Alan M. Delamater
David G. Marrero *Editors*

Behavioral Diabetes

Social Ecological Perspectives for Pediatric and Adult Populations

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Editors
Alan M. Delamater
Department of Pediatrics
University of Miami Miller School of Medicine
Miami, FL, USA

David G. Marrero
Center for Border Health Disparities
University of Arizona
Tuscon, AZ, USA

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We dedicate this book to the memory of Julio Santiago, MD, and Richard Rubin, PhD, two friends and colleagues who helped to support and energize the field of behavioral diabetes. This book is also dedicated to the new generation of researchers who are continuing to advance the field.

Spectacular contributions from leaders in the behavioral aspects of diabetes. This book is a must read for all clinicians taking care of patients with diabetes (children and adults). The authors have masterfully described how individual characteristics, in addition to the social, physical, and political environments in which behaviors occur, all influence management. In integrating the individual chapters, Drs. Delamater and Marrero highlight the role of behavioral interventions and demonstrate how such awareness is critical to achieving optimal diabetes outcomes.

Desmond Schatz
Professor of Pediatrics
University of Florida College of Medicine, Gainesville, FL, USA

This book, edited by Delamater and Marrero, is a comprehensive overview of the extremely important topic of behavioral diabetes. The issues encompassed in this book have evolved greatly over the last few decades, and the editors have done a spectacular job in having the key experts on each of the many topics review the literature while at the same time keeping it practical for both clinicians and researchers. Given the explosion of information on this topic dealing from pediatrics to geriatrics, this book should be present on the bookshelves of all interested in this topic.

Irl B. Hirsch
Professor of Medicine
University of Washington, Seattle, WA

Delamater and Marrero explore the expansive landscape of behavioral diabetes through a socioecological perspective to help us better design and evaluate strategies to address the overwhelming burden that diabetes can present to the patient and their families. As biomedical and bioengineering efforts have given us a plethora of new therapies to address glucose aberrations, it has become even more important that we must imbed these breakthroughs in a system of care and support that enables the patient and their loved ones to not only survive, but to thrive and achieve unencumbered by the stress, strain, discrimination, and imposed adversity often associated with managing diabetes. The chapters in this book are authored by experts in the field, representing a diversity of evidence and discussion that enable readers to truly explore their own thoughts and approaches. Behavioral Diabetes provides a wealth of information for both clinicians and researchers involved in the care of children, adolescents, and adults with diabetes.

Francine R. Kaufman
Chief Medical Officer, Senseonics
Distinguished Professor Emerita of Pediatrics at USC
The Center for Endocrinology, Diabetes & Metabolism
Children's Hospital Los Angeles

Foreword

I am often presumed to be a psychologist as well as a physician, since I am a "Professor of Medicine, Pediatrics, and Psychology." That is not the case. My focus is on diabetes, from cradle to grave – hence appointments in both Medicine and Pediatrics. However, long ago, I realized that the most difficult aspect of diabetes management was dealing with the psychological aspects and that if there was to be meticulous glycemic control, one must understand the various stressors in the life of the patient and the family. That led to two things: first, having behaviorally oriented people on our diabetes management team, and, second, exploring research questions that included the interaction of psychosocial and behavioral support in improving the care of type 1 diabetes. I ended up with an appointment in psychology in order to serve on advisory and dissertation committees of the many psychology students who worked in our unit.

Alas, I was short-sighted. In this book, Delamater and Marrero have expanded the notion to include not just the patient and family and their biological and psychological issues. They have developed and explored an ecological model of health behavior that includes the communities, organizations, and culture in which the patient and family live. And they go further in noting that all of this is influenced by society in general, including government policies.

Over the past few years, we have become accustomed to reading tragic stories of patients with type 1 diabetes having to ration their insulin and dying as a result of not having affordable insulin as an option. Thinking about this in the context of the broad ecosystem highlights how multiple issues – at all levels – impact the lives of patients.

This book is a unique contribution to the field – it is the first time in one volume that all levels of the social ecological model are comprehensively discussed in relation to diabetes management – with an emphasis also on the different issues in pediatric and adult populations. The editors have assembled an impressive array of international experts who collectively have tackled the various components of the ecosystems impacting diabetes management. Moreover, the editors made a conscious effort to encourage senior authors to work with junior colleagues in constructing their chapters. Not only did this bring contemporary concepts to the table, it also allowed the next generation of diabetes clinician investigators to better appreciate the complexities of dealing with the ecosystem impacting diabetes.

The readers will find that they are rewarded by exploring this novel approach to thinking about diabetes. Delamater and Marrero are to be commended for their outstanding effort.

Jay S. Skyler
Professor, Division of Endocrinology, Diabetes, & Metabolism
Deputy Director - Diabetes Research Institute
University of Miami Miller School of Medicine
Miami, FL, USA

Acknowledgments

We greatly appreciate the outstanding work done by all of the authors in this volume – their contributions provide a scholarly summary of the field in each area and point the way to future clinical and research efforts. We also acknowledge the assistance and support of the Springer team, including Janice Stern, who supported the original book concept, and Lilith Dorko and Sara Yanny-Tillar, who guided the book to completion.

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Contributors

Ronald T. Ackermann Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Barbara J. Anderson Baylor College of Medicine, Houston, TX, USA

Katherine L. Aparicio Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA

Naeem Aslam National Institute of Psychology, Quaid-i-Azam University, Islamabad, Pakistan

Ashley C. Baker Psychological Sciences and the Health Sciences Research Institute, University of California, Merced, CA, USA

Samantha A. Barry-Menkhaus Oregon Health & Science University, Portland, OR, USA

Lindsay Blevins The Institute for Family Health, New York, NY, USA

Augustina M. A. Brands Franciscus Gasthuis & Vlietland Hospital, Rotterdam, The Netherlands

Reid Burch Oregon Health & Science University, Portland, OR, USA

Ashley M. Butler Baylor College of Medicine, Houston, TX, USA

Texas Children's Hospital, Houston, TX, USA

Stuart Chalew Division of Endocrinology/Diabetes, Department of Pediatrics, School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, USA

Division of Endocrinology, Children's Hospital of New Orleans, New Orleans, LA, USA

Sue Channon Centre for Trials Research, Cardiff University, Cardiff, UK

Lila S. Chertman Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Miami Miller School of Medicine, Miami, FL, USA

Marshall H. Chin Department of Medicine, Section of General Internal Medicine, University of Chicago, Chicago, IL, USA

Persis V. Commissariat Pediatric, Adolescent, & Young Adult Section, Section on Clinical, Behavioral and Outcomes Research, Harvard Medical School, Joslin Diabetes Center, Boston, MA, USA

Denis Daneman Department of Paediatrics, University of Toronto, Toronto, ON, Canada

The Hospital for Sick Children, Toronto, ON, Canada

Karishma A. Datye Ian M. Burr Division of Pediatric Endocrinology and Diabetes, Vanderbilt University Medical Center, Nashville, TN, USA

Alan M. Delamater Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA

Leonard E. Egede Department of Medicine, Division of General Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

Center for Advancing Population Science (CAPS), Medical College of Wisconsin, Milwaukee, WI, USA

Rebecca L. Emery University of Minnesota School of Public Health, Minneapolis, MN, USA

Meredyth A. Evans Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Edwin B. Fisher Department of Health Behavior, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Lawrence Fisher University of California, San Francisco, San Francisco, CA, USA

Lynda K. Fisher The Center for Endocrinology, Diabetes and Metabolism, The Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Steven Fox Department of Pharmaceutical and Health Economics, University of Southern California, Los Angeles, CA, USA

Tracy Georges Baylor College of Medicine, Houston, VA, USA

Texas Children's Hospital, Houston, TX, USA

Ann E. Goebel-Fabbri Dr. Goebel-Fabbri, LLC, Brookline, MA, USA

Jeffrey S. Gonzalez Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Department of Medicine (Endocrinology) & Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, USA

The Fleischer Institute for Diabetes and Metabolism, Albert Einstein College of Medicine, Bronx, NY, USA

New York Regional Center for Diabetes Translation Research, Albert Einstein College of Medicine, Bronx, NY, USA

John W. Gregory Division of Population Medicine, School of Medicine, Cardiff University, Cardiff, UK

Margaret Grey Yale University School of Nursing, Orange, CT, USA

Michael A. Harris Oregon Health & Science University, Portland, OR, USA

Vicki S. Helgeson Psychology Department, Carnegie Mellon University, Pittsburgh, PA, USA

Claire J. Hoogendoorn Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Rachel Hopkins State University of New York Upstate Medical University, Syracuse, NY, USA

Elbert Huang Department of Medicine, University of Chicago, Chicago, IL, USA

Sarah S. Jaser Ian M. Burr Division of Pediatric Endocrinology and Diabetes, Vanderbilt University Medical Center, Nashville, TN, USA

Kevin Joiner University of Michigan School of Nursing, Ann Arbor, MI, USA

Naomi S. Kane Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Maura Kepper School of Public Health, Louisiana State University Health Sciences Center, New Orleans, LA, USA

Rachel P. Kolko Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Natalie Koskela Oregon Health & Science University, Portland, OR, USA

Lori M. Laffel Pediatric, Adolescent, & Young Adult Section, Section on Clinical, Behavioral and Outcomes Research, Harvard Medical School, Joslin Diabetes Center, Boston, MA, USA

Tianyi Lu Department of Pharmaceutical and Health Economics, University of Southern California, Los Angeles, CA, USA

Jamil A. Malik National Institute of Psychology, Quaid-i-Azam University, Islamabad, Pakistan

Jessica A. Marino Psychological Sciences and the Health Sciences Research Institute, University of California, Merced, CA, USA

David G. Marrero Center for Border Health Disparities, University of Arizona, Tucson, AZ, USA

Dayna E. McGill Pediatric, Adolescent, & Young Adult Section, Section on Clinical, Behavioral and Outcomes Research, Harvard Medical School, Joslin Diabetes Center, Boston, MA, USA

Juliane Menting Department of Medical Psychology, Amsterdam Public Health (APH) Research Institute, VU University Medical Center, Amsterdam, The Netherlands

NIVEL, Netherlands Institute for Health Services Research, Utrecht, The Netherlands

Carmen Mironovici Division of Endocrinology/Diabetes, Department of Pediatrics, School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, USA

Division of Endocrinology, Children’s Hospital of New Orleans, New Orleans, LA, USA

Rebecca Myerson Department of Population Health Sciences, University of Wisconsin Madison, Madison, WI, USA

Danielle Neuman Division of Internal Medicine, Department of Medicine, University of Miami Miller School of Medicine/Jackson Memorial Hospital, Miami, FL, USA

Elisabeth Northam Royal Children’s Hospital, Melbourne, VIC, Australia

Anne Peters Department of Medicine, University of Southern California, Los Angeles, CA, USA

Elizabeth R. Pulgaron Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA

Juan F. Roy Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Richard Scribner School of Public Health, Louisiana State University Health Sciences Center, New Orleans, LA, USA

Elizabeth A. C. Sellers Pediatrics and Child Health, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada

Children’s Hospital Research Institute of Manitoba, Winnipeg, MB, Canada

Amit Shapira Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Frank J. Snoek Department of Medical Psychology, Amsterdam Public Health Research institute, Amsterdam University Medical Centers, Vrije Universiteit, Amsterdam, The Netherlands

Patrick Y. Tang Department of Health Behavior, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Paula M. Trief State University of New York Upstate Medical University, Syracuse, NY, USA

Elizabeth L. Tung Department of Medicine, Section of General Internal Medicine, University of Chicago, Chicago, IL, USA

Victoria L. Valledor Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA

Eelco van Duinkerken Department of Medical Psychology, Amsterdam University Medical Centers, Amsterdam, The Netherlands

Center for Epilepsy, Instituto Estadual do Cérebro Paulo Niemeyer, Rio de Janeiro, Brazil

Meredith Van Vleet Psychology Department, Carnegie Mellon University, Pittsburgh, PA, USA

Elizabeth M. Venditti Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Francesco Vendrame Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Miami Miller School of Medicine, Miami, FL, USA

Anthony T. Vesco Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Northwestern University's Feinberg School of Medicine, Chicago, IL, USA

Alaina P. Vidmar The Center for Endocrinology, Diabetes and Metabolism, The Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

David V. Wagner Oregon Health & Science University, Portland, OR, USA

Julie Wagner UConn Health, Farmington, CT, USA

Rebekah J. Walker Department of Medicine, Division of General Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

Center for Advancing Population Science (CAPS), Medical College of Wisconsin, Milwaukee, WI, USA

Jill Weissberg-Benchell Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Brandy A. Wicklow Pediatrics and Child Health, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada

Children's Hospital Research Institute of Manitoba, Winnipeg, MB, Canada

Deborah J. Wiebe Psychological Sciences and the Health Sciences Research Institute, University of California, Merced, CA, USA

Joni S. Williams Department of Medicine, Division of General Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

Center for Advancing Population Science (CAPS), Medical College of Wisconsin, Milwaukee, WI, USA

Chapter 1
Introduction

Alan M. Delamater and David G. Marrero

In the past decades, the complexity and sophistication of treatments for diabetes has increased dramatically (Garber et al., 2015). Despite these advances, however, many people with diabetes continue to have less than optimal metabolic control and suffer from preventable complications and reduced quality of life (Bagnasco et al., 2014; Inzucchi et al., 2015). This gap between optimal, evidence-based medicine, and actual clinical practice illuminates the central role of the patient in implementing optimal management plans in daily life. The increasing awareness that patients' play a central role in achieving optimal outcomes has also given rise to the understanding that self-management is vastly more complex than the individual exercising "self-control." In addition to individual characteristics, the social, physical, and political environments in which behaviors occur have great influence on how persons manage their diabetes. Indeed, family and peer dynamics, access to different modes of health care, barriers in the workplace, and national health policies all contribute to diabetes outcomes. For patients and clinicians, these ecological factors create the context in which behaviors occur. This awareness highlights the importance of patient supported approaches to achieving optimal diabetes outcomes (Inzucchi et al., 2015).

This interplay between the individual and the context in which he or she behaves has shifted in important ways over the past few decades. Previously, we thought that simply providing information about "best" treatment strategies would change health care and health behaviors. It was widely held that all that was necessary to change clinical practice was to inform doctors of the reasons or research behind recommendations and that changing individual health behavior was a simple matter of explaining the importance of performing specific actions and then patients would readily comply with those recommendations (Lorig & Holman, 2003; Steed, Cooke, & Newman, 2003).

Achieving behavior change in the clinical setting is not such a simple matter (Delamater, 2006). In the later decades of the twentieth century, the view of clinicians and patients as obedient adopters of facts and recommendations was replaced by two, somewhat divergent viewpoints: those emphasizing characteristics of the individual versus those emphasizing the role of the broader contexts of economics, communities, organizations, cultures, and policies (Marrero et al., 2013). Psychosocial therapies for individuals with diabetes have benefited from this latter view (Delamater et al., 2001). In this

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A. M. Delamater (✉)
Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA
e-mail: adelamater@med.miami.edu

D. G. Marrero
Center for Border Health Disparities, University of Arizona, Tuscon, AZ, USA

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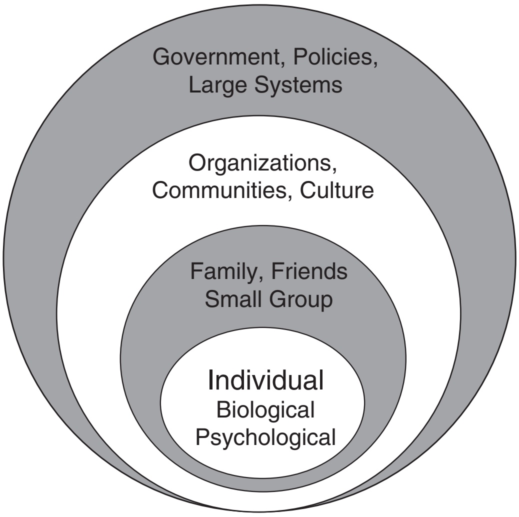
Fig. 1.1 Ecological model of health behavior



context, this book examines the synthesis of individual and context using a social ecological perspective and explores implications and lessons for clinical practice and development of improved approaches to promoting engagement in diabetes care, effective diabetes self-management, and quality of life among those pediatric and adult populations with diabetes. This is consistent with the recommendations of professional diabetes organizations such as the International Society of Pediatric and Adolescents Diabetes and the American Diabetes Association, which have both published guidelines for the psychosocial care of individuals with diabetes (Delamater et al., 2018; Young-Hyman et al., 2016).

To help structure this discussion, we have elected to use the social ecological framework for understanding how a range of broad contextual factors interact and influence individuals and their behaviors (Bronfenbrenner, 1979; Glanz et al., 2008). As shown in Fig. 1.1, in the ecological model of health behavior (Fisher et al., 2002), the individual (both psychological and biological aspects) operates within the context of family, friends, and small groups, which are in turn, embedded within several layers of larger social contexts.

Just as people influence their families and are influenced by them, families influence communities and vice versa. How communities can facilitate or inhibit diabetes management are in turn influenced by government policy, cultures, and overall society. Thus, an important principle of the social ecological model is that factors at different levels influence each other, and these inter-level influences are often reciprocal. It allows us to understand the range of factors that put people at risk for negative and positive outcomes associated with diabetes self-management. The overlapping rings in the model illustrate how factors at one level influence factors at another level.

Besides helping to clarify these factors, the model also suggests that in order to improve health outcomes, it is necessary to consider and act across multiple levels of the model at the same time. This approach is more likely to sustain prevention and treatment efforts over time than any single intervention.

How this Book Is Organized

Using the social ecological model, we define key issues at each level for both pediatric and adult populations with diabetes, since the issues they experience are different, focusing on different developmental and contextual factors. Thus, there are parts that focus on the individual, the social/family level, the community level including health-care systems, and finally the policy level. Each part presents research findings on the current state on knowledge and what interventions have been used to address the issues.

The first main section of the book begins with chapters that focus on children and adolescents (Parts I through VI), starting with a chapter that updates the epidemiology and current strategies for pediatric medical management. We then explore *individual-level factors* with chapters on the biobehavioral and neuroendocrine influences on development of diabetes in children; distress and quality of life; depression and anxiety; eating disorders; the effects of diabetes on neurocognitive function; and individual-level intervention approaches.

Consideration is then given to *social-level factors* with chapters on family influences; the role of peer support; social-level intervention approaches with an emphasis on family therapies; and enhancing peer support and coping.

We then review *community-level factors*, with chapters discussing demographic influences and health disparities; the impact of medical systems and patient-provider relationships and transition of care to diabetes outcomes; and diabetes prevention in communities and schools. Finally, we focus on *policy-level factors* with a discussion on how health care, insurance, and school policy affects diabetes management. The section on children and adolescents concludes with a discussion of main research findings and implications for clinical practice and research.

The second section of the book focuses on *adults* with diabetes (Parts VII through XII). It also begins with a chapter that updates the epidemiology and current treatment of adults. We then explore issues at the *individual level* that include biobehavioral factors in the etiology of diabetes; distress and quality of life issues; depression and anxiety; eating disorders; neurocognitive function; and individual-level intervention approaches.

Social-level factors are then explored with chapters discussing the role of family and peer support; social-level interventions with an emphasis on family-based therapies; and social-level interventions including enhancing peer support. This is followed by chapters discussing *community-level factors*, including demographic influences and health disparities; the influence of medical systems and patient-provider relationships; and the social-community-level context of weight loss interventions and diabetes prevention.

We conclude this section of the book on adults with consideration of *policy-level* factors. The focus here is on how health care and insurance policy affect diabetes management. The section on adults concludes with a discussion summarizing the main findings and their implications for clinical practice and research.

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Part I
Medical Management of Diabetes in Children and Adolescents

Chapter 2
Update on Medical Management of Diabetes in Children and Adolescents: Epidemiology and Treatment

Denis Daneman

Diabetes mellitus encompasses four conditions or groups of conditions:

(i) Type 1 diabetes, a largely autoimmune condition with peak onset in childhood, but increasing incidence in adults and highly variable incidence around the world
(ii) Type 2 diabetes, predominantly a disorder of adulthood but seen more frequently in high-risk groups during adolescence associated with the rapid rise in childhood obesity
(iii) Gestational diabetes, which is a rare consideration in adolescence;
(iv) Other less common causes including monogenic diabetes, neonatal diabetes, and diabetes associated with certain disorders including some endocrine disorders (e.g., Cushing's syndrome), certain medications (e.g., glucocorticoids, L-asparaginase), and disorders such as cystic fibrosis-related diabetes mellitus

For a complete list of these conditions, see Craig et al. (2014).

In this chapter, the focus will be on the epidemiology of types 1 and 2 diabetes and on the major components of day-to-day management in both types of diabetes.

Epidemiology and Pathogenesis of Type 1 Diabetes

Type 1 diabetes has its peak onset in mid- to late-childhood, although there is no age at which individuals are no longer susceptible to developing this disorder. The incidence of type 1 diabetes varies from as high as >50/100,000 youth under 15 years of age/year in Finland to as low as <1 in China. Since the 1950s, when incidence rates began to be carefully documented, annual increases of between 2% and 5% have been recorded in the high-incidence countries. Besides Scandinavian countries, other high-incidence areas include Canada (highest in Newfoundland and Prince Edward Island),

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The author has no disclosures or conflicts of interest to declare.

D. Daneman (✉)
Department of Paediatrics, University of Toronto, Toronto, ON, Canada

The Hospital for Sick Children, Toronto, ON, Canada
e-mail: Denis.daneman@sickkids.ca

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the UK, Australia, and the USA (Patterson et al., 2009, 2014). The reasons for these regional differences are not easily forthcoming but do suggest environmental influences since adjacent communities of similar genetic makeup can have vastly dissimilar incidence rates for type 1 diabetes: e.g., Finland vs Russian Karelia; Sardinia vs rest of Italy; and Newfoundland vs rest of Canada (Kondrashova, Seiskari, Ilonen, Knip, & Hyöty, 2013; Newhook, Penney, Fiander, & Dowden, 2012; Songini, Mannu, Targhetta, & Bruno, 2017).

What is also known is that when certain populations migrate from low- to high-incidence areas, the immigrant population soon reaches the same incidence as the established population; the best example of this is migration of South Asians to the UK (Harron et al., 2011). There is evidence of a declining age of presentation of type 1 diabetes with an increased incidence of 21% in those under 20 years of age from 2001 to 2009 (Dabelea et al., 2014). There is also a suggestion of a leveling off in incidence in Sweden and Finland since 2000.

The data points to genetic-environmental interactions in the causation of type 1 diabetes. The underlying mechanisms for this remain elusive but are pivotal in the development of a more complete understanding of the pathogenesis of the disease and of therapeutic approaches to interrupt the inexorable process of pancreatic beta cell destruction.

In the 1980s, Eisenbarth postulated a 6-phase process in the development of type 1 diabetes, a model which remains relevant more than 30 years later (Eisenbarth, 1986):

1. First, genetic susceptibility sets the stage upon which an immune disruption occurs. We are all born with genes that determine our level of susceptibility to developing diabetes (e.g., the most important genes are linked to the major histocompatibility antigens: DR3 and 4 enhance susceptibility, while DR2 confers a degree of protection).
2. Second, a presumed triggering event is needed to convert susceptibility into pathophysiology (exposure to cow's milk protein or certain viruses remain contenders for this triggering role).
3. Third, the appearance of antibodies against specific beta cells proteins (e.g., ICA, GAD, insulin autoantibodies, IA2, ZnT8) signals the presence of autoimmune attack on the beta cells (often termed "insulitis"). Individuals with more than one diabetes-related antibody detected have more than an 80% likelihood of developing type 1 diabetes over the next 15 years (Arif et al., 2014). This beta cell response provides markers of the autoimmune attack on the beta cells rather than acting as the agents damaging the beta cells.
4. Fourth, beta cell function begins to decline with loss of first phase insulin secretion.
5. Fifth, when declining insulin secretion reaches a critical point, hyperglycemia supervenes and clinical diabetes becomes apparent.
6. Finally, the beta cells go through a partial recovery phase ("honeymoon period") after which there is ongoing decline until no more beta cell function is measurable. The majority but not all individuals with type 1 diabetes will progress to complete lack of insulin secretion within 3–5 years of diagnosis.

Epidemiology and Pathogenesis of Type 2 Diabetes

Since the 1970s, there has emerged, slowly at first and then more rapidly, an increasing incidence of type 2 diabetes, most particularly in high-risk groups such as Aboriginal Canadians and Americans, African- or Caribbean-Americans, Hispanics, and South Asians (Zeitler et al., 2014). In general, this rising incidence of type 2 diabetes has paralleled the steep rise in childhood and adult obesity (Dabelea et al., 2014). A massive epidemic of type 2 diabetes was predicted as a result of the rising obesity but has not occurred in most places. Nevertheless, the incidence of type 2 diabetes in children and adolescents has been increasing in recent years.

In the USA, type 2 diabetes accounted for 21% of those with new-onset diabetes in individuals 15–19 years of age (Dabelea et al., 2014). More recently, data from the SEARCH Study in the USA revealed a rate of type 2 diabetes of 8.1/100,000 in 10–14-year-olds and 11.8 in 15–19-year-olds (Dabelea et al., 2007). In Canada, the incidence of type 2 diabetes is 1.54 per 100,000 under 18-year-olds, highest by far (over 12/100,000) in the Oji-Cree communities of Northwestern Ontario and Manitoba (Amed et al., 2010). This has been ascribed to a mutation in the HNF1alpha gene. In the presence of this gene, type 2 diabetes emerges at an earlier age and lower weight (Triggs-Raine et al., 2002).

Type 2 diabetes in young people has been associated with adolescent development (average age of onset is 13 years), is faster in onset than in adults, and has not only insulin resistance but a decline in beta cell function as its dominant features. The decline in beta cell function likely accounts for the 6–25% frequency of DKA at presentation in youth with type 2 diabetes (Zdravkovic, Daneman, & Hamilton, 2004; Zeitler et al., 2014).

Presentation of Type 1 and Type 2 Diabetes

The most common presentation of type 1 diabetes in the high-incidence countries is with signs and symptoms of hyperglycemia, namely, polyuria, polydipsia, and polyphagia in the face of weight loss. The diagnosis is usually made within a few days or weeks of emergence of these symptoms. If the symptoms are overlooked, the child or teen may develop diabetic ketoacidosis (DKA) due to significant dehydration related to the osmotic diuresis caused by the hyperglycemia and acidosis caused by production of ketones as a result of fat metabolism to provide an alternative energy source to glucose (Bui et al., 2010; Usher-Smith, Thompson, Ercole, & Walter, 2012).

DKA occurs in anywhere from <10% to 60% of individuals with new-onset type 1 diabetes, the frequency being inversely proportional to the incidence of type 1 diabetes in that community (suggesting that when the incidence is high then awareness is better and DKA is less likely to supervene) (Usher-Smith et al., 2012). Also, the frequency of DKA at diagnosis is correlated with the societal income inequality level, suggesting that in these unequal countries, access to care may vary (Limenis, Shulman, & Daneman, 2012).

Beyond diagnosis, DKA occurs under a limited number of conditions all associated with severe insulin deficiency, and all preventable (Bui et al., 2004; Jefferies et al., 2015), including:

1. Insulin omission that is either deliberate or unintentional. Deliberate insulin omission may occur in the context of an eating disorder where omission of insulin induces hyperglycemia and glycosuria, the loss of calories causing weight loss.
2. Pump failure will lead to rapid dissipation of insulin and development of DKA.
3. Intercurrent illness with marked counterregulatory hormone responses will lead to DKA unless appropriate adjustments in insulin dose are made.

Many, if not most, youth with type 2 diabetes are asymptomatic, and the diagnosis is made by oral glucose tolerance testing in high-risk patients. Some, however, have typical symptoms of hyperglycemia, and DKA is present at diagnosis in 6–25% (Dabelea et al., 2014; Zdravkovic et al., 2004). The presence of DKA may lead erroneously to a diagnosis of type 1 diabetes in such youth.

Occasionally a diagnostic dilemma arises as to whether an individual has type 1 or 2 diabetes: this is resolved by testing for the presence of antibodies and by observing the natural history of the disorder. Features highly suggestive of type 2 include obesity, acanthosis nigricans, polycystic ovarian syndrome, dyslipidemia, and a strong family history of type 2 diabetes.

Children presenting under 6 months of age should be assessed for genes related to neonatal diabetes (KCNJ11, ABCC8, INS, and more). Beyond 6 months of age, genetic analysis should be done in multiplex families with an autosomal dominant inheritance pattern (HNF1alpha/4alpha, GCK, HNF1beta) (Cameron and Wherrett, 2015).

Management of Type 1 Diabetes

Type 1 diabetes is a lifelong condition with serious short- and long-term complications. The short-term complications are those of hypoglycemia and ketoacidosis, both of which can be limited by careful attention to day-to-day diabetes care. The long-term diabetes-related complications are divided into the microvascular, affecting eyes, kidneys, and nerves, and macrovascular, involving cardiovascular, cerebrovascular, and peripheral vascular circulations.

There is unequivocal evidence derived mainly from the Diabetes Control and Complications Trial (DCCT) and its follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC) study, demonstrating a very close correlation between level of glucose control, as assessed by HbA1c levels, and the onset and progression of all of the long-term complications (DCCT Research Group, 1993; DCCT/EDIC Study Research Group, 2016). The message is simple: achieve and maintain as near normal glucose control as possible; however, the means to do so remain imprecise at best. Only a small proportion of children and teens maintain near normal glycemia.

Given our knowledge of complication prevention, the goals of therapy ought to be dogmatic: in other words, we know the relationship between control and complications and must share these with the children and adolescents with diabetes and their families. Where pragmatism comes in is in the methods used to achieve the dogmatic goals. At the same time, hypoglycemia remains a major barrier to achieving these goals.

A thorough knowledge of diabetes and its ramifications, as well as a thorough knowledge of the technical aspects of therapy (insulin injection, pump infusion, glucose monitoring, nutrition planning) are essential. Nonetheless, we must not overlook the behavioral or psychosocial aspects of care as the final common pathway by which the knowledge is applied (Cameron, Northam, Ambler, & Daneman, 2007).

Health-care outcomes according to the Ecological Perspectives Model depend on factors operating in five domains: two, societal and community, represent the macroenvironment, while the other three, institutional, interpersonal, and intrapersonal, reflect the microenvironment in which individual health care occurs. Inadequate attention has hitherto been paid to the so-called social determinants of health, specifically poverty (and its associated food and shelter insecurity), lack of education, race/ethnicity, and refugee/immigrant status, as moderators of diabetes outcomes.

In virtually every situation in diabetes studied, social determinants of health are a major contributor to outcome, always unidirectionally; that is to say, the more disadvantaged the child with diabetes and their family is, the worse the outcomes, be they metabolic control, quality of life, or other variables (Inman et al., 2016a, 2016b). Health-care professionals involved in care of children and adolescents with type 1 diabetes must be aware of these relationships, as well as any and all programs to overcome these health inequities. Since most of us live in multidimensional societies (based on diversity of race, language, educational level, refugee/immigrant or native born, religion, and more), health care must of necessity be responsive to the differing needs of individual patients.

Health equity differs from equality in a very fundamental way. While equality means that everyone gets the same, health equity means that everyone gets what they need to succeed. These are difficult concepts to bring into law, and some countries function more effectively (e.g., Scandinavian countries) than do others in this respect.

The major international diabetes organizations have all published Clinical Practice Guidelines which are online and accessible under relevant websites for the International Society for Pediatric and Adolescent Diabetes (ISPAD), the American Diabetes Association, and Diabetes Canada. In this chapter, the guidelines of the ISPAD are referenced to demonstrate treatment aspects for convenience and because of their development by international experts.

The essential components of diabetes care in children and adolescents are:

1. *Appropriate care*. There is universal agreement that the child or adolescent with type 1 diabetes is best served by care provided in the context of an interdisciplinary team and that this care is evidence-based and family-centered (Cameron & Wherrett, 2015; Daneman, 2006). The core members of the diabetes team, in addition to the child/family unit, include a pediatric endocrinologist (or pediatrician with expertise in diabetes care), a diabetes nurse (often referred to as the nurse educator, although their role extends beyond education to all aspects of care), a diabetes dietitian (implying expertise in both childhood nutrition and nutrition planning in diabetes), and a mental health professional (social worker, psychologist). The major features of the team are that they develop a common philosophy of treatment that is evidence-based and that the child and family must be integrated into this team. Furthermore, the lines between the roles of the team members ought to be overlapping. The extended team will include those individuals in the community with whom the child or adolescent is in regular contact, e.g., school personnel, extended family, sports coaches, and more. This helps to safety-proof particularly younger children with diabetes when out of direct parental or primary care giver care.
2. *Acquisition of knowledge*. There are two aspects to the knowledge that the family is required to acquire: first, the technical skills (see below), and, second, a thorough understanding of what diabetes means, what needs to be done to keep it under good control, and what to expect in both the short- and longer term. This includes information about hypoglycemia and DKA. The amount and speed of information imparted to the family will depend on their ability to process it at the time of initial diagnosis when their emotional response to this new reality is expected to be at its strongest.
3. *Technical skills*. Rapid acquisition of these skills is needed to avoid lengthy hospitalization (or hospitalization at all) at the time of diagnosis. By this is meant the ability to perform the technical skills expertly and safely without oversight of the team members. With respect to blood glucose monitoring, this means everything from finger pricking, use of the glucose meter to insertion and use of continuous glucose monitoring equipment when indicated; and with respect to insulin how to give an injection using syringes or pens to appropriate use of an insulin infusion pump. Use of glucagon to reverse severe hypoglycemia is also a necessary skill to be acquired, though hopefully seldom required. Accurate and safe performance of the technical skills allows most appropriate application of the cognitive side of regimen adjustment and good glycemic control achievement and maintenance.

   Most insulin regimens at present fit into the basal-bolus format whether using long-acting insulin analogs to provide the basal and fast-acting analogs for boluses pre-food intake or using fast-acting insulin infusion via a pump. The uptake of insulin infusion pumps has increased exponentially over the past decade or so (Shulman, Miller, Stukel, Daneman, & Guttmann, 2017). This is increasingly being coupled with the use of glucose sensors providing continuous glucose measurement (Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, 2009). What is clear is that these technologies do not in and of themselves lead to better glycemic control; rather, it is up to the individual with diabetes to apply the technologies to their best advantage. A glucose sensor coupled to a pump programed to make adjustments may lead to implantable artificial pancreases, thereby bypassing the need for patient-based decision-making.

   The concern about these new technologies is that they may become unattainable except by those in the richest countries with excellent health benefits. This raises the possibility of an increasing gap in treatment availability between haves and have-nots (Gale, 2005). What is also evident is that the cost of the supplies for diabetes has risen significantly with newer insulins, pumps, and sensors.

4. *Nutritional planning*. The meal planning required for a child or adolescent with type 1 diabetes is often cited by families as the most difficult part of the diabetes treatment regimen. Meal planning has become much more simplified with the application of "carbohydrate counting" and dosing insulin based on ambient blood sugar and expected intake of carbohydrate. Nonetheless, for many this is the major disruption to their prediabetes lifestyle.
5. *Psychosocial surveillance and intervention*. Since diabetes is a lifelong condition with many short- and long-term consequences, it is no wonder that not only at the time of diagnosis, but throughout its course, it is a significant source of stress to the child/adolescent and his/her family. Furthermore, the presence of mental health issues in the child/adolescent or other family member is often a major barrier to achieving the goals of therapy. The response to these stresses is addressed in other chapters of this book and should not be overlooked (Cameron et al., 2007). The presence of a mental health professional on the diabetes team is an imperative as is their involvement with those individuals having the most difficulty adjusting to their diabetes routines.
6. *Realistic goals*. Developing a diabetes care plan with reasonable and realistic goals is an essential part of the treatment of this condition. All families ought to understand from the outset that the achievement and maintenance of as near normoglycemia as possible is the ultimate goal. Nonetheless, this is rarely achieved in childhood or adolescence. The clinical practice guidelines of the International Society for Paediatric and Adolescent Diabetes target an HbA1c below 7.5% as a general goal (see Table 2.1). For some this may be impossible to achieve without significant hypoglycemia. This means for some individuals goals with small steps to their achievement will need to be developed.

It should be noted that the ISPAD recently updated the guidelines for glycemic control to aim for HbA1c less than 7.0% (<53 mmol/mol) for those with access to comprehensive care (DiMaglio et al., 2018).

7. *Screening for comorbid conditions and complications* (Kordonouri et al., 2014). Since type 1 diabetes is an autoimmune disorder, it is not surprising that other organ-specific autoimmune conditions may be more frequent in these children and teens, specifically autoimmune (Hashimoto's) thyroiditis and celiac disease (gluten enteropathy). Screening for these two conditions should begin soon after diagnosis and be repeated at regular intervals. At diagnosis, screening with TSH and antithyroid peroxidase antibodies is recommended, followed in asymptomatic individuals by TSH every second year. Celiac screening is recommended at diabetes diagnosis and every 1–2 years thereafter. This entails detection of tissue transglutaminase and/or anti-endomysial antibodies. Some debate continues as to the value of a gluten-free diet in those with asymptomatic celiac disease.

   Second, screening for diabetes-related micro- and macrovascular disease begins in early adolescence with retinal and urinary screening for diabetic retinopathy and microalbuminuria respectively. Detection of clinically evident complications during adolescence is now exceedingly uncommon (Table 2.2).

Table 2.1 Target indicators of glycemic control. Modified from ISPAD Clinical Practice Consensus Guidelines 2014 Compendium (Rewers et al., 2014). Goals should be modified according to individual circumstances

	Optimal	Suboptimal	High risk
HbA1c (DCCT standard)	<7.5%	7.5–9%	>9%
Plasma glucose: fasting/preprandial	4–8 mmol/L	>8	>9
Postprandial	5–10	10–14	>14
Bedtime	6.7–10	<4.2/>9	<4.4/>11
Nocturnal	4.5–9	<4.5/>9	<4.4/>11

Table 2.2 Screening for vascular complications

Retinopathy: Annually from age 10 or onset of puberty using fundus photography or mydriatic ophthalmoscopy
Nephropathy: Annually from age 10 or at onset of puberty using urinary albumin creatinine ratio or first morning albumin
Neuropathy: unclear
Macrovascular complications: after age 10 using annual BP and lipid profile every 5 years

Modified from Kordonouri et al. (2014)

8. *Crisis management*. *Intercurrent illness* in a child with type 1 diabetes has the potential to seriously disrupt the stability of the diabetes. This could result either from inadequate food intake in the face of ongoing insulin injection or infusion leading to hypoglycemia, or the stress from illness elevating the counterregulatory hormones, and thereby amplifying the associated hyperglycemia and ketosis. It is essential that, during an illness, the child or adolescent monitor their sugar 4–6 times daily and adjust insulin accordingly.

   The other crisis of note relates to the *hypoglycemia* that occurs in all people with diabetes. Hypoglycemia occurs as a result of the mismatch between insulin supply and glucose need. In those without diabetes, the exquisite response of the pancreatic beta cells to changing blood glucose concentrations is able to prevent hypoglycemia. In those receiving insulin by injection, either decreased glucose supply by changes in intake or increased demand for glycogen breakdown during exercise can precipitate hypoglycemia in the ongoing presence of injected or infused insulin.

   Mild, occasional hypoglycemia that can be recognized and treated before it becomes severe is one of the prices to be paid for the achievement of excellent metabolic control. Severe hypoglycemia with neuroglycopenia is to be avoided at all costs. When an episode of severe hypoglycemia does occur, glucagon should be available in the home for immediate administration.
9. *Transitions of care*. Type 1 diabetes is a disorder of transition. First, there are the transitions to a new lifestyle at the time of diagnosis which incorporates diabetes management. Then, there are the transitions from one approach to therapy (e.g., multiple daily injections to pump therapy), and finally from one age stage to the next culminating in the transition from the family-centered care in the children's diabetes clinic to patient-oriented care in the adult hospital (Daneman & Nakhla, 2011; Nakhla & Daneman, 2012). It is important to navigate these transitions as smoothly as possible.

Integration of all of these aspects of care provides a formidable challenge to most families with a child newly diagnosed with type 1 diabetes. It is clear that those families capable of achieving this integration without too much in the way of lifestyle disruption will achieve the best outcomes, in terms of HbA1c levels, quality of life, and freedom from complications. For many, however, the reality is that diabetes poses major challenges to their well-being. The good news is that the longevity of people with type 1 diabetes has increased significantly in parallel to declining complications (Miller, Secrest, Sharma, Songer, & Orchard, 2012).

Management of Type 2 Diabetes

In brief, the first challenge with regard to type 2 diabetes is to consider the diagnosis in anyone with high-risk characteristics (childhood obesity plus high-risk group, acanthosis nigricans, polycystic ovarian syndrome, dyslipidemia), perform appropriate screening (fasting plasma glucose, 2 hour post-glucose challenge and/or HbA1c), and institute therapy appropriate for the severity of the condition.

Recent data reveal that, at diagnosis, 85% of youth with type 2 diabetes are overweight or obese compared to only 24% of those diagnosed with type 1 diabetes (Shaw, 2007). Furthermore, at diagnosis many youth with type 2 diabetes already have early signs of micro- and macrovascular disease, hypertension, dyslipidemia, and fatty liver. Although the long-term prognosis of type 2 diabetes in youth is uncertain, the expectation is of serious health complications by age 40 and loss of about 15 years of life expectancy (Rhodes et al., 2012).

Lifestyle changes including enhanced activity and reduced caloric intake should be instituted in all patients. In those that are metabolically unstable, intensive initial insulin therapy is indicated followed in time by withdrawal of insulin and use of metformin may be possible. Insulin and metformin are, in fact, the only two medications approved for use in type 2 diabetes in young patients. The goals of therapy should be to achieve and maintain near normoglycemia. The TODAY Trial compared three arms: monotherapy with metformin vs metformin plus rosiglitazone vs metformin plus intensive lifestyle intervention. The most effective was metformin combined with rosiglitazone, although the latter is not approved for younger individuals (The TODAY Study Group, 2012). Disappointingly, almost 50% of the study subjects in the TODAY Trial failed to achieve the goals of therapy. There are a number of medications for therapy of type 2 diabetes in the adult population, but most remain untested and unapproved in teens with the disorder.

Conclusions

Since the discovery of insulin in 1922 at the University of Toronto, there has been a transmutation of type 1 diabetes from uniformly lethal to a chronic disorder with important short- and long-term health implications. Modern therapy has contributed to a significant delay in onset and progression of complications. The prevention or reversal of type 1 diabetes is eagerly awaited but does not appear imminent.

At the same time, the obesity epidemic worldwide has seen the rapid emergence of type 2 diabetes and its ramifications especially in high-risk populations at increasingly younger ages. This latter sequence threatens to overwhelm the health-care systems of some of the world's emerging economies.

In both types of diabetes, the challenge is to provide optimal and equitable health care to all, paying attention not only to the disordered biochemistry but also to the behavioral and psychosocial aspects, as well as the social determinants of health.

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Part II

Individual Level Factors in Children and Adolescents

Chapter 3
Neuroendocrine and Biobehavioral Influences on Diabetes in Youth

Persis V. Commissariat, Dayna E. McGill, and Lori M. Laffel

Childhood and adolescence are marked by continuous physical and emotional development, which may be impacted by the development of diabetes. This chapter explores multiple neuroendocrine and biobehavioral factors as they relate to the development of type 1 diabetes (T1D) and type 2 diabetes (T2D), as well as the early progression of these diseases. The occurrence of type 1 diabetes as well as type 2 diabetes is multifactorial, including contributions from genetic factors and the environment. Further, the development of both types of diabetes reflects multistage processes, with different factors interacting at different times. For example, neuroendocrine and biobehavioral factors may influence or trigger the development of the autoimmunity that initiates beta cell destruction in T1D, while different factors may impact the progressive loss of beta cell function. Similarly, with respect to T2D, a constellation of factors may lead to insulin resistance, which may be followed by glucose intolerance (or prediabetes), and then by frank T2D; each of these stages may result from multiple factors acting at different times. In T2D, there is fundamental resistance to insulin action along with pancreatic beta cells that cannot increase insulin production sufficiently to defend against the insulin resistance, resulting in the onset of T2D. Further, there may be exhaustion of beta cell function over time, leading many patients with T2D to require exogenous insulin. In the following sections, we will describe the occurrence of T1D and T2D in youth, as well as the potential contributions of genetics, environmental factors, stress, family factors, lifestyle behaviors, puberty, depression, and adaptation as they relate to the development and progression of diabetes in young persons.

P. V. Commissariat · D. E. McGill · L. M. Laffel (✉)
Pediatric, Adolescent, & Young Adult Section, Section on Clinical, Behavioral and Outcomes Research, Harvard Medical School, Joslin Diabetes Center, Boston, MA, USA
e-mail: lori.laffel@joslin.harvard.edu

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Incidence and Prevalence

The incidence of T1D in youth in the United States varies by race and ethnicity. A recent analysis by the SEARCH for Diabetes in Youth Study, a large multisite population-based study in the United States, examined trends in incidence from 2002 to 2012 and reported that there was an increase in incidence of T1D over that period from 19.5 cases per 100,000 youth per year in 2002–2003 to 21.7 cases per 100,000 youth per year in 2011–2012 (Mayer-Davis, Dabelea, & Lawrence, 2017). This study group also found that the incidence of T1D was the highest among non-Hispanic white children (incidence rate of 27.0 cases per 100,000 youth per year in 2011–2012) and the lowest among American Indian (6.5 per 100,000) and Asian/Pacific Islander children (9.7 per 100,000) (Mayer-Davis et al., 2017). The incidence of T1D peaks around ages 10–14, and the incidence rate was noted to be increasing significantly in all age groups except very young children 0–4 (Mayer-Davis et al., 2017; Pettitt et al., 2014). The SEARCH group estimated 166,984 youth under the age of 20 years old in the United States had type 1 diabetes in 2009. Notably, in youth with T1D, the overwhelming majority do not have a family history of diabetes; a positive family history of T1D has been suggested in up to 15% of youth with T1D (Insel et al., 2015).

The increasing incidence of T2D in youth is a serious problem around the world in recent years (Mayer-Davis et al., 2017; Pinhas-Hamiel & Zeitler, 2005), arising from the increase in childhood overweight and obesity. Rates of T2D are very low in children under 10 years old, before the onset of pubertal insulin resistance (which will be discussed later in the chapter). The SEARCH for Diabetes in Youth Study found no cases of T2D in children 0–4 years old (in a population of over 1.2 million youth in that age group) and only 19 cases in children 5–9 years old (also over 1.2 million youth in that age group; incidence rate of T2D was 0.8 per 100,000 person-years). A recent analysis of incidence trends from 2002 to 2012 from this study group found that in adolescents 10 to 14 years old, the most recent incidence rate of T2D was 12.1 per 100,000 youth per year and in those 15 to 19 years old, 12.9 per 100,000 youth per year. There was a significant increase in incidence of T2D over that period of time, from 9.0 cases per 100,000 youth per year in 2002–2003 to 12.5 cases per 100,000 youth per year in 2011–2012 (Mayer-Davis et al., 2017). The SEARCH group estimated 20,262 youth under the age of 20 years old in the United States had type 2 diabetes in 2009 (Pettitt et al., 2014). A detailed review by Pinhas-Hamiel and Zeitler describes rates of T2D in youth around the world (Pinhas-Hamiel & Zeitler, 2005). In the United States, over 75% of youth with T2D have a first- or second-degree relative with T2D (Rosenbloom, Silverstein, Amemiya, Zeitler, & Klingensmith, 2009). One study reported that 83% of youth with T2D had a family history of diabetes (Gilliam et al., 2007). Various risk factors, in addition to overweight/obesity, including genetics, the in utero environment, and early childhood influences, have been proposed for the development of T2D in youth.

Type 2 diabetes is seen in youth of all races, but there is a much higher occurrence among those of racial/ethnic minority status. The SEARCH for Diabetes in Youth Study found that the incidence of T2D was the highest among American Indian, African American, and Asia/Pacific Islander youth (incidence rates per 100,000 of 25.3, 22.3, and 11.8, respectively, in 10–14-year-olds and 49.4, 19.4, and 22.4, respectively, in 15–19-year-olds) and the lowest among non-Hispanic white children (3.0 in 10–14-year-olds and 5.6 in 15–19-year-olds) (Dabelea et al., 2007). Minorities were also more likely to have a family history of diabetes than non-Hispanic white youth, likely related to the higher occurrence of T2D among racial and ethnic minorities (Copeland et al., 2011; Gilliam et al., 2007).

Genetics

The primary genetic associations of T1D involve the human leukocyte antigen (HLA) class II region encoded by genes within the major histocompatibility complex (MHC) chromosome 6p21 (Barrett et al., 2009). There are several HLA alleles associated with genetic susceptibility for T1D (HLA-DR3, DQB1∗0201 and HLA-DR4, DQB1∗0302 in particular) (Pociot et al., 2010) and other HLA alleles associated with protection from type 1 diabetes (e.g., HLA-DR2, DQB1∗0602) (Pugliese et al., 2016). The pathogenesis of T1D in those with a genetic predisposition by nature of HLA-risk alleles involves progression from altered immune function to development of autoantibodies to tissue inflammation to clinical disease. At each stage of progression, both genetic and environmental factors may be at play (Jerram & Leslie, 2017).

There is a clear association between certain HLA haplotypes and diabetes-associated autoantibodies, including insulin autoantibodies (IAA), glutamic acid decarboxylase 65 autoantibodies (GADA), insulinoma antigen 2 autoantibodies (IA-2A), and zinc transporter 8 autoantibodies (ZnT8A) (Ilonen et al., 2017). Children with positivity for two or more islet autoantibodies have the greatest risk of progression to T1D. One large multicenter study showed that 70% of children with two or more islet autoantibodies developed T1D at 10-year follow-up (Ziegler et al., 2013). Another large study of first-degree relatives of persons with T1D showed that 88% of relatives with two or more islet autoantibodies developed T1D in 20-year follow-up (Gorus et al., 2017). This study also revealed that positivity of IA-2A or ZnT8A, antibodies to two proteins usually found in the beta cells, in individuals with multiple autoantibodies was associated with more rapid progression to diabetes. It is important to highlight that beta cell destruction results from T-cell mediated autoimmunity, and the antibodies are only markers of this process. There are currently no proven therapies that can alter a half progression of the autoimmune beta cell destruction. However, recent international registry studies have indicated that children with T1D who participated in screening studies and were identified at risk either through family history of T1D (BABYDIAB) (Winkler, Schober, Ziegler, & Holl, 2012) or through presence of HLA risk genotypes at birth (TEDDY) (Larsson et al., 2011) were significantly less likely to present in diabetic ketoacidosis at diagnosis compared to the general population.

Genetic associations with T2D are well-described in the adult literature but only more recently in children and adolescents. A large meta-analysis identified nine genetic loci associated with altered fasting glucose levels in children and adolescents: ADCY5, CRY2, GLIS3, PROX1, SLC2A2, G6PC2, MTNR1B, SLC30A8, and GCK (Barker et al., 2011). A recent study by Cropano and colleagues revealed that a variant in the TCF7L2 gene impairs beta cell function and hepatic insulin sensitivity and thus increases the risk of prediabetes and T2D in obese adolescents (Cropano et al., 2017). Epigenetic modifications that occur in the prenatal period may also be associated with obesity and metabolic disease in childhood (Godfrey et al., 2011).

Environmental Factors

The relationship between genetic and environmental factors in the development of T1D is not well-understood, but several environmental risk factors have been proposed and studied; these are summarized in a review article by Rewers and Ludvigsson (Rewers & Ludvigsson, 2016). In general, there is some evidence to support associations between the development of T1D and viral infections (enteroviruses in particular), although the mechanism is not entirely clear (Krogvold et al., 2015; Stene & Rewers, 2012). There are suggestions of associations, although more research is needed, in the relationship between T1D and the intestinal microbiome, particularly related to caesarean delivery, early childhood diet, and antibiotic use (de Goffau et al., 2013; Endesfelder et al., 2014;

Murri et al., 2013). There is no evidence or very little evidence of associations between the development of T1D and vaccines (Morgan, Halliday, Campbell, Cardwell, & Patterson, 2016). There is also very little empirical support for the "hygiene hypothesis," which proposes that improved hygiene has led to decreased frequency of childhood infections and higher rates of autoimmune diseases (Rewers & Ludvigsson, 2016). There is also very limited evidence for the "accelerator hypothesis," which postulates that excessive weight gain in early childhood may cause the development of islet autoantibodies due to a "stressed beta cell" responding to the need for more insulin in the setting of overweight/obesity and thus lead to T1D (Elding Larsson et al., 2016; Wilkin, 2001). However, childhood overweight or insulin resistance may promote progression from islet autoimmunity with failing beta cell function to overt T1D (Hypponen et al., 1999; Rewers & Ludvigsson, 2016).

Another interesting demographic pattern related to the onset of T1D is month of diagnosis and seasonality. One study assessing month of diagnosis across 105 centers worldwide found that in the northern hemisphere, T1D cases peaked during the colder months of October–January and decreased during the summer months of June–August, while the southern hemisphere showed opposite effects (Moltchanova, Schreier, Lammi, & Karvonen, 2009). Others suggest a pattern of T1D diagnoses based on birth month. For example, higher rates of T1D have been reported for those born in the warmer months of spring and summer versus those born in the colder months in more northern parts of the United States (Kahn et al., 2009), Ukraine (Vaiserman et al., 2007), Sweden (Samuelsson, Johansson, & Ludvigsson, 1999), and New Zealand (Willis et al., 2002), as summarized in a chapter by Maahs (Maahs, West, Lawrence, & Mayer-Davis, 2010). One potential reason for this pattern may be related to maternal vitamin D levels, as vitamin D can affect immune cells and beta cells (Maahs et al., 2010). However, this pattern is inconsistent across studies and geographical locations.

Various pregnancy and fetal factors have been associated with the development of T2D in offspring. One such factor is maternal diabetes, which has been associated with obesity in offspring and increased BMI in late childhood (Crume et al., 2011; Pettitt, Baird, Aleck, Bennett, & Knowler, 1983; Wright et al., 2009). In turn, higher BMI in childhood has been associated with higher risk of later impaired glucose tolerance and T2D (Sinha et al., 2002; Weiss et al., 2005). A second prenatal risk factor for T2D in offspring is higher maternal BMI (Juonala et al., 2013). The link between maternal overweight/obesity and later T2D in offspring is partly explained by the association between higher maternal BMI and childhood overweight/obesity in offspring (Mingrone et al., 2008; Salsberry & Reagan, 2005). Additionally, maternal obesity can alter insulin sensitivity and secretion in offspring and impact systemic inflammation and neurohormonal activity, all of which can increase risk of T2D in offspring (Lieb et al., 2009; Mingrone et al., 2008).

Stress and Trauma

Traumatic events and various life stresses can impact both T1D and T2D through physiologic and behavior-based mechanisms. Trauma and stress induce a physiologic response that leads to release of counterregulatory hormones, which oppose insulin action. Counterregulatory hormones, namely, cortisol, epinephrine, norepinephrine, growth hormone, and glucagon, all can lead to hyperglycemia. For example, an acute illness in childhood can lead to "stress hyperglycemia," which resolves without sequelae (Herskowitz-Dumont, Wolfsdorf, Jackson, & Eisenbarth, 1993). Further, a stressful event or traumatic episode that induces counterregulation can lead to hyperglycemia, particularly in persons who have inadequate endogenous beta cell function reserve.

Past research has postulated a link between stressful or traumatic experiences and risk of developing T1D, though there is no unanimous support of this notion. One theory suggests that stressful experiences early in life are associated with development of T1D. Mothers' experiences of stressful life events, particularly divorce and domestic violence, in the 2.5 first years after the birth of their child have been associated with an increased risk of diabetes-related autoimmunity in children, independent of family history of T1D (Sepa, Frodi, & Ludvigsson, 2005). An older study found that negative life events as experienced by the child, including a change in family structure, serious illness or injury in the family, and deaths in the family, in the first 2 years of life were also associated with increased risk of T1D (Thernlund et al., 1995), while another study suggested that stressful life events during the ages of 5–9 years old were associated with the onset of childhood T1D (Hagglof, Blom, Dahlquist, Lonnberg, & Sahlin, 1991). A more recent prospective study of more than 10,000 children in Sweden found that those who had experienced a serious life event in childhood had a higher risk of a future diagnosis of T1D, even after controlling for heredity, BMI, size for gestational age, parent education, and mother's employment status (Nygren, Carstensen, Koch, Ludvigsson, & Frostell, 2015). While speculative, psychological stressors may impact autoimmune responses (Rewers & Ludvigsson, 2016).

Recent reviews of the literature have suggested there is no linkage between stress and development of T1D. One systematic review of the literature stated a lack of evidence supporting the stress link from large controlled trials (Cosgrove, 2004). Another more recent review showed mixed results from studies comparing adverse childhood experiences and diabetes risk with several notable issues: few studies examined the association in children rather than adults, the range in types of adverse event studied, the need for a consistent measure of adverse events to facilitate comparisons among studies as well as comparison of the timing, frequency, and severity of the adverse events in relation to diabetes (Huffhines, Noser, & Patton, 2016).

Stress has also been found to impact the progression of diabetes after diagnosis. Past studies have found that stress is indirectly related to poor glycemic control as it negatively affects self-care behaviors (Farrell, Hains, Davies, Smith, & Parton, 2004; Helgeson, Escobar, Siminerio, & Becker, 2010). More frequent stressful life events have been shown to negatively impact adherence, glycemic control, self-efficacy, quality of life, and family conflict (Commissariat et al., 2017).

Physical and emotional stresses have also been associated with T2D in youth. First, stress can lead to overeating, which can lead to overweight/obesity, both potent risk factors for T2D. Physical, emotional, and/or chronic stress in childhood may impact the body's stress response, thus affecting metabolic functioning and growth, and may lead to early-onset obesity and T2D (Pervanidou & Chrousos, 2012). Additionally, chronic emotional stress, particularly anxiety, may lead to emotional eating as a coping mechanism and result in loss of control over eating behaviors (Goossens, Braet, Van Vlierberghe, & Mels, 2009). Disordered overeating will also affect weight, insulin resistance, and risk for type 2 diabetes.

Family Factors

There are likely multiple demographic and family factors related to onset, presentation, and diagnosis of T1D and T2D. Many factors may also impact the progression of diabetes and success related to various treatments.

Family demographics have been shown to be associated with the risk of developing T1D in youth. One study found that risk of T1D had an inverse relationship with number of siblings and was positively associated with maternal factors indicative of lower SES, such as an unmarried mother, inadequate prenatal care, or Medicaid insurance. Additionally, maternal BMI of 30 kg/m^2 or higher was associated with increased risk of diabetes (D'Angeli et al., 2010). In youth with T2D, both youth and family demographics are associated with T2D in youth. Large studies in the United States (TODAY and SEARCH) report that youth with T2D tend to be primarily female, of racial/ethnic minority status, and have overweight/obesity, low socioeconomic status, and a family history of diabetes (Copeland et al., 2011; Nadeau et al., 2016). Similarly, a recent analysis from the Pediatric Diabetes Consortium

T2D Registry of 503 youth at the time of diagnosis found that youth with T2D were primarily females, Hispanic, and had a family history of T2D. Family demographic factors often found in youth with T2D include single-parent households, parents with no more than a high school education, and household incomes rarely over $25,000 (Klingensmith et al., 2016).

The American Diabetes Association (ADA) has encouraged age-appropriate family support and involvement in managing diabetes in youth in the ADA's medical and psychosocial standards of care (American Diabetes, 2017; Young-Hyman et al., 2016). The family is critically important in the management of childhood diabetes, for both T1D and T2D. A literature review of family interactions in pediatric T1D reported that warm and collaborative family involvement in care was associated with better health outcomes and quality of life (Jaser, 2011). Interventions aimed to encourage family involvement have also found that family teamwork in managing T1D prevented deterioration in glycemic control in adolescents with longer durations of diabetes (Laffel et al., 2003) and improved glycemic control in those adolescents with particularly suboptimal A1c levels (Katz, Volkening, Butler, Anderson, & Laffel, 2014; Wysocki et al., 2006).

Numerous studies have suggested that family support and family lifestyle behaviors also play a role in health outcomes in youth with T2D. One qualitative study showed that parents reported struggling to serve as positive role models for healthy lifestyle behaviors, especially when other members of the family were obese or if parents believed that healthier eating behaviors did not cohere with their parental instinct to feed their child (Mulvaney et al., 2006). Another study showed that better glycemic control in T2D was associated with more parent involvement in diabetes care, particularly outside the home (Anderson, Cullen, & McKay, 2005).

Lifestyle Behaviors

Certain lifestyle behaviors appear to contribute to diabetes risk. Lifestyle factors associated with T1D have focused primarily on the impact of certain lifestyle behaviors, like dietary habits and physical activity, on blood glucose levels following diagnosis. Few lifestyle behaviors have been explored in relation to the development of T1D. Studies have focused primarily on early nutrition, suggesting that early termination or lack of breastfeeding and early exposure to cow's milk are risk factors for T1D (Atkinson & Ellis, 1997). Additionally, exposure to foods containing gluten within the first 3 months of life rather than exclusive breastfeeding has been suggested to increase the risk of T1D in infants (Chmiel et al., 2015). Lifestyle changes have also been suggested to affect the progression of T1D. For example, exercise has been postulated as a means to preserve beta cell function in patients with recent onset T1D. A recently published pilot study involving older teens and adults ages 16–60 randomized 58 individuals to an exercise intervention or control group within 3 months of diagnosis. After 12 months, the rate of beta cell function loss was similar between groups, although there was a suggestion of greater insulin sensitivity in participants in the exercise intervention group (Narendran et al., 2017).

On the other hand, multiple behavioral factors contribute to the development of T2D, centered around obesity caused by excessive calorie consumption, infrequent physical activity, and more sedentary behavior (Pulgaron & Delamater, 2014). These factors appear to be particularly difficult to manage in youth and become particularly problematic during pubertal growth and development. Multiple studies have documented the persistence of unhealthful lifestyle behaviors in youth with T2D after diagnosis, which include overeating and consumption of unhealthy foods such as fast food and sugary drinks (Rothman et al., 2008), infrequent physical activity (Rothman et al., 2008; Shaibi, Faulkner, Weigensberg, Fritschi, & Goran, 2008; Wilmot & Idris, 2014), and more sedentary behaviors (Kriska et al., 2013; Wilmot & Idris, 2014). While the Look AHEAD study and Diabetes Prevention Program in adults demonstrated the benefit of lifestyle management on reduced progression to T2D and on preservation of glycemic control (Herman et al., 2017; Look Ahead Research Group, 2014), studies in pediatric patients have been less supportive of lifestyle interventions. For example, the HEALTHY study, which implemented a longitudinal school-based intervention for overweight/obese children in middle schools, found that students who participated in the school-based intervention did show a reduction in various secondary measures of adiposity and fasting insulin levels, but no changes were shown in mean blood glucose compared to students in control schools (Group et al., 2010). Similarly, the TODAY study showed no added benefit of supplementing metformin treatment with an intensive lifestyle intervention for the preservation of glycemic control in youth with relatively recent onset T2D (Narasimhan & Weinstock, 2014).

Lifestyle modifications require substantial effort, self-control, and organization that may not be present in many youth. Involving families in lifestyle interventions may ease the burden on the child or adolescent while providing support and more opportunities to implement healthy, new behaviors. Given the SES and racial/ethnic disparities found in pediatric T2D populations, prescribed lifestyle interventions may be more difficult to implement and maintain. The ADA has suggested a family-centered approach to lifestyle modifications in youth with T2D, with particular attention to the interplay of culture and nutrition, as well as the availability of resources based on the family's means (American Diabetes Association, 2017).

Puberty

It is well established that insulin resistance develops as part of normal pubertal development in children both with and without diabetes (Amiel, Sherwin, Simonson, Lauritano, & Tamborlane, 1986; Jeffery et al., 2012; Raab et al., 2013). Other factors such as physical activity, diet, and the menstrual cycle also contribute to pancreatic beta cell function and insulin resistance (Cree-Green, Triolo, & Nadeau, 2013; Jeffery et al., 2012). Research clearly shows that glycemic control worsens in adolescents as compared to younger children or adults, due to physiological changes (Hamilton & Daneman, 2002). Further, psychosocial issues during adolescence also impact adherence and, in turn, glycemic control.

In persons with T1D, this insulin resistance often leads to increased insulin requirements, and may lead to deteriorating glycemic control at times when there is a delay between the onset of insulin resistance and titration of insulin dosing in youth around the time of puberty. Ongoing studies are investigating the relationship between puberty and pancreatic autoimmunity in youth, and how this might influence the development of T1D (Ziegler, Meier-Stiegen, Winkler, Bonifacio,, & Teendiab Study Group, 2012). In those with obesity and a genetic predisposition for T2D, the insulin resistance of puberty may lead to the development of diabetes.

Deteriorating diabetes self-care behaviors during adolescence result from typical developmental issues, as teens may place greater emphasis on peer approval rather than on diabetes self-management. Adolescents often experiment with limits, risk-taking, and rebellion in an attempt to establish independence and control their destiny, though this may negatively affect diabetes care and glycemic control (Frank, 2005). These phenomena are applicable to both T1D and T2D, as adolescents may find that self-care behaviors amplify their differences from their peers. For example, adolescents with T1D may feel burdened and uncomfortable by the visibility of their insulin administration or glucose checks, the appearance of wearing devices, or what people may think if the teen has a hypoglycemic reaction in front of others. Adolescents with T2D may experience similar struggles with visibility of the illness by trying to maintain a healthy diet when peers may not, by taking medications, or by checking glucose levels. Additionally, there may be added stress and embarrassment related to weight gain or being overweight or obese. Many studies have reported high rates of nonadherence in youth with T2D, potentially due to the fact that youth with T2D may not experience many symptoms of hypoglycemia compared with youth with T1D (Pulgaron & Delamater, 2014).

Depressive Symptoms: Metabolic and Inflammatory Markers

Persons with both T1D and T2D often have elevated levels of inflammatory markers along with dysregulated metabolism (Rabinovitch & Suarez-Pinzon, 2007; Sochett et al., 2017; Tilg & Moschen, 2008). These metabolic influences, systemic inflammation, and immune system dysregulation may play a role in the relationship between diabetes (and glycemic control) and depressive symptoms, although the details of the interplay and the directionality of the effect is not well-described. Inflammatory markers such as C-reactive protein, serum amyloid A, apolipoprotein B, leptin, lipoprotein A, and interleukin-6 have been associated with depressive symptoms in youth with diabetes (Hood et al., 2012). A recent meta-analysis of several studies of neuroimaging in adults with diabetes has revealed thalamic atrophy in persons with T1D and reduced global brain volume as well as regional atrophy in the hippocampi, basal ganglia, or orbitofrontal and occipital lobes in persons with T2D (Moulton, Costafreda, Horton, Ismail, & Fu, 2015). Biological mechanisms may play a role in mediating the link between depression and diabetes and might shed light in the future upon new targets for intervention.

We have shown that youth with new-onset T1D who endorse depressive symptoms in the first month after diagnosis had poorer glycemic control with a higher HbA1c 6 months after diagnosis, compared with youth with new-onset diabetes who did not endorse high levels of depressive symptoms in the first month (McGill et al., 2017). Further, those youth who experienced partial remission (honeymoon period) 6 months after diagnosis were significantly less likely to have clinically elevated depressive symptoms compared with those youth who were not in partial remission after living with T1D for 6 months. A study by Grey and colleagues found that in the first 6 weeks after diagnosis of T1D, children ages 8–14 endorsed more feelings of depression, dependency, and withdrawal than their self-selected peers without diabetes. At one-year follow-up, children with T1D appeared to have adjusted to their diagnosis, as they endorsed no psychosocial differences compared with their peers. However, at 2 years post-diagnosis, they reported twice the amount of depression and adjustment issues (Grey, Cameron, Lipman, & Thurber, 1995). The TODAY study reported high rates of depressive symptoms in teens with T2D, as well as both high rates of depression and diminished quality of life when associated with binge eating behaviors (Anderson et al., 2011; TODAY study group et al., 2011). This may point to bi-directionality in the association between reported depressive symptoms and poorer glycemic control.

Conclusion

This chapter aimed to describe of the various factors associated with the development and progression of T1D and T2D in the pediatric population. There are currently no approaches to prevent the onset of T1D, although research continues to explore immunomodulatory therapies. With respect to T2D, adult studies have demonstrated opportunities to prevent progression from glucose intolerance to frank diabetes with intensive lifestyle interventions, though such approaches have not yielded positive results in the pediatric population. Despite these deficiencies, there are extraordinarily effective treatments for the management of both T1D and T2D in youth as well as across the lifespan. Managing the progression of both T1D and T2D requires an orchestrated approach to management, including an appreciation of the neuroendocrine and biobehavioral factors that may be involved.

Diabetes demands substantial responsibility on the part of the youth and family in order to adhere to the complex treatment regimen with the goal of optimizing glycemic control. These self-care responsibilities are often burdensome and likely to interfere with many of the typical developmental stages of childhood and adolescence. In order to maximize both biomedical and psychosocial outcomes following the diagnosis of diabetes, it is important that both the patient and family adapt to the diagnosis and its treatment regimen. A number of factors influence adaptation to diabetes, including demographic factors, psychological responses, and personal and environmental factors (Nadeau et al., 2016; Whittemore, Jaser, Guo, & Grey, 2010). The interaction of these factors may influence a child or adolescent's acceptance of diabetes, which may, in turn, impact overall physical and mental well-being. It is important to periodically evaluate a child or adolescent's response to the diagnosis and continuing management of diabetes and to provide support that encourages acceptance and family involvement in the management of either T1D or T2D.

The extent to which a child or adolescent is able to adapt, accept, and positively identify with a diagnosis of diabetes may impact his or her future treatment adherence and health outcomes (Commissariat, Kenowitz, Trast, Heptulla, & Gonzalez, 2016). This highlights the importance of adaptation to a chronic illness that requires extensive work and responsibility on the part of the patient and family for the foreseeable future. Acceptance and adaptation are enhanced with support from the family and ongoing education from the healthcare team. There is, understandably, an emotional adjustment period to any new diagnosis of diabetes. However, following this initial adjustment, it is important to maximize opportunities to incorporate a positive mental framework around diabetes and its self-management as part of one's life. These efforts by the patient, family members, and healthcare team can guide the patient to disease acceptance and make self-management less physically and emotionally burdensome. Thus, diabetes, along with its many neuroendocrine and biobehavioral influences, from diagnosis and during its progression, can become manageable.

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Chapter 4

Distress and Quality of Life

Jamil A. Malik and Naeem Aslam

Psychological distress and quality of life are interlinked factors that have both generic and specific connotations. In the general population, there is considerable empirical evidence that suggests an association between distress and quality of life. Within the distress and quality of life spectrum, a cyclic mechanism of functioning seems to work: an increase in distress decreases quality of life and decline in quality of life further escalates distress. Out of the cyclic spectrum they both seem to work together as negatively correlated antecedents of several consequences and correlated outcomes of several clinical conditions. In this chapter, we focus on research aimed at understanding psychological distress associated with diabetes and diabetes-related quality of life in pediatric populations with type 1 and type 2 diabetes.

Diabetes-Specific Distress

Daily life chores including household and work-related strains are potential sources of distress. In our daily life, we are confronted and manage routine stressors. Often, however, we know that even with our best management skills there is something that is never going to be finished or we may never be able to accomplish a task. If the tasks are not able to be eliminated, and we are compelled to continue the task, they have the potential to instigate psychological distress. Psychological distress may include the feelings of worthlessness, poor work performance, chronic sadness, lack of interest and involvement in daily activities, etc. (Lovibond & Lovibond, 1995). In the context of diabetes self-management, monitoring and keeping records of blood glucose, never missing medications, carrying medications everywhere, adjusting insulin, injecting insulin, programming time for physical activity not as a healthy lifestyle yet just to ensure health, counting carbohydrates, and meal planning are among the routine stressors and part of everyday life that may lead to psychological distress. These tasks may be burdensome and have physical, emotional, and psychosocial effects irrespective of age, gender, and other socio-demographics. Pediatric populations are particularly more vulnerable for developing psychological distress when they compare themselves with their counterparts without

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J. A. Malik (✉) · N. Aslam
National Institute of Psychology, Quaid-i-Azam University, Islamabad, Pakistan
e-mail: ja.malik@nip.edu.pk

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diabetes. Compounding this is the fact that children and adolescents are in a stage of life in which their coping mechanisms are not matured. It is difficult for them to cope with emotional consequences resulting from a discriminated lifestyle of their age group.

The daily strains and stressors resulting from self-management demands are recognized as diabetes distress. For the past few decades, health professionals and more specifically mental health professionals have been trying to understand the mechanism and nature of diabetes distress. Moreover, they strive to comprehend, what is diabetes distress? How is diabetes distress different from general distress? What are potential indicators and consequences of diabetes distress? What are its demographic and psychosocial correlates? How should diabetes distress be assessed? How and when should we intervene in diabetes-related distress? Empirical literature demonstrates that distress is two to three times higher in people with diabetes, despite the fact that the majority of the cases of distress are under-recognized (Badescu et al., 2016). However, in the following review, we present the theoretical and empirical literature that addresses diabetes-related distress and quality of life and their reciprocal relationship among children and adolescents with diabetes. We incorporate the demographic and psychosocial correlates and give a generic conceptual model of care for diabetes distress and quality of life in the patients with diabetes mellitus.

Among the multifaceted dimensions of diabetes-related distress, the stress associated with the diagnosis of diabetes is of prime importance. Studies have shown that distress resulting from diagnosis of this illness is escalated during the honeymoon period (Nieuwesteeg et al., 2016; Viaene, Van Daele, Bleys, Faust, & Massa, 2017). The diagnosis itself is stressful not only for the children and adolescents but also for the parents and caretakers (Chaney et al., 1997; Northam, Anderson, Adler, Werther, & Warne, 1996). The complexity associated with the treatment regimen is also a major source of strain for parents of diabetic children, affecting almost every aspect of their daily life (Greening, Stoppelbein, & Cheek, 2016) and making them vulnerable for development of negative emotional consequences (Landolt, Vollrath, Laimbacher, Gnehm, & Sennhauser, 2005). Although longitudinal follow-up has shown a decline in psychological strain over a period of 1 year, it is evident that family functioning is affected in a complex way (Northam et al., 1996).

Other studies have shown severe psychological consequences and risk of posttraumatic stress in parents of children diagnosed with diabetes (Greening et al., 2016; Landolt et al., 2002). It has been reported that parental stress might also be a result of severe fear of hypoglycemia (Viaene et al., 2017), but whatever the source, distressed caregivers may become another potential source of escalating distress for children diagnosed with diabetes (Cunningham, Vesco, Dolan, & Hood, 2011). Indeed, studies have shown that caregiver and parental stress is related with children stress and also directly and indirectly to glycemic control of children (Cunningham et al., 2011; Haugstvedt, Wentzel-Larsen, Graue, Sovik, & Rokne, 2010; Stallwood, 2005; Viaene et al., 2017). In a follow-up study, Nieuwesteeg et al. (2016) showed that over a longer period, fathers are more stressed and face more burden of care as compared to mothers. It has been also demonstrated that poor health outcomes of children are linked with greater parental general stress whereas diabetes-specific stress was associated with better child outcomes (Helgeson, Becker, Escobar, & Siminerio, 2012; Hilliard, Monaghan, Cogen, & Streisand, 2011). It is, however, suggested that each area of parent functioning related to diabetes distress should be addressed by using behavioral interventions to gain maximum benefits in terms of child mental health and diabetes management (Streisand, Swift, Wickmark, Chen, & Holmes, 2005).

Among children and adolescents, distress faced at the time of diagnosis (Hannonen et al., 2015) and during the honeymoon period is not only associated with changes in lifestyle and adjustment to the complex and burdensome treatment regimen (Malik & Koot, 2009) but also to concern about the development of complications associated with diabetes (Beck et al., 2012; Landolt et al., 2005; Sismanlar et al., 2012). The awareness related to risk of various complications, particularly fear of hypoglycemia, and worries about day-to-day management demands might be the underlying sources of distress among newly diagnosed pediatric patients. Poor family resources is also identified as another significant factor that correlated with diabetes-related distress (Auslander, Bubb, Rogge, & Santiago, 1993). Poor family resources may indirectly increase distress through escalation in family stress and distortions in family functioning (Northam et al., 1996; Viaene et al., 2017). Even though the onset of the disease is considered among the significant points of time that are associated with distress (Hannonen et al., 2015), people with diabetes are vulnerable for development of diabetes distress throughout the course of the disease. The emotional component of diagnosis of a chronic condition like diabetes can be activated by any trigger and any point in time starting from diagnosis itself. Hence, more rigorous assessment and intervention for the diabetes distress particularly at the time of diagnosis and during the honeymoon period may have an additive value (Delamater et al., 2014).

Several longitudinal studies have shown varying patterns of distress after diagnosis of diabetes in pediatric populations (Law, Walsh, Queralt, & Nouwen, 2013; Northam et al., 1996). Empirical investigations have acknowledged that development through the stage of adolescence for children with diabetes increases difficulties in psychological management of the disease (Cho, Craig, & Donaghue, 2014; Huston, Blount, Heidesch, & Southwood, 2016) resulting in poorer glycemic control (Samuelsson et al., 2016). Other than diagnosis, factors like change in treatment regimen, change of doctor, onset of a complication, change in healthcare plan, and changing or adding medications are commonly associated with exacerbating diabetes distress. These situations may lead to experiences of higher emotional distress in some patients at some point in time after diagnosis. Facing and dealing with these spells of distress usually become a part of routine management of the disease, but at times this distress may become very challenging. Healthcare professionals should evaluate and assess the emotional distress and psychological comorbidity of children and adolescents in their regular treatment regimen for better management of the disease (Delamater et al., 2014; Delamater, Patino-Fernandez, Smith, & Bubb, 2013).

Studies have shown variant correlates of psychological distress among children and adolescents with diabetes mellitus from physiological measures to psychosocial and psychiatric outcomes. The prime of all these correlates is the clinical outcome, i.e., glycemic control. It is suggested that diabetes distress has a very complex role in the way that it directly and indirectly affects glycemic control through impact on self-management (Jaser, Patel, Xu, Tamborlane, & Grey, 2017). Regarding direct link between diabetes distress and glycemic control, previous studies have shown mixed findings. For example, one study showed that various indicators of diabetes-related stress including parental criticism and no control over food choice, particularly snacking, are directly associated with poor glycemic values (Delamater et al., 2013). Parental and adolescent distress resulting from parent-adolescent conflict over self-care responsibilities is also related to poor glycemic control (Anderson et al., 2009). Other studies have shown that poor glycemic control is also indirectly related to elevated distress through use of withdrawn coping (Luyckx, Seiffge-Krenke, & Hampson, 2010).

Adherence to the diabetes treatment regimen is considered another important clinical correlate of diabetes distress (Baucom et al., 2015; Hains, Berlin, Davies, Parton, & Alemzadeh, 2006; Mumtaz, Haider, Malik, & La Greca, 2016; Tran, Wiebe, Fortenberry, Butler, & Berg, 2011). Studies have shown that diabetes distress has a direct impact on adherence to treatment with increased distress worsening adherence to treatment (Baucom et al., 2015; Hains et al., 2006). The importance of adherence in diabetes management is undeniable as it directly affects everyday life of patients and increases risk of both acute and long-term complications (Rausch et al., 2012). Diabetes self-care tasks are a consistent correlate of diabetes distress, and adherence to treatment is challenging for adolescents with elevated distress (Larson, Moneta, Richards, & Wilson, 2002). Disruption in negative affect is reported as a common cause for both elevation in diabetes distress (Rao, Hammen, & Poland, 2010) and increased nonadherence (Hilliard, Herzer, Dolan, & Hood, 2011). It has been established that late adolescence is associated with elevated stress as the daily distress of diabetes management is pooled with more generic yet future-oriented stress related to financial and career pursuits (Baucom et al., 2015). Hence, older adolescents with diabetes are less likely to regulate their healthy behaviors resulting in poor disease management, such as skipping meals and engaging in sedentary activities (Baucom et al., 2015). Other studies showed associations of both increased diabetes-specific and general stress with lower adherence resulting in poorer metabolic control (Farrell, Hains, Davies, Smith, & Parton, 2004; Malik & Koot, 2009). The link between diabetes distress and adherence is elaborated with decline in effective coping strategies (Baucom et al., 2015; Tran et al., 2011).

Among sociodemographic correlates of diabetes-specific distress, gender has been frequently studied (Forsander, Bogelund, Haas, & Samuelsson, 2016). Experts say that "Yes, gender matters" even for pediatric populations at an early age due to unsuitability of higher levels of physical activity in girls as compared to boys (Sundberg, Forsander, Fasth, & Ekelund, 2012). Other factors include differences in hormonal change for girls and boys making diabetes management more complex and increasing risk of complications in this period of age (Cho et al., 2014), specifically for girls (Hochhauser, Rapaport, Shemesh, Schmeidler, & Chemtob, 2008; Samuelsson et al., 2016). Girls with type 1 diabetes have reported higher disease burden than boys (Chaplin et al., 2009). It is concluded that female adolescents are particularly vulnerable to diabetes distress and would benefit from additional support (Forsander et al., 2016).

Family-related factors are other important correlates due to the significance of the role of family in management of diabetes. Though we have already discussed the relationship between parent and child distress related to diagnosis, the literature suggest a more complicated link during the growth of children through adolescence with variant nature and degree of parental involvement (Law et al., 2013). Disagreement between parents and their children about responsibility for self-management has been associated with diabetes distress among children (Law et al., 2013). Along with other developmental changes, children with diabetes are assumed to manage their disease with the increased shift of responsibility for self-care from their parents to themselves (Anderson et al., 2009). Depending on the child's stage of readiness, this can make them more vulnerable to diabetes distress.

Along with adolescents, the parents of an adolescent diagnosed with diabetes also go through challenges in modifications of their degree of involvement in transfer of responsibility for child care (Dashiff, 2003). While both parents and children are facing this stressful challenge, they see each other's role differently, with adolescents seeing themselves as more independent and capable to take care of their diabetes (Butner et al., 2009) than their parents. This discrepancy may hinder a successful responsibility shift from parents to adolescents resulting in psychological distress in both adolescents (Pomerantz & Eaton, 2001) and their parents (Eckshtain, Ellis, Kolmodin, & Naar-King, 2010; Haugstvedt, Wentzel-Larsen, Rokne, & Graue, 2011). It is suggested that better sharing and timely transfer of responsibility from parents to adolescents is critical for good health-related outcomes (Schilling, Knafl, & Grey, 2006).

Besides demographic correlates, studies examining psychosocial correlates of diabetes distress have addressed both risk and protective factors including social support (Malik & Koot, 2011, 2012), self-efficacy (Law et al., 2013), resilience (Huston et al., 2016; Yi-Frazier et al., 2015), emotion regulation (Huston et al., 2016; Larson et al., 2002), appraisal (Streisand, Mackey, & Herge, 2010), cognitive distortions (Farrell et al., 2004), and stress coping mechanisms (Jaser et al., 2017). Among protective factors, social support has been a focus of research, and empirical literature indicates that social support may function as both direct and indirect predictors of diabetes distress and quality of life (Malik & Koot, 2009). Social support, either from parents (Hanson, Henggeler, & Burghen, 1987) or friends (Malik & Koot, 2012), is negatively associated with diabetes distress. From a developmental perspective, it is suggested that for adolescents, support from friends may be more important than parental support, the latter due to its potential conflict with development of autonomy. Social support from both parents and friends is also reported to moderate the effect of diabetes distress on psychological consequences (Malik & Koot, 2009). Recent empirical findings on social support suggest that an active involvement of both family and friends is needed to address diabetes distress, particularly for female adolescents who may require extra support (Forsander et al., 2016).

Resilience has also been reported as an important protective factor. Resilience has been shown to work against the rising of distress in diabetes patients and predicted better glycemic control (Yi, Vitaliano, Smith, Yi, & Weinger, 2008). When facing stress, people with low levels of resilience showed worse self-care behaviors and poor glycemic control compared to people with high resilience. It is suggested that interventions should incorporate strategies to boost resilience to reduce diabetes distress and to get desired health outcome in adolescents with type 1 diabetes (Yi-Frazier et al., 2015). It has been shown that interventions aimed at promoting resilience have helped improving coping and emotional well-being resulting in better self-care and health outcomes (Burton, Pakenham, & Brown, 2010).

This association has been extended to the underlying mechanism of maladaptive coping (Yi-Frazier et al., 2010). It has been shown that adolescents' ways of coping with their diabetes distress are associated with depressive symptoms, adherence, and even glycemic control (Delamater, Kurtz, Bubb, White, & Santiago, 1987; Graue, Wentzel-Larsen, Bru, Hanestad, & Sovik, 2004). The coping studies have addressed distress ranging from approach/avoidance to control-based coping from cross-sectional to longitudinal designs (Hapunda, Abubakar, van de Vijver, & Pouwer, 2015; Jaser et al., 2017). Although it has been shown that adolescents with diabetes use different coping styles compared to healthy adolescents, particularly for seeking professional help, a great deal of similarity was found in the coping styles of adolescents with diabetes to their parental coping styles (Pisula & Czaplinska, 2010). Longitudinal models have shown that adolescents' coping with stress is interrelated with psychological symptoms and glycemic control across time and have a reciprocal pattern of relationship (Luyckx et al., 2010).

Diabetes-Specific Quality of Life

Quality of life (QoL) is a complex construct with a composition of diversity of indicators ranging from societal or community well-being to a very specific assessment of the situation of individuals (Felce & Perry, 1995). Some people consider happiness as the prime indicator of QoL, while others have a more materialistic approach. The diversity of the concept is indicated by the various definitions of QoL (Baker & Intagliata, 1982; Liu, 1976). Generic measures of QoL include both objective and subjective indicators from a broad range of life domains (Felce & Perry, 1995; Rose et al., 1998). QoL in pediatric populations was not a focus of scholarly attention until the 1980s (Eiser & Morse, 2001). Initially, QoL of children was addressed using functional indicators such as school attendance, social relationship, and physical abilities (Ditesheim & Templeton Jr., 1987).

These early efforts helped in developing an understating of QoL by emphasizing that children have ability to adapt to a situation caused by a critical life event (i.e., diagnosis of a chronic condition, stress, or injury) and highlighting the significance of children's own understanding of such a critical situation and disability (Eiser & Morse, 2001). In chronic illness, evaluation of treatments typically involve multifaceted shifts in morbidity, changes in physiologic measures, side effects of treatments, and burdens faced by families and patients (DCCT, 1988). In such conditions, the conceptualization of QoL is dominated with disease-specific aspects of life. When considering diabetes-specific QoL, we refer to well-being and health-related indicators predominantly related to the disease that are assessed using measures with the potential to address specific issues (i.e., meal planning/restrictions, insulin management, hypoglycemia, glucose testing, etc.) of diabetes management (Rubin & Peyrot, 1999).

Several measures focusing on diabetes-specific QoL have been developed. These include (but are not limited to) the Diabetes Quality of Life Measure – DQOL (DCCT, 1988), the Diabetes-39 (Boyer & Earp, 1997), Diabetes Treatment Satisfaction Questionnaire – DTSQ (Lewis, Bradley, Knight, Boulton, & Ward, 1988), the Problem Areas in Diabetes – PAID (Polonsky et al., 1995), and the PedsQL diabetes module (Varni et al., 2018).

For the last two decades, health-related QoL in patients with diabetes has been fairly well studied. For instance, patients with type 2 diabetes have a doubled risk level for comorbid distress that hampers their QoL (Schram, Baan, & Pouwer, 2009). Health professionals are concerned with the QoL of patients who often struggle with diabetes management (Aalto, Uutela, & Aro, 1997). Studies suggest, however, that the diagnosis of diabetes has little effect on QoL at the time of diagnosis and continuing for the first few years of the disease (Edelman, Olsen, Dudley, Harris, & Oddone, 2002). Diagnosis itself is a compromise to life with the patient's awareness of their inability to continue with a regular life course and that they have to adjust their lifestyle activities considering their diabetes self-management tasks (Delamater et al., 2014; Malik & Koot, 2009). In addition, the label that comes with a chronic disease diagnosis may have some short-term effects on QoL (Sparring et al., 2013).

Given the complexity and diversity of the health-related QoL construct, the few studies showing that diagnosis of diabetes doesn't adversely affect QoL (Edelman et al., 2002) are not sufficient for drawing the conclusion that diagnosis and early adaptation does not negatively impact QoL. More evidence is needed with different measures of QoL addressing at least three domains (physical, social, and psychological well-being) and incorporating samples with diverse sociodemographic profiles (Aalto et al., 1997). Despite the fact that experts agree on the significance of patients' subjective evaluation of their QoL, a qualitative approach may reflect more precise results of being diagnosed with diabetes. It is not surprising to find differences in QoL even under similar circumstances (i.e., same physiological indicators, severity, and complications) due to varying ability of individuals to cope with adversity (Murillo et al., 2017; Testa & Simonson, 1996, 1998). Children and adolescents may be the best source of identification for QoL indicators in managing diabetes (Ausili et al., 2007; Shakya-Vaidya, Povlsen, Shrestha, Grjibovski, & Krettek, 2014). Wagner, Abbott, and Lett (2004) found differences in children's conceptualization of diabetes-related QoL domains: younger adolescents give importance to diabetes with the rationale of self-care behaviors compared to older adolescent who emphasized health with the rationale of living with diabetes.

Empirical literature addressing QoL in patients with diabetes suggests several factors that may act either as consequences or causal factors to worsen QoL (Aalto et al., 1997; Delamater et al., 2014; Malik & Koot, 2009; Rubin & Peyrot, 1999). These factors include sociodemographic, disease-specific, and psychosocial correlates of QoL. Sex and age of the patients are among the frequently studied demographic variables. Studies have consistently showed that boys scored high on QoL measures than girls (Chaplin et al., 2009; Hanberger, Ludvigsson, & Nordfeldt, 2009; Murillo et al., 2017). Low values of females particularly on positive well-being are associated with their tendency toward emotional reactions (Narasingarao, Manda, Sridhar, Madhu, & Rao, 2009). It is concluded that being female is among the significant potential risk factors for lower QoL particularly in the dimensions of mobility, self-care, usual activities, and pain/discomfort (Sparring et al., 2013). It is however, important to note that females appeared to have better disease knowledge (Lemes Dos Santos, Dos Santos, Ferrari, Fonseca, & Ferrari, 2014) but somehow unable to translate it into practice (Shakya-Vaidya et al., 2014).

Age is another important demographic variable incorporated in studies addressing QoL of children and adolescents with diabetes. Some studies have shown a negative association between age and QoL (Glasgow, Ruggiero, Eakin, Dryfoos, & Chobanian, 1997; Hahl et al., 2002; Klein, Klein, & Moss, 1998), while others reported nonsignificant associations (Malik & Koot, 2009; Peyrot & Rubin, 1997). The contradiction might be a result of varying age of diagnosis. With increased disease duration, a decline in QoL is expected particularly in physical functioning (Murillo et al., 2017; Rubin & Peyrot, 1999). Though studies reported better health-related outcomes of being young (Wagner, Muller-Godeffroy, von Sengbusch, Hager, & Thyen, 2005), it is recommended that age at diagnosis or duration of diabetes should be used as a control to estimate a precise relationship between age and QoL in children and adolescent with diabetes.

Studies have also indicated poor health-related QoL outcomes in children with diabetes with low socioeconomic status (SES) (Froisland et al., 2013; Hassan, Loar, Anderson, & Heptulla, 2006; Puri, Sapra, & Jain, 2013; Tahirovic, Toromanovic, Tahirovic, & Begic, 2013) and with low maternal education (Froisland et al., 2013; Murillo et al., 2017; Puri et al., 2013). This is contrary to a report of adult patients with diabetes who reported low QoL with higher education and SES (Glasgow et al., 1997).

Studies looking at differences in QoL across race and ethnic background also have mixed findings (Kalyva, Abdul-Rasoul, Kehl, Barkai, & Lukacs, 2016), either with nonsignificant differences (Glasgow et al., 1997; Peyrot & Rubin, 1997) or with lower QoL in African-American, minorities, and immigrants (Goh, Rusli, & Khalid, 2015; Jhita et al., 2014; Kaholokula, Haynes, Grandinetti, & Chang, 2006; Shallcross et al., 2015; Wee, Li, Cheung, Fong, & Thumboo, 2006).

Among diabetes-specific correlates of QoL, clinical indicators such as poor glycemic control (Froisland et al., 2013; Keller et al., 2016; Murillo et al., 2017; Puri et al., 2013; Tahirovic, Toromanovic, Tahirovic, Begic, & Varni, 2012), longer duration of diabetes (Abdul-Rasoul, AlOtaibi, Abdulla, Rahme, & AlShawaf, 2013; Buresova, Veleminsky Jr., & Veleminsky Sr., 2008; Malik & Koot, 2009), and presence of diabetes complications (Alva, Gray, Mihaylova, & Clarke, 2014; Hahl et al., 2002; Jacobson et al., 2013; Peasgood et al., 2016; Solli, Stavem, & Kristiansen, 2010) are well documented in empirical literature. While earlier studies failed to show a relationship between glycemic control and QoL (Anderson, Fitzgerald, Wisdom, Davis, & Hiss, 1997; Weinberger et al., 1994), recent studies suggest a relationship between poor glycemic control and lower QoL (Abdul-Rasoul et al., 2013; Froisland et al., 2013; Murillo et al., 2017; Puri et al., 2013; Tahirovic et al., 2012). It is yet not clear, however, what predicts what and most researchers suggest a cyclic relationship between glycemic control and QoL (Malik, Batool, & Nawaz, 2016). The studies that fail to establish a link between glycemic control and QoL used generic measures compared to recent studies using more disease-specific measures. Overall, the empirical data suggest a relationship that should be further investigated to confirm reciprocity. The available data suggest that extra effort for good glycemic control is beneficial in reducing the burden of care and results in improved QoL (Rubin & Peyrot, 1999).

It is well established that duration of diabetes can worsen QoL (Abdul-Rasoul et al., 2013), yet other factors including age of patient and age at diagnosis confound these findings (Rubin & Peyrot, 1999). An overall view of time-related factors suggests an impact of chronicity on QoL. For instance, chronicity of diabetes is associated with a substantial decline in QoL (Buresova et al., 2008). Follow-up studies involving control groups have shown that the QoL of individuals with diabetes is significantly decreased after 15 years and 24 years of diagnosis (Sparring et al., 2013). The chronicity itself might have a spurious effect, as studies have shown that adherence to treatment also declines with increased duration of diabetes (Murillo et al., 2017; Sud, Marcon, Assor, Daneman, & Mahmud, 2012). Adherence and QoL are positively related factors suggesting that a decline in adherence may deteriorate perceived QoL (Chew, Sherina, & Hassan, 2015). Improved diabetes care in pediatric populations resulting in better adherence is associated with lower mortality and morbidity in later life (Samuelsson et al., 2016). Thus, the underlying mechanism for the effect of diabetes duration on QoL might involve a mediating role of treatment adherence.

It seems logical to expect an indirect effect of duration of diabetes with the explanation that over the course of diabetes, a decrease in adherence may result in poor QoL. A review of the adherence literature proposes a chain of causal processes rather than simple indirect effects of duration of diabetes on QoL through treatment adherence. Much of the adherence literature has shown poor glycemic control (Sloan, Bethel, Lee, Brown, & Feinglos, 2004; Song & Kim, 2009) and development of diabetes complications for nonadherent patients (Fukuda & Mizobe, 2017; Gibson et al., 2010; Shivashankar et al., 2016; Simpson, Lin, & Eurich, 2016; Yu, Yu, & Nichol, 2010). On the other hand, studies show poor QoL for patients with complications compared to patients without complications (Alva et al., 2014; Hahl et al., 2002; Jacobson et al., 2013; Peasgood et al., 2016; Solli et al., 2010). For example, a study showed that foot problems were associated with substantial loss in health-related QoL (Peasgood et al., 2016). Another study investigated the effect of seven different incident diabetes complications (stroke, heart failure, myocardial infarction, ischemic heart disease, renal failure, blindness, and amputation) and showed that having any one of the seven complications was associated with significant reduction in QoL, even controlling for age, sex, and economic region (Hayes et al., 2016). Given that time-related factors (age of the patient, age at diagnosis, and duration of the illness) are directly associated with health-related QoL, a conclusion for a causal chain may be drawn particularly for duration of diabetes when considering the above cited literature. A logical causal chain may be determined starting from chronicity to decline in adherence to poor glycemic control to development of complications resulting in a decline is health-related QoL. Hence, it is imperative that longitudinal models should develop a clear understanding for the effect of time-related factors and even for time-invariant determinants of QoL (Alva et al., 2014).

Several studies have investigated the role of psychosocial correlates in health-related QoL of children and adolescent with diabetes (Achuko, Walker, Campbell, Dawson, & Egede, 2016; Allan, Flett, & Dean, 2008; Byrne et al., 2012; de Vries et al., 2014; Eckert, 2012; Joensen, Almdal, & Willaing, 2016; Kong et al., 2013; Puri et al., 2013; Rubin & Peyrot, 1999; Zhu, Fish, Li, Liu, & Lou, 2016). Qualitative studies also have shown the significance of psychosocial determinants of QoL including relationships, family responsibilities, rewarding life, spiritual life, material support, social support, general stress, helplessness, fear, anger, and depression (Choe, Padilla, Chae, & Kim, 2001). The significance of psychological aspects in QoL has been conferred across cultures (Kong et al., 2013). Allan et al. (2008) showed that youth with type 2 diabetes are more optimistic about their health-related QoL than their parents. Others have shown that perceived discrimination (Achuko et al., 2016) and stigma (Gredig & Bartelsen-Raemy, 2016) have a significant effect on QoL, reinforcing the need to address it in children soon after diagnosis of diabetes.

Eating problems are a major issue of youth diagnosed with diabetes and are therefore a major concern of clinicians caring for these patients. Body mass index (BMI) has been reported to have a negative relationship with health-related QoL (Hlatky et al., 2010). Group et al. (2011) showed that youth with type 2 diabetes had serious impairment in QoL due to clinical and subclinical levels of binge eating. Parental perception of child functioning at school is also associated with QoL. In addition, parents of adolescents diagnosed with type 1 diabetes showed elevated concerns about their school functioning and an elevated fear of hypoglycemia which was associated with lower QoL (Herbert et al., 2015). Maternal involvement is important in diabetes care, yet it is recommended that such an involvement should be adjusted to the developmental levels of children to get optimal health-related outcomes (Wiebe et al., 2005).

Research on coping has shown diverse effects of various types of coping on QoL (Jaser et al., 2017; Jaser, Linsky, & Grey, 2014). It is reported that use of problem-solving and positive thinking strategies as primary and secondary coping skills predicted fewer problems with QoL compared to use of avoidance coping strategies (Jaser et al., 2017). Puri et al. (2013) developed a profiling of children at risk of development of psychological and cognitive problems resulting in poor QoL. The study was conducted as part of the DAWN youth project and concluded that in a setting where resources are limited, a priority for behavioral and cognitive evaluation should be given to children with recent diagnosis, older age onset, poor glycemic control, low SES, and low maternal education. These children are at a higher risk of development of psychological issues and impaired QoL (Puri et al., 2013). Others have reported that social and financial support along with interventions to promote physical activity and to enhance coping skills against psychological distress might be effective in improving health-related QoL (Shiu, Choi, Lee, Yu, & Man Ng, 2014).

Certain factors appear to have complex patterns related to adjustment to having diabetes. For example, one study suggested that both emotional distress and treatment-related frustration may have a positive role initially yet may become barriers to achieve positive health outcomes in the long run (Weinger & Jacobson, 2001). Patients' attitudes to accept challenges and their level of motivation and hope are among the protective factors against harmful consequences of diabetes on both mental and physical components of QoL. Hence, it has been recommended that patients' perspectives should be given importance in the translation and interpretation of the meaning of illness (Walker, Lynch, Strom Williams, Voronca, & Egede, 2015); patients' attitudinal barriers should also be addressed in intervention plans (Weinger & Jacobson, 2001). Further support in achieving favorable outcomes in health-related QoL has been reported with interventions addressing diabetes empowerment ability, self-efficacy (Zhu et al., 2016), and resilience in children and adolescents (Yi-Frazier et al., 2015).

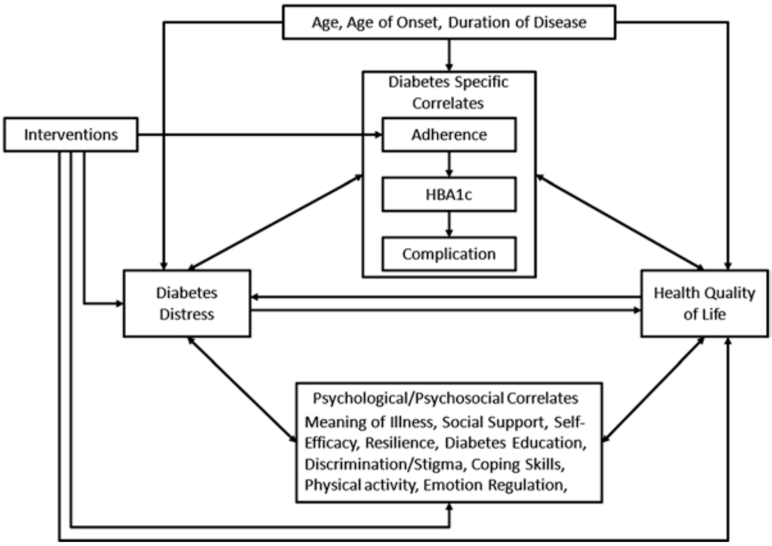

Fig. 4.1 Conceptual model of care for diabetes distress and health-related quality of life

Conceptual Model of Care

In light of the research literature in this area, a generic conceptual model of care addressing both psychological distress and health-related QoL is proposed. The model, presented in Fig. 4.1, includes common correlates of diabetes distress and health-related QoL in children and adolescents with diabetes. Precision may be added in the model by specification of suitable interventions addressing respective correlates.

Conclusions

It can be concluded that both psychological distress and health-related QoL have common grounds in children and adolescents with diabetes. Starting from sociodemographic factors, i.e., age, gender, socioeconomic status, ethnicity, and family culture, to diabetes-specific physical and physiological indicators, i.e., age of onset/diagnosis, duration of diabetes, glycemic control, and diabetes complications, to behavioral and psychological factors, i.e., treatment adherence, fear of hypoglycemia, discrimination and stigmatization, meaning of illness, burden of self-care and management of diabetes, family functioning, social support, resilience, self-efficacy, emotion regulation, and coping styles, seem to have similar underlying mechanisms but in reverse direction for diabetes distress and health-related QoL. With a direct negative relationship and with these common underlying grounds both diabetes distress and diabetes-related QoL seems to work in a cyclic process. It is recommended that tailored interventions addressing any of the common correlates, distress, and QoL should be carefully evaluated. Interventions should be prioritized based on their commonality in the underlying mechanism of diabetes distress and QoL spectrum. Given the reciprocal nature of relationship, future research should use longitudinal designs to determine several potential feedback loops in understanding the underlying mechanisms of diabetes distress and QoL for pediatric patients.

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Chapter 5
Depression, Diabetes-Related Distress, and Anxiety in Pediatric Diabetes

Meredyth A. Evans, Anthony T. Vesco, and Jill Weissberg-Benchell

Youth with type 1 diabetes (T1D) face a demanding disease with complicated daily self-care tasks, including blood glucose monitoring, insulin administration, food calculations, and monitoring of physical activity. As children transition to adolescence, they also face the challenges of coping with the social, emotional, and biological changes associated with developing into a young adult. Negotiating the typical developmental tasks of adolescence while also managing the daily demands of T1D can lead to poor adherence as well as increased emotional burden. Data suggest that youth with T1D are at increased risk for depression, diabetes-specific emotional distress, and anxiety (Hood et al., 2006; Reynolds & Helgeson, 2011; Delamater, de Wit, McDarby, Malik, & Acerini, 2014; Delamater et al., 2018; Herzer & Hood, 2009), which are also associated with a decline in daily self-care behaviors and glycemic control (Hilliard, Wu, Rausch, Dolan, & Hood, 2013; McGrady, Laffel, Drotar, Repaske, & Hood, 2009; Herzer & Hood, 2009).

There are a variety of factors that influence the development and course of depression and anxiety in youth with T1D including individual, family, and sociocultural factors. These factors need to be considered in order to provide effective treatment for youth with diabetes who are experiencing or at risk for symptoms of depression and anxiety. Identification of the factors that can influence anxiety and depression in this population may also lead to the development of policies and practices, such as routine psychological screening, that could prevent the onset and progression of psychological disorders in this population.

Depression in Type 1 Diabetes

Much of the literature addressing depression in the context of T1D has focused primarily on symptom prevalence and intraindividual demographic factors that influence depressive course. In a meta-analysis conducted by Reynolds and Helgeson (2011), youth with T1D reported more depressive symptoms ($d = 0.26$) as well as more clinical depression ($d = 0.40$) based on standard measures of depressive

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M. A. Evans · A. T. Vesco · J. Weissberg-Benchell (✉)
Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Northwestern University Feinberg School of Medicine, Chicago, IL, USA
e-mail: jwbenchell@luriechildrens.org

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severity relative to children without diabetes. Moreover, a 2015 population-based cohort study of children with T1D ($n = 17{,}122$) and their healthy siblings compared risk of psychiatric disorders with that of non-related children without diabetes matched on demographics (Butwicka, Frisén, Almqvist, Zethelius, & Lichtenstein, 2015). Participants were followed until their 18th birthday and were born between 1973 and 2009 and were divided into birth cohorts based on time of diagnosis of T1D: 1973–1986, 1987–1996, and 1997–2009. The prevalence of a diagnosed psychiatric disorder, adjusting for age, sex, year of diagnosis, socioeconomic, and perinatal factors, was approximately two times higher in individuals with T1D relative to those without diabetes; however, the risk of psychiatric disorders decreased marginally over the course of the study period compared to matched controls. The authors suggest that advances in diabetes care (e.g., intensive insulin regimens allowing greater flexibility in schedule and diet) likely contribute to this finding. Butwicka et al. (2015) reported that the prevalence of a diagnosed mood disorder, suicide attempt, and anxiety disorders is approximately twofold higher (hazard ratios of 2.0, 1.6, and 1.6, respectively) for youths with T1D. Siblings of children with diabetes did not demonstrate an increased risk for developing either a mood or an anxiety disorder, suggesting that biological and/or psychological aspects of T1D that are associated with the increased risk.

At diagnosis, children with T1D endorse higher depressive and anxious symptomatology than children without diabetes. Some evidence suggests that symptoms remit after 1 year and increase again after 2 years (Grey, Cameron, Lipman, & Thurber, 1995). A more recent study found that the risk for a psychiatric disorder was highest during the first 6 months following the diagnosis of T1D, regardless of the age at which participants were diagnosed (Butwicka et al., 2015). The higher risk for psychiatric disorders, including depression, at the point of diagnosis may be due to challenges inherent in adjusting to a new diagnosis and to the demands and intensity of a daily treatment regimen.

Some studies suggest that youth with T1D experience periods of depressive symptoms throughout their lifetime. Studies have reported that depressive symptoms are highest at 4 and 10 years after diagnosis (Grey et al. 1995; Grey, Whittemore, and Tamborlane 2002). In contrast, other studies suggest that the risk of depressive symptoms decreases over time (Butwicka et al., 2015) or that they are initially low and remain consistently low 5 years after diagnosis (Hood et al., 2014). It may be that premorbid depressive symptoms account for the course of depressive symptoms throughout the life span (Johnson, Eiser, Young, Brierley, & Heller, 2013).

Typical factors associated with depressive symptoms in the general pediatric population include older age, female gender, and familial stress or dysfunction (Calles, 2007; Twenge & Nolen-Hoeksema, 2002). Many of these factors are also associated with depressive symptoms in youth with diabetes. For example, in the SEARCH study for diabetes, higher prevalence of depressed mood was associated with female gender, older age (in girls), racial minority status, lower parental education, and lower family income (Lawrence et al., 2006). Notably, the SEARCH study involved a mixed sample of youth with type 1 and type 2 diabetes, and demographic associations with depressed mood were not examined separately between these populations. Studies that exclusively included youth with T1D also show that there is a higher prevalence of depressive symptoms in girls (de Wit & Snoek, 2011; Hood et al., 2006), older adolescents (Riley, Duke, Freeman, Hood, & Harris, 2015), and youth from lower socioeconomic backgrounds (Silverstein et al., 2015). Additionally, there is evidence that comorbid obesity can increase the risk for depressive symptoms (Silverstein et al., 2015). Taken together, there are a variety of individual factors that increase the risk for depression in youth with T1D. Longitudinal studies using diverse samples of youth with T1D across age, SES, and race will further clarify the differences in depressive symptoms across various populations.

A handful of studies reveal positive correlations between depressive symptoms and glycemic control, as measured by hemoglobin A1c in youth with T1D. For example, a 1% increase in A1c is associated with significantly increased probability of experiencing a clinically elevated depressive episode (Hassan, Loar, Anderson, & Heptulla, 2006). Moreover, elevated depressive symptoms are significantly associated with higher A1c values 1–2 years after endorsing such symptoms (Helgeson, Siminerio, Escobar, & Becker, 2009; Whittemore et al., 2002). Another study demonstrated that an increase in depressive symptoms is associated with an increase in A1c and that this association between mood and glycemic control is moderated by adherence to blood glucose monitoring; i.e., if youth check blood sugars, depressive symptoms are not associated with A1c (Hood, Rausch, & Dolan, 2011; McGrady et al., 2009). These studies suggest that the relationship between depressive symptoms and glycemic control may be bidirectional. More research using longitudinal, prospective data could identify the mechanisms that link depressive symptoms and A1c. Future research may also identify additional factors that influence this link, including familial and social factors.

Depressive symptoms in youth with T1D do not appear to resolve as children mature into adults. The maintenance of depressive symptoms over time may be explained by the social pressures placed on adolescents as they age. Emerging adults (i.e., individuals between age 18 and 29 years of age) face many challenges as they negotiate the change in roles from living with parents to living on their own and becoming increasingly self-reliant. This period of development is characterized by economic and relational instability, identity exploration, and feeling “in-between” the stages of adolescence and adulthood (Arnett, Žukauskienė, & Sugimura, 2014; Shulman & Connolly, 2013). Many emerging adults also endorse inadequate levels of social support (Arnett et al., 2014). In considering the unique challenges associated with emerging adulthood, managing medical concerns like diabetes that often involve social stigma may cause further emotional disturbance and stress.

Emerging adults with diabetes have the added pressures of learning the many practical skills of living with diabetes, including finding an adult endocrine provider, attending appointments regularly, navigating the channels of insurance practices, obtaining insulin and other necessary diabetes supplies, administering insulin, and monitoring blood glucose levels while meeting all of the other demands of early adulthood. In a study by Hislop, Fegan, Schlaeppi, Duck, and Yeap (2008), approximately one-third of emerging adults with T1D reported clinically significant depressive symptoms, and nearly one-quarter demonstrated severe depression. For these depressed emerging adults, mean A1c values were significantly higher than their non-depressed counterparts. One study found that diabetes-related medical complications in adults were associated with depressive symptoms, and as the number of medical complications increased, depressive severity increased as well (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001).

Family Factors Associated with Depression in Type 1 Diabetes

A social ecological framework highlights the influence of the family system on depressive symptomatology in youth with T1D. When children are young, parents are primarily responsible for all aspects of diabetes management. As children mature, they begin to assume more responsibilities for diabetes but typically still require parental support. For example, research suggests that adolescents who experience ongoing support with diabetes management from their caregivers have better diabetes adherence via more frequent blood glucose monitoring (Vesco et al., 2010). Moreover, research shows that family communication and problem-solving abilities are associated with either the development of or protection from depressive symptoms in youth with diabetes. In a study of 102 adolescents with T1D, Grey et al. (2002) found that depressive symptom severity was associated with lower family adaptability, lower family cohesion, and less warm and caring diabetes-related family behaviors. Additionally, Wu and colleagues found that increased adolescent depressive symptoms are associated with decreased parental involvement with diabetes care (Wu, Hilliard, Rausch, Dolan, & Hood, 2013).

Furthermore, data suggest that parental psychological distress is associated with suboptimal family functioning. Maternal depression is significantly associated with lower child quality of life and maladaptive family function (Jaser, Whittemore, Ambrosino, Lindemann, & Grey, 2008). In a study conducted by Cunningham, Vesco, Dolan, and Hood (2011), caregiver symptoms of depression and anxiety were independently associated with youth glycemic control. Parental diabetes-specific burden (i.e., feeling overwhelmed by task management) impacted both of these relationships, although the link was stronger between parent depressive symptoms and youth glycemic control. Maternal depression appears to increase the risk of inpatient admissions due to diabetic ketoacidosis or intractable hypo−/hyperglycemia (Butwicka, Zalepa, Fendler, Szadkowska, & Mlynarski, 2013).

In summary, depression is more prevalent in youth with T1D than in youth without T1D, particularly for girls, for racial minorities, and for youth originating from lower socioeconomic backgrounds. In recent studies, rates of depressive symptoms and depression have been falling although there is no clear understanding of what may cause depression at any given point of the course of T1D. Future research should identify how medical aspects and events related to T1D influence depressive course, how role negotiation and identity formation impact T1D and depression during emerging adulthood, and family factors associated with the etiology of depression.

Diabetes-Specific Emotional Distress in Type 1 Diabetes

As discussed above, depressive symptoms are prevalent in T1D, but not all youth experience such symptoms; however, many youth with T1D experience emotional distress related to the daily burden of living with diabetes (Hagger, Hendrieckx, Sturt, Skinner, & Speight, 2016). The emotional reactions to the daily burdens of diabetes management are known as *diabetes-specific emotional distress* and refer to non-pathological worries, concerns, and fears specific to living with diabetes (Fisher et al., 2010; Fisher, Gonzalez, & Polonsky, 2014). Recent literature highlights differences between diabetes distress and depression. As Fisher et al. (2014) discuss, clinical depression is not explicitly related to a precipitant or stressor, and a diagnosis is given when the required number of symptoms is present for a specified duration. In a study of adults with T1D, over 90% of individuals reporting high levels of depressive symptoms also demonstrated high levels of diabetes-specific emotional distress. When individuals with high depressive symptomatology were evaluated via a structured diagnostic interview, the number of individuals with diagnosable depression dropped significantly (Fisher et al., 2016).

Diabetes distress is more closely associated with glycemic control than clinical depression, and depression is more strongly associated with general life stressors, diabetes complications, and lower educational level than diabetes-related emotional distress. Careful consideration of the differences between depression and diabetes distress is important, since the two constructs are separate but related. For example, Fisher et al. (2014) state that individuals presenting with high diabetes distress will likely benefit from education and problem-solving around diabetes challenges, whereas people experiencing clinical depression may need a higher level of intervention such as cognitive behavioral therapy or medication.

Hagger et al. (2016) recently published a systematic review examining correlates of diabetes-specific emotional distress among adolescents with T1D. Approximately one-third of adolescents with T1D endorse diabetes-specific emotional distress (Hagger et al., 2016). The majority of the studies reviewed by Hagger et al. (2016) reveal small-to-moderate associations between distress and glycemic control, and three out of five studies showed no association between diabetes-specific emotional distress and adherence. It is possible that individuals react differently to diabetes-specific distress, such that some individuals may engage in more diabetes monitoring in response to distress, whereas others may engage in avoidant behaviors that decrease adherence. In Hagger and colleagues' review, there were strong correlations (r's ranging from 0.53 to 0.76) between distress and depression among the reviewed studies suggesting that distress and depression are interrelated (Boland, Grey, Mezger, & Tamborlane, 1999; Weissberg-Benchell & Antisdel-Lomaglio, 2011).

Family Factors Associated with Diabetes Distress in Type 1 Diabetes

Similar to its influence on depressive symptoms, family factors also play a role in the development of diabetes-specific distress in youth with T1D. Research suggests that diabetes-specific emotional distress is associated with negative family functioning (Singh, Farruggia, & Peterson, 2013; Weissberg-Benchell & Antisdel-Lomaglio, 2011). When caregivers disagree on their child's diabetes management, diabetes-specific conflict within the home is elevated. Specifically, when fathers are less involved or do not communicate with mothers, the association between caregiver discrepancies regarding diabetes management and glycemic control is higher (Sood et al., 2012). In addition to caregiver discrepancies, when youth with T1D and their parents disagree on who completes diabetes tasks and how often, they are more likely to experience family conflict (Miller & Drotar, 2003) and worse glycemic control (Anderson, Auslander, Jung, Miller, & Santiago, 1990; Butner et al., 2009). Additionally, parental nagging, criticism, and coercion are associated with worse adherence in adolescents with diabetes (Duke et al., 2008; Patton, Dolan, & Powers, 2006).

The theoretical model of miscarried helping (Anderson & Coyne, 1991) offers one way of understanding the relationship between diabetes-specific emotional distress and family functioning. Specifically, when a parent is worried and concerned about their child's health and well-being, they may express that concern in a manner that is not perceived by their child as supportive or helpful. In particular, their concerns may be perceived as nagging, intrusive, or judgmental. The youth may then feel blamed or criticized for less than optimal diabetes outcomes (e.g., higher blood glucose levels than expected). As a result, youth may decrease their communication and collaboration with their parent in an effort to avoid negative feelings and interactions. Parents may respond to this decrease in communication and collaboration by increasing their attempts at expressing worry and concern, which may then be perceived as even more intrusive by their child. Eventually, both parent and youth are frustrated, concerned, and possibly demoralized, leading to an ongoing cycle of missed opportunities for collaboration and problem-solving. Understanding the normative nature of this cycle, which occurs because parents are worried about their children's health, may help diabetes providers offer effective support and guidance to families who are struggling with such interactions.

There is evidence to suggest that positive family interactions are associated with better diabetes-related quality of life and psychological functioning in youth with T1D. For example, Faulkner and Chang (2007) revealed that youth who perceive higher levels of family warmth and caring endorse a lower impact of their diabetes on daily living, fewer worries about diabetes, higher levels of diabetes self-care behaviors, and higher quality of life. Similarly, higher family social support is also related to higher diabetes-related quality of life in adolescents with T1D (Pereira, Berg-Cross, Almeida, & Machado, 2008). One longitudinal study found that when youth with T1D perceived high levels of diabetes-related family and social support, they endorsed higher levels of positive well-being 6 months later (Skinner, John, & Hampson, 2000).

In addition to family functioning, parenting style may also influence overall well-being in youth with T1D and their parents. For example, Jaser and Grey (2010) found that child-centered parenting (i.e., high awareness and attention to a child's needs, emotions, interests, and abilities) and positive reinforcement were associated with better quality of life and lower depressive symptoms in adolescents with T1D. Additionally, Monaghan and colleagues found that parents who have a more authoritative parenting style (i.e., showing high levels of warmth and setting consistent limits with reasonable expectations) have lower levels of stress related to parenting a child with T1D (Monaghan, Horn, Alvarez, Cogen, & Streisand, 2012).

Positive family functioning can also influence diabetes behaviors and health outcomes. Wiebe et al. (2005) found that children with T1D who perceived their mothers to be collaborative when responding to diabetes problems (e.g., extreme high or low blood glucose levels) had better adherence and glycemic control. Similarly, Wysocki et al. (2009) found that when caregivers engaged in collaborative diabetes involvement, youth with T1D had significantly lower A1c levels, better adherence, higher levels of diabetes-related quality of life, and lower levels of depressive symptoms. Furthermore, when both the primary and secondary caregivers had high levels of collaborative involvement in their child's diabetes management, youth had significantly lower A1c values, and the parents subsumed significantly higher levels of responsibility for the child's diabetes management (Wysocki et al., 2009).

Overall, there is research evidence to suggest that positive and negative aspects of family functioning are associated with distress levels and quality of life in youth with T1D and their parents. Furthermore, there is a relationship between family functioning and diabetes health outcomes in youth. More research using longitudinal, prospective data can identify the ways in which family functioning might predict or influence the development of diabetes distress and diabetes health outcomes in youth with T1D.

Treatment Interventions for Depression and Distress in Type 1 Diabetes

There are individual, group, and family-based interventions that positively impact psychological and health outcomes for youth with T1D. However, interventions targeting depressive symptoms specifically are limited. Cognitive behavioral therapy can be effective in reducing depressive symptoms in adolescents with type 1 diabetes. McGrady and Hood (2013) conducted a pilot study of the effectiveness of a manualized cognitive behavioral therapy (CBT) intervention for adolescents with T1D. They found that individuals who participated in the intervention endorsed a significant reduction in depressive symptoms and improvements in diabetes management. Another group conducted a pilot study for a group-based CBT intervention with Puerto Rican adolescents with T1D and found that individuals who participated endorsed reductions in depressive symptoms, anxious symptoms, and hopelessness, as well as improvements in their self-concept and self-efficacy in managing diabetes (Rosselló & Jiménez-Chafey, 2006).

There are psychological/behavioral interventions that train youth in assertiveness, problem-solving, and stress management that positively influence diabetes outcomes and quality of life. For example, coping skills training (CST) consists of six small-group sessions to help youth cope with their lives in the context of diabetes management. Skills include social problem-solving, cognitive behavior modification, and conflict resolution through the use of role-plays and feedback from therapists (Grey, Boland, Davidson, Li, & Tamborlane, 2000). Grey and colleagues found that adolescents who received CST showed greater improvements in glycemic control, quality of life, and the use of assertiveness skills 12 months later compared to a control group that did not receive CST (Grey et al., 2000). Grey and colleagues also conducted a multi-side randomized study to investigate the effectiveness of an Internet-based version of CST called TeenCope. Adolescents with T1D either completed the TeenCope program or an Internet-based diabetes education program. After 12 months, participants could then choose to participate in the program that was not initially assigned to them. Those completing both programs showed improvements in glycemic control (as measured by A1c), quality of life, social acceptance, and self-efficacy, as well as lower perceived stress and diabetes-related family conflict at the 18-month follow-up compared to youth who competed only TeenCope or only diabetes education (Grey et al., 2013). Grey et al. (2009) also evaluated a group-based version of CST for younger children and their parents (children and parents received CST separately) and compared them to joint parent-child group-based diabetes education sessions. They found that youth in both groups showed improvements in quality of life, depressive symptoms, coping with diabetes, and better diabetes self-efficacy. The authors suggest that the general social support received from group-based intervention may serve as a mediator for treatment.

Family-based interventions that focus on collaborative problem-solving and communication between youth with T1D and their caregivers also lead to positive psychosocial outcomes. Behavioral family systems therapy for diabetes (BFST-D) is one of the most extensively researched family-based interventions for youth with T1D. BFST-D consists of four different components that cover problem-solving training, communication skills training, cognitive restructuring, and family roles and responsibilities as they relate to diabetes engagement. Studies show that participation in BFST-D leads to reductions in depressive symptoms in youth and improvements in glycemic control, diabetes adherence, and diabetes-related family conflict (Riley et al., 2015; Wysocki et al., 2006, 2007, 2008). BFST-D can also be delivered using Skype, with similar effectiveness as delivering the intervention in person (Harris, Freeman, & Duke, 2015).

In summary, there are individual-, group-, and family-based interventions that contribute to positive psychosocial and diabetes outcomes in youth with T1D. Pilot studies using CBT to target depressive symptoms have shown promising results; however, future studies using larger sample sizes are needed. Additionally, future research should investigate the aspects of existing interventions that are most effective in producing positive change. Furthermore, identification of the potential barriers that influence the feasibility and accessibility of psychosocial interventions for depressed youth with T1D and their families is needed. The positive outcomes associated with both family- and group-based interventions for youth with T1D highlight the importance of incorporating the individual, family, and social spheres of a child's life into treatment.

Anxiety in Type 1 Diabetes

The literature on psychosocial functioning in youth with T1D has primarily examined depression and diabetes-related distress; less is known about anxiety in the context of T1D. Research shows that between 13% and 21.3% of youth with T1D endorse clinically significant anxiety symptoms and approximately 18.4% of youth are diagnosed with an anxiety disorder (Bernstein, Stockwell, Gallagher, Rosenthal, & Soren, 2013; Herzer & Hood, 2009; Silverstein et al., 2015). With regard to gender, there is some evidence that girls endorse higher anxiety levels and more worries about hypoglycemia than boys (Naar-King, Idalski, et al., 2006).

Anxiety in youth with T1D is associated with psychosocial and metabolic outcomes, including worse glycemic control, lower quality of life, and reductions in diabetes self-management behaviors (Garrison, Katon, & Richardson, 2005; Herzer & Hood, 2009;; Herzer, Vesco, Ingerski, Dolan, & Hood, 2011; Naar-King, Idalski, et al., 2006). In a study conducted by Herzer and Hood (2009), higher adolescent anxiety was associated with higher A1c and lower blood glucose monitoring frequency, even when controlling for sociodemographic factors, diabetes illness duration, and depressive symptoms. Naar-King and colleagues (2006) investigated factors associated with adherence in an urban population of predominantly African American youth with T1D from low-income families. They found that adherence was significantly correlated with anxiety and depressive symptoms; however, this association was no longer significant when controlling for depressive symptoms, externalizing symptoms, and sociodemographic variables. The authors found that externalizing symptoms were more closely associated with adherence and A1c than internalizing symptoms, such as anxiety. The differences between Naar-King and colleagues' (2006) findings from those of Herzer and Hood (2009) may be due to the differences in the ethnicity of the study populations. Future research in this area should include racially and economically diverse youth with T1D, as there are likely individual and environmentally based differences that influence anxiety and diabetes management.

Anxiety can also contribute to fears and worries specific to diabetes-related tasks and complications. For example, research shows that trait anxiety (e.g., anxiety that is stable over time and that may predate a diabetes diagnosis) is associated with increased fear and worry about hypoglycemia and with difficulty differentiating between physiological anxiety and symptoms related to high or low blood glucose (Gonder-Frederick et al., 2006; Herzer & Hood, 2009). Youth with higher levels of both state anxiety (e.g., anxiety in response to a stressful or threatening situation) and trait anxiety experienced more frequent hypoglycemic events and were less likely to check their blood glucose (Gonder-Frederick et al., 2006; Herzer & Hood, 2009).

Research also reveals that youth can develop a fear of hypoglycemia due to the potentially severe and life-threatening consequences of low blood glucose. For example, studies show that hypoglycemic episodes can increase an adolescent's general fear of hypoglycemia (Al Hayek, Robert, Braham, Issa, & Al Sabaan, 2015; Herzer & Hood, 2009). Additionally, fear of hypoglycemia is higher when a child has previously lost consciousness during a hypoglycemic episode and/or experienced symptoms of hypoglycemia in front of friends or at school (Al Hayek et al., 2015). Fear of hypoglycemia and the health consequences of severe hypoglycemia are also associated with general measures of anxiety (Al Hayek et al., 2015). Research shows that general anxiety in youth with T1D can increase the likelihood of diabetes-specific hospitalizations (Garrison et al., 2005). Taken together, elevated levels of anxiety are associated with diabetes-specific health events and vice versa. Future research using longitudinal data will be helpful in identifying the temporal relationship between anxiety and diabetes health events in youth with T1D. Early identification of anxiety symptoms in youth may lead to intervention and prevention of poor health outcomes.

While high levels of anxiety are associated with negative health outcomes in youth with T1D, there may be an optimal level of anxiety that increases an individual's attention to their diabetes self-care tasks. The Yerkes-Dodson theory postulates that when a task is difficult or requires low motivation, there is an optimal amount of stress or anxiety for promotion of good performance (Broadhurst, 1959). In the context of diabetes, some anxiety may increase an individual's motivation to engage in diabetes tasks. However, when anxiety is highly elevated, youth with T1D may experience increased distress, impairing their ability to manage their diabetes effectively. Long-standing anxiety can contribute to rumination about diabetes tasks, short- and long-term health consequences, avoidant and maladaptive coping behaviors, a perceived loss of control, feelings of embarrassment, dependence on others, and guilt and frustration (Gonder-Frederick, Nyer, Shepard, Vajda, & Clarke, 2011). More research is needed on the mechanisms that lead to increased anxiety in youth with T1D and on the optimal levels of anxiety that may contribute to adaptive diabetes management.

Family Factors Associated with Anxiety in Type 1 Diabetes

There is limited research on the relationship between family processes such as diabetes-related family conflict and anxiety. Existing studies suggest that parental anxiety and diabetes-related family conflict may influence diabetes outcomes in youth with T1D. For example, higher maternal anxiety is associated with higher A1c and more frequent diabetes-related absenteeism from school and social activities for youth with T1D (Cameron, Young, & Wiebe, 2007). Additionally, increased diabetes-specific family conflict is associated with higher A1c in youth and higher levels of parental anxiety (Williams, Laffel, & Hood, 2009). Herzer et al., (2011) found that anxiety levels impact the relationship between family conflict and A1c. Specifically, when youth anxiety levels are higher, there is a stronger relationship between family conflict and A1c. There may be a bidirectional relationship between anxiety and family conflict, and future studies are necessary to clarify the mechanisms that link anxiety, family conflict, and A1c. It is also necessary to consider the potential influence of caregiver anxiety on diabetes management and health outcomes in youth with T1D. For example, parent trait anxiety significantly correlates with trait anxiety in youth (Gonder-Frederick et al., 2006; Herzer & Hood, 2009). Furthermore, adolescent worries related to the anxiety-inducing aspects of hypoglycemia show moderate associations with parent trait anxiety (Herzer & Hood, 2009). There is likely a bidirectional influence of family/social interactions and individual anxiety impacting diabetes health outcomes. Taken together, these findings imply that it is important to consider multiple individual, social, and ecological risk factors for poor diabetes management including anxiety, depression, behavioral issues, and systemic barriers (e.g., access to health care and treatment). More research is needed on the mechanisms by which family factors interact with and influence anxiety and diabetes outcomes in youth with T1D.

Treatment Interventions for Anxiety in Type 1 Diabetes

There is limited information in the literature regarding interventions for anxiety in youth with T1D. A small study on the effectiveness of a cognitive behavioral intervention for anxiety in youth with T1D revealed that four out of a total of six participants who participated in the intervention had an improvement in anxiety symptoms (Hains, Davies, Parton, & Silverman, 2001). Briery and Rabian (1999) found that participation in a week-long diabetes camp over the summer resulted in improvements in trait anxiety. Further work is necessary to understand interventions for anxiety in the context of T1D.

Depression in Type 2 Diabetes

There is limited research on the prevalence of depression in children and teens with type 2 diabetes (T2D). Youth with T2D manage their diabetes through daily diabetes tasks including checking blood sugars, managing weight with diet and exercise, and taking oral medication and/or daily insulin injections. Similar to youth with T1D, these daily tasks can become burdensome for many youth with T2D and can contribute to diabetes-specific emotional distress and psychological difficulties. Furthermore, youth with T2D often have the burden of managing two chronic health conditions: T2D and obesity (Nadeau & Dabelea, 2008). Additionally, T2D disproportionately impacts youth from ethnic and racial minority backgrounds and those who are socioeconomically disadvantaged (Copeland et al., 2011) and groups that have less access to medical and mental health care (Marrast, Himmelstein, & Woolhandler, 2016; Price, Khubchandani, McKinney, & Braun, 2013; Strickland, Jones, Ghandour, Kogan, & Newacheck, 2011),who are exposed to a higher frequency of stressful life events and are at a higher risk for the development of psychological disorders (Anderson & Mayes, 2010; Reiss, 2013). The daily burden associated with managing T2D as well as the disproportionate percentage of low income and minority youth with T2D highlights the need to better understand the prevalence of mental health difficulties in this vulnerable population as well as the broader cultural and societal impacts on youth with T2D.

Current research findings on depressive symptoms in youth with T2D suggest they endorse higher rates of depressive symptoms compared to their peers without diabetes and when compared to youth with T1D (Hood et al., 2014; Lawrence et al., 2006; Silverstein et al., 2015). As part of the multicenter, national SEARCH study, researchers administered the Center for Epidemiologic Studies Depression Scale (CES-D) to 2266 youth with T1D and 371 youth with T2D and found that males with T2D had higher rates of moderate-to-severe depressive symptoms compared to males with T1D (Lawrence et al., 2006). Females with T1D or T2D and with health comorbidities were at a higher risk for clinically significant depressive symptoms than females without health comorbidities. Older age was also a risk factor for clinically significant depressive symptoms for females with T1D and T2D (Lawrence et al., 2006). Dabelea et al. (2009) found that 21.9% of Navajo youth with T2D who participated in the Navajo SEARCH study endorsed depressive symptoms at a severe level. Furthermore, Silverstein et al. (2015) administered the Children's Depression Inventory short form version to 329 youth with T2D and 261 youth with T1D and found that 22% of participants with T2D endorsed clinically significant depressive symptoms, which was nearly twice as high as the youth with T1D (Silverstein et al., 2015).

Depressive symptoms in youth with T2D can have a detrimental effect on diabetes self-care and glycemic control. Higher depressive symptoms in youth with T1D and T2D are associated with worse glycemic control and a higher frequency of emergency department visits (Lawrence et al., 2006; Silverstein et al., 2015). Katz et al. (2016) examined depressive symptoms and diabetes adherence in the 699 youth with T2D (ages 10–17 years old) who were part of the multicenter clinical trial, the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY), and found that those children with higher depressive symptoms at baseline showed worse adherence to their diabetes over time. This finding is consistent with research on adults with T2D, which has revealed associations between higher depressive symptoms and worse adherence and health outcomes (De Groot et al., 2001; Gross et al., 2005; Lustman et al., 2000; Young-Hyman et al., 2016).

Research within the adult T2D literature suggests that the relationship between depressive symptoms and T2D is bidirectional, such that the presence of a preexisting depressive disorder may be a risk factor for the development of T2D (Brown, Majumdar, Newman, & Johnson, 2005; Musselman, Betan, Larsen, & Phillips, 2003) and/or the development of diabetes and the subsequent burden of living with a chronic illness can contribute to the development of depression. Suglia, Demmer, Wahi, Keyes, and Koenen (2016) investigated the association between depression in adolescents and the later development of T2D in adulthood using data from the Longitudinal Study of Adolescent to Adult Health and found that adolescent girls who reported high levels of depressive symptoms were more likely to develop T2D 13 years later. Additionally, depressive symptoms in children are associated with higher fasting insulin and insulin resistance concurrently and later during their adolescent years (Hannon, Rofey, Lee, & Arslanian, 2013; Jaser, Holl, Jefferson, & Grey, 2009; Shomaker et al., 2010, 2011). Individuals who have a history of depression may be at higher risk for T2D due to changes in unhealthy eating behaviors (which may increase weight) as well as decreased activity levels and reduced exercise (Weissman et al., 1996). Additionally, medications used to treat a preexisting psychiatric condition may also contribute to the development of T2D in youth. Specifically, atypical antipsychotics, which were originally used to treat schizophrenia spectrum disorders in youth (Kumra et al., 2008) but are now used more broadly for children presenting with a variety of mental health concerns including affective disorders (Cooper, Hickson, Fuchs, Arbogast, & Ray, 2004; Zuddas, Zanni, & Usala, 2011), have been found to increase the risk of weight gain and the development of T2D in children (Almandil et al., 2013; Baeza et al., 2017; Galling et al., 2016). Within the adult literature, there is also evidence that some antidepressant medications may increase the risk of developing T2D by contributing to weight gain and higher blood glucose levels (Rubin et al., 2008).

At this time, the biological, behavioral, and intraindividual factors linking depression and T2D in youth are unclear (Tabák, Akbaraly, Batty, & Kivimäki, 2014). Preexisting depression may lead to the development of diabetes through factors associated with depression such as inactivity, unhealthy eating, and weight gain. Children treated with atypical antipsychotic medications for preexisting psychiatric conditions may also be at risk for the development of T2D diabetes due to side effects of the medication such as weight gain and insulin resistance (Almandil et al., 2013; Baeza et al., 2017; Galling et al., 2016). It is also important to consider the daily burden associated with managing a chronic illness such as T2D, which can contribute to the development of emotional distress and depressive symptoms in some youth. More research using longitudinal prospective data is necessary to better understand the link between depression and T2D in children and adolescents. Furthermore, it would be beneficial for pediatricians and primary care providers to screen for depressive symptoms in their patients, especially those who are overweight or identified as having prediabetes. Early detection of depressive symptoms may lead to earlier intervention and prevention of negative health outcomes such as weight gain, insulin resistance, and subsequent diagnosis of T2D. It is also important to regularly screen for depressive symptoms in youth with T2D in order to provide treatment early so as to prevent further emotional distress and negative health outcomes.

Treatment Interventions for Depression in Type 2 Diabetes

There is limited research on psychological interventions for youth with T2D with comorbid depression. There is considerably more research available on the effectiveness of psychological interventions for reducing depressive symptoms and glycemic control in adults with diabetes (Van der Feltz-Cornelis et al., 2010). A meta-analysis by Markowitz, Gonzalez, Wilkinson, and Safren (2011) found support for the use of cognitive behavioral interventions and antidepressants in the reduction of depressive symptoms in adults with T1D and T2D and adolescents with T1D. Their analysis did not include any studies investigating the effectiveness of psychological interventions for youth with T2D. There is some research on depression prevention interventions for youth who are at risk for T2D. For example, Shomaker and colleagues (2016) conducted a randomized controlled, parallel group study in which adolescent girls identified as overweight/obese and endorsing mild-to-moderate depressive symptoms were assigned to participate either in a depression prevention cognitive behavioral program or in a health education control group. They found that adolescents in both groups experienced a decrease in depressive symptoms post-intervention and a reduction in depressive symptoms was associated with improved insulin sensitivity across both groups. These findings suggest that the group atmosphere was the key factor contributing to the improvement in depressive symptoms in this population. It is possible that social support and a sense of shared experience were most beneficial.

In summary, the research available on depression in youth with T2D diabetes suggests that they are at a higher risk for developing depressive symptoms than youth with T1D or youth without diabetes. More research using longitudinal, prospective data is needed to understand the link between depression and T2D. There is a need to assess for depression in youth with T2D and to identify effective interventions to treat it due to the link between depressive symptoms and poor diabetes outcomes. Currently there are no studies examining interventions that specifically target depression in youth with T2D. Clearly, more research is needed on the effectiveness of interventions for youth with T2D. There is research on family-based interventions such as BFST-D for youth with T1D with promising results, including reductions in depressive symptomatology and diabetes-related family conflict and improvements in diabetes outcomes (Riley et al., 2015; Wysocki et al., 2008). Family-based interventions such as this one may also have similarly promising results in youth with T2D. More research is needed to assess psychological and behavioral interventions for youth with T2D for their effectiveness in reducing psychological symptoms and improving adherence, glycemic control, and long-term health outcomes.

Anxiety in Type 2 Diabetes

To the authors' knowledge, there are no published studies on the prevalence of anxiety symptoms and anxiety disorders in youth with T2D. In the adult literature, there is evidence that adults with T2D have higher rates of anxiety disorders than adults without diabetes. Specifically, adults with T2D have higher rates of generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder compared to those without diabetes (Dos Santos et al., 2014; Fisher et al., 2008). One population-based study by Li et al. (2008) found that adults with T2D had a higher prevalence of a lifetime anxiety disorder by 20%, compared to adults without diabetes. Hispanic young adults (ages 18–29) with T2D had higher prevalence rates of anxiety compared to their same aged counterparts without diabetes (Li et al., 2008). Similar to depressive symptoms, there may be a link between anxiety symptoms in individuals with T2D and worse health outcomes. For example, lifetime anxiety and depression in adults with T2D are risk factors for psychopathology, reductions in diabetes self-care behaviors, and worse glycemic control (Whitworth et al., 2016). Naicker et al. (2017) also found that anxiety symptoms in adults with T2D were associated with a higher mortality risk. Given the evidence for increased risk for anxiety symptoms in adults with T2D, more research is needed in order to understand the prevalence of anxiety in children and teens living with T2D and the impact this may have on physical and emotional health. Additionally, further understanding of anxiety at critical points of development particularly from adolescent to emerging adult years within the context of T2D would be beneficial given the societal pressures placed on individuals during this time as discussed earlier in this chapter.

Overall, there is evidence that youth with T2D are at risk for elevated depressive symptoms and may also be at risk for anxiety symptoms, given the increased prevalence of anxiety in adults with T2D. Comorbid depression in youth with T2D and comorbid anxiety in adults with T2D are associated with worse adherence and worse glycemic control (Katz et al., 2016; Lawrence et al., 2006; Silverstein et al., 2015; Whitworth et al., 2016). Anxiety and depression in the general pediatric population appear to negatively affect social, physical, and academic functioning (Jaycox et al., 2009), which can lead to deleterious effects on overall emotional well-being, quality of life, and physical health. Routine and standardized screening for depressive and anxiety symptoms in youth with T2D in diabetes clinic is necessary in order to better understand the prevalence of comorbid anxiety and depression in this population and for the purpose of early detection, intervention, and prevention of negative emotional and physical health outcomes.

Psychosocial Screening for Youth with Diabetes

The American Diabetes Association (ADA) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) recommend regular screening and assessment of depression and anxiety in youth with diabetes (American Diabetes Association, 2017; Delamater et al., 2014, 2018; Young-Hyman et al., 2016). ISPAD guidelines also recommend that providers assess family-related factors such as diabetes-specific family conflict and stressors as well as diabetes-specific communication, parental monitoring, and responsibility for diabetes tasks. Assessment of these factors is especially appropriate for those families experiencing significant stress, adjustment concerns, or who present with language or cultural barriers. Given the evidence that T2D disproportionately affects youth from ethnic/minority and lower socioeconomic backgrounds, it may be particularly helpful to assess for the stressors and barriers that contribute to psychopathology and poor health outcomes in these populations.

There are a handful of studies that have documented the implementation of psychological screening protocols for youth with T1D at routine diabetes visits; however, the research on screening in youth with T2D is sparse. The majority of studies on screening in youth with T1D have demonstrated both the feasibility and clinical utility of routine screening (Boogerd et al., 2015; Corathers et al., 2013; Hilliard, Herzer, Dolan, & Hood, 2011; Schwartz, Cline, Axelrad, & Anderson, 2011; Zenlea et al., 2014). One study by Silverstein et al. (2015) examined results of depression screening in youth with T1D and T2D using the Children's Depression Inventory across eight pediatric diabetes clinics and found higher rates of depression in youth with T2D than T1D; however, the study did not discuss how the screeners were administered in the clinics or their overall feasibility, acceptability, and clinical utility. Given the increased risk for depression in youth T2D, the associations between depression and diabetes health outcomes, and the high rates of T2D in youth coming from vulnerable and disadvantaged populations, regular screening in this population is imperative. Regular screening is useful for early identification of psychological symptoms, appropriate intervention (e.g., referral to a mental health provider), and ultimately the prevention of worsening psychopathology and/or poor diabetes outcomes.

Conclusion

Depressive symptoms, diabetes-specific emotional distress, and symptoms of anxiety appear to be common among children and adolescents with diabetes. Therefore, routine psychosocial screening and appropriate follow-up are necessary to identify those who may be struggling, in order to provide appropriate support and treatment. Ultimately, having dedicated mental health professions integrated within diabetes teams on a full-time basis would best serve this need and guarantee that all youth with diabetes are receiving interdisciplinary care. It is also important that diabetes care providers consider the family and social environments in which children live and manage the daily diabetes tasks.

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Chapter 6
Eating Disorders in Youth with Diabetes

Karishma A. Datye and Sarah S. Jaser

Introduction

Youth with diabetes are at a significantly increased risk for eating disorders and their associated morbidity and mortality compared to the general youth population (Colton, Olmsted, Daneman, et al., 2015; Jones, Lawson, Daneman, Olmsted, & Rodin, 2000). Therefore, it is critical for providers to understand the complexities in diagnosing and treating youth with diabetes and coexisting eating disorders. In the general population, eating disorders are most commonly diagnosed in youth, with current estimates of the prevalence of anorexia nervosa in young females of 0.3% and prevalence of bulimia nervosa in young females of 1% (Hoek, 2006). While eating disorders have been predominantly reported and researched in White females, the gender and ethnicity gap may be closing. A recent national sample of US youth found equal lifetime prevalence of anorexia nervosa in males and females and higher lifetime prevalence of bulimia nervosa in Hispanic youth than non-Hispanic White youth (Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011). The prevalence of eating disordered behaviors is even higher than diagnosed disorders: the Centers for Disease Control and Prevention's study of Youth Risk Behaviors found that 10.6% of high school students reported that they did not eat for 24 hours or more to lose weight, 5% took diet aids without a doctor's advice, and 4% vomited or used laxatives to keep from gaining weight (Eaton et al., 2010). Thus, while behaviors that meet criteria for diagnosis of eating disorders are fairly rare in the general population, disordered eating behaviors are quite common and, as we will highlight, are even more common in youth with diabetes.

It is important to consider eating disorders and disordered eating behaviors in the context of diabetes, as the incidence of these problems in youth with diabetes is much higher than the general population (Colton, Olmsted, Daneman, et al., 2015). For example, a European study of youth with type 1 diabetes found that 28% of females and 9% of males reported disturbed eating behaviors at a level that warranted additional investigation by a clinician (Wisting, Froisland, Skrivarhaug, Dahl-Jorgensen, & Ro, 2013). Notably, youth with type 2 diabetes are also at increased risk for eating disorders; in the large multi-site TODAY study, a quarter of youth with type 2 diabetes reported binge eating behaviors (Wilfley et al., 2011).

Given the high prevalence of these disorders and the serious clinical sequelae reported in this population, providers need to be aware of the current literature to guide clinical practice. Thus,

K. A. Datye · S. S. Jaser (✉)
Ian M. Burr Division of Pediatric Endocrinology and Diabetes, Vanderbilt University Medical Center, Nashville, TN, USA
e-mail: sarah.jaser@vumc.org

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Table 6.1 Description of DSM-5 criteria for feeding and eating disorders seen more commonly in youth with diabetes

DSM-5 diagnosis (American Psychiatric Association, 2013)	Description
Anorexia nervosa	Failure to meet energy requirements, exhibited through considerably low body weight. Concomitant disturbance in body image and fear of weight gain
Bulimia nervosa	Repeated binge eating (eating more than most people would in a short period of time) with loss of control of eating, accompanied by behaviors intended to stop weight gain. Behavior occurs weekly, for 3 months (on average)
Binge eating disorder	Repeated binge eating behaviors with loss of control (as above), without the above behaviors intended to stop weight gain

the purpose of this chapter is to provide an overview of eating disorders in youth with diabetes and to focus specifically on type 1 and type 2 diabetes, ongoing research in these areas, and recommendations for providers.

Feeding and Eating Disorders in the DSM-5

The most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) has updated the "Feeding and Eating Disorders" section to better classify and diagnose patients with these disorders (American Psychiatric Association, 2013). Previously (DSM IV), patients were diagnosed with "eating disorder not otherwise specified (EDNOS)" when they did not meet the full criteria for anorexia nervosa or bulimia. This category ultimately was a "catch all" for several different diagnoses and was less clinically useful in terms of understanding the needs of a particular patient. Further, the variety of patients given this diagnosis made meaningful research on these disorders difficult (Call, Walsh, & Attia, 2013).

The DSM-5 section on feeding and eating disorders specifies formal diagnostic criteria for the following disorders: pica, rumination disorder, avoidant/restrictive food intake disorder, anorexia nervosa, bulimia nervosa, binge eating disorder, other specified feeding or eating disorder, and unspecified feeding or eating disorder (American Psychiatric Association, 2013). One significant change in the DSM-5 is the formal diagnosis of binge eating disorder, which had previously been classified under EDNOS. Additionally, several changes were made to the diagnostic criteria of anorexia nervosa and bulimia nervosa, allowing for more specificity in patients being diagnosed with one of these disorders, rather than EDNOS. Table 6.1 summarizes the eating disorders characterized in the DSM-5 that are seen most frequently in youth with diabetes.

While there are no specific diagnostic criteria to aid clinicians in diagnosing eating disorders in youth with diabetes, the DSM-5 explicitly states that patients with diabetes on insulin therapy may use their medications inappropriately to aid in weight loss goals. Specifically, the DSM-5 notes that patients with anorexia nervosa and diabetes may purposefully alter insulin doses to decrease weight gain or promote weight loss and patients with bulimia nervosa may exhibit similar behaviors during binge eating episodes (American Psychiatric Association, 2013). It is important, therefore, for clinicians to understand that these youth are at higher risk for eating disorders than the general population and to monitor weight, linear growth, and adherence to therapy carefully.

Diabetes in Youth

Diabetes is one of the most common chronic pediatric conditions, and given its rising prevalence in the pediatric population (Dabelea et al., 2014), it is important for both general pediatricians and endocrinologists to understand the increased risk of eating disorders in this population. Importantly, patients with different types of diabetes may be at increased risk for specific types of eating disorders. Therefore, classifying a patient's diabetes appropriately may aid providers in understanding the specific types of eating disorders and disordered eating behaviors for which they may be at risk.

A national population-based study of youth with diabetes (SEARCH) found that in 2009, over 190,000 youth had been diagnosed with diabetes in the United States (Pettitt et al., 2014). Type 1 and type 2 diabetes characterize nearly 98% of patients in the SEARCH cohort (Pettitt et al., 2014). Other types of diabetes (e.g., monogenic diabetes, transplant-related diabetes, cystic fibrosis-related diabetes) are seen in a very small minority of youth with diabetes; therefore, the focus of this chapter will be on eating disorders in youth with type 1 and type 2 diabetes. The next two sections focus on type 1 and type 2 diabetes separately and review the eating disorders seen in each type of diabetes.

Type 1 Diabetes and Feeding and Eating Disorders

Type 1 diabetes is an immune-mediated disorder causing destruction of the pancreatic insulin-producing beta cell and ultimately leading to an insulin deficiency (American Diabetes Association, 2018). In the SEARCH data, 87% of youth had a diagnosis of type 1 diabetes. Type 1 diabetes can be diagnosed in youth and adults; however, three-quarters of cases are diagnosed in children under 18, with 2 peaks of diagnosis between ages 5 and 7 and around the time of puberty (American Diabetes Association, 2018; Sperling, 2014). Therefore, by the time patients become young adults, they may have been living with type 1 diabetes for the majority of their lives. While classic symptoms of new-onset diabetes include weight loss, increased urination, and increased thirst and hunger (Sperling, 2014), it is important to note that the percentage of youth with type 1 diabetes who are overweight or obese is now similar to that of the general population (Minges, Whittemore, & Grey, 2013).

Prior to the discovery of insulin in the 1920s, type 1 diabetes was a fatal disease (Roth et al., 2012); however, the discovery of insulin, the development of insulin analogs (Vajo & Duckworth, 2000), and evidence from the landmark Diabetes Control and Complications Trial (DCCT) (DCCT Group, 1993) advanced the treatment of type 1 diabetes, demonstrating that tight glycemic control reduced the complications related to type 1 diabetes. The intensive treatment regimen recommended for type 1 diabetes involves checking blood sugars several times per day, counting carbohydrates, and, most importantly, giving basal, meal, and correction insulin (American Diabetes Association, 2018). While patients are encouraged to eat a healthy diet similar to their peers without diabetes, they are also counseled on how carbohydrates are metabolized in patients with diabetes and what healthy carbohydrate consumption means (American Diabetes Association, 2018).

Several aspects of the diagnosis and treatment of type 1 diabetes, such as counting carbohydrates, focus on food, and insulin administration, may increase patients' risk for developing an eating disorder. First, counting carbohydrates and close attention to carbohydrate intake during meals are tasks relatively unique to patients with diabetes, and this intense focus on food from the time of diagnosis may place patients with type 1 diabetes at an increased risk of eating disorders. Additionally, patients are educated early in their diagnosis that carbohydrates are not metabolized properly without insulin, and often patients who present with new type 1 diabetes have lost a significant amount of weight that is typically regained after starting insulin therapy. Finally, patients with type 1 diabetes may intentionally manipulate or withhold insulin doses to promote weight loss or decrease weight gain, a phenomenon called "diabulimia" (Colton, Olmsted, Daneman, et al., 2015; Jones et al., 2000; Mathieu, 2008). While eating disorders are seen in patients with and without type 1 diabetes, patients with type 1 diabetes may be at increased risk of eating disorders due to their unique treatment plan regarding food composition and intake and dependence on insulin.

Several studies have shown an increased risk of eating disorders in youth with type 1 diabetes as compared to their peers without diabetes. For example, Jones and colleagues found in a cross-sectional study that girls with type 1 diabetes age 12–19 years of age had an increased risk of a DSM-IV eating disorders (OR 2.4) and specifically had an increased risk of bulimia nervosa, eating disorders not otherwise specified, and subthreshold eating disorders (Jones et al., 2000). In this study, participants with eating disorders, with subthreshold eating disorders, and with non-disordered eating, *all* reported insulin manipulation: 42% in the participants with eating disorders, compared to 18% and 6% in the other groups, respectively (Jones et al., 2000). This cross-sectional study demonstrates not only the increased risk of eating disorders in youth with diabetes but also that the misuse of insulin to aid in weight loss goals is relatively common.

While the cross-sectional study described above provides evidence for an increased risk of eating disorders in youth with type 1 diabetes, more recent longitudinal studies have confirmed this finding. A prospective study by Colton and colleagues found a high incidence of disturbed eating behavior and eating disorders in young females with type 1 diabetes over 14 years (Colton, Olmsted, Daneman, et al., 2015). The authors enrolled 126 participants (girls between 9 and 13 years of age) and interviewed participants at baseline and at six additional time points throughout the study (last time point 10–14 years after baseline). The authors found that the mean age of onset of disturbed eating behavior was 18.3 years and mean age of developing an eating disorder was 22.6 years (Colton, Olmsted, Daneman, et al., 2015). Although there was significant attrition (56% participation at the last time point) during the 14-year study period, the authors reported that, after accounting for loss to follow-up, the chance of developing an eating disorder during the study was 60% and the chance of developing disturbed eating behavior was 79%. Several different disturbed eating behaviors were reported, but during the final interview, Colton and colleagues found that 27% of participants reported omitting insulin to aid in weight control (Colton, Olmsted, Daneman, et al., 2015). Results from this longitudinal study further support the increased risk of disordered eating in youth with type 1 diabetes.

While patients with type 1 diabetes are at increased risk of eating disorders, characterizing the type of eating disorders for which patients are at greatest risk has been challenging. The study by Colton and colleagues (above) demonstrated that participants were diagnosed with anorexia nervosa, bulimia nervosa, eating disorder not otherwise specified, and subthreshold eating disorder; however, there was no comparison to healthy control subjects (Colton, Olmsted, Daneman, et al., 2015). Results from a meta-analysis (Mannucci et al., 2005) found that patients with type 1 diabetes are at increased risk of bulimia nervosa but not anorexia nervosa (notably, the meta-analysis did not include diagnoses of EDNOS), and Jones and colleagues demonstrated an increased risk of bulimia nervosa, EDNOS, and subthreshold eating disorders (Jones et al., 2000). However, the recent updates to the DSM-5 allow for better classification of eating disorders, and it is therefore possible that patients previously diagnosed with EDNOS will increasingly be diagnosed with anorexia nervosa, bulimia nervosa, or binge eating disorder.

It may also be important to study gender differences in disordered eating behavior in youth with diabetes. For example, a small study of disordered eating behavior in youth with type 1 diabetes ($n = 50$) found some gender differences in behaviors – while both genders reported concerns with weight, body shape, and overexercising, only females also reported binging behaviors (Wilson, Smith, Coker, Hobbis, & Acerini, 2015). There are limited data on gender differences in youth with diabetes and disordered eating behaviors; additional research is necessary to characterize the eating disorders diagnosed in patients with type 1 diabetes and to understand the gender differences that may exist.

Eating disorders in otherwise healthy populations are associated with increased morbidity and mortality (Arcelus, Mitchell, Wales, & Nielsen, 2011), but patients with type 1 diabetes are at further risk for diabetes-related health complications, making eating disorders especially concerning in this population. Several studies have demonstrated that patients with type 1 diabetes and eating disorders or disordered eating behaviors have worse glycemic control (as defined by hemoglobin A1c) than patients with type 1 diabetes without an eating disorder (Jones et al., 2000; Rydall, Rodin, Olmsted, Devenyi, & Daneman, 1997; Scheuing et al., 2014). Additionally, Scheuing and colleagues found significantly higher rates of severe hypoglycemia in patients with type 1 diabetes and eating disorders, higher frequency of diabetic ketoacidosis, and increased risk of retinopathy in patients with type 1 diabetes and bulimia nervosa (Scheuing et al., 2014). Similarly, Rydall and colleagues showed that patients with type 1 diabetes and highly disordered eating not only had significantly higher rates of retinopathy, but that disordered eating contributed more strongly to the model predicting retinopathy than other risk factors (such as duration of diabetes and hemoglobin A1c itself) (Rydall et al., 1997).

Given that patients with poor metabolic glycemic control are at increased risk for macrovascular and microvascular disease (monitored through blood pressure, albuminuria screening, lipid profile, and retinal exams) (DCCT Research Group, 1994), it is also concerning that patients with type 1 diabetes and eating disorders have worse glycemic control than patients with type 1 diabetes without eating disorders. Prospective longitudinal studies are needed to further describe the increased morbidity and mortality seen in patients with type 1 diabetes and eating disorders; however, the existing data strongly suggest that these patients have worse glycemic control and increased risk for retinopathy.

Given the incidence of disordered eating behavior in youth with type 1 diabetes, and the morbidity associated with eating disorders noted above, it is important for clinicians to diagnose disordered eating behaviors in their patients. Screening tools used in youth without diabetes may not effectively screen youth with diabetes given circumstances unique to type 1 diabetes (e.g., close attention to diet, ability to manipulate insulin for weight loss). To address this issue, Markowitz and colleagues validated a disordered eating screening tool in youth with type 1 diabetes (Markowitz et al., 2010) and found that the tool could be completed relatively quickly (less than 10 minutes) and was therefore appropriate for use in clinical settings. In a separate study, Colton and colleagues demonstrated that depressive symptoms and disordered eating behaviors are often seen concurrently (Colton, Olmsted, Daneman, & Rodin, 2013); therefore clinicians should consider screening for disordered eating behaviors in patients that report depressive symptoms (and conversely should consider screening for depressive symptoms in patients with disordered eating behaviors). Additionally, clinicians should consider screening for eating disorders when patients have rapid weight loss, worsening/poor glycemic control, and poor adherence to therapy. Implementing screening will necessitate treatment plans for previously unidentified eating disordered behaviors. In the next section, we review the recommended treatments for this population.

Treatments for Eating Disorders in Type 1 Diabetes

While there are limited studies regarding effective treatments for patients with eating disorders and type 1 diabetes, a recent review article discussed some important points that must be considered when starting treatment (Goebel-Fabbri, 2009). Patients should be treated with a multidisciplinary team including (but not limited to) an endocrinologist, mental health provider, nutritionist, and nurse. Additionally, patients should be counseled that if they have been withholding insulin to aid in weight loss, they may experience weight gain, hypoglycemia, and other symptoms as insulin administration increases. This point is key, as patients may become frustrated as they gain weight after increasing their insulin doses. Finally, the diabetes treatment team needs to set reasonable goals for the patient as they resume their appropriate insulin regimen as setting goals for tight glycemic control may not be feasible.

While there are no large clinical trials studying patients with type 1 diabetes and coexisting eating disorders, Dickens and colleagues examined glycemic and psychological outcomes in multidisciplinary residential treatment in women with type 1 diabetes and coexisting eating disorders (Dickens, Haynos, Nunnemaker, Platka-Bird, & Dolores, 2015). This study retrospectively reviewed glycemic control and psychological symptoms in 29 women admitted to a multidisciplinary residential treatment facility. The treatment goals included improving skills to manage thoughts of disordered eating that may affect diabetes management. The authors found an improvement in glycemic control and improvement in the eating disorder inventories used to assess their treatment. Although this was not a randomized clinical trial, the data are promising and suggest a treatment option for these patients.

Another retrospective study examined "day hospitalization" for patients with type 1 diabetes and eating disorders using cognitive behavioral therapy principles (Colton, Olmsted, Wong, & Rodin, 2015). The program was available to patients with and without diabetes, and 37 patients with type 1 diabetes were retrospectively identified who attended the day hospital treatment. Interestingly, only 53% of patients diagnosed with an eating disorder and type 1 diabetes attended day hospital treatment. Of those that completed 4 or more weeks of treatment, 6 had a "good outcome," 14 had an "intermediate outcome," and 12 had "poor outcome" (referring to improvement in BMI and resolution of specific disordered eating behaviors), with better outcomes seen in patients without diabetes (Colton, Olmsted, Wong, & Rodin, 2015). It is unclear why so many patients with type 1 diabetes and eating disorders may have opted not to participate in day hospitalization and why treatment outcomes were better in individuals without diabetes compared to those with diabetes.

Clearly, patients with type 1 diabetes are at risk for disordered eating behaviors, and these behaviors put them at risk for worsening control of their diabetes (and diabetes-related comorbidities). While some therapeutic options are available for patients with type 1 diabetes and eating disorders, additional research is needed to learn the best treatment for these patients.

Type 2 Diabetes and Feeding and Eating Disorders

Type 2 diabetes is characterized by insulin resistance and inability to release adequate insulin to overcome this resistance, ultimately leading to hyperglycemia (Sperling, 2014). The insulin resistance seen in type 2 diabetes is typically due to obesity, while insufficient insulin release is likely related to genetic factors (which is an active area of investigation) (Sperling, 2014). Although type 2 diabetes affects a smaller percentage of youth (11% of youth with diabetes in the SEARCH cohort), rates of type 2 diabetes are rising with the increase in obesity in youth (Pettitt et al., 2014). The mean age of onset of type 2 diabetes in the SEARCH cohort was 13.7 years (Pettitt et al., 2014). Additionally, the racial/ethnic distribution of type 2 diabetes differs from type 1 diabetes; the highest prevalence of type 2 diabetes was noted in Native American and black youth, while the highest prevalence of type 1 diabetes was noted in non-Hispanic white youth (Pettitt et al., 2014).

The treatment for type 2 diabetes varies by the severity of diabetes. In youth with type 2 diabetes and mild hyperglycemia, the first-line treatment is metformin (oral medication) coupled with lifestyle changes. Metformin decreases glucose made by the liver and increases insulin sensitivity (Sperling, 2014). Although several other oral medications can be used to treat type 2 diabetes, metformin is the only oral agent that is FDA-approved to treat children with type 2 diabetes. Patients with more poorly controlled diabetes (evidenced by significant hyperglycemia or hemoglobin A1c over 8–9%) are treated with insulin, in addition to oral therapy with metformin and lifestyle interventions. Patients with type 2 diabetes who are treated with insulin therapy must also learn to check blood sugars, count carbohydrates, and administer basal and meal insulin, and the treatment then becomes similar to patients with type 1 diabetes (American Diabetes Association, 2018).

The American Diabetes Association (ADA) recommends the same glycemic goals for type 1 and type 2 diabetes in youth and states that a multidisciplinary team is needed to help patients achieve these goals (as in type 1 diabetes) (American Diabetes Assocation, 2018). However, the ADA further recommends that patients with type 2 diabetes also work toward lifestyle modifications, noting that patients and their families should exercise, eat a healthy diet, and target a healthy weight (American Diabetes Association, 2018). While specific dietary recommendations vary from patient to patient, the ADA recommends, at minimum, that diabetes educators and other providers discuss healthy food choices and the importance of portion control with patients. The ADA also recommends that youth with type 2 diabetes should participate in 60 minutes of physical activity per day (American Diabetes Association, 2018).

The Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study, one of the largest studies of type 2 diabetes in youth, was a randomized clinical trial to compare the effects of oral medications with and without lifestyle changes, on glycemic control (Zeitler et al., 2012). The investigators found that, 5 years after starting metformin alone, approximately 50% of participants failed to meet the study's treatment goals of maintaining HbA1c levels of less than 8%. Participants who received metformin plus an intensive lifestyle modification program showed improvements in BMI compared to the other study groups, but there was no statistically significant difference between groups in terms of the primary HbA1c outcome. Thus, the TODAY study demonstrated that, over 5 years, about half of participants with type 2 diabetes failed to meet treatment goals with metformin alone, and these participants therefore must be treated with insulin (in addition to metformin and lifestyle changes). This study also demonstrated the difficulties in treating youth with type 2 diabetes and the need for additional treatment options in this group.

Although the pathophysiology in type 1 and type 2 diabetes are quite different, the treatment goals are identical. While patients with type 2 diabetes may be treated with or without insulin (depending on their blood sugars), a cornerstone of therapy in type 2 diabetes is a focus on lifestyle changes. Patients are taught the importance of a healthy lifestyle, portion control, and minimizing unhealthy options (e.g., sweet drinks, processed foods). This focus on diet and lifestyle may similarly place patients with type 2 diabetes at risk for developing eating disorders. Additionally, many youth with type 2 diabetes may eventually need treatment with insulin, and these patients may then be at risk for the disordered eating behaviors seen in youth with type 1 diabetes.

Few studies have examined disordered eating behaviors in youth with type 2 diabetes; however, studies of adults with type 2 diabetes demonstrate that this population is also at risk for eating disorders. For example, a recent study of over 300 adult patients with type 2 diabetes conducted by Nicolau and colleagues examined the prevalence of disordered eating behaviors in this population (Nicolau et al., 2015). They found that approximately 14% of participants screened positive for an eating disorder, with binge eating disorder being most prevalent. Additionally, when these participants were compared to controls (matched for age, gender, and BMI but without a history of diabetes or eating disorders), more participants with type 2 diabetes had "pathological eating patterns" (11% vs. 0%, $p = 0.05$), and the proportion of participants with binge eating disorder was higher among participants with type 2 diabetes as compared to the control group (12.2% vs 4.3%; $p = 0.01$) (Nicolau et al., 2015). While this study was a cross-sectional study of adults with type 2 diabetes, it demonstrates that these patients are potentially at risk for disordered eating behaviors.

Similarly, the TODAY study found that many patients with type 2 diabetes had disordered eating behaviors (Wilfley et al., 2011). As part of the TODAY study, participants with type 2 diabetes were asked to complete an inventory assessing eating disorders (Wilfley et al., 2011), and based on the inventory results, 20% of participants were classified as subclinical binge eaters, and 6% were classified as binge eaters. Both of these groups had worse quality of life than non-binge eaters (based on the quality of life inventory use), and clinical binge eaters reported more depressive symptoms (Wilfley et al., 2011). This study highlights that youth with type 2 diabetes are at risk for disordered eating behaviors, and assessing youth for these behaviors may be important, particularly among youth who describe problems with quality of life.

Given the limited number of studies in youth with type 2 diabetes, the literature on disordered eating behaviors in obese youth may be relevant. In a study by Lourenco and colleagues, youth who were seeking treatment in an outpatient obesity clinic were asked to complete an inventory about binge eating behavior (Lourenco et al., 2008). Of 128 youth in the study, 40% of participants met criteria for moderate or severe binge eating. These findings are pertinent to youth with type 2 diabetes, as obesity is a major risk factor for developing type 2 diabetes (Sperling, 2014). Of note, given the high prevalence of binge eating and disordered eating behaviors seen in obese patients, it is difficult to know if obesity, type 2 diabetes, or both obesity and type 2 diabetes are independent risk factors for developing disordered eating behaviors.

On the other hand, data also suggest that patients with certain eating disorders may be at risk for developing type 2 diabetes. Raevuori and colleagues retrospectively reviewed adult patients treated for eating disorders at a local hospital over a 15-year period and studied prevalence of type 2 diabetes prior to starting treatment and over the course of each patient's treatment (Raevuori et al., 2015). The authors found that patients treated for bulimia nervosa and binge eating disorder had increased odds of pre-existing type 2 diabetes (which they defined as patients having a prescription for a diabetes medication using national prescription registries) with an OR of 5.83 (95% CI 2.8–12.1) and 8.78 (95% CI 4.32–17.9), respectively. Additionally, the authors found that the lifetime prevalence of type 2 diabetes among patients treated for bulimia nervosa was 2.44 (95% CI 1.72–3.46) and binge eating disorder was 12.9 (95% CI 7.39–22.5) (Raevuori et al., 2015). There was no difference in rates of type 2 diabetes among patients treated for anorexia nervosa. Both men and women treated for bulimia nervosa or binge eating disorder had higher lifetime prevalence of type 2 diabetes. While there were several limitations to this study, including the lack of diabetes-related data (BMI, metabolic parameters) and the retrospective design, the authors found high rates of type 2 diabetes in patients with binge eating disorder (both prior to starting treatment for binge eating disorder and then after starting treatment for binge eating disorder). Patients with bulimia nervosa actually had a higher risk of type 2 diabetes before starting treatment compared to after starting treatment. Findings from this study emphasize the link between eating disorders and type 2 diabetes and highlight the need for prospective research in this area.

Additional research is also needed to understand the metabolic complications for patients with type 2 diabetes and concomitant eating disorders. Research from patients with type 1 diabetes and eating disorders suggests these patients are at risk for worsening glycemic control, hypoglycemia, and retinopathy (Jones et al., 2000; Rydall et al., 1997; Scheuing et al., 2014). However, the types of eating disorders seen in patients with type 2 diabetes are different than those seen in type 1 diabetes. Additionally, the pathophysiology of type 1 and type 2 diabetes is different, and the treatment for these diseases is different. Therefore, it is unclear if the complications associated with type 2 diabetes and eating disorders differ from those seen in patients with type 1 diabetes and eating disorders. In the study of adult patients with type 2 diabetes by Nicolau and colleagues described above, there was no statistically significant difference in glycemic control or several other metabolic parameters between the type 2 diabetes participants with and without a positive screen for binge eating (Nicolau et al., 2015). It is difficult to interpret this finding, however, given the cross-sectional nature of the study. Thus, longitudinal cohort studies of patients with type 2 diabetes and eating disorders are needed to determine their risk for similar complications.

Taken together, the research in youth with type 2 diabetes, obese youth, and adults with eating disorders supports a link between type 2 diabetes and disordered eating behaviors. Although the underlying mechanisms and specific risk factors for this association are unclear, the data suggest that youth with type 2 diabetes are at risk for disordered eating behaviors. Interestingly, the direction of the association between eating disorders and type 2 diabetes is yet to be determined, as there is also evidence that patients with eating disorders may be at increased risk for developing type 2 diabetes. Additional longitudinal research is needed to understand the long-term health risks of type 2 diabetes and eating disorders and whether patients with type 2 diabetes and eating disorders are at risk for worsening glycemic control and other diabetes-related comorbidities at rates similar to those observed in youth with type 1 diabetes.

Summary, Clinical Recommendations, and Future Directions

Recent research suggests that disordered eating behaviors are prevalent in youth with diabetes, and these behaviors may have negative effects on glycemic control and other diabetes-related comorbidities, making this an important area of evaluation and treatment. These data also demonstrate that youth with diabetes who do not meet diagnostic criteria for eating disorders may still engage in disordered eating behaviors and that insulin misuse is a common method of weight loss in this population, with serious associated complications. It is important, therefore, for diabetes providers to consider insulin manipulation and other disordered eating behaviors when assessing the adherence (Jaser & Datye, 2016), glycemic control, and overall health of their young patients with diabetes. While it is common for adolescents with diabetes to express diabetes "burnout" and associated poor adherence to therapy (Borus & Laffel, 2010), it is important for providers to consider that patients may be intentionally withholding insulin to aid in weight loss goals. Providers should consider discussing recent weight gain or weight loss and any concerns about body image with patients as intentional nonadherence to insulin therapy may not be obvious. While many youth with type 2 diabetes may not be prescribed with insulin therapy, it is important for providers to assess adherence to therapy in type 2 diabetes, especially as new therapeutic agents with different mechanisms of action become available. Additionally, providers should be cautious when praising youth regarding weight loss. If a patient is reinforced for weight loss, it may create a cycle leading to increased or unhealthy weight loss. Instead, patients should be praised for healthy behaviors and eating choices.

Evidence supports that patients with type 1 diabetes and eating disorders are at risk for deteriorating glycemic control, hypoglycemia, and retinopathy, but the long-term effects of eating disorders in patients with type 2 diabetes are not yet known. While youth with type 2 diabetes appear to be at greater risk for binge eating disorders (as compared to other eating disorders), it is possible that prescribing insulin for youth with type 2 diabetes increases the risk for "diabulimia" and its associated morbidity. Longitudinal, descriptive studies are needed to determine the long-term complications that may be seen in youth with type 2 diabetes and eating disorders.

Importantly, youth with diabetes and eating disorders require special treatment. Providers that are comfortable treating youth with eating disorders may not understand the intricacies of diabetes management and therefore may not feel comfortable or have the appropriate training to treat youth with diabetes. While an optimal treatment for youth with diabetes and eating disorders has not yet emerged, it is clear that a multidisciplinary treatment team is crucial to optimize treatment of a patient's eating disorder and diabetes.

Youth with type 1 and type 2 diabetes are at increased risk for eating disorders and disordered eating behaviors, and understanding the signs and symptoms of eating disorders along with the potential for worsening glycemic control and diabetes-related complications is important. Current research is focusing on better characterizing the types of eating disorders seen in youth with diabetes and understanding the best options for screening and treating these patients. Although the full extent of the long-term complications of coexisting diabetes and eating disorders is not yet known, youth with type 1 diabetes and eating disorders are at increased risk of worsening glycemic control and retinopathy. Therefore, increased provider awareness of disordered eating behaviors and eating disorders is critical when treating youth with diabetes.

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Chapter 7
Effects of Diabetes on Neurocognitive Function of Children

Elisabeth Northam

Background

The brain is one of the major organ systems affected in children and adolescents with type 1 diabetes (TID). A constant supply of glucose to the brain is critical for normal cerebral metabolism. Developing brains, in particular, have high cerebral energy needs associated with brain growth and 'neural pruning' and may be more sensitive than adults to glucose fluctuations (Arbelaez, Semenkovich, & Hershey, 2013). Current possibilities for insulin delivery and glucose regulation to treat TID are far from ideal. Thus cerebral glucose levels are often abnormal, even in well-controlled type TID, leading to a number of pathophysiological processes that potentially affect the developing brain.

Hyperglycaemia is associated with accelerated formation of advanced glycation end products (AGEs), as well as impaired insulin signalling and oxidative stress, ultimately leading to axonal degeneration and neuronal damage/loss (Arbelaez et al., 2013; Sima, 2010; Tomlinson & Gardiner, 2008). Intracellular calcium toxicity and uncontrolled release of excitatory amino acids, such as glutamate and aspartate, trigger a cascade of events during hypoglycaemia that may also result in neuronal damage (Arbelaez et al., 2013). There is evidence that constantly fluctuating glucose levels may be even more neurotoxic than episodic glycaemic extremes (Russo, Higgins, Werther, & Cameron, 2012). A number of other neuroendocrine processes are disrupted in TID, including abnormal fluctuations in cortisol, C-peptide and insulin growth factor-1, all of which potentially affect brain function at critical stages of neurodevelopment (Arbelaez et al., 2013; Csajbok & Tamas, 2016; Sima, 2010).

There is increasing awareness that TID has the potential to alter central nervous system (CNS) function, particularly in children and adolescents with the disease. Our understanding of the causal mechanisms that underlie changes in brain structure and cognition, however, is incomplete, and we are yet to develop a coherent model of brain-behaviour relationships specific to TID. In rare cases, an individual suffers a brain injury directly attributable to severe DKA or a catastrophic hypoglycaemic event, but generally CNS changes in TID differ from other forms of brain injury where a single, well-defined insult damages the brain. In TID, as with other metabolic disorders, there is potential for ongoing neurotoxicity and often a lack of clarity about the timing of putative insults. However, the impact of the disease on brain is not simply cumulative – if it were, the relationship between duration of disease and

E. Northam (✉)
Royal Children's Hospital, Melbourne, VIC, Australia
e-mail: Lis.Northam@rch.org.au

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CNS function would be much stronger than it is, and by early-mid adulthood individuals with early onset disease would be more clearly impaired than is the case. Interactions between disease effects and neurodevelopmental processes are possible, indeed likely, although still largely speculative.

This chapter will review current knowledge about neuropathological changes in the brain and cognition in children and adolescents with TID, noting our relative failure, to date, to define precise causal mechanisms and demonstrate meaningful, disease-specific linkages between brain and behaviour. The question as to whether the subtle changes found in brain structure and function matter in the everyday life of individuals with diabetes will be discussed from an ecological perspective.

Pathological Brain Changes in TID

Neuroimaging studies have documented morphologic and neuro-metabolite changes in the central nervous systems of children with the disease (Arbelaez et al., 2013; Moulton, Costafreda, Horton, Ismail, & Fu, 2015), although findings have implicated different brain regions and reported variable associations with illness-specific risk factors (Northam & Cameron, 2013). This lack of consistency may reflect differences in the ages of children studied, timing of insult as a function of neurodevelopmental stage, inconsistent definitions of disease-related variables and different neuroimaging and statistical approaches. A meta-analysis of paediatric neuroimaging studies in TID (Moulton et al., 2015) concluded that there was no evidence for a reduction in whole-brain grey matter (GM) volumes, but there were significant regional effects. This conclusion reflects findings from individual studies showing reduced GM volumes compared to controls in the anterior cingulate (Kaufmann et al., 2012), thalamus, parahippocampal gyrus and insular cortex (Northam et al., 2009), hippocampus (Ho et al., 2008), precuneus/cuneus (Kaufmann et al., 2012; Marzelli et al., 2014) and cerebellum (Marzelli et al., 2014).

Conversely, Marzelli et al. (2014) noted increased GM volume in the prefrontal, insula and temporal pole regions in their study of very young children (mean age 7 years) with early onset disease. In longitudinal follow-up of this sample, neuroimaging was repeated after 18 months. Children with TID exhibited significantly less growth of cerebral GM and cortical surface area between time points than age-matched healthy controls (Mazaika et al., 2016), a similar finding to that reported by Perantie et al. (2011), although in the latter study, reduced GM was specifically related to hyperglycaemia exposure. Of interest, change in blood glucose level at the time of scanning from baseline to follow-up was negatively correlated with change in GM volumes in Mazaika et al. (2016), suggesting that fluctuating blood glucose levels in children with TID are associated with corresponding fluctuations in brain volumes.

Animal models suggest that white matter (WM) is particularly sensitive to dysglycaemia in the context of the rapid myelination that occurs during neurodevelopment (Malone, Hanna, & Saporta, 2006) and empirical findings in human studies are largely consistent with this. Volumetric studies in paediatric samples show WM changes in the middle frontal region and thalamus (Northam et al., 2009), temporal lobe (Kaufmann et al., 2012; Northam et al., 2009) and occipital lobe (Kaufmann et al., 2012). Consistent with the effect reported above for GM, growth in WM over an 18-month interval was less in young children with TID than in controls (Mazaika et al., 2016), a finding that has been reported previously in a cross-sectional study conducted by Aye et al. (2011). Recent studies have used sophisticated diffusion tensor imaging (DTI) to study the functional connectivity of WM in children with TID and have documented widespread changes, compared to controls, particularly implicating temporal and parietal regions, hippocampus and thalamus (Antenor-Dorsey et al., 2013; Aye et al., 2012; Barnea-Goraly et al., 2014).

Magnetic resonance spectroscopy (MRS) studies demonstrate metabolite abnormalities in both adults (Lyoo et al., 2009; Makimattila et al., 2004) and children (Northam et al., 2009; Sarac et al., 2005) with TID. Glutamate, an excitatory neurotransmitter, was higher in the frontal brain in adults with TID than in healthy controls and metabolite levels correlated with lifetime glycaemic control in the sample studied by Lyoo et al. (2009). Compared to controls, *N*-acetylaspartate (NAA) levels were lower, suggestive of neuronal loss, while choline and myo-inositol were elevated, consistent with increased membrane turnover in youth with TID, particularly impacting the frontal lobes and basal ganglia 12 years after disease onset in a longitudinal cohort study (Northam et al., 2009), with similar metabolite changes reported by Sarac et al. (2005). EEG abnormalities, including reduced cortical connectivity (Cooray, Hillienmark, & Brismar, 2011; Hyllienmark, Maltez, Dandenell, Ludvigsson, & Brismar, 2005) and altered cerebral perfusion (Salem, Matta, Tantawy, Hussein, & Gad, 2002), provide further evidence of pathophysiological brain changes in children and adolescents with TID.

Associations between glycaemic extremes and brain changes have been a focus of particular interest in TID. A history of mild to moderately severe hypoglycaemia was not associated with WM volumes in several cross-sectional reports (Antenor-Dorsey et al., 2013; Barnea-Goraly et al., 2014), but appeared to inhibit growth in occipital/parietal WM over a 2-year period in the prospective study conducted by Perantie and associates (2011). A history of seizures in the context of hypoglycaemia has been associated with reduced total GM volumes (Ho et al., 2008), as well as with regional effects on the thalamus (Northam et al., 2009), left superior temporal (Perantie et al., 2007) and occipital/parietal (Perantie et al., 2011) brain regions. In a paradoxical finding, greater exposure to severe hypoglycaemia was associated with larger hippocampal volumes in the study by Hershey et al. (2010). These authors interpreted their findings as reflecting a pathological reaction to hypoglycaemia in the developing brain involving gliosis, a reactive neurogenesis or disruption of normal synaptic pruning.

Chronic hyperglycaemia has also been associated with adverse CNS changes in youth with TID. Volume reductions have been documented in whole-brain GM (Perantie et al., 2011) and cortical surface area (Mazaika et al., 2016), as well as regional effects on the cuneus/precuneus (Antenor-Dorsey et al., 2013; Perantie et al., 2007), right parietal (Kaufmann et al., 2012) and bilateral temporal-occipital regions and cerebellum (Marzelli et al., 2014). These are similar brain regions to those shown to be impacted by hyperglycaemia in adult samples where pathology is likely to impact cognitive skills such as attention, memory and language skills (Musen et al., 2006). Arbelaez et al. (2013) point out that the superior parietal lobule (cuneus/precuneus) is a critical part of the default mode network and also has the highest baseline metabolism of the whole brain; hence it is not surprising that this region may exhibit a heightened vulnerability to glycaemic perturbations. Studies have also reported increased GM volumes in prefrontal and insular cortices in hyperglycaemia-exposed children (Marzelli et al., 2014; Perantie et al., 2007), a counter-intuitive finding that has been interpreted as an inflammatory response to increased oxidative stress when blood glucose levels are elevated. Higher cumulative hyperglycaemia and glucose variability appeared to reduce WM growth in the splenium of the corpus callosum, bilateral superior parietal lobe and inferior frontal fasciculus (Maurus et al., 2012), while diffusion tensor imaging studies reveal an association between chronic hyperglycaemia and altered DTI parameters (Antenor-Dorsey et al., 2013; Aye et al., 2012). Hyperglycaemia-associated changes in WM were particularly evident in children with younger age of disease onset and longer disease duration (Barnea-Goraly et al., 2014).

Diabetic ketoacidosis (DKA) is a severe metabolic crisis involving extreme hyperglycaemia, ketone production and acidosis that arises as a result of marked insulin deficiency and ketonuria. During the acute phase, DKA has been associated with altered conscious state (Nadebaum, Scratch, Northam, & Cameron, 2012), EEG abnormalities (Mackay, Molesworth, Northam, Inder, & Cameron, 2016), widespread subclinical cerebral oedema (Glaser et al., 2006), metabolite changes (Cameron et al., 2014; Wootton-Gorges et al., 2007) and altered DTI parameters (Cameron et al., 2014). While many of these CNS abnormalities do not persist after resolution of the acute metabolic crisis, Cameron et al. (2014) documented lower frontal WM NAA levels, suggestive of neuronal necrosis, 6 months post DKA. In a recent report (Siller et al., 2016), children who had presented in DKA at TID diagnosis had lower radial, axial and mean diffusivity in WM at 3 months, providing further evidence of brain changes that persist beyond the initial insult.

Neuropsychological Findings

Given the pathophysiological brain changes noted above, it is not surprising that meta-analytic studies have documented subtle decrements in Full Scale IQ in both adults (Brands, Kappelle, Biessels, Kessels, & de Haan, 2005; Tonoli et al., 2014) and children (Gaudieri, Greer, Chen, & Holmes, 2009; Naguib, Kulinskaya, Lomax, & Garralda, 2009; Tonoli et al., 2014) with TID. In a particularly robust test of the impact of childhood-onset TID on intellectual functioning, Lin, Northam, Werther, and Cameron (2015) calculated change scores using measures of IQ obtained at diagnosis and at follow-up 12 years later and showed a greater decline in Verbal and Full Scale IQ in the TID cohort than was evident in the healthy controls. The impact of TID on intellectual functioning is subtle. IQ scores are consistently within the average range but lower than those of age-matched healthy controls (Cato et al., 2014; Lin et al., 2015; Northam et al., 2009; Patino-Fernandez et al., 2010; Perantie et al., 2008), and there is evidence reviewed below that appears to be of functional significance.

The few studies to date that have attempted to link IQ scores in TID with structural changes in brain have largely produced null findings, but Marzelli et al. (2014) did find evidence of atypical morphology/function relationships in their sample of younger children with TID. The expected positive correlation between GM volume in cerebellar-occipital regions and medial prefrontal regions was evident in control subjects, but not in the TID group. IQ was reduced in boys with early onset TID relative to girls in one report (Schoenle, Schoenle, Molinari, & Largo, 2002), but Naguib et al. (2009) found no significant gender effect in their meta-analytic review of the literature. The specific cognitive skills that appear most vulnerable in children with TID include attention, executive functions (planning, organising, goal setting, problem solving, mental flexibility), psychomotor efficiency and information processing speed (Cato et al., 2014; Kaufmann et al., 2012; Kirchhoff, Jundt, Doty, & Hershey, 2016; Naguib et al., 2009; Schwartz et al., 2014; Tonoli et al., 2014). Deficits in these skills are theoretically consistent with pathology in fronto-temporo-parietal brain regions and subcortical structures described above although few studies to date have attempted to directly correlate brain pathology and cognitive impairment.

Attempts to identify specific diabetes-related risk factors for TID-related cognitive sequelae have proved inconclusive. A relationship between early disease onset and cognitive impairment is the most robust finding (Gaudieri et al., 2009; Lin et al., 2015; Lin, Northam, Rankins, Werther, & Cameron, 2010; Patino-Fernandez et al., 2010; Schoenle et al., 2002). Effect sizes were ‘moderate’ in children diagnosed prior to 5–6 years and small when comparing children with disease onset after 6 years and their age-matched peers in the meta-analysis conducted by Gaudieri et al. (2009). Attention, memory/new learning and executive skills appear to be particularly vulnerable to early disease onset (Gaudieri et al., 2009; Lin et al., 2010).

Associations between cognitive impairment and glycaemic perturbations are less consistent and are possibly complicated by the U-shaped relationship between blood glucose levels and cognitive deficit demonstrated in field studies (Gonder-Frederick et al., 2009) where both high and low blood glucose levels are associated with performance decrements. Given the obvious alteration in conscious state that accompanies falling blood glucose levels, it is not surprising that the focus has traditionally been on hypoglycaemia as the explanation for cognitive deficits in TID. In fact, the ‘early onset’ effect just described is often interpreted as a proxy for recurrent severe hypoglycaemia that is common, but often unrecognised and poorly documented, in young children (Battelino et al., 2011).

Aye et al. (2011) found that IQ indices were reduced in children with a positive history of a hypoglycaemia, while Naguib et al. (2009) reported a negative effect of severe hypoglycaemia on verbal memory. Blasetti et al. (2011) conducted a meta-analysis of studies examining the relationship between hypoglycaemic seizure history and cognitive deficit and found evidence for an association, particularly compromising memory/learning (medium effect sizes) and verbal intelligence/language skills (small effect sizes). These authors concluded that impaired memory secondary to neuropathological changes in medial temporal brain regions, including the hippocampus and basal ganglia, compromise language development over time. However, Ryan (2008) drew attention to the number of studies that have failed to find this association (Gaudieri et al., 2009; Schoenle et al., 2002; Strudwick et al., 2005) and argued that other diabetes-related risk factors must be at play. For example, the ‘early onset’ effect may reflect chronic hyperglycaemia at this sensitive developmental stage as parents deliberately aim for higher blood glucose levels to avoid hypoglycaemia. Certainly, the Diabetes Control and Complications Trial (2007) failed to find evidence for hypoglycaemia-related cognitive decline in young adults followed prospectively over an 18-year period, suggesting that even if an association between hypoglycaemia and cognitive deficit exists in the young child, adolescents and adults exhibit some form of cerebral adaptation to low blood glucose levels.

In adults, long-term exposure to hyperglycaemia increases the risk of hypertension and cerebrovascular disease, which, in turn, are associated with cognitive deficits, particularly slowed psychomotor speed (DCCT, 2007; Sima, 2010). There is now increasing concern that chronically elevated blood glucose levels may be a risk factor for cognitive difficulties from much earlier in the course of the illness. Studies of children with TID have identified associations between chronic hyperglycaemia and lower IQ (Aye et al., 2011, 2012; Cato et al., 2014; Kirchhoff et al., 2016; Patino-Fernandez et al., 2010; Perantie et al., 2008; Schoenle et al., 2002), as well as specific deficits in working memory (Lin et al., 2010; Tonoli et al., 2014), executive functions (Cato et al., 2014; Kaufmann et al., 2012) and processing speed (Kirchhoff et al., 2016; Schwartz et al., 2014). The DCCT noted improved psychomotor speed with better metabolic control (DCCT, 2007) suggesting a direct relationship between elevated blood glucose levels and some aspects of cognitive functioning. More recently, Kirchhoff et al. (2016) found that within-individual decreases in hyperglycaemia exposure were associated with improved visuospatial ability and increased processing speed. However, these authors also found better delayed memory performance in children with poorer metabolic control documented at each of three time points over a 5-year period. They interpreted this intriguing finding as consistent with the possibility that greater hyperglycaemia may indicate lesser exposure to severe hypoglycaemia and thus be protective against the negative impact on memory noted above (Blasetti et al., 2011). It is equally possible that improved performance may simply reflect a ‘practice’ effect where children become familiar with stimuli that have been presented on multiple occasions.

There are a number of possible explanations for the complex picture that emerges from studies examining associations between disease variables and neurodevelopmental outcomes. Reliable ascertainment of metabolic control history is problematic, particularly when such information is gathered retrospectively. In vivo measurement of many of the variables that may contribute to TID-related effects on the CNS, such as disturbances in insulin homeostasis, C-peptide, IGF-1, neurotransmitter function and counter-regulatory hormone responses, is difficult, if not impossible given current technologies, but may be important. In fact, Sima (2010) argued, based on animal models, that cognitive deficits in TID may result from insulin and C-peptide deficiencies and their impaired signalling rather than hyperglycaemia per se. A study conducted by Benedict and colleagues (Benedict, Nelson, Schunk, Sullwold, & Seaquist, 2006), which found insulin-dependent brain region and task-specific effects on neuronal activity, provides some support for this suggestion, although it should be noted that participants were healthy (nondiabetic) adults.

It is often hard to pinpoint the timing of putative neural insults, and most children experience multiple disease-related risk factors, making it extremely difficult to identify specific causal mechanisms. Furthermore, neurotoxic effects may be cumulative and/or synergistic, thus confounding attempts to identify specific risk factors. For example, Lin et al. (2010) found that youth with a combination of two or three illness risk factors (i.e. early onset TID, hypoglycaemic seizure/coma or chronic hyperglycaemia) performed more poorly on language tasks, working memory and mental efficiency, than youth with no or one risk factor. A greater negative impact of hyperglycaemia on visuospatial ability in children with earlier rather than later onset disease was documented by Kirchhoff et al. (2016), while children who had experienced both DKA and severe hypoglycaemia tended to have lower IQ in another report (Cato et al., 2014).

Finally, an interaction between developmental stage and disease processes has been postulated. Biessels, Deary, and Ryan (2008) suggest that the chronic disturbance of glucose and insulin homeostasis inherent in TID exerts deleterious effects on the brain during critical periods of CNS change, such as during neurodevelopment in childhood and in mid to later adulthood when adults with the disease exhibit a form of ‘accelerated ageing’ or early neurodegeneration. Ryan (2008) further argues that the peri-onset phase, with the progressive decline in endogenous insulin secretion, prolonged untreated hyperglycaemia, and changes in blood-brain barrier permeability that precede diagnosis, may represent a third critical period of TID-related neurotoxicity. A more recent report (Schwartz, Axelrad, & Anderson, 2014) documenting cognitive deficits, particularly psychomotor slowing and impaired verbal fluency and visuomotor integration skills within days of diagnosis, is consistent with Ryan’s hypothesis, as is data from animal models showing reduced dendritic connections and impaired spatial maze learning within weeks of streptozotocin-induced diabetes (Malone, Hanna, & Saporta, 2008). Ryan (2008) speculates that peri-onset brain changes may alter subsequent neurodevelopmental trajectories and represent a marker of future neurobiological vulnerability to subsequent brain insults including the glycaemic extremes inherent in TID. Longitudinal follow-up of the cohort studied by Swartz et al. (2015) using a combination of neuroimaging and neurocognitive assessment at regular intervals may provide an opportunity to test this hypothesis.

Functional Outcomes

Even subtle decrements in cognitive capacity can impact on children engaged in ongoing learning and skill development, and there is compelling evidence that children with TID exhibit compromised academic achievement (Desrocher & Rovet, 2004). In a large Finnish sample, childhood onset TID was associated with reduced academic grades at secondary school completion and with lower employment rates thereafter (Persson et al., 2013). Children who developed diabetes prior to 6–7 years appeared at particular risk of academic underachievement in a Swedish population register-based study, and this early onset effect was independent of metabolic control history (Dahlquist & Kallen, 2007; Hannonen et al., 2012).

In contrast, a population study in Western Australia found lower academic test scores only in those children with poorly controlled diabetes (Cooper, McNamara, de Klerk, Davis, & Jones, 2016). Youth with TID had lower rates of school completion and work/study participation than healthy controls in a longitudinal cohort study (Northam, Lin, Finch, Werther, & Cameron, 2010), despite having similar intellectual potential (IQ) at diabetes onset 12 years previously. In addition to impacting academic achievement, subtle cognitive dysfunction may impair daily living skills and affect independent decision-making in self-management of diabetes. TID-related damage to WM tracts and to brain regions that form part of the default mode network described above are likely to reduce speed of information processing and compromise the capacity to integrate information across different brain regions and neural systems, skills that are critical for timely and effective decision-making in diabetes management. Consistent with this possibility, McNally, Rohan, Pendley, Delamater, and Drotar (2010) reported an association between deficits in executive skills such as goal setting, planning, organising, working memory and mental flexibility, with reduced treatment adherence and poor metabolic control although they were unable to discern the direction of effects in a cross-sectional design.

The functional implications of pathophysiological brain changes in TID are not limited to cognition, academic achievement and adaptive functions. Meta-analytic reviews show that depression, eating and other affective disorders occur more commonly in both children (Buchberger et al., 2016; Reynolds & Helgeson, 2011) and adults (Anderson, Freedland, Clouse, & Lustman, 2001; Lustman et al., 2000) with TID than in healthy controls. Increased risk for psychiatric morbidity, including elevated rates of suicidality, was confirmed in a very recent population-based Swedish study

(Butwicka, Frisen, Almqvist, Zethelius, & Lichenstein, 2015). Psychological difficulties in TID are associated with poor metabolic control, leaving individuals at 'double jeopardy' for poor mental and physical health outcomes (Hassan, Loar, Anderson, & Heptulla, 2006; Johnson, Eiser, Young, Brierley, & Heller, 2013; Lustman et al., 2000; Northam et al., 2010). Adolescence is a time of increased illness demands and mental health burden for youth with TID (Cameron & Northam, 2012). Hormonal fluctuations and increased insulin resistance at puberty directly affect blood glucose levels, increasing the risk for hyperglycaemia and poor longer-term metabolic control even in treatment-compliant adolescents (Daneman, 2006). However, treatment adherence is also known to deteriorate in adolescence (Daneman, 2006). Optimal disease management, which is challenging at any time, is particularly unpalatable to adolescents as it conflicts with many of the normal developmental tasks of this period such as the desire for increasing autonomy, a spontaneous lifestyle and a propensity for risk taking. This desire to live 'in the moment' is in direct conflict with pressure to adhere to a rigid disease management regimen in pursuit of a seemingly distant goal of minimising risk for diabetes complications in the life.

Psychopathology in TID populations has traditionally been interpreted as secondary to the emotional impact of a serious chronic illness with onerous demands for daily self-management and lifestyle adjustments. However, McIntyre et al. (2010) note that the brain regions subserving affective functions, such as the prefrontal cortex and limbic structures, are those shown to be affected in neuroimaging studies in TID (e.g. Ho et al., 2008; Northam et al., 2009; Perantie et al., 2007), leading these authors to suggest that diabetes-related structural and biochemical disturbances in the brain may affect emotional wellbeing directly, leaving individuals with the disease more vulnerable to mood disturbance and increased risk of mental health difficulties in general. For example, Lyoo et al. (2009) reported elevations in prefrontal glutamate-glutamine-y-aminobutyric acid levels and mild depression in young adults with TID, with both biochemical changes and affective symptoms showing a linear relationship with lifetime hyperglycaemia exposure. Causal mechanisms are still speculative, and it is possible that psychological symptoms in individuals with TID may be a cause or a consequence of hyperglycaemia, or indeed arise directly, but independently, from the same set of TID-related biochemical brain changes. In one recent report, children spent increased time in normoglycaemia and exhibited improved behaviour and mood after commencing on insulin pump therapy, consistent with the possibility that a reduction in glycaemic perturbations is associated with improvements in mental health (Knight et al., 2009). Self-reported behaviour problems 2 years after commencing pump therapy were significantly associated with metabolic control, and there was a trend for similar association based on parent report (Knight, Northam, Cameron, & Ambler, 2011).

Assessment, Management and Intervention

Improved understanding of the aberrant neurophysiology that is inherent in TID holds promise for neuroprotective therapies that, over time, may reduce morbidity in both cognition and mental health in children with TID. For example, there is preliminary evidence that secondary metabolic substrates such as pyruvate, lactate, ketone bodies and medium chain triglycerides may offer neuroprotection against glycaemic perturbations, but this work is still in its infancy, particularly in paediatric populations (Northam & Cameron, 2013). In contrast, there is a robust literature and several meta-analytic reviews (Hood & Nansel, 2007; Winkley, Miranda-da-Cruz, & Sonneville, 2006) of psychological interventions in TID showing significant reduction in psychological distress and a marginally positive effect on metabolic control. Standardised interventions with a theoretical foundation were more efficacious than theoretical, ad hoc programmes, and there was no evidence of positive benefit in adults with TID, suggesting that intervention in childhood is critical. Evidence from a longitudinal cohort study suggests that behavioural problems that predate the diagnosis of TID predict ongoing psychological morbidity and poor metabolic control (Northam et al., 2010), making children with premorbid difficulties an obvious focus for early intervention. Cameron and Northam (2012) argue that universal screening at the time of diagnosis and during periods of increased risk, such as developmental transitions, is feasible and cost-effective as well as reducing individual and family distress and long-term health morbidity. Clinic wide, proactive interventions to promote resilience and enhance coping have been trialled with some success (Serlachius et al., 2016; Westrupp, Northam, Lee, Scratch, & Cameron, 2015). The advantage of this preventive approach is that it allows more individualised multidisciplinary resources to be directed to children and families with severe psychopathology.

Much less attention has been paid to preventive and remedial cognitive and educational interventions in TID than has been directed to addressing psychological vulnerability. Greater awareness on the part of clinicians, parents and teachers of the risk for neurocognitive deficits in TID is an important first step if academic underachievement is to be reduced and rates of school completion improved in children with this disease. Access to neuropsychological assessment for children presenting with unexplained academic under achievement or exhibiting difficulties in managing the problem-solving demands inherent in optimal disease management should be a routine part of clinical care in TID but will require increased funding support. It is critical that any testing of children with TID is conducted, while blood glucose levels are within 5.0 mmol/l–15 mmol/l to ensure that performance is not affected by intercurrent hypo- or hyperglycaemia.

Summary

A constant supply of glucose to the brain is critical for normal cerebral metabolism and the glycaemic perturbations and other physiological changes inherent in TID potentially affect the activity and survival of neural cells. Downstream effects on cognition, adaptive skills and mental health are now well recognised, but causal mechanisms are still imperfectly understood, and we are yet to develop a coherent model of brain-behaviour relationships that is specific to TID. It is clear, though, that TID onset in childhood has very particular implications for quality of life and academic and professional success across the lifespan. Following diagnosis, all subsequent neurodevelopment and mastery of new skills occur in the context of potentially neurotoxic disease processes.

Optimal management of TID places enormous demands on both cognitive and psychological resources of the individual, and it is not surprising that risk of mental health disorders is increased in TID populations. For children and adolescents, these demands are present at a time when all the normal developmental challenges are co-occuring. That many patients grow up well in the face of these demands are impressive and should encourage even greater efforts to better understand the impact of the disease on the brain, neuro-cognition and mental health so that we may better help those who struggle. There is already a burgeoning literature reviewing efficacy of psychological interventions to foster greater resilience in individuals with TID, and this work should continue. New technologies mean that neuroprotective therapies are now within the realm of possibility, as are attempts to understand links between metabolite profiles and mental health vulnerability.

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Chapter 8
Individual-Level Intervention Approaches in Pediatric Diabetes Management

Sue Channon and John W. Gregory

Introduction

The focus of this chapter is on the individual-level intervention approaches in pediatric diabetes populations. The aim is to provide an overview of the "stand-alone" individual-level interventions for children and young people that have been described in the published literature while also including some multicomponent interventions where the work with the individual comprises the most significant part of the intervention design.

Type 1 diabetes mellitus (T1D), for both children and adults, poses a risk to both physical and psychological health. The aim of any intervention delivered in a diabetes service is to optimize the biopsychosocial health outcomes for the young person, both in the short and the long-term. For children and young people living with T1D, a positive outcome would be to minimize its impact, maximize the positive protective factors in their lives, and achieve as close to the physical and psychological outcomes that they would have reached without T1D. They want services to be delivered by professionals who know them well, who understand the complexities of their daily life. They want individualized, collaborative care which will include setting an agenda and being given choices (Curtis-Tyler, Arai, Stephenson, & Roberts, 2015).

Any intervention, be it individual, group, or family, needs to take into account that the risks and protective factors the young person experiences will not only depend on their individual and social circumstances but will change over time with their age and stage of development (Whittemore, Jaser, Guo, & Grey, 2010). T1D affects not just the person diagnosed but also their family and wider system. The social-ecological model (Bronfenbrenner, 1979) takes this a step further, linking systems thinking with developmental psychology and looking at the multidirectional relationships between the young person and the context in which they are living and developing. In pediatric services, many of the interventions have the family system in mind such that "stand-alone" interventions are now very much in the minority. However, recognizing the complexity of T1D management and the uniqueness of each person's circumstances, practitioners need a range of interventions to draw upon

S. Channon (✉)
Centre for Trials Research, Cardiff University, Cardiff, UK
e-mail: ChannonS2@cardiff.ac.uk

J. W. Gregory
Division of Population Medicine, School of Medicine, Cardiff University, Cardiff, UK
e-mail: gregoryjw@Cardiff.ac.uk

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to enable them to individualize the intervention to the needs of the young person including individual-level interventions.

One of the common questions raised when considering individual interventions is the age at which it becomes feasible and appropriate. Many published interventions specify an age band, often identifying a lower age limit with most individual interventions having been designed with the high school age population in mind and also excluding young people with learning or developmental disabilities. The most important aspect to consider is that the intervention approach is matched to the capacity of the child and also to be mindful that the published literature reflects research studies which tend to be conservative, bearing in mind issues of consent and capacity which in clinical practice in an ongoing clinical relationship with the child would be easier to judge on an individual basis. For individual psychotherapeutic approaches, there is no defined general lower age limit; for example, play therapists work on an individual level with very young children and children with learning disabilities. To conduct a cognitive behavioral therapy (CBT)-based intervention, a child has to have reached the stage where they can "compare" thoughts and beliefs and understand that having a thought can cause them to behave in a particular way. With individual differences, this stage of development is not defined by a specific age; however, most studies with children under 7 years of age have worked with parent and child, and some have suggested that the approach is more effective with parents alone in this young age group (Cartwright-Hatton et al., 2011).

Where possible the decision about who to work with also needs to reflect the issue to be discussed. For example, if the presenting problem seems to be around family communication, then it would be preferable to work with the family. However, the approach taken also needs to match the patient's agenda, so while family work might in principle be preferable, if the family will not attend such a session or the young person wants to be seen alone, then individual work could help. If the focus of the work is around independence, developing self-care skills, etc., this might be most appropriately dealt with on an individual basis. Other pragmatic considerations in considering individual work is the availability of suitably trained practitioners and the skill set within the team who are working with the young people and their family. In the interventions to be described, the practitioners' background will be described wherever that information is made available.

The interventions discussed in this chapter are presented in three main sections: psychotherapeutic approaches (or "talking therapies") which occur in addition to routine care; individual interventions within routine care; and telemedicine.

Psychotherapeutic Approaches: "Talking Therapies"

Cognitive Behavior Therapy (CBT)

CBT is widely used as an evidence-based approach to depression and anxiety that aims to work on the relationship between cognitions, behavior, and emotional response to situations. The CBT model as developed by Beck (Beck, 1976) has the central premise that our thoughts mediate the relationship between an event and our emotional, behavioral, and physiological reactions to that event. By helping the client become more aware of those associations, they are then able to challenge their negative thoughts and thinking patterns and work on making their thinking patterns more adaptive. It focuses on current problems rather than past difficulties, and is very structured, trying to break down negative cycles of thinking, feeling, and behavior, making problems more manageable.

It has been used with young people with chronic health conditions, although unlike the positive impact for adults with diabetes, the evidence in T1D in adolescents is less clear (Thorpe, Fahey, Johnson, Thorpe, & Fisher, 2014), possibly due to the limited size and design of the studies. Much of the CBT in T1D with adolescents has been conducted in a group format, often led by doctoral-level psychologists (Hains, Davies, Parton, Totka, & Amoroso-Camarata, 2000; Serlachius et al., 2014). These interventions have not had a significant impact on HbA1c, but in some studies, there has been evidence for improved psychosocial well-being on measures of coping self-efficacy and quality of life (Serlachius et al., 2014). Others have combined individualized and family work in multicomponent approaches (Stanger et al., 2013). There have been some small uncontrolled studies of individual level CBT for adolescents with T1D, addressing anxiety, anger, and stress (Hains, Davies, Parton, & Silverman, 2001). In an uncontrolled pilot study of CBT with 9 adolescents with subclinical depression (McGrady & Hood, 2013), 12 sessions of individual level CBT were delivered by doctoral and postdoctoral level practitioners. At the end of the intervention, the depressive symptoms had declined, and the young people were reporting improved diabetes self-management, although there was no significant change in glycosylated hemoglobin A1c (HbA1c). However, there has been no randomized trial of individual level CBT intervention for youth with T1D and subclinical or clinical depression, so any indicators of effectiveness have yet to be adequately tested.

Motivational Interviewing

Motivational interviewing (MI), “a person-centered counselling style for addressing the common problem of ambivalence about change” (Miller & Rollnick, 2013), has been increasingly used by a range of health professionals in their practices across various settings to engage their service users in thinking about change. MI is often used as a stand-alone intervention but also as an adjunct to other approaches, in particular to promote engagement with an intervention (Lundahl et al., 2013).

MI comprises four broad processes, engaging, focusing, evoking, and planning, which the practitioner uses not in a linear fashion but in a flexible combination depending on the needs of the patient. The relationship is a collaboration in which the practitioner fully accepts the young person’s autonomy and, rather than trying to drive the patient in a particular direction, they work to evoke the patient’s own intrinsic motivation for positive change. The core skills, derived from person-centered counselling, are asking open questions; affirming patient’s qualities, strengths, and effort; reflective listening; and summarizing. MI practitioners use these core skills to help their patients explore their own views about change and engage with movement toward positive change. Information and advice can be provided by the practitioner but only when it is in response to a patient request or with their permission to ensure it doesn’t compromise the patient’s autonomy (to choose to engage with or reject the information) or the collaborative nature of the relationship.

Motivational interviewing with its focus on shared agendas, collaboration and autonomy, has a natural fit with the aspects of care that young people have identified as important to them (Curtis-Tyler et al., 2015). While its early development was in work with adults, since the late 1990s, it has been increasingly used in services for children and young people, particularly in the field of pediatric health behavior change, and it is included in the recommended approaches in the UK National Guidelines for management of pediatric diabetes (NICE, 2015).

There has been one review and two meta-analyses of MI interventions in pediatric health behavior change in recent years (Cushing, Jensen, Miller, & Leffingwell, 2014; Gayes & Steele, 2014; Suarez & Mullins, 2008). Overall, across health behaviors, the conclusions suggest that MI interventions produce small but significant effect sizes when MI is compared to usual care or waiting list control groups. Across these three reviews, five studies of MI in pediatric diabetes published up to 2012 were identified. The three earlier studies all published in 2003 were pilot studies using MI as a stand-alone individual intervention (Channon, Smith, & Gregory, 2003) or in group interventions in which MI was combined with other forms of therapy such as CBT, solution-focused approaches, and narrative therapy (Knight et al., 2003; Viner, Christie, Taylor, & Hey, 2003). These studies showed that it was feasible to use MI with teenagers and that there was potential for positive outcomes at least in the short-term.

One of these pilot studies (Channon, Smith, & Gregory, 2003), the only one of the published MI interventions to be delivered on an individual basis, was followed by a randomized trial of MI with teenagers with T1D in which the MI was delivered on an individual basis by a postgraduate psychologist trained in MI approach (Channon et al., 2007). MI was compared with nondirective support, and the study had HbA1c as the primary outcome. The intervention period was for 1 year, and the young people received an average of four MI-focused consultations. The key findings were of a significant change in HbA1c that was maintained 12 months after the end of the intervention alongside positive changes in well-being and quality of life for those young people.

In the more recent RCT included in the reviews, two sessions of education delivered in MI-consistent style by a diabetes educator were compared with two sessions of structured diabetes education (SDE) for adolescents with an HbA1c >9% (74.9 mmol/mol) (Wang et al., 2010). Over the 6 months of follow-up, the SDE group had significantly lower adjusted mean HbA1c value than the MI group with no differences on any of the psychosocial measures. In a smaller pilot study published since the reviews (Stanger et al., 2013), MI was combined with CBT with the CBT component adding coping skills designed to improve decision-making. This was primarily an individual-level intervention, delivered by Masters level clinicians with the young people, but it was combined with a family-based contingency management intervention to reinforce desired behaviors, in this instance blood glucose monitoring, using financial rewards. The intervention was weekly for 14 weeks, and at the end of the intervention, blood glucose monitoring was increased, and HbA1c was significantly improved. However, there was no control group and no longer-term follow-up, so the effectiveness of this intervention needs to be explored in a larger study.

The conclusion from the two meta-analyses published in 2014 is that overall, MI interventions for adolescent health behaviors appear to produce a small but significant effect which is sustained in those studies with longer follow-up averaging 33 weeks (Cushing et al., 2014; Gayes & Steele, 2014).

One aspect of the MI reviews that stands out, as it does with CBT, is how few studies have been published relating to the use of MI with pediatric diabetes populations. Could this be because of equivocal findings in MI studies with adults with diabetes? Despite overall small to moderate effect sizes in health behavior change in medical and primary care settings (Lundahl et al., 2013; Vanbuskirk & Wetherell, 2014), there is less effectiveness in areas such as self-care behaviors, eating disorders, and medication adherence. A large study of motivation enhancement therapy (MET) with adults with sub-optimal glycemic control (Ridge et al., 2012) found MET was ineffective alone and was best combined with CBT.

What can we learn from the other studies implementing MI in other pediatric health contexts? Interventions that include parent-child sessions yield the greatest effect sizes (Gayes & Steele, 2014), so it may be that individual-level interventions need to be combined with more family-focused aspects, and this would be crucial in developing the intervention for younger children. In terms of practitioners, community health workers seem to be most effective in working with adolescents, but the training and background of interventionists are often unclear, so this needs to be clarified. Given Wang's results (albeit in a small study), do we make a mistake to combine it with an education focus? What is the optimum number of sessions? Currently there are far more questions than answers, but MI does still hold promise that has yet to be explored adequately.

Personal Trainer Model

In an approach that was described as "guided by the principles of motivational interviewing, applied behavior analysis, and problem-solving," Nansel and colleagues (Nansel et al., 2009) developed a diabetes personal trainer intervention for young people aged 11–16 years with T1D. This six-session intervention with additional phone calls was delivered over a 2-month period by trained nonprofessionals (usually graduate students in health-related subjects) who used a structured problem-solving approach to work on areas of diabetes management the young person identified as difficult and was compared to usual care. The results showed a sustained intervention effect on HbA1c at 1- and 2-year follow-up for those in middle adolescence (13–16 years) rather than the pre-early adolescent subgroup. The authors suggest that their results support the use of this type of youth-focused intervention for the mid-adolescence group as they develop more autonomy with their diabetes management and that potentially a parent-child focused intervention may suit the younger age group.

Individual Interventions as Part of Routine Care

Goal Setting

Individualized goal setting is also a key component of the WICKED (Working with Insulin Carbs, Ketones, and Exercise to Manage Diabetes) program in Sheffield, UK (Eiser et al., 2013). This intervention is for 16–21-year-olds. It is integrated into routine care and aims to increase clinic efficacy, enhance knowledge and self-care among young people, as well as facilitate family communication and support. The primary outcomes are HbA1C, depression, and diabetes distress. The theoretical models underpinning the intervention are Arnett's model of emerging adulthood (Arnett, 2000), the theory of social cognition (Bandura, 1986), and to improve staff communication and implementation intention (Gollwitzer, 1999) to enhance standard care through improved consistency and recording. The young people receive individualized goal setting to enhance implementation intention and to build self-efficacy. This aspect of the program is delivered by psychology graduates who work with the young person to identify achievable goals which are then recorded at the post-clinic team meeting. There are also group-based modules of education for the young people, with individualized follow-up, and also a four-session family communication program with groups of parents (who meet separately to the young people).

Preconception Counselling

A preconception counselling intervention, READY-Girls, has been developed for teenagers with T1D (Fischl et al., 2010) with the goal of reducing the incidence of reproductive complications. In a randomized controlled trial comparing READY-Girls to standard care, the 13–19-year-olds in the intervention group viewed two CD-ROMS, read a book, and received a brief nurse counselling session during three consecutive clinic visits over a 9-month period. The intervention led to improved knowledge and perceived benefits about preconception counselling, and also the young women in the intervention arm sought more additional pre-conception counselling information than those receiving standard care. With low direct costs of delivering the intervention (and costs which could be lower with information being placed on the web) and high costs of adverse reproductive outcomes, this was a cost-effective intervention that also seemed to enhance patient-professional interaction.

Health-Related Quality of Life

Health-related quality of life (HRQoL), which includes physical symptoms, functional status, cognitive, psychological, and social functioning, is often referred to as an important factor in diabetes management and is included in clinical guidelines as an area for review and discussion to ensure young people are coping (Whittemore et al., 2010). Exploring HRQoL as part of routine care was the focus of an intervention developed in the Netherlands (de Wit et al., 2010) in which the young person completed a HRQoL questionnaire immediately prior to routine clinic appointments and the results were made available to the young person and practitioner to inform the discussion in the ensuing consultation. It was a 12-month intervention with three successive appointments, and the results indicated that it significantly improved teenagers' psychosocial well-being and their satisfaction with care with the exception of those with the poorest control (HbA1c >9.5%). In the 12-month follow-up, the positive gains had been lost, showing that for gains to be maintained, they need to be reviewed regularly using the structure of a formal instrument. This approach would also have the added benefit of highlighting issues around mental health that might otherwise get missed.

Self-Monitoring

On example of an intervention designed to increase self-monitoring was EPIC (Evidence into Practice Information Counts) (Noyes et al., 2014). This RCT tested the impact of an individually tailored age-appropriate diabetes diary and information pack for children and young people aged 6–18 years with T1D. The aim was to support decision-making and self-care with a specific focus on insulin management and blood glucose monitoring. The RCT recruited 337 children and young people from 11 UK centers in 2010–2011. However, there was poor take-up of the diaries and the EPIC packs, with the intervention being no more effective than receiving diabetes information in an ad hoc way.

Telemedicine

Telemedicine (TM) is the use of telecommunication and information technologies to provide clinical health care at a distance and is an area of significant development in recent years with the increasing sophistication and availability of technology. The hope is that it helps to reduce barriers, be they related to distance, engagement, or resources, adding a welcome dimension to clinical services but also improving access to those communities who struggle to engage with usual methods of delivering care. With technology often at the heart of young people's communication, it might also be hoped to have a better fit with the way they want to approach their own self-care. One of the difficulties describing work in this field is the ever-changing nature of the technologies and the interventions that are emerging.

In a review of the literature on the impact of TM interventions on the management of T1D in youth published in 2010 (Shulman, O'Gorman, & Palmert, 2010), the interventions mostly involved transmission of blood glucose data followed by unsolicited scheduled clinician feedback. The results did not demonstrate beneficial impact on HbA1c or diabetes complications though there did appear to be indicators that this was an idea worth pursuing for young people at greater risk such as those with higher HbA1c concentrations. However, the nature of these interventions will have now been superseded with the advance of technology, but it will be of interest to see if the outcomes and conclusions resonate with the same themes.

Phone

One example of using phone contact in a randomized trial design was the study by Lawson and colleagues (Lawson, Cohen, Richardson, Orrbine, & Pham, 2005) who targeted 13–17-year-olds who had an HbA1c >8.5% for more than 6 months. They were randomized to usual care or usual care plus

6 months of weekly, standardized telephone contact with the diabetes nurse educator who would discuss their blood glucose levels of that week and how to manage them in the following week. While the early indicators at 3 months were of a positive impact on quality of life and family support, by 6 months this impact was not sustained. One conclusion from these results is that we need to be more sensitive to the point at which a helpful intervention becomes an irritant or ceases to help working with the young person's agenda. Also, the authors described significant difficulty getting hold of the young people which is a reminder that just because technology is convenient to deliver an intervention does not mean it is necessarily more effective or easier to use.

Text messaging is clearly an approach that offers a low cost, feasible intervention. However, in a review of studies using text messaging (Herbert, Owen, Pascarella, & Streisand, 2013), retention was not particularly good, satisfaction of young people with the intervention was mixed, and there was also no clear link with clinical outcomes. If services are going to consider using new methods of communication, they need to engage young people in their development in a timely manner to avoid the risk in this fast-moving field that interventions seem outdated before their introduction.

Internet and Electronic Communication

Delivery of interventions electronically either entirely or as part of the intervention has significant advantages. It is consistent with young peoples' approach to seeking information in their daily life, and they can have a degree of choice about when and where they can access it. If it is linked to the clinic, it can be delivered in clinic contexts where there are limited personnel and consultation space. It also maximizes flexibility with opportunities for web-based modules to offer tailored education for particular populations or needs.

In the DAILY (Daily Automated Intensive Log for Youth) trial (Kumar, Wentzell, Mikkelsen, Pentland, & Laffel, 2004), a handheld personal digital assistant (PDA), equipped with a wireless modem and blood glucose data management software, was provided to 40 young people. Half the group were randomized to receive just the device, while the intervention group received the device along with an integrated motivational game (DiaBetNet) in which the participants would guess a blood glucose level following collection of three earlier readings (Game Group). Over 90% of all young people transmitted their results at least once in a 4-week period, and over 65% of the participants transmitted a median of four BG results a day. The use of the motivational game increased the frequency of monitoring, reduced the frequency of hyperglycemia, and appeared to increase satisfaction with the use of the device.

In a feasibility study using Yourway, an Internet-based self-management intervention for 13–17-year-olds with type 1 diabetes, six multimedia stories were made available over an 11-week period, describing scenarios that typified barriers to self-care experienced by young people (Mulvaney, Rothman, Wallston, & Lybarger, 2010). Approaches to problem-solving and coping with the situation were provided, and participants were encouraged to engage in problem-solving exercises. This was completed individually, but participants were also able to access social networking via a peer forum, compare their response to others in the study, and receive prompts and help from a problem-solving expert (although there was no interaction with diabetes clinicians through the website). The intervention was rated highly by participants, the majority of whom accessed every story at least once. While an intention-to-treat analysis showed no difference to usual care, an as-treated analysis did show significant improvements in self-care and problem-solving, suggesting this intervention has promise as an additional resource to engage young people with problem-solving around their diabetes care.

Rajkumar and colleagues (Rajkumar et al., 2015) have been exploring the feasibility of using a computer-delivered intervention in clinic with an adolescent African-American population. This three-session intervention known as the "3 Ms" (Medication, Meter, and Meals) is delivered at 3–4-month intervals to match clinic attendance and is designed to increase motivation for diabetes self-management, based on an information-motivation-behavior skills model of health behavior change and MI approaches. The first session lasts approximately 20 minutes and includes psychoeducation about the importance of daily diabetes self-care tasks using clips of a physician and a young person providing a personal account of the experience with diabetes. Then an avatar is used to take the young person through a series of activities to identify their motivation for engaging in particular activities of self-care, culminating in a statement of goals that are set by the young person which are then also sent to the young person in a letter, confirming the goals they have set. The avatar reflects back the young person's responses, using affirmations to boost self-efficacy and statements emphasizing personal choice. The second and third sessions lasting 5–10 minutes are based around the goals the young person has set and how they have engaged with these goals in the interim. The feedback from the 23 young people aged 10–13 who took part in the study showed high satisfaction with the intervention and a very high completion rate with 78% completing all three sessions. The design offers the opportunity to integrate the intervention into routine clinical practice.

Developing effective coping skills strategies has been the focus of the work of Grey and colleagues for many years with a range of studies exploring the development of coping skills around self-management as children transition into adolescence to minimize the deterioration in metabolic control that occurs in this developmental phase. The coping skills programs have traditionally been delivered in a group context, but the most recent iteration of this has been delivered via the internet, firstly in TEENCOPE (Grey et al., 2013) and then combining that with an educational program to create Teens.connect (Whittemore et al., 2015). TEENCOPE was a series of five 30-minute interactive sessions that were completed by young people individually but who were part of virtual groups who all completed the sessions within the same time frame of a week. They all posted their responses and were able to see each other's responses and had a moderated discussion board to share their experiences of practicing the coping skills (to recreate as far as possible the experience of group work while in practice working as an individual).

In a randomized controlled trial, TEENCOPE was compared to the Internet education program Managing Diabetes. There was good engagement with both programs: TEENCOPE participants completed 82% of sessions and Managing Diabetes participants completed 74% of sessions. At 12 months there were no significant difference between the two groups on primary outcomes. However in the crossover study design, the participants were offered the second intervention at 12 months, and those that engaged with both interventions had lower HbA1c, higher quality of life, improved self-efficacy, lower perceived stress, and lower diabetes family conflict at 18 months. In order to explore the impact of integrating these two interventions, TEENCOPE was integrated with Managing Diabetes into an Internet coping skills and education program called Teens.connect.

In the pilot trial (Whittemore et al., 2015), Teens.connect was compared to Planet D, an open access generic support program for diabetes. Initial consent rate was high at 85%, but actual participation was lower. Only 69% completed any lesson, and only 31% received an adequate "dose" of 8–10 lessons. This was lower than expected given the findings from the earlier studies, but a key difference was that in the previous intervention studies, participants received more frequent and individualized prompts and lessons were released weekly, whereas in this study all the lessons were available from the beginning.

So it seems that the Internet can be used to engage young people and has great potential to add value into clinical care processes, but these need integrated prompting, structure, and possibly a motivational component. It also needs a "personal" element in the nature of the prompts, the feedback received, etc.; otherwise young people disengage. There is an ever-growing number of mobile technologies featuring software program apps aimed at supporting young people's self-management of their long-term condition (Majeed-Ariss et al., 2015), but there is a lack of good quality studies as yet which evaluate their effectiveness and identify the key "active ingredients" needed to support young people.

Discussion

One conclusion that can be drawn from looking at this area of individual interventions is just how few face-to-face interventions specifically for the young person with diabetes there are. Clearly a rapidly growing area will be in technology-based interventions, many of which will be individual but weaving in group-based elements. The review by Gayes and Steele of MI interventions showed that interventions based on work with parents and children are more effective particularly with younger children (Gayes & Steele, 2014), so it may be that developing individual interventions is really only crucial with adolescence. In the work with individuals, it is important to remember that interventions that focus solely on direct, behavioral processes involved in diabetes management are less likely to be effective if they neglect emotional, social, and family processes (Hood, Rohan, Peterson, & Drotar, 2010).

Taking this wider perspective is perfectly possible when working with an individual, but the practitioners need to ensure that they adopt this systemic view. Young people want diabetes to be seen in the context of their life, and our approach to it as a practitioner needs to reflect this, with our interventions designed to reflect the system that the young person lives in even if those other people such as family and friends are not in the room. There are individual-focused interventions in adult services that we can learn from and consider whether there are elements that can be transferred into a pediatric context, particularly for adolescents, e.g., 3DFD (3 Dimensions of Care for Diabetes) (Doherty, Gayle, & Ismail, 2015), which provides a coordinated service for those with sub-optimal glycemic control delivering help for psychological, medical, and social domains.

We need to have multiple types of interventions to support young people with diabetes; one type of intervention is not going to fit all; it is certainly not going to work for all in the long-term, needing to change and develop as the young person's needs change and develop. Rather than seeing results that diminish after 6 months simply as an intervention that didn't work, we need to consider whether it has its place as part of a series of short-term interventions. Maybe it is simply not possible in the context of such significant developmental change for one intervention to achieve long-term effectiveness. Teams need a menu of approaches to enable them to offer long-term support, and individual approaches need to be part of the toolkit alongside family and community interventions.

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Part III
Social Level Factors for Children and Adolescents

Chapter 9
Family Influences

Ashley M. Butler, Tracy Georges, and Barbara J. Anderson

Introduction

Since the earliest writings on the child with a chronic physical illness, a transactional relationship has been described between the chronically ill child and the family. In this transactional relationship, the family has been seen as having important influences on the physical and emotional health of the child, and the family system has also been seen as being significantly influenced by the chronic illness itself (Gerhardt, Berg, Wiebe, & Holmbeck, 2017). In this chapter, while recognizing this transactional relationship in which *the family influences the child* with a chronic illness and *is influenced by the chronic illness*, we will review the empirical research on the many family processes and parent behaviors that influence children and adolescents with diabetes, including youth with type 1 diabetes (T1D) and youth with type 2 diabetes (T2D).

Because there have only recently been sufficient numbers of youth with T2D to participate in research studies, there is currently very little empirical data on family influences on youth with T2D. Therefore, while we review the few studies that exist on youth with T2D, most of this chapter addresses family influences with respect to youth with T1D. It is important to note that the majority of research studies reviewed here are cross-sectional in design, and thus conclusions can only speak to relationships or associations—not causal influences—between family factors and health and behavior outcomes in youth with diabetes . We highlight those few longitudinal studies that begin to shed light on the directionality of influence between child and family behaviors.

First, we review research which documents a relationship between sociodemographic characteristics of the family and health and behavior outcomes in the child and adolescent with diabetes . Next, we review research on how the type or quality of general family interactions, as well as maternal and paternal symptoms of depression and anxiety, influence youth with diabetes. Finally, we review research on how different types of diabetes-specific family behaviors, such as diabetes-specific family conflict and parental-perceived burden of diabetes management , relate to behavior and health outcomes

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A. M. Butler · T. Georges
Baylor College of Medicine, Houston, TX, USA

Texas Children's Hospital, Houston, TX, USA
e-mail: ambutler@bcm.edu; txgeorge@texaschildrens.org

B. J. Anderson (✉)
Baylor College of Medicine, Houston, TX, USA
e-mail: bja@bcm.edu

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in children and adolescents with T1D. Throughout we include only empirical reports published since the release of the findings of the Diabetes Complications and Control Trial (DCCT) (DCCT Research Group, 1993) in 1993, as this landmark study established an intensive insulin regimen as the standard of care for youth with T1D, which changed the landscape for the family management of diabetes. We conclude with next steps in research on family influences in pediatric diabetes as well as clinical implications of the research reviewed in this chapter.

Family Demographics and Social Determinants of Health

Research has traditionally included the term *demographic factors* to describe the social and economic characteristics of families of children with diabetes . The most often studied demographic characteristics are children's race/ethnicity and insurance status, family structure, parental marital status, educational attainment, occupation, and income. Further, studies have often assessed the *socioeconomic status* of the family, which is a composition of parental education, income, and occupational status (Matthews & Gallo, 2011). Given these demographic factors are nonmodifiable or very challenging to modify, we also address, when available, studies that have identified potentially modifiable mediators of the relationships between demographic factors and health outcomes.

We also address research in T1D on *social determinants of health*, which has emerged in the literature to describe demographic factors, as well as other related constructs that consist of the social and physical environments of children and families. The World Health Organization defines the *social determinants of health* (SDOH) as aspects of the social and physical environments in which youth and their families live, as well as the wider set of systems shaping the conditions of their daily life (World Health Organization, 2017). Among children with diabetes, parental literacy and health status are social determinants that have been examined in their relationships with health behaviors and outcomes.

Race/Ethnicity Racial/ethnic disparities in diabetes health outcomes have been documented in the growing literature on racially/ethnically diverse youth with T1D. *Health disparities* are defined as differences in health outcomes that are closely linked with social, economic, and environmental disadvantages (U.S. Department of Health and Human Services Office of Minority Health, 2015). Despite controlling for socioeconomic status in analyses, cross-sectional investigations have showed that African American youth have worse glycemic control (Agarwal, Jawad, & Miller, 2015; Clements et al., 2016; Delamater et al., 1999; Willi et al., 2015), higher rates of diabetic ketoacidosis and hypoglycemic events (Willi et al., 2015), and more deaths (Saydah, Imperatore, Cheng, Geiss, & Albright, 2017) compared to non-Hispanic whites. One longitudinal study that examined racial/ethnic differences in changes in glycemic control found no difference between African Americans and non-Hispanic whites during adolescence and young adulthood (Clements et al., 2016). Yet, African American youth begin to show poorer glycemic control early in the disease course (Clements et al., 2014; Frey, Templin, Ellis, Gutai, & Podolski, 2007). Thus, African American children have relatively greater deteriorations in metabolic control shortly after disease onset, but the pattern of glycemic changes that occur later in the disease course is not different from non-Hispanic whites. Hispanic adolescents have also been found to have worse glycemic control and higher rates of diabetic ketoacidosis and hypoglycemic events compared to non-Hispanic white youth, but these differences were diminished in analyses that controlled for socioeconomic status (Clements et al., 2016; Willi et al., 2015).

In contrast to T1D which most often occurs in non-Hispanic white youth, there are disparities in the incidence of T2D among Hispanic, African American, and American Indian children. Approximately 80% of youth with type 2 diabetes are from these racial/ethnic minority backgrounds (Klingensmith et al., 2016). African American and Hispanic children with T2D have also been found to have poorer glycemic control compared to non-Hispanic whites (Copeland et al., 2011). Regarding psychosocial factors, African American and Hispanic youth and families report poorer quality of life and family burden from diabetes management, respectively (Rhodes et al., 2012).

Overall, little is known about factors that mediate racial and ethnic disparities in the incidence of T2D or in health outcomes of T1D or T2D. Given family socioeconomic status is difficult to change, there is an ongoing need to identify modifiable factors that can be addressed to close the gap in T1D outcomes for Hispanic and African American youth. While research conducted by Willi et al. (2015) showed health-care differences in therapeutic modality (i.e., insulin pump use) for T1D across racial/ethnic groups, determining whether creating equalities in therapeutic modality can reduce disparities in outcomes for African American or Hispanic youth is not known.

Insurance Status Insurance status is often considered a marker of level of access to health care. Indeed, youth with T1D who have public insurance are more likely to have poorer glycemic control and cardiovascular disease risk factors (Majidi et al., 2014) compared to those with private insurance. It is important to note that the associations between public insurance status and worse health outcomes were eliminated in analyses controlling for insulin regimen (i.e., insulin pump therapy vs. insulin injections) (Majidi et al., 2014). Thus, poorer T1D health outcomes among youth with public insurance may be due, in part, to being less likely to have access to insulin pump therapy than youth with private insurance. Overall, little is known about the relationship of insurance status to health behavior and outcomes among youth with T2D.

Family Structure Youth who live in homes with a larger ratio of children to parents have poorer glycemic control, and this relationship is mediated by lower adherence and greater diabetes-related family conflict (Caccavale, Weaver, Chen, Streisand, & Holmes, 2015). Additionally, studies have consistently documented that youth with T1D living in homes with single parents have poorer glycemic control (Mazarello Paes et al., 2017), as well as low parental involvement and parental over-involvement in diabetes management (Mullins et al., 2011). Taken together, while family structure is difficult to change, these findings suggest that adherence and diabetes-specific family behaviors are important modifiable mediators of the influence of family structure on health outcomes.

Parent Education, Family Income, and Socioeconomic Status (SES) The research has been mixed regarding different measures of family socioeconomic status and diabetes outcomes in youth. Research that used a composite measure of SES (combined measure of parent education and occupation) showed poorer glycemic control among adolescents with T1D from lower SES families (Caccavale et al., 2015). Similarly, research has shown that low family income is associated with poorer glycemic control and that this relationship is mediated by low adherence and lower parental acceptance of their child (Drew et al., 2011). However, no significant association between maternal educational attainment and glycemic control trajectory over a 3-year period during childhood and young adolescence was found in a study conducted by Rohan et al. (2013). It is important to note, however, one study showed higher levels of paternal education were related to better glycemic control in adolescents (Johns, Faulkner, & Quinn, 2008). These studies indicate that income alone and combined indices of low SES are risk factors for poorer metabolic control in T1D.

Relatively few studies have investigated the role of parent education or family income or socioeconomic status and T2D health behaviors and outcomes. According to the TODAY study, the largest group of well-characterized American adolescents with rigorously defined type 2 diabetes, the large majority of youth with T2D, are from low socioeconomic backgrounds. Approximately 70% of parents have high school education or less (Klingensmith et al., 2016), and 40% of families have a yearly income of $25,000 or less (Copeland et al., 2011; Klingensmith et al., 2016). The TODAY study found no association between family income or parent education and medication adherence among youth with T2D (Katz et al., 2016). These studies in T2D show that low SES may play a role in T2D onset but may not significantly influence adherence among youth who develop T2D.

Parental Literacy Better parental general literacy skills are associated with better metabolic control in children with T1D (Ross, Frier, Kelnar, & Deary, 2001). More recent research has also shown that the literacy and numeracy skills of caregivers influence glycemic control of youth (Hassan & Heptulla, 2010; Pulgarón et al., 2014). Qualitative research has shown that parents with low literacy reported confusion by diabetes jargon, preferred hands-on teaching from diabetes education, and wished for information to be communicated in simple language, broken down into key points, and repeated (Howe, Cipher, LeFlore, & Lipman, 2015). The next section focuses on the roles of general family interactions and parental symptoms of anxiety and depression in diabetes health behaviors and outcomes.

General Positive Family Interaction Patterns

Over the past two decades, many studies have documented a strong relationship between general positive family interaction patterns and optimal health outcomes in youth with T1D. Nurturing, warm, and caring family behaviors have been reported to be related to improved adherence and quality of life in youth with T1D (Faulkner & Change, 2007; Grey, Boland, Sullivan-Bolyai, & Tamborlane, 1998; Hoey et al., 2001; Wysocki et al., 1996). Hanson and colleagues (Hanson, De Guire, Schinkel, & Koleterman,1995) reported that high family cohesion and low family conflict were related to better metabolic control and positive adherence in adolescents with T1D. Jacobson and colleagues (Jacobson et al., 1994) reported that youth who reported high levels of family expressiveness (the encouragement to act openly and express feelings directly) at diagnosis had better glycemic control at the 4-year follow-up assessment and boys, who reported more family cohesion and less general conflict at diagnosis, were in better glycemic control at the 4-year follow-up assessment. Similarly, Grey and colleagues (Grey, Boland, Yu, Sullivan-Bolyai, & Tamborlane, 1998) reported that adolescents with T1D who reported that their families provided general guidance had better glycemic control than adolescents who reported their families were less warm and caring. Taken together, these findings from cross-sectional studies indicating an association between positive family interactions and better glycemic control are in accord with results from research using longitudinal designs.

In one of two prospective longitudinal-observational studies, Cohen and colleagues (Cohen, Lumley, Naar-King, Partridge, & Cakan, 2004) followed a cohort of youth (mean age = 11.7 years) with T1D from low-SES and minority ethnic/racial families over 4 years and reported that family adaptability (the ability of a family system to change its roles and relationship rules in response to situational and developmental demands) was related to better glycemic control in older children, while in younger children, higher family adaptability was related to poorer glycemic control. They also found that cohesive families (positively engaged family relationships) at baseline had children with better adherence and had daughters (but not sons) with better glycemic control at follow-up. In another longitudinal study of adolescents with T1D, Helgeson and colleagues (Helgeson, Siminerio, Escobar, & Becker, 2009) also found gender differences in family relationships and metabolic control over 4 years. They reported that good family relations were associated with better metabolic control for girls but not for boys. In sum, the longitudinal studies suggest that positive influence of general family interaction patterns on adherence and glycemic control is not uniform across different age groups or gender.

General Family Conflict and Life Stress

Non-diabetes-specific, negative family interaction qualities such as lack of parental warmth or caring and lack of family cohesion and high levels of general family conflict have consistently been shown to be associated with frequency of diabetic ketoacidosis (DKA) and poor glycemic control (Grey et al., 1998; Pereira, Berg-Cross, Almeida, & Machado, 2008). In a longitudinal study of youth with

T1D from diagnosis, Jacobson and colleagues (Jacobson et al., 1994) reported that the child's perception of general family conflict *assessed at diagnosis* was the strongest predictor of poor adherence to multiple aspects of the diabetes care regimen over the 4-year follow-up period. Similarly, Hanson, De Guire, Schinkel, and Kolterman (1995) reported that poor metabolic control and poor adherence behaviors were related to more conflictual family relationships. These studies demonstrate the important role of family conflict in outcomes of youth with T1D.

In contrast, little is known about the role of general family conflict in youth with T2D. While few studies have examined the role of family conflict or life stress among youth with T2D, one study showed that experiencing more frequent stressful life events was associated with poorer adherence to oral medications by youth with T2D (Walders-Abramson et al., 2014). Anderson (2012) identified stressors unique to minority parents of youth with T2D, such as lack of access to health and mental health care, working multiple jobs, and caring for relatives with complications of T2D.

Parenting Style

Parenting style is the emotional context for specific parenting behaviors, and this emotional climate is said to be stable over time (Darling, & Steinberg, 1993). Parenting styles are usually discussed as typologies characterized by the parent's level of sensitivity to and expectations for their child's behavior (Baumrind, 2005). In the "authoritative parenting style," parents have high sensitivity and warmth toward their child along with high expectations for the child's behavior. In addition, in the "authoritative parenting style," conflict is minimized as the parents set consistent, realistic limits on children's behavior while displaying warmth and sensitivity to their child's needs and feelings (Baumrind, 1991). Davis and colleagues reported that in a group of 4- to10-year-old children with T1D, mothers with an "authoritative parenting style" had children with better adherence and glycemic control (Davis et al., 2001). Similarly, in an older age group (8–11-year-olds) with T1D, Monaghan and colleagues (Monaghan, Horn, Alvarez, Cogen, & Streisand, 2012) reported that mothers of these preteens who self-identified as using an authoritative parenting style also reported less parenting stress and had preteens with better adherence to the T1D regimen.

In an Israeli sample of adolescents (11–18 years; mean age of 14.4 years) with T1D, Shorer and colleagues (Shorer et al., 2011) studied the parenting styles of both mothers and fathers and reported that an authoritative parenting style in fathers was related to better glycemic control and adherence, while a permissive parenting style in mothers was related to poor adherence. For both mothers and fathers, endorsing a general feeling of parental helplessness was related to poor glycemic control and poor adherence to treatment in their adolescents with T1D.

Taking a more molecular look at the parenting styles of mothers and age of adolescents with T1D, Butler and colleagues (Butler, Skinner, Gelfand, Berg, & Wiebe, 2007) studied adolescents (11–17 years; mean age = 14.2 years) and focused on two components of the authoritative parenting style: *psychological control* refers to the parent trying to control the child's thoughts and feelings through guilt and criticism; and *firm control* refers to parental monitoring of adolescents' activities and setting behavioral limits. Adolescents of all ages who perceived their mothers as using psychological control had greater depressed mood. Firm control was strongly associated with greater depressed mood among older adolescents but less strongly among younger adolescents. Maternal acceptance was associated with better adolescent adherence, irrespective of the adolescent's age. The investigators conclude that maternal parenting style is associated with well-being in adolescents with T1D, but the relationship is complex and moderated by adolescent age (Butler et al., 2007).

With respect to youth with T2D, Saletsky and colleagues (Saletsky, Trief, Anderson, Rosenbaum, & Weinstock, 2014) studied the parenting styles for diabetes-related tasks and for normative developmental tasks in a cohort of parents and adolescents with recent-onset T2D. Youth who perceived less parental control and more autonomy in day-to-day tasks as well as in diabetes tasks were more likely to adhere to their T2D medication regimen. The authors concluded that a less authoritarian (more authoritative) parenting style toward diabetes tasks predicted better medication adherence in this group of youth with T2D. In reviewing the parenting style literature in pediatric diabetes, Anderson (2011) concluded that for optimal family management of both T1D and T2D, parents should be encouraged to adopt an authoritative parenting style with respect to management of diabetes.

Maternal Symptoms of Depression and Anxiety

Parents have a central role in the management of T1D in children and adolescents. For this reason, characteristics of parents have been studied as to their influence on behavioral and health outcomes in youth with T1D. Mothers of children and adolescents with T1D report higher levels of depressive symptoms than women in the general population (Clayton, et al., 2013; Jaser, Linsky, & Grey 2013). Several recent studies have documented elevated levels of depressive symptoms in mothers caring for children with T1D (Driscoll et al., 2010; Horsch, McManus, Kennedy, & Edge, 2007; Jaser & Grey, 2010; Jaser, Whittemore, Ambrosino, Lindemann, & Grey, 2009). Driscoll and colleagues (Driscoll et al., 2010) reported that elevated levels of depressive symptoms in caregivers of children with T1D were associated with less caregiver education, more family stress, older age of the child, and poor glycemic control. In a large sample of youth with T1D and their caregivers (82% mothers), Hood (2009) reported that caregivers with high levels of depressive symptoms themselves reported higher levels of youth depressive symptoms when compared with caregivers with low levels of depressive symptoms.

Several recent studies (Butwicka, Zalepa, Fendler, Szadkowska, & Mlynarski, 2013; Clayton et al., 2013) have reported that high levels of maternal depressive symptoms predicted higher utilization of health care (ER visits and hospitalizations) in their children with T1D. In one of the first studies to try to identify the mechanisms by which maternal depressive symptoms relate to poor health outcomes in youth with T1D, Wiebe and colleagues (Wiebe et al., 2011) followed young adolescents with T1D and their mothers over a 16-month period and found that when maternal depressive symptoms were low, maternal involvement in diabetes management was associated with lower adolescent depression, better adherence, and better metabolic control. Similar findings were reported by Mackey and colleagues (Mackey et al., 2014) who used structural equation modeling with a large cohort of young adolescents with T1D and reported that maternal depressive symptoms were directly associated with less parental monitoring of diabetes tasks as well as more diabetes conflict and poor adolescent adherence.

Compared with studies of maternal depression, fewer studies of general maternal anxiety have been conducted. In a systematic literature review, Whittemore and colleagues (Whittemore, Jaser, Chao, Jang, & Grey, 2012) reported that the prevalence of anxiety symptoms in parents of children with T1D ranged from 21% to 59%. Cameron and colleagues (Cameron, Young, & Wiebe, 2007) studied trait anxiety in mothers of adolescents with T1D and found that maternal trait anxiety is associated with high maternal involvement and overprotectiveness. Furthermore, for younger adolescents, maternal trait anxiety was associated with poorer glycemic control and higher levels of school absenteeism, while for older adolescents, maternal trait anxiety was associated with lower autonomous motivation for diabetes self-care and lower levels of positive mood.

Streisand and colleagues (Streisand et al., 2008) studied parents of newly diagnosed children with T1D and examined the relationship between anxiety and depressive symptoms and general pediatric parenting stress (i.e., assesses the general stress involved in parenting a child with a chronic illness, and not diabetes-specific stress). Parents who scored in the clinical range for depression and anxiety showed increased pediatric parenting stress. The authors discuss the vulnerability to anxiety and depression of parents following the diagnosis of T1D and the importance of intervention early in the disease course. Grey (2009) studied mothers of children with T1D less than 8 years old and found that 21% had clinically significant levels of anxiety symptoms and 24% had clinically significant levels of depressive symptoms. Maternal symptoms of anxiety and depression were strongly related to fear of hypoglycemia, which is discussed in the next section on diabetes-specific stresses. Overall, the relatively large body of literature focused on mothers shows that maternal symptoms of anxiety and depression are common and greater symptoms influence poorer glycemic control, adherence, and negative diabetes-specific family behaviors.

Paternal Symptoms of Depression and Anxiety

There is relatively little research on fathers' influences on youth with T1D compared to mothers' influences, although the few studies that have been published shine an important light on a potential target of intervention to improve outcomes in youth with T1D. Wysocki and Gavin (2006) studied paternal involvement in pediatric chronic disease management in six chronic disease conditions (asthma, cystic fibrosis, T1D, phenylketonuria [PKU], inflammatory bowel disease, and spina bifida). These conditions were selected because these chronic diseases had complex medical regimens and "empirical data and clinical observation indicate that effective family adaptation is critical to successful management of these conditions" (Wysocki & Gavin 2006, p. 502). These investigators found that in all disease groups, more paternal involvement in disease management was associated with maternal well-being and with healthier marital and family functioning (Gavin & Wysocki, 2006). They also reported that in adolescents, more paternal involvement was associated with better adherence and quality of life but not with health status or health-care utilization (Wysocki & Gavin, 2006, p. 502).

Mitchell and colleagues (Mitchell et al., 2009) investigated pediatric parenting stress, child behavior, participation in diabetes management tasks, and parental psychological resources in fathers of children 2–6 years old with T1D. Results indicated that fathers who experience more state anxiety and whose children display more behavior problems report higher levels of pediatric parenting stress than those with lower anxiety and fewer child behavior problems. While fathers of very young children with T1D experience lower levels of pediatric parenting stress than mothers, the correlates of fathers' stress are unique and may have implications for fathers' general psychological functioning and for their children's behavior.

Examining paternal involvement in T1D with an older cohort of youth (7–14 years of age) using a new validated measure of fathers' involvement in diabetes management tasks, Hansen and colleagues (Hansen, Weissbrod, Schwartz, & Taylor, 2012) found that for fathers in this study, 44% reported clinically significant sleep problems, 23% reported clinically significant anxiety, and 19% reported clinically significant depressive symptoms. They also found that better child adherence was significantly related to maternal perceptions of the father's helpfulness. While mothers reported significantly more anxiety and higher levels of pediatric parenting stress, mothers and fathers had comparable rates of depressive symptoms. Fathers whose children had worse glycemic control also reported significantly higher frequency of pediatric parenting stress. In summary, existing research indicates that paternal psychological stress and symptoms of anxiety and depression play a different though important role from maternal variables in relation to health and psychosocial outcomes in children with T1D. Studies of the influence of a range of different diabetes-specific parental behaviors and stressors will be reviewed in the next section.

Diabetes-Specific Stressors and Parental Behaviors

Fear of Hypoglycemia Parents fear a range of consequences from hypoglycemia/severe hypoglycemia for their child—seizures, loss of consciousness, brain damage, and even death (Gonder-Frederick, Nyer, Shepard, Vajda, & Clarke, 2011). In a recent study of "contemporary rates of severe hypoglycemia" in youth with T1D (Katz, Volkening, Anderson, & Laffel, 2012), the authors discuss that while there is variability in reported rates of hypoglycemia, severe hypoglycemia remains common in youth with T1D. In their sample, longer duration of T1D was associated with a higher rate of severe hypoglycemia, while age, HbAlc, and sex were not. However, other investigators have reported that age is related to incidence of severe hypoglycemia, with an increased risk of hypoglycemia with younger age (Levine et al., 2001). Severity of hypoglycemic episodes and not the frequency of hypoglycemic episodes is most strongly related to parental fear of hypoglycemia. As parental fear of hypoglycemia increases, parental quality of life decreases; however, a history of severe hypoglycemic episodes experienced by parents was not related to decreased quality of life for the parent (Johnson, Cooper, Davis, & Jones, 2013). Other studies have reported that parental fear of hypoglycemia may result in increased anxiety about diabetes management, obsessive blood glucose monitoring, deliberately keeping blood glucose levels too high, and relationship stress (Gonder-Frederick et al., 2011).

In the context of the evidence summarized earlier in this chapter on the association of symptoms of parental depression and anxiety with outcomes in the child with T1D, several investigators have reported that parental fear of hypoglycemia is related to symptoms of parental anxiety and depressive symptoms. Patton and colleagues (Patton, Dolan, Smith, Thomas, & Powers, 2011) reported that increased general parenting stress and symptoms of depression were associated with increased fear of hypoglycemia in parents of younger children, while Streisand and colleagues (Streisand, Swift, Wickmark, Chen, & Holmes, 2005) reported similar findings for parents of older youth with T1D. Overall, parental fear of hypoglycemia is common, is related to diabetes management behaviors, and often co-occurs with increased parental stress, as well as depressive and anxiety symptoms.

With respect to the influence of parental fear of hypoglycemia, empirical studies about the relationship between parental fear of hypoglycemia and the child’s glycemic control are inconsistent. Several investigators have reported a significant association between higher parental fear of hypoglycemia and worse glycemic control in their child (Clarke et al., 1998; Haugstvedt, Wentzel-Larsen, Rokne, & Graue, 2011). On the other hand, other investigators have *not* found an association between maternal fear of hypoglycemia and HbA1c levels (Gonder-Frederick et al., 2006; Jaser, Whittemore, Ambrosino, Lindemann, & Grey, 2008; Marrero, Guare, Vandagriff, & Fineberg, 1997; Patton, Dolan, Henry, & Powers, 2008). Across ages of children and adolescents, parental fear of hypoglycemia has been shown to correlate only modestly with child and adolescent fear of hypoglycemia (Gonder-Frederick et al., 2011). In summary, the preponderance of evidence suggests that high levels of parental fear of hypoglycemia affect both parental health and quality of life (Barnard, Thomas, Royle, Noyes, & Waugh, 2010) which, as documented earlier in this chapter, have been shown to be associated with the quality of life, psychosocial functioning, and glycemic control of youth with T1D.

Perceived Caregiver Burden of Type1 Diabetes Several conceptual models have been suggested to explain the complex nature of stress processes as caregivers adapt to the needs of their growing children and adolescents with chronic physical conditions and chronic illnesses (Raina et al., 2004). Parents of very young children with T1D have reported that the two greatest sources of diabetes burden are fears about hypoglycemia and the profound responsibility of caring for a very young child with T1D which demands “constant vigilance” (Sullivan-Bolyai, Deatrick, Gruppuso, Tamborlane, & Grey, 2003). In one of the few studies of the perceived diabetes burden of both mothers and fathers of youth with T1D, Haugstvedt and colleagues (Haugstvedt, Wentzel-Larsen, Rokne, & Graue, 2011) reported that long-term diabetes health concerns were the greatest diabetes burden for mothers and fathers. In addition, mothers and fathers reported similar perceived diabetes burden for family disruption due to diabetes, for the child’s current mental and physical problems, and for restrictions on the child’s social and school activities. While overall frequency of blood glucose monitoring was not related to diabetes burden, frequency of nighttime blood glucose monitoring was associated with increased diabetes burden. For mothers, but not for fathers, higher family burden was associated with higher levels of general emotional distress.

Several investigators have reported that higher parental-perceived burden of T1D management is strongly associated with poorer glycemic control (Butler et al., 2008; Law, Walsh, Queralt, & Nouwen, 2012; Markowitz et al., 2012). However, Cunningham and colleagues (Cunningham, Vesco, Dolan, & Hood, 2011) reported that caregiver burden around diabetes management mediated the relationship between caregiver psychological distress and glycemic control. In their study perceived diabetes burden was more strongly related to caregiver depressive symptoms than to caregiver anxiety symptoms.

Parental Involvement in Diabetes Management

The importance of sustained developmentally appropriate parent involvement in diabetes management has been linked to optimal adherence and optimal glycemic outcomes (Anderson, 2012; Anderson, Ho, Brackett, Finkelstein, & Laffel, 1997; Wiebe et al., 2005). Ellis and colleagues (Ellis, Templin, Naar-King, & Frey, 2008) contributed an important clarification of the construct of "parental monitoring" with respect to chronic illness, Furthermore, Martire and Helgeson (2017) made an important distinction between" parental involvement" in illness management and "parental controlling behavior" and "parental autonomy support." Because in this chapter we are addressing family influences on children with T1D from infancy through adolescence, we will focus this section on "parent involvement" defined as parent behaviors that take some responsibility for remembering diabetes management tasks, for executing diabetes management tasks, or for acting on the information learned from diabetes management tasks, such as from blood glucose monitoring.

Greater collaborative involvement or "teamwork" between caregivers and adolescents has been documented to be related to improved glycemic control (Anderson et al., 1997, 2009; Berg et al., 2008; Wiebe et al., 2005). Parental responsibility for T1D management tasks declines over the adolescent years, which can be a risk factor for poor adherence and glycemic control if parental involvement declines before the child or adolescent has the maturity and motivation to manage T1D more independently (Wiebe, Helgeson, Berg, 2016; Wysocki et al., 1996). When children or adolescents prematurely take on the burden of managing diabetes alone, the result is often chronic feelings of failure leading to "diabetes burnout" and a complete lack of adherence to the diabetes regimen (Anderson, 2012). In fact, Wiebe and colleagues (Wiebe et al., 2014) found that declines in parental responsibility over adolescence were associated with decreased adherence when adolescents with T1D did not have a strong sense of diabetes self-efficacy. It is important to note that several demographic factors have been found to be associated with the level of parental involvement in T1D management. Lord et al. (2015) found that adolescents living in single-parent homes and racial/ethnic minority adolescents experience less parental collaborative involvement, as well as greater parental over-involvement in diabetes management tasks.

Balancing parental involvement in T1D management with adolescent self-care autonomy is challenging. In addition to the problems of parental under-involvement discussed above, the consequences of parental over-involvement or intrusive parental involvement will also undermine adolescent adherence and glycemic control (Berg et al., 2013; Wiebe et al., 2005). Well-intentioned parental helping that is excessive or untimely and causes the youth with T1D to feel "shamed and blamed" is called "miscarried helping" (Anderson & Coyne, 1991; Harris et al., 2008). Therefore, the interpersonal challenges faced by adolescents with T1D and their parents in managing T1D with parental involvement appropriate for the adolescent's level of diabetes self-efficacy, diabetes autonomy, and diabetes skills often become a source of conflict between adolescents and parents, and as discussed below, diabetes-specific conflict in the family is consistently found to be strongly associated with poor psychosocial and health outcomes.

Diabetes-Specific Family Conflict

Hood and colleagues (Hood et al., 2006) found that report of higher levels of family diabetes-specific conflict by both youth with T1D and their parents was associated with poorer youth emotional functioning. Williams and colleagues (Williams, Laffel, & Hood, 2009) reported that for youth with T1D in poor control, both youth and parents reported increased family conflict, and furthermore, psychological distress in both parents and youth was related to increased diabetes-specific family conflict. The presence of diabetes-specific family conflict was associated with poorer youth-reported diabetes-specific quality of life as well as higher A1c in a global sample of youth with T1D (Anderson et al., 2017). These studies, based on cross-sectional designs, address the likely bidirectional relationship between family conflict and poor glycemic control and between family conflict and youth and parent psychological distress. Similar findings were reported by Rybak and colleagues (Rybak et al., 2017) who studied adolescents with T1D and parents and found that greater agreement between parents and youth on family functioning and lower diabetes-specific conflict was associated with lower HbA1c and higher health-related quality of life.

In a 6-month prospective, longitudinal study of adolescents with T1D, Ingerski and colleagues (Ingerski, Anderson, Dolan, & Hood, 2010) found that younger adolescents who took greater responsibility for diabetes management tasks and reported greater family conflict at baseline monitored their blood glucose less frequently at 6 months. In addition, for adolescents and parents who reported greater diabetes-specific family conflict at baseline, adolescents had worse glycemic control at 6 months. In a second longitudinal study of adolescents with T1D, Hilliard and colleagues (Hilliard, Guilfoyle, Dolan, & Hood, 2011) found that diabetes-specific family conflict reported by adolescents at baseline predicted deteriorations in frequency of blood glucose monitoring at 6 months and poor glycemic control at 1 year. Further reports from this group (Hilliard, Wu, Rausch, Dolan, & Hood, 2013) found higher levels of negative family communications around blood glucose monitoring, and diabetes-specific family conflict at baseline both predicted poor blood glucose monitoring adherence and poor glycemic control in adolescents 18–24 months later.

There are very few studies of diabetes-related family conflict in families living with youth with T2D. In an important qualitative study of parents of youth with T2D, St. George and colleagues found that adherence problems were consistently high in youth with T2D and that parents felt that they needed to learn more facts about T2D management, as well as positive parenting skills around diabetes management tasks (St. George et al., 2017). In one of the few quantitative studies of youth with T2D and their parents, in a 12-month study of parents of adolescents with recent-onset T2D, parent-youth conflict around normative and diabetes tasks at baseline and 6 months did not predict medication adherence at 12 months (Saletsky et al., 2014). Moreover, in racial/ethnic minority families, there are multiple challenges to the positive involvement of parents in their youth's adherence to T2D management (Anderson, 2012).

Summary and Clinical Implications

The research evidence on family influences in pediatric diabetes reviewed here documents the strong bidirectional relationships between parent behavior and emotional and health outcomes in youth with T1D. There is consensus that a warm and supportive parenting style whether measured by general or diabetes-specific measures with clear and realistic expectations for youth behavior is linked to optimal psychosocial functioning in youth with T1D, to good adherence, and to optimal glycemic control. Harsh, critical family interactions are associated with poor behavior and health outcomes in youth with T1D. Parental symptoms of depression and anxiety are closely tied to greater perceived burden of diabetes.

The longitudinal studies reviewed document that vicious cycles of negative family behavior and family conflict can begin early in the disease course and drive poor youth outcomes. The research also shows that youth who have public insurance, live in homes with a large ratio of children to parents or with single parents, have low family SES, or have parents with lower literacy skills have poorer diabetes health behaviors and outcomes. Cross-sectional and qualitative studies have begun to shed light on modifiable factors that mediate the relationships of some of these demographic and social factors with outcomes. These factors include adherence behavior, family conflict, insulin regimen, parental involvement in diabetes management, and the quality of diabetes education.

While much research has documented racial/ethnic disparities in health outcomes and, to a lesser extent, disparate emotional outcomes, few quantitative studies have examined the role of general or diabetes-specific family influences on outcomes of minority youth. This lack of research may likely be due to the relatively smaller number of minority youth with T1D and because it is only recently that the number of youth with T2D has been sufficient to allow adequate study. Multi-site studies with large numbers of minority youth with T1D and T2D are needed to determine whether general or diabetes-specific aspects of family factors or both play a role in disparities in diabetes adherence and health outcomes (Butler, 2017).

To move the field of family influences in pediatric diabetes forward, future studies must broaden the concept of family to include fathers and siblings. More longitudinal and observational studies will also help to advance the field. Cross-sectional studies have little promise of contributing any new information at this time. Prospective studies using naturalistic observational methods to assess family and youth behavior are needed. More studies that use both generic and diabetes-specific measures of family interactions are needed.

The research findings reviewed here suggest several lessons for the clinical care of youth and families living with diabetes:

- At diagnosis, screen mothers and fathers for symptoms of depression and anxiety, and refer for counseling those parents who screen above clinically significant cutoff levels.
- At regular intervals, screen parents for perceived burden of diabetes management, and provide resources and referrals for parents endorsing high levels of diabetes burden.
- Routinely screen parents of youth with T2D for stressors and stressful life events.
- Periodically define and role-play how an authoritative parenting style works with respect to diabetes management tasks (for both challenges and for strengths) across child and adolescent development.
- Regularly encourage developmentally appropriate parent involvement in diabetes management tasks. Cultural sensitivity should be used when addressing parent involvement in racial/ethnic minority families.
- At every clinical encounter, assess for diabetes-specific family conflict, work to resolve conflict if there are modifiable factors involved (especially around unrealistic parental expectations for blood glucose levels or youth behavior), and if conflict is severe and entrenched into family routines, refer for counseling.

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Chapter 10
Friend and Peer Relationships Among Youth with Type 1 Diabetes

Meredith Van Vleet and Vicki S. Helgeson

Adolescence is an interesting developmental stage in which individuals begin to establish independence from parents, and peer and friend relationships take a more prominent role. Extensions of attachment theory stipulate that while children turn to their parents for sources of support, belonging, and behavioral norms, individuals gradually transfer some of these responsibilities to their peers during adolescence (Allen & Land, 1999). Correspondingly, research has found adolescents spend more time with their peers (Larson & Verma, 1999) and have strong desires to develop a close friend group at this age (Collins, Gleason, & Sesma, 1997). Because friendships and peer relationships become more important in adolescence, such relationships are likely to influence adolescents' well-being and behavior. For adolescents with type 1 diabetes, these relationships may not only impact psychological well-being but also self-care behavior and, subsequently, health outcomes.

Self-care regimens for individuals coping with type 1 diabetes are exceptionally complex, involving frequent blood glucose testing, administering insulin, monitoring one's diet, and consistent exercise. Adherence to this regimen prevents hypoglycemia or hyperglycemia in the short term and serious complications (including heart disease, kidney disease, nervous system disease, and lower limb amputation) in the long term (Hood, Peterson, Rohan, & Drotar, 2009). In childhood, the brunt of these self-care responsibilities is often managed by parents. As children mature into adolescents, they begin to take a more active role in their self-care. This is often a difficult transition for adolescents (Holmes et al., 2006). Not surprisingly, research has found glycemic control is poorer at this developmental stage (Greening, Stoppelbein, Konishi, Jordan, & Moll, 2007).

Given that peer and friend relationships assume a new importance during adolescence when self-care and glycemic control become problematic for individuals with type 1 diabetes, it is important to investigate the influence of such relationships on well-being and self-care. Friends or peers may exert positive influences on well-being and self-care by providing emotional support intended to make adolescents feel loved, cared for, and good about themselves or by providing instrumental support, such as offering advice or physical assistance when needed. Such support may be directed toward the adolescents' diabetes or be more general (i.e., not specifically related to diabetes). Conversely, peers

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M. Van Vleet · V. S. Helgeson (✉)
Psychology Department, Carnegie Mellon University, Pittsburgh, PA, USA
e-mail: vh2e@andrew.cmu.edu

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and friends can also exert negative influences on well-being and self-care if they are a source of conflict. Peers may directly interfere with adolescents' self-care. Conflict that is unrelated to diabetes in friendships and peer relationships may also elicit psychological distress and indirectly impair self-care. In other words, friendships and peer relationships are likely to be sources of support and conflict, which can either facilitate or hinder well-being and self-care. We review work in this area and summarize relations of friend or peer relationships to psychological well-being and diabetes outcomes.

Literature Search

We identified peer-reviewed journal articles investigating links between friend or peer relationships and psychological and diabetes outcomes among adolescents with type 1 diabetes. Following procedures outlined in a previous review in this area (Palladino & Helgeson, 2012), we selected 1990 as the earliest year of publication for our literature review. Self-care recommendations became much stricter at this time, because of findings from the Diabetes Control and Complications Trial (DCCT, 1993). Thus, research focused on diabetes self-care before this time period is not comparable to more recent research. First, we identified articles previously discussed in a literature review conducted by one of the co-authors which focused on links of friend and peer relationships to diabetes self-care and glycemic control (Palladino & Helgeson, 2012). Second, we identified additional articles focused on these topics that were published since the previous review article was written (from 2010 to 2016). Third, we built on this previous review by identifying articles that examined relations of friend and peer relationships to *psychological* outcomes among adolescents with diabetes. Thus, articles were included in our review if they occurred between 1990 and 2016, involved a sample of adolescents or emerging adults with type 1 diabetes (under 25 years old), and studied links between peer or friend relationships and psychological health outcomes, diabetes self-care, or glycemic control.

Searches were conducted in PsycINFO and MEDLINE. Search terms used included (a) either "peer" or "friend"; (b) "adolescents," "teens," or "children"; (c) "diabetes," "diabetic," or "1DDM"; and (d) "self-care," "adherence," "compliance," "A1c," "glycemic control," "depression," "well-being," "adjustment," or "stress." All articles needed to include at least one keyword from each of the groups described above. This yielded a total of 162 separate literature searches. In addition to the 24 articles identified in a previous review of this literature (Palladino & Helgeson, 2012), 34 additional articles were identified in the literature searches. After further review of these 34 articles, 8 met criteria for inclusion in our review. Articles most often did not fit inclusion criteria because they did not include measures of friend or peer support or conflict. This resulted in a total of 34 articles included in our review.

The Current Review

Below we review findings from studies investigating links of friend or peer relationships to psychological well-being and diabetes outcomes among children and adolescents with type 1 diabetes. First, we present studies that focus on friend or peer support. We organize these studies according to whether they assess *general* friend or peer support (support that is not specific to diabetes self-care contexts) or *diabetes-specific* support (e.g., support focused on diabetes self-care). It should be noted that, unless otherwise specified, the support scales used in the reviewed studies involved aggregates of both emotional support (support intended to make recipients feel better emotionally) and instrumental support (support involving provision of tangible assistance or advice) such that the effects of one form of support could not be distinguished from the other. Second, we summarize research that examines friend or peer conflict. As with the previous section, we differentiate between studies that examine general friend conflict from those that investigate links between diabetes-specific friend conflict and outcomes. We focus on two sets of outcomes: psychological well-being (e.g., depression, perceived stress, risk behaviors) and diabetes outcomes (self-care, glycemic control). Unless noted otherwise, studies are cross-sectional and do not include covariates in analyses.

General Support from Peers and Friends

Below we review literature examining relations of general peer or friend support (support not specific to diabetes contexts) to psychological and diabetes outcomes. Unless otherwise specified, all studies either employed the Perceived Social Support from Friends Questionnaire (Procidano & Heller, 1983) or Berndt and Keefe's (1995) friendship questionnaires to assess friend support.

Psychological Outcomes Ten studies examined relations between general friend or peer support and psychological outcomes. Of these studies, five revealed links between general peer support and less psychological distress. In a sample of 64 children (ages 7–15) attending diabetes camp, more positive peer relations (feeling less lonely, more socially adequate, and having higher peer status) were linked with better diabetes adjustment (Kager & Holden, 1992). Similarly, in a sample of 66 adolescents (*M* age = 14 years), general perceived peer support, measured with four items from the Norbeck Social Support Questionnaire (Norbeck, Lindsey, & Carrieri, 1983) reworded to reflect all of one's friend and peer relationships, was related to better diabetes adjustment (Thomas, 1997). A survey study of 34 children (6–12.4 years old) and 41 adolescents (12.5–16 years old) found less friend support was related to greater internalizing and externalizing symptoms (Varni, Babini, Wallander, Roe, & Frasier, 1989). Children's peer support accounted for 46% of the variance for internalizing symptoms and 35% of the variance for externalizing symptoms, and adolescent peer support explained 54% of the variance for internalizing symptoms and 25% of the variance for externalizing symptoms. In longitudinal work, general friend support reported in one's senior year of high school predicted decreases in perceived stress (but not depression) 1 year later among a sample of 117 emerging adults (Helgeson et al., 2014a).

The fifth study was a longitudinal investigation that linked greater combined peer and family support with less depression 6 months later, controlling for sex, socioeconomic status (SES), and illness duration (Skinner & Hampson, 2000). Increases in combined family/peer support from year 1 to year 2 were also linked with less depression and greater well-being at the 6-month follow-up. However, given that the authors combined peer support and family support into a composite measure, the effects of support from peers cannot be disentangled from support provided by family.

Three studies revealed more complicated relations between general friend support and psychological outcomes. In an ecological momentary assessment (EMA) study (Helgeson, Lopez, & Kamarck, 2009), adolescents between the ages of 13 and 16 first completed baseline measures of general friend support. Then, over the course of 4 days, adolescents reported every 2 hours whether they interacted with a friend and the extent to which the interaction was enjoyable or upsetting. Baseline measures of general friend support and an aggregate of daily enjoyable interactions with friends were unrelated to psychological outcomes. However, sex interacted with adolescents' aggregates of enjoyable interactions over the 4-day period in predicting depressive symptoms. Specifically, enjoyable interactions with friends were more strongly linked with fewer depressive symptoms for females than males. A longitudinal study of adolescents (11–13 years) found no association between general friend support and psychological well-being 1 year later, controlling for body mass index (BMI), pubertal stage, and parents' social status (Helgeson, Reynolds, Escobar, Siminerio, & Becker, 2007). Again, sex and general friend support interacted in predicting psychological well-being. In this case, friend support was more strongly linked with better psychological well-being for *males* than females in this study. Further longitudinal work with the same sample at age 17 found that friend support interacted with parent control in predicting alcohol use 1 year later (Helgeson et al., 2014a). When parent control was high, alcohol use increased from year 1 to year 2—except when emerging adults reported high friend support. This suggests that friend support buffered the negative relation of parent control to alcohol use.

Two studies revealed no association between friend or peer support and psychological outcomes. In a study involving the same emerging adult sample described in the previous paragraph, general friend support at age 12 was unrelated to depressive symptoms, alcohol use, or smoking at age 19 (Helgeson et al., 2014b). Because friends are likely to change between age 12 and age 19, it may not be surprising that friend support at age 12 did not predict outcomes at age 19. Another study, involving a sample of 74 adolescents who varied widely in age (12–18 year), found general peer support was unrelated to depression, controlling for sex, SES, and illness duration (Skinner & Hampson, 2000).

Summary Overall, there is evidence that general friend support is associated with enhanced psychological well-being, but findings are not consistent across studies and some relations are complicated. It is important to note, however, that one of the five studies that found general friend support to be related to psychological health combined friend and family support into a single measure—obscuring the unique effects of friend support and family support. Three studies revealed more complicated relations between friend support and psychological well-being. Two found that sex played a role in the relations between friend support and psychological well-being, but this role was inconsistent across the two studies. Finally, one found parent control played a role in the link between friend support and psychological well-being. Taken together, the literature in this area provides suggestive evidence that general friend support is linked with psychological well-being among youth with diabetes. This research, however, hints that individual differences or environmental factors (sex, parent control) may play a role in the relation between friend support and psychological outcomes.

Diabetes Outcomes Seven studies examined the association of general friend or peer support to diabetes self-care. Support was related to better self-care in three of these studies. Specifically, greater general peer support was related to better dietary adherence but unrelated to insulin administration or blood glucose testing in a sample of adolescents who were 12–18 years old (Skinner & Hampson, 1998). Likewise, in a follow-up of this sample, peer support was combined with family support and was linked to one aspect of self-care. Specifically, greater combined peer/family support and increases in peer/family support were linked with better dietary adherence but were unrelated to insulin administration or blood glucose testing 6 months later (Skinner & Hampson, 2000). As mentioned earlier, the combined peer/family support measure is problematic in interpreting these findings. In an investigation by Thomas (1997) involving two samples of adolescents ($n = 89$; M age = 14 years), one found no association between general peer support and diabetes self-care outcomes, but the second ($n = 66$) linked greater general peer support to greater diabetes adherence, but not adherence when placed under social pressure (as measured in questionnaires). General peer support was also unrelated to adolescents' daily reports of exercise, injection regularity, dietary adherence, or frequency of testing one's blood glucose in telephone interviews over the course of 6 days.

More complex relations between friend support and self-care emerged in two investigations, the latter of which involved multiple publications and analyses. Baseline measures of friend support and enjoyable friend interactions were unrelated to self-care in the EMA study previously described (Helgeson et al., 2009). However, sex interacted with enjoyable friend interactions in predicting self-care, such that enjoyable interactions were more strongly linked to better self-care for females than males. In a sample of emerging adults, greater general friend support in one's senior year of high school had no relation to self-care 1 year later, but friend support interacted with parent control in predicting self-care (Helgeson et al., 2014a). Friend support helped to buffer the impact of low parent controlling behavior on self-care; that is, friend support predicted better self-care in the absence of parent controlling behavior. Two other longitudinal investigations involving the same sample found no relationship between general friend support at age 12 and self-care at age 13 (Helgeson et al., 2007) or 19 (Helgeson et al., 2014b).

Nine studies investigated the relation of general friend support to glycemic control. General friend or peer support was unrelated to glycemic control in six of these studies (Helgeson et al., 2007, 2014a; Helgeson et al., 2009; Kager & Holden, 1992; Thomas, 1997 Study 1 and Study 2). General friend support was related to *poorer* glycemic control in three studies. In a longitudinal study, friend support was related to poorer glycemic control in cross-sectional analyses, but did not predict *changes* in glycemic control over the course of 2 years (Helgeson, Reynolds, Siminerio, Escobar, & Becker, 2008). In a follow-up of this sample, the same pattern emerged. Friend support was related to poorer glycemic control over the span of 4 years (controlling for age, method of insulin treatment, pubertal stage, parent SES, and BMI), but did not predict *changes* in glycemic control over this time period (Helgeson, Siminerio, Escobar, & Becker, 2009). In a different evaluation of these same youth, general friend support at age 12 was associated with poorer glycemic control 7 years later (Helgeson et al., 2014b).

Summary There is little evidence that general friend support is associated with better diabetes outcomes. Three studies found friend support was related to better self-care, but all three studies showed links to only one of several self-care behaviors and one of these studies combined friend and family support into a single measure. Two studies painted more complicated relations between general friend support and self-care, suggesting other individual difference variables or environmental factors (i.e., sex, parental control) play a role in this relation. Collectively, these studies provide weak evidence that general friend support is related to better self-care.

There is also no evidence that general friend support is protective in terms of glycemic control. Six of nine studies found no association between general friend support and glycemic control, and three studies found opposite relations. These three studies imply that friend support is problematic for glycemic control.

Diabetes-Specific Support from Friends and Peers

Here we summarize research examining relations of diabetes-specific support from friends and peers to psychological and diabetes outcomes. Measures of diabetes-specific support were more heterogeneous than general measures of support. Two studies adapted the Diabetes Family Behavior Checklist (Schafer, McCaul, & Glasgow, 1986) for use with peers. Several studies measured diabetes-specific support with the Diabetes Social Support Inventory (La Greca, Auslander et al., 1995). Unless noted otherwise, studies reviewed below used one of these two measures.

Psychological Outcomes Little work has examined links between diabetes-specific support provided by friends and psychological health outcomes. Skinner and Hampson (1998, 2000) found no association between diabetes-specific peer support and depression. Likewise, diabetes-specific friend support was also unrelated to well-being in a sample of 55 Spanish adolescents who varied widely in age (12–19 years; de Dios, Avedillo, Palao, Ortiz, & Agud, 2003). Work by Thomas (1997) revealed a complex, indirect link between diabetes-specific peer support (measured with the diabetes peer support subscale of a modified version of the Diabetes Family Behavior Scale; McKelvey et al., 1993) and psychological well-being. In an investigation involving 66 adolescents (*M* age = 14 years), greater comfort with reaching conflict resolutions with friends predicted disclosing more about diabetes to peers which, in turn, predicted greater diabetes-specific warmth and caring from peers and, ultimately, better diabetes adjustment (Thomas, 1997).

Summary Two of the three studies investigating relations of diabetes-specific support to psychological outcomes found no associations. The other revealed a complex, indirect link involving comfort with resolving conflict with friends and diabetes self-disclosure. Overall, this work suggests that links between diabetes-specific support and psychological outcomes may be indirect, but more work is needed in this area before conclusions can be drawn.

Diabetes Outcomes Twelve studies investigated the impact of diabetes-specific friend support on diabetes outcomes. Five empirical studies and two qualitative studies suggest associations between diabetes-specific support and better self-care. Qualitative work found adolescents who had better compliance reported that their friends "silently" supported their self-care (accommodated diabetes self-care, provided reminders about self-care) or had no effect on their self-care (Kyngas, Hentinen, & Barlow, 1998). Other interview work suggested peer acceptance of diabetes helped teenagers integrate their self-care demands into their daily routine (Karlsson, Arman, & Wikblad, 2008).

In quantitative work, a study of 96 adolescents (ages 10–16 years) with poor metabolic control (HbA1c $> 8\%$) found peer support was linked with better diabetes management after controlling for externalizing symptoms, family and provider relations, and age (Naar-King, Podolski, Ellis, Frey, & Templin, 2006). Likewise, illness-specific friend support was also related to better adherence in a sample of 300 Finnish adolescents coping with diabetes and other chronic illnesses (Kyngas & Rissanen, 2001). However, the researchers did not distinguish between adolescents who had diabetes and adolescents who had other chronic illnesses in this study. Skinner and Hampson (1998) linked diabetes-specific peer support with better blood glucose monitoring, but not insulin administration. Consistent with these findings, Bearman and La Greca (2002) found diabetes-specific friend support was unrelated to *overall* adherence but that friend support specifically focused on blood glucose testing was related to more frequent blood glucose monitoring. In Thomas' (1997) dissertation work, Study 2 revealed several complex, indirect links between perceived diabetes-specific peer support and diabetes self-care outcomes. Specifically, comfort with conflict resolution with peers predicted greater diabetes disclosure, which predicted diabetes-specific peer warmth and caring which, in turn, predicted greater compliance. Similarly, through the paths of comfort with conflict resolution and diabetes disclosure, diabetes-specific peer warmth and caring predicted less diabetes mismanagement, greater adherence in social pressure situations, and greater injection regularity.

However, five studies found no association between diabetes-specific friend or peer support and self-care. Two studies with wide age ranges found diabetes-specific support was unrelated to adherence (La Greca, Auslander et al., 1995; Pendley et al., 2002). When asked to imagine a series of adherence scenarios, adolescents' (ages 10–18 years old) diabetes-specific friend support was unrelated to anticipated self-care difficulties in scenarios (Hains et al., 2007). In Study 1 of Thomas' dissertation work (1997), diabetes-specific peer support was unrelated to self-care or frequency of blood glucose testing in a sample of 89 adolescents. Finally, an intervention designed to increase peer support and diabetes knowledge had no impact on self-care (Greco, Pendley, McDonell, & Reeves, 2001). However, this sample was quite small ($n = 21$).

Six studies examined associations between diabetes-specific support and glycemic control, and this work has produced mixed results. Two studies found no association between diabetes-specific support and glycemic control (de Dios et al., 2003; Thomas, 1997). Other work found no association between diabetes-specific peer support (measured by questionnaire) and glycemic control but found adolescents who reported more peers in their diabetes support team had better glycemic control (Pendley et al., 2002).

More complicated relations between diabetes-specific friend support and glycemic control were revealed in three studies. In Study 2 of Thomas' dissertation work (1997), an indirect path was revealed between diabetes-specific peer warmth and caring and glycemic control, such that comfort with conflict resolution with friends predicted greater diabetes self-disclosure to friends, which led to greater diabetes-specific peer warmth and caring which, in turn, predicted better glycemic control.

Hains et al. (2007) found no direct association between friend support and glycemic control. However, friend support moderated the link between diabetes stress and glycemic control in a peculiar way. Rather than buffering or weakening the relation between diabetes stress and poor glycemic control, the relation was *stronger* when friend support was high. Another unanticipated finding was a link between satisfaction with diabetes-specific school support (which included one item measuring support from friends in class) and poorer glycemic control 6 months later (Lehmkuhl & Nabors, 2008). In addition, glycemic control at baseline interacted with friend support in predicting glycemic control at follow-up, such that friend support was related to better glycemic control at follow-up only for those who had lower HbA1c at study start. It is important to note, though, that this study did not control for baseline measures of glycemic control. Furthermore, since the support measure also included support provided from others who were not friends (e.g., nurses, teachers), it cannot be determined the extent to which this complicated link reflects support provided by friends versus support provided by others.

Summary Research investigating links between diabetes-specific friend support and self-care is mixed. Five empirical studies and two qualitative studies suggest friend support is associated with better self-care. One of these studies revealed a complicated, indirect link involving comfort with conflict resolution and diabetes self-disclosure in diabetes-specific peer support predicting self-care. Yet, diabetes-specific support provided by friends and peers was unrelated to self-care in four other studies, and an intervention that increased peer support found no effect on self-care. In sum, findings from this work provide weak evidence at best that diabetes-specific friend support is associated with better self-care.

Overall, the literature found diabetes-specific friend support was unrelated to glycemic control. Three studies revealed no link between support and glycemic control. One study revealed a link between a less traditional measure of diabetes-specific friend support (but not a traditional self-report measure) and better glycemic control. Three other studies revealed complex, indirect, or unexpected associations between friend support and glycemic control. One study found that comfort with conflict resolution and diabetes self-disclosure predicted peer support which, in turn, predicted glycemic control. One study found that when friend support was high, diabetes stress was more strongly associated with poorer glycemic control which is opposite of stress-buffering predictions. Finally, one study found that diabetes-specific friend support predicted better glycemic control for those who had better glycemic control at the beginning of the study. In sum, empirical evidence linking diabetes-specific friend support to glycemic control is scarce and inconsistent.

General Conflict with Peers and Friends

Studies investigating links between general friend conflict and outcomes are described below. These investigations measured friend conflict with the Test of Negative Social Exchange (Ruehlman & Karoly, 1991) or the negative subscales from Berndt and Keefe's friendship questionnaire (1995) to assess general friend conflict, unless stated otherwise.

Psychological Outcomes Research has revealed somewhat consistent links between general friend conflict and poorer psychological health. Of the five studies to examine links between general friend conflict and psychological outcomes, four found conflict was associated with greater psychological distress. In longitudinal work with adolescents, general friend conflict was linked with poorer psychological well-being and declines in well-being 1 year later (Helgeson et al., 2007). Poorer peer relationships (measured with two items from the Quality of Life Scale for Children and Adolescents; Wu, Liu, & Meng, 2006) were also linked with more depression in a study of 136 children (ages 8–19) with diabetes in China (Guo et al., 2012). Daily upsetting interactions with friends were related to more depressed mood, anxiety, and anger in an EMA study of adolescents (Helgeson et al., 2009). Sex also interacted with aggregate measures of upsetting interactions with friends in predicting depressive symptoms. Specifically, conflict was more strongly associated with more depressive symptoms for female than male adolescents. In longitudinal work (Helgeson et al., 2014a), general friend conflict among high school seniors was related to increases in depressive symptoms, perceived stress, alcohol use, binge drinking, a greater drive for thinness, and more bulimic symptoms 1 year later. Parent support buffered the negative effects of general friend conflict on bulimic symptoms. That is, friend conflict was linked with increases in bulimic symptoms when parent support was low. However, other work involving this same sample found general friend conflict reported at age 12 was unrelated to depression, stress, or risk behavior at age 19 (Helgeson et al., 2014b). Again, in this study, it may be unreasonable to expect that friends at age 12 are the same friends at age 19.

Summary Taken together, the findings from this work provide moderate evidence that general friend conflict is linked with a variety of indicators of psychological distress, including depressive symptoms, perceived stress, negative mood, and poorer well-being. Two studies revealed that individual differences and environmental factors (i.e., sex and parental support) influenced the relations between general friend conflict and psychological distress. Overall, empirical work indicates general friend conflict is associated with psychological distress.

Diabetes Outcomes Four studies examined links between general friend conflict and diabetes self-care. In one study (Helgeson et al., 2009) cross-sectional measures of general friend conflict were related to worse self-care among a sample of adolescents between 13 and 16 years old. However, EMA data obtained in this study revealed no associations between aggregates of upsetting interactions with friends over a 4-day period and diabetes self-care. In a 7-year longitudinal sample of emerging adults (Helgeson et al., 2014b), general friend conflict at age 12 predicted poorer self-care at age 19. Two longitudinal investigations of the same sample showed no links between general friend conflict and self-care 1 year later among 12-year-old adolescents (Helgeson et al., 2007) or 17-year-old adolescents (Helgeson et al., 2014a).

Only four studies investigated links between general friend conflict and glycemic control. Two studies revealed associations between general friend conflict and poorer control. One longitudinal study of adolescents found general friend conflict predicted decreases in glycemic control over 4 years (Helgeson, Siminerio, et al., 2009). Other work revealed a cross-sectional link between greater friend conflict and poorer glycemic control (Helgeson, Lopez, et al., 2009). Furthermore, sex interacted with friend conflict in predicting glycemic control, indicating that friend conflict was especially predictive of poorer glycemic control for females compared to males. Yet, EMA data from this same study found no association between an aggregate measure of upsetting interactions with friends and glycemic control. Two longitudinal investigations found general friend conflict was unrelated to glycemic control 1 year later (Helgeson et al., 2014a) or 7 years later (Helgeson et al., 2014b).

Summary Only five studies have examined links between general friend conflict and diabetes outcomes. The work in this area is limited in part by the fact that all of the data come from one laboratory, with three of the four publications being based on the same dataset sampled at different points in time. Although work in this area has been longitudinal and statistically sophisticated, links between conflict and self-care are inconsistent. Half of this work has linked conflict with poorer self-care, while the other half has found conflict was unrelated to self-care. Therefore, it is difficult to interpret findings from this literature as a collective. At best, this work provides suggestive evidence that friend conflict impedes diabetes self-care.

Likewise, the four studies from the same lab examined links between general friend conflict and glycemic control. Two studies (involving the same sample of emerging adults) found associations between general friend conflict and poorer glycemic control, and two studies found no such links. Overall, these findings provide only suggestive evidence that general friend conflict is related to poorer glycemic control.

Diabetes-Specific Conflict with Friends and Peers

Next, we review the literature linking diabetes-specific conflict with peers and friends with psychological and diabetes outcomes. The vast majority of this research was qualitative in nature and did not include measures of diabetes-specific conflict. Instead the literature largely investigated psychological and diabetes outcomes of adolescents who perceived conflict with their friends and peers.

Psychological Outcomes Research examining links between diabetes-specific friend conflict and psychological health outcomes has been sparse. When asked to predict how their friends and peers would react in hypothetical diabetes adherence scenarios, adolescents who reported their friends and peers would react negatively also reported higher overall diabetes stress (Hains et al., 2007). Relatedly, adolescents (ages 10–18) who reported higher diabetes-specific interpersonal/peer stress also reported higher *overall* diabetes stress (Berlin, Rabideau, & Hains, 2012). To the best of our knowledge, no other work has examined such links.

Summary Only two cross-sectional studies examined relations between diabetes-specific friend conflict and psychological outcomes. Both studies suggest a relation between diabetes-specific friend conflict and psychological distress, but more research is needed in this area for conclusions to be drawn.

Diabetes Outcomes Eight studies (five qualitative and three quantitative) investigated relations between diabetes-specific friend conflict and self-care. The five qualitative studies indicated that adolescents often perceive peers as an obstacle to their self-care. In interviews with a small sample ($n = 20$) of adolescents adjusting to a new insulin pump, peer interactions were commonly reported as problematic for self-care (Berlin et al., 2006). Likewise, teenagers commonly reported situations involving peers (especially interpersonal peer conflict and eating at school) as obstacles to their dietary adherence (Schlundt et al., 1994). Similarly, when a sample of adolescents was interviewed about their friends' behavior in self-care contexts, describing one's friends as dominant was associated with poor adherence (Kyngas et al., 1998). Work focused on identifying barriers to diabetes management found that adolescents (13–17 years old) and parents of adolescents reported peer interactions as one such important barrier. However, parents of children (8–12 years old) did not find peer interactions to be a barrier to self-care (Cox et al., 2014). A study assessing interest and feasibility of a peer-mentoring program for adolescents with diabetes echoed these findings. One third of their sample of adolescents (ages 13–18) reported social barriers to their self-care—particularly embarrassment over testing their blood glucose in social settings. In contrast, young adults (ages 19–25) in this study reported no such barriers (Lu et al., 2015).

In quantitative work, a study in which adolescents were presented with scenarios in which they had to choose between being adherent and acting in a way to satisfy peers, older adolescents (ages 15–17) chose less adherent responses than younger adolescents (ages 11–14) or children (ages 8–10), despite the fact that they had more advanced problem-solving skills. Moreover, older adolescents also recognized that they *should* be adherent in the scenarios, even though they chose otherwise (Thomas, Peterson, & Goldstein, 1997). Relatedly, adolescents who predicted that their friends and peers would react negatively in hypothetical self-care scenarios also anticipated more adherence difficulties (Hains et al., 2007). Additional work found that adolescents who had greater extreme peer orientation (EPO, an individual difference variable involving greater susceptibility to peer pressure) also had poorer self-care (Drew, Berg, & Wiebe, 2010).

Five studies investigated links between diabetes-specific friend conflict and glycemic control. One study found adolescents who identified peer interactions as a barrier to their self-care also had poorer glycemic control (Cox et al., 2014). Similarly, adolescents who expected friends and peers to react negatively in hypothetical self-care scenarios had poorer glycemic control (Hains et al., 2007). This association was mediated by greater anticipated adherence difficulties and diabetes stress. In related work, higher EPO was associated with poorer glycemic control (Drew et al., 2010). The quality of one's relationship with one's parents moderated this link, indicating that adolescents who had better relationships with their parents and lower EPO had better glycemic control. However, one study found no association between diabetes-specific interpersonal/peer stress and glycemic control (Berlin et al., 2012). Likewise, another study found no association between choosing to be nonadherent in scenarios pitting adherence against peers' desires and glycemic control (Thomas et al., 1997).

Summary As a collective, work examining associations between diabetes-specific friend conflict and diabetes outcomes has been qualitative. Six studies investigating associations between diabetes-specific friend conflict and self-care suggest that greater conflict is associated with poorer self-care. Three of these studies suggest that age is likely to play a role in the relation of diabetes-specific friend conflict to self-care, indicating older adolescents' peer interactions are more problematic to their self-care than those of children or emerging adults. Less consistent relations were found when it came to diabetes-specific friend conflict and glycemic control. Of the five studies investigating links between diabetes-specific conflict and glycemic control, two suggest conflict with friends and peers is related to poorer control, and two revealed no link between conflict and glycemic control. One study indicated that relationships with parents and susceptibility to peer pressure both matter in predicting glycemic control. This research provides very weak evidence that diabetes-specific friend conflict is associated with poorer glycemic control and hints that other important individual differences and environmental factors (EPO, relationships with parents) play a role in the link between conflict and glycemic control.

Discussion

Although relationships with friends and peers are thought to play a large role in adolescence, little work has examined associations between such relationships and psychological well-being and diabetes outcomes for adolescents with type 1 diabetes. To date, the work in this area suggests that general friend support may be beneficial to adolescents' psychological well-being and (less consistently) self-care. There are several reasons why this may be the case. Support received from friends may buffer against stress (Cohen & Wills, 1985), which is detrimental to health and well-being. Friend support may also communicate feelings of acceptance, belonging, and social competence, which may in turn improve psychological well-being. These proposed improvements in self-perceptions and reductions in stress may boost one's perceived ability to carry out self-care responsibilities and lead to actual implementation of self-care.

Surprisingly, the research reviewed suggests general friend or peer support is either unrelated to glycemic control or may be detrimental to adolescents' glycemic control. Making sense of this counterintuitive pattern is more difficult. Adolescence is characterized as a time of fluctuations in glycemic control (Greening et al., 2007). This has been explained as both a result of poorer self-care (La Greca, Swales, Klemp, Madigan, & Skyler, 1995) and biological changes (Goran & Gower, 2001). These fluctuations may partially explain the lack of consistent links between friend support and glycemic control, but they do not explain why support would be associated with *poorer* glycemic control. One potential explanation is that when adolescents have high-quality, supportive friendships, they become immersed in their friendships to the point that they simply become distracted from their self-care routines, resulting in poorer glycemic control over time. On the other hand, general friend support could have negative consequences on glycemic control because the support provided is of low quality. Friends are likely to have less practice in providing support than the adults in adolescents' lives. As a result, support attempts by friends may be clumsy, may be perceived as unhelpful, or unintentionally undermine effective self-care and glycemic control.

Friend or peer support focused on adolescents' diabetes was unrelated to psychological outcomes. This may be the case because, unlike general forms of support, diabetes-specific support draws attention to the adolescent's illness and may make adolescents feel different from their friends. While general forms of support are likely to communicate feelings of acceptance and belonging (and fitting in with one's friends), diabetes-specific support may unintentionally single out adolescents with diabetes. Given that adolescents with type 1 diabetes often express a desire to feel "normal," this type of support may be a double-edged sword (Commissariat, Kenowitz, Trast, Heptulla, & Gonzalez, 2016). Moreover, friends may not be the most knowledgeable of network members when it comes to providing instrumental diabetes-specific support. Ill-informed or miscarried support from friends may make adolescents feel misunderstood and undermine well-being.

Similar to results involving general measures of support, diabetes-specific support was inconsistently linked with better self-care. Half of this work found that support was beneficial for overall self-care, while half found support was beneficial specifically for blood glucose monitoring (but not other forms of self-care). Studies examining links between diabetes-specific support and glycemic control were inconclusive. As mentioned above, this may be the case because other adolescents may not have the necessary knowledge to provide effective diabetes-specific support.

Thus, the degree to which adolescents share their diabetes knowledge with their friends (and the accuracy of the knowledge shared) is likely to contribute to the effectiveness of friend diabetes-specific support. This idea was most strongly supported by Thomas' work (1997), which focused on the role of diabetes self-disclosure in peer relationships and its influence on psychological and diabetes outcomes. This work showed that diabetes-specific peer support influenced diabetes adjustment, self-care, and glycemic control via self-disclosure. That is, general peer support predicted greater diabetes self-disclosure which predicted greater diabetes-specific peer support and, in turn, psychological and diabetes outcomes. When peer relationships are more supportive, adolescents may disclose more to their friends about their diabetes. This disclosure leads friends to provide more diabetes-specific support, which then leads to greater psychological well-being, self-care, and glycemic control. Related qualitative work also highlights the importance of self-disclosure in the route from diabetes-specific peer support to self-care. In a diabetes camp study, adolescents with diabetes and their peers indicated that peers needed more diabetes knowledge and coaching in order to better help with self-care (Lehmkuhl et al., 2009). Relatedly, Commissariat et al. (2016) found that the majority of adolescents in their sample indicated that they were happy that they shared diabetes information with their friends, because friends became more involved in their self-care afterward (reminded them to test their blood glucose or take their insulin). These patterns hint that friends may be a valuable source of diabetes-specific support, once they are equipped with appropriate diabetes knowledge. An important vehicle through which peers are likely to acquire this knowledge is self-disclosure. Future research should further examine self-disclosure as a key antecedent to effective diabetes-specific friend support.

General friend conflict was consistently linked with psychological distress. Friend conflict is likely to be a strong source of stress, in and of itself, which may exhaust psychological resources in dealing with other ensuing stressors (diabetes related or not). Arguments or tensions with friends may communicate feelings of rejection, or not fitting in, which may undermine self-esteem. These sources of conflict may be internal (perceived or imagined) or external (explicitly communicated by friends) to adolescents. Being placed in situations in which adhering to one's self-care regimen is inconsistent with friends' plans or desires is also likely to be, itself, a source of frustration and distress.

Regarding diabetes outcomes, half of the literature found general conflict was related to poorer self-care and glycemic control, while the other half found conflict was unrelated to self-care and glycemic control. Conflict with friends may lead to worse self-care and glycemic control simply because conflict may captivate adolescents' attention and distract from their normal self-care routines. Conflict is also likely to be stressful and detract from adolescents' abilities to problem-solve in self-care contexts. Indeed, properly caring for oneself while one is dealing with the additional burden of friend conflict is likely a difficult cognitive and emotional challenge.

In comparison to the research focused on general friend conflict, the literature focused on diabetes-specific friend conflict was smaller and more qualitative in nature. Although qualitative work strongly suggests that diabetes-specific friend conflict is related to poor psychological health and poor diabetes outcomes, surprisingly few studies directly assess diabetes-specific friend conflict to examine these associations. This work found diabetes-specific conflict was linked with greater psychological distress. On the other hand, diabetes-specific conflict was less consistently linked with diabetes outcomes. Half of the literature found no association, while half revealed links between conflict and poorer self-care and glycemic control. One reason why diabetes-specific friend conflict may lead to poorer self-care and glycemic control is intentional nonadherence. When friends' wishes or plans conflict with self-care responsibilities, adolescents may intentionally stray from their self-care routines in order to appease friends. Work in this area hints that adolescents (but not children or emerging adults) may be more likely to fall prey to peer pressure in such scenarios. Again, the work reviewed in this area has been largely qualitative. More empirical work is needed in order to draw conclusions.

Moderator Variables

One reason for the inconsistent findings across the review is that there are several potential variables that may moderate the relation of friend support and conflict to psychological and diabetes outcomes. A sizeable portion of the studies reviewed indicated that relations often depended on individual difference variables or environmental factors. In particular, several studies found that sex moderated these links, typically showing that links between friend relationships and outcomes were stronger for females than males. The combination of these findings hints that females' psychological well-being and self-care are more influenced by support and conflict provided by friends and peers than males.

There are several possible explanations for these findings. First, friends may play a larger role in the lives of female than male adolescents. Second, friends may be more involved in the diabetes care of female than male adolescents. Related work suggests that females with diabetes receive more diabetes support, regardless of who is providing the support, than males (Bearman & La Greca, 2002; La Greca, Auslander et al., 1995; Skinner & Hampson, 1998; Skinner, John, & Hampson, 2000). Alternatively, females may be more influenced by their friends' or peers' opinions, acceptance, or hostility than males. Finally, it is possible that these sex differences are a reflection of friends' or peers' gender. Research has found that friendships between two females are characterized by more intimacy than friendships involving two males (Barry, Madsen, Nelson, Carroll, & Badger, 2009; Bauminger, Finzi-Dottan, Chason, & Har-Even, 2008; Linden-Andersen, Markiewicz, & Doyle, 2009; Swenson & Rose, 2009). Thus, females may be more influenced by their friendships and peer relationships because they have higher quality friendships (with other females) than males (who are more likely to have friendships with other males). These are all unanswered, intriguing questions awaiting future research.

Parent relationships are another potential moderator. Several studies reviewed indicated that adolescent relationships with friends and parents should not be considered in isolation. Positive aspects of one relationship domain appear to offset problems in the other. This makes sense, given that mid-adolescence is characterized as a period in which attachment needs and behaviors are gradually transferred to one's closest peers and romantic relationships (Allen & Land, 1999). Future research should track the degree to which parent and peer relationships work together in impacting psychological well-being and diabetes outcomes over time during this important developmental stage.

Age is also an important variable to consider in examining the links between peer and friend relationships and psychological well-being and diabetes outcomes. This review covered studies that involved children as young as 6 years old through emerging adults as old as 19 years old. Clearly, friends play a different role in the lives of children, early adolescents, and emerging adults. As adolescents grow older, their peer relationships are likely to become more complex and qualitatively different from their peer relationships in childhood. Although none of the studies directly assessed age as a moderator in the link between friend conflict and diabetes outcomes, interesting patterns emerged, hinting that age influences the link between friend conflict and diabetes outcomes. Several studies indicated that adolescents perceive more social barriers to self-care, while children (Hains et al., 2007) and emerging adults do not (Lu et al., 2015). When posed with scenarios in which their self-care needs were pitted against the wishes of their peers, older adolescents reported that they would go along with their peers or friends more often than younger adolescents—despite having more advanced problem-solving skills and a clearer understanding of the consequences of failing to adhere to their self-care regimens (Thomas et al., 1997). This set of findings suggests that peer influence on self-care may peak in older adolescence and subside over time. However, a substantial amount of work is needed in this area examining differences in these age groups and changes in the relation between peer interactions and diabetes outcomes over time.

Other individual differences are also likely to moderate associations of relationships with friends and peers to well-being and diabetes outcomes. Socioeconomic status (SES) may influence this link. Lower SES homes may include single-parent families or two parents who work long hours. If parents are absent from the home after school, adolescents may be more likely to spend those hours with friends and peers. Over time, adolescents from lower SES households may become more influenced by support and conflict within their friendships than adolescents from higher SES households. Other personality characteristics (e.g., optimism, neuroticism) are also likely to influence the strength of links between relationships with friends and psychological well-being and diabetes outcomes. Few of these potential moderator variables have been explored, leaving this an exciting avenue for future research.

Directions for Future Research

Several advancements are needed to strengthen this neglected research area. First, finer distinctions need to be made in the measurement of friend and peer support and conflict. None of the work reviewed distinguished instrumental support from emotional support provided by friends and peers, despite the fact that La Greca, Auslander, and colleagues (1995) found that peers were a greater source of emotional support than instrumental support. Instead, measures aggregated across multiple forms of support. This may explain some of the inconsistent links revealed between support and outcomes. If only emotional support is beneficial to well-being and diabetes outcomes, combining emotional support and instrumental support into a single measure may have obscured the link between emotional support and outcomes. Examining the effects of both general and diabetes-specific support in the same study would also allow researchers to determine if one form of support is more predictive of well-being and self-care than the other. This work could inform researchers designing interventions aimed to improve peer support. For instance, in the only investigation to simultaneously measure both general and diabetes-specific peer support, Thomas (1997) found general peer support led to greater disclosure, which predicted greater diabetes-specific peer support, and psychological and diabetes outcomes, in turn. This chain of relationships suggests it may be most advantageous for interventions to first focus on fostering general peer support before turning attention to diabetes-specific peer support.

Future research should also make finer distinctions regarding the relationships in which friend and peer support and conflict occur. First, very few studies distinguish between relationships with peers versus friends. One study reviewed differentiated between friend relationships and peer relationships in some of their measures (but not all) and found no difference in how adolescents expected peers versus friends to react in self-care scenarios (Hains et al., 2007). Peers are others of the same age with whom adolescents may interact on a normal basis but with whom they do not share a special bond or feel an affiliation. Friends, on the other hand, are others with whom adolescents choose to spend time and with whom they feel an emotional connection. Because adolescents are likely to care more about their friendships than relationships with peers, it seems likely that friends should matter more to one's psychological well-being and self-care than relationships with peers. On the other hand, adolescents may group others who are of the same age and who are unhelpful or a source of conflict into the category of "peer" rather than "friend." If this is the case, researchers may find that peers are the primary source of general and diabetes-specific conflict and such relationships are likely to have a negative impact on psychological well-being, self-care, and glycemic control. Friends, on the other hand, may be more supportive and assimilate adolescents' diabetes self-care needs into their plans. Friendships may even grow as a result of other adolescents' positive or benign responses to adolescents' self-care. In other words, peers may become a primary source of conflict, while friends may become a key source of support.

Empirical attention should also focus on understanding more specific friend and peer relationships and their impact on psychological and diabetes outcomes. When it comes to peer relationships, it may be difficult for adolescents to imagine a particular person or group of people when asked to imagine their "peers" (in comparison to when they are asked to think of their friends). Future research should consider studying more specific peer groups, such as classmates, teammates, or after-school activity groups, to improve the quality of participant responses and add new depth to this research area.

Among adolescents' friendships, two warrant special empirical attention. Best friends and romantic partners are likely people with whom adolescents feel particularly close. They are also likely to be the first people adolescents turn to for support or belonging. For these reasons, conflict with best friends and romantic partners is also likely to be especially difficult. Thus, support and conflict from best friends and romantic partners in particular are likely to influence psychological well-being and diabetes outcomes. However, only one study has examined relations of romantic partner support and conflict to psychological and diabetes outcomes (Helgeson et al., 2015), and no research to date has examined relationships with best friends and their associations with psychological and diabetes outcomes.

Another exciting avenue for future research is to examine friend and peer relationships with other adolescents who have diabetes. Although there is a growing body of qualitative research and work developing interventions to increase peer-to-peer support among adolescents with type 1 diabetes (Boogerd, Noordam, Kremer, Prins, & Verhaak, 2014; Hanberger, Ludvigsson, & Nordfeldt, 2013; Kichler, Kaugars, Marik, Nabors, & Alemzadeh, 2013; Markowitz & Laffel, 2011; Nordfeldt, Hanberger, & Bertero, 2010), very little work has examined the impact of peer relationships or friendships with other adolescents who have diabetes on well-being and diabetes outcomes. Relationships with friends who also have diabetes may be a tremendous source of diabetes-specific support that is of high quality. Such friends or peers know the difficulties of self-care and have the necessary knowledge to help in administration of self-care. Furthermore, they also have firsthand experience in having friends without diabetes who may intentionally or unintentionally interfere with self-care needs, validating adolescents' feelings in such circumstances. Thus, friends or peers who also have diabetes are likely to be an invaluable source of support.

In order to advance this research area, more sophisticated methods of measuring friend and peer support and conflict need to be developed. All of the work reviewed involved self-reported *perceptions* of support and conflict. More objective measures, using observational methods or a modified version of the revised class play method (Masten, Morison, & Pellegrini, 1985), would add new richness to the data and improve external validity. These more objective measures would also be advantageous in ruling out other underlying personality characteristics in explaining relations of friend and peer relationships to psychological well-being and diabetes outcomes.

Future work should investigate potential mechanisms underlying links between friend and peer relationships and outcomes. To date, Hains et al. (2007) and Thomas (1997) are the only researchers to have tested potential mechanisms. Hains et al. (2007) found that diabetes-specific conflict with peers was linked to poorer glycemic control because adolescents who perceived more peer conflict expected their peers to respond negatively to self-care demands, which increased diabetes-specific stress. Thomas (1997) found adolescents who were comfortable with resolving conflicts with friends had greater general friend support, which led them to disclose more about their diabetes to friends, which led their friends to provide more diabetes-specific support, and which ultimately predicted psychological well-being and diabetes outcomes. We suspect there are several other mechanisms that could partially explain these links. Friend support is likely to cultivate feelings of acceptance and self-esteem, which may explain links between support and psychological well-being. Diabetes-specific support may increase diabetes-specific self-efficacy either by providing tangible assistance which facilitates self-care or by instilling confidence in the adolescents' ability to take care of their own diabetes needs. This enhanced self-efficacy may, in turn, predict better self-care and glycemic control.

The mechanisms by which conflict with friends is associated with psychological and diabetes outcomes also need to be explained. Conflict with friends may lead to feelings of rejection and decreased self-esteem and, in turn, poorer well-being. Alternatively, conflict may simply consume a substantial amount of adolescents' attention and distract them from their self-care, leading to poorer self-care and glycemic control. Lansing and Berg (2014) also propose that deficits in self-regulation may underlie both poor self-management of chronic illness and interpersonal problems. All of these remain exciting untested mechanisms that may explain links between friend relationships and psychological well-being and self-care.

Finally, future work should also investigate predictors of friend support and conflict among adolescents with type 1 diabetes. Two studies have identified resiliency, agency, communion, and unmitigated agency and communion as important players in predicting general friend support and conflict. One such study found resilience (defined as high self-esteem, mastery, and optimism) was associated with greater friend support, less conflict, greater likelihood of being in a romantic relationship, and fewer romantic breakups among a large sample of emerging adults with type 1 diabetes and healthy controls (Helgeson et al., 2015). The second study, involving this same sample of emerging adults, found communal and agentic traits were linked with more friend support and less conflict, while unmitigated agentic and communal traits were associated with less support and more conflict over time. Unmitigated communion also predicted poorer diabetes health over time (Helgeson & Palladino, 2012). Thomas' work (1997) also points to social competence as a potential predictor of general peer support, finding that adolescents who had more confidence in reaching conflict resolutions with friends had greater peer support. This is, to the best of our knowledge, the only work to examine predictors of friend support and conflict among adolescents with type 1 diabetes. There are many important individual differences that are likely to impact friend support and conflict that have not been examined (e.g., self-esteem, attachment security). Furthermore, predictors of diabetes-specific friend support and conflict still remain unexplored territory.

Although researchers and adolescents alike describe friends and peers as important to well-being and diabetes self-care, the empirical work that has examined the impact of these relationships to the well-being and self-care of youth with type 1 diabetes is small. The literature thus far suggests that support provided by friends and peers is associated with better psychological well-being. For diabetes outcomes, support was less consistently linked to better self-care and was either unrelated to glycemic control or related to poorer glycemic control. Conflict was associated with psychological distress and somewhat less consistently linked to poorer self-care and glycemic control. More sophisticated work, using a variety of methods and exploring more specific relationships among peers and friends in adolescence, is needed to further expand this research area. We urge researchers to delve deeper to further understanding of these relationships, which take on new weight and meaning in adolescence. There is a wealth of information waiting to be discovered about how these important relationships may impact the health and well-being of youth with diabetes. Much exciting work lies ahead in this area.

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Chapter 11

System Overload: Interventions that Target the Multiple Systems in which Youth with Type 1 Diabetes Live

Samantha A. Barry-Menkhaus, Natalie Koskela, David V. Wagner, Reid Burch, and Michael A. Harris

Youth with type 1 diabetes (T1D) who have difficulties adhering to the medical regimen are at increased risk for suboptimal glycemic control (i.e., higher HbA1c values), medical complications during youth, and longer-term complications into adulthood (Danne et al., 2001; Group, 1993; Quittner, Espelage, Ievers-Landis, & Drotar, 2000). Though many children and adolescents with T1D encounter problems adhering to the treatment regimen and experience above-target HbA1c values (Wood et al., 2013), there is a subgroup of the pediatric T1D population who experience a multitude of life challenges that result in poorer adherence, poorer glycemic control, earlier onset of complications, and the disproportionate use of healthcare resources. This group of high-risk youth with T1D requires innovative approaches that can reduce and/or prevent the aforementioned negative health outcomes.

Some youth with T1D are vulnerable to negative diabetes-related outcomes based on individual risk factors. For example, youth with behavioral or mental health concerns are at increased risk for poor glycemic control, suboptimal adherence, and increased healthcare costs (Anderson et al., 2002; Cohen, Lumley, Naar-King, Partridge, & Cakan, 2004; Leonard, Jang, Savik, Plumbo, & Christensen, 2002; Peitte, Richardson, & Valenstein, 2004). Additionally, individuals of lower socioeconomic status (SES) and/or ethnic minority status are at high risk for diabetes-related complications (e.g., Drew et al., 2011; Willi et al., 2015), as are youth in adolescence (Harris, Hood, & Weissberg-Benchell, 2014), in emerging adulthood (Gill et al., 2014), and/or transitioning from pediatric to adult care (Lotstein et al., 2013). As such, treatments for this population would benefit from components that consider and target relevant individual risk factors.

While individual risk factors are important to consider, youth with T1D exist within complex systems. For example, family, school, and medical systems each play an important role in youth development, and functioning within and across these systems often impacts diabetes. Within the family system, parental stress, unemployment, and mental health concerns are among the family factors associated with poorer diabetes management and negative diabetes-related outcomes (Cameron et al., 2008; Harris et al., 2014; Rumburg, Lord, Savin, & Jaser, 2017; Stallwood, 2005; Whittemore, Jaser, Chao, Jang, & Grey, 2012). In addition, low levels of parental support for diabetes care, interparental conflict, and low family cohesion are also linked to inadequate diabetes management and associated health concerns (Cameron et al., 2008; Cohen et al., 2004; Hilliard, Wu, Rausch, Dolan, & Hood, 2013; Jacobson et al., 1994; Lancaster, Gadaire, Holman, & LeBlanc, 2015). Thus, treatments which

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S. A. Barry-Menkhaus · N. Koskela · D. V. Wagner · R. Burch · M. A. Harris (✉)
Oregon Health & Science University, Portland, OR, USA
e-mail: harrismi@ohsu.edu

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neglect parent- and family-level variables may be insufficient for treating many youth with T1D, especially those with high social vulnerability.

Youth with T1D are also influenced by additional systems (e.g., school, medical system) and the interactions between these various systems. For instance, in the school environment, there is a positive association between access to trained school personnel and glycemic control (Wagner, Heapy, James, & Abbott, 2006). In addition, youth who are exposed to school environments with inadequate training for employees and/or a lack of full-time trained nursing staff are likely at greater risk for negative outcomes (Hayes-Bohn, Neumark-Sztainer, Mellin, & Patterson, 2004; Hodges & Parker, 1987; Lindsay, 1987; Nabors, Lehmkuhl, Christos, & Andreone, 2003; Wysocki, Meinhold, Cox, & Clarke, 1990). Furthermore, within the medical setting, access to standard and subspecialty care (Bindman et al., 1995), continuity of providers (Rewers et al., 2002), and multidisciplinary staffing (Danne et al., 2001) are among the factors that may contribute to disparities in glycemic control across clinics. Moreover, poor quality or low frequency of interactions between the family system and the medical system (e.g., diabetes care providers) has been implicated in poorer glycemic control and more DKA admissions (Hanson et al., 1988; Jacobson, Hauser, Willett, Wolfsdorf, & Herman, 1997; Kaufman, Halvorson, & Carpenter, 1999). Given that youth with a combination of risk factors within and across a number of systems are a particularly vulnerable group (Wagner, Stoeckel, Tudor, & Harris, 2015), treatments which can effectively impact these contexts and related interactions should be well positioned to improve diabetes management and associated outcomes (e.g., health, care, medical expenditures).

Behavioral Interventions

There are numerous behavioral health interventions for youth with T1D, which differ from one another in meaningful ways. When examining interventions for T1D, it seems useful to consider several factors. For example, is the intervention designed to impact a single system, several systems, or all systems in which a youth is embedded? The location of the intervention is also of importance, as many interventions are delivered in a clinical care setting or office that does not represent the places where youth spend their time, while other interventions are delivered in settings in which youth spend the majority of their life (e.g., home, school, neighborhood). Interventions can also vary by delivery method, as some interventions are delivered face-to-face, whereas others rely on telephonic, web-based, text support, or a combination of these delivery methods. Finally, the accessibility of these interventions is also an important component, as the majority of interventions appear to be accessible only during typical business hours (i.e., 9–5 pm, Monday through Friday), the most convenient times for providers. Few interventions seem ecologically valid, meaning that they have a high degree of generalizability of intervention to real-world settings based on provider involvement at the times and in the settings which the problems occur (Brown, 2002). There are trade-offs associated with all of these factors, and thus model care may include the flexible choosing of intervention components based on risk stratification related to youth and family needs.

Single System Approaches

Not surprisingly, the majority of interventions developed for T1D predominantly focus on a single system. Although extensive literature suggests that multiple systems may contribute to adherence difficulties and poor diabetes outcomes for youth (Naar-King, Podolski, Ellis, Frey, & Templin, 2006), many youth benefit from interventions designed to impact a single system and therefore may be targeted by multiple single system interventions. Unfortunately, such an approach runs the risk of being too reductionistic and negatively impacted by siloed service provision.

Individual interventions Given the importance of adherence and glycemic control to long-term health outcomes (Hood, Rohan, Peterson, & Drotar, 2010), many interventions aim to promote diabetes management by targeting direct, behavioral processes (e.g., blood glucose monitoring, insulin administration, coordination of dietary intake). However, a recent meta-analytic review suggests that interventions focusing on behavioral processes alone without emphasizing emotional, social, and family processes are unlikely to have a significant impact on glycemic control (Hood et al., 2010). For example, several interventions target direct behavioral processes by addressing possible gaps in T1D management comprehension, but while these educational interventions are generally associated with increased knowledge, most have little to no influence on glycemic control (Bloomgarden et al., 1987; Murphy, Rayman, & Skinner, 2006). Similarly, interventions that target youth mental health concerns (e.g., CBT for depression) have demonstrated success in improving mental health symptoms but not glycemic control (Huang, Wei, Wu, Chen, & Guo, 2013; Li et al., 2017).

Some interventions contain multiple components designed to influence individual risk factors in numerous manners. For example, cognitive-behavioral treatment (CBT) for diabetes-related behavior change incorporates coping skills training, cognitive restructuring, behavioral role-play, and/or motivational interviewing related to diabetes management. Although CBT for T1D has yielded promising improvements to glycemic control and quality of life (QoL) at 1-year follow-up (Grey, Boland, Davidson, Li, & Tamborlane, 2000; Stanger et al., 2013), studies of CBT at the individual level (i.e., without involving other systems) have failed to demonstrate efficacy with diverse, high-risk samples (Cook, Herold, Edidin, & Briars, 2002; Grey et al., 2000; Stanger et al., 2013). As vulnerable populations often evidence risk factors across other systems, youth-based interventions that do not involve other systems may be less effective.

A rapidly developing area of research during recent years has included the risk associated with the transition from pediatric to adult care during a vulnerable developmental period. Transition programs have utilized the following methods: targeted education and skills training for patients; support programs for young adults; the identification of coordinators to assist in the transition process; joint clinics with staff from both pediatric and adult services; distinct clinics for young adults; and enhanced documentation to improve the transfer of care (Agarwal et al., 2017; Peters, Laffel, & Group, 2011; Sheehan, While, & Coyne, 2015). Results of preliminary studies suggest that transition programs are associated with improved clinic attendance and fewer diabetes-related hospitalizations post-transition, with limited improvements to glycemic control. However, well-powered RCTs are necessary in order to further assess outcomes of transition interventions and to develop an understanding of the effective aspects of these multicomponent programs.

Family system interventions Few interventions have been designed to impact the family system without including the youth with T1D (see the section "Multisystem Interventions" for a review of interventions that target both the individual with T1D and the family). Parent-to-parent support groups may be promising interventions designed to provide mentoring for parents of children with T1D (Channon, Lowes, Gregory, Grey, & Sullivan-Bolyai, 2016). However, while similar parent-to-parent mentoring and support groups have been associated with positive outcomes for parents of children with a number of chronic conditions (Shilling et al., 2013), assessments of effectiveness in T1D samples have not yet been published.

School system interventions Preliminary research in the area of classmate interventions suggests that diabetes education interventions for the peers of individuals with T1D in the school environment may be associated with improved diabetes-related quality of life (QoL) (Wagner et al., 2006). Education interventions directed at others in the school environment (e.g., teachers) have produced improvements in knowledge of diabetes (Gesteland, Sims, & Lindsay, 1989; Jarrett, Hillam, Bartsch,

& Lindsay, 1993; Siminerio & Koerbel, 2000; Vanelli et al., 1999); however, the effects of school personnel training on diabetes-related outcomes for youth with T1D are currently unknown. Given the association between access to trained school personnel and improved glycemic control (Wagner et al., 2006), an increased understanding of diabetes education interventions for daycare providers, teachers, nurses, and other school personnel who interact with children with T1D is indicated.

Several resources exist to strengthen communication between parents, medical providers, and school personnel, but interventions evaluated with scientific rigor have been minimal. Toolkits and guidelines exist for parents and medical professionals, respectively, to facilitate improved communication and partnership with school systems and daycare settings (American Diabetes et al., 2012; Wolff, 2014).

Medical system interventions Though healthcare reform may not typically be considered an "intervention," policy developments and large-scale changes to the healthcare environment can significantly impact, albeit indirectly, the type and quality of care patients with diabetes can access. For example, in 2015 the Medicare Access and CHIP Reauthorization Act (MACRA) introduced the Quality Payment Program, a new approach to payment that rewards high-quality patient care delivery and care coordination and encourages alternative payment models (APMs) (AAFP, 2016, 2017; CMS, 2015). APMs are payment approaches that incentivize focusing on cost-efficient and high-quality care rather than volume and care duplication (CMS, 2016, 2015). By 2018, the Department of Health and Human Services (HHS) hoped to have 50% of Medicare payments in alternative payment models (CMS, 2015). Given the trickle-down effect from Medicare policies to other areas of insurance (e.g., Medicaid), these large-scale changes will undoubtedly impact the care being received by youth with diabetes. Still, while APMs are a promising way to improve care quality for diabetes patients, it is noteworthy that some APMs are more successful than others, and it is vital to find APMs effective in serving various populations and systems (Barry et al., 2017).

While policy indirectly impacts an individual's medical care, aspects of clinical practice can also have significant impact on health outcomes. For example, interventions aimed at improving sociodemographic and cultural competencies for medical providers, as well as efforts to increase access to medical care and well-trained interpreters, have demonstrated short-term improvements (Barkin, Balkrishnan, Manuel, & Hall, 2003; Health, 2000; Jacobs et al., 2001; Peña Dolhun, Muñoz, & Grumbach, 2003; Thom, Tirado, Woon, & McBride, 2006). While provider interventions are essential to improving care for these vulnerable groups, the fact that racial and ethnic minorities tend to be underrepresented in pediatric clinical research limits the culturally tailored, empirically supported treatments available to providers through these training programs (Clay, Mordhorst, & Lehn, 2002; Prieto, Miller, Gayowski, & Marino, 1997; Ross & Walsh, 2003).

Other smaller scale aspects of the medical system may indirectly impact patient care. For example, work-related satisfaction for staff in clinical practices has been associated with patient-perceived quality of care and satisfaction with care (Rossberg, Melle, Opjordsmoen, & Friis, 2008). Similarly, a study of nurses and patients across the USA and several European countries yielded results that suggest more satisfactory work environments for nurses, and smaller patient-to-nurse ratios correlate with increased care quality, patient satisfaction, and patient safety (Aiken et al., 2012). While these cross-sectional studies do not constitute interventions, they demonstrate areas of potential medical system interventions in need of further research.

Multisystem Interventions

There are several interventions that have been effective in targeting both direct and indirect processes involved in diabetes management. The following interventions are multicomponent in nature, address problems across a number of systems by assessing youths' broader contexts, and involve the individual with T1D *and* individuals who play important roles in diabetes care across systems.

BFST Behavioral family systems therapy (BFST) uses a combination of family-based skills training interventions (e.g., functional and structural family therapy, communication skills training, problem-solving, cognitive restructuring) to address obstacles to health behaviors in vulnerable youth. The psychologist uses standard behavioral therapy techniques such as instruction, feedback, modeling, and rehearsal to engage the family in learning targeted skills. Behavioral homework, which encourages family members to practice specific skills at home, is assigned at each session and reviewed at future sessions. BFST has demonstrated significant improvements to self-reported and directly observed parent-adolescent interactions and diabetes-specific conflict in families of youth with T1D (Wysocki et al., 2006); however, standard BFST was not successful in improving adherence or glycemic control. Thus, BFST was revised to specifically target diabetes-related behavioral problems. In addition, length of BFST was extended to 6 months, other family members or systems relevant to T1D management were included, and participating caregivers experienced a 1-week simulation of living with T1D. These changes generated an adaptation of BFST for diabetes (BFST-D), and results of large BFST-D randomized controlled trials (RCTs) have demonstrated improvements to family functioning, as well as adherence and HbA1c, with an estimated moderate effect on glycemic control (Wysocki et al., 2007).

MST Multisystemic therapy (MST) is a family-based treatment that includes regular home visits, frequent phone communication, structural and strategic family interventions, and cognitive-behavioral therapy strategies based on each family's specific needs. Originally developed for youth involved in juvenile delinquency and their families, this intensive home- and community-based treatment has been adapted for youth with T1D experiencing poor glycemic control and is meant to intervene directly within the systems that affect adherence and glycemic control. Interventions involve the youth with T1D, the family, *and* the broader community (e.g., peers, school, medical team) as needed.

MST has been shown to be efficacious for youth with T1D and chronically poor glycemic control (Ellis et al., 2004). Multiple studies have documented significant improvements to health outcomes and reduced costs of care. When compared to nontreatment controls, MST has demonstrated significant increases in frequency of blood glucose testing and decreases in hospital admission rates, with an estimated small effect (i.e., 0.10) on glycemic control (Ellis et al., 2004, 2007). In addition, youth in MST experienced significantly fewer hospitalizations at up to 24 months post-MST compared to standard medical care (Ellis et al., 2008). Furthermore, improvements to diabetes-related stress, parental overestimation of adolescents' responsibility for completion of diabetes care, and parent reports of the parent-provider relationship have been documented (Carcone et al., 2015; Ellis, Frey, et al., 2005; Naar-King, Ellis, Idalski, Frey, & Cunningham, 2007). Taken together, these MST findings highlight the ability of interventions to effectively improve outcomes across relevant systems demonstrating ecological validity.

Novel Interventions in Children's Healthcare Novel Interventions in Children's Healthcare (NICH; Harris et al., 2013) is an intensive, multicomponent behavioral health intervention for youth with complex medical conditions, which was developed to improve glycemic control and associated negative outcomes for youth with repeated DKA who are recurrently hospitalized due to poor glycemic control. NICH services include a combination of family-based problem-solving, care coordination, and case management. NICH interventionists deliver services in the youth's natural environment (e.g., home, school, clinic, community); are available to families 24 hours per day, 7 days per week; and utilize telecommunication to increase frequency of service provision. Daily telecommunication (e.g., text messages, phone calls, web-based video chat) is individualized based on youth and family characteristics and is commonly used to monitor blood glucose levels and insulin intake, to provide frequent positive reinforcement for adherence, and to problem-solve during crises (e.g., DKA events) (Wagner et al., 2016).

Unlike other systemic interventions, NICH was originally developed for youth with complex chronic medical conditions like T1D and continues to target youth with repeated DKA. Data suggests NICH is associated with significant reductions in ED visits, improvements in glycemic control, and reductions in yearly healthcare costs for a subgroup of youth who appear especially vulnerable to repeat DKAs (Harris, Wagner, & Dukhovny, 2016; Wagner, Barry, Stoeckel, Teplitsky, & Harris, 2017). Although there has yet to be an RCT involving NICH, the improvements in glycemic control and avoidable utilization associated with program involvement are comparable if not greater than those demonstrated by MST.

Other Approaches Various other systemic interventions for T1D exist as well. Many focus specifically on the family system, with notable developments to family-based interventions in the last decade (Katz, Volkening, Butler, Anderson, & Laffel, 2014; Murphy, Wadham, Hassler-Hurst, Rayman, & Skinner, 2012; Nansel, Iannotti, & Liu, 2012). For example, the WE-CAN intervention (Nansel et al., 2009) focuses on (1) improving disease management problem-solving, (2) improving parent-child cooperation and communication, and (3) facilitating appropriate sharing of disease management responsibilities by coaching in the following areas: working together as a family to set goals; exploring possible barriers and solutions; choosing the best solutions; acting on a plan; and noting the results. A large RCT evaluating the WE-CAN intervention (Nansel et al., 2012) yielded a significant improvement in HbA1c at 2-year follow-up compared to baseline and controls.

Other family-based intervention studies have demonstrated improvements in family involvement, with less promising changes to glycemic control. A 2-year RCT evaluating the efficacy of standard care with the addition of monthly telephone outreach by a Care Ambassador and family-based psychoeducational interventions provided at each quarterly visit (Katz et al., 2014) demonstrated significantly increased parental involvement compared to the standard care group; however, no significant changes to HbA1c, diabetes-specific family conflict, or youth QoL across treatment groups were reported (Katz et al., 2014). The Families, Adolescents, and Children's Teamwork Study (Murphy et al., 2012; Murphy, Wadham, Rayman, & Skinner, 2007) demonstrated that participation in a four-session structured education group focusing on skill building, parental responsibility, and communication was associated with improved parental involvement and HbA1c at 12 months (Murphy et al., 2007), but a follow-up study was not able to replicate HbA1c findings, with poor group attendance being a notable barrier (Murphy et al., 2012).

Other multisystem interventions focus on both peers and families. For example, one small study used the KIDS Project intervention for youth with T1D and their parents (Kichler, Kaugars, Marik, Nabors, & Alemzadeh, 2013), emphasizing rapport building during adolescent groups and family collaboration, negotiation, and problem-solving during family-based groups. Improvements to youth-specific QoL and parent involvement were reported at 4 months posttreatment, but changes in HbA1c were not demonstrated. Another multisystemic intervention that has attempted to incorporate a "support team" beyond the family system alone requests that patients identify at least three people from their extended family, peer group, or neighborhood to attend the first session of this in-home intervention (Pendley et al., 2002). Initial results of this pilot found perceived peer and family support to have no significant correlation with improvements in glycemic control, although peer participation did significantly and positively correlate with glycemic control.

Other interventions have focused on the adolescent peer relationships without intervening on the family system. For example, one small study recruited adolescent and best friend dyads to attend four support group and education sessions, which emphasized topics of diabetes treatment, reflective listening, problem-solving, and stress management (Greco, Pendley, McDonell, & Reeves, 2001). After the intervention, adolescents with diabetes and their peers showed increases in support and knowledge, while parents, although not part of the intervention, reported significantly less diabetes-related conflict. There were no significant changes, however, to global peer support or adherence, and glycemic control was not measured. Thus far, studies examining treatments that intervene on the peer system are limited by small sample sizes.

Improvements over Time Recent improvements in distal technology efficacy and access provide opportunities for individual and systemic interventions to increase reach and effectiveness. Electronic technology has become a common way to communicate, access information, and manage personal healthcare, with estimates suggesting there are now over 7.1 billion wireless subscribers worldwide with over 70% living in low- and middle-income countries (LMICs) (Kay, Santos, & Tarkane, 2011; TeleGeography, 2015). Therefore, distal technologies (e.g., text messaging, telephone coaching, electronic portals) for diabetes management have become integral and beneficial parts of many diabetes care interventions, including those focused on families and systems.

Advancements in telehealth have been important to the advancement of NICH, an intervention that utilizes telecommunication regularly to intervene in the moment and across systems. Interventionists frequently use text messages, phone calls, and web-based video chats to monitor insulin intake and blood glucose levels, to provide frequent positive reinforcement for adherence, and to problem-solve during crises. In general, telecommunication allows interventionists to increase frequency of service provision and maximize efficiency (Wagner et al., 2016). Evaluations specific to text messaging suggest that more than half of NICH interventionists' texts to patients and caregivers are sent outside of business hours (i.e., evenings and weekends) and that caregivers are more likely than patients to receive "behavioral intervention" texts from interventionists (Wagner et al., 2016). In addition, sending more text messages to caregivers is associated with a greater decrease in number of hospital admissions during the NICH intervention, whereas no correlation has been found between text messages to youth themselves and changes to number of admissions (Wagner et al., 2017). Taken together, these data suggest that (1) technology may present a unique opportunity for increasing contact points between healthcare providers and individuals/caregivers, particularly during hours that patients and families typically do not have as much access to support, and (2) increasing contact points between providers and families in this way may be associated with positive diabetes-related outcomes.

While the NICH intervention was established with telehealth strategies at the center of intervention development, existing interventions that have not previously incorporated telehealth have begun demonstrating success when doing so. For example, one study of 90 adolescents with T1D and their parents found that those who received BFST-D via videoconferencing had no significantly different outcomes, including outcomes specific to therapeutic alliance, than those who received the treatment in a traditional clinic setting (Riley, Duke, Freeman, Hood, & Harris, 2015). Changes in family conflict, miscarried helping, and adjustment to illness were not significantly different between the two groups, and in both groups, youth and parents reported significant reductions in family conflict and miscarried helping and improvements in acceptance of diabetes (Duke, Wagner, Ulrich, Freeman, & Harris, 2016). The same youth showed significant reductions in depressive symptoms and improvements in overall family functioning from pre- to posttreatment (Riley et al., 2015), as well as statistically significant improvements in adherence and glycemic control from pre- to posttreatment that were maintained at 3-month follow-up, regardless of which means of treatment delivery they received (Harris, Freeman, & Duke, 2015). Results of these telehealth studies suggest the potential for positive changes across systems (e.g., family, communication between provider and family) while also potentially addressing risk factors relevant to SES (e.g., lack of transportation, cost of childcare) and geographic location (e.g., rural location).

Case Example

When considering the need for multisystem interventions, we find it useful to provide a case example that exemplifies the barriers experienced by the most vulnerable youth with T1D. Below we describe a patient who was referred to NICH (Harris et al., 2013) and include minor changes to identifying information.

Jimmy was a 14-year-old boy diagnosed at age 7 with T1D. He lived with his mother, her partner, and three older siblings in a rural community. He had a trauma history, including recent removal from his father's care due to physical abuse. On an individual level, Jimmy was previously diagnosed with attention-deficit hyperactivity disorder (ADHD), posttraumatic stress disorder, and major depressive disorder, for which he received regular therapy with a psychologist and medication management through psychiatry. On a family level, his mother and her partner were in recovery from methamphetamine dependence and were using a combination of marijuana and alcohol daily at the time of NICH referral. In addition, there was reportedly high parent-child conflict, low supervision and monitoring, and low family cohesion. Both parents reported their own poorly managed medical conditions which exacerbated their difficulty in helping Jimmy manage T1D. Jimmy spent the majority of his time with "delinquent" peers who did not support his diabetes management and academic success and detracted from caregivers' attention by using their home as a transitory living arrangement.

Jimmy was referred due to suboptimal adherence resulting in four DKA episodes in the prior year and an HbA1c consistently at or above 14%. His family struggled to regularly attend diabetes clinic appointments and did not bring his glucometer when attending. He had previously been referred for both office- and videoconferencing-based behavioral health but infrequently attended and received little benefit from such interventions. Jimmy was living over 25 miles from the diabetes clinic, and his caregivers had an adversarial relationship with the diabetes care team due to past reports to Child Protective Services (CPS). Ironically, reports suggested that CPS was unwilling to remove him from his mother's care due to liability associated with medical foster care. In addition, when he was voluntarily placed elsewhere, he displayed moderate health improvements (e.g., HbA1c of 11.4; 0 missed clinic visits) which quickly declined after the death of his foster caregiver and subsequent return to his parents' care.

When involved in a multisystem and ecologically valid intervention (i.e., NICH), Jimmy received coordinated intervention designed to impact him, the multiple systems in which he was embedded, and the interactions between those systems. For example, Jimmy received individual behavioral skills training related to T1D management that included frequent and immediate reinforcement of management skills (e.g., blood glucose monitoring, insulin delivery). He and his parents also received skills training related to coping with strong emotions, parent-child communication, and communication between family members and other relevant individuals (e.g., school staff, members of medical team). His parents received skills training focused on supervision, monitoring, and positive reinforcement. Jimmy and his family received these home- and community-based interventions through in person, through one-on-one and group meetings, as well as through frequent conversations via text message and phone.

Jimmy's interventionist also worked with other systems; his medical team was provided with psychosocial information they were previously unaware of as well as suggestions regarding communication styles that appeared to work best for Jimmy and his family. Jimmy's interventionist worked face-to-face with extended family members and family friends to increase monitoring and reinforcement across adult. The increased monitoring across systems provided Jimmy's parents with much-needed respite, indirectly improving their interactions with Jimmy and their engagement in treatment. The interventionist worked with his parents to reduce his association with delinquent peers while also meeting with his peers to engage them in assisting Jimmy when outside of the home.

Care was coordinated directly with school officials, mental health providers, medical staff, and family members to ensure that all systems that directly interacted with Jimmy were partnering effectively. Furthermore, Jimmy and his family were provided with case management services designed to build skills related to accessing transportation to appointments, getting medical supplies in a timely fashion, and accessing evidence-based psychological and psychiatric services to address Jimmy's mental health concerns. Finally, Jimmy and his family were provided with around-the-clock access to his interventionist which included problem-solving, crisis management, and frequent check-ins and reinforcement related to T1D management in addition to other important aspects of his life (Wagner et al., 2016, 2017).

Jimmy represents one of many youth with T1D with comorbid social vulnerability that impacts their ability to successfully respond to individual- and office-based interventions. Other examples include a 6-year-old girl with T1D “couch-surfing” with her homeless father as he attempted to recover from heroin dependence, a 17-year-old young woman with an intellectual disability living with caregivers with serious mental health concerns (e.g., borderline personality disorder) and regular involvement in domestic violence, and a 13-year-old boy with major depressive disorder living in severe poverty and with a history of using his insulin for self-harm. As expected, interventions that are not designed to address these social risk factors were unable to successfully treat these youth.

Discussion

In recent years, there has been a call for interventions that specifically target high-need, high-cost (HNHC) patients (Blumenthal, Chernof, Fulmer, Lumpkin, & Selberg, 2016). America’s health system cannot be significantly improved until it better addresses the needs of its most vulnerable: HNHC patients who warrant increased attention due to their major healthcare problems and the frequency of their healthcare utilization. In order to best help this population, it is essential to have a thorough understanding of the needs of these patients across systems, create interventions that offer them high-quality and highly integrated care, and disseminate these effective intervention programs on a national level (Blumenthal et al., 2016). This final objective is key, as accelerating the wide-scale adoption of programs is both important and challenging. As this chapter highlights, intensive interventions that focus not only on the individual but also on factors within and across the systems involved in diabetes care (e.g., BFST-D, MST, NICH) have demonstrated success with HNHC youth with T1D in terms of glycemic control, treatment adherence, diabetes-related functioning, QoL, and other relevant areas. These programs, although expanding slowly, have not yet become the standard model of care for HNHC patients.

Systemic interventions are important from a strictly financial perspective as well. The care of HNHC individuals is indeed costly; these individuals compose about 5% of the population but account for approximately 50% of the country’s annual healthcare spending (Blumenthal et al., 2016). Although much of the financial data represent adult healthcare costs, many medically and social vulnerable youth inevitably mature to become HNHC adults. Thus, it is imperative to work toward reducing costs for high-risk individuals. Systemic interventions provide a promising option, although providers’ wariness of the up-front investments required to implement these interventions is an oft-cited barrier to increased dissemination (Blumenthal et al., 2016). In the long term, however, systemic interventions have demonstrated cost-effectiveness for people with chronic medical conditions compared to individually focused interventions. For example, youth with T1D who received multisystem intervention (MST) demonstrated significant reductions (i.e., 61%) in direct hospital costs, while youth receiving standard care evidenced a near doubling of costs (Ellis, Naar-King, et al. 2005). Similar short- and long-term cost benefits have been shown by multisystem interventions with other at-risk populations such as youth involved in violent crime and youth with substance dependence (Dopp, Borduin, Wagner, & Sawyer, 2014; Schoenwald, Ward, Henggeler, Pickrel, & Patel, 1996), so it seems reasonable to assume that healthcare systems which utilize evidence-based multisystem interventions for pediatric populations should also continue to reap additional savings over time. The long-term benefits of systemic interventions, therefore, far outweigh the initial costs of implementing the interventions, and the accelerated widespread adoption of such programs could significantly decrease costs for high-risk and complex patients.

Unfortunately, we spill much ink detailing the cost savings likely associated with multisystem interventions for HNHC youth when the improvements in youth health and QoL should be argument enough. Although demonstrating the financial value of such services is encouraged (Harris et al., 2016), there is a stronger argument that we should be providing children and families with the level of care that most effectively meets their needs, even if this service costs more. Ironically, as detailed by Harris (2017), when it comes to problems with health behaviors, we typically start with the least aggressive or intensive treatment despite the wealth of literature indicating that youth with multiple social risk factors likely will not show improvements with standard medical and behavioral treatment alone. However, when it comes to medical care, if a child is experiencing severe DKA, providers don't hesitate to hospitalize, and payers don't balk at costs associated with intensive care.

Why this same model is not applied to behavioral health remains a mystery. Indeed, a more effective and morally grounded decision-making process would utilize risk stratification resulting in referral and financial approval of multisystem interventions for children like Jimmy *before* they experience multiple DKAs and chronically high HbA1c. Instead, our current system is slow to respond, reactive as opposed to proactive, and ripe for poor short- and long-term health outcomes for these children that will result in poor health and QoL in adulthood, high burden for their family, and significant costs to the healthcare system and society. Although the majority of children and adolescents with T1D will not require multisystem and ecologically valid interventions, those at greatest risk needed these services yesterday.

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Chapter 12
Social Level Interventions: Enhancing Peer Support and Coping in Pediatric Diabetes Populations

Margaret Grey and Kevin Joiner

Peer Support and Coping Skills Training for Children and Adolescents with Diabetes

Nearly a quarter century has passed since landmark studies in type 1 and type 2 diabetes demonstrated that maintaining optimal glycemic control through intensification of diabetes treatment and self-management dramatically reduces the incidence and prevalence of complications (DCCT Research Group, 1993; UKPDS Group, 1998). Yet, epidemiological evidence indicates that reaching target goals for glycemic control remains a challenge for most youth (Wood et al., 2013; Zeitler et al., 2012). Tremendous advances in treatment (e.g., automated pump and continuous glucose monitoring technologies) are being made that hold great promise for facilitating maintenance of optimal control. There is widespread recognition also that self-management support provided as a routine part of care plays a pivotal role in developing, mastering, and sustaining self-management skills (American Diabetes Association, 2016). Many youth, however, are at risk for receiving inadequate self-management support (Jaacks et al., 2014). Thus, a key priority is the development of engaging and effective interventions for youth and their families that facilitate mastering and sustaining self-management skills.

The need for innovative models of self-management support to improve care for people with chronic conditions including diabetes was one of the main findings highlighted in the Institute of Medicine (IOM) report, *Priority Areas for National Action: Transforming Health Care*. High-quality, efficient, and effective self-management support was defined in the report as “the systematic provision of education and supportive interventions to increase patients’ skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support” (IOM, 2003, p. 52). The report concluded that in order for transformative change in the delivery of self-management support to take place, empirical evidence of the effectiveness of interventions is essential. Furthermore, the report recommended the application of

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M. Grey (✉)
Yale University School of Nursing, Orange, CT, USA
e-mail: Margaret.grey@yale.edu

K. Joiner
University of Michigan School of Nursing, Ann Arbor, MI, USA
e-mail: Kljoiner@med.umich.edu

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frameworks, models, and concepts including the Chronic Care Model (Wagner et al., 2001) and the Medical Home (American Academy of Pediatrics, 2002).

Appropriate self-management support for children and adolescents varies by age and length of time since diagnosis. During early childhood (infancy (age 0–12 months), toddler (age 13–26 months), and early childhood (age 3–7 years)), preventing low and high blood glucose levels and knowing what to do when they occur dominate parent and guardian caregivers' needs (Chiang, Kirkman, Laffel, & Peters, 2014). Parents and guardians need to develop and master these "survival skills" soon after diagnosis (Swift, 2009). The focus of self-management support is initially on gaining problem-solving and diabetes management skills. The initial phase often entails abruptly assimilating a complex regimen into daily routines. Many technical skills need to be developed and mastered in a short period of time, including blood glucose testing, insulin administration, assessment and treatment of hypoglycemia, and ketone testing. Parents may experience strong emotional and psychological responses (Delamater et al., 2001), feeling overwhelmed with the constant demands of caring for a young child with diabetes. Loneliness and isolation are common experiences particularly among mothers (Smaldone & Ritholz, 2011; Sullivan-Bolyai, Deatrick, Gruppuso, Tamborlane, & Grey, 2003). Some parents may experience extreme stress and may develop symptoms consistent with anxiety or depression.

Children of young school age (age 7–11 years) are capable of learning many tasks of diabetes management. Blood glucose testing can often be performed independently, and as they learn more mathematics, they can count carbohydrates and understand requirements for bolusing. For most children, however, the complexities of insulin adjustment and carbohydrate coverage require the ongoing help of their parents or guardians (Chiang et al., 2014). Because they are curious developmentally, they tend to enjoy learning rules and participating in their care.

In adolescence (age 12–19 years), there is a transition from shared management to increased independence (Chiang et al., 2014). Adolescence is also associated with increases in risk-taking behaviors, including using alcohol and drugs, cigarette smoking, and sex (Jaser, Yates, Dumser, & Whittemore, 2011). The hormonal changes of puberty also result in higher glycosylated hemoglobin (A1C) levels (Amiel, Sherwin, Simonson, Lauritano, & Tamborlane, 1986) that may create conflict in families. Navigating these transitional issues while maintaining continued parental involvement presents challenges for adolescents with diabetes and their families. Issues that rise to the forefront in adolescence include negotiating roles and dealing with conflict. Adolescents with diabetes are also at risk for eating disorders and depression (Delamater et al., 2001).

The needs of children and adolescents with diabetes and their families are influenced by environmental and individual characteristics. Environmental influences change as children progress through different periods of developmental, behavioral, and physical growth. Thus, it is important to consider both social and developmental perspectives. For example, for all school-age children and adolescents, it is important to consider the roles of peers and schools as part of the social environment.

Reviews in the area of psychosocial structured self-management interventions for adults with type 1 and type 2 diabetes have been published previously (e.g., Brownson & Heisler, 2009; Tang, Ayala, Cherrington, & Rana, 2011), but there are few such reviews of the literature on interventions focused on children. Brownson and Heisler (2009) conducted a review describing roles and duties of peers in Diabetes Self-Management Education (DSME) and Diabetes Self-Management Support (DSMS) programs, and Tang et al. (2011) conducted a review of volunteer-based peer support programs in diabetes care, but studies focused on children and adolescents were not included in the reviews. More recently, Raphael, Rueda, Lion, and Giordano (2013) evaluated the role of lay health workers in the care of pediatric chronic conditions, but only four studies were included of youth with diabetes. Thus, in this chapter, we review the literature from 2000 to 2018 on peer support and coping skills training as approaches to the provision of self-management support and discuss the implications of this body of research for future research, clinical practice, and health policy.

Search Strategy

The online database *Medline* was searched for studies of peer support programs in diabetes care for children and adolescents, using terms including peer, shared medical appointments, promotora, community health worker, mentor, lay health worker, lay health educator, and patient navigator. A second search was conducted for studies of programs to enhance coping skills. The search was limited to articles published from the year 2000 to 2018. The inclusion criteria were as follows: (1) studies of a program in which volunteer peer support or coping skills training in diabetes care was a primary goal; (2) participants were children or adolescents (age < 20 years) with diabetes or family caregivers of children or adolescents; (3) studies were conducted in the United States; and (4) the article was published in English. A total of nine studies were identified for inclusion in the review of peer support, and after review, seven were included in this review (Table 12.1). A total of 12 studies were identified for inclusion in the review of coping skills training programs, and after review, 12 were included (Table 12.2).

Table 12.1 Studies of peer support in youth with diabetes

Author(s) (Date)	Sample	Intervention	Findings
Parents of children with type 1 diabetes			
Sullivan-Bolyai et al. (2004)	42 mothers of children with newly diagnosed type 1 diabetes	Peer mentoring for mothers of children (age < 10 years) with newly diagnosed type 1 diabetes	Intervention group had lower concern, perceived less of a negative impact on their family, and awareness of more resources
Sullivan-Bolyai et al. (2010)	60 mothers of children with newly diagnosed type 1 diabetes	Peer mentoring for mothers of children <13 years with newly diagnosed type 1 diabetes	Improved overall family management of diabetes
Sullivan-Bolyai, Bova, Lee, and Gruppuso (2011)	28 fathers of children with newly diagnosed type 1 diabetes	Peer mentoring for fathers of children (age < 13 years) with newly diagnosed type 1 diabetes	Fathers in the intervention group had improved confidence. They also had more worry about raising a child with a chronic illness
Adolescents with type 1 diabetes			
Greco, Pendley, McDonell, and Reeves (2001)	21 adolescents, age 10–18	Psychologist-led group program for teens with diabetes and their friends	Pre/post measures showed increased knowledge in youth with diabetes, increased in self-perception in friends, and decreased family conflict by parental report
Cook, Herold, and Edidin (2002)	53 adolescents, age 13–17	Advanced practice nurse led Choices program	Intervention group showed increased blood glucose testing compared to usual care control and had within-group improvements in problem-solving and A1c levels
Sims and Haines (2011)	6 adolescents, age 13–17	Group program led by peers with type 1 diabetes	Over time increase in A1c levels
Floyd et al. (2016)	37 adolescents, age 12–16, 47% minority	Shared medical appointments	Improved quality of life (e.g., adherence, school function, psychosocial function, barriers, communication) and stabilization of A1c levels

Table 12.2 Studies of coping skills training in youth with diabetes

Author(s) (Date)	Sample	Intervention	Findings
Type 1 diabetes			
Grey, Boland, Davidson, Li, and Tamborlane (2000)	77 youth, age 12–20	Group-based coping skills training program	Coping skills group had significantly better metabolic control, quality of life, and self-efficacy compared to a usual care control group
Grey et al. (2013)	320 youth, age 11–14, 37% minority	Web-based TEENCOPE coping skills training program with additional advanced diabetes education	Both programs over time improved A1C levels, quality of life, social acceptance, and perceived stress and reduced family conflict
Whittemore et al. (2015)	124 teens, age 11–14, 25% minority	Web-based Teens. Connect coping skills training program with additional advanced diabetes education	Over time, those that received the intervention had improved A1C and lowered perceived stress
Mulvaney, Rothman, Wallston, Lybarger, and Dietrich (2010)	72 adolescents, age 13–17	Web-based self-management intervention	Improved self-management and improved problem-solving using as-treated analyses. Intervention group A1C levels remained constant while control group increased
Anderson, Brackett, Ho, and Laffel (1999)	85 pre- and young adolescents, age 10–15 years	Clinic-based family teamwork program	Teamwork group had no major deterioration in parent involvement in insulin administration or blood glucose monitoring as well as less family conflict over 12 months
Laffel et al. (2003)	105 children and adolescents, 8–17 years	Clinic-based family teamwork program	Reduced A1C levels in the teamwork group; increased parent involvement, but no increase in family conflict
Holmes, Chen, Mackey, Grey, and Streisand (2014)	226 young adolescents, age 11–14, 25% minority	Clinic-based individual coping skills training and teamwork	Both groups demonstrated no deterioration in outcomes over time, but the Coping Skills Training and Teamwork group had greater improvements in adherence to self-management and A1C levels
Grey et al. (2009)	82 preadolescents, age 8–12	Group-based coping skills training program	Over time both the intervention and the education control showed lower impact of diabetes management on quality of life, improved coping, improved self-efficacy, lower level of depressive symptoms, and improved family functioning
Ambrosino et al. (2008)	82 school-age youth, age 8–12	Group-based coping skills training for youth and their parents	Improved quality of life, coping, self-efficacy, and depressive symptoms compared to an education control group
Grey, Jaser, Whittemore, Jeon, and Lindemann (2011)	181 parents of teens with type 1 diabetes	Group-based coping skills training program for parents of teens (< 13 years) with type 1 diabetes	Over time both groups had improved quality of life, coping, and less responsibility for treatment management

(continued)

Table 12.2 (continued)

Author(s) (Date)	Sample	Intervention	Findings
Type 2 diabetes prevention			
Grey et al. (2009)	198 seventh grade students at risk for type 2 diabetes, 45% Hispanic, 49% African American	Nutrition and physical activity education and coping skills training delivered by teachers in the classroom	Improvement over time in both groups in body weight, lipids, depressive symptoms, and reduction of metabolic risk on oral glucose tolerance tests. No significant change in BMI
Whittemore, Jean, & Grey (2013)	384 high school students at risk for type 2 diabetes, 65% minority	HEALTH[e]TEEN, web-based curriculum of nutrition and physical activity education and coping skills program delivered in schools	High participation and satisfaction, but no significant change in BMI

Peer Support for Youth with Diabetes

Peer support is "the provision of emotional, appraisal, and informational assistance by a created social network member who possesses experiential knowledge of a specific behavior or stressor and similar characteristics as the target population, to address a health-related issue of a potentially or actually stressed focal person" (Dennis, 2003, p. 329). Accordingly, peer support in diabetes self-management involves structured or unstructured exchange between individuals with diabetes or between individuals affected by diabetes (e.g., a family caregiver for a youth with diabetes). A number of different models exist that may incorporate peer support. Peer mentoring programs often match individuals of different levels of self-management experience. Groups can be led by peers. Groups led by health workers can involve peer exchange. Programs can facilitate peer exchange with remote delivery via various distance-based modalities such as telephone, email, and web-based and/or mobile applications. They may be based on theory or previous research. Settings of programs may vary, with some offered in the clinic and others in the community. Thus, peer support can be viewed as mutually beneficial assistance exchanged between two or more individuals with diabetes (or family caregivers of young children with diabetes) (Heisler, 2010).

Peer Mentors for Parents While the majority of peer support programs are for children and adolescents who have diabetes themselves, the model has also been applied to the support of parents with children with newly diagnosed diabetes. Since such interventions may affect outcomes for the children, we included these studies. Although peer support programs for families are common clinically, we were unable to locate any other studies of the outcomes of these interventions in the recent past.

Sullivan-Bolyai et al. (2004, 2010, 2011) developed and evaluated an intervention designed to provide peer support for parents of children with newly diagnosed type 1 diabetes using a peer mentor model (Sullivan-Bolyai et al., 2004, 2010, 2011). The intervention was based on the Ireys curriculum (Ireys, Sills, Kolodner, & Walsh, 1996). The Ireys curriculum had been shown to be an effective means of facilitating peer support in parents of children with special needs (Ireys, Chernoff, DeVet, & Kim, 2001) and was adapted for the needs of parents of children with newly diagnosed diabetes. Informational support in the curriculum consists of a set of topics described as "survival skills." These topics include helping the child to grow and develop, caregiver day-to-day management responsibilities, siblings, behavior/discipline, dealing with doctors and the medical system, dealing with specific daycare or school-related issues, and out-of-school activities/issues (e.g., baby-sitting, camps, and parties). Affirmational and emotional support are also provided, and topics include relationship with spouse/significant other, relationships with other family members, parents' physical and emotional health, problems with other children in the family, work- and job-related stress, concerns with safety and community problems, moving, parents' reaction to intervention, parents' own childhood experiences, and comments made by friends, family, and strangers. Mentors also help parents identify and use sources of family and community support (Sullivan-Bolyai et al., 2004).

Parent-mentors were mothers of one or more children with type 1 diabetes who were carefully selected based on a set of criteria that indicated they could serve as an experienced guide and role model. These criteria included evidence of mentorship qualities of successful experience caring for their own child's diabetes, being knowledgeable regarding issues involved in caring for a young child with diabetes, and other traits that indicated they would be an effective mentor (e.g., worked well with others, good listener, assertive, empathetic, nonjudgmental). Mentors were supervised through quarterly meetings and telephone calls after each mentor-parent interaction.

The effectiveness of the program was tested initially in a 6-month randomized controlled trial with a delayed control group design (Sullivan-Bolyai et al., 2004). Mothers who received the intervention expressed fewer concerns about managing their child's diabetes, perceived less negative impact of the condition on the family, and reported awareness of more community resources. Their level of confidence in managing their child's diabetes day-to-day management remained unchanged, as did the child's glycemic control. Measures of cost, number of emergency room or acute care visits, and number of calls made to the diabetes team were not changed.

In a subsequent 12-month randomized controlled trial (Sullivan-Bolyai et al., 2010), eight of the ten parent-mentors were designated as mentors for the intervention group and received training in the adapted curriculum used in the previous study. The other two parent-mentors were not trained and served as mentors for the control group. Compared to controls, there was no difference between groups at 3, 6, or 12 months in the parent outcomes of concern, confidence, worry, impact on family, or perceived social support. In a companion study (Sullivan-Bolyai et al., 2011), the efficacy of the intervention on fathers was evaluated. Compared to controls at 12 months, fathers who received the intervention were found to be more confident in managing their child's diabetes but also more worried. There were no significant differences in outcomes of parent concerns, impact on family, or perceived social support.

Adolescent Peer Support Unlike parent support programs, there has been substantial work to develop peer support programs for adolescents with type 1 diabetes. There are a number of examples of interventions with professional-led group visits with peer exchange in adolescents with type 1 diabetes that have been evaluated. Greco et al. (2001) studied the effects of a psychologist-led group program in adolescents and their invited friends. The intervention consisted of a series of four weekly 2-hour group sessions for groups of three to six pairs. Each session followed a detailed written manual and included didactic content as well as interactive games and exercises. Sessions covered topics including etiology, physiology, and treatment of diabetes; listening and general problem-solving skills; problem-solving skills; and stress management. In the session on listening and general problem-solving skills, developmentally appropriate scenarios were employed. Small incentives (e.g., sugarless gum or diet soda) were awarded for completion of homework, which was assigned each week. The adolescents and their friends demonstrated increased understanding of self-management post-intervention; however, perceived peer support did not improve. There was a decrease in diabetes-related conflict by parental report, but not by adolescent self-report.

A randomized controlled trial to examine the effect of a group program, Choices, was conducted with 53 adolescents with type 1 diabetes over a 6-week period (Cook et al., 2002). Choices was developed based on a previous study in which children and adolescents and their parents were asked to share problems they had encountered in their diabetes care and how they had resolved the problems. An advanced practice nurse led the program in 2-hour weekly group sessions. The topics included making choices and keeping records, planning meals, timing your insulin, getting back on track, making adult decisions, and dealing with the impact of diabetes. Participants identified their own goals and attainment strategies.

Follow-up data collected 6 months after enrollment showed no significant differences between the two groups in adolescents' problem-solving skills, independent responsibilities, or A1c levels. The intervention did result in improved daily mean blood glucose monitoring frequency. In qualitative interviews conducted after completion of the intervention, participants reported enjoying the peer interaction and the discussions that occurred in the program.

Sims and Haines (2011) also reported on the development of a peer support program for adolescents with type 1 diabetes led by pharmacists. They used the US Diabetes Conversation Map to guide the educational part of the program. The conversation map is a tool for facilitating group education on self-management. Six participants completed follow-up evaluations and reported improvements in adherence to lifestyle modification despite worsening of metabolic control over 6 months of follow-up.

One way to include peer support in the provision of care to youth with diabetes is the use of shared medical appointments. Shared medical appointments are used to provide education and clinical care in an interactive manner between patients and healthcare providers. Floyd et al. (2016) developed a shared medical appointment approach that focused on self-management, communication skills, goal setting, glucose pattern recognition, and peer/diabetes team support. Visits also included usual clinical activities along with the group session. In a pretest-posttest analysis, 37 adolescents, age 12 to 16 years, were found to have stable A1c levels and significant improvements in quality of life. These results suggest that shared medical appointments may be a useful approach to incorporating peer and professional support in clinical care for young adolescents. Davis and Vitagliano (2015) noted that such shared appointments may represent the opportunity to develop learning communities among youth with type 1 diabetes.

Coping Skills Training

Coping skills training is a psychosocial self-management intervention focused on improving the coping skills of social problem-solving, communication skills, cognitive-behavioral modification, and stress management. Coping skills training is focused less on behavioral processes directly related to diabetes self-management and more on processes that indirectly affect how youth self-manage. Consistent with Social Cognitive Theory (Bandura, 1986, 1997), coping skills training is based on the premise that youth gain in self-efficacy through deliberate practice and rehearsal of skills resulting in a higher level of confidence. Increased self-efficacy, in addition to increasing the ability to cope successfully with management of chronic conditions, may decrease risk of other disadvantageous psychological sequela that sometimes occur including depression and anxiety.

Coping Skills Training for Adolescents Grey and colleagues developed a coping skills training intervention for adolescents with type 1 diabetes. The intervention, described in detail by Davidson, Boland, and Grey (1997), consisted of six sequential sessions in which participants engaged in a series of role-playing scenarios. Scenarios were examples of common social situations that often require making choices and decisions while taking into account diabetes care needs. Themes of the scenarios included choosing food in social situations, avoiding drugs and alcohol, and independence/dependence conflicts with parents. Grey et al. (1998) evaluated the coping skills training program in combination with intensive diabetes management in adolescents with type 1 diabetes in a randomized controlled trial. In a report of the short-term effects of the intervention over a period of 6 months, they showed that the group who received the coping skills intervention had improved A1c levels and improved self-efficacy and quality of life compared to an intensively managed control group with usual care (Grey et al., 1998). To evaluate the longer-term effects, follow-up data after 12 months were analyzed. The intervention group had improved A1c levels, medical and diabetes quality of life, and self-efficacy, compared to the group that received intensive diabetes management alone (Grey et al., 2000). In male participants, the intervention did not significantly increase the incidence of hypoglycemia, but in females, there was an increased incidence of weight gain and hypoglycemia.

Because many adolescents were too busy with school and sports activities to attend group sessions, Grey and colleagues adopted the coping skills training program to an Internet-based format (Whittemore, Grey, Lindemann, Ambrosino, & Jaser, 2010). Using a multiphase, multi-method approach, the Internet coping skills program, TEENCOPE, was developed and consisted of five sessions on the same skills related to self-talk, communication skills, social problem-solving, stress management, and conflict. They also developed an Internet-based diabetes education program for adolescents, Managing Diabetes, which consisted of four weekly sessions on glucose control, nutrition, exercise and sick days, and new diabetes technology. In a multi-site study comparing TEENCOPE to Managing Diabetes over 18 months of follow-up, the investigators found that A1C levels remained stable over time in an age group where they would be expected to rise and that those who participated in both programs had better A1C levels and quality of life compared to those who participated in only one (Grey et al., 2013). In a follow-up study designed to test whether the combined program, Teens. Connect, would be prescribed by diabetes providers, the authors reported that the dissemination approach was acceptable to the providers but that youth were less likely to complete the program without reminders (Whittemore et al., 2015).

Another approach to improving self-management in adolescents with diabetes was taken by Mulvaney et al. (2010). The intervention was designed to reduce barriers to self-management and was based also on social learning theory. In a randomized trial comparing the self-management intervention with usual care, improvements in self-management, problem-solving, and A1C levels were found in the as-treated analyses, but not in the intent-to-treat analysis.

Anderson et al. (1999) developed a family-focused teamwork intervention to improve glycemic control, family conflict, and quality of life in youth with type 1 diabetes transitioning to adolescence. The intervention involved structured meetings with patients and parents at quarterly diabetes visits. Importantly, the focus of the discussion was on issues that are of concern to both parents and youth with diabetes, about developing self-management and addressing conflict as the youth seek more independence. The research assistant presented brief modules addressing sharing diabetes tasks and resolving conflict and then provided a forum for patients and parents to discuss the topic. After the intervention, the research assistant helped the family to negotiate a responsibility-sharing plan, in which each individual's responsibility for maintaining various components of the treatment regimen was outlined. Each session of the intervention lasted approximately 15 minutes. In a randomized controlled trial, the Teamwork group showed improvements in glycemic control after 1 year, compared to a group receiving standard multidisciplinary diabetes care. However, the Teamwork intervention group did not show significant improvements in family conflict or quality of life (Laffel et al., 2003).

Building on work by Anderson, Laffel, and colleagues on teamwork and on the coping skills training research described above, Holmes et al. (2014) developed a clinic-based intervention that combined the two approaches. They compared the more intensive family teamwork with coping skills intervention to a diabetes education treatment delivered as adjunctive care at quarterly medical visits. In contrast to previous studies, the lower intensity intervention without coping skills training was associated with improved self-management and more effective communication skills.

Coping Skills Training for Younger School-Age Children To study whether needs of school age children (age 6–11 years) with type 1 diabetes and their parents could be met with an age-appropriate version of the coping skills training intervention, Grey et al. (2011) conducted a randomized controlled trial with a 12-month follow-up period. Modules on the same topics as described above were delivered in small groups of two to five children over 6 monthly sessions. Concurrently, parents of children met in separate groups to learn the same skills. After the separate sessions, parents and children met together to discuss the coping skills that they learned and how they could support each other. Control participants received group-based standard education paced similarly to the intervention. Analyses of the data were conducted to evaluate outcomes after 6 and 12 months (Ambrosino et al., 2008). Parents who received the coping skills program reported more improvement in family adaptability, and children showed greater improvement in life satisfaction, and these outcomes were sustained at 12 months of follow-up (Grey et al., 2011).

Coping Skills Training to Prevent Type 2 Diabetes in Youth As the incidence of type 2 diabetes increased, especially among racial and ethnic minority youth, Grey and colleagues (2009) developed a multifaceted intervention for youth at risk for type 2 diabetes that consisted of nutrition and physical activity education, coping skills training, and health coaching. The intervention was delivered by health or biology teachers trained by the investigators. In a study where high schools in a minority community were randomized, students in both groups showed improvements in anthropometrics, lipids, metabolic status, and depressive symptoms. This intervention was later translated to an Internet format and was called HEALTH[e]TEEN (Whittemore, Jeon, & Grey, 2013). The authors then conducted an implementation study of the program compared to a wait list control and found that while health behaviors improved in the experimental group, body mass index (BMI) and weight were not different in the 6 months of follow-up (Whittemore, Jeon, & Grey, 2013).

Gaps in the Research

While there has been substantial research on peer support of diabetes management in adults, there are a limited number of studies that examined the efficacy of peer support of children and adolescents with diabetes and their families. Sullivan-Bolyai's studies of peer mentor programs for parents of young children with type 1 diabetes suggest that programs led by trained peers with appropriate training may be useful for these young families. These findings are consistent with those of previous studies with adults that suggest that trained peer leaders can be very successful in improving self-management with diabetes (Lorig et al., 2001). Larger studies are necessary to confirm these findings. Only one program for adolescents led by trained peers has been evaluated in a small study of six subjects (Sims & Haines, 2011). Clearly, further studies of peer-led programs for adolescents are warranted.

Most of the peer support studies in adolescents reviewed used a healthcare professional to lead group meetings. Group programs were led by a variety of health professionals – advanced practice nurses, psychologists, pharmacists, and others. Each of these interventionists was associated with improved outcomes. To draw conclusions about whether there are differential effects of programs led by different types of professionals, further studies that compare outcomes across group leaders are needed.

Nearly all of the studies of peer support programs reviewed were of interventions that were conducted face-to-face. Particularly for youth who are busy with sports, school activities, and the like, evaluation of peer support interventions delivered via telephone, email, and web-based and/or mobile applications is important to evaluate, since they are likely to meet the needs of more youth. Quite complex interventions have been developed and delivered using these modalities in treating depression, for example (Mohr et al., 2012). Given the proclivity of youth to use smartphones to communicate, mobile applications might be a very useful approach to be studied.

It is interesting that in these studies of peer support programs, the outcomes studied were primarily related to improvements in knowledge and adherence to the diabetes regimen. Peer support interventions are usually based on the idea that the provision of peer support will improve self-efficacy or self-confidence that would lead to improved self-management or adherence. This finding suggests that many of these interventions may have been targeted more toward DMSE as opposed to peer support specifically. In addition, few of these reports contained a clearly articulated framework or process by which the outcomes were hypothesized to occur.

Characteristics of the participants of peer support programs need to be considered and studied as moderators of outcomes. Pertinent user characteristics that need to be considered include demographics (age, gender, socioeconomic status), cognitive and emotional factors (self-efficacy, knowledge, health literacy, mood), and coping skills. The lack of diversity in the samples is a notable gap. Although about 75% of youth with type 1 diabetes are White (Bell et al., 2009), Delamater and colleagues have shown consistently that minority youth have poorer outcomes than their White counterparts (Naranjo, Schwartz, & Delamater, 2015). We found no recent trials in which peer support interventions in populations with limited English proficiency were evaluated. Peer support interventions that focus on culturally appropriate concerns may help these youth to achieve better outcomes than more generic programs.

A major gap that we found in this literature is the lack of studies that evaluate peer support self-management interventions for youth with type 2 diabetes and their families. Even in the TODAY trial (Zeitler et al., 2007), diabetes education and support was provided to youth and families individually. Given the difficulties with improving lifestyle behaviors in this population, research on such interventions for youth with type 2 diabetes and their families is sorely needed.

There have been more trials of coping skills training programs than on peer support programs, although most are with adolescents with type 1 diabetes. One trial used coping skills training along with nutrition and physical activity education and health coaching to improve metabolic state in minority youth at high risk for type 2 diabetes. Findings from the majority of these studies suggest that these approaches have potential to improve outcomes for adolescents. It is less clear whether coping skills training programs enhance care of younger children with type 1 diabetes. It may be that teaching coping skills during the younger school-age years would help to ease the transition to adolescence, but such longitudinal studies have not been conducted.

One of the strengths of the studies of coping skills training programs is the clarity of the hypotheses about the processes through which these programs are hypothesized to work. For example, Jaser et al. (2014) examined the mediators of outcomes in the TEENCOPE trial and found that self-efficacy mediated effects on quality of life and in TEENCOPE, stress reactivity, and primary and secondary control coping mediated treatment effects. It is clear that more studies of this type need to be conducted so that we can understand how such programs work.

In this literature on both peer support and coping skills training programs, the lack of implementation and dissemination research is a gap that needs to be addressed. The works by Laffel and colleagues on the Teamwork intervention (Laffel et al., 2003) and that of Whittemore et al. (2015) were the only such studies. If similar programs are to be incorporated into clinical practice, questions of how best to disseminate information about such programs and how to assure completion of the programs using tested implementation approaches need to be answered.

Clinical Implications

To meet the needs of children and adolescents with diabetes and their families and facilitate self-care in meaningful ways, DSME/S programs have changed as traditional views in healthcare are replaced by a new paradigm emphasizing partnerships between a prepared interdisciplinary healthcare team and an activated patient and family. Incorporating peer support and coping skills training in DSME/S programs is an innovative way diabetes care may enhance support in children and adolescents (Haas et al., 2014; Marrero et al., 2013). Such programs must be adapted to the evolving healthcare delivery environment. Time and cost constraints make it difficult to provide these services, and these difficulties may force health professionals to prioritize acute issues over psychosocial needs. Faced with these challenges, it is critical that strategies for enhancing the availability of peer support and coping skills programs for children and adolescents with diabetes and their families are evaluated and implemented in practice or made available in ways that do not interfere with practice patterns. How to pay for the cost of such programs is not clear, however. It is possible that the ability to provide such support programs may be improved with potential changes to healthcare reimbursement with the Patient Protection and Affordable Care Act.

Self-management support programs that are integrated with clinical care may facilitate the adjustment of medications and other treatment regimen factors. For example, adoption of shared medical visits for adolescents might provide opportunities to provide peer support as well as training in coping skills. For younger children, a companion parental program may be an important element to provide peer support for parents as children begin to transition to adolescence. Both parents and youth need support as the shift of responsibilities for diabetes care occurs.

A major area in the social environment for youth is schools. The findings by Grey et al. (2009, 2013) of preventive lifestyle interventions integrated with a school-based program that demonstrated high levels of engagement in diverse samples of adolescents are intriguing. Innovative partnerships such as these that extend type 2 diabetes prevention interventions into the classroom may help reach at-risk youth and provide support for improving dietary behaviors and physical activity for all youth. Positive effects of such efforts may include not only positive changes in health outcomes and better quality of life but also decreased feelings of isolation and “differentness” that youth at risk or with type 2 diabetes often experience (Mulvaney et al., 2008).

It is complicated to evaluate psychosocial self-management interventions in Latino/Hispanic children and adolescents with diabetes and their families since they often speak multiple languages and use interpreters when receiving diabetes care. Latino/Hispanic children and adolescents with diabetes and their families are rarely studied, and much remains unknown regarding their experiences, but Latinos/Hispanics are the fastest-growing ethnic/racial group in the country. Studies of such programs for peer support or coping skills in this at-risk population are sorely needed.

Conclusions

Research on approaches to facilitate development and mastery of skilled self-management practices can serve to improve provision of effective high-quality patient-centered care for children and adolescents with diabetes and their families. Much more work needs to be done, especially with regard to the evaluation of programs provided in practice and determination of what programs work best on what outcomes and for whom.

Peer support and coping skills training approaches have been shown to be effective in supporting the development and mastery of skilled self-management practices in children and adolescents with type 1 diabetes and their families. It is important to understand factors associated with health disparities and less desirable health outcomes. Further research in this area has the potential to guide diabetes care and influence policy decisions, ultimately benefiting children and adolescents with diabetes and their families and the communities in which they live.

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Part IV
Community Level Factors for Children and Adolescents

Chapter 13
Demographic Influences and Health Disparities

Carmen Mironovici, Maura Kepper, Richard Scribner, and Stuart Chalew

Introduction

Diabetes mellitus is one of the most common incurable, chronic diseases of childhood. The incidence of both type 1 and type 2 diabetes mellitus (T1D, T2D) has been increasing in children. Both types of diabetes are associated with development of serious metabolic complications and increased morbidity and mortality. The incidence and prevalence of diabetes, success in achieving optimal management, outcomes, and risk for developing later complications have been found to vary between patients of different race, ethnicity, and socioeconomic backgrounds. It is often challenging to separate differences due to race and ethnicity which might be related to genetic and biologic factors from the impact of the environment and socioeconomic factors on the occurrence of diabetes and outcome of treatment. This chapter will review our evolving understanding of these factors on childhood diabetes.

Social and Physical Environmental Factors Influencing Diabetes and Subsequent Health

Social and physical environmental factors at the neighborhood level can be linked to behavioral risk and biological processes that promote chronic diseases such as obesity, diabetes, and cardiovascular disease (Miller, Chen, & Parker, 2011). Therefore, inequalities in the conditions in which individuals live, work, and play can lead to inequalities in health. Poor and minority populations are more likely to be exposed to unfavorable social, food, and physical activity environments that predispose residents to obesity and metabolic dysfunction (Frech & Kimbro, 2011; Lampard, Jurkowski, Lawson, & Davison, 2013). An analysis of neighborhood-level data in 100 metropolitan areas with the largest child populations (comprising 45 million children) found that black and Latino children consistently live in more disadvantaged neighborhoods than white children and a large portion of black and Latino children consistently live in both poor families and poor neighborhoods (Acevedo-Garcia, Osypuk, McArdle, & Williams, 2008).

C. Mironovici · S. Chalew (✉)
Division of Endocrinology/Diabetes, Department of Pediatrics, School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, USA

Division of Endocrinology, Children's Hospital of New Orleans, New Orleans, LA, USA
e-mail: schale@lsuhsc.edu

M. Kepper · R. Scribner
School of Public Health, Louisiana State University Health Sciences Center, New Orleans, LA, USA

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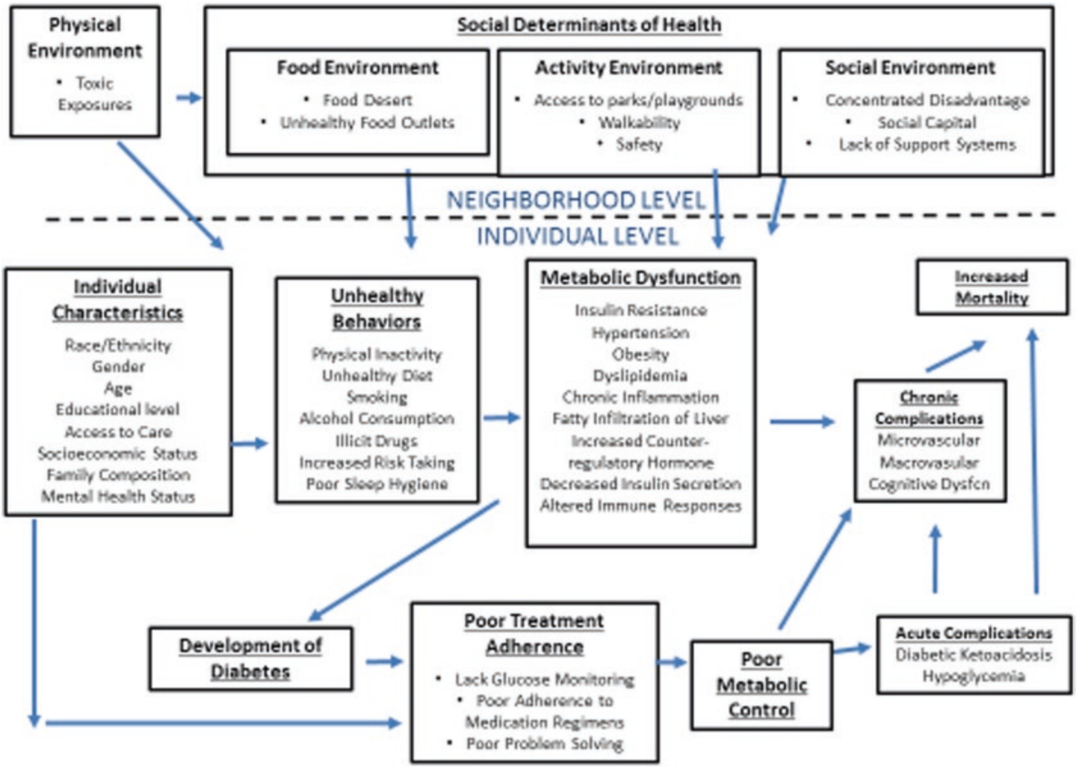

Fig. 13.1 Proposed schema of how environmental and social determinants may influence development and progression of obesity, diabetes, and their complications

The relationship between the environment and diabetes occurrence and deleterious health outcomes is complex due to the variety of exposures that can potentially lead to a state of metabolic dysfunction. Figure 13.1 outlines a proposed schema of how neighborhood and environmental factors influence development of diabetes and its complications. Although specific mechanisms have not been fully identified, both direct and indirect effects may occur (Diez Roux, 2003; Smalls, Gregory, Zoller, & Egede, 2015, 2016). The direct effects on an individual may occur from environments that result in chronic psychosocial stress (e.g., high crime neighborhoods, concentrated disadvantage, abusive family environments) (Blair, Raver, Granger, Mills-Koonce, & Hibel, 2011; Danese & McEwen, 2012; McEwen, 2004; Schulz et al., 2012; Steptoe et al., 2014). For example, environmental stress may result in chronic activation of insulin counter-regulatory hormones especially through the hypothalamic pituitary adrenal (HPA) and the sympathetic adrenal medullary (SAM) systems.

McEwen, a neuroendocrinologist, was the first to propose a relationship between chronic stress and metabolic dysfunction (McEwen, 1998, 2000). He theorized that conditions of stress lead to reactive homeostatic responses or “allostasis” by an individual. Chronic stress could produce prolonged/repeated activation of such responses with “allostatic overload” which would cause pathologic “wear and tear” on both body and brain. In vulnerable individuals these changes may contribute to obesity, dysglycemia, dyslipidemia, inflammation, immune dysfunction, insulin insensitivity, and hypertension.

Researchers in a variety of disciplines have assessed the influence of chronic stress from living in a disadvantaged neighborhood environment (Doamekpor & Dinwiddie, 2015; Geronimus, Hicken, Keene, & Bound, 2006; Schulz et al., 2012; Theall, Drury, & Shirtcliff, 2012; Weiss, Bremer, & Lustig, 2013). From National Health and Nutrition Examination Survey (NHANES) data, Theall and colleagues found that nondiabetic adolescents living in neighborhoods characterized with high concentrated disadvantage had a 69% greater odds of increased allostatic load, which includes higher fasting glucose and lower insulin insensitivity, compared with adolescents living in low disadvantage neighborhoods (Theall et al., 2012). A recent study that looked specifically at the stress-related end points of allostatic load (i.e., cardiovascular, inflammatory, neuroendocrine, and cholesterol responses) confirmed that allostatic load may be a mechanism by which stressful environments contribute to T2D risk (Steptoe et al., 2014). However, other studies examining the influence of allostatic load specifically among diabetic patients have reported equivocal findings (Carlsson, Nixon Andreasson, & Wandell, 2011; Mattei, Demissie, Falcon, Ordovas, & Tucker, 2010). The relationship between social stress in the environment and causation of T1D remains uncertain. Potentially mechanisms which alter the immune system or contribute to decreased insulin sensitivity from allostatic overload might accelerate the clinical presentation of T1D (Booker, 2010; Fourlanos, Harrison, & Colman, 2008; Islam, Srinivasan, & Craig, 2014; Wilkin, 2009). At present there is no connection of allostatic overload associated with autoimmune beta-cell destruction (Dayal, Samprathi, Jayaraman, Kohat, & Bhalla, 2016).

With regard to the management of diabetes, there are several studies that documented a relationship between stressful social environments and glycemic control. Zuijdwijk and colleagues studied glycemic control among their pediatric T1D population in terms of zip codes deprivation indices (Zuijdwijk, Cuerden, & Mahmud, 2013). They found significantly higher levels of HbA1c among the T1D patients residing in high deprivation zip codes. Coulon and colleagues also found that residing in census tracts with higher concentrated disadvantage was associated with a significantly higher HbA1c among their black T1D patients. Thus neighborhood factors may contribute to challenges in the management of pediatric diabetes (i.e., medication adherence, pump type, etc.). It should be kept in mind that blacks may be disproportionately disadvantaged compared to the white population making it difficult to parse out the influence of social/environmental factors from that of race (Coulon et al., 2017).

The indirect pathway implicates environments that promote unhealthy behaviors (i.e., physical inactivity and/or a poor diet) that lead to adverse health outcomes, including T1D and T2D. This poses a particular challenge for children with diabetes who require consistent adherence to self-care behaviors (i.e., diet and physical activity) and management regimens that are often challenging and complex (Billimek & Sorkin, 2012; Smalls et al., 2015).

The contribution of unhealthy diets to the obesity and diabetes in the USA is well recognized. Research indicates that access to healthy food outlets (i.e., markets offering high-quality food products at the lowest cost as compared to stores that sell mostly prepared, high-calorie foods and little fresh produce, at higher prices) results in healthier food intake. A study in adults observed that for each additional supermarket near the individual's home (within the census tract), there was a related 32% increase in fruit and vegetable intake among blacks and an 11% increase among whites (Larson, Story, & Nelson, 2009). The differential availability of healthy food outlets according to the racial and income composition of neighborhoods may be contributing to the differences in diabetes prevalence between African-American and White individuals (Franco, Diez Roux, Glass, Caballero, & Brancati, 2008).

Despite known benefits of physical activity for diabetes prevention and management, levels of physical activity remain inadequate, especially among disadvantaged populations (Chimen et al., 2012; Colberg et al., 2010; Michaliszyn & Faulkner, 2010). In general, youth may be getting less than optimal physical activity (Katzmarzyk et al., 2016). But physical activity is significantly reduced in ethnic minority groups and individuals from socioeconomically disadvantaged backgrounds (Singh, Kogan, Siahpush, & van Dyck, 2008). Disparate levels of physical inactivity not only contribute to obesity but also result in differences in cardiorespiratory fitness across racial groups (Katzmarzyk et al., 2016). Multiple factors of a child's environment can contribute to physical inactivity: poor access to safe places to play (greenspace, parks/playgrounds), longer distances from home to school, and lack of sidewalks, bike lanes, and safe intersections to cross streets (Ball et al., 2010; Burdette & Hill, 2008; Ding, Sallis, Kerr, Lee, & Rosenberg, 2011; Foster & Giles-Corti, 2008; Kimbro, Brooks-Gunn, & McLanahan, 2011). Furthermore, children with local environmental barriers to physical activity often lack the resources to acquire physical activity outside their neighborhood (e.g., sports teams that are financially burdensome and require transportation) (Carver, Timperio, Hesketh, & Crawford, 2010).

Additional consideration should be placed on how environments impact children's health prior to birth. There is growing recognition that exposure to environments characterized by social or nutritive stress during early developmental stages (e.g., fetal overnutrition) can result in epigenetic changes predisposing affected individuals to adolescent obesity and metabolic dysfunction. There is concern that exposure to stressful environments (i.e., social or nutritive stress) may begin to have an influence during early developmental stages of life (Fall, 2011; Miller et al., 2011). *The developmental origins perspective proposes that exposures during critical periods of intrauterine development when there is a high degree of* genomic plasticity can result in permanent physiologic changes predisposing the affected individual to later obesity and metabolic dysfunction (Bateson et al., 2004; Fall, 2011, 2013). For example, fetal overnutrition, which may be due to the mother's environment, may result in predisposing their offspring to adolescent obesity and metabolic dysfunction (Miller et al., 2011).

Measuring Social and Physical Environmental Influences

Research has embraced the social-ecological perspective to focus on how social and physical environmental factors contribute to racial and ethnic disparities in the development and health outcome of chronic diseases such as diabetes. Measuring neighborhood factors that influence health and determining the geographic scale (i.e., census tract, block group, or spatial buffer around an individual's residence) that appropriately captures an individual's exposure can be challenging. Social determinants of health are defined using numerous variables (built environment, social capital, crime, income inequality, segregation, etc.) and measured using a variety of methods (e.g., archival sources, direct observation, questionnaires) at varied geographic scales (block group level, census tract level, 1 mile spatial buffers, etc.); this variability has produced inconsistent associations to chronic diseases, including diabetes, and has limited public health efforts (Diez Roux & Mair, 2010).

The majority of research examining environmental influences of health uses archival sources, such as census data, or individual perceptions of his or her environment, as these methods are cost-effective and efficient (Odgers, Caspi, Bates, Sampson, & Moffitt, 2012; Sampson, Raudenbush, & Earls, 1997). However, archival sources are often limited in the variables measured and geographic resolution (census tract or block group level). An individual's perceptions of their environment, although important, are not objective measures of a neighborhood environment. Observation methods, such as Systematic Social Observation (SSO), allow for objective data collection of certain variables such as presence of graffiti, litter, dilapidation, street safety measures, etc. that are not available through archival sources (Kepper et al., 2017; Odgers et al., 2012). Technological advancements have enabled SSO to be performed virtually using Google Street View which has increased the feasibility (decreasing time and costs) of performing SSO while maintaining the reliability of this measure (Brownson, Hoehner, Day, Forsyth, & Sallis, 2009; Kepper et al., 2017; Odgers et al., 2012; Schaefer-McDaniel, Caughy, O'Campo, & Gearey, 2010).

Incidence and Prevalence of Diabetes in Children

Diabetes is one of the most common chronic diseases of childhood affecting approximately 200,000 children and adolescents in the USA (CDC, 2014a). More than 23,000 new cases of diabetes of all types are estimated to be diagnosed among pediatric population each year (CDC, 2014b, American Diabetes Association, 2013). Furthermore, the SEARCH for Diabetes in Youth study (SEARCH study), a large multiethnic population-based, observational study of youth under the age of 20, reported an increasing incidence of both T1D and T2D over the last two decades, particularly among minority youth (Dabelea et al., 2014; Lipman et al., 2013; Mayer-Davis et al., 2017).

T1D T1D is caused by a deficiency in the ability to secrete insulin, most frequently due to autoimmune destruction of the pancreatic insulin producing beta-cells in genetically predisposed individuals (American Diabetes Association, 2013). Initiation of the autoimmune damage may occur after exposure to an environmental trigger (American Diabetes Association, 2013). T1D is the predominant form of diabetes in youth, affecting 1 in every 300 children and adolescents in the USA (Pettitt et al., 2014; Writing Group for the SEARCH for Diabetes in Youth Study Group, Dabelea et al., 2007). The SEARCH study reported that 97% of children diagnosed with diabetes below the age of 10 years had T1D, compared to 62% of diabetic youth aged 10–14 years and 42% of diabetic youth aged 15–19 years (Dabelea et al., 2014).

Over the years the incidence of pediatric T1D has been increasing (Lipman et al., 2013; Mayer-Davis et al., 2017), with a trend toward younger age of onset (Dabelea et al., 2014; S. S. Group, 2004; Vehik et al., 2007; Wolfsdorf, Glaser, Sperling,, & American Diabetes, 2006). SEARCH data from the USA found an upward trend in incidence rates for T1D, from approximately 15,900 new cases diagnosed per year in the USA in 2002–2003 to 17,900 new cases in 2011–2012, with an overall 1.8% annual increase in incidence of T1D (Mayer-Davis et al., 2017).

Race/ethnicity is an important factor in the distribution of new cases. Although the incidence of T1D in white youth is fourfold higher than in minority youth (Dabelea et al., 2014; CDC, 2014a), whites had the smallest annual increase in incidence (1.2% per year) of all racial/ethnic groups in the USA compared to 2.2% annual increase for blacks and 4.2% for Hispanics (Mayer-Davis et al., 2017). The age- and gender-adjusted rate of T1D for white youth was 27.4/100,000 in 2009, which was increased from 24.4/100,000 in 2002 (Lawrence et al., 2014). Among blacks, the annual T1D incidence was 15.7 per 100,000 in the 0–9 years age-group, increasing to approximately 17 per 100,000 in youth aged 10–19 years (Writing Group for the SEARCH for Diabetes in Youth Study Group, Dabelea et al., 2007). In the 10–14 years age-group, black females had a significantly higher incidence (26.1/100,000 per year) than black males (16.7/100,000 per year) and not different from incidence in white females of same age (29.1/100,000 per year) (Mayer-Davis et al., 2009). But the highest increase of T1D incidence in African-Americans (220%) has been noticed in children younger than 5 years of age, from 3.8 /100,000 in 1990 to 12.2/100,000 in 2009, as demonstrated from a 20-year retrospective review of the Philadelphia Pediatric Diabetes Registry (Lipman et al., 2013). The incidence of T1D in Hispanic children and adolescents was between that of whites and African-Americans (CDC, 2014a; Lawrence et al., 2009). SEARCH data from 2008 to 2009 reported an incidence of approximately 15 per 100,000 in Hispanic children younger than 10 years and approximately 18 per 100,000 in youth 10–19 years of age (Lado & Lipman, 2016).

The prevalence rate of T1D exceeded T2D for both genders and all pediatric age-groups. The overall prevalence of physician-diagnosed T1D in youth aged 0 through 19 years was 1.48 per 1000 (Dabelea et al., 2014). For children aged 0–9 years, prevalence was 0.44 per 1000 and increased with age to 1.59 per 1000 for youth 10–19 years old (Dabelea et al., 2014). There was approximately equal prevalence between both genders. By 2009, the overall prevalence rate had increased significantly to 1.93 per 1000, representing an increase of 21.1% over the 8-year period (Dabelea et al., 2014). Whites have the highest prevalence of the disease, 2.55 per 1000 (Dabelea et al., 2014), but T1D is increasingly affecting youth of racial/ethnic minorities (S. f. D. i. Y. S. Search for Diabetes in Youth Study Group, Liese et al., 2006). African-American children aged 0–9 years have a relatively low prevalence of 0.57 per 1000, but by the age of 10–19 years, an estimated 2.04 per 1000 have T1D (2.17/1000 among African-American girls and 1.91/1000 among African-American boys) (Marshall Jr., 2005; Mayer-Davis et al., 2009). Across age and gender groups, up to 50% of African-American youth with T1D were overweight or obese (Mayer-Davis et al., 2009), compared with 30% of Whites (Bell et al., 2009) and 44% of Hispanics (Lawrence et al., 2009).

Projections based on SEARCH data suggest that the number of youth with T1D will nearly triple in the USA, from 179,387 in 2010 to 587,477 in 2050 (Imperatore et al., 2012). The predicted increase will occur primarily among minority race/ethnic groups (Imperatore et al., 2012). The great racial variability and rapid increase in incidence of T1D in specific racial/ethnic groups are significant and not yet understood.

T2D T2D is caused by a combination of resistance to insulin and inadequate compensatory rise in insulin secretion (American Diabetes Association, 2013). Pediatric T2D is characterized by familial predisposition, increased central body fat, female-to-male predominance, and greater occurrence in certain ethnic groups (Mayer-Davis et al., 2017).

T2D was rare in children before the 1990s, accounting for less than 3% of all cases of new-onset diabetes in adolescents (D'Adamo & Caprio, 2011), and considered a disease of the middle-aged and elderly. Since that time it has been increasingly diagnosed in older children and adolescents, although T1D remains the main form of pediatric diabetes worldwide. In some locales up to 45% of new cases of diabetes in older children are attributed to T2D (Bobo et al., 2004; Pinhas-Hamiel & Zeitler, 2005). About 5000 new cases are diagnosed in the USA each year (Dabelea et al., 2014). The average age of onset of T2D in youth is 13 years of age, coinciding with physiological occurrence of pubertal insulin resistance (Rosenbloom, Silverstein, Amemiya, Zeitler, & Klingensmith, 2009). The diagnosis is rarely made in children aged 0–9 years (Dabelea et al., 2014).

The increase in cases of T2D in youth has been strongly correlated with increased occurrence of childhood obesity over the past two decades (Kaufman & Shaw, 2007; Pinhas-Hamiel & Zeitler, 2000, 2005; "Type 2 diabetes in children and adolescents. American Diabetes Association," 2000), suggesting a causal relationship, particularly when the obesity is central and related to decreased physical activity (Alberti et al., 2004). More than 90% of youth with T2D were overweight or obese at diagnosis, compared with 35% of those with T1D (Hamman et al., 2014; Liu et al., 2010; Scott, Smith, Cradock, & Pihoker, 1997). Average BMI at diagnosis is typically in high 30s (Abbasi, Juszczyk, van Jaarsveld, & Gulliford, 2017). The prevalence of obesity among children and adolescents in the USA has significantly increased in the past three decades. Obesity increase has been more pronounced among African-American and Hispanic youth than among whites, specifically black males and Hispanic females (Skinner & Skelton, 2014; Sturm, 2002). Physical inactivity is one of the major contributors to obesity. White children and adolescents were found to have higher physical activity levels than other ethnic groups, with boys usually more active than girls, regardless of race (Calle, Thun, Petrelli, Rodriguez, & Heath Jr., 1999). Increased body adiposity leads to insulin resistance and the need for increased compensatory insulin secretion (Krauss et al., 2000; Williams & Kelley, 2000). Central obesity, in particular, is an important determinant of insulin resistance leading to hyperinsulinemia (Byers et al., 2002; Tatsumi et al., 2015). Individuals who cannot adequately increase insulin in the face of insulin resistance become dysglycemic (Cali et al., 2009; Taksali et al., 2008). The strong relationship between obesity and T2D has given rise to the term "diabesity" (Astrup & Finer, 2000; Anjum, 2011; Farag & Gaballa, 2011).

Although T2D disproportionately affects certain minority populations in the USA, notably Native Americans, African-Americans, and Mexican Americans (Dabelea et al., 1998; Neufeld, Raffel, Landon, Chen, & Vadheim, 1998), the disease occurs in all races (Rosenbloom et al., 2009; Writing Group for the SEARCH for Diabetes in Youth Study Group, Dabelea et al., 2007). African-American children are five times as likely as white children to develop T2D (Hamman et al., 2014). In minority communities, the occurrence of childhood T2D may exceed that of T1D (Spanakis & Golden, 2013).

Pediatric obesity in high-risk minority communities has been linked with racial differences in insulin sensitivity evident in childhood (Golden et al., 2012; Goran, Bergman, Cruz, & Watanabe, 2002). One study comparing white and black obese children found that higher insulin secretion levels compensate for lower insulin sensitivity in whites, but not in blacks, suggesting a greater diabetogenic risk from obesity among African-Americans (Conway et al., 2018). SEARCH data from 2002 to 2012 reported an increase in overall incidence of T2D by 4.8% per year, which significantly differed by race. The highest rate of new cases of T2D in youth ages 10–19 was observed in Native Americans (8.9% annual increase in incidence), followed by blacks (6.3%) and Hispanics (3.1%), compared to whites (lowest increase, 0.6%) (Mayer-Davis et al., 2017). Overall females have a higher rate of new diagnosed cases per year (6.2%) compared to males (3.7%) (Mayer-Davis et al., 2017).

Economic and ethnic disparities in youth with T2D parallel the disparities in obesity among youth, with ethnic minority and lower socioeconomic status (SES) children more likely to be obese than white, middle-class youth (Delva, O'Malley, & Johnston, 2006; Pulgaron & Delamater, 2014; Tang, Chen, & Krewski, 2003). Environmental factors such as lower SES, general lack of physical activity, greater occurrence of in utero exposure to hyperglycemia, improper diet (Arslanian, Saad, Lewy, Danadian, & Janosky, 2002), and exposure to neighborhood stresses appear to increase risk for obesity and development of T2D (Shaw, 2007; Singh, Siahpush, & Kogan, 2010).

The occurrence of pediatric T2D is also strongly associated with gender. Among African-Americans, about twice as many girls as boys have T2D (D'Adamo & Caprio, 2011). During puberty, which is associated with the peak of physiologic insulin resistance (Moran et al., 1999), African-American girls aged 10–14 years are twice as likely as African-American boys of the same age to develop T2DM: 1.47/1000, compared with 0.67/1000 in African-American boys (Bulger, Shubrook, & Snow, 2012; Mayer-Davis et al., 2009). At puberty, the annual incidence of T2D was 29.8/100,000 in black girls and 12.2/100,000 in black boys (Writing Group for the SEARCH for Diabetes in Youth Study Group, Dabelea et al., 2007). This may be associated with earlier puberty onset, lower levels of physical exercise, and greater degrees of obesity in girls than in boys (Alberti et al., 2004). Among youth aged 15–19 years, the incidence of T2D exceeded that of T1D for female subjects, but not for males (Mayer-Davis et al., 2009). However, the boys catch up later in prevalence and among adults, more males than females are diagnosed with T2D (Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services, 2017).

In comparison, the incidence rates of T2D in Hispanic children aged 10–14 years were 6.8 per 100,000 girls and 4.7 per 100,000 boys. The rates increased among Hispanic youths aged 15–19 years: 12.5 per 100,000 for female subjects (exceeding the incidence of T1D in this group) and 11 per 100,000 for male subjects (Lawrence et al., 2009). The gender difference previously described in black adolescents with T2D was not present in Hispanics (Lawrence et al., 2009).

Pediatric T2D has a strong family predisposition (D'Adamo & Caprio, 2011) for insulin resistance, increased weight gain, and subsequent inadequate compensatory secretion of insulin (Defronzo, 2009; Lyssenko et al., 2008). These factors may be more prevalent in certain ethnic populations. For example, African-American children aged 7–11 years have increased insulin resistance and significantly higher insulin levels than age- and BMI-matched white children (Reinehr, 2013; Uwaifo et al., 2002). Pima Indians may have a genetic predisposition to insulin resistance and an increased risk for T2D (Dabelea et al., 2011). Caucasian children have higher sensitivity to insulin, likely due to their association with a T2D protective genetic variant (Van Name & Santoro, 2013).

An overall average annual increase in pediatric T2D was noted between 2001 and 2009 in both genders, all age-groups, and ethnicities (white, Hispanic, and African-American) (Mayer-Davis et al., 2017). The prevalence of T2D in 2001 was 0.34 per 1000 and 0.46 per 1000 in 2009, with an overall increase in prevalence of 30.5% over the 8 years (Dabelea et al., 2014). Increasing from childhood, the prevalence of T2D in adolescents reached 1.20 per 1000 in Native Americans (SEARCH for Diabetes in Youth Study Group, 2004), 1.06 per 1000 in African-Americans (Mayer-Davis et al., 2009), and 0.45/1000 in Hispanics (Lawrence et al., 2009). For Native American youth aged 10–19, the rate of new cases of T2D is now higher than for T1D (Writing Group for the SEARCH for Diabetes in Youth Study Group, Dabelea et al., 2007). In comparison, whites between 10 and 19 years have the lowest rate of T2D: 0.18/1000 persons (Bell et al., 2009). Projections suggest that there will be a fourfold increase in the number of youth living with T2D in 2050 compared with data from 2010 (Imperatore et al., 2012). The obesity epidemic in children and adolescents with a sedentary life style is a major contributor to the increase in incidence rate of pediatric T2D in the USA being among the highest in the world (Narasimhan & Weinstock, 2014; Singh, Shaw, & Zimmet, 2004; Writing Group for the et al., 2007).

Complications of Diabetes in Youth

Youth with diabetes are at risk for development of both acute and chronic metabolic complications of the disease. Risk for diabetes complications varies depending on type of diabetes, ethnicity, age, duration of disease, pubertal status, and metabolic control of the disease.

Acute Complications Acute life-threatening complications such as diabetic ketoacidosis (DKA) and hypoglycemia occur more often in children with T1D (Cengiz et al., 2013). DKA and hypoglycemia are serious complications and have been associated with considerable morbidity and mortality (Dunger et al., 2004). DKA can occur at presentation of T1D in families who do not recognize and seek medical attention for the typical symptoms of hyperglycemia (Usher-Smith, Thompson, Sharp, & Walter, 2011). After diagnosis of diabetes, DKA is preventable as patients and families are more aware of the symptoms and signs of metabolic decompensation and have access to glucose testing and assessment of ketones. Delay in treatment and seeking medical intervention increases the severity of acidosis and dehydration in DKA (Wolfsdorf et al., 2006).

Racial/ethnic/socioeconomic differences are associated with the risk for occurrence of DKA (Cengiz et al., 2013). African-American youth are more likely to be hospitalized for DKA than white or Hispanic patients (Lipton, Good, Mikhailov, Freels, & Donoghue, 1999). Greater risk for DKA has been associated with higher HbA1c levels and less frequent blood glucose monitoring in African-American diabetic youth (Cengiz et al., 2013). Hyperosmolar decompensation in T2D in the absence of ketoacidosis is a serious and rare complication which carries a greater risk of cerebral edema, thrombosis, and death compared with DKA (Zeitler et al., 2011). It appears to occur most often in obese African-American males (Zeitler et al., 2011).

Hypoglycemia in youth with diabetes is an acute adverse effect of treatment with glucose-lowering medications, particularly of intensive insulin therapy in patients with T1D, and therefore can be a critical limiting factor in diabetes management (McGill & Levitsky, 2016). One of the findings of the Diabetes Control and Complications Trial (DCCT) was that improved glycemic control which lowered mean blood glucose levels led to increased occurrence of hypoglycemic episodes ("Hypoglycemia in the Diabetes Control and Complications Trial. The Diabetes Control and Complications Trial Research Group," 1997). Paradoxically, the T1D Exchange reported that acute symptomatic episodes of severe hypoglycemia were twice as frequent among African-American youth than white patients even though the African-American patients had higher HbA1c levels and were less likely to be on insulin pump or multiple daily injection management (Willi et al., 2015).

Youth-onset T2D carries a lower risk for hypoglycemia than T1D (U. K. H. S. Group, 2007), but T2D patients who experience episodes of hypoglycemia may have an increased risk of cardiovascular disease and higher mortality, as suggested by the results of the ACCORD trial in adults (Hempe et al., 2015; Seaquist et al., 2012). Abnormally low plasma glucose concentrations, prolonged episode duration, and high frequency of episodes increase the risk for morbidity in patients (American Diabetes Association Workgroup on Hypoglycemia, 2005). Acute symptoms of hypoglycemia (hunger, shakiness, weakness, rapid heart rate, cold sweat, drowsiness, headaches) are caused by activation of the sympathetic nervous system and adrenal catecholamine counter regulatory response in both T1D and T2D patients. The effects of excessively released epinephrine on the cardiac work load are significant, increasing the heart rate, systolic blood pressure, myocardial contractility, stroke volume, and cardiac output and predisposing to arrhythmias (Nordin, 2010). During episodes of hypoglycemia, the cerebral blood supply with its metabolic fuel decreases and may become insufficient generating symptoms of neuroglycopenia (difficulty concentrating, weakness, dizziness, confusion and irritability to seizures, loss of consciousness, and even death) (Cryer, 1999).

The neurocognitive impairment during hypoglycemia can have potentially deleterious and cumulative long-term effects on intellectual function, particularly in young children (Davis & Jones, 1998). Asvold et al. reported lower cognitive scores overall in children with diabetes who had experienced severe hypoglycemic episodes than in those without history of hypoglycemia (Asvold, Sand, Hestad, & Bjorgaas, 2010). The long-term complications of recurrent hypoglycemia may also include impaired awareness to hypoglycemia and weight gain from preventive overfeeding, with negative impact on insulin resistance and risk of cardiovascular diseases (Cryer, 2004).

Chronic Complications Long-term diabetes complications are often broadly classified as being microvascular or macrovascular. Microvascular disease is related to longstanding damage to small blood vessels which leads to retinopathy, nephropathy, and neuropathy (Dabelea et al., 2017). Macrovascular disease is related to accelerated atherosclerosis and changes in large vessels which cause cardiovascular disease including heart attack and stroke (Dabelea et al., 2017). The DCCT, EDIC, and UKPDS studies showed that microvascular disease in adults could be prevented with improved glycemic control (Diabetes Control and Complications Trial Research Group, Nathan et al., 1993; Gubitosi-Klug & DCCT/EDIC Research Group, 2014; UK Prospective Diabetes Study (UKPDS) Group, 1998; Nathan & DCCT/EDIC Research Group, 2014). Data from SEARCH indicates a substantial prevalence of diabetes-related complications and comorbidities in both types of diabetes at a young age, higher for all outcomes among adolescents and young adults with T2D compared with T1D at similar ages and diabetes duration (Dabelea et al., 2017).

In T1D patients the microvascular complications start developing within 5–7 years of the onset of diabetes but rarely before the onset of puberty (Dabelea et al., 2017). The risk for occurrence of complications increases with poor glycemic control, longer duration of diabetes, and puberty onset (Diabetes Control and Complications Trial Research Group, Nathan, Genuth, Lachin, Cleary, et al., 1993). Because of its insidious onset, T2D may be present untreated for a prolonged period of time before diagnosis. Thus, microvascular complications may be found early in the course of T2D, sometimes at the time of diagnoses or soon after (Dabelea et al., 2017; Dean & Sellers, 2007; Pinhas-Hamiel & Zeitler, 2007). Complications of T2D can progress faster than in youths with T1D (Pinhas-Hamiel & Zeitler, 2007). Among early-onset T2D patients, ethnic minorities appear to be disproportionately affected by diabetic complications and comorbidities (Dabelea et al., 2017; Golden et al., 2012). By 8 years after diagnosis, about 75% of patients with childhood onset of T2D had at least one microvascular complication from diabetes compared with one in three T1D patients (Dabelea et al., 2017). The SEARCH study found that diabetic nephropathy, retinopathy, and peripheral neuropathy occurred over twice more often in youth with T2D than with T1D (Dabelea et al., 2017). Nearly 20% of youth with T2D participating in the study developed kidney disease versus 6% of those with T1D, peripheral neuropathy in 18% of T2D patients versus 9% of T1D, and retinopathy in 9% of T2D versus 6% of T1D youth (Dabelea et al., 2017).

Risk factors for heart disease are also more frequent in patients with T2D. The SEARCH study reported greater hypertension (22% versus 10%) and arterial stiffness (48% versus 12%) in patients with T2D compared with T1D. The exception was the prevalence of cardiovascular autonomic neuropathy, which was similar in youth with either T2D or T1D (Dabelea et al., 2017). Adjustments for differences in age, sex, race/ethnicity, BMI, waist-height ratio, mean arterial blood pressure, and glycemic control over time did not remove the excess prevalence of microvascular complications among young patients with T2D compared with T1D (Dabelea et al., 2017).

In addition to micro- and macrovascular complications of diabetes, children and adolescents with T2D are prone to develop obesity-related complications, including hypertension, intrahepatic fat accumulation, and metabolic syndrome, which further increase their cardiovascular risk (Cali et al., 2009;

Pinhas-Hamiel & Zeitler, 2007). T2D with onset in childhood or adolescence also appears to progress faster than the adult-onset T2D, determined by accelerated failure of beta-cell function in youth (Gungor & Arslanian, 2004), and has a more aggressive course in the development of complications, as the results of TODAY study have shown (Narasimhan & Weinstock, 2014).

Retinopathy The reported prevalence of diabetic retinopathy by the SEARCH study was found to be higher among minority adolescents with T2D (Dabelea et al., 2017). Retinopathy, including dilated retinal venules and microaneurysms, may start very early in the course of pediatric T2D (Sultan, Starita, & Huang, 2012). Retinopathy often remains asymptomatic during childhood and adolescence (Sultan et al., 2012). Retinopathy was found in 17% of children and adolescents diagnosed with T1D for more than 5 years (Lado & Lipman, 2016), usually in the pre-proliferative stage. The prevalence was higher in minority youth with diabetes (23.9%) when compared with white youth (15.3%) (Lado & Lipman, 2016). This was further supported by data from the National Health and Nutrition Examination Survey (NHANES) which found diabetic retinopathy and visual impairment in 26.5% in African-American and Hispanic patients compared with 18.2% in whites (Golden et al., 2012). The retinopathy tends to progress faster and to be more severe in African-Americans compared to whites, with the risk of visual impairment fourfold higher in African-Americans (Roy, 2000). Insulin resistance at puberty may be an accelerator for progression of vascular complications including retinopathy (Bognetti et al., 1997; Cho, Craig, & Donaghue, 2014).

Hypertension The presence of diabetes increases the risk of developing hypertension (Volpe, Battistoni, Savoia, & Tocci, 2015). One-quarter of youth with T1D (Dean & Sellers, 2007; Eppens et al., 2006; Muntner, He, Cutler, Wildman, & Whelton, 2004) and up to 36% in T2D youth develop high blood pressures (Dean & Sellers, 2007). The prevalence of hypertension is higher in African-Americans with diabetes (33.5%) than in whites (28.9%) and Hispanics (20.7%) (Hajjar & Kotchen, 2003). Higher prevalence of hypertension in African-Americans has been associated with increased rate of obesity (Ogden, Carroll, Kit, & Flegal, 2014).

Hypertension is a major risk factor for diabetic nephropathy/end-stage renal disease (ESRD) and peripheral arterial disease (Mortensen et al., 1990). Diabetes and hypertension induce endothelial dysfunction, vascular remodeling, and vascular stiffness, promoting and accelerating high blood pressure-related organ damage (Volpe et al., 2015). Occurrence of increased blood pressure has been associated with level of glycemic control (Torchinsky et al., 2004). At cardiac and vascular levels, hypertension may increase the carotid artery intima-media thickness, leading to atherosclerosis in childhood and development of later clinically significant cardiovascular disease than in nondiabetic individuals (Kotb, Gaber, Salama, Nagy, & Elhendy, 2012; Lilje et al., 2017). At renal level, hypertension can be associated with increase in microalbuminuria in youth with diabetes (Mortensen et al., 1990) and is therefore one of the major risk factors for development of diabetic nephropathy (National High Blood Pressure Education Program Working Group on High Blood Pressure in & Adolescents, 2004). Heredity may also predispose to nephropathy, supported by the association, found within families, between history of parental hypertension and nephropathy risk in diabetic offspring (Roglic et al., 1998; Rudberg, Stattin, & Dahlquist, 1998). Higher occurrence of hypertension in black youth with diabetes may be a mechanism for the higher prevalence of nephropathy and vascular disease in this ethnic group (Mortensen et al., 1990).

Nephropathy Renal changes in susceptible patients begins soon after diabetes onset and may accelerate during puberty, leading to microalbuminuria, an early clinical marker of diabetic nephropathy (Bogdanovic, 2008). Renal hypertrophy is thought to precede the augmented glomerular filtration, which occurs in 25–50% of diabetic patients (Zerbini et al., 2006). Blood pressure is usually normal in this stage (Bogdanovic, 2008). Glomerular hyperfiltration is the predisposing factor to diabetic nephropathy (Dahlquist, Stattin, & Rudberg, 2001) . Microalbuminuria develops 7–10 years after diagnosis in about a third of T1D patients (Bogdanovic, 2008; Schultz et al., 1999). Elevations in blood pressure are associated with subsequent development of moderately increased microalbuminuria, and patients with microalbuminuria had higher blood pressures than those without albuminuria (Guntsche et al., 2002).

Diabetic nephropathy seems to progress faster in adolescents with T2D: after 5–10 years of diabetes, microalbuminuria is found in 18–72% of patients and overt diabetic nephropathy in 5–27% of patients (Maahs et al., 2007; Pinhas-Hamiel & Zeitler, 2007). The onset and progression of diabetic nephropathy are strongly correlated with longer duration of diabetes and poor long-term glycemic control, puberty (Amin et al., 2008; Schultz et al., 1999), hypertension, obesity, dyslipidemia, and family history of diabetic complications (Gungor, Hannon, Libman, Bacha, & Arslanian, 2005) and are commonly associated with other microvascular complications, particularly diabetic retinopathy (Bojestig, Arnqvist, Hermansson, Karlberg, & Ludvigsson, 1994; Harvey et al., 2001; Hovind et al., 2003). Gross proteinuria is accompanied by a steady rise in blood pressure and a declining glomerular filtration rate (Bogdanovic, 2008), leading to renal failure in up to 10% of diabetic patients after 10 years duration of the disease (Amin et al., 2008; Dart, Sellers, & Dean, 2012; Hovind et al., 2003; Sochett & Daneman, 1999). Overt diabetic nephropathy is very rare in childhood and adolescence (Bogdanovic, 2008). As microalbuminuria progresses to gross proteinuria, irreversible kidney damage occurs, and there is an increased risk of progression to end-stage renal disease, which is higher in youth with T2D than with T1D (Dart et al., 2012).

Occurrence of diabetic nephropathy is much higher in black, Native American, and Hispanic pediatric patients compared with whites (Alberti et al., 2004; Gungor et al., 2005; Rosenbloom, Joe, Young, & Winter, 1999). African-Americans are disproportionately affected by hypertension and early-stage (microalbuminuria) and end-stage renal disease (ESRD) and have the highest mortality from ESRD of all races (S. f. D. i. Y. S. Group, Liese et al., 2006). African-Americans with diabetes have higher rates of end-stage renal disease than whites even after adjustment for socioeconomic and access to care factors (Karter et al., 2002), suggesting a possible genetic predisposition to hypertension and nephropathy among African-Americans (Bulger et al., 2012).

Pima Indian youth with T2D have high incidence of diabetic nephropathy and high prevalence of hypertension (18%) and microalbuminuria (22%) at diagnosis (Bogdanovic, 2008). Progression of renal impairment in Pima Indian children is manifested by microalbuminuria in 60% of patients and gross proteinuria in 17% of patients, between 20 and 29 years of age (Bogdanovic, 2008).

The increased risk of developing diabetic kidney disease and eventual kidney failure in early adulthood is thus of concern in patients from ethnic minorities with youth-onset T2D (Krakoff et al., 2003). Compared to T1D children, youth with T2D are also at higher risk for developing other primary renal diseases, as IgA nephropathy or membranoproliferative glomerulonephritis, with early progression to ESRD (Dart et al., 2012).

Neuropathy Chronic hyperglycemia may impair the small blood vessels supplying the nerves and the myelin nerves sheaths, causing slower nerve conduction and impaired sensory perception (Trotta, Verrotti, Salladini, & Chiarelli, 2004). Children and adolescents with diabetes can develop peripheral (sensorimotor) and autonomic neuropathy (Moser et al., 2013; Ringel et al., 1993; Trotta et al., 2004). Symptomatic diabetic neuropathy is rare in children and adolescents with both types of diabetes. However, subclinical impairment of neurologic function has been reported in 50–68% of pediatric patients with duration of diabetes of 5 years or longer for T1D (Hyllienmark, Brismar, & Ludvigsson, 1995; Jaiswal et al., 2013). Nerve conduction studies were suggestive of subclinical nerve damage in up to 25% of children newly diagnosed with diabetes (Trotta et al., 2004). After adjustment for glycemic control, age, and gender, youth with T2D had almost four times the prevalence of diabetic peripheral neuropathy compared to patients with T1D (Jaiswal et al., 2013). Prevalence rates for diabetic peripheral neuropathy in T2D youth were comparable with those reported in adults (30–40%) (Jaiswal et al., 2013). Other studies suggest that development of diabetic neuropathy in patients with pediatric-onset T2D is more aggressive than in T1D (Song, 2015). Older age, longer duration of disease, microalbuminuria, and cardiovascular risk factors such as central obesity, hypertension, and atherogenic lipid profile may be risk factors for neuropathy in youth with T2D (Jaiswal et al., 2013).

White youth are more likely to develop diabetic sensorimotor neuropathy (47%) compared to African-Americans (37%) and Hispanic Americans (35%) (Bao, Wong, Wang, & Low, 1999). In contrast, Hispanic Americans had a higher prevalence rate (51%) of autonomic neuropathy, demonstrating at least one abnormal test for heart rate variability and postural blood pressure control (Verrotti, Chiarelli, Blasetti, & Morgese, 1995). The prevalence rates of autonomic neuropathy were found similar for African-American and white children with T1D (45% and 44%, respectively) (Verrotti et al., 1995). Subclinical autonomic dysfunction can be detected within the first 2 years of diabetes diagnosis, but symptoms of autonomic neuropathy generally occur long after diagnosis, most often presenting as heterogeneous dysfunctions affecting the autonomic nervous system (cardiovascular, gastrointestinal, genitourinary, sudomotor, or ocular) (Verrotti, Loiacono, Mohn, & Chiarelli, 2009). Among these, cardiovascular autonomic neuropathy may become severe, potentially fatal in later life (Verrotti et al., 2009). Reduction of heart rate variation (Trotta et al., 2004) and of baroreflex sensitivity, causing daytime blood pressure elevation, is a manifestation which could occur early in the course of either diabetes type (Dalla Pozza et al., 2007; Krause, Rudiger, Bald, Nake, & Paditz, 2009). Puberty appears to enhance the development of diabetic cardiac autonomic dysfunction (Bognetti et al., 1997; Karavanaki & Baum, 2003).

Macrovascular (Large Vessel) Pathology Diabetes can also lead to gradual development of cardiovascular disease and risk of stroke in later adult life (Maahs et al., 2014). Clinically significant macrovascular complications (stroke, coronary heart disease, and peripheral vascular diseases) are rare in children and youth with diabetes and may become clinically significant decades later, even though vascular changes as increased arterial stiffness and associated high blood pressures can begin at disease onset (Urbina et al., 2010). As a result of long-term exposure to hyperglycemia, advanced glycosylation end products (AGEs) accumulate progressively in vessel wall collagen, accelerating the atherosclerotic process in large vessels (Brownlee, Cerami, & Vlassara, 1988). There is also evidence that hyperglycemia stimulates the intracellular reactive oxygen species (ROS) formation, decreases natural antioxidant defense mechanisms, and so induces large vessel damage (Nishikawa et al., 2000).

Cardiovascular Complications Depending on the techniques used, pathological alterations in cardiac and peripheral vascular function can be identified early in the course of pediatric diabetes (Hensel et al., 2016; Lilje et al., 2017). Endothelial dysfunction occurs earlier in T2D than in T1D in children and adolescents and is more prevalent in males than females, who are more likely to develop early atherosclerotic changes (Harrington, Pena, Gent, Hirte, & Couper, 2010; Lilje et al., 2017). Among adolescents with T2D, African-Americans have thicker and stiffer vessels than age-matched white patients (Shah, Dolan, Gao, Kimball, & Urbina, 2012) and may be more predisposed to stroke and myocardial infarction later in life (Urbina et al., 2009). Children with T1D also have reduced left ventricular size and decreased stroke volume even in the absence of hypertension or nephropathy, which is thought to represent a metabolically induced cardiomyopathy (Hensel et al., 2016). As a consequence, the myocardial contractility is decreased in children with longstanding and poorly controlled diabetes (Gotzsche, Darwish, Gotzsche, Hansen, & Sorensen, 1996).

Youth with diabetes have an overall sixfold increased risk for any vascular disease (Dabelea et al., 2017), contributing to 7–13-year decreased lifespan in T1D patients compared with nondiabetic controls (Nathan & the Diabetes Control and Complications Trial Group, 2014; Petrie et al., 2016). Paradoxically in adults with diabetes, African-Americans had lower incidence of macrovascular complications but higher mortality rate from coronary artery disease, strokes, and congestive heart failure, compared to whites (Golden et al., 2012). In fact, African-Americans have the highest mortality rate from coronary artery disease associated with diabetes of any ethnic group in the USA (Golden et al., 2012).

Dyslipidemia Dyslipidemia is part of the "metabolic syndrome" present in 42% of young individuals with obesity (Centers for Disease Control and Prevention, 2010). Dyslipidemia is more common in T2D children than in obese children without diabetes (Specht et al., 2013) and is an important risk factor for later development of cardiovascular disease and atherosclerosis (Newfield, Dewan, & Jain, 2008). At diagnosis of T2D, approximately half of the adolescents had an LDL-cholesterol ≥130 mg/dL and triglycerides levels ≥200 mg/dL (Pinhas-Hamiel & Zeitler, 2007). In a study of Mexican American and black adolescents with newly diagnosed T2D, 61% had triglyceride concentrations greater than 150 mg/dL, 54% had total cholesterol greater than 200 mg/dL, 46% had LDL cholesterol greater than 130 mg/dL, and 44% had HDL cholesterol levels of less than 35 mg/dL (Newfield et al., 2008).

The SEARCH study evaluated the prevalence of dyslipidemia in 1963 patients with T1D and 283 patients with T2D older than 10 years of age (Kershnar et al., 2006) and demonstrated a statistically significant association between poor glycemic control and higher concentrations of total cholesterol, LDL cholesterol, triglycerides, and non-HDL cholesterol in youth with either T1D or T2D, persistent after adjustment for age, gender, race/ethnicity, duration of diabetes, and BMI (Petitti et al., 2007). The T2D group had a more atherogenic lipid profile for a similar elevation of HbA1c, with higher proportions of fasting serum total cholesterol, higher LDL cholesterol and triglycerides, and of lower HDL cholesterol levels: 33%, 24%, 29%, and 44%, respectively, compared with young T1D patients (19%, 15%, 10%, and 12%) (Kershnar et al., 2006). Higher triglycerides are linked to higher insulin resistance and represent an important risk factor for the development of cardiovascular disease (Hamman et al., 2014; Reinehr, 2013). African-Americans have lower triglycerides levels compared with both whites and Hispanics (Sumner, 2009; Sumner et al., 2010), likely due to low hepatic fat, low apolipoprotein CIII, and high lipoprotein lipase levels (Sumner et al., 2005). Despite lower triglycerides, higher insulin resistance likely drives the accelerated development of cardiovascular pathology in black adolescents and young adults compared with whites (Sumner et al., 2005).

Skin Advanced Glycation End Products It has been suggested that AGEs are a mechanism underlying chronic complications of diabetes (Goh & Cooper, 2008; Stirban, Gawlowski, & Roden, 2014). Tissue AGEs have been assessed using invasive biopsy techniques and laborious assay methods. Recently noninvasive methods using measurement of skin fluorescence have been used to estimate the burden of AGEs in youth with diabetes (Bos, de Ranitz-Greven, & de Valk, 2011; Felipe et al., 2011; Shah et al., 2013). Skin AGEs (sAGEs) are higher in youth with diabetes than chronologic age-matched controls without diabetes (Baez et al., 2014; Felipe et al., 2011; Shah et al., 2013) and increase with age and HbA1c. The sAGE levels of matched diabetic and nondiabetic youth overlap, so sAGE is not a definitive approach to diagnosis of diabetes in this age group (Baez, Shah, Felipe, Maynard, & Chalew, 2015; Baez, Shah, Felipe, Maynard, Lefevre, et al., 2015; Shah et al., 2013). The impact of race, ethnicity, and SES on sAGE is unclear. The technology may have limitations in patients with dark skin complexion (Baez et al., 2015). Higher sAGEs have been associated with nephropathy and retinopathy (Genuth et al., 2015). Thus the technology may be helpful in identifying patients at early risk for diabetes complications.

Nonalcoholic Fatty Liver Disease (NAFLD) NAFLD, a condition associated with excessive weight gain, is common in pediatric patients with T2D, dyslipidemia, and abdominal obesity (Nadeau, Klingensmith, & Zeitler, 2005). At the time of T2D diagnosis, 25% of pediatric patients have NAFLD (Nadeau et al., 2005; Van Name & Santoro, 2013). The prevalence of NAFLD increases with age up to 74% of T2D adult patients (Dai et al., 2017; Leite, Salles, Araujo, Villela-Nogueira, & Cardoso, 2009). Insulin resistance within the liver, adipose tissue, and skeletal muscle is implicated in the pathogenesis of NAFLD, leading to increased lipolysis with accumulation of large triglyceride droplets within hepatocytes (Newton et al., 2016; Van Name & Santoro, 2013). The diagnosis is often challenging due to absent or nonspecific signs and symptoms. NAFLD may be suspected based on elevated levels of liver transaminases, mainly alanine aminotransferase (ALT), in clinical chemistry (Lomonaco, Chen, & Cusi, 2011). NAFLD encompasses a broad spectrum of disease severity and outcomes from isolated steatosis in its mildest form, which follows in general a benign and stable clinical course, to more advanced steatohepatitis (NASH) with varying degrees of inflammation and fibrosis, that may progress to cirrhosis in 15–25% of patients later in childhood or adulthood (Musso, Gambino, Cassader, & Pagano, 2011). Rarely there is advance to hepatocellular carcinoma (Alisi, Locatelli, & Nobili, 2010; Lindback et al., 2010; Loomba, Sirlin, Schwimmer, & Lavine, 2009).

T2D was found to be a strong independent factor for progression to hepatic fibrosis, in a cross-sectional study at 12 pediatric US clinical centers including 675 children with biopsy-confirmed NAFLD, most of whom were obese Hispanic males (Newton et al., 2016). With similar BMI and HbA1c, higher prevalence of NAFLD in Hispanic compared to black and white obese T2D youth is likely associated with more severe insulin resistance in the Hispanic group (Browning et al., 2004; Hudson, Nunez, & Shaibi, 2012; Mohanty et al., 2009). Genetic factors were suggested to confer predisposition to development of NAFLD in Hispanic youth (Schwimmer et al., 2009). However, the NAFLD progression to nonalcoholic steatohepatitis (NASH) was more prevalent in white children (Newton et al., 2016). Severity of liver injury is strongly associated with higher risk of atherosclerosis in T2D youth, which is independent of the degree of obesity and insulin resistance (Nobili et al., 2010). In patients with T1D and T2D, the presence of NAFLD increases the risk of both macrovascular (Targher et al., 2007) and microvascular complications, mainly nephropathy and retinopathy (Targher et al., 2008; Targher et al., 2010).

Other Complications Youth with diabetes are also prone to other complications. Poor growth and delayed puberty can occur in children with poorly controlled T1DM (Lado & Lipman, 2016). Arthropathy, hearing loss, and cognitive problems can also develop in patients over time (Reinehr, 2013).

Mortality Although prevalence and incidence of pediatric diabetes have been increasing, there has been no corresponding increase in diabetes mortality in this age group. (CDC, 2014b; Centers for Disease Control & Prevention, 2007). According to data from the Center for Disease Control, the total number of deaths from diabetes in children and adolescents of 228 (0.97 per 1 million) from 2012 to 2014 was lower than the rate of 265 (1.15 per million population) between 2000 and 2002 (Centers for Disease Control & Prevention, 2007; Saydah, Imperatore, Cheng, Geiss, & Albright, 2017). Racial/ethnic differences in the mortality rate of children and adolescents with diabetes, however, persisted from 2000–2002 to 2012–2014. Despite the higher prevalence and incidence of T1D in white children aged 1–19 years, African-American children continued to have the highest diabetes death rates (2.04 per million population) when compared with white (0.92) and Hispanic (0.61) patients (Saydah et al., 2017).

Acute diabetes complications (diabetic ketoacidosis more often than hyperosmolar coma) were the primary cause of all diabetes-related deaths within 10 years of diagnosis (Calle et al., 1999; Patterson et al., 2007; Secrest, Becker, Kelsey, Laporte, & Orchard, 2010). Seizures or coma resulting from severe hypoglycemia account for 5–10% of diabetes-related mortality, with children younger than 5 years of age being at the highest risk (Shafiee, Mohajeri-Tehrani, Pajouhi, & Larijani, 2012). Cardiovascular disease and diabetic nephropathy become the leading causes of mortality in adulthood, decades after diabetes diagnosis, with highest rates recorded in African-Americans (Secrest et al., 2010; Wong, Constantino, & Yue, 2015). Differences in mortality between racial and ethnic groups have been ascribed to differences in access to health care, health services, and differences in diabetes self- and parent-management education (Miller et al., 2016; Todd, Armon, Griggs, Poole, & Berman, 2006; Valenzuela et al., 2014).

Race and Differences in Pediatric Diabetes Treatment Outcome

The Diabetes Control and Complications Trial (DCCT) conducted in adult patients with T1D (The DCCT Research Group, 1987) and the United Kingdom Prospective Diabetes Study (UKPDS) in adult T2D patients ("Implications of the United Kingdom Prospective Diabetes Study. American Diabetes Association," 1998) demonstrated the importance of glucose-lowering treatment for the prevention of chronic diabetes complications. Therapy which reduced mean blood glucose (MBG) concentration, and consequently HbA1c, toward physiologic levels prevented the development and progression of microvascular complications (Nathan & DCCT/EDIC Research Group, 2014). These findings led to the publication of HbA1c and MBG treatment goals for adults and children in order to facilitate prevention of chronic complications (Chiang, Kirkman, Laffel, Peters, 2014; ISPAD, 2018). However, most children and adolescents with diabetes, regardless of race/ethnicity, do not achieve goal for metabolic control (Beck et al., 2012; S. S. Group, 2004; Willi et al., 2015). Studies have documented persistently higher HbA1c and MBG in African-American and Hispanics patients with T1D compared with white patients (Kamps, Hempe, & Chalew, 2010; Kirk et al., 2006, 2008; Marshall Jr., 2005). Multiple factors may contribute to differences in HbA1c outcomes between ethnicities.

African-American patients have found to have lower rates of adherence to management than white patients. Self-monitoring of capillary blood glucose (SMBG) is important in order to achieve glycemic control while reducing the hypoglycemic events (Lado & Lipman, 2016; Mayer-Davis et al., 2009). The more frequent the blood is tested for glucose, the more frequent adjustments can be made to reach glycemic goals. Frequency of glucose testing is inversely correlated with HbA1c (Chalew et al., 2018). Frequency of glucose testing is inversely rated to age (Chalew et al., 2018). Several studies have shown lower rates of SMBG among African-Americans, compared with whites even after adjustment for age (Mayer-Davis et al., 2009). The mean number of SMBG measurements per day was 6.1 in whites and 5.4 in African-Americans (Mayer-Davis et al., 2009). Barriers to SMBG were identified, including lower socioeconomic status and education level, which are more prevalent in minorities, including African-Americans (Stanescu, Lord, & Lipman, 2012). Increased clinic attendance is associated with lower HbA1c; clinic attendance is higher for white youth with diabetes, compared to African-Americans (Kim, Elmi, Henderson, Cogen, & Kaplowitz, 2012; Pulgaron & Delamater, 2014; Urbach et al., 2005).

African-American youth consistently are reported to receive less intensive insulin regimens (multiple daily injections or insulin pumps) than white youth (Beck et al., 2012; Paris et al., 2009; Willi et al., 2015). While 26.3% of white children were using insulin pumps, only 12.3% of Hispanic and 5.3% of African-American children were using those devices (Paris et al., 2009). In the T1DM Exchange trial, white children were 3.6 times more likely to be on insulin pumps than African-American children, even after adjusting for gender, age, diabetes duration, and socioeconomic status (Beck et al., 2012; Willi et al., 2015). The number of Hispanic children on insulin pumps was directly correlated with the income levels (Willi et al., 2015). In all three racial/ethnic groups, HbA1c values were lower for pump users versus multiple daily injections or fixed-dose injections (Willi et al., 2015). The difference in HbA1c between pump users and fixed dose injection was greatest for African-American patients (Willi et al., 2015). However HbA1c levels were still higher in black patients when mode of insulin delivery and age were controlled (Fig. 13.2) (Willi et al., 2015), suggesting that the mode of insulin delivery alone does not explain ethnic disparity in glycemic outcome (Chalew, 2015).

If the only factor influencing the level of HbA1c were MBG, then there should be no difference in HbA1c between racial/ethnic groups after statistical adjustment for MBG. However, multiple studies in various adult populations have found that African-Americans have higher HbA1c levels even after adjustment for glucose levels (Herman & Cohen, 2012). Kamps et al. found that HbA1C in African-American patients with T1D exceeded that of whites on average by approximately 0.8% after adjustment for MBG levels (Kamps et al., 2010). Subsequent studies in youth indicate that the MBG-independent racial disparity in HbA1c is not associated with differences in red blood cell (RBC) indices or iron status (Fig. 13.3) (Hamdan & Chalew, 2017; Hamdan et al., 2016). These data suggest the possibility of MBG-independent factors as the cause of differences in HbA1c levels between African-American and white patients.

MBG-independent racial disparity in HbA1c would lead to estimated average glucose derived from HbA1c to be overestimated in African-Americans patients. Unrecognized, this difference could

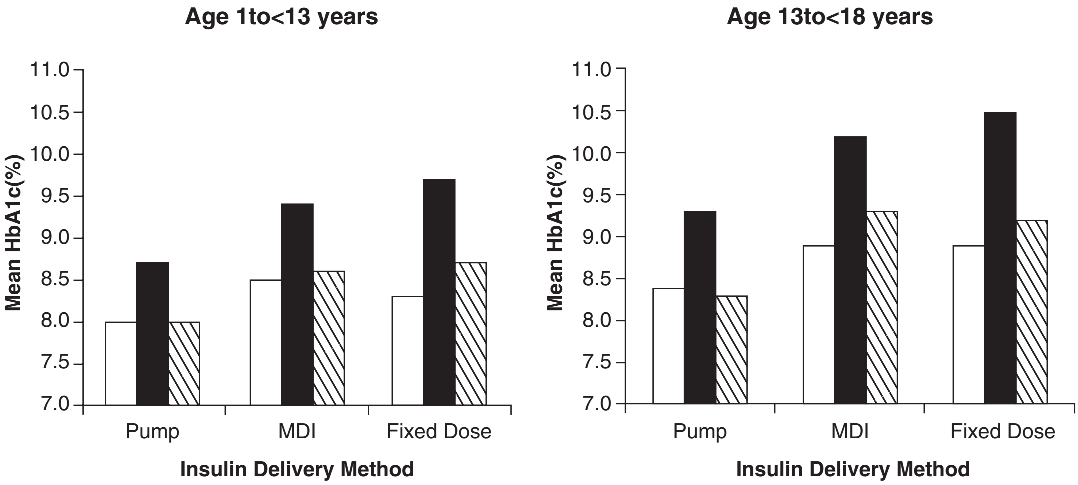

Fig. 13.2 Mean HbA1c by race/ethnicity, mode of insulin delivery and age among young patients in the Type 1 Diabetes Exchange Study. Blacks have higher HbA1c compared to the other groups regardless of mode of insulin delivery and age (white bar, non-Hispanic white; black bar, non-Hispanic black; striped bar, Hispanic). (From reference Willi et al., 2015)

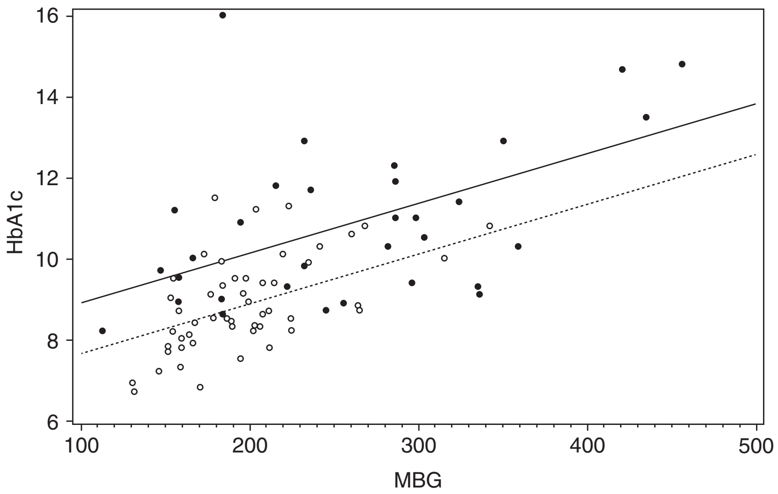

Fig. 13.3 Relationship between HbA1c and mean blood glucose (MBG in mg/dL) by race. Blacks have higher HbA1c at any given level of MBG compared to whites. This difference persists even after adjustment for age, gender, CBC indices, and iron status. Thus factors besides MBG contribute to racial disparity in HbA1c and need to be taken into account when using HbA1c as a metric for diagnosis and management of diabetes. Blacks, black dots and solid regression line; whites, open circles and dotted regression line. (From reference Hamdan et al., 2016)

lead to over diagnosis of diabetes in African-Americans, as well as may lead to more aggressive insulin therapy in African-American patients, with higher occurrence of symptomatic hypoglycemia (Chalew, 2015). Indeed the T1D Exchange Study reported higher occurrence of symptomatic hypoglycemia in African-American patients even though they had higher HbA1c and MBG levels (Cengiz et al., 2013; Willi et al., 2015). The etiology of MBG-independent racial disparity in HbA1c is unclear. MBG-independent differences in HbA1c may further contribute to risk of complications that cannot be influenced by glucose-lowering treatments (Chalew, 2015; Chalew, Hempe, & McCarter, 2009), but this possibility needs to be clarified by additional research.

Implications for Practice

As outlined above it can be challenging to separate observed racial/ethnic differences in occurrence of diabetes, use of state-of-the-art insulin delivery systems, adherence to treatment, treatment outcomes, and predisposition to complications from socioeconomic/environmental factors which may be more prevalent in one ethnic/racial group compared to others. Poverty, lack of family resources, and impoverished neighborhood environment may combine and contribute to the development of diabetes as well as present obstacles to adherence with diabetes treatment. Cost may dictate choice of glucose monitoring device, test strips, insulin type, and insulin delivery system as well as accessibility to specialist care and frequency of clinic visits. The T1D Exchange and other studies reported that a higher percentage of African-American than white children with diabetes were living in poverty, had limited access to healthy food sources and safe places to play and exercise, and live in high crime neighborhoods (Beck et al., 2012; Mayer-Davis et al., 2009). Young African-American patients were more likely to live in a single-parent household and have parents with lower educational attainment (Mayer-Davis et al., 2009; Schwartz, Cline, Axelrad, & Anderson, 2011). Greater than 50% of African-American children with type 1 and 63% of African-American children with type 2 diabetes reported living with only one parent (S. S. Group, 2004). Depressed patients with diabetes adhere poorly to self-management behaviors and as a result have poorer glycemic control and increased risk of diabetic complications (Chalew et al., 2018; Gonzalez et al., 2008). African-American patients are more likely to suffer from depression, less likely to report their depressive symptoms, and thus often miss opportunities treatment of depression, which may contribute to poorer diabetes outcome (Bulger et al., 2012; Wagner, Tsimikas, Abbott, de Groot, & Heapy, 2007).

Health provider-related factors may underlie some disparities in treatment outcome. Minority children with T1D receiving suboptimal culturally competent care (Waitzfelder et al., 2011) from providers who don’t communicate effectively or are not considerate of specific cultural factors may reduce family confidence and efficacy in self-care for diabetes (Heisler, Bouknight, Hayward, Smith, & Kerr, 2002; Piette, Schillinger, Potter, & Heisler, 2003). When a family’s level of education is low, a provider’s ability to communicate with that family may be impaired. In youth withT1D, higher caregiver literacy, but not child literacy, has been linked with better glycemic control (Pulgaron et al., 2014). The Institute of Medicine (IOM) has reported that racial and ethnic minorities often receive a lower quality of health care when compared with white majority population, independent of SES, insurance coverage, age, or comorbidities (Fiscella & Sanders, 2016). African-American and Hispanic diabetic patients receive less intensive pharmacological treatment than white diabetic patients and are less likely to have their treatment intensified to improve glycemic control (Coulon et al., 2017; S. f. D. i. Y. S. Group et al., 2006; Marshall Jr., 2005). Fewer numbers of young African-American patients on insulin pumps may reflect health provider differences in assessment, recommendation, and support for this therapy among African-American families (Miller et al., 2015).

The continued disparity in occurrence of diabetes and diabetes treatment outcomes between ethnic groups indicates the need for innovation and redesign of management practices. Better understanding of differences in how neighborhood/environmental and cultural factors influence behaviors and health outcomes is necessary to develop effective intervention strategies for youth with diabetes (Coulon et al., 2017). Furthermore, better insight into how biological factors may contribute to differences in HbA1c and proclivity to complications is needed. Specially designed interventions addressing multiple levels of change including the patient/family, provider, technology, health-care organization, and community may prove ultimately successful.

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Chapter 14
Medical Systems, Patient-Provider Relationships, and Transition of Care

Brandy A. Wicklow and Elizabeth A. C. Sellers

Introduction

The word "transition" is derived from the Latin "transire" meaning to "go across" and is defined as "the process or a period of changing from one state or condition to another" (Oxford English Dictionary Online, 2016). Healthcare transition refers to the transition of care for youth with a chronic disease from pediatric-oriented healthcare services to adult-oriented services. Transition of healthcare is a process, not a discrete event, starting in the adolescent years and extending into adulthood (Blum, 2002). The primary goal of transition is to ensure that the move from pediatric to adult healthcare services occurs seamlessly, resulting in continuity of care in a comprehensive, developmentally appropriate manner. The transition of care of youth with chronic illness to adult care has been identified as a significant issue since the early 1980s when increasing numbers of young people with chronic illnesses began to survive into adulthood (Blum, 2002).

Diabetes, both type 1 and 2, is a chronic illness significantly impacted by the transition from pediatric to adult care and therefore requires a focused and purposeful transition processes to optimize lifelong health outcomes (Peters & Laffel, 2011). The transition period is complicated by a life-course period of transitioning in other domains including a move away from parent responsibility and control to independent decision-making, changing family, peer and romantic relationships, and new demands of work or school. Late adolescence and young adulthood are periods of significant change in all realms of life including social, family structure, education, and vocational choices. In addition, diabetes self-management is complex and demands daily attention, with adolescence being a high-risk period for poor glycemic control (Mortensen et al., 1998; Wood et al., 2013). This is likely attributable to the psychosocial challenges of adolescence complicated by the physiologic changes of puberty.

Brandy A. Wicklow and Elizabeth A.C. Sellers contributed equally to the writing of this chapter.

B. A. Wicklow · E. A. C. Sellers (✉)
Pediatrics and Child Health, Max Rady College of Medicine, Rady Faculty of Health Sciences,
University of Manitoba, Winnipeg, MB, Canada

Children's Hospital Research Institute of Manitoba, Winnipeg, MB, Canada
e-mail: bwicklow@exchange.hsc.mb.ca; esellers@exchange.hsc.mb.ca

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The concept of "the emerging adulthood," as a unique and distinct period of life in the industrialized world, was introduced by psychologist Dr. John Arnett (Arnett, 2000). This period of life bridges adolescence and adulthood and typically spans the period from 18 to 25 or 30 years of age. The emerging adulthood is described as a period characterized by an "age of identity exploration" and "an age of possibilities" (Arnett, 2000). This is the period where the young adult finds their niche within their peer group, family, and society. It is also where personal identity is established and important educational and vocational choices are made. For the emerging adult with a chronic illness, it is the developmental period when they assume more responsibility for self-care and interaction with their healthcare team. For the young person living with diabetes, it is often the end of a long relationship with their pediatric healthcare providers and the introduction of a new provider and model of care that can add to the complexity of their lives. It is not surprising that this period is associated with deterioration in glycemic control and a decrease in adherence to medical regimens and clinic attendance (Mortensen et al., 1998; Wood et al., 2013). Efforts to prevent transition-related shortcomings include the development of several models of provision of transitional care to prepare and support the emerging adult within the context of their lives and developmental stage. These models are discussed below.

In the United States, risk-taking behaviors often associated with adolescence, such as substance use, unprotected sex, and risky driving behavior, are, in fact, higher in the emerging adult years (Callahan & Cooper, 2010). Young adults also have higher rates of unintentional injury and suicide compared to their adolescent counterparts with the emerging adult having double the mortality of adolescents (Park, Paul Mulye, Adams, Brindis, & Irwin Jr., 2006). In addition, within the US medical system, this is the period during which there is the lowest rate of healthcare coverage and the highest rates of poverty (Park et al., 2006). It should not be surprising that interaction with the healthcare system during the emerging adulthood is characterized by a decrease in routine or preventative ambulatory care visits and an increase use of emergency room visits compared to the adolescent (Callahan & Cooper, 2010). The complexity of this period of change is further increased for young people with diabetes who are also balancing the day-to-day challenges of diabetes management and transfer to adult care systems. In Canada, the mortality rate in the 20–29 year age group in those living with diabetes is four times that of their peers without diabetes (Public Health Agency of Canada, 2011).

The rates of both childhood onset type 1 and type 2 diabetes are increasing worldwide. Overall, the incidence of type 1 diabetes in children and adolescents is increasing 4% per year (Patterson, Dahlquist, Gyurus, Green, & Soltesz, 2009). Childhood onset type 2 diabetes is also increasing. In the United States, the prevalence of type 2 diabetes in children rose by 30.5% between 2001 and 2009 (Dabelea et al., 2014), and in Central Canada, the incidence doubled between 2006 and 2011 (Sellers, Wicklow, & Dean, 2012). Thus, the population requiring support through the transition processes is growing. The Diabetes Complications and Control Trial in type 1 diabetes revealed the importance of target glycemic control to prevent long-term vascular complications. Significant reductions in complication rates in the intensive management arms of the trial highlight the importance of the transition period as a high-risk period, which may, in part, determine the lifelong financial and physical burden of illness for these patients and society. Another concern is newer evidence demonstrating that children diagnosed with type 2 diabetes develop vascular complications aggressively and at an earlier age than their adult counterparts (Dart et al., 2012, 2014). This illustrates the urgent need for (1) methods to assess transition readiness in youth and their families, (2) interventions to address deficits in transition readiness, (3) programs of successful transition that address the differences in providers and models of care, and (4) support for emerging adults to adapt to the new healthcare system.

We review here several aspects of transition of youth with both type 1 and type 2 diabetes to adult healthcare services. This includes models of transition care; patient, provider, and program characteristics; and the assessment of a patient's transition readiness. In addition, we will address gaps in our understanding of this process and future needs to best support the population of adolescents and emerging adults with type 1 and type 2 diabetes.

Current Recommendations and Guidelines

Several recent clinical practice guidelines and recommendations have been published based on the state of current evidence and expert opinion on transition of care of emerging adults with diabetes (Peters & Laffel, 2011; Singh, Anderson, Liabo, & Ganeshamoorthy, 2016). Recommendations are based on patient and provider characteristics and healthcare systems and infrastructure. All of the guidelines and recommendations acknowledge the high-risk developmental stage of the emerging adult who is gaining psychosocial maturity while facing increasing demands for independent decision-making, time management, and organizational skills. They recognize the different training and healthcare practices of pediatricians and adult physicians and the fundamental differences in healthcare provision between pediatric and adult care. Pediatric care is often touted as being family centered, socially oriented, and informal with adult care being person centered, disease oriented, formal, and focused on disease management. The American Diabetes Association (ADA) position statement in 2011 included recommendations for transition content starting a minimum of 1 year prior to transfer. This should include information on self-management, scheduling appointments, and ensuring adequate and proper supplies for diabetes management. They further recommend information be provided regarding the differences in the pediatric and adult services and healthcare insurance to allow patients and families to adequately prepare for adult clinical appointments. Finally, they recommend provision of clinical summaries and patient care plans and progress to both the family and the new healthcare provider (Peters & Laffel, 2011).

A recent summary of the recommendations of the Institute for Health and Care Excellence (NICE) outlines practical strategies to operationalize the concepts important in the transition process. For example, they report on the need to develop clear transition services, including the identification of a key named worker. This individual would help to coordinate care, arrange appointments, travel to appointments, aid with scheduling around school and work, and facilitate access to information about community supports and advocacy opportunities. They recommend the development of a personal summary of care needs and history that includes a component of patient preferences. The NICE recommendations also identify the time spent on transition content as an important factor, suggest that planning for transition commence as early as age 14 years, and span a minimum period of 6 months preceding transition to 6 months following transition (Singh et al., 2016).

Transition of Care Models

As numbers of emerging adults with chronic disease increase, transitional care models have become an important focus, and major challenge, for healthcare practitioners. Different approaches to the transition of care of emerging adults from pediatric clinics to adult services can be categorized by transition staff (one-on-one nurse coordinator, transition coordinator, or navigator), method (specific transition visit, web-based and written transition information), and healthcare provision (joint pediatric/adolescent and adult clinics, young adult clinics). Models of care have been examined by qualitative assessment of individual perceptions of the transition process, youth's desired transition services, and quantitative assessments of outcomes including number of patient visits, time gaps in care, and measures of metabolic control. Existing literature suffers from significant limitations with few randomized controlled trials of transition models and many retrospective cohort studies with limited numbers of subjects.

Continuity in Transition

The different models of transition services for young adults each attempt to address the vulnerability and complexity of the patient's stage of development and components of chronic illness management. Continuity of care is a theme that arises as important throughout the different transition models and is the basis for several proposed methods of transition services. Seven relevant continuities have been described related to healthcare transition, including continuities of experience, information, cross-boundary, flexible, longitudinal, relational, and developmental (While et al., 2004). A more recent evaluation of continuities in models of practice (Allen et al., 2012) identified cultural continuity as an additional important concept in care provision. Cultural continuity is a continued commitment to adolescent healthcare and is focused care on the specific needs of adolescents and young adults. These authors outlined the central nature of relational (personal relationships between caregiver and patient), longitudinal (the infrastructure through which care is provided), and cultural continuity (shared practices and approaches to care provision between pediatricians and adult physicians) that facilitates continuity in management and flexibility of care. The importance of these continuities can be observed in the development of transition programs that employ a key person with a personal connection to the patient who supports the patient through the transition process. Longitudinal continuity is exemplified in the development of joint pediatric and adult clinics, which occur in the pediatric care setting, with the same charting systems and the same laboratory services. Although empirically derived information to inform the transition process has been limited, many of the clinical models continue to design transition around these continuities, and many have found improvements in patient engagement over traditional patient transfer processes.

Transition Staff/Transition Coordinator

A recent Cochrane review outlined four randomized trials of transition models implemented for youth with chronic illness; however only one of these studies focused on youth with type 1 diabetes (Campbell et al., 2016). In that study, a transition coordinator model was implemented with the coordinator responsible for making the initial adult clinic appointment and providing telephone support with the emerging adults at 1 week and 3, 6, and 12 months post-discharge from pediatric care (Steinbeck et al., 2015). This model focuses on a transition coordinator to prove relational continuity as the young person moves from the familiar pediatric services to the unfamiliar adult-oriented healthcare services. In addition, individual patients received electronic copies of healthcare information on adult services and healthcare practices for ongoing diabetes management. They also received a paper copy of the referral sent to the adult clinic. The study failed to show any significant improvements in engagement and retention in adult services, diabetes-related hospitalizations, or hemoglobin A1c between the intervention group and the group who received a standard transfer. The authors speculated that this might have been due to the high rates of retention in both groups and the participation of self-selected patients who were already more engaged in their care. Other transition programs utilizing the concept of relational continuity and employing a transition coordinator have shown improvements in hemoglobin A1c and reduction in hospital admissions post-transition (Holmes-Walker, Llewellyn, & Farrell, 2007) and a decrease in fall out of care (Van Walleghem, Macdonald, & Dean, 2008). A Canadian clinical trial study group is undertaking a current randomized control trial that is also employing the transition coordinator as a central component and link to both pediatric and adult care services and education and support through the transition period. The trial will measure clinic attendance and measures of metabolic control at 2 years post-transition (Spaic et al., 2013).

Transition: Method of Information Transfer

Huang and colleagues (Huang et al., 2014) delivered transition material to emerging adults with type 1 diabetes, cystic fibrosis, and inflammatory bowel disease in a web-based format with SMS to deliver a skills-based intervention which consisted of an 8-month self-management program targeting self-management skills and information on monitoring of disease symptoms. With the understanding that many of the psychosocial issues of chronic disease management in this population are shared, the study aimed to determine if a more generalized transition model would benefit young adults with different chronic diseases. They concluded that generalized transition content focused on disease engagement and skill-based learning resulted in significant improvements in disease management tasks, health-related self-efficacy, and patient-initiated communications with healthcare staff (asking questions). In a similar study of 12 pediatric outpatient clinics in Germany, Schmidt et al. (Schmidt, Herrmann-Garitz, Bomba, & Thyen, 2016) tested the effectiveness of a generic transition-oriented patient education program on health services participation and quality of life. The study included patients with cystic fibrosis, type 1 diabetes, and inflammatory bowel disease. The intervention included an interactive group-based patient education program led by a psychologist and pediatrician, based on improving/developing self-empowerment, self-efficacy, and self-activation skills. The educational intervention included eight modules each lasting 60–90 minutes completed over two consecutive days to a minimum of four adolescents. The module topics included transfer to adult medicine (systems and provision); the new doctor-patient relationship (considerations for new MD and the role as a patient); health insurance; future employment; social and family support and conflict; resources for stress management; sharing diabetes with friends, family, and romantic partners; resource activation; and risky behaviors. Reported outcomes included improvements compared to baseline and the usual care group in transition competence and self-efficacy scales, work, and school-related preparedness and condition-related knowledge.

Structured Transition Programs

A study based in Italy compared outcomes from a historical type 1 diabetes patient cohort (pre-structured transition program) that were transferred to adult services with a traditional referral letter to a cohort who participated in a structured transition program (Cadario et al., 2009). This program included a pediatrician who followed patients through the transition process, provided individual assistance with transition, and discussed relevant issues to transition. Both the pediatric and adult care provider participated in the final pediatric visit and the initial visit to adult care services. Patients were provided with a copy of their health information sent to the adult physician. Young adults who participated in the structured transition program had increased visits to adult providers, fewer gaps in care, improved complication surveillance, and lower A1c 1 year post-transition and reported a better subjective experience of transition compared to the historical cohort (Cadario et al., 2009). Similarly, the evaluation of a structured transition program consisting of diabetes-specific education, case management, and access to a young adult diabetes clinic and transition website revealed no change in patient follow-up visits from pediatric to young adult care, improved glycemic control, reduced hypoglycemia, and improved global well-being compared to a usual care control group (Sequeira et al., 2015).

Transition: Joint Healthcare Provision

Sparud-Lundin and colleagues found greater attendance to adult clinic appointments if patients participated in a combined pediatric-adult clinic or were transitioned to a specific young adult clinic as opposed to patients who were transferred directly into adult care (Sparud-Lundin, Ohrn, & Danielson, 2010). The importance of cultural continuity is exemplified by a prospective cohort study that demonstrated no deterioration in metabolic control post-transition if the familiar pediatric clinic routines were maintained in the adult follow-up program (Neu et al., 2010).

Transition: Patient and Parent Experiences

Qualitative reports have shed light on the experiences of transition for patients and families and can be used to identify unmet needs in the transition process. Despite the increasing awareness of the importance of successful transition for ongoing optimal health services utilization, health knowledge, and well-being post-transition, in a survey of emerging adults with type 1 diabetes, 21% of respondents reported a lack of transition process with transfer of care occurring by physician to physician letter of referral only.

In a survey sample of adults aged 22–30 years with type 1 diabetes, many reported having no purposeful transition process. Themes included the desire for a structured transition that included an explanation of the differences between pediatric and adult healthcare provision, expectations for the culture of adult care, and specific programming to orient emerging adults to the logistics of transition. Based on their findings, the authors recommend the inclusion of a peer-based mentoring model as part of a transition model (Garvey et al., 2014). Another study of patient perspectives on transition found that patients felt preparation needed to start early, and they needed the opportunity to interact independently with the healthcare team prior to transition of care. In addition, many patients described wanting logistical help in identifying adult services that would be a "good fit" for them. Many stated they felt they were unprepared for the brevity of the visits once they entered adult care (Hilliard et al., 2014). Another survey-based study of transition services in the United States reported 52.5% of patients did not receive adult care recommendations by their pediatric provider. In addition, over one quarter of patients felt worried or apprehensive about the transition of care that may have led to the 25% lapse in care of greater than or equal to 1 year post-transition. Patients reported wanting more information on the use of technology in diabetes management, how to introduce diabetes to others, tools for advocacy in the workplace or academic settings, life skills (cooking, shopping, driving, leaving home), and how to communicate with a medical team (Raymond, Duke, Shimomaeda, & Harris, 2013).

Psychological Assessment

Both the American Diabetes Association and the International Society of Pediatrics and Adolescent Diabetes recommend screening for common psychological comorbidities of type 1 diabetes (including depression and anxiety) that are associated with poor metabolic control (Delamater, de Wit, McDarby, Malik, & Acerini, 2014; Peters & Laffel, 2011). Adolescents with psychological disorders have poorer metabolic control, a higher risk of failing to transition to adult diabetes care, and increased risk of loss to follow-up (Northam, Lin, Finch, Werther, & Cameron, 2010; Reynolds & Helgeson, 2011). However, these comorbidities often go unrecognized in adolescents with type 1 diabetes, and screening is uncommon within the context of a busy inter-professional clinic. The transition process may be complicated by psychological difficulties/comorbidities that have not been recognized by the pediatric care providers (Silverstein et al., 2015). Recently, a group undertook formal screening for diabetes distress, disordered eating, and depression within a tertiary care transition clinic. Chart reviews were performed to determine if any psychological comorbidity had previously been identified. They found a high rate of previously undetected cases of depression, diabetes distress, and, most significantly, disordered eating in both males and females. They postulate that identification of concerns during the transition process (and facilitation of support services) may play a critical role in the successful transition of many emerging adults (Quinn et al., 2016). The implementation of a formal psychological screening process and intervention to address concerns identified within the transition years has yet to be formally evaluated. There is a dearth of information related to psychological comorbidities in youth with type 2 diabetes.

Special Considerations: The Transition of Youth with Type 2 Diabetes Mellitus

There are no reports in the published literature specific to the transition or process of transition of youth with type 2 diabetes. There is, however, data to suggest that there are significant social-environmental-economic challenges in the population of youth with type 2 diabetes that add to the complexity of transition (Van Walleghem, MacDonald, & Dean, 2012). In Manitoba, Canada, the majority of adolescents with type 2 diabetes are of self-declared First Nation status, and 80% live in rural or remote communities outside of urban centers. In this population, 24.4% of young women with type 2 diabetes had a documented pregnancy, and 11% of young men had become fathers before the age of 18 years. At 18 years of age, only 17.6% had completed high school, and 30% had achieved less than a grade 9 education. In addition, 20% had had an in-patient admission for a mental health issue under the age of 18 (MacDonald, 2014).

Similar challenges are seen in the baseline description of the TODAY study cohort of youth with type 2 diabetes (Anderson et al., 2011; Copeland et al., 2011). In the TODAY cohort, the majority of participants were members of racial minority groups. Total family income was less than $25,000 in 41% and < $ 50,000 in three quarters of the participants. Less than 40% of participants lived in a home with both biologic parents, and 47% lived with their mother alone. In addition, the highest level of education obtained by the primary caregiver was less than high school graduation in more than a quarter of the families. These characteristics and the challenges faced by youth and emerging adults with type 2 diabetes make it likely that the transition process for youth with type 2 diabetes will need to address these issues in order to be successful.

Story Lines

An increased understanding of the complexity of the experience of youth with type 2 diabetes and the early default to primary care experienced in the Manitoba pediatric type 2 clinic lead, in part, to the development of a project entitled “Story Lines” (MacDonald, 2014). The purpose of this project was to understand the experience of living with diabetes from the perspective of the youth with type 2 diabetes. This included how they experienced interaction with the healthcare system and reasons for defaulting from care. In addition to in-depth individual interviews, the medium of visual arts (writing, drawing, painting, and sculpture) was used to allow youth to communicate through creative expression. While the results of this project are now just emerging, it is the hope that an improved understanding of the patient experience of living with type 2 diabetes and experience of interaction with the healthcare system can be used to inform the development of culturally appropriate programs to support both youth and emerging young adults with type 2 diabetes (MacDonald C, 2014).

Role of Parents/Carers in the Transition Process

In a qualitative study, Allen and colleagues explored the role of parents in the transition of adolescents with type 1 diabetes to adult care services in the United Kingdom (Allen, Channon, Lowes, Atwell, & Lane, 2011). The majority of adolescents identified their mothers as their principle care provider. They conducted a series of three interviews with young people and separately with their mothers over a 12–18-month period during which the transition of healthcare services occurred. Semi-structured questions were used to gain an understanding of their engagement with healthcare services, their transition experience, and their service preferences.

They found that mothers play an active role in assisting adolescents with diabetes management and continue to do so as they transition. As emerging adults, young people continued to use their mothers for discussion and support even if they have made independent decisions about their management (Allen et al., 2011). They conclude that services for young adults need to recognize the continuing role that the parents, in particular mothers, play in the lives of young adults. Additionally, while adolescents identify talking with their provider and receiving transition-specific materials as helpful, they identified parents as a greater support in the transition process. They emphasize that the process of healthcare transition needs to be in step with the emerging adults' socio-ecologic reality. Most emerging adults maintain many interdependencies with their parents – including living within their parents' home and receiving healthcare coverage under their parents' healthcare plans. The typical adult health service focus on the individual is out of step with this reality. Similarly, in a report from the United States, youth with type 1 diabetes identified parental support as a critical element in a successful transition process (Polfuss, Babler, Bush, & Sawin, 2015). Supporting parents in the transition of their role from supervisor (of the young adolescent) to supporter (of the emerging adult) may be an important factor in the transition process (Polfuss et al., 2015).

These findings suggest that services for emerging adults need to recognize the continuing role of the parent or carer and support formal incorporation of them into the transition process. The period of transition may more appropriately require a combined model of care that incorporates components of both the pediatric family-centered model and the adult, patient-centered model. Conversely, the lack of an identified carer who plays an active role in the life of the adolescent/emerging adult may help identify youth at particular risk during the transition process (Allen et al., 2011; Polfuss et al., 2015).

Characteristics of Adolescents/Emerging Adults

Factors that predict successful transition are important to inform the development of tools for successful transition. Measures of readiness for healthcare transition are also important to predict whether an adolescent will be successful in accessing care in the adult system. Traditionally, the focus has been on individual age, knowledge, and behaviors to determine transition readiness. However, more recently, this field of research has expanded to evaluate the role of the family, community, and society in a social-ecological model of healthcare transition. Differences in pediatric and adult healthcare settings, differences in patient and provider relationships and communication, and differences in insurance healthcare coverage from adolescent to adult healthcare are important factors to consider in the transition process. The ability of the emerging adult to adapt to these differences is an important determinant of successful transition. Individual characteristics, social supports, and the healthcare system itself play a role in the adaptation of a patient to the new adult healthcare model. Transition readiness is a dynamic concept that has measureable and modifiable components making it an important focus of any transition program aimed to optimize engagement of emerging adults in the adult healthcare setting.

Individual Characteristics: Transition Readiness

Healthcare transition readiness has been defined as the affective, behavioral, and cognitive capacity of the adolescent and his or her primary support system to prepare for, begin, continue, and complete the healthcare transition process (Betz, 2004, 2008). A variety of transition readiness scales have been developed to identify those adolescents who succeed in transition based on higher levels of readiness for the transition (Schwartz et al., 2014). Many of these scales, including the Self-Management Skills Assessment Guide (SMSAG), the Transition Readiness Assessment Questionnaire (TRAQ), and the California Healthy and Ready to Work (HRTW) Transition Assessment Tool, are self-reported assessment tools that examine readiness for transition by assessing an individual's ability for self-management. These include participation in medical decision-making, medication adherence, and knowledge of their condition (Betz, 2000; Cohen et al., 2015; Sawicki et al., 2015; Wood et al., 2014). These scales have been found to be valid and reliable in small test populations with different chronic illnesses, and reports suggest transition readiness is related to age, disease severity, participation in a transition clinic, low anxiety, and high confidence with adult providers. However, these early tools focus mainly on the individual's features of readiness and fail to take into account the social-ecological environment within which emerging adults are undergoing transition of care.

The ON TRAC transition questionnaire includes few external factors in the determination of transition readiness (Paone, Wigle, & Saewyc, 2006) and assesses six domains including (1) self-advocacy and self-esteem; (2) independent/self-management of healthcare behaviors; (3) sexual health; (4) social supports; (5) educational, vocational, and financial planning; and (6) health and lifestyle. A recent update to the tool was trialed with 200 adolescents with various chronic illnesses (36% type 1 diabetes) (Moynihan, Saewyc, Whitehouse, Paone, & McPherson, 2015). The authors found that only 27% of 17-year-olds and 62% of 18-year-olds met the cutoff criteria for readiness to transition. Age of participant had the strongest relationship with overall transition readiness; however, psychosocial maturity had the strongest relationship with behavioral scores regardless of age. Only a weak correlation was found between participant age and psychosocial maturity suggesting that age may not be an optimal proxy for maturity and age-based transition programs may benefit from the addition of maturity-based assessments of readiness. This is illustrated by a study comparing healthcare management behaviors between adolescents and young adults, with the young adults scoring higher in healthcare management behaviors. However, less than one half of young adults studied reported consistently managing their healthcare independently, making healthcare appointments, and understanding insurance issues. This suggests that age alone may not be the best predictor of transition success (Annunziato et al., 2011). Williams et al. reported that adolescent medical self-management scores were strongly associated with scores of functional independence but had small and nonsignificant correlations with age (Williams, 2009).

Patient-provider communication has repeatedly been found to be an important component of transition readiness. Patients report being more engaged in clinical appointments if the provider includes them in the conversation regarding their health (Garvey et al., 2012; Sawicki et al., 2011). Adolescents and emerging adults desire the opportunity to be a main partner in healthcare communication, and frequency of transition discussions has been found to be a stronger predictor of transition readiness than age (van Staa & Sattoe, 2014; van Staa, van der Stege, Jedeloo, Moll, & Hilberink, 2011). Increased patient participation in health visits leads to improved self-care and better outcomes in adults with chronic illness (Croom et al., 2011; van Dam, van der Horst, van den Borne, Ryckman, & Crebolder, 2003).

A study from the Southern United States examined the relationship between perceived health locus of control – the belief that an individual's health is under their own control (internal) or that one's health is under the control of others or chance – and readiness for healthcare transition from pediatric to adult care (Nazareth et al., 2016). The survey of 16–17-year-old adolescents with chronic disease (19% with type 1 diabetes) revealed that transition readiness was positively correlated with the perception that the doctor and patient have control over the disease while other external loci of control (family and chance) were negatively associated with transition readiness and medication adherence. This study is one example of the importance of the patient-provider relationship in preparing the youth for transition.

External Level Factors-Transition Readiness

The UNC TRxANSITION Scale (Ferris et al., 2012) is administered by a healthcare provider and incorporates a component of physician and medical chart verification of patient responses. In addition to the standard measures of readiness, including patient and parent characteristics, it includes additional external variables including school and work environments, reproduction, insurance, and new providers. In 41 adolescents with chronic kidney disease (Fenton, Ferris, Ko, Javalkar, & Hooper, 2015), this scale identified family cohesion to be a significant predictor of emergency room visits and medication adherence. Disease-related risk factors including age at diagnosis, disease burden, and disease severity were not associated with transition readiness. In a separate study, the TRAQ (Transition Readiness Assessment Questionnaire) scale predicted self-reported medication adherence and number of emergency room visits in the prior year. Higher transition readiness scores were seen in youth who were older, lived in two-parent households, and have higher levels of health literacy (Beal et al., 2016).

The Social-Ecological Model of Adolescent and Young Adult Readiness to Transition (SMART) assessment tool for transition expands upon individual- and family-based readiness and examines transition readiness of the patient in the context of a social-ecological framework (Schwartz et al., 2013; Schwartz, Tuchman, Hobbie, & Ginsberg, 2011). This model, validated in cancer survivors, emphasizes the multiple factors and stakeholders in the transition process including patients, parents, insurance, demographics and cognition, knowledge, beliefs, motivations, self-efficacy, relationships, and psychosocial functioning.

Measures of transition readiness appear to be an important component of the preparation of the adolescent and emerging adult for the move to an adult-based healthcare model. Research thus far has shown that individual, family, and community variables can influence a patient's transition readiness. Tools that can determine areas that are less developed than others (e.g., communication, social support) allow a tailored approach to best prepare each patient for transition. To date, most tools that have been tested in emerging adults with type 1 diabetes have included these youth among a bigger sample of youth with other chronic diseases. Future studies, limited to type 1 diabetes, may help to clarify which tools provide the best information on transition readiness in this particular population. Studies aimed to understand readiness for transition in type 2 diabetes are also essential. In addition, as these measures of transition readiness are relatively new, long-term follow-up to determine their ability to predict successful transition is lacking (Schwartz et al., 2014).

Measures of Successful Transition

The measures of successful transition have traditionally included hemoglobin A1c, acute and chronic complications, continuity of post-transition care, self-management skills, disease-specific knowledge, rates of complication screening, and diabetes-related quality of life. Pierce and Wysocki (Pierce & Wysocki, 2015) have suggested an expanded measure of success taking into account the multidimensional nature of healthcare transition and the impact of systems on the progression from transition readiness to successful healthcare transition. These authors propose that systems including social supports, relationship with providers, educational attainment, and workplace environment mediate the relationship between transition readiness and healthcare transition outcomes. The impact of these multifactorial systems on transition outcomes has been reported. The lack of the adult healthcare provider name and contacts, competing life priorities, and insurance problems were all significantly associated with gaps in healthcare continuity (Garvey et al., 2012).

Summary and Conclusions

The importance of healthcare transition in diabetes is well recognized as evidenced by the development of many national and international guidelines. However, many of the recommendations within these guidelines are consensus based. There remains limited evidence to guide the development of transition programs. With the increasing rate of both type 1 and 2 diabetes of youth onset, there is an increasing need for evidenced-based programs that will support successful transition to adult-oriented services without metabolic deterioration or gaps in care.

Healthcare transition from pediatric-oriented to adult-oriented healthcare services occurs during a particularly vulnerable and unique life stage from late adolescence into the emerging adulthood. An understanding of the characteristics and challenges of this period of life is an essential component of any transition care model. Evidence to date supports the importance of continuity, in particular cultural, longitudinal, and relational, as important characteristics of successful programs. In addition to incorporating these important characteristics, there is a need to develop and evaluate programs that include the medical, social, and psychological aspects of diabetes care in the context of the social-ecological realities of the individual. While there will likely be components of healthcare transition common to both type 1 and type 2 diabetes, the unique medical aspects of type 2 diabetes and the unique (socio-ecologic) characteristics of this population support the development of programs specifically designed to best serve this vulnerable group.

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Chapter 15
Diabetes Prevention in Schools and Communities

Elizabeth R. Pulgaron, Victoria L. Valledor, Katherine L. Aparicio, and Alan M. Delamater

Introduction

The purpose of this chapter is to review type 2 diabetes (T2D) in children and adolescents, at risk for T2D, and discuss research relating to primary and secondary prevention of T2D in youth clinical implications of these models. T2D occurs when insulin secretion is inadequate to meet the increased demand due to insulin resistance (Ramkumar & Tandon, 2013). Many epidemiologic studies have shown that T2D has increased dramatically over recent years in children and adolescents with the average age of onset being 13 years of age (Rosenbloom, Silverstein, Amemiya, Zeitler, & Klingensmith, 2008). The incidence varies among ethnic groups, but generally the range is 1–51/1000 (Fagot-Campagna et al. 2000; Shaw, 2007). Incidence of T2D is highest among Native American Indians and lowest among non-Hispanic white youth, with those from Hispanic, Black, and Southern Asian ethnic backgrounds also having a higher incidence of T2D (Chen, Magliano, & Zimmet, 2011; Cizza, Brown, & Rothe, 2012; Ramkumar & Tandon, 2013; Shaw, 2007).

The SEARCH for Diabetes in Youth population-based study found that ethnicity was a factor among 10–19 year olds diagnosed with T2D in the United States (Hamman et al. 2014), with relatively greater representation among ethnic minority youth including Black, Hispanic, Asian/Pacific Islanders, and Native Americans. Youth at risk for or diagnosed with T2D are also more likely to be of lower socioeconomic status (SES) backgrounds. Furthermore, the trend of susceptibility of youth from ethnic minorities and lower SES developing T2D seems to parallel the disparities in obesity among youth (Pulgaron & Delamater, 2014). Children are more likely to become obese or develop T2D if they are from an ethnic minority group and from low-income families, when compared to white, middle-class youth (Delva, O'Malley, & Johnston, 2006; Pulgaron & Delamater, 2014).

There are several risk factors for T2D in youth, with the most common being obesity. Furthermore, most overweight and obese children have metabolic abnormalities associated with insulin resistance even if they have yet to develop T2D (Kim & Caprio, 2011). Other risk factors for T2D in youth are impaired glucose tolerance and metabolic syndrome (Sinha et al. 2002; Weiss et al. 2004); many of these youth also have hypertension and hyperlipidemia. Insulin resistance in the preteen years has been shown to predict increased body mass index (BMI), impaired fasting glucose, and T2D by age

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E. R. Pulgaron · V. L. Valledor · K. L. Aparicio · A. M. Delamater (✉)
Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA
e-mail: adelamater@med.miami.edu

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18–19 years (Morrison, Glueck, & Horn, 2008). These are also all considered metabolic comorbidities of obesity in children and adolescents. Other risk factors include positive family history of T2D and in utero exposure to hyperglycemia (Fetita, Sobngwi, Serradas, Calvo, & Gautier, 2006). In fact, 75% of T2D cases in youth have a strong family history of T2D (Rosenbloom et al., 2008). Overweight Hispanic children with a positive history of T2D constitute a high-risk group as they already demonstrate impaired glucose tolerance (Goran, Bergman, & Avilla, 2004). Furthermore, small size at birth, large for gestational age, offspring to mothers with T2D or gestational diabetes, and puberty are also risk factors for developing childhood T2D. Girls are 1.3–1.7 times more like to develop T2D than boys (Delva et al., 2006; Ramkumar & Tandon, 2013).

Obesity is not only a risk factor for T2D in children and adolescents, it is also the most common comorbidity (Fagot-Campagna et al., 2000; Rosenbloom et al., 2008). Over 85% of children diagnosed with T2D are considered either overweight or obese. Poor glycemic control in youth with T2D can lead to serious health complications, such as retinopathy, neuropathy, and nephropathy, and cardiovascular disease (Dean & Sellers, 2007; Pinhas-Hamiel & Zeitler, 2007a). Typically, glycemic control begins to deteriorate within 2 years after diagnosis of T2D, increasing risk for these comorbidities (Levitt Katz et al., 2011). Studies have also linked mental health diagnoses to obesity and T2D. For example, the prevalence of psychiatric disorders such as depression and disordered eating (e.g., binge eating) tend to be higher among youth with T2D than those without (Walders-Abramson, 2014).

The major goal of T2D treatment is to achieve normoglycemia. Normoglycemia is achieved through daily oral medication (metformin), and sometimes insulin is prescribed, along with daily monitoring of blood glucose, as well as other daily medications (Rosenbloom et al., 2008). While medical treatment is important, adopting healthy lifestyle behaviors and achieving a healthy weight are important to successfully achieve normoglycemia (Pulgaron & Delamater, 2014).

Lifestyle behaviors are targeted through behavioral interventions. A key issue in treatment is patient and family education to improve medication adherence and lifestyle modification to reduce obesity (Pinhas-Hamiel & Zeitler, 2007b). However, these lifestyle behaviors are difficult to change because the unhealthy habits that lead to obesity and T2D are already well established by the time of diagnosis. While family interventions help with children at risk for T2D, adolescents are more independent and do not rely on their parents as much to feed them and provide them with physical activity as would a small child. This is why interventions that deal directly with the adolescent or young adult are important. Nevertheless, integrated behavioral and medical team management of T2D appears to be the most effective approach for successful management (Pulgaron & Delamater, 2014).

There is little evidence for the optimal treatment of T2D in youth, but it is clear that both medical and lifestyle intervention is needed (George & Copeland, 2013). The results of the TODAY trial indicated that over half of the patients failed to attain durable glycemic control over the course of the nearly 4-year study (TODAY Study Group, 2012). Given the increasing incidence of T2D in youth, the increased risks for morbidity, and the difficulties in attaining good glycemic control, it is imperative to determine the best ways to reduce risk factors for T2D and prevent it from occurring in the population. This chapter will review primary and secondary prevention programs aimed at reducing T2D in youth; most of these intervention studies occurred in school and community settings. Future directions for research and clinical practice will also be discussed.

Primary Prevention of T2D in Youth

Primary prevention focuses on preventing the onset of disease by reducing its incidence. Primary prevention is applied before there is any evidence or symptoms of the disease. It is a population-level intervention because it focuses on preventing disease in everyone. Very few studies have focused on primary prevention as a means to reduce the incidence of T2D in children. We review two such studies below that consider obesity and metabolic measures such as fasting insulin and glucose as primary outcomes: the HEALTHY study and the Bienestar study.

Considerable research has also examined various ways to prevent obesity in children, and we review three representative studies that focus on these outcomes as they are relevant to T2D prevention. Most studies in this are educational and behavioral interventions that aim to promote a healthier lifestyle by increasing physical activity and improving dietary intake. Many controlled studies have shown school-based interventions to have some success in improving children's dietary and physical activity habits, as well as improving their weight status (Pulgaron & Delamater, 2014). It is reasonable to assume that reducing obesity may offer our best hope in the prevention of T2D.

The HEALTHY study (HEALTHY Study Group, 2009a, 2010) was a primary prevention intervention aimed at reducing the risk of T2D, primarily through obesity prevention, in middle school students. A pilot study by this group conducted with 1740 eighth graders from 12 schools demonstrated a high prevalence of risk factors for T2D: 49% were overweight; 40.5% had impaired fasting glucose; and 36.2% had fasting insulin greater than 30 microU/ml (Baranowski et al. 2006). The HEALTHY study was conducted with 6358 sixth graders in 42 middle schools: 21 of these schools received a multicomponent intervention, while the other 21 served as a control group. In order to qualify for the study, schools had to be representative of the adolescent population at risk for developing T2D, including schools with a high proportion of ethnic minority and low SES children. At baseline there were already high risks for T2D in these youth: 49.3% were overweight or obese; 16% had impaired fasting glucose; and 6.8% had high-fasting insulin levels (HEALTHY Study Group, 2009b).

The intervention was applied school-wide, so all students were exposed; however, the HEALTHY study focused on a specific cohort. Students enrolled in the cohort were followed from sixth to eighth grade. The participants underwent measurements of body mass index (BMI), waist circumference, and fasting glucose and insulin levels. The intervention employed by the HEALTHY study consisted of four integrated components: nutrition, physical activity, behavioral knowledge and skills, and communications and social marketing. Newsletters and informational packets with tips on how to reinforce behavioral goals were sent home. Volunteer peers were trained to help deliver certain intervention components.

Upon completion of the study, there were no significant differences between the study groups on the prevalence of overweight and obesity. However, children in the intervention schools had significantly lower BMI and BMI z-scores, waist circumference, and fasting insulin (HEALTHY Study Group, 2010), suggesting such programs may reduce T2D risk. The main limitation of the HEALTHY study was the feasibility and sustainability outside a controlled study environment. Even with significant resources, the intervention was unable to meet its primary goal of reducing the prevalence of overweight and obesity in sample, indicating how difficult these changes are to achieve in at-risk youth.

Another school-based primary prevention program to prevent T2D was the Bienestar Health Program (Treviño et al. 2004). A previous study by this group found a high rate of T2D risk factors in 173 Mexican-American 9-year-old children, with increased body fat, a high prevalence of T2D in family members, and poor dietary and physical activity habits (Treviño, Marshal, Rodriguez, Baker, & Gomez, 1999). The Bienestar Program was a randomized trial of 1419 low-income Mexican-American fourth grade students. Twenty-seven elementary schools were randomly assigned to either the intervention or a control group. The intervention group received health programming over 7 months focused on reducing high-risk behaviors associated with T2D. The health sessions aimed to (1) decrease dietary saturated fat intake, (2) increase dietary fiber intake, and (3) increase physical activity in children. The intervention was delivered via the classroom, home, school cafeteria, and after-school care programming. Participants attended on average 32 out of 50 possible sessions. The primary outcome was fasting capillary glucose; secondary outcomes included body fat, physical fitness, and dietary intake.

There was a significant reduction in fasting glucose for children in the intervention group, while the control group increased over time. Secondary outcomes also favored the intervention group, with increased physical fitness and dietary fiber consumption. While the program made some meaningful changes, it is unclear if the participants maintained long-term changes or if it is feasible to replicate this type of program given the intensity and cost of this type of intervention. Nevertheless, the Bienestar study did demonstrate that high-risk fourth grade children can achieve a significant reduction in fasting blood glucose and some improved lifestyle behaviors that have implications for the prevention of T2D.

We now discuss three representative school-based studies which had the aim of obesity prevention and decreasing T2D risk factors such as sedentary behavior and poor dietary intake, but did not include measures related to metabolic risk such as fasting glucose and insulin or insulin resistance. The Healthier Options for Public School Children (HOPS)/OrganWise Guys was a quasi-experimental controlled study in which an elementary school-based obesity prevention program was delivered to keep children at a normal, healthy weight and improve their overall health status and academic achievement (Hollar et al., 2010). Over 4500 elementary school students, almost half of them Hispanic (48%), participated in the study. The intervention focused on providing nutritious foods in school-provided meals, engaging children in a nutrition and healthy lifestyle curriculum, and increasing opportunities for physical activity throughout the school day.

For the subset of the cohort who qualified for free or reduced lunch, significantly more children in the intervention condition stayed within the normal BMI range (Hollar et al. 2010). Girls experienced significantly decreased diastolic blood pressure compared to controls at the end of the 2-year intervention. Systolic blood pressure also decreased for girls, but this was only significant after the first year; after the second year, the trend continued but was not statistically significant. BMI also decreased significantly for girls in the intervention group compared to controls (Hollar et al., 2010).

The “Active by Choice Today” (ACT) randomized controlled trial aimed to increase physical activity in low SES and ethnic minority adolescents (Wilson et al. 2011). This school-based trial was conducted in 24 middle schools. The objective was to increase physical activity among at-risk ethnic minority youth via a motivational plus behavioral skills intervention delivered during the school year with summer programming. The ACT program consisted of homework completion, physical activity that students selected each week, and behavioral and motivational coaching on developing strategies for increasing physical activity in their home environments. The control condition was a health education program focused on nutrition, stress management, drug prevention, and dropout prevention. It included hands-on activities related to general health and homework completion; however, there was no physical activity component.

Compared to the students in the control schools, those in the intervention program engaged in an average of 27 more minutes of physical activity per week during school time, although changes in physical activity outside of school time were not significant. Participants in the ACT program reported enjoying the program more and having more choices in their activities. Although measures of adiposity were not reported, this study demonstrated that physical activity levels could be increased in a high-risk group of adolescents via a school-wide program (Wilson et al., 2011).

Eskicioglu et al. (2014) conducted a school-based intervention in a remote and isolated area of Canada with Native American children, a population at high risk for T2D. This study was a quasi-experimental trial with a control arm that was completed across two school years. The objective of the study was to assess the efficacy of an after-school, peer-led, healthy living program on waist circumference, BMI, self-efficacy, and knowledge of healthy living behaviors. Fourth grade students participated in a 5-month intervention led by high school mentors. Students in the control arm were those that were unable to participate in the program or fifth grade students. Post intervention, there was a significant decrease in waist circumference and BMI z-scores between the intervention and control conditions. The intervention group also had improved knowledge of healthy dietary choices. The study limitations include self-selection bias, investigators partially knowing who was in and who was not part of the intervention, and carry-over effects of fifth graders who previously participated in the program. Similar to the studies previously described, there was also limited parent involvement.

Secondary Prevention

Secondary prevention focuses on detecting a disease in its earliest stages before symptoms appear, and slowing or stopping its progression, focusing on those individuals at increased risk for the disease. Secondary prevention programs have been tested in various settings such as schools, after-school programs, and residential programs. The formats and delivery style vary. Some include traditional face-to-face counseling, while others have incorporated technology and telehealth. We review several representative secondary prevention interventions that target overweight youth who are at increased risk for T2D and include metabolic measures as outcomes.

Scott and colleagues (2013) used school clinic data to identify youth who are at risk for T2D. These researchers conducted chart reviews of school-based health clinic medical records of 971 children in grades 1 through 5. They found that about 40% of the sample was overweight, 49% belonged to an ethnic minority group identified as high-risk for developing T2D, 27% had signs of acanthosis nigricans, and 48% had a family history of diabetes. When risk factors were combined, 39% of the sample met criteria for T2D screening. This study indicated the value and importance of using school clinical data to identify children who may be at risk for T2D and getting them appropriate referrals.

A randomized study was conducted in the school with 73 Latino overweight eighth grade students (Rosenbaum et al., 2006). The 3–4-month intervention consisted of one weekly class on nutrition education and three times per week of aerobic exercise. Results showed intervention students had decreased adiposity and improved insulin sensitivity relative to control students. Another school-based study targeted 8–12-year-old Latino youth at high risk for T2D based on their overweight status, having a positive family history of T2D, and being from an ethnic minority group (Coleman et al. 2010). Sixty-two children and 82 parents participated, receiving 10 90-minute sessions focused on healthy lifestyle habits. While parents showed improved outcomes in terms of increased physical activity and lower body weight, children did not evidence any improvements in BMI. These findings were further limited by the lack of a control group.

A school-based intervention was performed in New Haven, CT, on 198 students at risk for T2D (Grey et al. 2009). Risk for T2D was determined if the student had a family history of T2D and if their BMI was above the 85th percentile for age and sex. Schools were randomized to either the control or intervention arm. All seventh grade children in the schools received a multifaceted school-based educational intervention with or without coping skills training and 9 months of telephone health coaching to reduce their risk of T2D (Jefferson et al. 2011). Participants were followed for 12 months. The main findings were that children in both groups showed some improvements in anthropometric and metabolic risk measures, but zBMI was not improved. However, children who received coping skills and health coaching exhibited greater improvements in 2-hour glucose during oral glucose challenge testing, as well as improved total cholesterol and triglycerides (Grey et al., 2009). One of the major limitations of the study was the lack of consistent attendance of intervention participants, with only 34% of the sample receiving at least half of the intervention. Therefore, the amount of content received by participants was limited. There was also a dropout rate of 27%.

While most controlled intervention studies of overweight youth have included white middle-class participants (Pulgaron & Delamater, 2014), the Bright Bodies Weight Management Program was developed to serve obese ethnic minority children of lower SES in New Haven, Connecticut. The program was an intensive program with classes focused on exercise and nutrition education held two times per week for 6 months and then meetings every other week for another 6 months; sessions were held at a school in the community, and parents were included in the program less frequently for nutrition and behavior modification. A randomized design was used to test the effects of the program on anthropometric as well as metabolic outcomes of 209 obese 12–16-year-old youth. The results of the program after 1 year of intervention showed improvements in measures of adiposity as well as metabolic parameters including improved glucose tolerance and insulin sensitivity (Savoye, Shaw, & Dziura, 2007; Shaw et al. 2009). These investigators evaluated the 2-year outcomes of participants completing the 1-year study, without additional intervention, and found sustained effects for improved BMI, percent body fat and total body fat mass, LDL cholesterol, and insulin resistance as measured by HOMA-IR (Savoye et al. 2011). However, these findings are limited by the significant attrition observed over the course of the 2-year follow-up.

A number of studies have evaluated the effects of dietary and exercise programs including strength training and aerobic exercise on weight and metabolic outcomes in overweight youth. Davis and colleagues (Davis et al. 2007) demonstrated in a pilot study with overweight adolescent Latino girls that a 12-week dietary intervention with reduced carbohydrates led to lower BMI, reduced carbohydrate intake, and increased fiber intake, whether the program was delivered at home or at school; glucose tolerance was unchanged. Another study by this group randomized 54 overweight Latino adolescents to either a 16-week nutrition and strength training program, nutrition alone, or a control condition. Although there was an observed improvement in glycemic response to oral glucose challenge, this study was underpowered, and the investigators concluded that a more intensive intervention was needed (Davis, Kelly et al. 2009).

In another small randomized study with 41 overweight Latina adolescents, the combination of nutrition with aerobic and strength training was associated with reduced fasting glucose and reduced adiposity (Davis, Yung et al. 2009). In a larger randomized controlled trial with 100 obese African-American and Latino adolescents, nutritional intervention, emphasizing decreased sugar and increased dietary fiber, was associated with improved insulin sensitivity; nutrition plus strength training resulted in decreased hepatic fat (Hasson et al. 2012). However, results depended on ethnic status: outcomes relating to glucose tolerance and total fat mass worsened for African-American youth, suggesting that response to dietary interventions may differ between African-American and Latino youth.

Circuit training (aerobic and strength training) with or without motivational interviewing was examined by Davis and colleagues (Davis et al. 2011) in a study of 38 overweight or obese Latina adolescents. Results were promising for circuit training in this study, with reductions in waist circumference and adiposity as well as fasting insulin and insulin resistance. An uncontrolled study of 29 Latino adolescents, 15 of whom were obese, showed that in a 12-week program with 4 times per week of aerobic exercise (2 times per week at the clinic and 2 times per week at home), there were reductions in insulin resistance and hepatic fat for the obese youth (van der Heijden et al., 2010). However, another small study did not show any beneficial effect on adiposity or insulin sensitivity for obese Latino adolescent boys at high risk for T2D participating in a home-based strength training program (twice per week) delivered over 16 weeks (Kelly et al., 2015). This series of studies addressing dietary intake, aerobic exercise, and strength training, while conducted with small samples and being underpowered, did include measures of metabolic risk and in general provides support for the notion that T2D risk factors can potentially be improved by interventions to increase physical activity (with both aerobic and strength training programs) and improve dietary intake.

Strength training was also evaluated in a small randomized pilot study by Shiabi and colleagues (Shiabi et al., 2006). Twenty-two overweight Latino adolescent boys were randomized to participate in two times per week of strength training for 16 weeks or to a control group without strength training. Results showed improved insulin sensitivity for boys receiving strength training, although there was significant attrition by the end of the study. A later study by this group (Shiabi et al., 2010) evaluated a diabetes prevention program delivered in a community-based health clinic. This was a lifestyle educational program for 102 obese Latino youth and their parents. At baseline, there was a high prevalence of risk factors for T2D. After 1 year, although there were only 50 youth returning for the follow-up evaluation, there were reductions in BMI, LDL-cholesterol, and fasting insulin, with increased HDL cholesterol. However, the lack of a control group and significant attrition limits the significance of these results. A small pilot study by this group of 15 obese Latino adolescents subsequently reported that a 12-week program delivered at a local YMCA including 1 session per week on healthy lifestyle education and 3 60-minute sessions per week of physical activity resulted in decreased BMI, waist circumference, sedentary behavior, and 2-hour glucose during OGTT, with increases in fitness and insulin sensitivity (Shiabi et al., 2012). Three youth dropped out, and there was no control group, but this finding nevertheless documents the potential benefits of community-based programming to reduce risk factors for T2D in high-risk youth.

Davis et al. (2012) randomized overweight, sedentary children from 15 elementary schools in Georgia to a low-dose exercise treatment, a high-dose exercise treatment, and a no treatment control group after-school program. This trial aimed to test the effect of aerobic training dose on insulin resistance, BMI, visceral fat, and fitness in these high-risk children and test moderation by sex and race. Participants were between the ages of 7 and 11 years and classified as overweight or obese. The study had 6 cohorts of 30–40 children over the course of 4 years. The exercise treatment took place after school for 10–15 weeks. Children were bused to a gymnasium and offered healthy snacks prior to exercise. The exercise conditions were equivalent in intensity but differed in duration depending on whether it was part of the low- or high-dose treatment. Monthly lifestyle education classes on topics such as diet, physical activity, and stress management were offered to all participant families. Results showed that reduction in insulin resistance was larger in the high-dose group than the low-dose group and control group. There were also dose-response benefits on body fat and visceral fat. Results did not vary by participant sex or race.

Low SES children living in urban centers are at risk for T2D, but many children in rural locations are also at risk, especially Native American youth. A culturally sensitive behavioral intervention was created for youth of the Eastern Band of Cherokee Indians and Navajo Nation (Sauder et al., 2018). The study included children between the ages of 7 and 10 with a BMI greater than the 85th percentile. The participants also had at least one caregiver willing to participate. The Tribal Turning Point (TTP) program consisted of 12 active learning group sessions, 5 youth/caregiver dyad motivational interviewing (MI) sessions, and a resource toolbox. The group sessions included physical activity, cooking demonstrations, a small meal, and or active craft projects. The Traffic Light Diet system was used to guide the nutrition component, and families were invited to an optional 60-minute kid’s workout to help them meet with physical activity goals each week. A positive reinforcement system in the form of “wellness bucks” was implemented to encourage participation in the program goals. The control group received general information about health and safety across three sessions. Intervention group attendance averaged 84%, and 97% of participants completed the study. BMI and waist circumference significantly increased over time for the control group, but not for the intervention group. However, there were no significant differences in fasting insulin, fasting glucose, HbA1c, insulin resistance (measured by HOMA-IR), or blood pressure between groups.

It can be challenging to recruit and retain participants outside of a school or afterschool-based program. One way to enable access to care and potentially reach a broader audience is through technology and telehealth. One example of secondary prevention program delivered via technology is the Pace-Internet for Diabetes Prevention Intervention (PACEi-DP; Patrick et al., 2013). PACEi-DP was a randomized controlled trial that compared three levels of intensity of an obesity intervention to usual care. One hundred and one mostly Hispanic adolescents were randomized to either usual care, a website (healthy lifestyle programming) only group, a website with monthly group sessions and follow-up phone calls, or to the website plus text messaging condition. Participants were overweight or obese 12–16-year-old adolescents at risk for T2D based on their being overweight, ethnic minority, having signs of insulin resistance, and a family history of T2D. After completing the 1-year intervention, there were decreases in sedentary behavior for the website only condition compared to usual care. There were no treatment effects for BMI, adiposity, physical activity, or dietary intake at the 12-month assessment.

Telehealth and technology-based interventions are often used to reach rural populations. Davis, Sampilo, Gallagher, Landrum, and Malone (2013) showed that offering multifamily group intervention via telehealth can be as effective as physician visits in reducing BMI and improving children’s dietary intake and physical activity habits.

Discussion

Few studies (Healthy Study Group, 2010; Trevino et al., 2004) have addressed the primary prevention of T2D in youth. It is noteworthy that in these studies, risk factors for T2D were already apparent in many participants prior to the intervention. Thus, primary prevention must begin at very early ages, as T2D risk factors are prevalent in many children in the elementary school-age years, particularly if they are overweight or obese. Clearly, more research needs to address the primary prevention of T2D in children. Nevertheless, these two studies have at least demonstrated that reductions in adiposity (Healthy Study Group, 2010) and fasting glucose (Trevino et al., 2004) can be achieved through school-wide programs to improve healthy lifestyle habits for all children.

The research literature is clear in establishing that the presence of obesity in youth is associated with increased T2D risk factors such as insulin resistance and decreased insulin sensitivity, especially so in children with a positive family history of T2D (Goran et al., 2004; Pulgaron & Delamater, 2014). Thus, studies to reduce T2D risk factors in high-risk youth, i.e., those with obesity, positive family history of T2D, ethnic minority status, and metabolic perturbations such as impaired fasting glucose, high-fasting insulin, and signs of insulin resistance, constitute an issue of considerable public health significance. Not surprisingly, much more research has addressed T2D risk reduction in children and adolescents already at increased risk. Secondary prevention efforts have targeted overweight and obese youth in various ways but mostly through weight reduction programs that aim to improve dietary and physical activity habits.

Hispanic youths, like American Indian youth, are at high risk for developing T2D. A recent review analyzed the results of lifestyle-based T2D prevention interventions targeting Hispanic youths (McCurley, Crawford, & Gallo, 2017). The review included 15 studies, 11 of which were randomized controlled trials and 4 were uncontrolled. BMI, BMI z-score, fasting glucose, and fasting insulin were the four commonly measured outcomes among all the studies (McCurley et al., 2017). Twelve of the fifteen studies measured participant BMI, and of those, 3 reported a significant reduction in mean BMI post intervention or when compared to the control group depending on the study (Davis, Kelly et al. 2009; Davis, Yung et al. 2009; Rosenbaum et al., 2006; Shaibi et al., 2010). Two studies found statistically significant reductions in fasting glucose between the intervention and control groups (Davis, Kelly et al. 2009; Davis, Yung et al. 2009; Treviño et al., 2004). Four out of nine studies that measured fasting insulin found a significant reduction in insulin (Davis et al., 2011; Healthy Study Group, 2010; Shaibi et al., 2010; van der Heijden et al., 2010). One study found an improved glycemic response during an oral glucose tolerance test (Shaibi et al., 2012).

Behavioral outcomes were also considered in this systematic review (McCurley et al., 2017). Eight studies examined self-reported changes in dietary intake, and six reported significant changes compared with controls (Davis et al., 2007; Davis, Kelly et al. 2009; Davis, Yung et al. 2009; Patrick et al., 2013; Shaibi et al., 2012; Weigensberg et al., 2014). Of all the studies examined in this review, the 11 randomized controlled trials presented the strongest evidence for behavioral interventions in reducing T2D risk in Hispanic youths. However, due to the small sample sizes, heterogeneity of intervention content, lack of stratification by sex, and other limitations, more research must be done to conclusively demonstrate that behavioral interventions are successful in this at-risk population (McCurley et al., 2017).

Many studies were school-based, as interventions in this setting offer advantages in terms of access to students at high risk. However, parental involvement, particularly with younger children, seems essential to successful risk reduction, and many of the studies reviewed in this chapter had limited parental involvement. Studies in which schools can deliver curriculums to improve the lifestyle habits of all children (e.g., Hollar et al., 2010) have great potential but depend on the willingness of school systems to incorporate such programming into an already crowded academic curriculum. Using the school as a site to deliver interventions after regular school hours seems very advantageous in terms of access by being in the neighborhood where families live and by potentially increasing parental involvement in such programs. This approach was used successfully in several studies to reduce T2D risk factors (e.g., Grey et al., 2009; Rosenbaum et al., 2006; Savoye et al., 2011).

A number of studies demonstrated improvements in physical fitness and body composition, as well as reduction in metabolic risk factors and improved insulin sensitivity, with increased physical activity through either aerobic or strength training exercise, and improved dietary intake via reduction in simple carbohydrates (e.g., Davis, Kelly et al. 2009; Davis, Yung et al. 2009; 2011; Shaibi et al., 2006; van der Heijden et al., 2010). More work is needed in this area as most of these studies were conducted with small underpowered samples and limited follow-up. It is also clear that the intensity and dose of these types of interventions may have been either insufficient to effect significant metabolic risk reduction or too intense so as not to be sustainable. More research should also address the settings best suited to effect long-term behavioral changes needed to reduce T2D risk, whether the home or school setting. For severely obese youth, residential camp settings also offer potential advantages (e.g., Huelsing, Kanafani, Mao, & White, 2010), but research addressing the sustainability of behavioral, weight, and metabolic changes is needed for such programs.

Another issue raised in this review concerns ethnicity and the cultural tailoring needed to work effectively with various populations. While quite a few studies have addressed T2D risk reduction in Latino youth (McCurley et al., 2017), several studies have included mixed samples of African-American and Latino youth (e.g., Grey et al., 2009; Savoye et al., 2011), without stratification for ethnicity; this is important because there is some evidence of differential metabolic effects of behavioral interventions depending on ethnicity (e.g., Hasson et al., 2012). Few studies have examined programs to reduce T2D risk in Native American youth, and the effectiveness of these depends on successful cultural tailoring (Sauder et al., 2018). More work with various ethnic populations at high risk for T2D is urgently needed.

Even if successful programs to reduce T2D risk factors are demonstrated through controlled research, delivering such programs to those that need it remains a challenge. While using the school or other community sites such as health clinics may be helpful strategies, another is the use of telehealth, which may be particularly helpful for youth living in rural areas. Research in this area is beginning, and results demonstrate the potential for the delivery of family-based weight control programs (Davis et al., 2013) or programs directly targeting adolescents (Patrick et al., 2013).

Conclusions

Given the increasing incidence of T2D in youth, the challenge of achieving optimal glycemic control, and the high risk for health complications in this population and eventual costs to society in terms of reduced quality of life and increased heath care utilization, the prevention of T2D in youth has become an urgent public health issue. Very little research at this point has demonstrated that primary prevention of T2D can be achieved, but available studies have shown that reductions in BMI and fasting glucose are possible through a public health approach targeting all children in the school setting. Finding ways to effectively reduce risk factors for T2D in high-risk children is another strategy to improve public health. However, the population that is at risk for T2D is a challenging group to engage, based on low SES and high rates of obesity and T2D in family members. Many such families are trying to manage multiple stressors, and attending to a disease that may or may not affect their children in the future may often not be viewed as a priority or alternatively may be viewed as an inevitability that cannot be prevented.

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Part V

Policy Level Factors for Children and Adolescents

Chapter 16
Health Care, Insurance, and School Policy Affecting Diabetes in the Pediatric Population

Lynda K. Fisher and Alaina P. Vidmar

Introduction

Both type 1 and type 2 diabetes (monogenic and other forms of diabetes are not specifically addressed in this chapter) in youth are noted to be increasing around the globe. Since landmark studies have shown that health outcomes are linked to glycemic control, efforts to improve diabetes management have increased. At the same time, advancements and improvements in insulin (human as well as rapid and long-acting insulin analogs), monitoring devices (both meters and continuous glucose monitoring systems), and insulin delivery systems (pens and pumps) have made diabetes management better able to meet changing glycemic targets, yet diabetes management has also become more challenging and complex. Strategies in delivery of care, data analysis, and benchmarking to improve glycemic control and prevent complications are growing internationally.

The cost of diabetes care supplies is also increasing, and there are places where the delivery of care and the availability of insulin make achieving new targets difficult. Even in high-income countries, the cost of care is an issue; this is especially the case currently in the United States, where the cost of insulin has become a huge issue. Insurance availability and affordability are critical to diabetes care. Diabetes care is not only delivered at home, but as children and youth with diabetes spend most of their weekday hours in school, the availability and quality of proper care and supervision of their diabetes are an added burden. This chapter will highlight some of these issues as well as consider epidemiological trends, treatment guidelines and goals of care, the pediatric health care model, and federal and state law and school policy affecting diabetes management in youth.

Epidemiological Trends in Pediatric Diabetes

Worldwide there has been an increased incidence and prevalence of type 1 (T1D) and type 2 diabetes (T2D) in children and adolescents (Dabelea, Bell, & D'Agostino, 2007; Fazeli Farsani, van der Aa, van der Vorst, Knibbe, & de Boer, 2013; Mayer-Davis, Lawrence, &Dabelea, 2017; IDF Diabetes Atlas 2017). The exact incidence and prevalence rates vary among countries based on population characteristics (Mayer-Davis et al., 2018; Fazeli Farsani et al., 2013; IDF Diabetes Atlas 2017). T1D

L. K. Fisher (✉) · A. P. Vidmar
The Center for Endocrinology, Diabetes and Metabolism, The Keck School of Medicine,
University of Southern California, Los Angeles, CA, USA
e-mail: lfisher@chla.usc.edu

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is caused by insulin deficiency following destruction of the pancreatic beta cells and is one of the most common chronic conditions in childhood (Chiang, Kirkman, Laffel, & Peters, 2014; Mayer-Davis et al., 2018). The incidence of T1D varies based upon age, gender, geography, family history, and ethnicity (Chiang et al., 2014; Dabelea et al., 2007; Mayer-Davis, Kahkoska, & Jefferies, 2018; IDF Diabetes Atlas, 2017). The incidence of T1D in children younger than 15 years is increasing (Patterson, Gyurus, & Rosenbauer, 2012). The incidence of youth with T1D worldwide ranges from 0.1 to 65 per 100,000 youth (Chiang et al., 2014; Mayer-Davis et al., 2017; Patterson et al., 2012). The percentage of European children with T1D is increasing with an overall annual increase of almost 4% (Patterson et al,. 2009, 2012). The SEARCH for Diabetes in Youth study reported that over 200,000 youth less than 20 years of age have T1D in the United States with an increased incidence of 21% from 2001 to 2009 (Dabelea et al., 2014; Pettitt, Talton, & Dabelea, 2014). SEARCH data indicates T1D increasing 1.4% annually from an incidence of 19.5 per 100,000 in 2001–2012 to 21.7 per 100,000 (Mayer-Davis et al., 2017). In Poland, rates documented prospectively in regional registries increased from 5.36 to 22.74 per 100,000 in youth <15 years from 1989 to 2012 (Chobot et al., 2017).

T2D accounts for 20% to 50% of new-onset diabetes cases diagnosed in patients less than the age of 20 (Imperatore, Boyle, & Thompson, 2012), with an increased incidence in ethnic minorities (Dabelea et al., 2014; Nadeau, Anderson, & Berg, 2016). T2D is a complex metabolic disorder with a multifactorial etiology composed of social, behavioral, and environmental risk factors triggering the effects of genetic susceptibility (Copeland, Silverstein, & Moore, 2013; Zeitler, Arslanian, & Fu, 2018; Zeraatkar, Nahari, & Wang, 2016). The pathophysiology is thought to result from a combination of beta-cell failure, insulin resistance, inflammation, glucotoxicity, and lipotoxicity (Fazeli Farsani et al., 2013; Scaramuzza, Cherubini, & Tumini, 2014). The prevalence of T2D in youth is increasing (Nadeau et al., 2016; Zeitler et al., 2018; Zeraatkar et al., 2016), with an incidence of 0–330 per 100,000 person-years and a prevalence of 0–5300 per 100,000 worldwide (Fazeli Farsani et al., 2013). Several European studies have reported prevalence rates of 0.21–2.3/100,000 person-years (Sharma, Nazareth, & Petersen, 2016). However, in the United States, the T2D prevalence among youth is approximately 12/100,000 person-years, with a 30.55 increase in prevalence between 2001 and 2009 and a 7.1% annual increase from 202 to 203 in 2011–2012 (Dabelea et al., 2014; Mayer-Davis et al., 2017).

Consensus Guidelines for Treatment Approach and Goals of Care

The International Society for Pediatric and Adolescent Diabetes (ISPAD) and the American Diabetes Association (ADA) have created consensus targets for glucose, hemoglobin A1c (HbA1c), blood pressure, lipids, and BMI for children and adolescents with T1D (DiMeglio, Acerini, & Codner, 2018; Danne, Phillip, & Buckingham, 2018; Scaramuzza et al., 2014; Smart et al., 2018). The Diabetes Control and Complications Trial (DCCT) showed a significant link between blood glucose control and development of diabetes-related complications in adolescents age 13 or older (Mahmud, Elbarbary, & Fröhlich-Reiterer, 2018; Zhang et al., 2016). Crucial to achieving glycemic control is an understanding of the effect of diet, physical activity, and insulin on blood glucose levels (DiMeglio et al., 2018; Hood, Peterson, Rohan, & Drotar, 2014; Prasanna Kumar, Dev, & Raman, 2014; Smart et al., 2018). To achieve good glycemic control, youth must monitor blood glucose levels multiple times per day and respond to those levels with intake of food or insulin administration (Corathers et al., 2015; Scaramuzza et al., 2014). In addition, they must administer insulin for all the food they consume. Insulin is administered by multiple daily injections or with an insulin infusion pump (Danne et al., 2018; Mezquita-Raya, Reyes-Garcia, & Moreno-Perez, 2013). Research indicates that only one-third of youth with T1D in the T1D Exchange study met the age-specific ADA and ISPAD targets for HbA1c of 7.5%, with the majority meeting target goal for blood pressure, lipids, and BMI targets (Wood, Miller, & Maahs, 2013); in 2018, the ISPAD HbA1c target was lowered to 7.0%. These results suggest that despite advances in strategies of care for youth with diabetes, significant barriers to achieving target HbA1c levels remain (Wood et al., 2013).

Most medications used for T2D have been evaluated for safety and effectiveness in persons older than 18 years (Mahmud et al., 2018; Nadeau et al., 2016). In fact, the studies in adults rarely have subjects in their 20s. There are limited evidence-based guidelines for the most effective therapy and medical management of adolescents with T2D (Nadeau et al., 2016; Nambam, Silverstein, & Cheng, 2016; Meehan & Silverstein, 2016; Scaramuzza et al., 2014). The treatment goal is normalization of blood glucose levels and HbA1c values, with the ultimate goal of reducing the risk of acute and chronic complications associated with chronic hyperglycemia (Oester, Kloppenborg, Olsen, & Johannesen, 2016; Zeitler et al., 2012). Treatment should include lifestyle behavior modification strategies and increasing physical activity (Onge, Miller, Motycka, & DeBerry, 2015; Zeitler et al., 2012). Weight control is critical for achieving these goals (Klingensmith, Connor, & Ruedy, 2016; Zeitler et al., 2012). If the treatment goal is not achieved with behavioral modification, pharmacologic therapy is indicated (Zeitler et al., 2018). Metformin and insulin are currently approved for use in patients younger than 18 years of age (Tamborlane, Haymond, & Dunger, 2016). Oral agents are first-line therapy for most patients (Katz, Anderson, & McKay, 2016; Zeitler et al., 2018).

The TODAY study reported that overall, 50% of patients with a mean duration of T2D of 6.8 months failed oral treatment alone, or a combination of metformin and intensive lifestyle modification, at a median of 11.5 months after initiation (Zeitler et al., 2012). The current recommendation is to start metformin as the first-line agent in those youth with T2D without metabolic decompensation, defined as a HbA1c > 10% (Gandica & Zeitler, 2016). Many youth with T2D present with secondary complications at diagnosis (Weinstock, Drews, et al., 2015). In addition, they are at risk of secondary comorbidities including dyslipidemia, hypertension, nonalcoholic fatty liver disease, polycystic ovary syndrome, obstructive sleep apnea, and psychological problems (Donaghue, Marcovecchio, & Wadwa, 2018; Mahmud et al., 2018; Zeraatkar et al., 2016). Given the long-term complications of T2D, optimal management is essential (Mezquita-Raya et al., 2013; Zeraatkar et al., 2016). Clinical practice guidelines have been developed to assist providers who care for youth with T2D (Zeitler et al., 2012, 2018; Zeraatkar et al., 2016).

Social Ecological Model of Pediatric Diabetes

There are multiple levels of influence on health behaviors in youth with diabetes including intrapersonal, interpersonal, organizational, community, and public policy levels. Attentions to developmental stages, family dynamics, and physiological differences are all essential in developing and implementing an optimal diabetes regimen (American Diabetes Association 2018; Chiang et al., 2014; Silverstein et al., 2015). Providers must identify the most relevant potential influences at each level to inform the development of comprehensive interventions that can systematically target mechanisms of change at several levels at a time (Pihoker, Forsander, & Fantahun, 2018). Improved health outcomes occur when behavior change is supported by environments, policies, and social support and when youth with diabetes are motivated to make those necessary changes.

Diabetes management throughout childhood and adolescence places substantial burdens on the youth and family (Corathers et al., 2015; Everest, Akhtar, & Sumego, 2016). Health-care providers must be capable of evaluating the educational, behavioral, emotional, and psychosocial factors that impact implementation of a successful treatment plan and work with the individual, family, and community to overcome those barriers and lead to improved health outcomes (Naughton, Yi-Frazier, & Morgan, 2014; Pihoker et al., 2018; Zhang et al., 2016). In this chapter, we examine the socio-ecological determinants that influence pediatric diabetes management and health outcomes, focusing on the modifiable domains such as pediatric health-care model, federal and state law, and school policy.

Pediatric Health-Care Model

Diabetes Self-Management Education

Diabetes self-management education and psychosocial support should be provided at diagnosis and regularly during follow-up visits, by a multidisciplinary health-care team consisting of physicians, clinical diabetic educators, nutritionist, and social workers and psychologists experienced with the educational, nutritional, behavioral, and emotional needs of the youth and their families (American Diabetes Association 2018; Everest et al., 2016; Gesuita, Skrami, & Bonfanti, 2016; Phelan, Lange, & Cengiz, 2018; Pierce & Wysocki, 2015). The diagnosis of diabetes may impact family function, psychosocial development, and school performance and place a financial burden on the family (Chiang et al., 2014; Weinstock, Drews, et al., 2015). Screening for psychosocial distress and mental health problems is an important component of ongoing care (Inman, Daneman, & Curtis, 2016; Luyckx et al., 2013). Psychosocial factors are significantly related to nonadherence, suboptimal glycemic control, reduced quality of life, and higher rates of acute and chronic diabetes complication (Hood et al., 2014; Luyckx et al., 2013; Naughton et al., 2014; Noser, Patton, Van Allen, Nelson, & Clements, 2016).

Diabetes self-management behaviors exist within individual, family, community, and health-care system domains (Modi, Pai, & Hommel, 2012; Schnell, Alawi, & Battelino, 2011). An individual child or adolescent's self-management practices and family and community support affect their ability to adhere to treatment guidelines and impact their health outcomes (Naughton et al., 2014; Modi et al., 2012). However, the youth's developmental stage impacts how they are able to traverse the health-care and school system as required for successful adherence to recommendations (Cameron, Garvey, Hood, Acerini, & Codner, 2018; Hilliard, Harris, & Weissberg-Benchell, 2012; Luyckx et al., 2013; Modi et al., 2012). Therefore, health-care teams must identify both nonmodifiable and modifiable components of the self-management regimen to individualize care for these youth and provide the specific support they require (Gesuita et al., 2016; Inman et al., 2016).

Within the family domain, non-modifiable components include socioeconomic status (SES), insurance coverage, and racial or ethnic minority status (Gesuita et al., 2016; Inman et al., 2016). A recent study looking at the effect of race and ethnicity indicated that despite adjusting for SES and clinical factors, black race was associated with significantly higher HbA1c trajectory in youth with T1D over the 9 years of the study (Kahkoska, Shay, Crandell, & Dabelea, 2018). The authors also reported that there was an association between Hispanic ethnicity and the highest HbA1c trajectory which did not disappear after adjustment for demographics, clinical variables, and socioeconomic status.

Modifiable family influences include parental involvement, parental stress, and family dynamics (Noser et al., 2016). Increased parental involvement and monitoring are associated with effective self-management (Luyckx et al., 2013). Interventions to reduce conflict and improve family communication demonstrate improved adherence rates and health outcomes among adolescents with T1D (Everest et al., 2016; Hilliard et al., 2016; Marrero et al., 2013; Naughton et al., 2014; Weinstock, Trief, et al., 2015).

Youth with diabetes have to manage their condition within the context of the community in which they live in (Gesuita et al., 2016; Modi et al., 2012). This includes schools, peer networks, neighborhood organizations, and community health-care organizations (Edwards, Noyes, Lowes, Haf Spencer, & Gregory, 2014; Noser et al., 2016). Youth spend a large portion of their day in the school setting, and therefore school policies and school staff knowledge of diabetes self-management strategies are essential; the lack of knowledge and skill may act as a barrier that has to be modified on a systemic level (Edwards et al., 2014; Jackson, Albanese-O'Neill, & Butler, 2015). Laws and policies are in place to ensure these self-management strategies can be completed effectively while the youth is at school (Jackson et al., 2015).Youth with diabetes often participate in health promotion camps, community gatherings, and online social networking which can positively influence self-management and improve health outcomes (Modi et al., 2012).

Finally, youth with diabetes are influenced by the clinical environment and the health-care team rapport (Pihoker et al., 2018). Centers where the diabetes multidisciplinary team have shared goals and work in concert to achieve HbA1c targets show lower HbA1c independent of how insulin is delivered (Skinner, Lange, & Hoey, 2018). In order to facilitate collaboration with the youth and family, providers must aid the youth in identifying individual barriers they are experiencing and work together with the parents and health-care team to improve shared decision-making and adherence to treatment regimen (Naughton et al., 2014). As the families interact within the clinical model during routine visits, they need to understand what the expectations are for the patient as well as the health-care team (Pihoker et al., 2018). Successful collaboration can result in improved patient-provider relationships which can result in improved health-care outcomes and family satisfaction and decreased stress associated with the chronic condition (Edwards et al., 2014; Katz et al., 2012; Pihoker et al., 2018). Across the Unites States and internationally, clinic programs have developed models to address the many complex factors that can result in poor diabetes control in children and adolescents (Limbers, Emery, Young, & Stephen, 2015; Scaramuzza et al., 2014). These programs often not only contain multidisciplinary health-care providers but also community health workers or interventionists who contact the families or patients frequently during the initial diagnosis period (Jackson et al., 2015; Prasanna Kumar et al., 2014; Zhang et al., 2016).

The ISPAD clinical practice guidelines for diabetes education emphasize the importance of utilizing patient-determined outcome measures to evaluate the efficacy of educational programs (Phelan et al., 2018) and outline what is needed for an effective multidisciplinary education program. These include health-care professionals "with a clear understanding of the special and changing needs of young people and their families as they grow through the different changes in stages of life." Diabetes education should be delivered with the child and their developmental and educational status in mind while paying attention to family, culture, and religious beliefs. The educators themselves should be continuing to advance their own knowledge of educational principles, insulin therapy, and new insulin delivery and monitoring technologies (Phelan et al., 2018).

In addition to well-designed educational programs founded on consensus guidelines, clinically relevant health-care policies must be created to support comprehensive system-based approach to pediatric self-management (Katz et al., 2012). Examples of such policies include Medicare's reimbursement of self-management education for diabetes educators (Katz et al., 2012; Pierce & Wysocki, 2015). Promoting access to preventive self-management has potential to save substantial costs to the health-care system by reducing preventable health-care utilization and illness-related morbidity associated with problematic self-management and nonadherence (Everest et al., 2016; Hood et al., 2009; Zeraatkar et al., 2016).

The Chronic Care Model (CCM) was developed in the 1990s to improve health-care outcomes for individuals living with chronic medical conditions. Identified were components that were believed to be essential for health-care systems to "encourage high-quality chronic disease care." These include "the community, the health system, self-management support, delivery system design, decision support, and clinical information systems." The CCM was later modified as the landscape in medical care changed to include patient safety, cultural competency, care coordination, community policies, and case management. Applications of the CCM to T1D management have found that systems and programs that were able to integrate patient-centered care, with patients and families, clinicians, researchers, health-care systems, payers, and policy makers working in concert, could have positive effects on diabetes management (Corathers et al., 2015).

Appropriate management of diabetes in children and adolescents requires access to medications, routine clinic visits, and medical supplies (Wolfgram, Sarrault, Clark, & Lee, 2013). Children without access to private health coverage may turn to public programs for medical coverage. The American Academy of Pediatrics has recommended that the federal government establish a benchmark to ensure uniformity of health benefits for children across states. In the Unites States, public programs such as Title V programs are unique because they designate eligibility based on diagnosis of a chronic disease (Wolfgram et al., 2013). Medicaid provides coverage for the most disadvantaged children, and State Children's Health Insurance Program (SCHIP) provides health coverage for children of modest means who do not qualify for Medicaid (Parish, Shattuck, & Rose, 2009. State-to-state variability in coverage exists as to Title V programs.

Barriers to Insurance Coverage

Medical care and pharmaceutical costs are escalating, and millions of Americans have been unable to both access and afford health insurance. The cost of health care in the United States is about twice that of most other comparable high-income countries, often with poorer outcomes (Papanicolas, Woskie, & Jha, 2018; Sawyer & Cox, 2018). In the Unites States, the Affordable Care Act and the expansion of Medicaid to cover those in many states have provided opportunities to extend benefits to those at below the 133% of federal poverty guidelines. It provided federal subsidies reducing premiums initially to 2% of income for those at the 133% of federal poverty with increase to 9.5% for those with incomes between 300% and 400% of poverty. It allows for children up to 26 years of age to be covered on parental insurance, and most importantly, it prohibits denial for preexisting conditions such as diabetes. States were mandated to create state or multistate exchanges to assist in the purchase of insurance. To assist those who could not afford to purchase insurance, temporary high-risk pools were designed to make the purchase and provision of insurance for those with current preexisting conditions. This extended to millions of uninsured the opportunity to be covered.

A part of the ACA mandated individuals to purchase health insurance or pay a penalty. This penalty was eliminated with passage of the 2017 tax bill so as of 2019 the incentive to purchase insurance no longer exists. This raises concern in that younger healthier individuals who no longer are penalized for not having insurance are dropping coverage. With healthier individuals leaving the pools, the cost of health is not spread out but again concentrated on those who are older (but less than age 65) and those with chronic medical illnesses who use more pharmaceuticals and have more frequent interactions with the health-care system; this is estimated to be between 2.8 and 13 million fewer insured and premiums of between 3% and 13% for bronze premiums (Eibner and Nowak, 2018).

For those who are able to obtain insurance, there are barriers of utilization especially for families of lower SES with state-funded insurance in accessing providers who accept their insurance, as well as the ability to take time from work to access care for themselves or their children. Access to medications may also be limited in type and supply. Out-of-pocket costs can also be a barrier to care for those with insurance both in the United States and in other high-income countries. About half of Americans have insurance through employers, and cost-sharing expenses have increased dramatically including deductibles. Although the United States has the highest access problems, high uninsured population, and high cost-sharing, these declined overall between 2004 and 2014, initially because of an increase in Medicare enrollment and recently because of ACA provisions (Rice et al., 2018).

These are significant issues for children with T1D (and T2D) who should have health-care appointments at least quarterly and require medications and testing supplies to safely manage their diabetes. Reimbursement for diabetes supplies, even for those with insurance, can be limited as many if not most plans in the United States limit the number of monthly test strips and may limit access to new technologies, such as insulin pumps and continuous glucose monitoring (CGM) devices, and do not necessarily cover access to all members of the multidisciplinary team such as psychologists.

Diabetes Management in the School Setting

Youth with diabetes have the right to participate in school just like any other child. Federal and state law provides legal protections for students with diabetes to ensure that they are given an equal educational opportunity (American Diabetes Association 2013; Jackson et al., 2015). The majority of children and adolescents with diabetes spend a large portion of their day in school or in some type of child care program (Jackson et al., 2015; Lawrence, Cummings, Pacaud, Lynk, & Metzger, 2015). Students with diabetes are more likely to succeed in school when there is collaboration in implementing a diabetes management plan at school (Phelan et al., 2018). Impaired glucose control has been shown to influence cognitive and structural maturation of the brain in youth with diabetes (Ferguson, Blane, & Wardlaw, 2005; Gaudiere et al., 2008; Mauras, Mazaika, & Buckingham, 2015; Perantie, Lim, & Wu, 2008; Semenkovich, Patel, & Pollock, 2016). Research indicates lower academic school performance in youth with T1D compared to students without diabetes, thought to be secondary to frequent absences due to disease demands and parental fear of acute complications occurring at school (Persson, Dahlquist, Gerdtham, & Steen Carlsson, 2013). Therefore, trained and knowledgeable staff is essential to provide a safe school and child care environment for children and adolescents with diabetes to ensure they achieve academic success and normal development (Chiang et al., 2014; Jackson et al., 2015).

In 2015, the American Diabetes Association (ADA) published a position statement to provide diabetes management recommendations for students with diabetes in the elementary and secondary school settings (Jackson et al., 2015). These were based on the ADA "Standards of Medical Care in Diabetes" and "Type 1 Diabetes Through the Life Span: A Position Statement of the American Diabetes Association" (Chiang et al., 2014; Nadeau et al., 2016). These documents provide health-care providers, school staff, and families with recommendations for appropriate diabetes management throughout the school day to ensure that all members of the care team have the information necessary to enable the youth to fully participate in the school day (American Diabetes Association 2013; Lawrence et al., 2015; Nadeau et al., 2016). The ISPAD clinical practice consensus guidelines 2018 contain an extensive chapter on the support and management of diabetes at school and a special chapter of the ISPAD guidelines addresses diabetes management in preschool settings was released in 2017 (Bratina et al., 2018; Sundberg et al., 2017). Both provide valuable information that outline procedures and practices that lead to appropriate and safe managment of diabetes in school.

Diabetes Medical Management Plan

To ensure that the student and school staff are familiar with the medical treatment regimen, an individualized diabetes medical management plan (DMMP) should be developed by the health-care provider in collaboration with the student and family to outline the student's daily diabetes management needs while at school (American Diabetes Association 2013; Jackson et al., 2015; Skinner et al., 2018). The aim of this document is to clearly state the tasks required and assign responsibilities for each task, based on the age and developmental stage of the student. These written guidelines are utilized ultimately to develop the 504 Plan or individual educational plan (IEP). This document should include specific instructions for each of the following: blood glucose monitoring (including frequency, timing, and location), insulin administration (storage of insulin, location of administration, and timing in relationship to meals), meals and snacks (amount, accessibility, and timing), management strategies for aberrant glucose values (access to food, water, glucagon, and insulin as needed), and guidelines for participation in physical activity, extracurricular activities, and field trips.

School Staff Members' Roles

The school staff should receive formal training to ensure all staff members understand a basic overview of diabetes, typical needs of students with diabetes, and recognition of hypoglycemia and hyperglycemia. For those staff members directly in contact with students with diabetes, they must be able to demonstrate competency in tasks such as blood glucose monitoring and insulin and glucagon administration in case of a situation in which the school nurse is not available. If a school nurse is available, they should act as a coordinator and provide care to the student with diabetes. The school must ensure that if the school nurse is not present, at least one trained school staff member is available to perform needed tasks while the student is at school, on a field trip, or participating in school-sponsored extracurricular activity (Lawrence et al., 2015).

Students' Roles

Those adolescents with diabetes who have demonstrated the ability to self-manage their diabetes should be permitted to carry their supplies, medication, and equipment at school and are thus responsible to monitor their blood glucose and administer insulin during the school day (Modi et al., 2012). For those students who perform their own diabetes management at school, nutritional information regarding school meals will need to be provided to them in advance (American Diabetes Association, 2013). All students, even those who can independently manage their diabetes, will need assistance in the event of a diabetes emergency (Cameron et al., 2018; Jackson et al., 2015).

Diabetes and the Law

Multiple federal laws exist to protect children and adolescents with diabetes in the United States. It is illegal for any school to discriminate against any student with a disability; in this case, diabetes is considered a disability. These include Section 504 of the Rehabilitation Act of 1973, the Individuals with Disabilities Education Act (IDEA), and the Americans with Disabilities Act (Jackson et al., 2015). Under Section 504 of the Americans with Disabilities Act, diabetes is considered a disability (American Diabetes Association et al., 2013). Therefore, federal law requires an individualized assessment, in writing, of any child or adolescent with diabetes under a 504 Plan or individualized education plan (IEP) (Jackson et al., 2015; Modi et al., 2012). Each plan must include the program modifications that will support the student and the school personnel to provide the services necessary to ensure the student with diabetes is able to participate in the full school day with as little interruption as possible (Hilliard et al., 2012; Jackson et al., 2015). This is accomplished by ensuring that staff members are able to assist the student in the following tasks: blood glucose checks, insulin or glucagon administration, recognition and management of hyper and hypoglycemia, and access to restrooms and food products as needed (Lawrence et al., 2015). Unfortunately, students with diabetes still face discrimination at school, which may manifest as not being allowed access to food during the school day or not receiving adequate time to monitor their blood glucose levels and administer insulin (American Diabetes Association 2013; Edwards et al., 2014; Jackson et al., 2015). The Americans with Disabilities Act works to ensure students with diabetes receive safe care while at school and prevent discriminatory practices.

Section 504 of the Rehabilitation Act of 1973

Multiple federal laws are in place to protect youth with diabetes as they traverse the school system. Section 504 of the Rehabilitation Act of 1973 is a federal civil rights law that prohibits recipients of federal financial assistance from discrimination on the basis of disability (Jackson et al., 2015; Lawrence et al., 2015). This means that schools that receive federal funding need to meet the needs of students with diabetes as well as meet the needs of students without disabilities. Section 504 does not require that students have any learning challenges. It equally protects honor students and those who struggle academically (American Diabetes Association 2013; Jackson et al., 2015).

The Americans with Disabilities Act

The Americans with Disabilities Act is a federal law that prohibits discrimination against qualified individuals with disabilities, including diabetes. The Americans with Disabilities Act protects parents and guardians from being fired and other adverse employment actions taken because of their child's disability (Jackson et al., 2015; Lawrence et al., 2015). It applies to public and private schools, preschools, child care centers, and camps except those run by religious institutions (Jackson et al., 2015; Nadeau et al., 2016). Students are covered by this legislation if they have a disability, defined as a physical or mental impairment, that substantially limits one or more major life activities (Jackson et al., 2015). For schools, these laws are enforced by the Office for Civil Rights (OCR) in the US Department of Education (Lawrence et al., 2015).

The administration of insulin at school by licensed individuals, mainly nurses, occurs in all states. In many states, there are laws that allow specially trained non-licensed individuals at school to administer insulin. In 18 of the 50 US states, there are no laws permitting trained non-licensed school staff to administer insulin, although in Louisiana, school principals may recruit non-licensed health aids for that purpose. Some states' laws are unclear on the issue or silent. In New Mexico, trained non-licensed staff can administer insulin using prefilled pens or insulin pumps. Many states allow non-licensed school staff to administer glucagon but not insulin. Most states have laws allowing non-licensed individuals to administer medication in emergency situations; in these states, the interpretation is that giving glucagon to treat a low glucose is an emergency and therefore is permitted, although the administration of insulin would not be permitted. In many states, older children are permitted to carry diabetes supplies with them and monitor glucose and self-administer insulin in all areas of the school. Current state-by-state information is readily available on the American Diabetes Association website (State Laws, Regulations and Policies for Diabetes School Care, www.diabetes.org).

Individuals with Disabilities Education Act (IDEA)

The IDEA is a federal law that provides federal funds to assist state and local agencies in making special education and related services available to eligible children with disabilities (Jackson et al., 2015; Lawrence et al., 2015). A child with a disability must meet the criteria for a disability and need special education and related services. The IDEA category of "other health impairment" includes diabetes as one of the health conditions listed (Jackson et al., 2015). IDEA is administered by the Office of Special Education Programs (OSEP) in the Office of Special Education and Rehabilitative Services (OSERS) in the US Department of Education. The IDEA regulations specify how school personnel and the parents/guardian, working together, develop and implement an IEP (Jackson et al., 2015).

International Perspectives

It is interesting to consider the how pediatric diabetes care varies by country. This is especially important to consider given the variation in glycemic control observed in different countries (Charalampopoulos et al., 2018). In this section, we consider this issue in several selected countries, including Sweden, the United Kingdom, Australia and New Zealand, and Italy, Spain, and Germany.

Sweden

Sweden has similar regulations as the United States and requires that each student has a mandatory, written action plan for diabetes self-care procedures. A study in 2014 evaluated the effect of a new national legislation in Sweden regarding diabetes management in schools (Sarnblad, Berg, Detlofsson, Jonsson, & Forsander, 2014). In July 2009, a new law was implemented which defined diabetes care in school as equivalent to home care and required schools to care for students with diabetes just as they would at home (Persson et al., 2013; Sarnblad et al., 2014). The components of this law required that a health-care professional created a detailed agreement outlining the diabetes-specific needs the child would have during the school day. The head teacher then had to arrange for the support needed. The law gives the diabetes specialist team the responsibility to spread knowledge about diabetes to the school staff, which is in line with the guidelines from International Society of Pediatric and Adolescent Diabetes (ISPAD).

This study was a national questionnaire-based survey examining parent, children, and diabetes team opinions about the support for children's diabetes self-care management in school (Sarnblad et al., 2014). Only around 40% of the children with T1D in Swedish schools had a written action plan for the treatment of hypoglycemia and a designated member of the school staff with principal responsibility helping the child with the diabetes self-care during the school day (Persson et al., 2013; Sarnblad et al., 2014). It was also reported that 21% of the parents regularly administered less insulin than they calculated would be needed for breakfast because of concerns about how to deal with hypoglycemia at school. In addition, parental satisfaction in school support increased from 55% to 65% over time (Sarnblad, Akesson, Fernstrom, Ilvered, & Forsander, 2016).

Other countries have their own issues, with little or no access to help with diabetes and other medical tasks at school. Although many have care guidelines for pediatric diabetes care, there are few mandated guidelines for diabetes care at school.

Australia/New Zealand

Australia has one of the highest incidences for T1D in youth, with over 10,000 youth with T1D nationally and an increasing incidence. The majority of these cases receive clinical care in tertiary academic centers with multidisciplinary teams (Cameron et al., 2013; Catanzariti et al., 2009; Clapin et al., 2016; Tran et al., 2014). In 2010, the Australian Pediatric Endocrinology Group formed a national Children's Diabetes Network that represented over 95% of young people with T1D in Australia and New Zealand to assess whether the goals of the universal intensive management of T1D in children had been achieved. The results of this study demonstrated that the clinician-to-patient ratios were significantly below accepted recommended levels. Although most patients were able to attend three monthly visits per year, access to all team members was limited. The broad conclusion from the audit was that less than one-third of young people with T1D were achieving the ISPAD target for glycemic control (Cameron et al., 2013).

In Australia, the Federal Government's Educational and Care Services National Law and Regulations state that "all services providing, or intending to provide, education and care must have a diabetes policy" (The Australian Children's Education and Care Quality Authority, 2017). A report detailing the results of a survey on diabetes in schools was published online in January 2017. The report identified inconsistencies, similar to the United States, across the country with no national approach to diabetes care in school. Some states and territories mandated individual diabetes management plans for individual students. Although there were educational materials available to schools along with information listing the rights of students with disabilities, specific information about how children with diabetes receive supervision and care at school for self-management tasks were not universal. The report also identified that teachers often did not have important information regarding diabetes and that parents reported a lack of understanding from teachers and schools about day-to-day diabetes care needed while at school. The report outlined these issues and made recommendations to improve diabetes care to schoolchildren across Australia (The Australian Children's Education and Care Quality Authority, 2017).

The Diabetes Committee of the Australian Paediatric Society recently created and promoted e-learning courses for schools and child care that are available at no cost to school personnel (Goss et al. https://www.t1d.org.au). These educational modules have been endorsed by ISPAD and have been used in schools in Victoria and other Australian states. There are no laws mandating their use; in Australia, state laws prevail as there are no national laws as to diabetes care in schools; however many school administrations have adopted their use.

United Kingdom

In a UK report from 2015, 66% of the diabetes centers had difficulties finding someone who could administer insulin, and 36% had difficulties finding someone who could take responsible for blood glucose testing for children while in the school setting. The United Kingdom enacted the Children and Families Act in England in 2014. It created guidelines for education, training, and formulation of individual self-care plans and educational material for all schools. When a child is diagnosed with diabetes or enters a new school, a plan of care is created by parents and the diabetes team in conjunction with the student and school. The school is obligated to train individuals who must be signed off for each individual student for their specific care plan. This includes insulin administration, provisions for exams, sports, and trips. Schools are not allowed to require parents to provide care at school (Children and Families Act, 2014).

Italy, Spain, and Germany

Italy and Spain do not have guidelines or formal obligations for the school staff to assist children with self-care. Germany does not have school nurses, although provisions for monitoring and guidelines exist to assure that children with diabetes have access to educational opportunities and are not permitted to be discriminated against. Children and adolescents in Germany are allowed to self-administer insulin at school, but often parents need to come to school to administer insulin for those too young to self-administer who may require insulin prior to lunch. Often longer-acting insulin is given in the morning, so students do not have to receive insulin prior to lunch at school. The use of insulin pumps is now more prevalent, and school staff are permitted to supervise. Many families with younger students who are not able to self-administer insulin have been able to apply for school assistants who are paid by the community and are trained to deliver insulin and meals and check glucose levels; however, parents must advocate for this type of assistance for their children.

Conclusions

As the incidence and prevalence of youth with diabetes have increased, awareness of the disease and its challenges have also increased around the globe. In developing countries, although diabetes is recognized more often and care has improved, access to insulin and glucose testing materials is still a significant challenge. In developed countries, standards of care for youth with diabetes are available through the national diabetes societies (e.g., American Diabetes Association, American Association of Diabetes Educators, Diabetes Canada, Diabetes UK, Diabetes Australia, German Diabetes Association), and international societies such as the International Diabetes Federation and ISPAD have published guidelines for care. In developed countries, access to insulin and diabetes supplies and new technologies are available, and intensification of diabetes care has become prevalent with targets for HbA1c, glucose, and "time in range." In the United Kingdom, centers now compete for funding based on their achievement of target glycemic control, screening for complications, etc. Benchmarking in countries like Sweden, the United Kingdom, Germany, and Austria has improved both mean A1c and numbers of individuals achieving target.

In some countries, government policy has driven improved diabetes care. For example, in the United States and Australia, standards of care and guidelines have set goals for care, but national laws have not mandated care, as states have control over what schools must do to provide care to students with diabetes. Recent data from the T1D Exchange indicates that fewer children, teens, and young adults achieve target A1c, with higher means especially in adolescents, despite new insulin products and advances in continuous glucose monitoring, pumps and integrated pumps (Foster et al., 2019). Although many states have laws that support appropriate diabetes care at school, many schools do not have enough staff to properly supervise students, and often parents feel compelled to come to school to provide care for their children. It appears that in countries where centers are identified as in Sweden and/or where there is competition for funds as in the United Kingdom, improvement in diabetes control is documented.

Another newer issue concerns the fact that insurance companies have been deciding which insulin, which antihypertensive or lipid lowering drug will be covered and which insulin pump must be ordered. This has interfered with physicians prescribing and patients receiving medically appropriate therapies. For those without access to any insurance, the cost is vastly more. This is the issue for a large proportion of youth with type 2 diabetes who are often economically disadvantaged and therefore cannot afford either medications or medical care.

As evidence increases that glycemic control is linked to medical complications of those with both T1D and type 2 diabetes, recommendations for target glucose levels, A1c, and time in range have changed to advance the goal of decreasing complications of diabetes. We know that for many youth, improved glycemic control with decreased hypoglycemia is possible with education, support, family, providers, and community effort. It is clear that advocacy for access to care, for expansion of insurance, and for state laws mandating care for students at school and children at daycare has improved the lives of those living with diabetes as well as significantly contributed to the safety of children at school. However, data from the TID Exchange indicate that we in the United States are still far from having a significant percent of youth <18 with ADA target HbA1c < 7.5% with only 17% achieving that goal and only 21% of adults achieving ADA target A1c < 7% and only 37% achieving A1c < 7.5%, who have access to care, medications, CGM devices, and insulin pumps.

Although policies around these issues have improved, as have medications and technologies, and standards of care and treatment guidelines are available nationally and internationally, we still have far to go in improving access to appropriate diabetes care, even in industrialized countries. Even in academic centers, medicine has become a business, with emphasis on efficiency and optimization of billing. Those who care for this vulnerable pediatric population need to continue to push for improved policy for delivering diabetes care, education, and support and advocate for appropriate guidelines and provision of proper diabetes care to preschool and school children as well as those in daycare, regardless of type of health insurance. Increasing coverage for diabetes supplies and care to young people with diabetes will improve their health and future.

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Part VI
Conclusions for Pediatric Populations

Chapter 17
Summary and Implications for Clinical Practice and Research in Pediatric Populations

Alan M. Delamater and David G. Marrero

In Parts I–V of this book are 15 chapters discussing the various levels of the social-ecological model as they related to diabetes management in pediatric populations. One recurring theme that appears in many of the chapters is the fact that the majority of youth with diabetes do not meet goals for optimal glycemic control, in spite of therapeutic and technological advances in treatment in recent years. Moreover, this disparity illuminates the limitations of relying on sophisticated technology alone to optimize diabetes clinical outcomes. When we consider the complexity of diabetes treatment and embrace the social-ecological nature of a lifestyle disease, it is not truly a surprise that advances such as newer insulin analogues, continuous glucose monitors, and insulin pumps have not resulted in optimal glycemic control.

Many may remember when nearly four decades ago, routine use of glycosylated hemoglobin A1c and blood glucose monitoring was first introduced into clinical practice. These did not turn out to be "magic bullets" that revolutionized clinical care. In fact, many patients made technical errors in their blood glucose measurement, falsified their blood glucose readings, did not utilize them for appropriate self-management, and did not even know their A1c or understand what it meant. Simply having technology available does not guarantee good diabetes management but certainly can facilitate it. The chapters in Parts I–V of this book detail and discuss the many factors that impact glycemic control in youth, including personal and social-familial factors, medical system and practice models, and environmental and policy factors.

In Chap. 2, Daneman updates the epidemiology of type 1 and type 2 diabetes (T1D, T2D) in children and adolescents and discusses management of both conditions, noting that only a small percentage of youth maintain near normal glycemia. As he observes, "its management depends more on psychosocial or behavioral factors, and indirectly on the social determinants of health." In discussing the latter, Daneman states they "are a major contributor to outcome, always unidirectionally; that is to say, the more disadvantaged the child with diabetes and their family is, the worse the outcomes, be they metabolic control, quality of life, or other variables." He further urges health-care professionals to be aware of these relationships and be responsive to the needs of individual patients.

A. M. Delamater (✉)
Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA
e-mail: adelamater@med.miami.edu

D. G. Marrero
Center for Border Health Disparities, University of Arizona, Tuscon, AZ, USA

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Treatment guidelines, such as those provided by the International Society of Pediatric and Adolescent Diabetes (ISPAD), state that optimal care is delivered by interdisciplinary teams and is evidence-based and family-centered, with extended team members based in the community (such as school personnel and sports coaches). In discussing new technologies in diabetes management, he observes that “these technologies do not in and of themselves lead to better glycemic control; rather, it is up to the individual with diabetes to apply the technologies to their best advantage.” Daneman also notes that “these new technologies…may become unattainable except by those in the richest countries with excellent health benefits…and raises the possibility of an increasing gap in treatment availability between haves and have-nots.”

A key factor in successful medical management of diabetes in youth is the recognition of mental health issues in young patients and/or their parents, as these constitute a barrier to achieving the goals of medical therapy. Therefore, Daneman states: “The presence of a mental health professional on the diabetes team is an imperative as is their involvement with those individuals having the most difficulty adjusting to their diabetes routines.”

He discusses diabetes care as a series of transitions: with diagnosis, a transition to a new lifestyle with a complex daily regimen; then, transitions to changing medical regimens over time; and finally, the transition from pediatric, family-focused care to patient-oriented care in the adult medical setting. While some patients and families may navigate these transitions well, for many “the reality is that diabetes poses major challenges to their well-being. The good news is that the longevity of people with type 1 diabetes has increased significantly in parallel to declining complications.” By contrast, management of T2D in youth presents special challenges, as many youth already present with health complications at the time they are diagnosed. Unfortunately, while the long-term prognosis of T2D in youth is uncertain, available data suggest that serious health complications may develop prior to age 40, with a consequent loss of life expectancy.

Daneman concludes by noting that modern therapies have resulted in a significant delay in the development and progression of significant health complications for youth with T1D but that the prevention or reversal of T1D does not appear to be forthcoming in the near future. However, the worldwide epidemic of obesity has led to increasing incidence of T2D, particularly in high-risk individuals at earlier ages than was previously observed, and the implications of this on health-care systems and some of the world’s emerging economies may be overwhelming. Clearly, for both T1D and T2D in youth, “the challenge is to provide optimal and equitable health care to all, paying attention not only to the disordered biochemistry but also to the behavioral and psychosocial aspects, as well as the social determinants of health.”

In Chap. 3, Laffel and colleagues consider the many neuroendocrine and biobehavioral influences on both T1D and T1D in youth. They note that the role of genetic and environmental factors (such as viral infection and stress) leading to T1D is not well understood and that there are currently no proven therapies to alter the path toward autoimmune beta-cell destruction, although research on immunomodulatory therapies continues. However, for young patients participating in autoimmune screening programs that were at increased risk for T1D, they were less likely to have ketoacidosis at diagnosis of T1D. While the impact of stress on the development of T1D is not clear, there is evidence indicating that increased stress may have adverse effects on diabetes management behaviors and glycemic control in young patients with T1D.

With regard to development of T2D in youth, they discuss various risk factors, including overweight/obesity, genetics, the in utero environment (i.e., maternal obesity and diabetes), early childhood influences, and puberty, all of which interact to lead to insulin resistance, glucose intolerance, and eventual T2D. In particular, they note the important role of stress as it may increase risk for obesity and T2D through disordered eating. Unhealthy lifestyle behaviors of youth with T2D have been documented, including excessive caloric intake (sweetened beverages and fast food), disordered eating, infrequent physical activity, and high levels of sedentary behavior. Unfortunately, available research indicates that lifestyle interventions for youth with T2D have not improved health outcomes at this point. As the authors note, “Given the SES and racial/ethnic disparities found in pediatric T2D populations, prescribed lifestyle interventions may be more difficult to implement and maintain.”

For both T1D and T2D, Laffel and colleagues observe that adolescence is a developmental period in which appropriate diabetes self-management behaviors are challenging to achieve and maintain and psychological factors such as depression may undermine diabetes management and glycemic control. The authors note the critical role of the family in managing childhood diabetes, whether T1D or T2D, and refer to the American Diabetes Association’s (ADA) medical and psychosocial standards of care that encourage age-appropriate family support and involvement in the management of diabetes in children and adolescents (ADA, 2017; Young-Hyman et al., 2016). They also note that the ADA “has suggested a family-centered approach to lifestyle modifications in youth with T2D, with particular attention to the interplay of culture and nutrition, as well as the availability of resources based on the family’s means” (ADA, 2017). The authors conclude by stating: “Managing the progression of both T1D and T2D requires an orchestrated approach to management, including an appreciation of the neuroendocrine and biobehavioral factors that may be involved.”

Chapters 4, 5, and 6 address three specific individual-level psychological factors: distress and quality of life; depression, diabetes-related distress, and anxiety; and eating disorders, respectively. In Chap. 4, Malik and Aslam review research related to quality of life in youths with diabetes, particularly as it relates to diabetes distress, and the mechanisms underlying the relationship between them. Psychological distress is common in young patients and is often experienced at diagnosis, associated with changes in lifestyle and adjustment to the complex medical regimen, concerns about potential health complications, fear of social stigma, and related to demographic factors. With regard to the latter, research indicates that adolescent girls seem to be especially vulnerable to distress and lower quality of life; the authors suggest more research is needed to understand these relationships in specific racial/ethnic groups as a function of sex, age, and diabetes duration. In general, research has shown that diabetes distress is associated with lower quality of life, and this relationship seems to be reciprocal; social support, resilience, and effective coping also appear to moderate this relationship. Quality of life of parents is also affected, as many experience distress related to their child’s diagnosis and ongoing diabetes management.

Although the authors note research has found lower quality of life in youths with poor glycemic control, they also state that “It is yet not clear, however, what predicts what and most researchers suggest a cyclic relationship between glycemic control and quality of life.” They present a conceptual model that helps to clarify the complex relationships between sociodemographic, clinical, psychosocial, and behavioral factors as they relate to distress and quality of life in youth with diabetes.

Chapter 5 continues discussion of psychological factors of depression, diabetes-related distress, and anxiety in youth with diabetes. Evan, Vesco, and Weissberg-Benchell review research demonstrating the effects of depression and anxiety on diabetes management as well as psychosocial functioning: these youth are at increased risk for poor regimen adherence and glycemic control, as well as psychological distress and perceived burden of ongoing diabetes management. Youth with diabetes are also at increased risk for development of depression and anxiety compared to children without chronic illness.

The authors discuss studies identifying risk factors for these psychological disorders, including family factors such as criticism and conflict, low cohesion, parenting style, and family psychiatric history. Other factors increasing risk for depression include female sex, older age, ethnic minority status, and lower family socioeconomic status. As the authors note, “Longitudinal studies using diverse samples of youth with T1D across age, SES, and race will further clarify the differences in depressive symptoms across various populations.” Given the important role of family factors in relationship to depression and distress in youth, the authors further recommend: “More research using longitudinal, prospective data can identify the ways in which family functioning might predict or influence the development of diabetes distress and diabetes health outcomes in youth with T1D.”

It is important to differentiate depression from diabetes-related distress. The authors state that "…depressive symptoms are prevalent in T1D but not all youth experience such symptoms; however, many youth with T1D experience emotional distress related to the daily burden of living with diabetes…The emotional reactions to the daily burdens of diabetes management is known as diabetes-*specific emotional distress*, and refers to non-pathological worries, concerns, and fears specific to living with diabetes" (Fisher, Gonzalez, & Polonsky, 2014). This is an important issue clinically, as patients experiencing distress may benefit from psycho-education and problem-solving, whereas those with depression may need more intensive psychological and/or family therapy.

Less research has addressed anxiety in youth with diabetes, but available evidence suggests that up to 20% of youth with diabetes experience significant anxiety, and this is associated with adverse health outcomes, including lower regimen adherence and quality of life, and poor glycemic control. While some studies have found diabetes-related family conflict and parental anxiety, the authors conclude: "More research is needed on the mechanisms by which family factors interact with and influence anxiety and diabetes outcomes in youth with T1D."

Given the importance of these psychological factors on diabetes outcomes in youth, it is surprising that relatively few studies have focused on therapies for these youth. There are some examples of controlled intervention research studies showing the benefits of stress management and coping skills training in youth with T1D, but not in those with clinically significant depression or anxiety. One recent randomized controlled trial evaluated a distress and depression prevention program for adolescents with T1D. One year after treatment, there were significant reductions in diabetes distress for adolescents receiving the resilience program, suggesting that diabetes distress can be prevented (Hood, Iturralde, Rausch, & Weissberg-Benchell, 2018). Clearly, more controlled intervention research is needed for young patients with diabetes who are identified as having significant depression, distress, and anxiety.

Few studies have examined depression and anxiety in youth with T2D. As Weissberg-Benchell and colleagues point out, based on the available research findings, these youth appear to have high risk for depression that is associated with worse health outcomes, but little is known about anxiety, or interventions that address either of these psychological factors in this patient population. The authors conclude by emphasizing the need for regular psychosocial screening and appropriate follow-up for depression, distress and anxiety as part of routine care, as recommended by professional societies such as the ADA and ISPAD (ADA, 2017; Delamater et al., 2018; Young-Hyman et al., 2016). Several studies have documented the feasibility of psychosocial screening in routine care of youth with T1D, but more research is needed in screening youth with either T1D and T2D and determining the outcomes of these programs in terms of providing evidence-based therapies and cost effectiveness.

In Chap. 6, Datye and Jaser review the literature on eating disorders and disordered eating in youth with T1D and T2D. Youth with diabetes are at heightened risk for both of these conditions compared with the general population of children and adolescents. It is important to note that eating disorder as a clinical condition is less common than disordered eating behaviors, which are fairly common in these patient populations. In the context of diabetes, research findings indicate that these conditions merit clinical attention because of their association with metabolic complications—not only poor glycemic control, but also increased risk for subsequent health complications such as retinopathy. Although more common in adolescent girls with T1D, eating disorders and disordered eating are becoming more frequent among boys as well as ethnic minority youth with T2D; in fact, research indicates that about 25% of youth with T2D exhibit disordered eating.

With regard to T1D, the authors state: "Several aspects of the diagnosis and treatment of type 1 diabetes, such as counting carbohydrates, focus on food, and insulin administration, may increase patients' risk for developing an eating disorder…patients with type 1 diabetes may intentionally manipulate or withhold insulin doses to promote weight loss or decrease weight gain, a phenomenon called "diabulimia." It is crucial for clinicians to be able to recognize disordered eating and diagnose eating disorders in their young patients. The authors describe several screening tools to be used particularly with patients with T1D who exhibit rapid weight loss, regimen non-adherence, and poor glycemic control. Unfortunately, at present there is a dearth of intervention research for youth with T1D and eating disorders, so this remains a research priority.

The authors note that few studies have examined disordered eating in youth with T2D. However, they discuss the findings from the TODAY Study which found that "20% of participants were classified as subclinical binge eaters, and 6% were classified as binge eaters. Both of these groups had worse quality of life than non-binge eaters, and clinical binge eaters reported more depressive symptoms." These findings provide further support for the need to assess youth with T2D for disordered eating and eating disorders in clinical practice. In addition, longitudinal research with cohorts of youth with T2D and eating disorders is needed to better understand their risk for health complications.

It is clear that youth with diabetes who also have disordered eating patterns or eating disorders require specialized treatment. As Datye and Jaser state: "While an optimal treatment for youth with diabetes and eating disorders has not yet emerged, it is clear that a multidisciplinary treatment team is crucial to optimize treatment of a patient's eating disorder and diabetes…increased provider awareness of disordered eating behaviors and eating disorders is critical when treating youth with diabetes."

There is a considerable research base addressing the effects of T1D on neurocognitive development of children and adolescents; however, very little is known about neurocognitive effects of T2D in youth and is urgently needed. In Chap. 7, Northam reviews the evidence for T1D focusing on morphological changes, altered cerebral growth trajectories, and reduced functional interconnectivity, which research suggests is more likely with early disease onset. There is evidence that chronic hyperglycemia has adverse effects on neurodevelopment of children, and also that constantly fluctuating glucose levels may be particularly harmful. While there is increasing recognition that T1D has the potential to adversely affect central nervous system function in children, as Northam states: "Our understanding of the causal mechanisms that underlie changes in brain structure and cognition, however, is incomplete and we are yet to develop a coherent model of brain-behavior relationships specific to TID." Understanding the causal mechanisms underlying the impact of T1D on neurocognitive function is the focus of ongoing research.

Research examining effects on neuropsychological function indicate, based on meta-analytic studies, have shown subtle decrements in IQ; scores are consistently in the average range but lower than age-matched control children. Specific cognitive skills impacted include information processing speed, attention and executive skills, working memory, and psychomotor function, particularly with early T1D onset and poor glycemic control. Research has also addressed functional outcomes. As Northam states, "Even subtle decrements in cognitive capacity can impact on children engaged in ongoing learning and skill development and there is compelling evidence that children with TID exhibit compromised academic achievement."

Northam observes that: "The functional implications of pathophysiological brain changes in TID are not limited to cognition, academic achievement and adaptive functions." Given the results of research indicating increased risks for psychological disorders in youth with T1D, and research identifying impacts of T1D on the neural substrates of affective functions (i.e., pre-frontal and limbic regions), she raises the intriguing possibility that diabetes-related structural and biochemical changes in the brain may directly impact on emotional well-being, increasing vulnerability to mood disturbance and risk for mental health problems. While causal mechanisms have not been clearly elucidated, "it is possible that psychological symptoms in individuals with TID may be a cause or a consequence of hyperglycemia, or indeed arise directly, but independently, from the same set of TID-related biochemical brain changes."

Northam concludes by advocating for universal screening of youth with T1D for psychological problems and providing them individualized interdisciplinary resources needed to promote good emotional adjustment and disease management. However, she notes that "less attention has been paid to preventive and remedial cognitive and educational interventions in TID than has been directed to addressing psychological vulnerability. Greater awareness on the part of clinicians, parents and teachers of the risk for neurocognitive deficits in TID is an important first step if academic underachievement is to be reduced." She further argues that access to neuropsychological assessment for children with unexplained academic underachievement or difficulties in problem-solving the demands of diabetes management should be provided as part of routine care.

In Chap. 8, Channon and Gregory review and discuss individual-level intervention approaches for youth with diabetes. They begin by noting there are relatively few studies targeting only youth as "stand-alone" therapies, as most behavioral intervention studies have also focused on family involvement. There is also the issue of age and developmental level to consider, as individual-level intervention approaches using cognitive behavioral therapy (CBT) or motivational interviewing (MI) require some degree of cognitive capacity on the part of the child. Thus, for the most part, individual approaches for youth with diabetes have mainly focused on work with adolescents with T1D.

The authors review studies with individual interventions conducted separately from and in addition to routine diabetes care, integrated within routine clinical care, or via telemedicine approaches. With regard to studies conducted separately from routine care, there are some reports of cognitive behavioral therapy (CBT) with adolescents with T1D, and these have shown improved well-being but no impacts on glycemic control. Channon and Gregory comment that "there has been no randomized trial of individual-level CBT intervention for youth with T1D and subclinical or clinical depression so any indicators of effectiveness have yet to be adequately tested."

More research, however, has been conducted with MI in adolescent populations, and a meta-analysis of this work indicated small to moderate effect sizes on various health behaviors. There have been five investigations (three of them pilot studies) since 2012 of MI with adolescents with T1D, either as stand-alone interventions or in combination with CBT or diabetes education, with all showing positive effects. In a multi-center randomized trial, adolescents receiving MI had significantly improved glycemic control and quality of life 12 months after intervention. There is also evidence that a personal trainer model, including MI and problem-solving approaches, led to improved glycemic control up to 2 years after intervention, but only for mid-adolescents (as compared with younger adolescents).

A number of studies have evaluated interventions delivered as to adolescents as part of routine care. These approaches generally have focused on individualized goal-setting, pre-conception counseling, discussions about quality of life, and self-monitoring. Positive results were reported for improved knowledge from pre-conception counseling and improved quality of life over time from clinic-based discussions with adolescents. More work in this area is needed. Goal-setting and self-monitoring approaches may need more intensive follow-up than the typical 3–4 months between routine clinic visits to have a more meaningful effect.

Telemedicine approaches present opportunities for increased therapeutic contact with youth in a modality they frequently utilize. Studies with phone and text messaging have not produced significant benefits on diabetes management. Results from several Internet-based diabetes self-management programs focused on problem-solving indicate feasibility of the approach and some support for improved outcomes. One of these, TEENCOPE, delivered coping skills training compared with diabetes education to adolescents individually by the Internet and demonstrated good engagement, with both groups having improved outcomes; those who received both programs in a later study phase had improved glycemic control, quality of life, and less family conflict at follow-up.

In discussing the findings from studies of individual-level interventions for youth with T1D, Channon and Gregory comment that developing such intervention approaches is needed primarily for adolescents, as intervention research with younger children typically must involve parents. They state that in such work, "…it is important to remember that interventions that focus solely on direct, behavioral processes involved in diabetes management are less likely to be effective if they neglect emotional, social, and family processes." They conclude by stating: "Teams need a menu of approaches to enable them to offer long-term support and individual approaches have their place on that menu, alongside family and community interventions. To optimize outcomes, it is important that the wider context within which the young person is managing their diabetes care is not neglected when offering such support."

In Part 3 of the book, Chaps. 9, 10, 11, and 12 examine social-level factors affecting diabetes management in youth. In Chap. 9, Butler, Georges, and Anderson review the empirical literature that examines family processes and parenting behaviors in relation to diabetes management. This large research base has firmly established the importance of family influences in T1D. In addition, research is increasingly supporting the role of the family in the management of youth with T2D, although relatively few studies have been reported. With regard to T1D, evidence indicates strong bi-directional relationships between family factors and psychosocial, behavioral, and health outcomes of youth. As the authors state, this is a "transactional relationship in which the family influences the child with a chronic illness and is influenced by the chronic illness."

At the sociodemographic level, it is clear that youth from single-parent, ethnic minority, and low SES families are at increased risk for a variety of problems in diabetes management. General family functioning factors such as conflict and cohesion have consistently shown significant relationships with diabetes management behaviors, glycemic control, and psychosocial functioning in youth, and these relationships appear to vary depending on children's age and gender. Individual parent factors such as depression, anxiety, low health literacy, and fear of hypoglycemia have also been reported to be associated with increased risks for youth. Diabetes-specific family behaviors such as conflict related to the regimen and parental perceived burden of diabetes management have consistently been associated with poor outcomes in youth, whereas authoritative parenting strategies including supportive, collaborative involvement, and clear and positive communications about diabetes management have been related to good health outcomes.

The authors note that most studies in this area used cross-sectional designs and point to the need for larger, prospective cohort studies to better understand how these family factors influence diabetes management in youth over time. Research is also needed investigating how family factors influence management of T2 in youth, the role of fathers and siblings, and studies using direct observational methodologies rather than self-report measures. Nevertheless, the research findings in this area are robust and indicate the need for health-care teams to be aware of these factors and assess their role in clinical practice. The goal is to improve family functioning by promoting family teamwork in managing the challenges of diabetes management.

Based on these findings and observations, the authors make several clinical recommendations. First, parents should be screened for psychological adjustment problems (e.g., depression and anxiety) at their child's diagnosis, and referred for appropriate treatment. Parents should also be screened over time for perceived burden of diabetes management and the presence of significant ongoing life stressors and provided resources and referrals as needed. Psycho-education for parents regarding authoritative parenting styles applied to diabetes management and encouragement of developmentally appropriate parental involvement over time would also be helpful. Finally, screening for diabetes-related family conflict should be conducted at every clinical encounter and families with severe conflict issues referred for further assessment and counseling.

In Chap. 10, Van Vleet and Helgeson address the role of friend and peer relationships in association with psychosocial well-being and diabetes management. The research in this area indicates that general friend support is associated with better well-being and, to a lesser extent, better diabetes management, but not with glycemic control. The findings with regard to diabetes-specific friend support were inconclusive. While general friend conflict was consistently associated with decreased well-being of youth with diabetes, relationships to diabetes management were mixed. Associations between diabetes-specific conflict and well-being and diabetes management outcomes were also variable. The authors conclude that "In sum, the literature on friend and peer relationships and their links to psychological well-being and diabetes outcomes is mixed. Future research can benefit from making finer distinctions in the conceptualization and measurement of friend and peer relationships, examining potential moderator variables, probing mechanisms underlying links between friend and peer relationships and outcomes, and by considering the broader social context (family relationships) in which such relationships are situated."

Social-level intervention approaches are the focus of Chaps. 11 and 12. In Chap. 11, Harris and colleagues discuss interventions that target multiple systems in youth with T1D. Consistent with the social-ecological model, it is clear that diabetes management occurs within and across multiple, complex systems, including individual, parent/family, peer, school, community, and health-care system levels. Much of the behavioral intervention literature has focused on individual- and family-level approaches, and many of these programs have been demonstrated to be efficacious in terms of psychosocial and behavioral outcomes, sometimes showing improvements in glycemic control (Delamater et al., 2018). Results from a meta-analysis showed that interventions that focus on behavioral processes as well as emotional, social, and family processes are more likely to have an impact on glycemic control (Hood et al., 2010).

In this context, Harris and colleagues review both single system and multisystemic intervention approaches for youth with T1D. For example, behavioral family systems therapy and multisystemic therapy are both family-based, multicomponent intervention approaches that have been shown to improve a variety of outcomes. These interventions are delivered outside of and in addition to the usual clinical setting. The authors also discuss Interventions delivered in other settings such as schools and within the health-care system setting. More research is needed to develop and evaluate interventions that occur in such settings that may require policy-level interventions, as well as targeting teachers and clinicians for specific training in alternative therapeutic approaches for youth with T1D.

The authors make the salient point that effective intervention requires identification of systems in which risk factors exist and then providing relevant interventions that address those issues where they occur. Some youth exhibit a combination of risk factors across a number of systems and are especially vulnerable to poor health outcomes including repeated hospitalizations for DKA. These high-risk, high-need youth need more intensive, multisystemic interventions than can typically be provided effectively in usual clinical care settings. The authors describe an innovative approach they developed, termed Novel Interventions in Children's Healthcare (NICH), that is described as "an intensive, multicomponent behavioral health intervention for youth…and include a combination of family-based problem solving, care coordination, and case management. NICH interventionists deliver services in the youth's natural environment (e.g., home, school, clinic, community), are available to families 24 h per day, 7 days per week, and utilize telecommunication to increase frequency of service provision."

Results from their initial studies show the promise of the NICH approach in improving health outcomes and cost savings and suggest that telehealth is a significant treatment component that increases points of therapeutic contact. More controlled trials are needed to demonstrate the effectiveness of NICH for this specific population of "high-need high-cost" youth with T1D. As the authors note, these patients are a relatively small group but account for a substantial share of health-care costs. Thus, there are challenging administrative and policy issues to solve before implementation of multisystemic interventions becomes feasible outside of the research setting. This is a priority area for future research in integrated behavioral health care.

In Chap. 12, Grey and Joiner focus on studies to enhance peer support and coping skills training for youth with T1D. Based on a systematic review of research since 2000, they identified and reviewed the results of seven studies addressing peer support and 12 studies evaluating coping skills training. There were a few studies in which parents of newly diagnosed children were provided support from other parents showing some improvements in terms of less worry and more confidence for parents in managing their child's diabetes. Several studies focused on group interventions designed to enhance peer support, including shared medical appointments.

Grey and Joiner point out that relatively few studies have examined the efficacy of peer support programs for youth with T1D and their parents. While such programs seem useful in terms of increased knowledge and some aspects of self-care, they seemed to focus more on diabetes self-management education and did not apparently aim to increase peer support specifically. Further, as the authors state, "few of these reports contained a clearly articulated framework or process by which the outcomes were hypothesized to occur." More research in this area is needed, especially for ethnically diverse youth and those with T2D, in which no studies have been reported.

Relatively more research has been conducted with coping skills training than with peer support. In general, the results of these controlled studies have shown the benefits of this intervention approach, usually delivered in face-to-face small group format, in improving diabetes management behaviors, quality of life, and glycemic control for adolescents with T1D. There is also evidence that coping skills training can be delivered via the Internet, including opportunities for peer interaction and support. However, as Grey and Joiner point out, "In this literature on both peer support and coping skills training programs, the lack of implementation and dissemination research is a gap that needs to be addressed."

In discussing the clinical implications of this research, the authors state: "...it is critical that strategies for enhancing the availability of peer support and coping skills programs for children and adolescents with diabetes and their families are evaluated and implemented in practice or made available in ways that do not interfere with practice patterns." One way to accomplish this is by incorporating such programs into diabetes self-management education programs that are integrated with clinical care.

Community-level factors that impact diabetes are addressed in Part 4 of the book, comprising Chaps. 13, 14, and 15, including health disparities influenced by demographic factors, medical system elements and transition of care issues, and diabetes prevention in communities and schools. In Chap. 13, Chalew and colleagues review studies that have documented health disparities in youth with diabetes, with ethnic minority and socioeconomically disadvantaged youth consistently exhibiting poorer health outcomes, including hospitalizations for DKA and higher risk for health complications related to chronic poor glycemic control. Studies also show that youth who live in high-deprivation environments (based on their zip codes) have worse glycemic control. The authors provide an informative discussion concerning methodological issues related to measurement of social and neighborhood-level environmental factors.

There is also evidence that ethnic minority and low-income youth are less likely to receive more technologically advanced intensive regimens such as pumps, although even when mode of insulin delivery is similar, Black youth still exhibit worse glycemic control than their White counterparts. As the authors observe: "Potentially the interplay of genetic, biological factors along with environment and socioeconomic influences contribute to continued health disparities among children with diabetes." More research is needed to better understand the factors that mediate these health disparities; changes in diabetes management need more cultural tailoring so optimal outcomes can be achieved by all patients (Naranjo, Schwartz, & Delamater, 2015).

Wicklow and Sellers discuss issues related to transition from pediatric to adult care in emerging adults with diabetes in Chap. 14, considering medical system models of care and patient-provider relationship factors. They provide an interesting discussion of the concept of transition readiness from pediatric to adult care and its measurement. Emerging adulthood is a crucial developmental time in the life course of youth with diabetes, as research has demonstrated decreases in regimen adherence and clinic attendance and deterioration of glycemic control during this period. Wicklow and Sellers discuss the differences between pediatric and adult medical care, the former being more family-focused and socially oriented, with the latter being more person-centered and disease-related. Many young people with diabetes "fall through the cracks" in the medical system of care during this transition, so this has been an important research topic in recent years.

The authors discuss clinical recommendations for this developmental period and note they are for the most part based on consensus guidelines advocated by professional organizations. There is a need for more research to improve the evidence base demonstrating the efficacy and effectiveness of programs that promote successful transition to adult care without gaps in care and worsening of glycemic control.

In summarizing, the authors state: "Evidence to date supports the importance of continuity, in particular cultural, longitudinal and relational as important characteristics of successful programs. In addition to incorporating these important characteristics, there is a need to develop and evaluate programs that include the medical, social and psychological aspects of diabetes care in the context of the social-ecological realities of the individual." They point to the very important continued role of parents, as well as patient-provider relationship factors such as clear communication about transition well in advance of actual transfer of care. They also recommend more work designed to promote transition in young patients with T2D, about whom little is currently known.

Although children at risk for development of T1D can be identified based on insulin autoantibodies, at present there is no way to prevent its eventual occurrence in high-risk children. The situation may be different with regard to prevention of T2D: high risk can be identified based on several factors, and efforts to prevent T2D in youth have been studied and shown to have some success. In Chap. 15, Pulgaron and colleagues review risk factors for the development of T2D, including obesity, family history of T2D, ethnic minority status, insulin resistance, and behavioral factors such as sedentary behavior, low levels of physical activity, and poor dietary intake. Review of the literature indicates that few studies have addressed the primary prevention of T2D in children, but available evidence indicates that school-wide programming emphasizing healthy lifestyle habits may reduce adiposity and fasting glucose.

More research has addressed secondary prevention efforts by providing interventions for youth at high risk for T2D. A number of controlled studies provide evidence supporting the benefits of intervention programs to increase physical activity, improve dietary habits, and reduce weight in obese youth, resulting in subsequent reduction in metabolic risk factors for T2D such as insulin resistance. Most of these programs were delivered in school or community clinic settings, but some have also taken place in the home setting. Pulgaron and colleagues discuss the need for more studies to examine the efficacy of T2D prevention programs delivered via telehealth, thereby increasing the reach of health behavior interventions to the greater population of at-risk youth. The authors conclude that the available evidence is promising but mostly consists of relatively small studies with limited follow-up. More large-scale, randomized controlled trials are needed to demonstrate the efficacy of interventions to reduce T2D risk factors and hopefully prevent T2D.

The policy level is addressed in Part 5 (Chap. 16) of the book by Vidmar and Fisher, who discuss health care, insurance, and school policies as they affect diabetes management in children and adolescents. The authors begin by observing that the costs of health care for patients with diabetes have been increasing in recent years, particularly the costs of insulin in the United States. There are significant issues with regard to insurance availability and accessibility, which are critical to diabetes care. This situation makes the challenge of achieving glycemic targets for youth with diabetes even more difficult. There is significant variability among insurance plans that may limit coverage with respect to essential diabetes management supplies such as glucose monitoring strips, pumps, and continuous glucose monitoring systems. Furthermore, some insurance plans may not cover the costs of care delivered by all members of the health-care team such as psychologists.

Vidmar and Fisher refer to the social-ecological model for pediatric diabetes care, stating: "Providers must identify the most relevant potential influences at each level to inform the development of comprehensive interventions that can systematically target mechanisms of change at several levels at a time…Improved health outcomes occur when behavior change is supported by environments, policies, social support, and when youth with diabetes are motivated to make those necessary changes." By understanding the social determinants at play, health-care providers need to identify modifiable components of the treatment regimen and individualize care to best support youth in their diabetes management efforts.

The authors discuss research findings showing variation in glycemic control among youth in eight countries (Charalampopoulos, Hermann, & Svensson, 2018). In discussing the factors accounting for this, they note that "…youth with diabetes are influenced by the clinical environment and the health care team rapport…Centers where the diabetes multidisciplinary team have shared goals and work in concert to achieve HbA1c targets show lower HbA1c independent of how insulin is delivered." Utilizing the chronic disease model for health-care delivery and the social-ecological framework for individualizing treatment provides clinicians with improved opportunities for their patients to achieve glycemic targets. Benchmarking in several European countries has resulted in reduced center-wide mean A1c and more patients achieving glycemic targets.

Because youth with diabetes spend a large part of their time in the school environment, it is essential that policies support appropriate diabetes management in that setting. Recommendations and guidelines for diabetes care in the school setting have been published by professional organizations such as the ADA and ISPAD. Vidmar and Fisher review federal laws that exist to ensure children with diabetes have access to the care they need while at school, discussing the American with Disabilities Act, Individuals with Disabilities Education Act, and Sect. 504 of the Rehabilitation Act of 1973. Despite this, they note that significant barriers still exist, and it is essential for health-care teams to advocate for their patients and support parents in dealing with school staff on behalf of their children. The authors provide an interesting discussion of international perspectives of these issues, considering how countries such as Sweden, the United Kingdom, Italy, Spain, Germany, Australia, and New Zealand have addressed these issues of pediatric diabetes management.

In concluding, the authors note that while there have been many advances in diabetes management medications and technologies, standards of care and treatment guidelines, as well as policies, there are still significant challenges. As they state: "Those who care for this vulnerable pediatric population need to continue to push for improved policy for delivering diabetes care, education and support, and advocate for appropriate guidelines and provision of proper diabetes care to preschool and school children as well as those in daycare, regardless of type of health insurance. Increasing coverage for diabetes supplies and care to young people with diabetes will improve their health and future."

Discussion and Conclusions

The chapters in this section of the volume have addressed all levels of the social-ecological model as they relate to management of diabetes in children and adolescents, highlighting research providing evidence for the importance of many individual-, social-, environmental-, and policy-level factors. From this review, it is evident that the social-ecological model provides not only a framework for research but also a guide for clinical decision-making at the patient level (Marrero et al., 2013).

Ever since the landmark DCCT was published in 1993, the challenge has been to translate those findings into real-world clinical settings. From the research reviewed here, it is clear that only a minority of children and adolescents in the United States achieve glycemic targets (Foster et al., 2019; Wood, Miller, & Maahs, 2013). This is also the case in other countries, although there is some evidence of improvements in recent years with benchmarking and government incentives supporting improved glycemic control at the center level.

We know that access to advanced diabetes management technologies such as insulin pumps and continuous glucose monitoring systems can improve glycemic control (DeSalvo, Miller, Hermann, & Maahs, 2018), but there are still many factors beyond technology that influence health outcomes. These include, for example, child race and ethnicity and family socioeconomic status; at the individual-level, psychological factors such as depression and anxiety and executive functioning; at the social level, family support and collaborative teamwork; and at the health-care system level, patient-provider relationships and team functioning. With regard to the latter, it is interesting that international variations in children's glycemic control can be attributed to some extent to whether the health-care team is consistent in discussing and setting glycemic goals with youth and their parents (Skinner, Lange, Hoey, 2018; Swift, Skinner, & De Beaufort, 2010).

Focusing on modifiable factors is important for effective diabetes management. Given the importance of psychosocial factors, effective diabetes management requires interdisciplinary care that includes mental and behavioral health professionals as part of the team (Delamater, 2012; Delamater et al., 2018). Yet there are significant barriers to achieving integrated behavioral health care in routine clinical diabetes settings (de Wit et al., 2014). Examples of integrated behavioral health care have demonstrated improvements in various psychosocial, behavioral, and glycemic health outcomes (Delamater et al., 2018). In addition, these intervention approaches have documented cost savings via reduced DKA hospitalizations (e.g., Ellis et al., 2008).

A major issue for pediatric diabetes management concerns the policy level: How can integrated behavioral health care be achieved? Integrated behavioral health care represents a strategy that can help to overcome common barriers such as access to mental health care for pediatric patients. We need, however, more research to demonstrate the effectiveness of integrated health-care delivery in community settings rather than academic research settings, as well as more evidence documenting the cost benefits associated with behavioral interventions, especially for high-risk youth. Such data demonstrating the benefits of integrated behavioral health care may help to convince policy makers to make required changes at the policy level.

In the United States, physical and mental health insurance plans are considered different and paid for by separate health insurance systems—i.e., the mental health “carve-out.” Health insurance for poor children in the United States is provided by Medicaid. However, Medicaid is administered at the state level, and states vary substantially in how psychological services for poor children are provided. Medicaid does not recognize psychologists as independent health-care providers in most states, so poor children with diabetes who also have psychological problems cannot typically be seen by psychologists; rather, they might be treated by less well-trained therapists in a community mental health center separate from and disintegrated with medical care.

Successful integration of behavioral health services in routine diabetes management in the United States will thus require major changes to existing models of reimbursement as well as the culture of health care. These changes must be driven by policy change. Single-payer models of health care as seen in many European countries offer some advantages toward integrated health care, but there are still significant challenges to adequately fund behavioral and psychological services that meet the mental health needs of children and adolescents with diabetes.

The excellent series of chapters in this section of the volume survey a large and impressive research base indicating the many factors at each level of the social-ecological model that influences diabetes management in pediatric populations. Not only do they point to the gaps in our understanding and identify needs for future research, they also provide the clinical implications of this evidence base for behavioral diabetes.

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Part VII
Medical Management of Diabetes in Adults

Chapter 18
Update on Diabetes Medical Management: Epidemiology and Treatment

Lila S. Chertman, Danielle Neuman, and Francesco Vendrame

Diabetes represents a group of metabolic disorders which is affecting a growing number of people worldwide. Diabetes increases the risk of developing disabling and life-threatening complications and in most developed countries is the leading cause of cardiovascular disease, adult-onset blindness, kidney failure, and lower-limb amputation. This chapter will focus on the current epidemiology and treatment of type 1 and type 2 diabetes in adults, although diabetes disorders can be classified into four major categories.

1. Type 1 diabetes: previously referred to as insulin-dependent diabetes or juvenile-onset diabetes, this form of diabetes affects mostly children and adolescents. It is caused by the autoimmune destruction of the insulin-producing beta cells in the pancreas. Insulin replacement therapy is an absolute requirement.
2. Type 2 diabetes: previously referred to as non-insulin-dependent diabetes, this is the main form of diabetes affecting adults. It is characterized by relative insulin deficiency and insulin resistance. Insulin replacement therapy is not an absolute requirement, at least initially.
3. Gestational diabetes: this form refers to diabetes diagnosed during pregnancy and excludes pre-existing diabetes.
4. Diabetes due to other causes: this group includes forms of diabetes caused by genetic defects in the function of insulin-producing cells or insulin action, such as the maturity-onset diabetes of the young (MODY) and type A insulin resistance; diseases of the exocrine pancreas such as cystic fibrosis, pancreatitis, and hemochromatosis; endocrinopathies such as acromegaly, Cushing's syndrome, and hyperthyroidism; and drug or chemical induced, for example, by the use of glucocorticoids, one of the main causes of new-onset diabetes after transplantation. For a complete list of the different forms of diabetes, refer to the American Diabetes Association position statement on diagnosis and classification of diabetes mellitus (American Diabetes Association, 2014).

L. S. Chertman · F. Vendrame (✉)
Division of Endocrinology, Diabetes and Metabolism, Department of Medicine,
University of Miami Miller School of Medicine, Miami, FL, USA
e-mail: fvendrame@med.miami.edu

D. Neuman
Division of Internal Medicine, Department of Medicine, University of Miami Miller
School of Medicine/Jackson Memorial Hospital, Miami, FL, USA

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The presentation of diabetes is heterogeneous and depends on the degree of hyperglycemia. In type 1 diabetes, classic symptoms of hyperglycemia include polyuria, polydipsia, weight loss, and blurry vision. When serum glucose exceeds the renal threshold for being reabsorbed, about 180 mg/dl, it is excreted in the urine causing osmotic diuresis and hypovolemia which in turn determine polydipsia. The weight loss is secondary to hypovolemia and increased catabolism caused by the reduced insulin secretion. The blurry vision is determined by the hyperglycemia-induced shifting in body fluids which causes swelling of the lens of the eye. A threatening complication is diabetes ketoacidosis. In subjects with type 2 diabetes, the disease is often asymptomatic, and the diagnosis follows regular blood testing. Classic symptoms of hyperglycemia can still occur but the weight loss is less frequent. Ketoacidosis in these individuals is rare, but in the event of marked hyperglycemia, a hyperglycemic hyperosmolar state characterized by significant dehydration can occur. Ultimately, for both type 1 and type 2 diabetes, the diagnosis is based on laboratory testing which should be confirmed with a second test unless the clinical picture is clear. The diagnosis of diabetes can be done by using either of the following tests: fasting plasma glucose ≥126 mg/dl; plasma glucose ≥200 mg/dL after a 75-gram glucose load; glycated hemoglobin A1c (HbA1c) ≥6.5%; and random plasma glucose ≥200 mg/dL with symptoms of hyperglycemia (American Diabetes Association, 2018). The HbA1c, although not very sensitive, is one of the most widely used criteria. This test measures the levels of glycosylation of the hemoglobin in red blood cells, and its value depends on the degree of hyperglycemia and life span of red blood cells. This parameter then reflects the average glucose level corresponding to the 120 day-life span of red blood cells, about 3 months.

Epidemiology and Pathogenesis of Type 1 Diabetes in Adults

Type 1 diabetes accounts for 5–10% of all forms of diabetes. Symptoms commonly manifest in childhood or adolescence, but the disease can also occur in the third, fourth, and even ninth decade of life (Diaz-Valencia, Bougnères, & Valleron, 2015). Few population-based studies have been conducted in adults since this condition affects mostly children. In addition, it is sometimes difficult to distinguish between those individuals with type 2 diabetes requiring insulin treatment from those individuals who are initially diagnosed with type 2 diabetes but then progress toward insulin dependence because of underlying autoimmunity. This latter condition which is at the junction of type 1 and type 2 diabetes accounts for about 4–14% of subjects with an initial diagnosis of type 2 diabetes and is referred to as LADA (latent autoimmune diabetes in adults), type 1.5 diabetes, NIRAD (non-insulin-requiring autoimmune diabetes), or SPIDDM (slowly progressive insulin-dependent diabetes mellitus) (Laugesen, Østergaard, & Leslie, 2015). Comparably to what is observed in children, the incidence of type 1 diabetes in adults reflects geographical variation and is higher in countries of Northern Europe compared to Southern Europe. The incidence in adults is however lower than in children (Diaz-Valencia et al., 2015). For example, Finland is the country with the highest incidence of the disease which in children is about 60 per 100,000 persons/year. Previous data report an incidence of the disease of 40.9 per 100,000 persons/year in the age group 0–14 years and 15.2 per 100,000 persons/year in the age group 30–34 years. In addition, in adults the disease seems to affect males more frequently. In the United States, within the age group of 18–44 years, new cases of type 1 diabetes are reported at about 17.5 per 100,000 persons/year for men and 13.6 per 100,000 persons/year for women (Gorham et al., 2009). As noted from these data, the incidence of type 1 diabetes is also increasing, and with a rate of about 3% per year, more cases of type 1 diabetes are expected in the general population.

The pathogenesis of the disease in adults resembles the mechanisms involved in children and adolescents although the process of beta cell destruction is likely to occur at slower rate. A combination of genetic and environmental factors triggers autoimmunity which causes the destruction of insulin-producing beta cells in the pancreas by autoreactive lymphocytes. Particular genetic arrangements of the MHC (major histocompatibility complex), which plays a crucial role in the regulation of immune responses, contribute to most of the genetic susceptibility. Autoimmunity is then triggered by the exposure to environmental factors which in children have been identified mostly as viruses, in particular *Enterovirus*, and dietary factors such as the early introduction of cow's milk proteins. The process of beta cell destruction is reflected by the appearance of autoantibodies directed against proteins expressed in the pancreatic beta cells. Autoantibodies represent the gold standard for the diagnosis and prediction of the disease and are directed against proteins such as insulin, GAD (glutamate decarboxylase), IA-2 (tyrosine phosphatase-like proteins insulinoma antigen-2), and ZnT8 (zinc transporter 8). With time, the process of autoimmune destruction of pancreatic beta cells results in hyperglycemia and then the clinical manifestation of the disease (Katsarou et al., 2017).

Epidemiology and Pathogenesis of Type 2 Diabetes in Adults

Type 2 diabetes is the most common form of diabetes representing about 90–95% of the total cases of diabetes. It is estimated that worldwide about 8.8% of the population or approximately 415 million people have diabetes in the age group 20–79 years with type 2 diabetes accounting for the vast majority of these cases (International Diabetes Federation, 2017). These staggering numbers become more daunting when one also considers that in this same group, there is another 7% of the population, about 318 million individuals with prediabetes, and that the projections for 2040 estimate an increase to 642 million people with diabetes. Data from the International Diabetes Federation Atlas 7 show that the prevalence is the highest at 11.5% in North America and the Caribbean, followed by the Middle East and North Africa at 10.7%, South and Central America at 9.6%, Western Pacific and Southeast Asia at 8.8%, and then Europe and Africa, respectively, at 7.3% and 3.8% (International Diabetes Federation, 2017). Type 2 diabetes is more frequent in urban rather than in rural areas and is associated with the aging population. There is no significant gender difference although the disease is slightly more frequent in males than females. In the United States, the prevalence reaches 22% in American Indians living in some areas of the Southwest, 12.7% in non-Hispanic blacks, 12.1% in people of Hispanic ethnicity, 8% in Asians, and 7.4% in non-Hispanic whites (Center for Disease Control and Prevention, 2017). This ethnic distribution is also reflected by data regarding the disease incidence during the period 2013–2015 which was higher in non-Hispanic blacks and people of Hispanic origin (9.0 and 8.4 per 1000 persons, respectively) compared to non-Hispanic whites (5.7 per 1000 persons). Not surprisingly, the incidence is also twice as high in those who have obtained less than a high school education, pointing to the underlying role of socioeconomic risk factors in addition to genetic risk factors.

The pathogenesis of type 2 diabetes is the result of a complex interplay between genetic and environmental factors where a combination of a defective insulin secretion and insulin resistance is the main cause of hyperglycemia. Subjects with a genetic predisposition to type 2 diabetes have an impairment in insulin secretion and action long before the development of the disease. Factors such as diets rich in carbohydrates and the lack of physical activity increase insulin resistance, meaning that an increase in insulin secretion is required in order to maintain glucose homeostasis. In subjects prone to type 2 diabetes, there is a lack of adaptation to this increase in insulin demand which eventually results in hyperglycemia. The chronic exposure to elevated levels of glucose also causes glucotoxicity which further impairs insulin secretion. In addition, several tissues are resistant to the action of insulin. At the level of the liver, the resistance to the suppressive action of insulin on glucose metabolism leads to glucose overproduction. This is also exacerbated by the lack of suppression of postprandial glucagon secretion from pancreatic alpha cells. At the level of the adipose tissue, the resistance to the antilipolytic effect of insulin increases levels of free fatty acids, promoting lipotoxicity and further damage to pancreatic beta cells. At the levels of the muscle, defects in insulin signaling prevent glucose transportation. Subjects with type 2 diabetes also demonstrate a decreased release of and decreased responsiveness to hormones known as incretins which increase insulin secretion in response to food intake and slow gastric emptying, inhibit glucagon secretion, and promote satiety. Finally, patients with type 2 diabetes seem to reabsorb an amount of glucose in the kidneys which is beyond the physiological level further worsening the glucose control (Defronzo, 2009; DeFronzo et al., 2013; Nauck, Baller, & Meier, 2004). Consequently, different defects in the pathways involved in glucose metabolism contribute to the development of hyperglycemia.

Diabetes Treatment

The goal of diabetes treatment is the prevention of diabetes emergencies and prevention of complications. Diabetes emergencies for type 1 and type 2 diabetes include diabetes ketoacidosis and the hyperosmolar hyperglycemic state, respectively. Hypoglycemia represents another possible complication which can occur in both cases. Long-term complications of hyperglycemia can be classified into two groups: microvascular and macrovascular. Microvascular complications include retinopathy, nephropathy, and neuropathy. Macrovascular complications include coronary artery disease, peripheral artery disease, and cerebrovascular disease. In this section we will discuss the targets of glucose control and the treatment options for the prevention of diabetes emergencies and complications.

Glucose Monitoring and the Glycemic Goals.

Blood glucose monitoring can be achieved using blood glucose monitoring systems (BGMS) or continuous glucose monitoring (CGM) devices. BGMS, such as glucometers, enable patients to perform point-of-care finger sticks for self-monitoring of blood glucose (SMBG). In the Diabetes Control and Complications Trial Research Group (DCCT), patients with type 1 diabetes and therefore insulin-treated, SMBG done at least four times per day contributed to slower progression of microvascular complications suggesting that patients should perform SMBG before meals and at bedtime (DCCT Research Group, 1993). A positive effect of SBMG on glucose control has also been shown in subjects with type 2 diabetes treated with insulin (Elgart, Gonzalez, Prestes, Rucci, & Gagliardino, 2016). The association between SBMG and improved HbA1c in patients who are non-insulin treated is less documented (Malanda et al., 2012). However, it is our opinion that SMBG in these patients can increase diabetes awareness and result in motivated individuals seeking care earlier than they would otherwise.

CGM devices have revolutionized glucose monitoring for individuals with type 1 diabetes since the first device was approved in the United States in 1999. CGM measures glucose in the interstitial fluid rather than blood and provides continuous feedback on estimated glucose levels and trends which can then be generated into customizable reports. These devices provide both the patient and health-care professionals a large aggregate of data that can be used to more accurately and safely achieve optimal glycemic control. They are also equipped with alarms for hypo- and hyperglycemia, a feature that prevents dangerous events from occurring. This is particularly beneficial in patients with hypoglycemia unawareness, which is of great concern in the elderly population. Both the GOLD (Glycaemic control and Optimisation of Life quality in type 1 Diabetes) and DIAMOND (Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes) trials showed significantly better glycemic control and possibly less hypoglycemic events with CGM compared to conventional SMBG in adults with type 1 diabetes and also in adults with type 2 diabetes who were insulin treated (Lind, Polonsky, Hirsch, & et al., 2017; Ruedy, Parkin, Riddlesworth, & Graham, 2017). Until recently the use of CGM required patients to perform SMBG several times daily for the confirmation of glucose levels, but in December 2016, the FDA (Food and Drug Administration) approved the Dexcom G5 CGM for making treatment decisions without additional finger stick testing which, however, must still be done twice daily for the calibration of the instrument. Of note, a new Dexcom G6 will soon become available. The requirement for patient calibration testing was more recently eliminated with the development of the FreeStyle Libre CGM. This device, approved by the FDA in 2017, also assesses interstitial glucose, and measurements become available to the patient simply by waving a mobile reader above the sensor. This CGM offers a safe alternative for patients who experience obstacles to frequent testing. Unlike the Dexcom system, however, it does not provide real-time alarms for hyper- and hypoglycemia and should therefore be used in caution in certain populations, such as those with hypoglycemia unawareness.

Once the diagnosis of diabetes has been established, recommended blood glucose targets include HbA1c < 7.0%, fasting blood glucose 80–130, and postprandial blood glucose <180. These simplistic targets however do not take into account the fact that the goals for blood glucose targets should be individualized for each patient based on their age, life expectancy, comorbidities, duration of diabetes, and risk for hypoglycemia. Therefore, more stringent targets with HbA1c < 6.5% are indicated for those individuals with a short duration of diabetes, long life expectancy, and no significant cardiovascular complications. In contrast, a less stringent goal of HbA1c < 8.0% represents a reasonable target for those individuals with history of severe hypoglycemia, limited life expectancy, several comorbidities, and advanced microvascular or macrovascular complications.

Lifestyle Intervention

Diabetes management reaches across multidisciplinary domains, beginning with lifestyle management which is an overarching term that encompasses diabetes self-management education and support, as well as nutrition counseling, physical activity, and smoking cessation. At its essence, this model emphasizes patient-centered care in which patients themselves are empowered to make self-management decisions to improve health-care outcomes. As part of this approach, patients should receive medical nutrition therapy by a registered dietician with a focus on healthy eating patterns of high-quality, nutrient-dense foods. They should be encouraged to replace refined carbohydrates, added sugars, and high-glycemic index foods with whole grains and a plant-based diet, maintaining consistency in daily carbohydrate intake so as to become familiar with the effects on glucose control from carbohydrate-containing foods. Dietary changes are particularly helpful for patients who are overweight or obese which is the case in most of those with type 2 diabetes. Weight loss is then recommended; at least 5% of initial body weight loss is associated with improved glycemic control, lipid profile, and blood pressure. Most adult patients with type 1 and type 2 diabetes should also engage in a physical activity of at least 150 min of moderate-to-vigorous physical activity spread over 3 days/week. In patients with type 1 diabetes, physical exercise has been associated with decreased mortality (Moy et al., 1993). However, the glucose response to physical activity is quite variable, and therefore a careful adjustment of insulin therapy to prevent hypoglycemia is required. In patients with type 2 diabetes, results of the Look AHEAD (Action for Health in Diabetes) trial evaluating intensive lifestyle intervention consisting of weight loss plus exercise compared to a control group receiving diabetes education indicated that those in the lifestyle intervention group achieved significantly greater sustained weight loss and improved cardiorespiratory fitness, blood glucose control, blood pressure, and lipid profile. These patients also reported significantly improved physical mobility and quality of life combined with decreased health-care costs (Pi-Sunyer, 2014; Wing et al., 2013). Despite these wide-reaching benefits, lifestyle change can be the most difficult to achieve and can be frustrating for both the patient and clinician when goals are consistently not being met.

Pharmacotherapy for Type 1 Diabetes

For patients with type 1 diabetes, insulin is the mainstay of treatment, but in the recent years, new drugs developed for treatment of type 2 diabetes have been also tested in patients with type 1 diabetes.

Insulin Replacement and Delivery

Since its first introduction in 1922, exogenous insulin has evolved into numerous preparations which can be classified based on their onset and duration of action (Table 18.1). Treatment is aimed at mirroring the physiological insulin secretion which is best achieved using the different insulin preparations in a basal-bolus fashion. Basal insulin, which inhibits hepatic glucose production over the course of the day and night, is commonly given once or twice daily as long-acting insulins such as insulin glargine, detemir, degludec, or intermediate-acting NPH (neutral protamine Hagedorn) insulin. Bolus insulin is then given as short-acting insulin, i.e., regular insulin or rapid-acting insulins such as lispro, aspart, and glulisine before meals. Some of these preparations have been recently developed as more concentrated formulations which can decrease the risk of hypoglycemia, as in the case of glargine U-300, and be particularly helpful for patients requiring higher insulin doses (Lamos, Younk, & Davis, 2016). Other preparations include premixed insulins which are mixtures of prandial and intermediate-acting insulins. They are available with different ratios and are generally given before breakfast and dinner. They offer limited possibility for insulin dosing adjustments and therefore are not recommended for the management of type 1 diabetes. Little flexibility for insulin dosing is also offered by the relatively new inhaled insulin which is available only in three fixed doses. Ultrafast-acting insulin has been recently developed but the experience is still limited. Interestingly, as the patents on conventional insulins have started to expire, “biosimilar” insulins have begun to emerge. Biosimilar insulins are highly similar versions of market-established biological insulins that have lost patent protection. They are expected to be less costly than their original molecules, thereby increasing access to preferred insulin regimens. Biosimilars must have the same primary structure as their originals, but they can differ in regard to some molecular characteristics and production techniques. At this time it is unclear if the current regulatory requirements are sufficient to assess biosimilarity. Nevertheless, the first biosimilar insulin glargine has already been introduced in the European Union as Abasaglar and the United States as Basaglar with more biosimilars expected to surface in the near future (Heinemann, Home, & Hompesch, 2015).

Insulin is generally administered subcutaneously using either multiple daily injections (MDI), which is most common, or continuous subcutaneous insulin infusion (CSII) also known as insulin pump therapy. Most patients with type 1 diabetes prefer MDI due to its simplicity; however CSII can more accurately mimic physiologic insulin secretion. CSII automatically delivers rapid-acting insulins by continuous subcutaneous infusion based on programmed rates which can be modified throughout the day to better match a patient’s individual demands and lifestyle. In addition CSII can also be used in conjunction with a CGM device as sensor-augmented insulin pump therapy. CSII is generally recommended for motivated patients with type 1 diabetes who are not able to reach their glycemic goals despite adherence to MDI because of extremely variable glucose levels, frequent episodes of severe hypoglycemia/hypoglycemia unawareness, extreme insulin sensitivity, or early morning rise in glucose levels (dawn phenomenon) (Grunberger et al., 2014).

Table 18.1 Insulin preparations

Category	Preparation	Onset of action	Peak of action	Duration of action	Use	Major characteristics
Ultrafast	Faster insulin aspart	16–20 m	91–133 m	1–3 h	Prandial	Flexible administration; improvement in postprandial glucose; lack of long-term clinical studies
Rapid-acting	Lispro	15–30 m	30–90 m	3–4 h	Prandial	Adjustable dosing; requires multiple daily injections
	Aspart					
	Glulisine					
	Inhaled insulin					
	Inhaled insulin	Seconds	12–17 m	2–3 h		No injections required, low risk of hypoglycemia; available only in three fixed doses; contraindicated in COPD/asthma
Short-acting	Regular	30–60 m	2–3 h	3–6 h	Prandial	Preferred insulin for intravenous therapy; higher risk of hypoglycemia when given subcutaneously compared to other prandial preparations
Intermediate-acting	NPH (isophane)	2–4 h	6–10 h	10–16 h	Basal	Generally given twice daily; has a peak effect which increases the risk of hypoglycemia
Long-acting	Glargine (G)	30–90 m	G: 8–16 h	G: 18–20 h	Basal	Almost no peak effect; low risk of hypoglycemia
	Detemir (D)		D: 6–8 h	D: 14 h		
	Degludec (T)		T: None	T: 24 h		
Premixed	NPH/regular 70/30	Variable	Variable	Variable	Mixed	Generally given twice daily; fixed ratio
	Lispro mix 50/50					
	Lispro mix 75/25					
	Aspart 70/30					
Concentrated	Regular U-500	Variable	Variable	Variable	Basal	Overcome significant insulin resistance; less volume/unit; may decrease injection frequency; variable risk of hypoglycemia depending by preparation; the U-500 can be used for both basal and prandial insulin requirements
	Humalog U-200					
	Glargine U-300					
	Degludec U-200					
Biosimilar	Glargine biosimilar	Comparable to glargine	Comparable to glargine	Comparable to glargine	Basal	Lower cost compared to original product, but lack of long-term clinical studies

m minutes, *h* hours

Hybrid Closed-Loop Systems

Technological advances for type 1 diabetes management have led to the development of HCL (hybrid closed-loop) systems. These devices integrate complex control algorithms, glucose sensors, and insulin pump therapy to automatically adjust basal insulin delivery rates according to CGM readings. Minimal input is required from the patient and is limited to the insulin request for mealtime coverage. Results from a multicenter trial in 124 subjects with type 1 diabetes, age range 14–75 years, showed that the use of Medtronic Mini-Med 670G HCL was associated with less glycemic variability, more time in the target range, no events of severe hypoglycemia or ketoacidosis, and reduced HbA1C compared to baseline data using sensor-augmented pumps (Bergenstal, Garg, Weinzimer, & et al., 2016). This system is currently FDA approved for patients older than 14 with type 1 diabetes. Closed-loop systems which deliver both insulin and glucagon have also been developed; however, larger studies must be conducted to test their efficacy.

Beta Cell Replacement

Rather than exogenously replacing the deficient hormone, select patients have the option to replace the entire pancreas or the pancreatic beta cells through pancreas or islet cell transplantation, respectively. Pancreas transplantation may be performed with or after a kidney transplant in patients with end-stage renal disease. Though transplantation may provide diabetic patients with a definitive treatment, its widespread use has been limited by donor/recipient suitability, organ disparity, and the requirement of lifelong immunosuppression. In addition, transplanted patients may experience diabetes recurrence as a side effect of the immunosuppressive drugs, organ rejection, or recurrence of autoimmunity (Vendrame et al., 2016). Overall transplantation should be reserved for subjects with type 1 diabetes who have recurrent ketoacidosis and severe hypoglycemia despite intensive management or for those who are already candidates for kidney transplantation. Compared to the transplantation of an entire organ, islet cell transplantation offers a less invasive approach to replace beta cells but remains investigational.

Additional Agents

Other agents which have been tested in patients with type 1 diabetes include amylin analogs, such as pramlintide, which reduces the increase in postprandial glucagon occurring in patients with diabetes, delays gastric emptying, and increases satiety. This medication is FDA approved for treatment of type 1 diabetes, but studies done mostly in the adult populations show it is associated with only a modest improvement in HbA1c, gastrointestinal side effects, and increased risk of hypoglycemia (Ratner et al., 2004; Whitehouse et al., 2002). Metformin, which is the mainstay of treatment for type 2 diabetes, has been tested in subjects with type 1, but although it may reduce the weight and the amount of insulin total daily dose, it is not associated with a significant improvement in glucose control (Vella et al., 2010). Other medications which have been developed for type 2 diabetes and have been tested in patient with type 1 diabetes include incretin-based therapies and SGLT2 (sodium-glucose co-transporter 2) inhibitors. The rationale for the use of incretins in patients with type 1 diabetes relies on their action on suppressing the glucagon release; the use of SGLT2 inhibitors relies on their action at renal level where they prevent the reabsorption of glucose. Results thus far have been variable, and consequently these therapies are not currently approved for treatment of type 1 diabetes.

Management of LADA

Patients with LADA express features of both type 1 and type 2 diabetes mellitus. Few clinical trials have been done in this population, and currently there is no standard approach for the treatment of these patients. Hypoglycemic agents alone or in combination with insulin can be used in patients with preserved insulin secretion, generally with low levels of autoantibodies against GAD. In contrast, individuals with higher titers of autoantibody against GAD are prone to rapid islet failure. These patients require close follow-up and may benefit from an early initiation of insulin therapy when glucose control deteriorates. There are no studies in favor or against the use of metformin in this population. The use of incretin-based therapy with drugs such as saxagliptin and linagliptin has been associated with preserved insulin secretion, but larger studies are needed (Buzzetti, Pozzilli, Frederich, Iqbal, & Hirshberg, 2016; Johansen et al., 2014). Thiazolidinediones which improve insulin content and have anti-inflammatory effects might be of potential interest but have several side effects. The use of sulfonylureas is discouraged since they increase the rate of deterioration of beta cells and therefore accelerate the progression toward insulin dependence (Landstedt-Hallin et al., 1999). In general, patients with LADA progress to insulin dependence more rapidly than patients with type 2 diabetes and will ultimately require management similar to patients with type 1 diabetes.

Pharmacotherapy for Type 2 Diabetes

Lifestyle modification is essential for all patients with diabetes, but pharmacotherapy should not be delayed if patients are not meeting targets. Various societies such as the American Diabetes Association and the American Association of Clinical Endocrinologists propose algorithms that are updated yearly in regard to which regimen a patient can be offered based on their glucose control. Importantly, when prescribing a regimen, the clinician must keep in mind the different aspects of the medications themselves, including adverse effects, aspects individual to patients such as comorbidities, age, therapeutic goal, adherence to treatment, and finally patients' preference. In general, for ease of use and patient compliance, oral medications are the first to be offered moving from monotherapy to combined therapy with two or more agents based on the response to treatment. The current consensus is that whenever possible metformin should be first-line treatment in patient with type 2 diabetes. Insulin can be started at any time depending on the severity of hyperglycemia and contraindications to other medications (Tables 18.1 and 18.2). Insulin is generally given as long-acting insulin in addition to oral agents, as premixed insulin or as a basal-bolus regimen, similar to what is done for patients with type 1 diabetes. Concentrated insulins are particularly suitable for patients with type 2 diabetes since high doses of insulin are often required to overcome insulin resistance. Selected patients with type 2 diabetes are also eligible for insulin pump therapy, for example, when they develop complications such autonomic neuropathy with gastroparesis.

In recent years, a lot of attention has been drawn by new classes of medications for treating type 2 diabetes. Postprandial glucose is regulated by several factors which include the secretion of a group of hormones by the intestine called incretins (Nauck et al., 2004). These hormones, which include GLP1 (glucagon-like peptide 1), can reduce gastric motility, stimulate the secretion of insulin, and also reduce postprandial glucagon levels. Eventually they are degraded by a protein called dipeptidyl peptidase-4. Modulators of this system called GLP1-RA (glucagon-like peptide-1 receptor agonists) and DPPIV (dipeptidyl peptidase-4) inhibitors have been developed. They are associated with low rates of hypoglycemia and do not cause weight gain. Specifically, in the case of GLP1-RA, they cause weight loss, whereas in the case of DPPIV inhibitors, they are weight neutral. Some of these medications besides improving glucose control can also exert a protective cardiovascular effect (Marso et al., 2016). Another interesting class of drugs is represented by the SGLT2 inhibitors which prevent the

Table 18.2 Antidiabetic medications other than insulin

Agent (class) *route*	Mechanism of action	HbA1c reduction	Advantages	Disadvantages
Metformin (biguanides) *oral*	Decrease hepatic glucose production	1–1.5%	Mild weight loss	GI side effects
			Low risk of hypoglycemia	Contraindicated in advanced renal disease
			Less CVD events	Rare risk of lactic acidosis
Albiglutide	Increase insulin secretion and decrease glucagon secretion, both in a glucose-dependent manner	1–1.5%	Weight loss	GI side effects
Dulaglutide	Slow gastric emptying		Low risk of hypoglycemia	Risk of pancreatitis, thyroid cancer
Exenatide	Increase satiety		Less CVD events[a]	Contraindicated in advanced renal disease
Liraglutide				
Lixisenatide				
Semaglutide (GLP-1 RA) *injection*				
Alogliptin	Increase insulin secretion and decrease glucagon secretion, both in a glucose-dependent manner	0.5–1%	Neutral effect on weight	Risk of pancreatitis, heart failure, skin reactions
Linagliptin			Low risk of hypoglycemia	Contraindicated or requiring renal dosing in advanced renal disease with the exception of Linagliptin
Sitagliptin				
Saxagliptin (DPP4 inhibitors) *oral*				
Canagliflozin	Block glucose reabsorption in the kidney, and increase renal excretion of glucose	0.5–1%	Weight loss	Risk of genitourinary infections, volume depletion/dizziness, diabetic ketoacidosis
Dapagliflozin			Low risk of hypoglycemia	Contraindicated in advanced renal disease
Empagliflozin (SGLT2 inhibitors) *oral*			Less CVD events[a]	
			Reduce blood pressure	
Glipizide	Increase insulin secretion	1–1.5%	Demonstrated efficacy in controlling hyperglycemia and reducing microvascular complications	Weight gain
Glimepiride				Increased risk of hypoglycemia, avoid in elderly
Glyburide (sulfonylureas) *oral*				Caution in renal and hepatic impairment
				Hastens beta cell dysfunction
Repaglinide	Increase insulin secretion	0.5–1%	Can be used in renal disease	Weight gain
Nateglinide (Meglitinides) *oral*			Low risk of hypoglycemia compared to sulfonylureas	Risk of hypoglycemia
				Frequent dosing

(continued)

Table 18.2 (continued)

Agent (class) *route*	Mechanism of action	HbA1c reduction	Advantages	Disadvantages
Pioglitazone rosiglitazone (Thiazolidinediones) *oral*	Increase sensitivity to insulin	1–1.5%	Reduce triglycerides	Weight gain
			Low risk of hypoglycemia	Risk of heart failure
			Possibly less CVD events	Risk of osteoporosis and bone fractures
Pramlintide (amylin analog) *injection*	Decrease glucagon secretion	0.2–0.7%	Modest weight loss	GI side effects
	Slow gastric emptying			Risk of hypoglycemia
	Increase satiety			Must be used with insulin
				Frequent injections
Acarbose	Slow intestinal carbohydrate digestion and absorption	0.5–1%	Neutral effect on weight	GI side effects
Miglitol (alpha-glucosidase inhibitors) *oral*			Low risk of hypoglycemia	Frequent dosing required
			Possible decreased CVD in prediabetes	
Colesevelam (bile acid sequestrants) *oral*	Increase hepatic bile acid production which may decrease hepatic glucose production; may increase incretin levels	0.5%	Low risk of hypoglycemia	GI side effects
			Decrease LDL cholesterol	Increase triglycerides levels
				May decrease absorption of other medications
Bromocriptine mesylate (dopamine D2 receptor agonist) *oral*	Increased insulin sensitivity and glucose disposal	0.1%	Reduced fasting and postprandial hyperglycemia without raising plasma insulin levels	GI side effects
			Low risk of hypoglycemia	Fatigue
				Headache
				Avoid use with other CYP3A4 inhibitors or ergot derivatives

GLP-1 RA glucagon-like peptide-1 receptor agonist, *DPPIV* dipeptidyl peptidase-4, *SGLT2* sodium-glucose co-transporter 2, *CVD* cardiovascular disease

[a] It does not apply to all medications of the same class

reabsorption of glucose at the level of the renal proximal tubules in the kidney-causing glucosuria (Whalen, Miller, & Onge, 2015). These medications improve HbA1c, cause weight loss, and also lower blood pressure. Moreover, a protective cardiovascular effect has been described for some SGLT2 inhibitors (Zinman et al., 2015). Overall, because of the pleiotropic effects of these new medications, it is currently debated if metformin should remain the first-line therapy (Pratley, 2016).

Diabetes Complications

Diabetes is a complex multi-system disease accounting for significant comorbidities. In 2014, 14.2 million emergency room visits and 7.2 million US hospital discharges listed diabetes as one of the diagnoses in adults aged 18 years or older. Discharges included 400,000 for ischemic heart disease, 251,000 for stroke, 108,000 for a lower-extremity amputation, and 168,000 for diabetic ketoacidosis. In the same year, a total of 52,159 people developed end-stage renal disease with diabetes as the primary cause (Center for Disease Control and Prevention, 2017).

In type 1 diabetes, the DCCT and follow-up Epidemiology of Diabetes Interventions and Complications Study Research Group (EDIC) trials served as groundbreaking studies revealing the importance of intensive glycemic management with multiple daily insulin injections compared to conventional therapy consisting of one or two daily injections (DCCT Research Group, 1993, 2016). The DCCT showed that after a follow-up of approximately 6.5 years, patients in the intensive glycemic management arm had an average HbA1c of 7% and decreased the early stages of microvascular complications by 35–76% compared to subjects in the conventional glycemic management group with an HbA1c of 9% (DCCT Research Group, 1993). The long-term EDIC follow-up revealed that the benefits on microvascular disease continued to persist, though to a lesser extent, despite HbA1c levels eventually equalized among the two groups. Results from these studies also suggested that the intensive treatment was associated with a decreased incidence of long-term macrovascular complications. After 30 years of follow-up patients, the intensive group continued to have a reduction of any cardiovascular disease up to 30%. It was also observed that a 10% decrease in HbA1c correlated with a 17% risk reduction of cardiovascular disease, showing that even small improvements in HbA1c can be important to the overall cardiovascular health of patients with type 1 diabetes (DCCT Research Group, 2016). Interestingly, there is also evidence that as patients transition into adulthood, there is a trend toward improvement in HbA1c levels. A study by T1D Exchange Clinic Network, a robust database of adults and children with type 1 diabetes from 77 clinical centers across the United States, reveals that glycemic control during childhood decreases from 8.3% in 2–4-year-olds to 8.1% at 7 years of age, worsens over time peaking at 9.2% in 19 years old, and then declines gradually reaching a plateau at 7.5%–7.8% after age 30 and then further dropping below 7.5% at age 65 (Miller et al., 2015). These data suggest that there is room for improvement across all ages and that patients acquire better awareness of diabetes control after age 30.

In type 2 diabetes, similar to what is observed in type 1 diabetes, large clinical trials have shown the importance of glucose control. The UKPDS (UK Prospective Diabetes Study Group) enrolled patients with newly diagnosed type 2 diabetes who were randomized to intensive treatment with a sulfonylurea or with insulin versus conventional treatment with diet. In the latter group, drugs were added if patients experienced symptoms of hyperglycemias or if the fasting plasma glucose was greater than 15 mmol/l (270 mg/dl). After 10 years of follow-up, subjects in the intensive treatment arm presented a median HbA1c of 7%, an overall reduction of microvascular complications by 25%, and a reduction in cardiovascular complications by 16% compared to patients with conventional treatment who achieved a median HbA1c of 7.9% (Holman, Paul, Bethel, Matthews, & Neil 2008; UKPDS Group, 1998). This cardiovascular outcome was further explored in three large clinical trials, ADVANCE (Action in Diabetes and Vascular Disease—Preterax and Diamicron Modified Release Controlled Evaluation), VADT (Veterans Affairs Diabetes Trial), and ACCORD (Action to Control Cardiovascular Risk in Diabetes). Surprisingly these studies didn't reveal any major cardiovascular benefit with the intensive glucose control although several explanations may explain this result (Skyler et al., 2009). It seems, however, that also for type 2 diabetes, the earlier the intensive treatment starts, the better is the outcome for both micro- and macrovascular complications. In addition, there is now evidence from large clinical trials that some GLP1-RA and SGLT2i provide cardiovascular benefits to patient with type 2 diabetes. In the LEADER trial, 9340 subjects with type 2 diabetes with or at increased risk of cardiovascular disease were treated with a GLP1-RA called liraglutide or placebo. The result of the trial showed that the treatment with liraglutide resulted in 13% relative reduction of major cardiovascular events and a 22% relative reduction in cardiovascular death (Marso et al., 2016). Similar results were also observed in another trial where 7200 individuals with type 2 diabetes and established cardiovascular disease were treated with the SGLT2 inhibitor empagliflozin or placebo. The study showed that patients taking empagliflozin had a relative reduction of 14% in major cardiovascular events and a relative reduction of 38% in cardiovascular death (Zinman et al., 2015). Overall with these new medications, we are moving to a new era where in addition to glucose control, it is now also possible to target the cardiovascular system. It should be noted however that these beneficial effects are not necessarily shared with the other molecules of the same class. For example, another GLP1-RA called exenatide didn't show a major effect on cardiovascular disease in patients with type 2 diabetes with or without cardiovascular disease compared to placebo.

In order to reduce the risk or slow the progression of complications, patients should be evaluated periodically for cardiovascular and microvascular complications. If patients are asymptomatic for cardiovascular disease, there are generally no indications for coronary artery disease screening as long as risk factors are treated. At every visit patients should have blood pressure measured and treated if it is above 140/90. In addition, most patients should be treated with cholesterol-lowering medications such as statins. As for microvascular complications, patients with type 1 diabetes should be assessed within 5 years from the diagnosis and annually thereafter for kidney disease, peripheral neuropathy, and retinopathy. Patients with type 2 diabetes should be similarly assessed for microvascular complications; however screening should start immediately at diagnosis since it is possible that the disease was undiagnosed for several years. Overall, glucose control, prevention, screening, and treatment of complications reduce the morbidity and mortality associated with diabetes.

Conclusions

Diabetes has become a global emergency in the adult population with type 2 diabetes accounting for most of the cases. The current trend mirrors the increased prevalence of obesity to the point that a new term "diabesity" has been used to indicate the combination of diabetes and obesity. These patients are at increased risk to have an adverse cardiovascular event. The arrival of new drugs able to target the cardiovascular system has further emphasized the importance of an approach that it is not limited to controlling the glucose levels. It is crucial that patients acquire awareness of diabetes and its complications. People often have a poor perception of this, especially those from ethnic minorities and low social economic status. The macrovascular events associated with the disease are often ignored. The result is an increased morbidity and mortality for both type 2 diabetes and type 1 diabetes. It is therefore imperative to invest in education, raise awareness in communities, and encourage and support behavioral changes. Achieving this aim will help improve both life expectancy and quality of life of patients with diabetes.

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Part VIII
Individual Level Factors in Adults

Chapter 19

Biobehavioral Factors Related to the Development and Course of Type 2 Diabetes and Cardiometabolic Impairment in Adults: The Critical Role of Weight, Diet, Physical Activity, and Other Lifestyle Behaviors

Elizabeth M. Venditti, Rebecca L. Emery, and Rachel P. Kolko

The Significance of Individual Biobehavioral Factors in the Dual Epidemics of Obesity and Type 2 Diabetes

The global epidemic of type 2 diabetes reflects the dramatic increase in obesity and unhealthy lifestyle behaviors that have occurred in rapidly modernizing societies worldwide. Although recent cross-sectional prevalence and incidence data from the Centers for Disease Control and Prevention (CDC) National Health Interview Survey suggest there may be a slowing in new cases of diagnosed diabetes among adults in the United States aged 20–79 years (Geiss et al., 2014), an effect potentially attributable to increased access to earlier preventive treatments there continues to be important heterogeneity by geographic region, gender, racial and ethnic subgroups, and varied socioeconomic environments. Moreover, absolute rates of type 1 and type 2 diabetes remain exceedingly high internationally, with an estimated 415 million people affected (95% of whom are estimated to have type 2 diabetes). Given that these prevalence rates are predicted to rise to 642 million by the year 2040 (IDF, 2015), research on biobehavioral factors is crucial to the development of effective prevention and intervention approaches aimed at reducing the human and economic burden of this disease.

In this chapter, we will focus specifically on individual-level lifestyle variables that, in the context of an obesogenic or “toxic” social and physical environment (Matthews & Matthews, 2011), are reliably linked to the development and course of obesity, type 2 diabetes, and associated cardiometabolic impairments in adulthood. These biobehavioral influences can be bidirectional and emerge throughout the life span; however we will focus solely on the expression of type 2 diabetes in adults in this chapter. We will review the primary pathophysiologic pathways that relate to the expression of type 2 diabetes; discuss the critical role of weight, diet, physical activity, and other lifestyle behavioral factors such as sleep, cigarette smoking, alcohol use, and psychosocial stress; and highlight promising research directions most likely to influence the development of effective treatments for type 2 diabetes.

E. M. Venditti (✉) · R. P. Kolko
Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
e-mail: vendittiem@upmc.edu

R. L. Emery
University of Minnesota School of Public Health, Minneapolis, MN, USA

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Some investigators have suggested that the developmental pathophysiology of type 2 diabetes, regardless of when it is diagnosed, may be conceptualized as a form of "accelerated aging" (Morley, 2008). Thus, attention to modifiable individual-level biobehavioral factors represents an effort to slow or prevent the natural history of this complex disease. Both cross-sectional and prospective epidemiologic evidence as well as findings from prevention and treatment research over the last several decades has helped to identify salient target risk factors associated with the onset of type 2 diabetes (Edelstein et al., 1997; Hamman et al., 2006), including age, gender, race, and ethnicity, that are unmodifiable. However, because the gestation period for type 2 diabetes (sometimes referred to as "prediabetes") may take several years (Meigs, Muller, Nathan, Blake, & Andres, 2003; Nathan et al., 2007), this extended period is amenable to lifestyle (e.g., behavioral weight loss programs, structured physical activity regimens), as well as pharmacologic and bariatric surgery interventions designed to counter emerging glucose impairments.

As research on the pathogenesis of insulin resistance, glucose homeostasis, β-cell dysfunction, and other high-risk states in the setting of excess adiposity advances (Kahn, Cooper, & Del Prato, 2014), there is also increased recognition of the heterogeneity in the pathogenesis of type 2 diabetes, thereby complicating efforts to demonstrate empirically what aspects of type 2 diabetes treatment can be unified and what needs to be individualized (Eckel et al., 2011). Although the promise of precision medicine through genetic research (Hivert, Vassy, & Meigs, 2014) is emerging, genetic risk studies to date have only slightly improved prediction of type 2 diabetes onset and course beyond common clinical risk indicators. Changes in the gene pool cannot explain the rapid increase in prevalence of diabetes over the last 50 years, and research suggests that a common behavioral intervention can be effective regardless of genetic load (Hivert et al., 2016).

The social-ecological model concerns itself with understanding and promoting health in all relevant environments (e.g., families, schools, communities), and the study of type 2 diabetes lends itself to this approach (shown in Fig. 19.1). Although diabetes is expressed at the individual level through a cascade of biobehavioral factors that influence onset, course, outcomes, and complications of the disease, there is widespread acknowledgment that interpersonal relationships, community factors, and broader public policies cannot be overlooked when examining these trajectories. Therefore, the advancement of diabetes prevention and diabetes care for all of society requires that biobehavioral relationships be evaluated using a social-ecological framework.

Obesity and the Pathophysiology of Type 2 Diabetes

Type 2 diabetes (herein referred to simply as diabetes) is diagnosed in the presence of impaired glucose homeostasis, resulting from an imbalance between glucose production and utilization (Leahy, 2005). Although the disrupted glucose regulation observed among individuals with diabetes is attributable to several interrelated factors (DeFronzo, 2009), it primarily has been shown to result from reduced insulin secretion from pancreatic β-cells and insulin resistance in muscle, liver, and adipose tissues (Kahn et al., 2014). The insulinemic abnormalities characteristic of diabetes promote additional cardiometabolic impairments, associated with heightened risk for cardiovascular disease (Emerging Risk Factors Collaboration, 2010; Juutilainen, Lehto, Rönnemaa, Pyörälä, & Laakso, 2005), stroke (Jeerakathil, Johnson, Simpson, & Majumdar, 2007; Najarian et al., 2006), and metabolic syndrome (Ford, Li, & Sattar, 2008).

Given the high level of cardiometabolic morbidity and mortality associated with diabetes, extensive research has identified factors associated with risk for the disease. Findings from genetic studies have led to increased consideration of diabetes as a hereditary condition (Billings & Florez, 2010; Frayling, 2007; Morris et al., 2012). However, additional evidence suggests that exposure to an obesogenic environment plays an integral role in the pathogenesis of diabetes above and beyond genetic

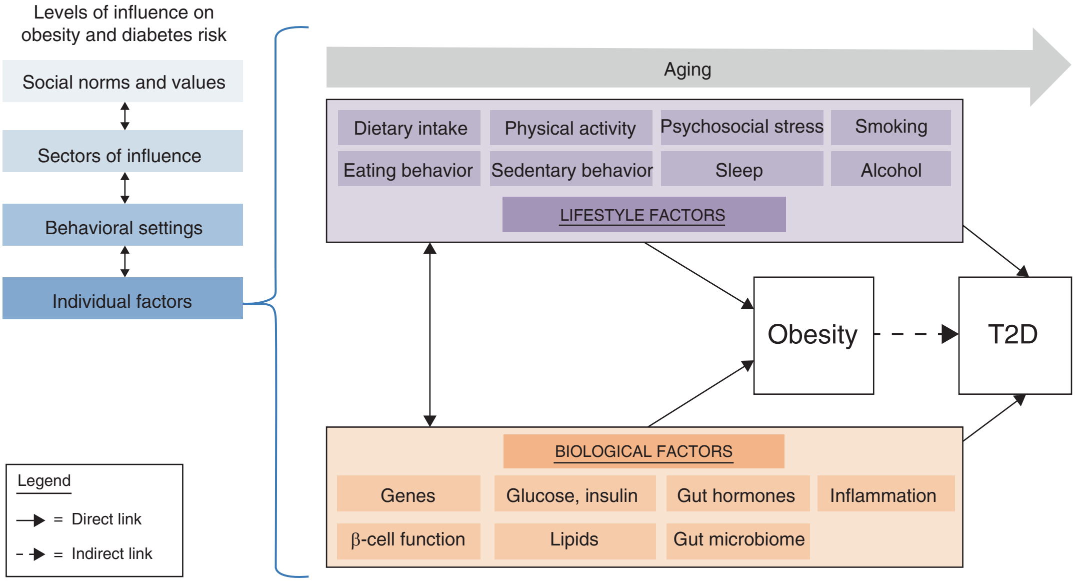

Fig. 19.1 Individual-level factors that influence obesity and diabetes risk in the context of aging

effects (Hivert et al., 2016). Diabetes and obesity indeed are highly associated, with some estimates documenting that 61% (Centers for Disease Control and Prevention, 2017) of individuals with diabetes also meet criteria for obesity, and over 85% (Centers for Disease Control and Prevention, 2004) of individuals with diabetes meet criteria for overweight and obesity combined. Additionally, reviews of these findings have verified that lifestyle behaviors shown to confer risk for obesity are inextricably linked to the development and progression of diabetes (Venditti, 2016). In particular, individuals whose lifestyle habits promote excess adiposity through a sustained positive energy balance, including overeating, physical inactivity, and sedentary behavior, are vulnerable to developing diabetes (Ravussin & Bogardus, 2000). Emerging evidence has further documented that poor sleep habits, cigarette smoking, heavy alcohol use, and psychosocial stress also serve as important lifestyle behaviors linked to the development of diabetes. Because prevention and treatment efforts aimed at reducing the disease burden of diabetes primarily focus on altering lifestyle behaviors, it is important to understand how such lifestyle behaviors uniquely contribute to the pathogenesis of diabetes. As such, the primary pathophysiologic pathways linked to the expression of diabetes, and the specific effects that the aforementioned lifestyle behaviors have on these pathways, will be reviewed herein.

The Role of Impaired Glucose and Insulin Regulation

The regulation of glucose production and metabolism is dependent on normal insulin sensitivity in central and peripheral tissues as well as normal insulin secretion from pancreatic β-cells, two processes that are disrupted in diabetes. The role of insulin sensitivity and insulin secretion in the natural history of diabetes has been extensively studied (Cersosimo, Triplitt, Mandarino, & DeFronzo, 2015; DeFronzo, 2004) and is discussed in greater detail in prior chapters of this volume. Prior to a biochemical diagnosis of diabetes, individuals at risk for developing the disease display chronic elevations in plasma glucose concentrations, resulting from a series of physiologic disruptions that lead to excessive glucose production in the liver (Cersosimo et al., 2015). The pancreatic β-cells respond to this hyperglycemic state by releasing insulin at higher rates to aid in glucose metabolism (Kahn et al., 2014).

However, the efficiency with which insulin-mediated glucose metabolism occurs diminishes over time, leading to chronic elevations in both glucose and insulin. Continuous exposure to insulin eventually causes central and peripheral tissues to become less sensitive to insulin action, thereby promoting the development of insulin resistance. To compensate for the development of insulin resistance in central and peripheral tissues, the pancreatic β-cells further increase insulin secretion (Kahn et al., 2014). Diabetes subsequently is diagnosed among individuals whose β-cells fail to appropriately augment insulin secretion to compensate for insulin resistance. Interestingly, individuals with obesity, who are not diabetic, show similar levels of insulin resistance as individuals with normal weight, who are diabetic, suggesting that obesity and diabetes are metabolically similar (DeFronzo, 1988). As such, attention to lifestyle behaviors that may be involved in the disruption of glucose homeostasis among individuals with obesity and diabetes is likely to be fruitful in understanding how to prevent or delay chronic metabolic diseases and associated complications.

The Role of Excess Lipids

Although adipose tissue is responsible for a relatively small proportion of glucose metabolism, it plays an important role in glucose homeostasis by regulating the release of free fatty acids (FFA) from stored triglycerides, which directly influence insulin action in liver and muscle tissues (Bays, Mandarino, & DeFronzo, 2004; Capurso & Capurso, 2012; Delarue & Magnan, 2007). Individuals who develop diabetes tend to have both excess adipose tissue and enlarged adipocytes that are resistant to the antilipolytic effects of insulin (Lönn, Mehlig, Bengtsson, & Lissner, 2010; Weyer, Foley, Bogardus, Tataranni, & Pratley, 2000). Such individuals consequently display chronic elevations in FFA and are at risk for developing lipotoxicity, a physiologic state characterized by high circulating levels of FFA. Sustained lipotoxicity ultimately leads to impaired insulin secretion and insulin resistance in liver and muscle tissues via increased glucose production (Kusminski, Shetty, Orci, Unger, & Scherer, 2009; Schaffer, 2003).

In addition to the association between excess adiposity and insulin resistance, accumulating evidence documents that the distribution of adipose tissue is uniquely predictive of how the body will respond to insulin (DeFronzo, 2009). In particular, individuals with visceral fat accumulation, characterized by preferential fat deposition in the abdominal and thoracic regions (colloquially referred to as the “apple shape”), tend to have higher rates of insulin resistance, hyperinsulinemia, and dyslipidemia than do individuals with gynoid fat accumulation, characterized by preferential fat deposition in the hips, thighs, and buttocks (colloquially referred to as the “pear shape”). This association largely has been attributed to the enhanced lipolytic activity of visceral fat cells, which leads to increased delivery of FFA and related triglyceride metabolites into liver and muscle tissues, thereby promoting insulin resistance in these regions (DeFronzo, 2004). Although more complete reviews of the impact of lipid metabolism on insulin resistance are available elsewhere (Bays et al., 2004; Capurso & Capurso, 2012; Delarue & Magnan, 2007), these findings emphasize that individuals with obesity, particularly visceral obesity, are at increased risk for developing diabetes as a consequence of lipotoxicity.

The Role of Inflammation, Gut Hormones, and the Gut Microbiota

The regulation of glucose and insulin and the accumulation of excess lipids also are linked to diabetes onset and course via additional physiological pathways, including inflammation, gut hormones, and the gut microbiota. We will briefly discuss these pathways and connect them to behavioral factors, in line with the scope and focus of this chapter.

Inflammation is associated with impaired insulin action and the development of insulin resistance, resulting from an increased production of inflammatory cytokines (Hardy, Czech, & Corvera, 2012). Inflammatory factors are highly associated with a constellation of behavioral risk factors that are themselves related to diabetes risk and maintenance, including dietary intake and eating behaviors, physical activity, sedentary behavior, sleep, cigarette smoking, alcohol consumption, and psychosocial stress. Additionally, gut hormones (e.g., glucose-dependent insulinotropic polypeptide [GIP], glucagon-like peptide-1 [GLP-1]) play an important role in insulin secretion. For example, individuals with both obesity and impaired secretion of gut hormones (e.g., decreased GLP-1 secretion) are at heightened risk for developing symptoms of diabetes, such as impaired insulin regulation (Holst, Pedersen, Wewer Albrechtsen, & Knop, 2017). Notably, bariatric surgery is emerging as an effective intervention for diabetes, given its association with weight loss, changes in gut hormones, and improvements in insulin resistance and β-cell function as well as glycemic control and reduced dependency on oral diabetes medications and insulin (Schauer et al., 2017). Relatedly, gastric bypass surgery affects the gut microbiota, and it's likely that the microbial alterations play a role in the weight loss and metabolic improvements found after bariatric surgery (Liu, Hu, Zhang, & Jia, 2017). Indeed, the type and abundance of gut microbiota are associated with energy homeostasis (e.g., increased energy harvest from diet, low-grade chronic inflammation, modulation of tissue fatty acid composition, peptide secretion), which in turn contribute to disruptions in insulin resistance and glucose metabolism (Brunkwall & Orho-Melander, 2017; Hage, Safadi, Salti, & Nasrallah, 2012).

In summary, impairments in glucose and insulin regulation, dyslipidemia, inflammation, gut hormone secretions, and the gut microbiota are interrelated and may potentially be addressed by modifying specific behavioral factors to reduce the risk or negative metabolic consequences of diabetes. The next section provides an in-depth discussion of the links between behavioral factors and strategies for modifying them to promote health.

The Influence of Behavioral Factors on the Pathophysiology of Obesity and Diabetes

In this section, we review several behavioral variables posited to impact diabetes onset and course, including dietary intake, eating behaviors, physical activity, sedentary behavior, sleep, cigarette smoking, alcohol use, and psychosocial stress. In addition, we discuss important biobehavioral associations and the potential for modification in individuals as they age.

Dietary Intake and Eating Behaviors

Dietary intake and eating behaviors are an important and often challenging component of diabetes risk and management, especially in the obesogenic environment promoted within the modern-day social-ecological context. Increases in calorie intake and unhealthy diet composition are related to the rise of obesity rates across the globe (Ezzati & Riboli, 2013). Specifically, when an individual regularly consumes more calories than he or she expends, a surplus of energy is created that is eventually converted to and stored as body fat, resulting in substantial increases in adipose tissue and excess weight gain (Blundell & Cooling, 2000). The accumulating fat mass observed in individuals with high calorie diets directly leads to additional physiologic impairments, including insulin resistance, glucose intolerance, and excess lipids, that promote the development of diabetes (Bastard et al., 2006; Carr et al., 2004; Thomas et al., 2004).

In addition to the impact of overall calorie intake on diabetes risk, studies show that the type and amount of specific nutrients consumed are related to diabetes risk and management, independent of adiposity and body weight (Ardisson Korat, Willett, & Hu, 2014), as are overall diet quality, dietary patterns, and eating behaviors. As such, several dietary factors associated with diabetes risk will be discussed in this chapter, with an emphasis on carbohydrate, fat, and protein consumptions, as these nutrient sources have the greatest influence on insulin regulation, diabetes onset, and diabetes management (American Diabetes Association, 2017).

Carbohydrates

One means of evaluating the quality of carbohydrate sources is the glycemic index, a measurement system that ranks sources of carbohydrates according to their impact on blood glucose levels (Wolever & Mehling, 2003). Relative to carbohydrates with a low glycemic index (e.g., most fruits, non-starchy vegetables, and whole grains), carbohydrates with a high glycemic index (e.g., white bread, starchy vegetables, and white rice) are digested and absorbed quickly into the bloodstream, leading to rapid elevations in blood glucose and subsequent increases in serum insulin levels (Ludwig, 2002). Another measure used to evaluate the quality of carbohydrate sources in certain food items is the glycemic load, which is calculated based on the glycemic index and accounts for the quantity of carbohydrates available in a serving and how much each gram of carbohydrate in that serving will raise blood glucose levels. Like the glycemic index, foods with a high glycemic load are associated with higher elevations in blood glucose levels than are foods with a low glycemic load. Notably, although measures of glycemic index and glycemic load are used widely in research and clinical care, there are some limitations with their calculation due to metabolic variability across individuals (Bhupathiraju et al., 2014).

Habitual consumption of foods with a high glycemic index or a high glycemic load initiates a cycle of hyperinsulinemia and insulin resistance that ultimately leads to glucose intolerance and β-cell dysfunction (Ardisson Korat et al., 2014). The hyperglycemic state that results from the consumption of carbohydrates with a high glycemic index or foods with a high glycemic load further prompts the liver to transform excess glucose into triglycerides for more efficient storage, which can lead to hypertriglyceridemia and increased circulating levels of FFA if sustained over time (Parks & Hellerstein, 2000). Results from a recent meta-analysis of prospective studies document the relations between carbohydrate intake and risk for diabetes, such that diets with higher glycemic index and higher glycemic load are linked to greater diabetes risk (Bhupathiraju et al., 2014). In contrast, dietary fiber, which represents a type of carbohydrate that is indigestible, has been shown to be inversely associated with diabetes risk in meta-analyses (Yao et al., 2014). Thus, monitoring and reducing intake of carbohydrates with a high glycemic index or high glycemic load while incorporating greater intake of dietary fiber may be useful in preventing diabetes onset and managing hyperglycemia in the context of diabetes.

Fats

As reviewed previously, higher total adiposity directly affects diabetes via lipotoxicity and insulin resistance (Ley, Hamdy, Mohan, & Hu, 2014). Although it is plausible that higher total fat intake would be indirectly associated with diabetes via weight gain, recent studies suggest that the type of fat consumed, rather than total fat intake, is associated with diabetes risk (Evert et al., 2013). In two cohort studies, the Nurses' Health Study and the Health Professionals' Follow-Up Study, associations between total fat intake and diabetes risk were not significant. However, increased intake of polyunsaturated fat and decreased intake of trans-fatty acids were associated with lower diabetes risk

(Ardisson Korat et al., 2014). Similarly, in the PREDIMED study, which examined the effects of a dietary fat intervention on diabetes risk, incident diabetes was not associated with baseline fat intake, though increased intake of saturated fat and animal fat was related to higher diabetes risk (Guasch-Ferre et al., 2017). Thus, diets that emphasize greater intake of unsaturated fats and lower intake of saturated fats, such as the Mediterranean diet, may be particularly helpful in the management of diabetes (American Diabetes Association, 2017).

Food Groups and Dietary Patterns

Beyond specific nutrients, several specific food groups and overall dietary patterns have been studied to determine their respective roles in either protecting against or promoting diabetes onset. For instance, dietary patterns characterized by high consumption of fruits and vegetables (Bazzano, Li, Joshipura, & Hu, 2008), low-fat dairy products (Ardisson Korat et al., 2014), nuts and legumes (Salas-Salvado et al., 2011), and whole grains (Aune, Norat, Romundstad, & Vatten, 2013) predict lower diabetes risk. In contrast, dietary patterns characterized by high consumption of red and processed meats (Ardisson Korat et al., 2014; Aune, Ursin, & Veierød, 2009), sugar-sweetened beverages (Malik et al., 2010), fried foods (Cahill et al., 2014), and salt (Liese, Nichols, Sun, D'Agostino, & Haffner, 2009) are related to a greater likelihood of developing diabetes.

Recent national guidelines emphasize wholemeal patterns and the importance of finding a dietary pattern that is sustainable in the context of diabetes prevention and management (American Diabetes Association, 2017). The 2017 American Diabetes Association Standards of Medical Care in Diabetes suggests that there are several diets, or eating patterns, that have demonstrated evidence for improving the course of diabetes and promoting weight management, including the Dietary Approaches to Stop Hypertension (DASH), Mediterranean, and other plant-based diets (American Diabetes Association, 2017). Such healthful eating patterns promote energy intake restriction and weight loss, which subsequently improve glycemic control (Evert et al., 2013). These guidelines further indicate that individuals' adherence to dietary patterns increases when the selected approach fits into their lives, which can be better achieved by taking behavioral and cultural factors into account (American Diabetes Association, 2017). For instance, the Mediterranean diet may be more easily adhered to when access to the foods and the style of eating are available. Notably, the dietary changes that are promoted across the Mediterranean, DASH, and plant-based diets can be customized to individuals' local settings and cultural background. In summary, a more complete understanding of the social-ecological context for target high-risk populations requiring diabetes prevention and control will be critical to further research on optimal dietary interventions.

Self-Regulatory Behavioral Strategies and Behavioral Adherence

Intervention trials have shown that the behavioral strategies and principles of social cognitive theory (Bandura, 1991), including self-monitoring (along with review of and feedback on progress), self-regulation, self-efficacy, goal-setting, reinforcement, problem-solving, and relapse prevention, are effective for weight management and reducing risk for diabetes (Hill-Briggs et al., 2011; Venditti, 2016). Given the role of meal timing in glucose metabolism and glycemic control, meal regulation also is a key component of weight management interventions and has particular relevance in the prevention and treatment of diabetes (Qian & Scheer, 2016; Reutrakul et al., 2014). The DiAlert trial, which applied social cognitive theory and promoted goal-setting related to healthful eating and physical activity, showed improvements in weight loss and systolic blood pressure among relatives of individuals with diabetes (Heideman et al., 2015). Moreover, a review of diabetes prevention programs suggests that intensive behavior change strategies, including self-monitoring, review of and feedback on progress, self-efficacy, goal-setting, reinforcement, problem-solving, and relapse prevention, delivered in both face-to-face individual and group settings typically included additional contacts with interventionists to promote adherence and maintenance of learned health behaviors (Baker, Simpson, Lloyd, Bauman, & Singh, 2011). The Look AHEAD trial, which targeted individuals with diabetes and obesity, used an intensive lifestyle intervention that included self-monitoring, self-regulation, goal-setting, and problem-solving (Look AHEAD Research Group, 2006) and was found to improve weight, glycated hemoglobin (HbA1c) levels, lipid levels, use of diabetes medications, blood pressure, fitness, depressive symptoms, and health-related quality of life (Look AHEAD Research Group, 2010, 2014a). Participants who received the intensive lifestyle intervention demonstrated greater engagement in weight management behaviors than those in the control condition, and individuals who more often used the weight management behaviors had a greater likelihood of maintaining weight loss than those who used the weight management behaviors less often (with higher likelihood of weight regain; Look AHEAD Research Group, 2014b). A recent meta-analysis of randomized controlled trials found that interactive self-management interventions may be useful for individuals with poorly controlled diabetes, particularly when including review of and feedback on progress, problem-solving, and goal-setting (Cheng et al., 2017).

Future studies are warranted to understand how social-ecological contexts (including culture, location, and availability of certain foods and eating patterns) can be utilized or enhanced to increase individuals' engagement in healthy eating behaviors that reduce risk for or promote healthy management of diabetes. In addition, research is needed to understand eating-related behavioral phenotypes (e.g., eating rate, binge eating, eating in the absence of hunger) and their expression in individuals at risk for or with diabetes to enhance the tailoring of intervention content and delivery. Furthermore, given that effective lifestyle intervention programs that address prevention and treatment of diabetes, dissemination and implementation efforts, along with policy initiatives to promote health across contexts, are critical to improving access to effective healthcare and support for diabetes prevention and management.

Physical Activity and Sedentary Behavior

Physical inactivity generally is defined as the failure to achieve recommended levels of weekly physical activity, whereas sedentary behavior refers to the engagement in activities, such as sleeping, sitting, and lying down, that do not increase energy expenditure substantially above resting level (Hamilton, Healy, Dunstan, Zderic, & Owen, 2008). Although physical inactivity and sedentary behavior are related constructs, they both contribute uniquely to cardiometabolic disease risk and are therefore typically considered independent predictors of cardiometabolic health outcomes (Hamilton, Hamilton, & Zderic, 2004; Hamilton et al., 2008; Wittink, Engelbert, & Takken, 2011). Most research examining the physiologic pathways linking physical activity to diabetes has focused on the beneficial effects of an active lifestyle on cardiometabolic factors. Treatment trials designed to increase physical activity through aerobic exercise or resistance training have documented concomitant reductions in body weight and visceral fat accumulation (Donnelly, Jacobsen, Heelan, Seip, & Smith, 2000; Irving et al., 2008; Slentz et al., 2011), enhanced insulin sensitivity and glucose tolerance (Cuff et al., 2003; Poehlman, Dvorak, DeNino, Brochu, & Ades, 2000; Ronald J Sigal et al., 2007), and improved lipid profiles (Eriksson et al., 1998; Jones, Doran, Leatt, Maher, & Pirmohamed, 2001; Lokey & Tran, 1989), which collectively mitigate risk for diabetes. This protective effect has been shown to be promoted through favorable alterations in body weight and body composition that lead to associated improvements in additional cardiometabolic risk factors (Kay & Singh, 2006; Lakka & Laaksonen, 2007; Salonen et al., 2015).

Physical activity indeed is associated with a cascade of metabolic effects that enhance fat oxidation (Goodpaster, Katsiaras, & Kelley, 2003; Talanian, Galloway, Heigenhauser, Bonen, & Spriet, 2007), prevent fat deposition (Kay & Singh, 2006; Lamarche, 1993), and build muscle tissue (Holloszy & Coyle, 1984), thereby reducing obesity risk and improving overall body composition (Donnelly et al., 2003; Irwin et al., 2003; Ross et al., 2000; Slentz et al., 2005). However, the relationship between physical activity and diabetes is not entirely explained by changes in body weight and body composition. The impact of physical activity on muscle tissue also directly improves insulin sensitivity, glucose tolerance, and lipid concentrations (Kiens, 2006) by increasing glucose uptake (Holten et al., 2004), enhancing insulin action (Miller et al., 1994; Ryan, Pratley, Goldberg, & Elahi, 1996), decreasing glycogen accumulation (Ebeling et al., 1993), and regulating FFA uptake and oxidation (Kiens, 2006).

In addition to the extensive research examining the physiologic factors driving the association between physical activity and diabetes, accumulating evidence has begun to focus more specifically on inactivity physiology to describe the distinct pathogenic role of sedentary behavior in promoting the disease (Hamilton et al., 2008; Wittink et al., 2011). Sedentary behavior is characterized by extended periods of muscular inactivity and reduced thermogenesis, which contribute to obesity risk and cardiometabolic abnormalities that subsequently increase the likelihood of developing diabetes (Hamilton et al., 2004, 2008; Wittink et al., 2011). For example, sedentary behavior is associated with decreased muscle glycogen synthesis (Bergouignan et al., 2016; Petersen et al., 2007), which leads to insulin resistance and inefficient glucose metabolism in muscle tissue (Jensen, Rustad, Kolnes, & Lai, 2011; Kida, Esposito-Del Puente, Bogardus, & Mott, 1990). The increased insulin resistance observed in muscle tissue among individuals engaged in prolonged sedentary behavior subsequently promotes dyslipidemia by diverting energy from carbohydrate intake away from muscle glycogen storage and into liver lipogenesis, leading to the development of hypertriglyceridemia and increased availability of circulating FFA (Petersen et al., 2007). Despite the advancements in understanding how sedentary behavior contributes to the pathogenesis of diabetes, this relationship remains an important area for future research advancement.

In line with these systemic cardiometabolic effects, accumulating evidence has implicated both physical inactivity and sedentariness as important behavioral contributors to the onset and course of diabetes. For example, meta-analytic findings have documented that regular participation in physical activity prospectively reduces the relative risk for diabetes by 15% to 55%, depending on the frequency and intensity of the physical activity engaged in (Aune, Norat, Leitzmann, Tonstad, & Vatten, 2015). Meanwhile, regular engagement in extended periods of sedentary behavior increases the relative risk for diabetes by 112% (Wilmot et al., 2012). Given the potency of these associations, prevention and treatment efforts aimed at reducing the disease burden of diabetes frequently include increased physical activity and decreased sedentary behavior as primary behavioral targets of intervention (Bassuk & Manson, 2005; Colberg et al., 2010; Laaksonen et al., 2005; Laaksonen, Niskanen, Lakka, Lakka, & Uusitupa, 2004; LaMonte, Blair, & Church, 2005; Powers et al., 2015; Sigal, Kenny, Wasserman, Castaneda-Sceppa, & White, 2006).

Most diabetes prevention and intervention programs have focused primarily on increasing moderate intensity aerobic physical activity with only nominal efforts to reduce sedentary behavior. Randomized controlled trials conducted over the past decade have produced mixed findings regarding the impact of increased physical activity on diabetes (Aune, Norat, et al., 2015). However, several large-scale prevention interventions, including the Finnish Diabetes Prevention Study (Laaksonen et al., 2005) and the Diabetes Prevention Program (Hamman et al., 2006), have documented that adults who achieve recommended levels of physical activity (e.g., 150 min of physical activity per week) are significantly less likely to develop diabetes than are their counterparts, even in the absence of reaching recommended weight loss goals.

Moreover, the Look AHEAD trial, one of the most extensive randomized controlled trials investigating the impact of an intensive lifestyle intervention on disease outcomes among adults with diabetes, further demonstrated that individuals assigned to an intensive lifestyle intervention that focused on improving dietary intake and increasing physical activity were more likely to achieve partial or complete remission of diabetes than were individuals assigned to an education control group (Gregg, Chen, Wagenknecht, & et al., 2012). However, the rates of remission remained relatively low after the 4-year treatment program, with only 7% of individuals in the intensive lifestyle intervention and 2% of individuals in the education control group reaching partial or complete remission of the disease. Despite the low remission rates, subsequent analyses showed that body weight, visceral adiposity, physical fitness, HbA1c levels, and additional cardiometabolic risk factors remained significantly improved through 6-year follow-up among individuals participating in the intensive lifestyle intervention relative to those in the education control group (Look AHEAD Research Group, 2013). Although it is difficult to disentangle the independent effects of changes in diet and physical activity on these outcomes, these findings suggest that engaging in healthier diet and physical activity regimens can have substantial impact on the pathophysiologic pathways linked to diabetes without necessarily promoting disease remission. Accordingly, physical activity remains an important lifestyle behavior for both the prevention and management of diabetes.

Sleep

Sleep is an emerging area of interest in relation to obesity, cardiometabolic impairment, and diabetes. Particularly, sleep quantity and quality are implicated in the onset and management of diabetes. A meta-analysis of studies that examined incident diabetes risk suggested that the lowest risk for diabetes was related to sleep duration of 7–8 h per day (Shan et al., 2015). Notably, in comparison to 7–8 h per day, shorter sleep duration (for every 1 h <7 h per day) and longer sleep duration (for every 1 h >7 h per day) were both associated with risk of diabetes in a U-shaped relationship. These results are similar to those found in a recent meta-analysis of studies in individuals diagnosed with diabetes, in which sleep duration (i.e., quantity) demonstrated a U-shaped association with glycemic control (Lee, Ng, & Chin, 2017). Specifically, compared to normal sleep duration, both short and long sleep durations were related to higher HbA1c levels. National Health Interview Study (NHIS) survey data also suggest that sleep patterns characterized by too few or too many hours are associated with an increased probability of obesity, diabetes, high blood pressure, and cardiovascular disease (Buxton & Marcelli, 2010).

Change in sleep duration over time also represents an important factor in the onset of diabetes and metabolic control. Among the Nurses' Health Study cohort, increases and decreases in sleep duration over a 14-year period were associated with higher diabetes risk in comparison to individuals who demonstrated no change in their sleep patterns (Cespedes et al., 2016). Notably, these results held after accounting for changes in diet, physical activity, and weight-related factors. Thus, the number of hours that an individual sleeps per night and the degree of change in sleep duration over time are useful to consider in the context of diabetes risk. Moreover, studies on sleep quality suggest that poorer sleep quality is also related to increased HbA1c levels (Lee et al., 2017). In particular, sleep disturbance is posited to affect diabetes management directly via glucose metabolism, as well as indirectly through appetite-related hormones such as leptin and ghrelin, and their associated effects on weight gain and subsequent insulin resistance (Lee et al., 2017). Additionally, research that takes circadian rhythms into account (e.g., extends beyond sleep quality and duration to include chronotype, eating patterns and timing of meals) suggests that the circadian system affects glucose metabolism and glycemic control; moreover, circadian system disruption is linked to risk for diabetes and obesity as well as diabetes management in patients with diabetes (Qian & Scheer, 2016; Reutrakul et al., 2014).

Given the emerging literature on sleep and circadian rhythms in relation to diabetes, future studies are warranted to examine the patterning of circadian rhythms in relation to diabetes onset and risk reduction as well as glucose management among individuals who have already developed diabetes. In addition, studying circadian rhythms and response to intervention may elucidate novel behavioral targets or help to inform precision medicine approaches that allow for tailoring of diabetes prevention or treatment delivery.

Cigarette Smoking

Meta-analytic findings show that current cigarette smokers have a 44% greater chance of developing diabetes than do nonsmokers (Willi, Bodenmann, Ghali, Faris, & Cornuz, 2007). Exposure to second-hand smoke further is associated with a heightened incidence of diabetes among nonsmokers (Wei, Meng, & Yu, 2015). Although the relationship between cigarette smoking and diabetes tends to be stronger among men than women, most studies indicate that both men and women smokers are at heightened risk for diabetes when compared to nonsmokers, with some estimates suggesting that approximately 12% and 2% of the total cases of diabetes are causally attributable to current smoking among men and women, respectively (Pan, Wang, Talaei, Hu, & Wu, 2015).

Cigarette smoking contributes to the expression of diabetes by promoting insulin resistance (Facchini, Hollenbeck, Jeppesen, Chen, & Reaven, 1992; Rönnemaa, Rönnemaa, Puukka, Pyörälä, & Laakso, 1996; Targher et al., 1997), glucose intolerance (Frati, Iniestra, & Ariza, 1996), disruptions in triglyceride metabolism (Razay & Heaton, 1995), and visceral adiposity (Mizuno et al., 2005). For example, cigarette smoking reduces insulin sensitivity by increasing circulating levels of hormones that have antagonistic effects on insulin action (Kapoor & Jones, 2005) and also by promoting high circulating levels of FFA via increased triglyceride metabolism (Targher et al., 1997). Increasing evidence further suggests that the relationship between cigarette smoking and diabetes may largely be driven by the effects of cigarette smoking on weight.

Emerging evidence documents that the relationship between cigarette smoking and weight is dose-dependent (Pan et al., 2015; Willi et al., 2007; Zhang, Curhan, Hu, Rimm, & Forman, 2011). Specifically, light to moderate cigarette smoking is linked to lower body weight and reduced risk for obesity (Albanes, Jones, Micozzi, & Mattson, 1987; Bouros et al., 2006; Flegal, Troiano, Pamuk, Kuczmarski, & Campbell 1995; Huot, Paradis, & Ledoux, 2004). These associations are attributable to the effects of nicotine, a stimulant that promotes a negative energy balance by increasing satiety signals and reducing motivational drive to eat (Audrain-McGovern & Benowitz, 2011; Bouros et al., 2006) as well as elevating resting metabolic rate and thermogenesis of adipose tissue (Andersson & Arner, 2001; Hellerstein et al., 1994). Conversely, heavy cigarette smoking is associated with heightened risk for both obesity (Chiolero, Jacot-Sadowski, Faeh, Paccaud, & Cornuz, 2007; Istvan, Cunningham, & Garfinkel, 1992; John, Hanke, Rumpf, & Thyrian, 2005; Rasky, Stronegger, & Freidl, 1996; Shimokata, Muller, & Andres, 1989) and elevated waist circumference (Molarius, Seidell, Kuulasmaa, Dobson, & Sans, 1997; Rosmond & Bjorntorp, 1999). Although the factors linking heavy cigarette smoking to increased adiposity are not fully understood, this relationship is hypothesized to result from heightened sympathetic nervous system activity that promotes visceral fat accumulation through increased cortisol secretion and altered levels of testosterone and estrogen (Balhara, 2012; Cena, Fonte, & Turconi, 2011; Chiolero, Faeh, Paccaud, & Cornuz, 2008).

In addition to the relationships among current cigarette smoking, weight, and diabetes, former cigarette smoking also is associated with a heightened incidence of diabetes for up to three decades after smoking cessation (Pan et al., 2015; Zhang et al., 2011), which may result from post-cessation weight gain. Indeed, individuals who quit smoking gain an average of 10 to 13 pounds in the first year following cessation (Audrain-McGovern & Benowitz, 2011; Ginsberg et al., 1997; Klesges et al., 1997), with greater amounts of post-cessation weight gain prospectively predicting risk for diabetes (Yeh, Duncan, Schmidt, Wang, & Brancati, 2010). Thus, although smoking cessation promotes extensive health benefits, both current and former smokers remain vulnerable to diabetes, primarily as a function of weight. Despite these strong associations, few studies have evaluated the impact of formal smoking cessation programs on diabetes outcomes, indicating a need for comprehensive diabetes prevention and intervention programs to include smoking cessation as a targeted treatment goal.

Alcohol Use

Despite extensive evidence linking alcohol use to cardiometabolic morbidity and mortality (Ajani et al., 2000; Kiechl et al., 1998; Koppes, Dekker, Hendriks, Bouter, & Heine, 2005; Reynolds et al., 2003; Rimm, Williams, Fosher, Criqui, & Stampfer, 1999), research examining the relationship between alcohol use and diabetes remains relatively sparse and controversial. Previous research has implicated alcohol use as both a risk factor for and a protective factor against the development of diabetes, with additional findings documenting no relationship between alcohol use and the disease (see Pietraszek, Gregersen, & Hermansen, 2010 for review). These discrepant findings are likely driven by the complex relationship between alcohol use and the pathophysiologic pathways involved in the development and progression of the disease (O'Keefe, Bybee, & Lavie, 2007). Previous research consistently has documented that consuming one to two alcoholic beverages per day substantially improves indicators of diabetes risk relative to less frequent alcohol use (Mukamal et al., 2003; Mukamal, Jensen, et al., 2005; Rehm, Sempos, & Trevisan, 2003), whereas heavier patterns of alcohol use and repeated engagement in binge drinking significantly worsen indicators of diabetes risk (Mukamal, Jensen, et al., 2005; Mukamal, Maclure, Muller, & Mittleman, 2005; Rehm et al., 2003). A meta-analysis of cross-sectional studies by Baliunas and colleagues (2009) confirmed that light to moderate alcohol use was associated with reduced risk for diabetes, whereas heavy alcohol use was associated with heightened risk for the disease. Taken together, these findings indicate that the association between alcohol use and risk for diabetes is dependent on the pattern of alcohol use. This association likely follows a J- or U-shaped pattern, whereby light to moderate alcohol consumption protects against diabetes relative to less frequent alcohol consumption and heavy alcohol use promotes diabetes.

Consistent with previous findings, the amount of and frequency in which alcohol is consumed can have both protective and exacerbating effects on distinct pathophysiologic pathways involved in the development and progression of diabetes. For example, light to moderate alcohol use is associated with metabolic effects that improve insulin signaling and subsequent glucose utilization among individuals with (Greenfield, Samaras, Hayward, Chisholm, & Campbell, 2005; Turner, Jenkins, Kerr, Sherwin, & Cavan, 2001) and without diabetes (Davies et al., 2002), though this effect is reversed when alcohol is consumed in high doses (Flanagan et al., 2000). Interestingly, the effect of alcohol on insulin action may be indirectly driven by the impact of alcohol on visceral adiposity (Bell, Mayer-Davis, Martin, D'agostino, & Haffner, 2000; Freiberg & Samet, 2005; Stampfer et al., 1988). Several studies have documented that the positive effect of alcohol on insulin resistance does not persist after measures of visceral adiposity are statistically accounted for (Bell et al., 2000; Stampfer et al., 1988). The loss of this effect is not surprising given the substantial and direct impact of visceral fat on insulin sensitivity and related indicators of diabetes risk (Bastard et al., 2006; Carr et al., 2004; Després & Lemieux, 2006; Hall, do Carmo, da Silva, Wang, & Hall, 2015; Thomas et al., 2004). However, the mechanisms linking alcohol use to visceral adiposity are not well-established (Traversy & Chaput, 2015) and require further elucidation to better understand how alcohol use contributes to both the prevention and promotion of diabetes risk (Guasch-Ferré et al., 2012).

Psychosocial Stress and Psychological Distress

The interaction of stress, distress, and diabetes pathophysiology reflects many aspects of the mind-body interaction. Psychosocial stress is an umbrella term used to refer to a range of psychological and emotional phenomena involving acute or chronic exposures to negative life events, developmental neglect and trauma, situational emotional reactivity, and/or job strain, each with potential to impact diabetes risk and progression (Hackett & Steptoe, 2017; Steptoe, 2016). Psychological distress, which may refer to symptoms of depression and anxiety (Peyrot et al., 2005) or personality traits such as anger or hostility (Goldbacher & Matthews, 2007), has also been studied in this biobehavioral context. Here we will examine some of the empirical findings on the stress-cardiometabolic disease relationship but first will review briefly a few key concepts in stress physiology because they highlight several of the biobehavioral concepts discussed in this review chapter (Fig. 19.1).

An often-studied physiologic mechanism linking stress and distress to diabetes is cortisol, a glucocorticoid hormone, so-named for its central role in glucose homeostasis. Research indicates that biobehavioral responses to stress are initially adaptive (i.e., they mobilize action in response to threat and heighten immune functioning) but eventually maladaptive. Notably, the chronic activation of biological systems involved in stress may be associated with either increased, prolonged, or diminished physiologic reactions and thus contribute to individual differences in health outcomes and disease vulnerability, including cardiometabolic disease and diabetes (Thayer & Sternberg, 2006). This process has also been referred to as “allostasis” or “allostatic load” (Gallo, Fortmann, & Mattei, 2014) and operationalized as the study of biobehavioral markers including health behaviors and neuroendocrine, cardiovascular, metabolic, and immune or pro-inflammatory factors. For example, it has been established that stress-induced sympathetic activation of the autonomic nervous system is associated with changes in blood pressure (Knowles & Reaven, 2016), heart rate, and cardiac output (Aune, ó Hartaigh, & Vatten, 2015) and that stress-induced parasympathetic activation is related to changes in heart rate variability (Licht et al., 2010). More specifically, studies of stress and diabetes course have focused on the dysregulation of the cardiovascular system, circadian/diurnal changes in cortisol, and the impact of chronic inflammation. Additionally, glucose and lipid impairments in relation to cellular energy demands have been associated with insulin resistance, weight gain, and potential damage to mitochondrial DNA (Picard, Juster, & McEwen, 2014; Picard & Turnbull, 2013).

Moreover, psychosocial stress has been associated with new-onset diabetes in initially healthy populations and as prognostic factor in the course of glycemic dysregulation. Epidemiological prospective studies, such as those conducted with the large Whitehall II occupational cohort in Britain, offer insight into stress-related risk factors, cortisol changes, and the course of pre-diabetes and diabetes (Hackett, Kivimaki, Kumari, & Steptoe, 2016; Hackett, Steptoe, & Kumari, 2014). This body of work has contributed significantly to an emerging paradigm regarding the social determinants of health (Marmot, 2005). For example, cumulative job strain (defined as a perception of high job demand with low control) has been shown to be associated with incident diabetes over an 18-year period in women with obesity, but not men (Heraclides, Chandola, Witte, & Brunner, 2012). In contrast, data from the IPD-Work Consortium examining 13 European cohorts (Nyberg et al., 2014) found that among persons with job strain, there was a modest but robust increase in the incidence of diabetes over 10 years, compared to those without job strain, even after accounting for baseline demographic factors (age, sex, socioeconomic status), lifestyle factors (physical activity, smoking, alcohol use), and BMI status. In another analysis of the same cohort, investigators assessed baseline psychological distress (symptoms of depression and anxiety from the General Health Questionnaire) to examine whether this construct was predictive of diabetes overall or by baseline cardiometabolic risk status (based on pre-diabetes status and Framingham risk scores [FRS]). Results indicated that among healthier individuals at baseline (those with normoglycemia or with pre-diabetes and a low FRS), psychological distress level was not predictive of diabetes development. However, among those with pre-diabetes and a high FRS, the odds of developing diabetes over 10 years was twice as likely among persons with psychological distress compare to those without symptoms.

Taken together, findings suggest that stress, distress, and diabetes are mutually influenced by the "wear and tear" of modern life and, as such, a social-ecological perspective that addresses such biobehavioral factors is needed to optimize the potential for prevention and intervention. Indeed, effective interventions for chronic stress and for diabetes typically address the health behaviors highlighted throughout this review (dietary habits, eating behaviors, physical activity, sedentary behavior, sleep, cigarette smoking, and alcohol use).

Biobehavioral and Social-Ecological Approaches in the Context of Healthy Aging

As referenced throughout this chapter, research that promotes understanding and modification of individual-level biobehavioral factors has strong potential to prevent or slow the natural history of type 2 diabetes. In line with the scope and focus of this volume, it is also apparent that adoption of a social-ecological and healthy aging perspective can increase the potency of such efforts. The cross-sectional and prospective epidemiologic evidence presented in this review would suggest that influencing social determinants of health across multiple contexts (e.g., family, social, cultural, work, healthcare, food, and physical environments) will allow for more robust biobehavioral outcomes in diabetes care (Fig. 19.1). Targeting and tailoring interventions to salient developmental risk periods that are sensitive to age, race/ethnicity, and gender-differences are also needed.

Life span perspectives have already become part of the landscape in biobehavioral diabetes research. For example, it has long been known that a history of gestational diabetes is a risk factor for the development of type 2 diabetes, and this has informed advances in lifestyle interventions for high-risk women (Ferrara, Hedderson, & Brown et al. 2016). However a social-ecological perspective broadens understanding and potential effectiveness when it encompasses a life course approach that aims to impact maternal and infant healthcare in a manner that would also influence childhood obesity risk (Dixon, Pena, & Taveras, 2012) and interrupt intergenerational cycles of maternal obesity (Gilman, 2016). Similar examples would include research agendas that seek to understand the associations between diabetes and frailty syndromes in aging individuals (Walston et al., 2006) or exploring social, workplace, or healthcare policies that aim to decrease cumulative stress burden to promote the health of individuals and communities (McEwen, 2006).

Conclusions

A critical review of empirical findings, many of which have been published in the past decade, highlights the importance and significance of biobehavioral factors associated with the natural history of cardiometabolic impairment and the onset and course of type 2 diabetes. If our scientific and societal objective is to combat the dual epidemics of obesity and type 2 diabetes, we conclude that a more comprehensive biobehavioral, social-ecological, and healthy aging framework is crucial to propel the research agenda forward. The evidence presented in this chapter confirms that innovative studies concerning the role of diet composition, eating habits and patterns, physical activity and inactivity, and variability in behavioral phenotypes over the life span, in relation to biomarkers inclusive of lipid, glucose, and insulin physiology, inflammatory processes, and the gut microbiome, will be most promising for the development of highly effective preventive and disease management approaches.

However, increased efforts are also needed to understand the impact of other behavioral lifestyle factors such as sleep, cigarette smoking, alcohol use, and psychosocial stress. The research that is being conducted in these areas, in association with neuroendocrine, cardiometabolic, immune function, and functional quality of life outcomes, widens the scope of diabetes-relevant inquiry and further highlights the critical importance of social-ecological and life span research approaches. We conclude that each of these areas of investigation, alone and in combination, has significant potential to yield benefits for the health and well-being of individuals and society.

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Chapter 20
Diabetes Distress and Quality of Life in Adults with Diabetes

Claire J. Hoogendoorn, Amit Shapira, Juan F. Roy, Naomi S. Kane, and Jeffrey S. Gonzalez

Introduction

The effects of chronic illness and its treatment on patients, including those with diabetes mellitus, have traditionally been quantified in terms of morbidity, mortality, and costs. The traditional model of healthcare has prioritized biological mechanisms of disease, often measured by surrogate biomarkers associated with clinical outcomes, placing primary importance on molecular, cellular, and genetic level of analysis at the expense of understanding psychological and social factors that may influence and be affected by disease processes and health outcomes (Engel, 1989). In contemporary diabetes care, positive findings regarding intensive treatment from landmark trials such as the Diabetes Control and Complications Trial (DCCT; DCCT Research Group, 1993) and the UK Prospective Diabetes Study (UKPDS; UKPDS Group, 1998) have contributed to the adoption of intensive treatment practices and a focus on the frequent evaluation of blood sugar levels, a surrogate for diabetes complications, as a standardized method for evaluating the adequacy of diabetes treatment and patient self-management.

However, the focus on surrogate outcomes to evaluate the benefits of diabetes care has not gone without serious criticism (e.g., Yudkin, Lipska, & Montori, 2011). Evidence from intensive glucose control trials in type 2 diabetes (T2D) shows significant benefits for patients in terms of reductions in hyperglycemia and a modest reduction nonfatal cardiovascular disease without any reduction in risk for cardiovascular- or all-cause mortality; however, these benefits are achieved at the expense of a twofold increase in risk of hypoglycemia, a direct and potentially dangerous side effect of intensive therapy (Kelly, et al., 2009). The mixed nature of these outcomes and evidence from some trials linking more intensive treatment to increased mortality risk for some patients with T2D (ACCORD

C. J. Hoogendoorn · A. Shapira · J. F. Roy · N. S. Kane
Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

J. S. Gonzalez (✉)
Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Departments of Medicine (Endocrinology) & Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, USA

The Fleischer Institute for Diabetes and Metabolism, Albert Einstein College of Medicine, Bronx, NY, USA

New York Regional Center for Diabetes Translation Research, Albert Einstein College of Medicine,
Bronx, NY, USA
e-mail: jeffrey.gonzalez@yu.edu

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Study Group, 2008) has led to a growing consensus that the relative benefits of intensive diabetes therapies should be weighed against the increased risk of negative outcomes, such as weight gain, hypoglycemia, and other side effects (Ismail-Beigi et al., 2010; Montori, Gafni, & Charles, 2006). For certain patients, particularly the elderly and frail, the risks of intensive therapy may often outweigh the benefits (Huang, Brown, Ewigman, Foley, & Meltzer, 2007; Lipska, et al., 2015). Thus, most recent treatment recommendations from the American Diabetes Association (ADA) recommend a patient-tailored approach in establishing goals for glycemic control and selecting treatments based on the patient's "preferences, needs, and values" (ADA, 2018 Standards of Care, page S60-S61).

In recent years, new technologies, such as continuous blood glucose monitoring, have allowed for the assessment of aspects of glycemic control not currently captured by A1c values, such as time-in-range and hypoglycemic events, but there is growing interest in also capturing patient-reported outcomes (PROs; Brown, Kennedy, Runge, & Close, 2016). The US Food and Drug Administration (2006) highlights that certain treatment effects can only be known by the patient (e.g., pain severity). Systematic inclusion of PROs can give valuable information that may otherwise be lost and could inform evaluations of treatment in terms that matter to patients.

From the first landmark trials of intensive therapy for diabetes, investigators have attempted to examine the patient's experience of living with diabetes and its treatment in terms of emotional distress and quality of life (QOL). This body of research draws attention to these PROs as representing important, patient-centered outcomes of diabetes care. The growing acceptance of Engel's (1989) viewpoint and recognition of the importance of these and other psychosocial factors in diabetes care has been most recently demonstrated by the publication of the first ever position statement from the ADA on *Psychosocial Care for People With Diabetes* (Young-Hyman et al., 2017). The cornerstone of this position statement is that diabetes care should prioritize health outcomes as well as quality of life and well-being. Indeed, ongoing evaluation of patient well-being by providers is framed as a standard of routine care. This position is in line with the priorities of those living with diabetes, who aim to improve their well-being and reduce their risk of complications and death while maintaining QOL (Bradley & Speight, 2002; Dismuke, Hernandez-Tejada, & Egede, 2014; Misra & Lager, 2008).

For diabetes treatments, psychosocial interventions, or system-level policy interventions to be evaluated in terms of PROs, such as diabetes-related distress (DD) and QOL, considerable challenges must be overcome in the conceptualization and measurement of these variables. Despite these challenges, there is substantial accumulated evidence to show that these PROs can be sensitive to aspects of the lived experience of individuals with diabetes in ways that are incompletely captured in blood glucose levels. A strong evidence base also demonstrates that these factors can predict important health outcomes, often at levels of magnitude that are similar or superior to the predictive power of surrogates, like A1c.

In this chapter, we first provide an overview of DD, discuss its relationship to depression and important diabetes outcomes, and review relevant DD measures. Next, we provide an overview of the measurement of QOL in diabetes, with a focus on HRQOL; discuss its differentiation from health status, its relationship to DD, and other constructs related to emotional distress; and provide recommendations for how to select an adequate measure for clinical practice and research. In addition, cultural, demographic, and social factors beyond the individual are described in relation to DD and HRQOL. Finally, future directions in diabetes DD and HRQOL research are discussed. In our review of the literature, we have integrated studies of type 1 diabetes (T1D) and T2D, although we recognize significant differences between these conditions, the evidence base does not support a separate review for each group.

Diabetes Distress

Introduction

Following a research tradition that seeks to understand an individual's experience of emotional distress in the context of specific stressful situations (e.g., Lazarus & Folkman, 1984; Rabkin & Struening, 1976; Selye, 1974), DD is reflective of the emotional impact of living with diabetes and its treatment and is often operationalized to include a variety of emotional experiences, such as feeling overwhelmed by the demands of self-management and worry about complications, as well as appraisals of diabetes-related burdens and stressors, and dissatisfactions with support from treatment providers and other significant others (Dunn, Smartt, Beeney, & Turtle, 1986; Polonsky et al., 1995; Polonsky, Fisher, Earles, et al., 2005b; Welch, Jacobson, & Polonsky, 1997). In contrast to psychopathological constructs, such as clinical depression, DD is not necessarily pathological. Rather, DD represents the patient's perception of problems related to diabetes that are viewed as burdensome and/or causing emotional distress. As such, DD is reflective both of the burdens of diabetes and the demands of diabetes treatment *and* one's perceived capacity to meet and cope with these demands and burdens.

A recent meta-analysis of 55 studies and nearly 37,000 participants estimated that clinically important levels of DD are experienced by 36% of all adults with T2D (Perrin, Davies, Robertson, Snoek, & Khunti, 2017). Although meta-analytic evidence is not available for the prevalence in T1D, where studies have compared levels of DD between adults with T1D and T2D, they have tended to find similar prevalence (e.g., Polonsky, Fisher, Earles, et al., 2005b). The most in-depth evaluation of DD in adults with T1D suggests a prevalence of 42% (Fisher et al., 2016), just above the 95% confidence interval (31–41%) for DD prevalence in T2D (Perrin et al., 2017). Evidence suggests that elevations in DD persist over time, in both T2D and T1D (Fisher, Skaff, et al., 2008; Fisher et al., 2016). In T2D, meta-analysis suggests that the prevalence of DD is not consistently related to the measure of diabetes distress used, study location, patient age, or ethnicity; the only variables evaluated that were consistently associated with increased prevalence of diabetes distress were female gender and a higher prevalence of depressive symptoms (Perrin et al., 2017). One recent study of a large population of 10,821 adults with T1D participating in the T1D exchange clinic registry used a single item to assess the frequency of feeling "stressed because of your diabetes" and found that approximately 42% reported "sometimes" and 20% reported "very often" experiencing DD (Boden & Gala, 2017).

Diabetes and Diabetes Distress

The demands of diabetes self-management are a significant source of distress among diabetes patients (Delahanty et al., 2007; Gask, Macdonald, & Bower, 2011; Vijan, Hayward, Ronis, & Hofer, 2005). Qualitative analyses have indicated that the burden of making lifestyle changes, implementing self-management routines, especially those related to insulin regimens, and achieving targets for glycemic control are relevant themes through which culturally diverse urban adults with T2D describe emotional distress related to their diabetes (Tanenbaum, Kane, Kenowitz, & Gonzalez, 2016). Data from Norway suggest that prevalence of DD is substantially higher in diabetes specialty care settings than in primary care, reflecting the poorer health and greater self-management demands of the patients typically seen in specialty care (Stoop et al., 2014). Certain aspects of diabetes self-management regimen, such as insulin injections and finger pricks to self-monitor blood glucose, tend to be viewed negatively by patients (Rubin, Peyrot, Kruger, & Travis, 2009). Among adults with T2D, DD is more prevalent among those on insulin therapy, as compared to those on oral medication regimens (Baek, Tanenbaum, & Gonzalez, 2014; Delahanty et al., 2007; Polonsky, Fisher, Guzman, et al., 2005a), and those taking insulin can report experiencing distress that is directly caused by the burdens of implementing insulin self-management, ideas of failure, self-reproach, and poor health associated with insulin and the social stigma that surrounds self-injections (Tanenbaum et al., 2016). Aspects of insulin self-management and blood glucose testing are also reflected in DD for adults with T1D (Boden & Gala, 2017; Fisher et al., 2016). Insulin use can also contribute to hypoglycemia (Yanai et al., 2015), and fear of hypoglycemia is particularly common among T1D patients (Joensen, Tapager, & Willaing, 2013) although such fear may not be uncommon among T2D patients, particularly those on insulin therapy regimens (Marrett, Radican, Davies, & Zhang, 2011; Tanenbaum et al., 2016). Fear of hypoglycemia is often triggered by distressing experiences with hypoglycemic episodes and can negatively impact one's sense of control and well-being, often building a barrier to engage in crucial self-management behaviors such as physical activity and following a flexible diet (Brazeau, Rabasa-Lhoret, Strychar, & Mircescu, 2008; Fisher et al., 2016). Fear of hypoglycemia and other broader manifestations of DD are also common among partners of adults with T1D (Polonsky, Fisher, Hessler, & Johnson, 2016).

Although the previously mentioned meta-analysis of T2D studies failed to demonstrate a relationship between variations in average levels of glycemic control observed in study samples and prevalence of DD, the effect was near the alpha level for significance ($p = 0.08$) (Perrin et al., 2017). A number of studies have shown a clear and consistent cross-sectional relationship between higher DD and poorer glycemic control in T2D (Boden & Gala, 2017; Delahanty et al., 2007; Fisher et al., 2007; Fisher, Glasgow & Strycker, 2010; Fisher, Hessler, Polonsky & Mullan, 2012; Fisher, Mullan, et al., 2010; Hessler et al., 2014; Schmitt, et al., 2015; Pandit et al., 2014), T1D (Strandberg et al., 2014; Zoffmann, Vistisen, & Due-Christensen, 2014; Fisher et al., 2015, 2016), and mixed T1D and T2D samples (Graue et al., 2012; Polonsky et al., 1995; Schmitt et al., 2015, 2016; Snoek, Pouwer, Welch, & Polonsky, 2000; Welch et al., 1997). Moreover, DD is also longitudinally associated with treatment adherence and glycemic control in T2D (Aikens, 2012; Fisher, Mullan, et al., 2010) and with missed insulin boluses and increases in A1c in T1D. In fact, glycemic control and DD have been shown to covary together longitudinally (Fisher, Mullan, et al., 2010; Zagarins, Allen, Garb, & Welch, 2012). Findings from a behavioral trial targeting DD also demonstrate significant covariation over time among regimen-related DD, medication adherence, physical activity, and glycemic control over time (Hessler et al., 2014).

Diabetes Distress and Depression

DD has been distinguished from psychiatric mood disorders, such as major depressive disorder (MDD), both at the conceptual and measurement levels and through a series of studies that generally show differential predictive validity in relation to glycemic control and self-management, despite modest to moderate levels of shared variance between measures of DD and measures of depression (Fisher, Gonzalez, & Polonsky, 2014; Gonzalez, Fisher, & Polonsky, 2011; Snoek, Bremmer, & Hermanns, 2015). Whereas MDD is based on a diagnostic system that is agnostic about etiology and contextual factors that might explain the experience of mental disorders, focusing instead on syndromes that are defined by the presence of an often arbitrary number of emotional, cognitive, and somatic symptoms, DD is a construct primarily defined by one's perceptions about the distressing nature of problems related to the situational context of diabetes. As such, DD is also distinct from general measures of distress that do not specify a diabetes-specific context (Fisher et al., 2014; Polonsky et al., 1995; Snoek et al., 2015).

One study showed that 84% of adults with T2D and elevated DD did not reach diagnostic criteria for MDD and 67% of those with MDD also reported elevated DD (Fisher et al., 2007); over 90% of adults with T1D who were identified as depressed in another study also reported elevated DD

(Fisher et al., 2016). This suggests that MDD is an insufficient construct to account for the experience of DD. Other evidence suggests that even clinician-assessed MDD symptoms can often be influenced by the situational context of diabetes and its management (Tanenbaum & Gonzalez, 2012; Tanenbaum et al., 2013). A review of the handful of studies examining shared variance between measures of DD and depression suggested moderate shared variance with measures of depressive symptoms (5–40% shared variance) but low overlap with measures of MDD (up to 2% shared variance) (Snoek et al., 2015).

Relatively few studies have examined independent effects of DD and depression in relation to diabetes outcomes, such as self-management and glycemic control. Although depressive symptoms are consistently correlated with poorer glycemic control (Lustman et al., 2000) and self-management (Gonzalez, Peyrot, et al., 2008) in diabetes, findings from a relatively smaller number of studies that assess DD and depression in adults with T2D or T1D generally support stronger and more consistent relationships between DD and poor diabetes self-management and control than are observed for measures of depressive symptoms (Aikens, 2012; Fisher et al., 2007, Fisher, Glasgow, et al., 2010, Fisher, Mullan, et al., 2010, 2016; Gonzalez, Kane, Binko, Shapira, & Hoogendoorn, 2016; Gonzalez, Shreck, Psaros, & Safren, 2015;). At least two studies suggest that observed relationships between depressive symptoms and glycemic control can be accounted for by DD (Schmitt et al., 2015; Van Bastelaar et al., 2010). When MDD is assessed using diagnostic interview methods, the gold standard of assessment, it is often not significantly related to diabetes self-management or glycemic control (Fisher et al., 2007, 2016). Thus, in research and practice, it is important to differentiate DD and depression in order to correctly identify the problems represented by these constructs and inform the selection of appropriate interventions and treatments (Fisher et al., 2014; Young-Hyman et al., 2017).

Measures of Diabetes Distress

A recent review suggested that when selecting a DD measure, it is important to consider the following: (1) type of diabetes; (2) intention to measure specific aspects of distress versus a single construct; (3) which aspects of DD are of interest (e.g., regimen, emotional burden); and (4) for intervention studies which aspects of DD are targeted by the intervention that would influence change in this outcome measure (Dennick, Sturt, & Speight, 2017). To identify general categories associated with the construct of DD, Dennick et al. (2017) used a bottom-up approach based on empirically identified subscales of various DD measures. These five categories included treatment regimen, food/eating, hypoglycemia, future/complications, and negative emotional experiences related to diabetes. Here we provide a brief review of the various widely used DD measures (Table 20.1) and identify other measures containing subscales that also capture DD and review how available measures of DD differentially capture the categories of DD identified by Dennick et al. (2017).

Early Measures Developed to Capture Diabetes Distress

The ATT39 (Dunn et al., 1986) and questionnaire on stress in diabetic patients-revised (QSD-R; Herschbach et al., 1997) were the first measures developed to assess DD but are not commonly used today and have been criticized for their face validity (Dennick et al., 2017). Specifically, both appear to more accurately assess beliefs and attitudes about diabetes, rather than one’s emotional response. For example, while the ATT39 has been described as a measure of DD (Esbitt, Tanenbaum, & Gonzalez, 2013; Snoek, et al., 2015; Dunn et al., 1986), individual items are focused on appraisals (e.g., “diabetes is the worst thing that ever happened to me”). Similarly, the QSD-R aims to assess

Table 20.1 Examples of measures of diabetes distress

Measure	Population	Items	Description and subscales	Reliability			Validity	
				Internal consistency				
				Item-total correlation	Cronbach's α	Test-retest correlation	Face/content	Convergent
Problems areas in diabetes (PAID)[a]	451 female adults with type 1 and type 2 insulin users from the USA	20	Initial development did not include subscales	0.32–0.84	0.95	NR	Items were selected based on diabetes healthcare providers and patient interviews. Items were revised after pilot data was collected	General emotional distress Fear of hypoglycemia Disordered eating Treatment adherence Diabetes complications HbA1c
Diabetes distress scale (DDS)[b]	683 type 1 and type 2 (insulin (50.4%/tablet 42.5%/diet alone 7.1%) from the USA	17	Items assess diabetes emotional distress over the past month across four domains of emotional burden, physician-related distress, regimen-related distress, and diabetes-related interpersonal distress. Responses are rated on a six-point Likert scale (not a problem – a very serious problem)	0.93	0.88–0.93	NR	Items were selected based on the input of healthcare providers and literature and revised after a pilot data was collected and feedback from patients was elicited	Depressive measure (CES-D) Treatment adherence (meal planning, exercise) Treatment regimen Cholesterol
Type 1 diabetes distress scale (T1-DDS)[c]	305 adults with type 1 from the USA and 105 adults with type 1 diabetes from Canada	28	Items assess the unique sources of distress that pertains to individuals with T1D over the past month, across seven domains of powerlessness, negative social perceptions, physician distress, friend/family distress, hypoglycemia distress, management distress, and eating distress. Responses are rated on a six-point Likert scale (not a problem – a very serious problem)	0.91	0.76–0.88	0.74	Items were selected based on qualitative interviews, literature review, and interviews of diabetes healthcare providers	Depressive measure (PHQ-8) Complications (just US sample) QOL measure (WHO-5) A1c Hypoglycemia worry scale

[a]Polonsky et al. (1995), [b]Polonsky, Fisher, Earles, et al. (2005b), [c]Fisher et al. (2015)

stress related to living with diabetes (Duran, Herschbach, Waadt, Strian, & Zettler, 1995; Herschbach et al., 1997), though some questions aren't related to diabetes (e.g., 'I suffer from wind') and others focus on appraisals rather than emotional responses to diabetes.

The Problem Areas in Diabetes (PAID)

This 20-item self-report questionnaire (PAID; Polonsky et al., 1995) was one of the first measures developed to measure emotional distress in diabetes (Snoek et al., 2000; Welch et al., 1997). The PAID covers a range of diabetes-specific sources of emotional distress, with the development based on input from diabetes care providers, interviews with diabetes patients, and pilot testing (Polonsky et al., 1995). While the PAID is perhaps most commonly used, it has been criticized for its length, and it does not fully address physician-related distress (Dennick et al., 2017; Polonsky, Fisher, Earles, et al., 2005b; Schmitt et al., 2016). The PAID was initially developed without subscales. Yet, Snoek et al. (2000) used factor analysis to identify four factors of emotional problems, treatment problems, food-related problems, and social support-related problems from a sample comprised of 1696 Dutch and American diabetes patients. However, this four-factor structure was not found in Chinese (Huang, Courtney, Edwards, & McDowell, 2010), Norwegian (Graue et al., 2012), Turkish (Huis in T' Veld et al., 2011), or US rural African-American (Miller & Elasy, 2008) samples. A more recent factor analysis by Schmitt et al. (2016) that included 628 German participants with diabetes showed a similar four-factor structure to that of Snoek et al. (2000), but item loadings differed somewhat, and analyses showed a different number of factors between T1D and T2D. These findings suggest that the PAID factor structure is not consistent cross-culturally or across diabetes types. One study using a nationally representative sample of adults with T2D in Australia found that the PAID had excellent psychometric properties after the removal of four items, suggesting promise for a shortened version (Fenwick et al., 2016). There is support for the PAID's sensitivity to change in response to educational psychological and medical interventions in T1D, T2D, and in mixed samples (Welch, Weinger, Anderson, & Polonsky, 2003).

The Diabetes Distress Scale (DDS)

This 17-item self-report measure was developed with the input of healthcare providers and patients, to assess four a priori domains. The DDS shows a reliable and generalizable factor structure and good internal reliability for the total score across all four subscales (Polonsky, Fisher, & Earles, 2005b). In a nationally representative sample of Australian adults, the emotional burden subscale showed the best psychometric properties followed by the regimen-related distress subscale (after the removal of item 5), while the physician and interpersonal distress subscales demonstrated poor psychometric precision (Fenwick et al., 2016). Fisher, Hessler, Polonsky, & Mullan (2012) identified cut points for classifying T2D patients as experiencing little or no DD, moderate DD, and high DD, based on the consistent pattern of curvilinear relationships between the DDS and A1c, diabetes self-efficacy, diet, and physical activity. Similar to the PAID, the DDS is most accurately conceptualized as identifying problem areas within the situational context of diabetes, rather than measuring emotional distress alone. Each item begins with, "Feeling that…" but what follows is a diverse set of feelings, appraisals, judgments, and beliefs. The DDS has been shown to be sensitive to change in psychological interventions (Hermanns et al., 2015; Quinn et al., 2017) and a glucose monitoring technology-based intervention (Mora et al., 2017). A brief two-item DDS (DDS-2) was developed for screening purposes by extracting two questions from the larger scale (Fisher, Glasgow, Mullan, Skaff, & Polonsky, 2008) and has been shown to accurately identify 96.7% of individuals at high risk of DD when compared with the full scale (Fisher, Glasgow, et al., 2008). However, it is unclear whether the DDS-2 shows acceptable internal consistency and content and criterion validity (Lee, Lee, Kim, & Moon, 2015).

The DDS was revised to create the 28-item Type 1 Diabetes Distress Scale (T1-DDS) to specifically address the unique challenges that adults with T1D face, across seven subscales (Fisher et al., 2015). The T1-DDS was found to have good internal consistency, excellent test-retest reliability, and good evidence of validity, including discriminant validity with measures of depression (Fisher et al., 2015; Fisher et al., 2016). A qualitative analysis of focus groups with adults with T2D suggests that those on insulin regimens reported aspects of DD that were better covered by the T1-DDS content than the DDS (Tanenbaum et al., 2016).

Subscales Assessing Diabetes Distress

Dennick et al. (2017) identified three measure subscales with adequate face validity to be included as measures of DD. This includes the "diabetes-specific well-being" subscale of the well-being questionnaire 28 (W-BQ28; Bradley, 2000; Speight & Bradley, 2002; Speight, Khagram & Davies, 2012), the "burdens and restrictions – daily hassles" subscale of the diabetes-specific quality of life scale (DSQoLs-R; Bott, Muhlhauser, Overmann, & Berger, 1998; Cooke et al., 2013), and emotional representations subscale of the illness perceptions questionnaire-revised (IPQ-R; Moss-Morris et al., 2002; Weinman, Petrie, Moss-Morris, & Horne, 1996).

These subscales tend to capture more general emotional experiences related to diabetes, rather than capturing the specific sources of distress, as the PAID and DDS do. This is particularly the case for the IPQ-R subscale which exclusively assesses emotional experience related to illness in general terms (e.g., "my illness makes me feel afraid"). The other two subscales also capture more general emotional responses, though they also include items tapping regimen-related distress. For example, the W-BQ28 diabetes-specific well-being subscale includes questions such as "I feel stressed by keeping to a schedule with my diabetes," while the daily hassles subscale of the DSQoLs-R includes the item "It bothers me that I have to spend so much time on my diabetes treatment." These subscales show adequate psychometric properties (Dennick et al., 2017).

Comparison of the Available DD Measures

As reviewed by Dennick et al. (2017), treatment regimen-related distress is most thoroughly captured by the DDS and T1-DDS but is also assessed by the PAID, the W-BQ 28 subscale, and DSQoLS-R subscale. Food and eating-related distress is most comprehensively captured by the PAID and T1-DDS but is also assessed by the DDS and DSQoLs-R subscale. Hypoglycemia-related distress is most captured by the T1-DDS and is also assessed by the PAID. The DDS does not capture hypoglycemia-related distress. Worry about the development of complications, and the future more generally, is assessed by the DDS, the T1-DDS, the PAID, and W-BQ28 subscale. The PAID also captures emotional distress surrounding complications that have already developed. Negative emotional experiences resulting from living with diabetes is covered more comprehensively by the PAID compared to the DDS and is exclusively assessed by the IPQ-R. The T1-DDS and DSQoLS-R subscale do not provide much or any coverage of this element.

When comparing the PAID and DDS, the PAID is focused more on problems related to food and covers a wider range of emotional concerns than the DDS (e.g., emotional burnout and nonacceptance of diabetes; worry about hypoglycemia), while the DDS is focused more on problems surrounding self-management and physician-related distress. Related to these content differences, Schmitt et al. (2016) showed that the PAID was associated more strongly with negative coping styles, depressive symptoms, and functional status, while the DDS was associated more strongly with measures of self-management and glycemic control.

Quality of Life in Diabetes

Introduction

Increasing appreciation of QOL as an important PRO in diabetes reflects a relatively recent reconceptualization of health, influenced by the growing recognition of the limitations of purely biomedical definitions and acceptance of contextual models of health and illness (e.g., Engel, 1977). In contrast to the dominant biologically reductionist approach, Engel and others championed a view of health that prioritized the patient's subjective experience alongside the results of blood tests and other biological data. Influential definitions had pushed against deficit models for a broader concept of health since at least 1948, when the World Health Organization (WHO) defined health as, "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (WHO, 1946). Fifty years later, the WHO further expanded the scope of patient outcome research and emphasized the importance of the individual's subjective perceptions of their experience when it defined QOL as "the individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns" (WHOQOL Group, 1998). As is evident from the WHO definition, measures of QOL should focus on the individual's subjective judgment of the quality of their life in comparison to some ideal, in light of perceived importance and personal expectations, and not simply reports of physical or cognitive functioning, somatic symptoms, negative or positive emotional states, or social integration (Leventhal & Colman, 1997; Carr & Higginson, 2001).

Research on life satisfaction represents another robust tradition of theoretical and empirical investigation relevant to conceptualizing QOL. From this perspective, QOL is inclusive of the experience of positive and negative emotional states, satisfaction with various domains of life, and overall life satisfaction (Diener, Suh, Lucas, & Smith, 1999). Similar to the WHO definition of QOL, this work also emphasizes the importance of the individual's subjective experience and preferences and avoids setting external criteria or normative definitions for QOL (e.g., Diener, 1984). The Satisfaction With Life Scale, the most widely used instrument in this research area, assesses respondents' extent of agreement with five statements about their satisfaction with life, the extent to which their life matches their ideals and expectations, and the overall conditions of their life (Diener, Emmons, Larsen, & Griffin, 1985). Studies evaluating life satisfaction interpret responses to this scale as reflecting how a person feels about life in the context of personal standards, preferences, and ideals (Diener & Suh, 1997). As such, this body of work adheres closely to the definition of QOL promoted by the WHO and others.

Standardizing the measurement of QOL in the vast number of research studies that have aimed to evaluate it has proven to be a difficult task. Early criticisms of the field already noted a failure of most studies to define QOL or to directly assess respondents' judgment of it, and a tendency to focus instead on domains of experience and functioning that were deemed to be important to QOL by the investigators rather than by the individuals whose QOL was in question (Guyatt, Feeny, & Patrick, 1993; Gill & Feinstein, 1994). As Katschnig (1997) puts it, a review of the literature would lead a reasonable observer to conclude that QOL is, "a loosely related body of work on psychological well-being, social and emotional functioning, health status, functional performance, life satisfaction, social support, and standard of living, whereby normative, objective and subjective indicators of physical, social and emotional functioning are all used" (p. 3–15; Katschnig, 1997). The diversity of these constructs and the often-overlapping measures used to assess them have led to considerable confusion in the literature.

Qualifying the scope of measurement by using the more specific label, HRQOL, does not avoid these definitional issues. Following from WHO's definition of QOL, HRQOL can be conceptualized as the impact of an illness like diabetes and its treatment on a person's life in ways that are significant to that person (Speight, Reaney, & Barnard, 2009). Thus, although the effects of health, illness, and treatment might be evident in overall measures of QOL, measurement of HRQOL provides an opportunity to focus on these particular effects, which might be more difficult to disentangle from the effects of other non-health-related factors that influence general QOL ratings. When individuals with diabetes are asked about what is important to their QOL and how diabetes affects these aspects, they tend to mention various domains of life, such as family, work and school, their social life, as well as leisure activities and holidays (Barnard, Speight, & Skinner, 2008; Walker & Bradley, 2002; Woodcock, Bradley, Plowright, Kennedy-Martin, & Hirsch, 2004). Thus, HRQOL in diabetes refers to an individual's perception of the ways that illness, health, and treatment influence the domains of their life that are most important to their QOL (Bradley & Speight, 2002; Moons, 2004; Rubin & Peyrot, 1999). Although the expected increased sensitivity of HRQOL to the effects of diabetes and its management represents an advantage over general QOL measures, the focus on health-related aspects of QOL has led to the proliferation of studies that endeavor to measure diabetes-related QOL with measures of patient-reported health status, diabetes symptoms, and self-management.

Differentiating HRQOL from Health Status in Diabetes

The most major conceptual models for QOL in the context of health and illness differentiate between health status, physical symptoms, and functioning on the one hand and QOL on the other. Health status is conceptualized as having a causal impact on QOL but is not synonymous with it. For example, Wilson and Cleary (1995) proposed that biological and physiological factors, symptom status, functional status, and general health perceptions interact with characteristics of the individual (e.g., values and preferences) and characteristics of the environment (e.g., social and psychological supports) to influence QOL, which is also influenced by other non-health-related factors (e.g., socioeconomics, life events, interpersonal relationships, work, etc.). However, the distinction between health status and QOL has been inconsistently operationalized and has led to much confusion in the literature, where measures of health status are often interpreted as indicators of QOL and/or incorrectly labeled as measures of QOL.

Although health status can have important impacts on QOL, poor health status or functioning is not always indicative of a low QOL (Albrecht & Devlieger, 1999; Bradley & Speight, 2002; Carr & Higginson, 2001; Testa & Simonson, 1996). The missing mechanism linking these constructs is the individual's judgment about how impairments in functioning influence QOL, involving a weighting of affected domains based on importance and on a consideration of QOL prior to illness onset or treatment initiation (Albrecht & Devlieger, 1999; Carr & Higginson, 2001; Leventhal & Colman, 1997). Patient-centered approaches to defining and measuring QOL, where respondents select relevant domains of QOL and weight their importance, suggest that physical health is more rarely mentioned as an important determinant of QOL than we might expect, particularly among older adults who generally experience the greatest levels of health-related functional impairment, relative to other age groups (Browne et al., 1994; Hickey, Barker, McGee, & O'Boyle, 2005; McGee, O'Boyle, Hickey, O'Malley, & Joyce, 1991). Individuals appear to place greater emphasis on physical functioning when reporting health status, while emotional functioning plays a larger role when appraising QOL (Smith, Avis, & Assman, 1999). These distinctions are especially important in the context of diabetes where pursuit of excellent health status, as indicated by near-normal blood sugar levels, could conceivably result in a deterioration in QOL if the experience of excessive treatment burden and side effects, increased risk for hypoglycemia, and restrictions in dietary freedom outweigh the experienced benefits of improved glycemic control (Bradley, 2001).

Interestingly, both the potential promise and the measurement-related limitations of QOL assessment in diabetes care are clearly illustrated by QOL data from the first two major landmark trials of intensive treatment in T1D and T2D that have had the greatest influence in modern diabetes care throughout the world, the DCCT (DCCT Research Group, 1993) and the UKPDS (UKPDS Group, 1998). The diabetes quality of life (DQOL) scale was specifically developed for use in the DCCT with the goal of elucidating the QOL-related costs and benefits of intensive treatment, which was recognized as being more demanding for patients to implement and self-manage than standard care. Content included items on: (1) satisfaction with both diabetes-related and general aspects of life; (2) impact of diabetes, as defined by a diverse set of items assessing psychological, physical and social functioning, and somatic experiences; (3) worry about not meeting family, social, vocational, and leisure goals; and (4) worry about negative physical, social, and relational consequences of having diabetes (DCCT Research Group, 1988).

Perhaps due to totaling of such diverse issues represented by item content (Bradley, 2001), the DCCT failed to demonstrate any differences between intensive and standard treatment arms (DCCT Research Group, 1993; DCCT Research Group, 1996). However, compelling longitudinal data from 23 years of follow-up of the DCCT cohort showed that DQOL total scores were able to significantly differentiate among those who experienced increased A1c, albumin excretion rate, mean blood pressure, body mass index, and occurrence of severe hypoglycemia. Lower DQOL scores were also associated with the development of diabetes complications, the experience of a greater number of somatic symptoms, and to psychiatric events; DQOL scores between intensive and conventional treatment arms continued to be equivalent (Jacobson et al., 2013). Thus, although the DQOL was based on patient input, at least somewhat specific to respondents' experience with diabetes and its management, was sensitive to diabetes-related health impairments, and captured emotional well-being as an important aspect of QOL, it was unable to show a benefit of intensive treatment in T1D.

The UKPDS investigators also recognized the importance of evaluating the effects of intensive treatment in terms of QOL for patients with T2D and included assessment of QOL as a patient-reported outcome of the trial (UKPDS Group, 1999). However, the measures used to capture QOL consisted of reports of positive and negative mood states, cognitive complaints, somatic symptoms, work satisfaction, and a health status measure assessing mobility, self-care, usual activities, pain, and anxiety, as well as an overall rating of perceived health, the EQ5D (Brooks, 1996; EuroQol Group, 1990). Contrary to expectations, results showed no significant benefit of intensive therapy across any of these "QOL" measures. Similar to the results for the DQOL in DCCT, significant relationships were observed for various indicators of QOL (primarily captured by mood states and general health status) and complications of diabetes and the experience of hypoglycemia (UKPDS Group, 1999). The UKPDS investigators' conclusion that their results demonstrate that the effects of intensive therapy on patient QOL "were neutral in effect" (UKPDS Group, 1999) has been appropriately criticized for being misleading (Bradley, 2001). As it involved assessment of neither patients' judgments about overall QOL nor the impact of diabetes on QOL, UKPDS results are mostly unable to address this question.

Currently ongoing landmark trials of diabetes treatments, such as the GRADE study, a large comparative effectiveness trial of intensive treatment regimens for T2D, continue to measure QOL with measures of health status and functioning, contributing to ongoing limitations in evidence for the costs and benefits of intensive diabetes treatment for QOL (Nathan et al., 2013). More routine assessment of QOL in such trials, in a manner that is consistent with the way it has been defined by experts and patients alike, through use of measures that avoid overlap with health status and other potential influences on HRQOL is necessary to address this question.

Associations Between Diabetes and QOL

The distinction between health status and QOL continues to be important when interpreting the QOL literature related to the presence of diabetes overall. For example, one of the few studies to examine longitudinal relationships between "HRQOL" across the T2D continuum (i.e., normal glucose tolerance, prediabetes, and T2D) showed reductions in physical functioning and increased psychological symptoms particularly when comparing prediabetes and T2D (Hunger et al., 2014). As the "HRQOL" measure used was, in fact, a measure of general health status (the SF-12), a more accurate interpretation would be that the presence of T2D is associated with reduced physical and emotional functioning, compared to those with prediabetes or normal glucose functioning. These findings are in line with other cross-sectional studies that have consistently shown reductions in physical and emotional functioning across groups of patients with normal glucose metabolism to those with prediabetes and T2D (Neumann et al., 2014; Seppälä, Saxen, Kautiainen, Järvenpää & Korhonen, 2013; Väätäinen et al., 2014). Similarly, individuals with T1D report reduced physical, mental, social, and role functioning compared to those without diabetes (e.g., Hänninen, Takala, & Keinänen-Kiukaanniemi, 1998).

Measures of patient-reported health status and functioning, often described by investigators as measures of HRQOL, have been associated with worse glycemic control among individuals with T2D (Goddijn et al., 1999; Kartal & İnci, 2011), T1D (Hassan, Loar, Anderson, & Heptulla, 2006; Jacobson et al., 2013; Nerenz, Repasky, Whitehouse, & Kahkonen, 1992; Wikblad, Leksell, & Wibell, 1996), and in mixed T2D/T1D samples (Lau, Qureshi, & Scott, 2004). However, it is important to note that these results are not consistently reported, with some studies showing no relationship between glycemic control and these measures (Lee et al., 2009; Lloyd, Sawyer, & Hopkinson, 2001; Sundaram, Kavookjian, Miller, Madhavan, & Scott, 2007; Weinberger et al., 1994). Hypoglycemic episodes and their severity have also been associated with self-rated physical and mental health status among individuals with T2D (Alvarez-Guisasola, Yin, Nocea, Qiu, & Mavros, 2010; Green, Fox, Grandy, & SHIELD Study Group, 2012). Some studies show that T2D patients treated with insulin report worse functional status and aspects of QOL than those treated through dietary management or with an oral antihyperglycemic medications (Redekop et al., 2002; Rubin & Peyrot, 1999). Insulin treatment has also been related with increased DD (Delahanty et al., 2007), a potential mechanism explaining impacts of treatment on HRQOL in diabetes. Insulin regimens are often viewed negatively by T2D patients (Rubin et al., 2009); however, disentangling the effects of insulin therapy from the effects of poorer health and more advanced diabetes is difficult outside the context of the randomized controlled trial. The development of diabetes complications is described as one of the most significant diabetes-specific determinants of QOL (Huang et al., 2007; Rubin & Peyrot, 1999). Diabetes complications and comorbid medical conditions have also been associated with reduced health status and functioning in T2D (Redekop et al., 2002; Wexler, et al., 2006) and in mixed samples of T1D and T2D (Coffey et al., 2002; Glasgow, Ruggiero, Eakin, Dryfoos, & Chobanian, 1997; Maddigan, Feeny, & Johnson, 2005). Thus, although many studies aim to assess QOL in diabetes, measurement limitations preclude clear conclusions. Evidence that a medical or behavioral intervention is associated with a decrease in symptoms or an increase in treatment satisfaction has little to say about the effects on QOL.

Few studies have used appropriate measures of HRQOL to examine the QOL impacts of various aspects related to diabetes (e.g., glycemic control, hypoglycemia, complications, insulin use). A recent multinational study using the Audit of Diabetes-Dependent Quality of Life (ADDQOL) in 5813 adults with T2D showed an overall negative impact of diabetes on QOL – nearly ¾ of patients reported that their QOL would be better without diabetes (Bradley et al., 2018). All QOL domains were negatively impacted by diabetes, with freedom to eat showing the highest weighted impact, followed by freedom to drink and feelings about the future. Optimal glycemic control was significantly associated with less negative impact of diabetes on QOL but not with ratings for overall QOL. Complications, comorbid conditions, and symptoms were also related to diabetes impact and overall QOL ratings. More intensive treatment regimens, including three or more oral agents or insulin, were associated with significantly worse QOL, and use of insulin alone was also associated with worse QOL. In contrast, a measure of patient-reported health status showed no significant relationships to glycemic control or treatment intensity, although they were related to complications, comorbid conditions, and symptoms (Bradley et al., 2018). Additionally, a study of 558 older Italian outpatients with T2D that included the ADDQOL showed that insulin use was associated with more negative QOL when compared with oral agents and showed a nonlinear relationship between perceived HRQOL and improved glycemic control over time (Abbatecola et al., 2015). Further, a double-blind RCT of 89 patients with diabetes and depression showed that antidepressant treatment decreased A1c and improved HRQOL, as measured with the D-39; however, D-39 scores improved regardless of treatment arm, and A1c was more closely associated with depression than HRQOL (Echeverry, Duran, Bonds, Lee, & Davidson, 2009). Furthermore, a retrospective cohort study from a self-management program RCT showed that change in A1c from baseline to 1 year was associated with improvements in diabetes-39 diabetes control and sexual functioning subscales (Khanna et al., 2012).

QOL and Emotional Distress in Diabetes

Diabetes behavioral interventions emphasize both DD and QOL as outcomes of focus (Peyrot & Rubin, 2007) but rarely compare the relationships between these two constructs. Studies including both measures as outcomes show consistent relationships between total QOL and DD scores (Arnold et al., 2004; Dismuke et al., 2014; Strine et al., 2008; Tol et al., 2015) and depressive symptoms and diabetes-specific QOL (Sundaram et al., 2007), though few studies have examined more detailed relationships between particular DD and QOL domains. Emotional well-being, and conversely emotional distress, is a component of QOL. For this reason, DD has been conceptualized as a singular determinant of the multidimensional concept of QOL (Glasgow et al., 1997). HRQOL measures often include diabetes-related emotional distress in their item content. Examples of item content that reflect DD include worries about the future of health (from the ADDQoL), being embarrassed because of diabetes (from Diabetes 39), and how often do you feel good about yourself (DQOL).

One study involving a T2D sample did examine relationships between DD and QOL domains using a generic QOL measure (Carper et al., 2014). This study found that DD was associated with an overall reduced quality of life, and particularly with reductions in perceived functioning in the achievement domain and, though marginally significant, with psychosocial growth (Carper et al., 2014). These associations likely reflect that QOL is a subjective multifaceted construct comprising both positive and negative conditions in the context of individual expectations for QOL with a chronic illness (Diener, 1984; Diener et al., 1999).

Assessing HRQOL in Diabetes

Despite the complex measurement issues already noted, earlier reviewers have conjectured that diabetes researchers and health professionals generally select HRQOL measures based on what has been previously used or by selecting a scale with “QOL” in the title regardless of its content (Polonsky, 2000). Instead, Fisher, Tang, and Polonsky (2017) have recommended a three-step process for selecting a good HRQOL for one’s research needs. First, specific anticipated immediate outcomes of intervention should be defined, such as improved flexibility in eating or reduced hypoglycemia. Second, how changes in these proximal outcomes might influence HRQOL for a specific group of patients should be specified. Finally, a HRQOL measure can be selected based on expected QOL impacts of these effects (Fisher et al., 2017). In some cases, specific measures can provide the most information. For example, Vileikyte et al. (2003) found that the Neuro-QOL, a measure designed specifically for patients with diabetic peripheral neuropathy and diabetes-related foot problems, was sensitive to clinical measures of neuropathic severity, whereas a more general measure of health status and functioning, the SF-12, was not. Table 20.2 provides examples of measures of QOL/HRQOL that conform to the conceptual definitions provided in this chapter and that have been widely used in diabetes.

Table 20.2 Examples of measures of diabetes-related quality of life

Measure	Population	items	Description and subscales	Reliability			Validity	
				Internal consistency				
				Item-total correlation	Cronbach's α	Test-retest correlation	Face/content	Convergent
Diabetes quality of life (DQOL)[a]	136 adults and 56 adolescents with type 1 diabetes from the USA	46	Items assess common issues of diabetes in those with type 1 diabetes on current functioning, regardless of treatment or self-monitoring methods across four domains of life satisfaction, treatment impact, diabetes worry, and social/vocational worry. Responses are rated on a five-point Likert scale (uses a range of scales some e.g., no impact-always effected; no worries-always worries)	0.92	0.66–0.92	0.78–0.92	The DQOL was developed as part of the DCCT. Items were selected based on literature review as well as patient and healthcare providers input, and pilot testing	Well-being Psychiatric symptom check list Adjustment to illness
Diabetes 39 (D-39)[b]	516 adults, the majority were persons with type 2 diabetes treated with insulin from the USA	39	Items assess how much diabetes and its treatment affects the persons QOL in the past month, across five domains of energy and mobility, diabetes control, anxiety/worry related to diabetes, social burden, and sexual functioning. Response are rated on a seven-point visual analogue (not affected at all – Extremely affected)	0.45–0.84	0.81–0.93	NR	Initial items were selected based on literature review, interviews with healthcare providers and patients, and pilot testing	Health status (SF-36)

Audit diabetes-dependent quality of life (ADDQoL)[c]	795 adults with type 1 and type 2 diabetes from the UK	20	18 scale-items assess the effects of diabetes across domains of freedom to eat, enjoyment of food, family life, employment/career life, sex life, physical activity, worries about the future, holidays or leisure activities, freedom to drink, confidence in ability to do things, friendships and social life, motivation to achieve things, ease of traveling, physical appearances, finances, living conditions, dependence on others, reactions from society	0.37–0.67	0.92	NR	Items were selected based on interviews of 12 adults with type 2 diabetes eliciting aspects of diabetes that effected their QOL, and discussions with professional healthcare providers	Treatment satisfaction (diabetes treatment satisfaction questionnaire)
Neuro-QOL[d]	418 adults with diabetic peripheral neuropathy and either type 1 or type 2 diabetes from the UK and USA	43	Items assess the specific effects of peripheral neuropathy and foot ulcers on persons with diabetes QOL across two scales of physical symptoms (pain, reduced feeling, diffuse sensory motor) and psychosocial symptoms (interpersonal/emotional burden, activity limitations)	Scales correlation,: 0.39–0.67	0.86–0.95	NR	Items were developed based on interviews with experts and patients, literature review, and pilot testing	NR

[a]DCCT Research Group (1988), [b]Boyer & Earp (1997), [c]Bradley et al. (1999), [d]Vileikyte et al. (2003)

Diabetes QOL (DQOL)

The 46-item DQOL was initially developed to be used as a measure of QOL in the DCCT that compared intensive to typical treatment among patients with T1D (DCCT Research Group, 1988) and is one of the earliest measures of HRQOL. The measure was also found to be applicable to T2D patients (Jacobson, 1997). Patients are asked to rate issues as it affects their current functioning (DCCT group, 1988), which places this measure in the domain of being a health status measure. Yet, the inclusion of satisfaction questions such as "How satisfied are you with life in general?" also aligns this with assessment of diabetes-specific QOL. Evidence for sensitivity to change has been inconsistent. The DQOL was found to be sensitive to simultaneous pancreas/kidney transplant compared to a kidney transplant alone in T1D (Nathan et al., 1991) but was not sensitive to an intervention of continuous insulin compared to multiple daily injections (Tsui, Barnie, Ross, Parkes, & Zinman, 2001). As noted above, the DQOL was not sensitive to the effects of intensive treatment in the DCCT.

The Diabetes 39 (D39)

The D-39 was developed almost a decade after the DQOL was introduced (Boyer & Earp, 1997). Design of this measure was done in two phases. During the initial phase, information was gathered from interviews with health professionals and diabetes patients, as well as from reviewing the literature and previously developed QOL measures. This led to the development of 92 questions that were then reduced down to 42 questions after pilot testing. In the second phase, individuals with diabetes completed the 42 item questionnaire, which was reduced down to 39 items after factor analysis. These 39 items ask about five domains: energy and mobility, diabetes control, anxiety and worry, social burden, and sexual functioning (Boyer & Earp, 1997). The D-39 was the first diabetes-specific measure to assess how a person's perceived functioning contributes to their overall sense of QOL, which clearly distinguishes it from health status measures. For example, the D-39 asks individuals with diabetes to rate "During the past month how much was the quality of your life affected by" which include responses such as "limited energy levels," "feeling depressed or low," or "diabetes in general." The D39 has been shown to be sensitive to a self-management intervention and changes in A1c (Echeverry et al., 2009; Khanna et al., 2012).

The Audit of Diabetes-Dependent Quality of Life (ADDQoL)

The 19-item ADDQoL was developed around the same time as the D-39 (Bradley et al., 1999), and like the D-39 improves on the DQOL in more directly assessing how functioning and the presence of diabetes impact one's overall sense of QOL. The development of the ADDQoL was based on review of previous QOL measures, as well as interviews with health professionals and patients, which led to the inclusion of 19 items pertaining to social, physical, and emotional domains (Bradley et al., 1999).

The ADDQoL was the first diabetes-specific HRQOL measure to include weights in its scoring that take into consideration the importance a patient places on various life domains in relation to their overall sense of QOL. In this way, a patient may report that diabetes very much impacts her or his physical abilities, for example, but if this aspect of their life is not important to them, a decrease in physical abilities will not have much of an impact on her overall ADDQoL score. Additionally, some domains have an option to select "not applicable" and are excluded from the total score if N/A is selected. The ADDQoL also includes assessment of overall QOL and impact of diabetes on overall QOL. One criticism of the ADDQOL is that it phrases questions as hypotheticals ("If I did not have diabetes…"), which is not recommended when assessing PROs (US Food and Drug Administration, 2006). The ADDQoL has been shown to be sensitive to treatment intensity and the presence of diabetes complications (Abbatecola, et al., 2015; Bradley, et al., 1999; Speight & Bradley, 2000) and to the effects of an educational intervention on flexible intensive insulin treatment (DAFNE Study Group, 2002).

The NeuroQOL

The 43-item NeuroQOL is a diabetes-specific measure of QOL that was designed and tailored to a specific set of issues related to diabetic peripheral neuropathy and related foot problems. The development of the NeuroQoL consisted of three phases: (1) items were developed based on discussions with experts, interviews with patients, and literature review; (2) pilot testing eliminated questions that did not meet criteria for inclusion; and (3) the measure was psychometrically validated among UK and US patients with well-characterized diabetic peripheral neuropathy (Vileikyte et al., 2003). The NeuroQOL captures functioning across six main domains: (1) pain and sensations of burning/throbbing in feet; (2) loss or reduction of feeling in the feet; (3) sensory motor symptoms while standing or walking, such as unsteadiness; (4) limitations in ability to perform daily work and leisure activities; (5) interpersonal issues including depending on others; and (6) emotional burdens associated with peripheral neuropathy. Additional domains assess sleep problems, side effects of medication, and overall impact of neuropathy. Finally, one item asks “Overall, I would rate my quality of life as” with the five-point response ranging from “excellent” to “poor.”

Cultural, Demographic, and Social Factors Related to QOL and DD

Contextual factors provide the ecological framework within which patients perceive and care for their health (Cabassa, Siantz, Nicasio, Guarnaccia, & Lewis-Fernández, 2014; Diez Roux, 2012) and have been consistently implicated in risk for the development of diabetes and in treatment outcomes among those living with T1D and T2D. These contextual factors include ethnicity, race, socioeconomic status, gender, and age, supporting a sociocultural-centered approach to understanding experiences of DD and HRQOL among diabetes patients.

Ethnicity, Race, and Socioeconomic Status

Prior research shows that individuals belonging to ethnic minority groups in the USA, particularly Blacks and Latinos, have a higher lifetime risk of developing diabetes when compared to non-Latino Whites (Centers for Disease Control and Prevention, 2014; Narayan et al., 2003). Diabetes also disproportionately burdens those from financially disadvantaged backgrounds (Kumari, Head, & Marmot, 2004; Spanakis & Golden, 2013). This increased burden appears to come from a variety of sources: disadvantaged individuals experience additional stressors in the healthcare system, including higher waiting time for services, less insurance coverage, and reduced quality of communication with physicians (El-Kebbi et al., 2003; Ferguson & Candib, 2002) and are less likely to receive diabetes education (Johnson, Ghildayal, Rockwood, & Everson-Rose, 2014). Patients receiving care from low-income clinics often have poorer glycemic control and higher DD (Pandit et al., 2014). Further, neighborhood distress is linked to low SES and can determine access to healthy foods, safe areas to exercise, and quality healthcare services (Brown et al., 2004) and has been associated with DD (Gariepy, Smith, & Schmitz, 2013).

These additional burdens can contribute to differences in patient reports of physical and emotional functioning as well as QOL. Specifically, ethnic minorities and lower SES individuals report a decreased functional status and higher emotional distress when compared to Whites and those with a higher SES in both T2D and T1D (Fisher et al., 2015; Goldney, Phillips, Fisher, & Wilson 2004; Narayan et al., 2003; Shallcross et al., 2015; Strandberg et al., 2014), as well as higher DD (LeBron et al., 2014). When considering our selected measures of HRQOL, limited information is available regarding associations with race/ethnicity and/or income. The majority of the validation papers include largely white samples, though the validation paper for the D-39 showed that the subsample with higher racial diversity and younger age consistently reported lower QOL compared to a homogenously white and older subsample (Boyer & Earp, 1997).

Factors Related to Gender and Age

Women and younger adults tend to report higher DD and worse functional status compared to men and older adults in both T2D and T1D samples (Boden & Gala, 2017; Boyer & Earp, 1997; Fisher et al., 2015; Glasgow et al., 1997; Goldney et al., 2004; Hessler et al., 2011; Irvine, Wright, Recchia, & De Carli, 1994; Nezu et al., 2014; Perrin et al., 2017; Rubin & Peyrot, 1999; Undén et al., 2008; Wexler et al., 2006). Gender differences may reflect increased negative social norms for women related to weight (Svenningsson, Marklund, Attvall, & Gedda, 2011), gender differences in coping and adjustment styles (Enzlin, Mathieu, & Demyttenaere, 2002), as well as structural gender inequalities. Age-related differences may reflect reduced self-management behaviors among younger patients (Albright et al., 2001; Bai, Chiou, & Chang 2009; Hessler et al., 2011), as well as higher expectations and greater demands in relation to functioning and health among younger compared to older adults. However, it should be noted that not all studies show consistent gender and age differences in DD (Baek et al., 2014) or health status and functioning (Boyer & Earp, 1997).

The relationships between gender, age, and assessments of overall QOL remain unclear, with several validation studies not reporting such relationships (Bradley et al., 1999; Vileikyte et al., 2003). No meaningful differences in overall QOL were found between the genders for the D-39 (Boyer & Earp, 1997). Yet, in the PANORAMA multinational study, an examination of the relationship between various PROs that included the ADDQoL and patient and illness factors showed that being male was associated with better health status and overall QOL as assessed by the ADDQoL, while being female was associated with greater fear of hypoglycemia (Bradley et al., 2018). In the same study, it was also found that being younger was associated with greater fear of hypoglycemia, better health status, and better overall QOL, while being older was associated with less perceived negative impact of diabetes on QoL (Bradley et al., 2018).

Conclusions

As healthcare providers are moving toward a broader model of health that places biological processes in the context of the individual's psychosocial and cultural environment, PROs such as DD and QOL have emerged as valid, reliable, and meaningful constructs reflecting aspects of a patient's health and well-being not fully captured by physiological measures alone.

Measuring the benefits and potential costs of diabetes care in terms of DD and QOL becomes particularly important for guiding care recommendations and informing shared decision-making among physicians and their patients. These decisions include whether a patient would benefit from more intensive treatments, taking into consideration the potential impact of intensive management on DD and QOL (e.g., Delahanty et al., 2007; Baek et al., 2014). Importantly, two treatments that similarly reduce A1c but differently impact DD or QOL should not be considered as equal options (Brown, Kennedy, Runge & Close, 2016). While landmark trials have begun including functioning and HRQOL measures as outcomes, the use of more sensitive measures and conceptual clarifications, particularly of HRQOL, would provide health professionals with a clearer picture of the relationship between various treatment options and patient experiences. Such knowledge could greatly improve shared decision-making, which has been increasingly emphasized in patient-centered diabetes care (Montori et al., 2006).

However, to ensure the best use of such PROs, it is of vital importance to improve conceptual clarity of the various PROs that are currently being used among diabetes patients, which has also been stressed by the FDA (US Food and Drug Administration, 2006). Specifically, the FDA has shown concern about psychometric properties and standardization of various PRO measures (Brown, et al., 2016; US Food and Drug Administration, 2006). In their guidance for industry (2006), the FDA proposes a process for PRO instrument development and modification, centered on four stages: (1) developing conceptual frameworks to identify concepts and domains that are important to individuals with diabetes; (2) creating instruments while considering item content, method of administration, period of recall, response scales, scoring and administration, and pilot testing; (3) assessing psychometric properties, including reliability, validity, sensitivity to change, and participant burden; and (4) modifying developed instruments to better reflect concepts and populations being assessed and improve method of administration or application to research. The incorporation of novel measurement techniques, including continuous glucose monitoring and ecological momentary assessment, represents an additional promising area for future research that can more adequately capture the within-person processes by which experiences with diabetes and its treatments are associated with the experience of DD and QOL. Retrospective reports of these constructs in study designs that attempt to relate these reports to distal outcomes (e.g., A1c) and crudely measured exposures (e.g., complications, yes/no) are limited in their ability to shed light on what is surely a bidirectional and dynamic process.

Several adjustments to measurement practices seem warranted based on the current review. Revision of DD measures to improve content validity would help move health providers toward measures of DD that meet regulatory standards for PROs to be used in clinical trials (Dennick et al., 2017; US Food and Drug Administration, 2006). Those constructing or revising measures should consider the wording of items, so that emotional responses are more clearly captured rather than cognitive or behavioral aspects related to an emotional response (Dennick et al., 2017). Qualitative studies could also help identify current omissions to the construct of DD and help identify additional domains not currently assessed by available measures. These efforts will hopefully allow us to more comprehensively measure DD in future studies and include measures of DD that meet international standards as primary research outcomes in clinical trials.

When considering HRQOL, agreement on conceptualization of HRQOL remains unclear, with some definitions focusing more on life satisfaction/well-being and others focusing more on overall life quality. Too often, studies use measures of health status and functioning in place of QOL, resulting in a significant loss of information regarding the patient's evaluation of their experience with medical treatments and other interventions related to diabetes prevention and control. Future work will need to further tease apart conceptual and measurement overlap between health and QOL. As pointed out by Fisher et al. (2017), HRQOL should be given equal status and importance as measures of glycemic control and self-care, in order to get a full picture of the impact of diabetes and the benefits and costs of various treatments and devices on individual patients.

Not only are QOL and DD central to a patient's health and disease outcomes, their assessment undoubtedly improves ethical, empathic, and efficient clinical practices and care. From a translational approach, as health professionals move forward in assessing PROs, it will be valuable to better understand the underlying biopsychosocial and cultural mechanisms linking PROs to objective measures of behavior and health (Young-Hyman et al., 2017). This biopsychosocial multidimensional view of diabetes transcends the individual to the broader cultural and ecological processes that surround patient's behavior in complex health and societal systems and will be essential to truly move toward a patient-centered model of diabetes prevention and care that focuses on outcomes that are important to patients.

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Chapter 21
Depression and Anxiety in Adults with Diabetes

Lindsay Blevins, Jeffrey S. Gonzalez, and Julie Wagner

Introduction

The earliest literature on psychological factors in diabetes tested the clinical hypothesis that type 1 diabetes was associated with personality factors that contributed to the development of the disease (Dunn & Turtle, 1981). Assessment of personality factors found no differences in samples of type 1 diabetes patients compared to the general population, refuting this hypothesis. In the 1990s, two landmark trials (the diabetes control and complications trial [DCCT] research group, 1993; UK prospective diabetes study [UKPDS] group, 1998) demonstrated both the unequivocal long-term benefits of glycemic control and, more importantly for our purposes, the intensive self-management required to achieve glycemic control. Living with type 1 or type 2 diabetes entails difficulties including a complex set of self-management behaviors, disruption of daily routines, experiences of hypo- and hyperglycemia, potentially uncomfortable social situations and aversive healthcare interactions, and onset of long-term complications. This spurred questions regarding whether people living with the burden of diabetes went on to develop higher rates of mental illness, or higher levels of subclinical symptoms of mental illness, than those observed in the general population. Ensuing studies documented that people with type 1 or type 2 diabetes were found to have high rates of mood, anxiety, and eating disorders and elevated subclinical symptoms of those disorders, although many initial studies did not include chronically ill comparison groups, thereby making it unclear whether the observed rates were attributable to diabetes per se or chronic illness more generally. The literature from this period also

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L. Blevins
The Institute for Family Health, New York, NY, USA

J. S. Gonzalez
Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA

Departments of Medicine (Endocrinology) & Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, USA

The Fleischer Institute for Diabetes and Metabolism, Albert Einstein College of Medicine, Bronx, NY, USA

New York Regional Center for Diabetes Translation Research, Albert Einstein College of Medicine, Bronx, NY, USA

J. Wagner (✉)
UConn Health, Farmington, CT, USA
e-mail: juwagner@uchc.edu

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documented that when a person with diabetes does develop significant psychological disturbance, their diabetes outcomes are worsened, including metabolic control, risks for long-term complications, hospitalizations, and even early mortality.

In the next decade, the landmark Diabetes Prevention Program in the United States (Knowler et al., 2002), and similar studies from other countries, established that healthy behavioral lifestyle changes confer the greatest modification of risk for type 2 diabetes compared to medications or placebo control. The focus on prevention of type 2 diabetes, combined with studies suggesting common biological underpinnings of metabolic dysregulation and mental illness (e.g., inflammation), led to larger, longitudinal studies that asked whether certain mental illnesses, or elevated subclinical symptoms, might increase risk for subsequent, incident diabetes. Moreover, individuals most at risk for diabetes, i.e., racial and ethnic minorities and those from low socioeconomic backgrounds, face unique experiences and exposures that can increase risk for depression and anxiety. Several prospective studies have since shown that social adversity and disorders, such as mood disorders, post-traumatic stress disorder, and serious and persistent mental illness, and/or the medications used in their treatments increase risk for subsequent type 2 diabetes. These studies have refined our understanding and led to the development of more sophisticated, *reciprocal*, biopsychosocial models of the interplay between psychological well-being and diabetes and their putative shared underpinnings. However, it remains unclear whether treating psychological risk factors such as depression or PTSD actually mitigates risk for onset of type 2 diabetes.

The types of psychological conditions that have been linked to adults with diabetes are varied, such as dementia (Ninomiya, 2014), substance use disorders (Walter, Wagner, Cengiz, Tamborlane, & Petry, 2017), eating disorders (Young-Hyman & Davis, 2010), and thought disorders such as schizophrenia (Perry et al., 2017). There is also a relatively small literature on psychological conditions in children with diabetes (Buchberger et al., 2016). This breadth of topics is beyond the scope of this chapter, however. Instead, this chapter will focus on the contextual factors associated with depression and anxiety in adults with diabetes. Whereas this chapter reviews depression and anxiety separately, it should be noted that it is difficult to study them in isolation due to symptom overlap and the tendency of depression and anxiety to co-occur. Excellent reviews of depression and anxiety in diabetes have been published in recent years (Holt, de Groot, & Golden, 2014; Smith et al., 2013), though none specifically address the environmental conditions beyond the individual's biological, psychological, and immediate social domains.

Researchers in the area of diabetes and mental health have a prevailing tendency to focus on individual level factors or perhaps just slightly beyond to immediate social domains such as family or patient-provider relationships. Such a tendency toward the individual may in part be due to training and professional discipline and associated lack of expertise in measurement and modeling of contextual factors. However, it should also be said that academic researchers tend to occupy a relatively privileged social standing that may blind them to the many ways in which deleterious contextual factors, rather than or in addition to individual factors, shape an individual's health and mental health outcomes. Indeed, cultures in the northern and western hemispheres – the provenance of much of this research – give primacy to the individual in determining her own fate. However, contextual factors such as geopolitical events, socioeconomic position, the healthcare system, and societal stigma hold promise for a comprehensive understanding of mental health in persons with diabetes. Indeed, environmental exposures beyond even the individual's awareness, to say nothing of control, such as certain toxins, may yet prove to be partly responsible.

Patients experiencing the psychological conditions under review may present with sufficient intensity, frequency, and duration to meet or exceed the threshold for a psychiatric diagnosis, e.g., major depressive disorder or generalized anxiety disorder. More frequently, however, patients present with subclinical symptoms that do not meet diagnostic criteria. Much of the research in this area has employed symptom checklists which preclude the determination of diagnosis per se. To the extent that the published literature allows, we will attempt to differentiate symptoms from diagnostic categories.

When the distinction is not clear from the literature or lacks particular importance, we will use the general terms "depression," "anxiety," or psychological conditions.

Living with diabetes can also create distress about the medical condition itself that, although related to depression and anxiety, may be qualitatively and quantitatively different. Unlike depression or anxiety, each of which is relatively circumscribed emotional experiences, *diabetes distress* refers to a broad spectrum of distress that may include worry, sadness, frustration, fear, feeling overwhelmed, or preoccupied. Yet, whereas depression and anxiety may be rooted in any number of precipitating factors, diabetes distress is de facto specifically rooted in the biopsychosocial impacts of diabetes (Fisher, Gonzalez, & Polonsky, 2014; Gonzalez, Fisher, & Polonsky, 2011). Another chapter in this volume specifically addresses diabetes distress. Therefore, in this chapter we refer to diabetes distress only where necessary to draw a distinction between it and depression or anxiety.

Depression

Major depressive disorder (MDD) is characterized by symptomatic episodes that last at least 2 weeks and include either marked loss of interest or pleasure and/or depressed mood in combination with several other somatic, psychological, and cognitive symptoms (American Psychiatric Association, 2013). Symptoms include appetite disturbance, changes in weight, insomnia/hypersomnia, psychomotor agitation/retardation, fatigue, feelings of guilt and worthlessness, diminished concentration, and recurrent suicidal ideation (American Psychiatric Association, 2013). Persistent depressive disorder (PDD; previously called dysthymia) is a less severe but more chronic presentation of depression with symptoms lasting at least 2 years. Subclinical elevations in depressive symptoms that comprise these diagnostic categories are also quite common and should be differentiated from these psychiatric disorders. Such elevations may be more reflective of emotional distress related to life stressors rather than MDD (Coyne, 1994). Although most studies of depression in diabetes target MDD as the construct of interest, they tend to use measures that are more suited to identifying elevations in depressive symptoms, leading to some inconsistency and inappropriate conclusions regarding what is reflected by these measures in the literature. Subclinical elevations in depressive symptoms may also be reflective of diabetes-related distress, which is conceptualized as reflecting emotional distress that is specifically caused by the burdens of living with diabetes and its management (Polonsky et al., 1995, 2005). These assessment issues will be discussed in detail in the section "Measurement" below. Readers are also referred to the chapter in this volume on diabetes-related distress.

Prevalence

MDD affects approximately 6.9% adults in the United States over a 12-month period (National Institute of Mental Health), while PDD affects 1.5% of adults in the United States over a 12-month period (National Institute of Mental Health). Research shows that the prevalence of depression is increased across a variety of chronic illnesses, including diabetes (Huang, Dong, Lu, Yue, & Liu, 2010). Meta-analyses of the available research literature on individuals living with type 1 or type 2 diabetes suggest that MDD is 1.2–2.2 times more likely to occur in adults diagnosed with type 2 diabetes compared to those without (Ali, Stone, Peters, Davies, & Khunti, 2006; Anderson, Freedland, Clouse, & Lustman, 2001). Relatively few studies have used the gold-standard assessment approach to diagnosis of depression, a semi-structured clinical interview of symptoms. Studies published subsequent to these meta-analyses suggest that when the gold standard clinical interview is used, elevations appear to be more modest than when depression is measured by self-report symptom scales (Ali et al., 2006; Barnard, Skinner, & Peveler, 2006; Fisher et al., 2008). Although much less evidence is available, according to international data collected via clinical interview from the World Health Organization's World Mental Health Surveys, PDD prevalence does not appear to be elevated among those with diabetes; the same data showed the odds of MDD were 1.4 times (95%CI: 1.2–1.6) higher for adults with diabetes as compared to those without (Lin et al., 2008).

Analysis of nationally representative data from the National Health and Nutrition Examination Surveys (NHANES) 2005–2010 showed that 12.6% of adults with diagnosed diabetes had a positive screening result on a widely used self-report measure for depressive symptoms. However, only 5.9% reported symptom patterns consistent with the diagnostic criteria for MDD (i.e., requiring low mood and/or anhedonia, with a minimum of five total depressive symptoms for more days than not) (Gonzalez et al., 2017). A similar difference in prevalence was seen in method for defining positive cases for depression in a study of 6172 adults with type 1 diabetes (T1D) from across the United States who participated in the T1D Exchange. Although 10.3% reached the commonly used screening cutoff for a total number of self-reported depressive symptoms, only 4.6% reported patterns and durations of symptoms that are consistent with MDD diagnostic criteria (Trief et al., 2014). A systematic review of studies of depression prevalence among adults with T1D concluded that evidence was not strong enough to confirm a significant increase in prevalence for adults with T1D (Barnard et al., 2006). However, far fewer studies have focused on adults with T1D, as compared to those with T2D. Although only 810 adults with T1D were included, nationally representative data is also consistent with depressive symptom presentations consistent with MDD criteria being somewhat lower in adults with T1D (6.3%) than for adults with T2D, especially when compared to insulin-treated adults with T2D (13.3%); differences in prevalence are less apparent when focusing on elevated depressive symptoms (Li, Ford, Strine, & Mokdad, 2008).

Measurement

The accurate assessment of depression in individuals with diabetes presents several challenges. First, there is considerable overlap between the symptoms assessed on depression scales and those of poorly controlled diabetes and/or poor health (e.g., sleep disturbance, fatigue, appetite disturbance). Evidence suggests that these somatic symptoms can lead to an overestimation of depression prevalence based on self-report scales in individuals with diabetes (Twist et al., 2013). Furthermore, qualitative analysis of depression symptom interviews suggests that patients often respond to questions about depression symptoms with explanations that emphasize a causal role of diabetes-related symptoms. For example, individuals may experience sleep disturbance that is explained by frequent nighttime urination or blood sugar self-testing (Tanenbaum et al., 2013; Tanenbaum & Gonzalez, 2012).

Second, self-report measures for depression symptoms can often be more reflective of situational stress than of the presence of a psychiatric condition (Coyne, 1994). In particular, there is a growing body of evidence that suggests that elevations in depressive symptoms can often overlap with diabetes-related distress or emotional distress that is specific to living with the challenges of living with diabetes and the burdens of its demanding self-management regimen (Fisher et al., 2014; Gonzalez et al., 2011).

Finally, accurate diagnosis of MDD and other depressive disorders requires clinical evaluation and judgment 2013 (American Psychiatric Association, 2013) and cannot be arrived at by a self-report of symptoms. Therefore, readily implemented depression screening protocols relying on patient self-reports cannot separate true-positive cases from false-positive cases without further evaluation (see section on Screening below). Although semi-structured clinical interviews are the gold standard of depression assessment in clinical and research settings, these are rarely used in either setting.

Directionality and Potential Mechanisms

Longitudinal studies have documented a bidirectional relationship between depression and diabetes (Campayo, Gomez-Biel, & Lobo, 2011; Golden et al., 2008; Mezuk, Eaton, Albrecht, & Golden, 2008; Pan et al., 2012). Meta-analyses of longitudinal studies found increased risk for T2D among those with elevated depressive symptoms (Nouwen et al., 2010; Rotella & Mannucci, 2013a, b). One meta-analysis of 13 longitudinal studies found that increases in depressive symptoms resulted in a 60% increased risk of developing T2D over a follow-up period ranging from 3 to 16 years (Mezuk et al., 2008). This increase in risk is comparable in magnitude to that associated with smoking (Willi, Bodenmann, Ghali, Faris, & Cornuz, 2007). Conversely, a meta-analysis of 11 longitudinal studies found 24% increased relative risk for the development of depression associated with diagnosed T2D over follow-up periods ranging from less than two years to 10 years among adults who did not have depression at baseline (Nouwen et al., 2010).

Some evidence suggests that these effects may be moderated by age. For example, the Longitudinal Study of Aging found that T2D was associated with increased risk of future depression among adults age 52–64, but this effect was not significant among older adults 65 and over (Demakakos, Zaninotto, & Nouwen, 2014). Similarly, data from the National Social Life, Health, and Aging Project, a national area probability sample of community-dwelling Americans 57–85 years of age showed that diabetes was most strongly associated with increased depression among those age 57–64, more modestly associated among those age 65–74, and was not significantly associated with depression among those 75–5 (Wexler et al., 2012).

If the associations between depression in the context of diabetes and worse health outcomes are causal, there are various biobehavioral mechanisms that could plausibly account for these relationships. First, depression has been consistently associated with suboptimal diabetes self-management and treatment adherence (Gonzalez et al., 2008). It is plausible that depression symptoms, such as problems with concentration, sadness, and loss of interest, could directly complicate the tasks of diabetes self-management. However, treatment studies for depression in diabetes have generally failed to demonstrate positive impacts on treatment adherence or diabetes self-management (Markowitz, Gonzalez, Wilkinson, & Safren, 2011). Biological pathways are also plausible mechanisms for a causal effect of depression and related emotional distress on glycemic control and health outcomes through associated changes in central nervous system functioning, dysregulation of the hypothalamic-pituitary-adrenal axis with associated elevations in cortisol and other stress-related hormones, and elevations in biomarkers for inflammation, such as inflammatory cytokines and highly sensitive C-reactive protein (Moulton, Pickup, & Ismail, 2015; Tabak, Akbaraly, Batty, & Kivimaki, 2014). Depression and stress-associated sleep disturbance may also represent a pathway with implications for insulin sensitivity and glycemic control. In general, little direct evidence is available for treatment effects on these pathways, and what is available has not demonstrated effects of treatment on measured biobehavioral mechanisms (e.g., Hermanns et al., 2015). More research is needed, and there is some indication of potential differences in relations between depression and these markers between T1D and T2D (Herder et al., 2018).

Patient and Illness-Related Risk Factors

The available evidence highlights a number of patient-level factors that predict elevated risk for depression in diabetes. Risk factors include relatively younger adult age (Li et al., 2008; Wexler et al., 2012), female sex (Ali et al., 2006; Anderson et al., 2001; Egede & Zheng, 2003; Li et al., 2008; Lin et al., 2008; Trief et al., 2014), and pregnancy in women (Kozhimannil, Pereira, & Harlow, 2009).

Contradictory results have been found in studies examining race and the prevalence of MDD in those with diabetes. While one study found that Native American/Alaskan Natives had the highest rates (27.8%), followed by non-Hispanic whites (9.5%) (Li et al., 2008), other studies have shown that racial minorities with diabetes have reported more depressive symptoms than Caucasians (Fisher, Chesla, Mullan, Skaff, & Kanter, 2001; Welch et al., 2007).

Elevations in depressive symptoms only appear to occur among individuals who are aware of their diabetes diagnosis; individuals diagnosed with diabetes for the first time based on screening are no more likely to be depressed than those with normal glucose metabolism (Tabak et al., 2014; Mezuk et al., 2013). Such a pattern is consistent with the hypothesis that the elevations in depression are due to the psychological burdens of living with a life-threatening illness and its demanding self-management regimen. However, it is also likely that individuals who have been previously diagnosed with diabetes are more symptomatic and would likely have more advanced diabetes than those who are unaware of their diagnosis. Among adults with T2D, those treated with insulin have been consistently found to have higher prevalence of depression than those managed with oral medications or lifestyle modification. Although this pattern is also consistent with the hypothesis that increased risk of depression among insulin-treated adults with T2D is explained by increased treatment burden, it is again difficult to tease out the effects of advanced diabetes and poor health on the one hand and treatment burden on the other in accounting for these differences. This hypothesis also fails to account for the relatively lower levels of depression among adults with T1D, who likely have the most difficult self-management demands but appear to have the lowest levels of depression (e.g., Li et al., 2008). Obesity, which is consistently associated with increased risk for depression, may be another factor that complicates these relationships.

Studies show that comorbid illness is correlated with depression in those with diabetes indicating that having additional medical conditions increases the risk of depression in those with diabetes. Elevated depressive symptoms were 2.5 times more common in adults with T2D and at least one additional chronic illness (i.e., arthritis, cardiovascular disease, stroke, cancer, lung disease (Pouwer et al., 2003). Additionally, functional disability was found more often in those with both diabetes and MDD compared to those who only had one diagnosis (Egede, 2004). Diabetes complications also appear to be risk factors for increased depressive symptoms in adults with both T1D (Gendelman et al., 2009) and T2D (van Steenbergen-Weijenburg et al., 2011), with the severity of complications correlating with severity of depressive symptoms (e.g., Vileikyte et al., 2005, 2009).

Associations with Treatment Outcomes

An early meta-analysis found significant associations between depression severity and poor glycemic control in adults with T1D and T2D; results indicated that the association between depression and worse glycemic control was strongest among studies that based the measurement of depression on diagnostic criteria versus those that relied on self-report scales (Lustman et al., 2000). However, a number of more recent studies that have examined changes in depression and glycemic control over time have failed to find significant relationships (Aikens, 2012; Aikens, Perkins, Lipton, & Piette, 2009; Fisher et al., 2010; Georgiades et al., 2007; Richardson, Egede, Mueller, Echols, & Gebregziabher, 2008).

Few studies have examined relations between variations in depression and glycemic control on a moment-to-moment basis. One study measured positive and negative mood states each evening for 21 days and found that adults with T2D who reported more negative mood states were significantly more likely to have higher fasting blood glucose levels the next morning than those who had lower levels of negative affective states over the day. No such relationship was found for positive affect, and no effect of glucose levels on subsequent mood states was observed (Skaff et al., 2009). Similarly, a small study that related twice-daily assessments by automated phone survey of positive and negative affective states showed that higher mean levels of negative affect were associated with higher mean glucose, greater percentage of hyperglycemic readings, and greater percentage of out-of-range glucose. Greater variability in positive affect was related to lower percentage of hypoglycemia (Wagner et al., 2017). An additional small study of 23 women with T2D also indicated some significant relationships between negative mood states and greater glycemic variability (Penckofer et al., 2012). Further research examining moment-to-moment variations in depression symptoms, emotional distress, and mood states in relation to measures of glycemic control and variability measured by CGM represents a promising area for further research into the mechanisms that might explain observed associations between depression and glycemic control (Wagner, Tennen, & Wolpert, 2012).

Another meta-analysis published in 2001 demonstrated consistent links between elevations in depression and a range of diabetes complications in T1D and T2D (Lustman et al., 2000). Although the available studies at the time were all cross-sectional, subsequent studies have identified depression as a significant independent predictor of incidence of diabetes complications over time (Black, 1999; Gonzalez et al., 2010; Katon et al., 2010; Lin et al., 2010; Roy, Peng, & Roy, 2007; Roy, Roy, & Affouf, 2007; Williams et al., 2010). More recent meta-analysis of studies evaluating mortality outcomes in longitudinal studies also show that depression is a significant independent risk factor for early mortality in adults with diabetes (Park, Katon, & Wolf, 2013).

Meta-analysis of 47 independent samples of children, adolescents, and adults with T1D or T2D also demonstrated that depression elevations are significantly and consistently associated with poorer treatment adherence and diabetes self-management, across a variety of self-care domains (Gonzalez et al., 2008). The consistency of depression's relationship to suboptimal diabetes self-management represents one behavioral pathway that may account for the association between depression and poor diabetes treatment and health outcomes. However, depression treatment studies in diabetes have generally failed to document a resulting improvement in diabetes treatment adherence or self-management (Markowitz et al., 2011). Treatment studies also show that improvements in depression severity may not always lead to improved glycemic control (Ell et al., 2010; Katon et al., 2004; Lin et al., 2006; Williams et al., 2010).

Anxiety

Various anxiety disorders have been studied relative to diabetes. Generalized anxiety disorder (GAD) is characterized by intense worry that is difficult to control. Those with GAD often have concerns about unrealistic scenarios. Symptoms include restlessness, concentration difficulties, irritability, muscle tension, and sleep issues. Panic disorder is characterized by unexpected intense anxiety attacks that relate to arousal of the sympathetic nervous system and often include somatic symptoms such as hyperventilation, racing heartbeat, and sweating. Post-traumatic stress disorder (PTSD) develops after an exposure to an event that threatens death, serious injury, or sexual violence. Symptoms include hypervigilance, intrusive memories, feelings of shame or guilt, nightmares, sensitive startle response, and sleep difficulties.

Prevalence

Rates of anxiety problems comorbid with diabetes vary by study due to differences in sample size, sampling strategy, methods for ascertainment of diabetes and anxiety, and whether anxiety symptoms or disorders are investigated. Cultural factors may also play a role in prevalence rates and reporting. Taken together, the evidence indicates a modestly higher rate of anxiety disorders among adults with diabetes compared to nondiabetes comparators. Smith et al. (2013) conducted a meta-analysis of 12 studies and found that diabetes was associated with both anxiety disorders, odds ratio (OR) = 1.20, and elevated anxiety symptoms, OR = 1.48 (1.02–1.93). The pooled OR for all studies that assessed anxiety was 1.25.

An early systematic review of primarily clinical studies found that approximately 20% of persons with diabetes have one or more diagnosable anxiety disorders (Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002). Subsyndromal anxiety disorder, unspecified, and elevated anxiety symptoms were found in 27 and 40%, respectively, rates which were higher than in control samples. GAD was the most prevalent, present in 14% of patients with diabetes. Epidemiological studies in US Behavioral Risk Factor Surveillance Survey (Li et al., 2008) and internationally (Lin et al., 2008) are not inconsistent with these rates, although studies that make comparisons across countries suggest that culture may influence rates of anxiety and symptom reporting in persons with diabetes (Lloyd et al., 2003).

In a rare longitudinal study, patients with T2D for an average of 8-year duration were assessed three times over 18 months and found that, compared to community adults, patients with diabetes displayed 123% increased risk for GAD and 85% increased risk for panic disorder.

Anxieties unique to diabetes may not be assessed by common anxiety symptom checklists. Worry about the possibility of serious, long-term complications is often rated as a distressing aspect of both T1D and T2D (Snoek, Pouwer, Welch, & Polonsky, 2000). Fear of hypoglycemia is also a common concern that may cause patients to avoid insulin use (Fidler, Elmelund Christensen, & Gillard, 2011) and allow blood glucose levels to exceed clinical targets in order to avoid hypoglycemic episodes (Shepard, Vajda, Nyer, Clarke, & Gonder-Frederick, 2014; Weinger & Lee, 2006). Hypoglycemia is unpleasant and potentially dangerous, and experiencing hypoglycemia in public may be embarrassing for the patient. Thus, some fear of hypoglycemia is normative and indeed adaptive. However, excessive fear of hypoglycemia can be problematic. Fear of hypoglycemia is associated with reduced quality of life, reduced productivity, and increased healthcare costs. In a sample of T1D patients, 25% met criteria for PTSD related to hypoglycemia (Myers, Boyer, Herbert, Barakat, & Scheiner, 2007).

A particularly problematic specific phobia is fear of invasive self-care behaviors such as injections, self-monitoring of blood glucose (SMBG), and insertion of subcutaneous insulin infusion devices (i.e., insulin pumps) and continuous glucose monitors. The lifetime prevalence of blood/injury/injection specific phobia is 3.5% in adults and does not appear to differ between persons with and without diabetes (Bienvenu & Eaton, 1998). Yet, subclinical fears of common diabetes-related procedures may be prevalent. One study found that 9% of diabetes patients using insulin reported anxiety symptoms related to self-injection (Mollema, Snoek, Heine, & van der Ploeg, 2001). Another study found these symptoms in 28% of insulin users and reported that half of these participants avoided injections (Zambanini, Newson, Maisey, & Feher, 1999). In the setting of diabetes, fear of invasive procedures can compromise self-care (Cemeroglu et al., 2015; Mollema, Snoek, Ader, Heine, & van der Ploeg, 2001; Wagner, Malchoff, & Abbott, 2005) and can also be a barrier to successful transition from oral agents to injections in T2D (Bahrmann et al., 2014).These fears are also associated with higher A1c (Berlin et al., 1997; Cemeroglu et al., 2015). A related problem is fear of invasive self-care behaviors in a *new location* on the body. Site rotation is important for avoiding damage to the subcutaneous tissue that can interfere with insulin absorption. Fear of pain is a common barrier to site rotation (Patton, Eder, Schwab, & Sisson, 2010).

Measurement

A key challenge in measuring anxiety in persons with diabetes is distinguishing symptoms of anxiety from symptoms of hypoglycemia. The adrenergic, affective, and cognitive symptoms of anxiety and hypoglycemia can be remarkably similar. Individuals with diabetes who report symptoms of anxiety and/or panic should be encouraged to self-monitor blood glucose while symptomatic. Symptoms of anxiety during euglycemia would be suggestive of an anxiety disorder. Making this distinction may require the input and expertise of the patient's diabetes healthcare provider.

Scales have been developed to assess diabetes-specific anxieties which have undergone psychometric analyses of varying rigor. Paper and pencil tools include the measure of diabetes-related fears (Taylor, Crawford, & Gold, 2005) which measures fears among patients with T1D. Fear of hypoglycemia can be measured with the Fear of Hypoglycemia Survey (FHS; Irvine, Cox, & Gonder-Frederick, 1991) and Fear of Hypoglycemia which is designed for pediatric patients (FOH; Kamps, Roberts, & Varela, 2005). Fear of various invasive procedures can be assessed with the Diabetes Fear of Injecting and Self-Testing Questionnaire (DFIST; Snoek, Mollema, Heine, Bouter, & van der Ploeg, 1997) and the Measure of Invasiveness and Skipping Self-Monitoring (MISS; Wagner et al., 2005). The Fear of Progression of Chronic Disease survey (Herschbach et al., 2005) assesses concerns about long-term outcomes that are relevant for, but not exclusive to, patients with diabetes.

Directionality and Mechanisms

The majority of studies have investigated the presence of anxiety in persons with extant diabetes, i.e., diabetes-anxiety. As described above, persons with diabetes may experience anxiety related to many facets of diabetes such as fear of complications, fear of invasive procedures, and fear of hypoglycemia. Living with and managing diabetes may also consume psychosocial resources that might otherwise be spent on managing nondiabetes life stressors, thus increasing anxiety symptoms in general.

There is also growing support for PTSD as a risk factor for incident T2D, i.e., PTSD-T2D. Several large, prospective studies have reported that the presence of PTSD at baseline increased odds of diabetes at follow-up, with odds ratios ranging from 1.3 (Miller-Archie et al., 2014) to 2.1 (Boyko et al., 2010). Vaccarino et al. (2014) examined 4340 twins from the Vietnam Era Registry who were followed for 19 years. The age-adjusted incidence of diabetes was higher in veterans with PTSD than without PTSD, odds ratio = 1.4. However, the within-twin analyses did not find an association between PTSD and diabetes for twin pairs that were discordant for PTSD. Findings suggest that biological and behavioral characteristics that occur within families may predispose to both PTSD and diabetes. Cross-sectional studies have found that PTSD increased odds of T2D even after controlling for other anxiety disorders (Weisberg et al., 2002), in a dose-response manner with more trauma events increasing likelihood of diabetes (Husarewycz, El-Gabalawy, Logsetty, & Sareen, 2014; Pietrzak, Goldstein, Southwick, & Grant, 2011). Studies conflict as to whether effects of PTSD are better accounted for by depression (Agyemang, Goosen, Anujuo, & Ogedegbe, 2012) or not (Vaccarino et al., 2014). PTSD is also a risk factor for metabolic syndrome in vulnerable populations (Heppner et al., 2009; Jin et al., 2009; Weiss et al., 2011). Future studies examining the PTSD-diabetes relationship should control for mood disorders and other anxiety disorders.

There are multiple putative biological pathways that might mediate a possible anxiety-diabetes association. Though few in number, studies of PTSD are the most informative in this regard. PTSD is associated with chronic hyperarousal of the sympathetic and renin-angiotensin-aldosterone system, the downstream effects of which include neurometabolic changes, inflammation, and oxidative stress (Levine, Levine, & Levine, 2014). Neuropeptide Y (NPY) is released during sympathetic activation. NPY accelerates diet-induced obesity and metabolic syndrome. Sympathetic arousal also results in increased catecholamines which can induce insulin resistance. PTSD is also associated with abnormalities in limbic-neuronal structure and function that contribute to central regulation of body weight.

PTSD is associated with behavioral factors related to obesity and diabetes, including sleep deprivation, sleep-disordered breathing, unhealthy lifestyles, and use of long-term atypical antipsychotics (Levine et al., 2014; Vaccarino et al., 2014). Individuals with PTSD also exhibit more emotional eating in response to stressors than those without PTSD (Talbot, Maguen, Epel, Metzler, & Neylan, 2013).

There is only limited support that anxiety disorders or symptoms other than PTSD increase risk for onset of T2D (Atlantis, Vogelzangs, Cashman, & Penninx, 2012; Engum, 2007). In a diverse sample of 2156 older adults initially free of diabetes mellitus followed over a 10-year period, a positive anxiety screen significantly predicted a diabetes diagnosis within the study period (Khuwaja et al., 2010). Yet, other work suggests that any association may be better accounted for by depression (Edwards & Mezuk, 2012).

Patient- and Illness-Related Factors

Women with diabetes show higher rates of anxiety symptoms than their male counterparts (De Melo, de Sa, & Gucciardi, 2013; Grigsby et al., 2002). Other studies document that younger individuals (Li et al., 2008), and those with longer diabetes duration (Trento et al., 2015) and medical comorbidities (Fisher et al., 2008), show the highest risk for anxiety disorders. Similarly, Fisher et al. (2008) found that risk of persistent anxiety disorders across time was associated with female sex, younger age, and medical comorbidities. Whereas one study found the prevalence of anxiety disorders to be approximately the same in both T1D and T2D (Grigsby et al., 2002), most studies that have examined prevalence have failed to differentiate between them (Smith et al., 2013). Fear of hypoglycemia is associated with history of severe hypoglycemia, frequency of nocturnal hypoglycemia, and frequency of self-monitoring. However, nondiabetes-related anxiety is also a strong predictor of fear of hypoglycemia, suggesting that an underlying tendency toward anxiety may at least partially account for fear of hypoglycemia (Anderbro et al., 2015).

Associations with Diabetes Outcomes

Anxiety about one's own health is fairly consistently related to poorer diabetes self-care behaviors in adults (Janzen Claude, Hadjistavropoulos, & Friesen, 2014; Kendzor et al., 2014). Panic episodes are associated with worse diabetes control, complications, diabetes symptoms, and lower perceived overall health in a sample of 4000 patients (Ludman et al., 2006). An early meta-analysis showed that whereas the presence of an anxiety disorder was associated with worse glycemic control, with a small effect size = 0.25, elevated anxiety symptoms were not (Anderson et al., 2002). Yet, a recent study of Hispanics found that the presence of anxiety symptoms was in fact associated with A1c (Kendzor et al., 2014). Further studies in adults are warranted with careful attention to ascertainment of anxiety as well as sociocultural factors. Further complicating interpretation of these findings, many studies of anxiety do not control for depressive symptoms. The studies of adults that do delineate the two suggest that diabetes distress (Strandberg, Graue, Wentzel-Larsen, Peyrot, & Rokne, 2014) and depressive symptoms (Gois, Dias, Raposo, do Carmo, & Barbosa, 2012) may be a better predictor of A1c than anxiety. In contrast, two pediatric studies documented that anxiety's effects on glycemic control were independent of depressive symptoms (Herzer & Hood, 2010; Herzer, Vesco, Ingerski, Dolan, & Hood, 2011).

Contextual Factors Associated with Risk, Treatment, and Outcomes of Depression and Anxiety in Persons with Diabetes

The term "contextual factors" is used here to refer to broad, environmental conditions beyond the individual's biological, psychological, and immediate interpersonal or social domains. Factors including geopolitics and migration, socioeconomic status, environmental exposures, differences in healthcare, and societal stigma all pertain to the intersection of mental health and diabetes. Whereas the research regarding contextual factors relating to risk for diabetes is well developed, the research regarding contextual factors relating to the intersection of mental health and diabetes is considerably more limited. The majority of this research pertains to depression as the literature on contextual factors in anxiety is relatively less developed.

Geopolitics and Migration

World events related to economic hardship, war, famine, and drought secondary to climate change are causing one of the greatest migration events in human history. Migration, and particularly forced migration, can have major consequences for health and mental health for migrants and their offspring. Although longitudinal data are scarce and cross-sectional findings are not entirely consistent, a pattern is emerging from the literature suggesting increased risk for mental health problems and T2D among refugee groups (Wagner, Berthold, et al., 2015). This pattern is thought to reflect the lifestyle shift toward urbanization and westernization but may also reflect common precursors for both disorders including trauma exposure and malnutrition.

Rates of major depressive disorder and elevated depressive symptoms are high among refugees as well as post-traumatic stress disorder and its symptoms (Fazel, Wheeler, & Danesh, 2005). For many, the symptoms become chronic. Data from Cambodian Americans may be informative in this regard since they are one of the longest settled refugee groups in the United States. For example, in face-to-face, linguistically appropriate interviews with 491 Cambodian American refugees, Marshall, Schell, Elliott, Berthold, and Chun (2005) found that even two decades after resettlement, premigration trauma increased odds of major depressive disorder, odds ratio = 1.56. Adult and child refugees settled in western countries are approximately 10 times more likely to have post-traumatic stress disorder than age-matched controls from their host countries (Fazel et al., 2005; Steel et al., 2009). As discussed earlier in the chapter, depression and PTSD are each risk factors for incident diabetes. Marshall and colleagues recently compared rates of diabetes between a household probability sample of US-residing Cambodian refugees ($N = 331$) and a probability sample of the adult US population ($N = 6360$) (Marshall et al., 2016). Using a laboratory-based A1c cutoff of >6.5%, they found 28% in the Cambodian sample as compared to 12% in the national sample. A separate study of self-reported diabetes among Cambodian refugees in New England showed exactly the same rate of diabetes (28%) (Berthold et al., 2014). Cambodian American rates of diabetes are not only higher than other Americans but also much higher than rates among Cambodians living in Cambodia (DM 5% rural, 11% urban) (Wagner et al., 2018).

Malnutrition is common for refugees and may be a common precursor to depression, anxiety, and diabetes. Refugee households may experience nutritional "double burden," i.e., households in which at least one member is overweight and at least one member is malnourished (Grijalva-Eternod et al., 2012). The quality of food assistance for refugees may contribute to both nutritional extremes. Studies from the Dutch Hunger Winter and the Jewish holocaust suggest that intrauterine exposure to starvation conditions may increase risk of adult obesity and T2D (Bercovich, Keinan-Boker, & Shasha, 2014; de Rooij et al., 2006) as well as depression (Brown, Susser, Lin, Neugebauer, & Gorman, 1995; Brown, van Os, Driessens, Hoek, & Susser, 2000).

Socioeconomic Status

Various indicators may be employed to measure socioeconomic status including food security. Food insecurity is a form of financial deprivation with particularly pernicious effects on health and mental health. Food insecurity refers to the uncertain or limited access to nutritionally adequate and safe foods in socially acceptable ways. In cross-sectional analyses of the National Health and Nutrition Examination Survey, approximately 10% of individuals with diabetes and 8.5% of individuals with prediabetes had severe food insecurity in the past year (Montgomery, Lu, Ratliff, & Mezuk, 2017). Food insecurity is independently associated with odds of having diabetes (Fitzgerald, Hromi-Fiedler, Segura-Perez, & Perez-Escamilla, 2011) and also with symptoms of depression and anxiety in persons with extant diabetes (Bermudez-Millan et al., 2016). Individuals with diabetes who are food insecure have been shown to have higher A1c than their food secure counterparts, and emotional distress partially mediates this relationship (Seligman, Jacobs, Lopez, Tschann, & Fernandez, 2012).

Other indicators of socioeconomic status include income, education, and health insurance status. Each has been associated with mental health in diabetes such that lower SES is consistently associated with worse mental health outcomes among persons with diabetes. For example, people with diabetes living below the poverty level have an increased prevalence of major depressive disorder compared to those above the poverty level (Egede & Zheng, 2003). Low health literacy is associated with elevated depressive symptoms in patients with T2D (Maneze, Everett, Astorga, Yogendran, & Salamonson, 2016). Among Hispanic patients with T1D, those with lower household income, with lower educational levels, and without private health insurance have an increased risk of depression (Trief et al., 2014).

Environmental Exposures

Disadvantage at the neighborhood level, rather than or in addition to the individual or household level, may also contribute to depression among individuals with diabetes. In the Look AHEAD study of weight loss among people with T2D, neighborhood-level socioeconomic status (% living below poverty) from the 2000 US Census was associated with mental health functioning (Gary-Webb et al., 2011). Compared to their counterparts living in the lowest tertile of neighborhood poverty (least poverty), those living in the highest tertile (most poverty) had significantly lower scores on mental health functioning. In another study of individuals with T2D followed for 12 weeks, patients in neighborhoods with high social affluence, high residential stability, and high neighborhood advantage were much less likely to have a pattern of persistent depressive symptoms over time with adjusted odds ratio = 0.06 (O'Donnell, de Vries McClintock, Wiebe, & Bogner, 2015). In the Diabetes Health Study (2008–2013), geospatial data from 1298 participants with T2D was paired with data from a depressive symptom checklist (Gariepy, Kaufman, Blair, Kestens, & Schmitz, 2015). Geographical material deprivation was associated with increased risk of depression, particularly in participants who were older or retired. More physical activity facilities, cultural services, and a greater level of greenness in the neighborhood were associated with a lower risk of depression, even after adjusting for confounders. Episodic or chronic concern about basic needs such as food, housing, and safety may cause anxiety and depressive symptoms. Yet some data also suggest a biological link between neighborhood conditions and mental health, showing that proximity to vegetated land cover, which is characteristic of higher SES neighborhoods, is associated with decreased allostatic load and individual biomarkers which are consistent with prevention of depression (Egorov et al., 2017).

Epidemiological studies have documented that environmental exposures, such as noise (Dzhambov, 2015) and air pollution (Balti, Echouffo-Tcheugui, Yako, & Kengne, 2014), increase risk for

T2D. Additional research suggests that air pollution may also increase risk for depression in persons who already have diabetes. For example, a study in Seoul, Korea, examined the association between levels of air pollution and depression-related emergency department visits among people with diabetes, cardiovascular disease, chronic obstructive pulmonary disease, asthma, and depressive disorder (Cho et al., 2014). Certain particulates significantly increased the risk of emergency visits for depressive episode, especially among individuals with pre-existing conditions including diabetes per se.

A relatively nascent area of research regards the role of endocrine-disrupting chemicals. It is well established that high doses of these chemicals are toxic, but there is also growing evidence regarding the deleterious effects of relatively low concentrations of substances used in food additives, pesticides, flame retardants, plasticizers, as well as personal care products and pharmaceuticals (see Kajta & Wojtowicz, 2013 for review). Chemicals used in these products can interfere with hormone receptors, hormone synthesis, or hormone conversion, increasing risk for metabolic dysregulation including diabetes (Chevalier & Fenichel, 2015). There is also preliminary evidence that in addition to effects on hormones, some endocrine disruptors are able to alter neuroplasticity, and substances capable of such effects are therefore known as *neuro*endocrine disruptors. They are implicated in the etiology of neurological disorders including anxiety and depression (see Masuo and Ishido, 2011 for review). Embryonic stages of central nervous system development appear most sensitive to neuroendocrine disruptors, so timing of exposure may be critical to their effects. There is evidence for epigenetic and transgenerational neuroendocrine-disrupting effects of some pollutants (Leon-Olea et al., 2014). Whereas the endocrine-disrupting effects of these chemicals are better established than their neurological disrupting effects, we highlight them here as a promising area of research and to underscore the broad array of environmental factors potentially involved in mental health problems associated with diabetes. More research is needed to investigate common and low-level chemical exposures in order to fully understand their potential effects.

Differences in Care

Rates of mental health screening, disclosure, detection, and treatment for patients with diabetes vary by racial and ethnic group. Reasons for these differences among patients with diabetes are likely multifactorial and may include healthcare provider bias, un- and underinsured status, lack of access to linguistically and culturally appropriate mental health services, and cultural attitudes toward disclosure and treatment. de Groot, Pinkerman, Wagner, and Hockman (2006) sampled adults with diabetes about their depression and depression treatment history. Rates of depression did not differ by ethnic group, and the majority (76%) of depressed participants reported some type of depression treatment. Yet, compared to their White counterparts, African Americans were less likely to report any depression treatment, receive antidepressant medications, or receive treatment from a mental health professional. In a small sample of adults with diabetes and elevated depressive symptoms, relative to Whites, African Americans were 6–12 times less likely to have ever discussed depression with anyone, discussed depression with their primary care physician, and been prescribed an antidepressant, and they were 25 times less likely to have seen a psychiatrist (Wagner, Perkins, Piette, Lipton, & Aikens, 2009). Yet, there were no significant racial differences in discussing depression with clergy or family members/friends suggesting that factors related to the healthcare providers or healthcare systems may have accounted for differences rather than any cultural taboo about discussing depression. Consistent with this hypothesis, data from rural African Americans with diabetes suggest that problems with the patient-provider relationship may impede detection of depressive symptoms (Kogan, Brody, Crawley, Logan, & Murry, 2007).

Patients may be aware of disparities in care, either in the general population or in their very own healthcare, and some patients may therefore be primed to attribute difficult provider interactions to discrimination. Self-reported exposure to discrimination in healthcare among people with diabetes may have implications for depression. Using survey data from the Diabetes Study of Northern California (DISTANCE), a race-stratified sample of Kaiser diabetes patients, racial and ethnic discrimination in healthcare was associated with having depression (Lyles et al., 2011). In a different study of African Americans with diabetes, self-reported racial and ethnic discrimination in healthcare was associated with increased depressive symptoms, as well as decreased likelihood of use of antidepressant medication (Wagner & Abbott, 2007).

However, differences in depression detection and treatment may not solely signal discrimination – they may also or instead reflect patient preferences for care. Although depression is perceived as a serious condition (Cabassa, Lagomasino, Dwight-Johnson, Hansen, & Xie, 2008) that is linked to diabetes, many Latinos report negative views of antidepressant medication (Cooper et al., 2003), citing concerns regarding side effects, fears about the addictive and harmful properties of antidepressants, worries about taking too many pills, attribution of lesser importance to antidepressant medications than other medications, and stigma of psychotropic medications (Ayalon, Arean, & Alvidrez, 2005; Cabassa et al., 2008). Compared to Whites, Latinos have been shown to be significantly less likely to fill an antidepressant prescription or to take the medication if filled (Harman, Edlund, & Fortney, 2004; Miranda & Cooper, 2004). In contrast, many Latinos have positive views of psychotherapy and may even view it as more acceptable than Whites do (Cooper et al., 2003) and report high receptivity to novel non-pharmacological approaches (Stacciarini, 2008; Wagner, Bermudez-Millan, et al., 2015).

It should be noted that disparities in care and patient preferences for treatment are not unrelated. When patients experience discrimination, mistrust, or lack of confidence in standard healthcare, they may prefer to rely on alternative or more traditional methods for addressing depression or anxiety. Traditional systems of medicine are common across cultures and may include home remedies, herbal therapies, and magico-religious healers (Purnell & Paulanka, 2003). Traditional systems of medicine often contain elements of historically rooted experiences and ideas. In a sample of Cambodians with high rates of depression and PTSD, whereas trust of traditional medicine was not deleterious, *distrust* of western medicine was related to higher chronic disease count that included diabetes, a decreased likelihood of ever having received a mental health screening, and decreased likelihood of having a primary care provider, and among those with a primary care provider, distrust of western medicine was associated with longer visit recency (Wagner et al., 2013).

Societal Stigma

Despite recent gains, significant societal stigma remains toward mental illness. Even among patients who do have access to quality care and confidence in its methods, many may experience shame, embarrassment, and fear of stereotypes and stigma which may discourage them from seeking help (Corrigan & Watson, 2002; Sartorius, Stuart, & Arboleda-Florez, 2012). Such concerns are not always unfounded. Mental health stigma is well documented among healthcare providers and varies significantly by specialty. Medical practitioners generally tend to have more negative attitudes toward people with mental illness compared to mental health professionals (Bjorkman, Angelman, & Jonsson, 2008; Hori, Richards, Kawamoto, & Kunugi, 2011; Smith & Cashwell, 2010). The vast majority of diabetes patients with behavioral or psychosocial needs present first, or exclusively, to their medical providers rather than to a mental health provider. Thus, physicians who hold mental health stigma may become barriers to disclosure of mental health symptoms and referrals for mental health treatment.

Unfortunately, mental health stigma may affect not only physician referral for mental healthcare, but also medical care for diabetes. Healthcare providers reporting higher levels of stigma may consistently question the ability of a patient with mental illness to follow treatment plans (Corrigan et al., 2014), which may result in the patient not being offered appropriate treatment options. A study of Medicaid enrollees during 2003–2004 compared patients with diabetes alone to those with diabetes plus a mental health comorbidity (Druss et al., 2012). Outcomes included diabetes performance measures (A1C testing, eye examinations, low density lipoproteins screening, and treatment for nephropathy) and hospitalizations. Presence of a mental condition was associated with decreased odds of obtaining two or more performance measures and increased odds of hospitalization. Consistent with this, mental health patients with diabetes report stigma and diagnostic overshadowing when seeking diabetes care (Nash, 2014). Similar findings from Australia and the Veterans Administration (Morden et al., 2010) suggest that differential diabetes care for patients with mental illness is not solely attributable to variation in reimbursement systems (Mai, Holman, Sanfilippo, Emery, & Preen, 2011).

Additionally, patients with T2D are often overweight which carries its own stigma. Self-reported exposure to weight stigma is related to depression and anxiety (Wu & Berry, 2018). Weight stigma among individuals with T2D is associated with a range of poor diabetes outcomes including psychological distress (Potter et al., 2015).

Conclusions and Future Directions

As a landmark development in its endorsement of psychosocial care as part of comprehensive diabetes care, the American Diabetes Association has recently released a position statement on the psychosocial care of individuals living with diabetes (Young-Hyman et al., 2016). Depression and anxiety both figure prominently in the position statement guidelines. Recommendations to providers of diabetes care include consideration of routine annual screening of all patients with diabetes for depression and screening for anxiety disorders in those exhibiting anxiety-related symptoms (Young-Hyman et al., 2016). Routine screening for depression is also recommended for all adults in the general population by the United States Preventive Services Task Force (Siu et al., 2016). The evidence reviewed in this chapter presents a sound rationale for the plausibility of benefits to screening for both depression and anxiety in individuals with diabetes – prevalence rates are higher, and if associations with poor health outcomes are causal, there could be downstream diabetes health benefits in addition to the improvements experienced immediately through successful identification and treatment of cases.

However, there is currently no direct evidence available to show that depression screening programs without integrated enhancements in depression care are effective in improving depression outcomes. They also generate a large number of false positives (e.g., Fisher et al., 2007, 2016). Critics have cautioned against routine screening in diabetes based on this lack of evidence and have argued that depression screening could unintentionally harm patients who do not derive benefit from treatment but who experience side effects and expose patients to distressing information related to being misidentified through a false-positive result. Routine screening involves significant cost and has the potential for consuming scarce mental health resources that are already unable to meet the needs of patients with mental illness that have already been self-identified or otherwise identified by their healthcare providers (Thombs, 2014).

Future research must address these limitations regarding screening for depression and anxiety in diabetes. Meanwhile providers should consider screening for problems related to depression and anxiety and should appreciate the importance of coordinating these efforts with systems to assure appropriate subsequent assessment, treatment, and follow-up. Consideration should include relative costs and benefits in light of available mental health resources and attempts to gain information on the prevalence of the problems noted above in the local patient population, as higher prevalence will generally lead to a better balance of false-positive to true-positive cases for any routine screening program. Readily usable instruments with strong psychometric properties are available for screening for the problems identified here and/or for following up on further assessment of symptoms reported in response to assessments of well-being that should be part of routine care for diabetes (Young-Hyman et al., 2016; Young-Hyman & Davis, 2010).

The information reviewed in this chapter also makes clear that depression and anxiety should be considered in terms of the context of diabetes treatment and self-management and in the broader, health systems and socioeconomic, cultural, historical, and political contexts that are relevant to understanding and developing interventions to address their root causes at multiple levels (e.g., targeting the individual, family, healthcare team, local community). This is one aspect of the psychosocial care of individuals living with diabetes that the position statement from the American Diabetes Association does not address in sufficient detail. This broader context is also given relatively less attention in clinical practice and research settings.

Nevertheless, it is clear from data reviewed here that access to adequate healthcare, exposure to societal stigma and discrimination, living in environments that present barriers to healthy living and involve noxious exposures, experience with migration and immigration status, and poverty are key aspects of the patient's life context that are as important to understanding clinical presentations of depression and anxiety and to treatment planning and coordination of mental healthcare as they are to understanding problems with diabetes self-management and treatment adherence. To guide multilevel interventions to improve the mental health as well as the physical health outcomes of diabetes care, greater attention to these issues is needed.

Although the data reviewed here make a compelling case for the importance of depression and anxiety in diabetes care, much of the available evidence is limited by small sample sizes and methodologically limited studies. As consensus grows about the importance of these and other patient-reported outcomes to evaluating diabetes treatments, a greater investment will be necessary in producing high-quality studies that evaluate approaches to care that can be translated into real-world practice. Despite an evidence base that is similar to that for depression, there has been far less attention paid to evaluation of treatment trials for problems related to anxiety, as compared to the number of studies evaluating treatments for depression. Moreover, as these problems tend to co-occur more often than they present separately, integrative treatments for problems related to combined anxiety and depression deserve further attention (e.g., Barlow et al., 2017).

Much of the research effort toward understanding the intersection of diabetes and mental health has attempted to clarify the temporal ordering and potential causality among depression, anxiety, and diabetes. It is also possible, indeed likely, that one or a number of common precursors may at least partially explain their co-occurrence. Genetics is most often noted as the potential common precursor, but the role of contextual factors receive relatively less attention. Greater attention should be focused on contextual factors as a class of potential mechanisms that might explain relationships between depression and anxiety on the one hand and diabetes and its outcomes on the other. Elucidating the contextual, psychological, behavioral, and/or biological pathways through which mental health problems influence, and are influenced by, diabetes could inform the development of treatments with greater impact. Researchers and clinicians in the northern and western hemispheres are influenced by an ethos of individualism. Diabetes and mental illness are multifactorial and global problems for which individual-level approaches will have important but limited impact. It is time that the field more seriously considers the factors beyond the individual that determine these important health outcomes.

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Chapter 22
Eating Disorders in Type 1 and Type 2 Diabetes

Ann E. Goebel-Fabbri

Type 1 Diabetes and Eating Disorders

Eating disorders in type 1 diabetes (T1D) are rarely understood or recognized outside the T1D patient and medical community. Even among diabetes health-care providers, there is often a sense of anxiety over what to do to help (Tierney, Deaton, & Whitehead, 2009). Disordered eating behavior (DEB) is common among adolescent girls and young women in the general population; however those with T1D are more likely to exhibit two or more DEBs than their peers without diabetes (Colton, Olmsted, Daneman, Rydall, & Rodin, 2004). DEBs have been defined as eating disorder thoughts or behaviors that happen less frequently than in formal eating disorder diagnoses yet still can present a deleterious impact on health status (De Groot, Golden, & Wagner, 2016). These may include dieting for weight loss, binge eating, calorie purging through self-induced vomiting, laxative or diuretic use, and excessive exercise (Olmsted, Colton, Daneman, Rydall, & Rodin, 2008).

In addition to these DEBs, women with T1D often turn to a unique behavior – intentional insulin restriction, inducing hyperglycemia and thereby purging calories via glycosuria. Prolonged exposure to hyperglycemia results in dehydration and the loss of fat and muscle. Insulin restriction can lead to rapid and dramatic weight loss but also increases the risk of both acute and long-term T1D complications as well as an increased risk of death (De Groot et al., 2016). Women with T1D and eating disorders are in poorer glycemic control with A1cs approximately 2 or more percentage points higher than similarly aged women without eating disorders – they also have higher rates of hospital and emergency room visits, higher rates of neuropathy and retinopathy, and more negative attitudes toward diabetes than women who do not report insulin restriction (Bryden et al., 1999; Polonsky et al., 1994; Rydall, Rodin, Olmsted, Devenyi, & Daneman, 1997). Even subthreshold DEBs, defined above, are strongly associated with significant medical and psychological consequences in the context of diabetes (Verrotti, Catino, De Luca, Morgese, & Chiarelli, 1999). In fact, simply endorsing insulin restriction alone was shown to increase mortality risk threefold over an 11-year follow-up period (Goebel-Fabbri et al., 2008).

It is important to note that not all people with T1D and eating disorders restrict insulin and may have more classic symptoms of anorexia nervosa or bulimia nervosa instead. However, the large majority of research in this area has focused on women who do have this particular eating disorder

A. E. Goebel-Fabbri (✉)
Dr. Goebel-Fabbri, LLC, Brookline, MA, USA

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symptom as part of their clinical picture. The media and lay public refer to an eating disorder involving insulin restriction as “diabulimia,” but this term is not a formal eating disorder diagnosis. This phenomenon will be the focus of the T1D portion of this chapter.

Research indicates approximately 31% of women with T1D report intentional insulin restriction and that rates continue to increase and peak by late adolescence and early adulthood (as many as 40% of women between ages of 15 and 30 years) (Polonsky et al., 1994). Evidence suggests women with T1D have a 2.4 times greater risk of developing an eating disorder and 1.9 times increased risk for developing subthreshold eating disorders than women without diabetes (Jones, Lawson, Daneman, Olmsted, & Rodin, 2000). Symptoms have also been shown to become more common, increase in severity, and persist over time (Colton et al., 2004; Peveler et al., 2005). Thus, it is important to note that eating disorders in T1D are not an exclusively adolescent phenomenon. In fact, the average age of onset of eating disorders in T1D is reportedly 23 years of age (Colton et al., 2015).

As mentioned above, eating disorder research in T1D has largely focused on those women who restrict insulin to purge calories. However, women with T1D can also meet classic diagnostic criteria for anorexia nervosa, bulimia nervosa, and binge eating disorder. Because these women with diabetes have not been widely studied, little is known about them. This may result in women who do not restrict insulin being under diagnosed. Clinicians should be alert to the fact that different types of eating disorders are still likely to present with significant medical risks and represent a notable women’s health problem in T1D. For example, a study of a national diabetes registry showed that the mortality rates over approximately 10 years were 2.5% for T1D alone, 6.5% for anorexia nervosa alone, and 34.8% for anorexia nervosa comorbid with T1D (Nielsen, Emborg, & Molbak, 2002).

Eating Disorder Risk Factors Associated with T1D

It remains unclear why girls and women with T1D have increased rates of eating disorders. However, women with eating disorders and T1D most likely have the same underlying biopsychosocial risks as women without diabetes. For example, eating disorders are known to have a strong genetic underpinning with a high co-occurring risk of depression and anxiety. People with diabetes have twice the risk of clinically significant depression than those without diabetes (De Groot, Freedland, Clouse, & Lustman, 2001). Prior struggles with weight and dieting appear to be other important risks. Women and girls with T1D are also slightly heavier than their peers without diabetes (Domargard et al., 1999). Women with diabetes are exposed to the same societal, peer, and family risk factors as those without diabetes.

Because T1D confers a higher risk for developing an eating disorder, there may also be some eating disorder risk factors that are unique to living with T1D itself. Specific aspects of diabetes management may even be iatrogenic in nature. For example, the Diabetes Control and Complications Trial (DCCT) (The DCCT Research Group, 1993) reported that along with the significantly decreased risk of diabetes complications, the group of patients under intensive diabetes management were 10.45 pounds heavier on average than the standard treatment group (The DCCT Research Group, 1988, 2001). Since having had prior struggles with weight is an identified eating disorder risk factor, it is possible that the possibility of weight gain associated with intensive diabetes management may add to that risk. However, this finding must be understood within the context of the quality of diabetes treatment tools available at the time of the DCCT trial.

The types of insulin and medical devices available to treat T1D have significantly changed and improved since the DCCT was conducted and published over 25 years ago. Intensive diabetes management during the DCCT was associated with frequent hypoglycemia, which requires treatment with glucose and therefore extra calories. This may have contributed to the weight difference noted above. Frequent hypoglycemia and the risk of related weight gain may be mitigated somewhat with the more tailored and finely tuned insulin protocols that are standard treatments today. The use of insulin pumps and continuous glucose monitors may not carry the same risk of weight gain as older treatment approaches because they offer the opportunity to more closely approximate the action of a healthy pancreas with physiologic insulin replacement.

Other aspects of diabetes treatment – as well as T1D itself – have also been proposed to increase the risk of eating disorders. The necessary attention to food portions and weight can parallel the rigid thinking about food, weight, and body image reported by women with eating disorders who do not have diabetes (Daneman, Olmsted, Rydall, Maharaj, Rodin, 1998; Goebel-Fabbri, Fikkan, Connell, Vangsness, Anderson, 2002). Frequent hypoglycemia or even perceived but not confirmed hypoglycemia has been found to be connected to disinhibited eating/bingeing, shame about bingeing, insulin restriction, and concomitant elevated A1c (Merwin et al., 2014). Increased anxiety and disgust over breaking “dietary rules” is also strongly associated with restricting insulin dosing for the food consumed (Merwin et al., 2015).

It has even been proposed that the eating-related blood glucose fluctuations associated with T1D might create a physiological propensity for disinhibited eating (Treasure et al., 2015). Other studies find that DEBs in T1D are strongly predicted by higher BMI, higher weight and shape concerns, lower self-esteem, depressed mood, and increased family conflict. Positive feelings about appearance, the absence of depression, and lower BMI may be factors that protect against eating disorders in this population (Colton, Olmsted, Daneman, Rydall, & Rodin, 2007; Goebel-Fabbri et al., 2002, 2011; Markowitz, Lowe, Volkening, & Laffel, 2009; Olmsted et al., 2008).

Lastly, although no research has examined this to date, other aspects of treatment may also present as possible risk factors. These include the way health-care teams engage with their patients around treatment goals and blood glucose values, the way patients and families are educated about T1D management and complications, and the way that patients themselves interpret and internalize aspects of their diabetes education. These aspects of diabetes treatment can foster certain attitudes and expectations in patients and families about how their diabetes management is meant to go. Perfectionistic personality traits are common in eating disorders. Such high expectations about blood glucose control can be unrealistic, leading to patient frustration, disengagement from self-care, and family conflict.

Taken together, these theories and findings support a model of disordered eating and T1D proposed earlier by Goebel-Fabbri et al. (2002) and adapted for inclusion here (Fig. 22.1).

Screening Tools

Olmsted (2008) advocates early and routine screening for eating disorder risk factors in T1D. Health-care teams working with adolescent and adult women with diabetes should be alert to patterns that could indicate the presence of DEBs. Warning signs may include extreme concerns about weight and body shape, unusual patterns of intense exercise (sometimes accompanied or followed by frequent hypoglycemia), unusually low-calorie meal plans, unexplained elevations in A1c values, repeated problems with DKA, and amenorrhea. However, identifying these problems is not sufficient to make an eating disorder diagnosis. Further screening and evaluation by a mental health professional familiar with eating disorders is required.

Early detection and intervention for DEB in the context of diabetes is important and requires effective and efficient screening tools. Longer, more complex questionnaires or interviews may be more appropriate for research, while briefer screening tools may be better adapted for a clinical setting. Research has examined the risks and benefits of using diabetes-specific screening tools, more widely used general screening tools, or general screening tools adapted to include some diabetes-related questions.

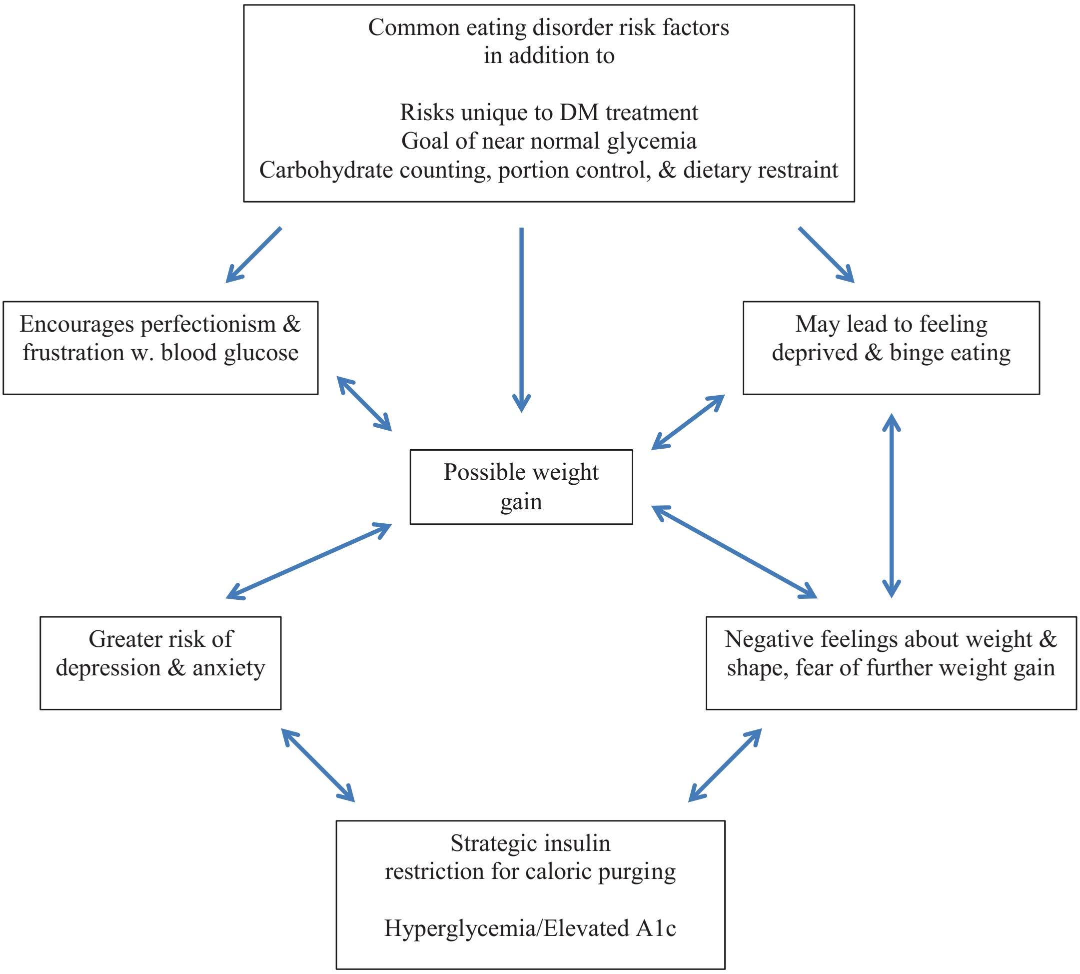

Fig. 22.1 Type 1 diabetes and eating disorders/insulin omission. (Adapted from: Goebel-Fabbri et al. (2002).

The Diabetes Eating Problem Survey – Revised (DEPS-R) is a validated 16-item questionnaire designed to detect disordered eating in T1D. It was validated in a cohort of 13- to 19-year-olds with T1D. It takes approximately 10 min to complete. The DEPS-R has not yet been validated in adult populations but has been used in many studies of eating disorders in T1D (Markowitz et al., 2010).

The mSCOFF is a brief screening instrument, consisting of five questions. It is based on the SCOFF, a reliable and valid screening tool that is widely used. The mSCOFF is an adaptation of the SCOFF which includes one diabetes-specific question – “Do you ever take less insulin than you should?” It was validated against the EDI-3, which has been used in eating disorder research for decades. Because it is so short, the mSCOFF may be more practical and easily adopted for use in routine clinical care (Zuijdwijk et al., 2014).

The final diabetes-specific screening tool that is currently available is the Screen for Early Eating Disorder Signs in Persons with T1D (SEEDS). It is an attempt to identify those patients who may be experiencing early signs of risk rather than those already engaged in actual eating disorder behaviors. It develops low risk, moderate risk, and high risk scores and creates both a total score and subscale scores for body image, feelings, and quality of life. Unlike the DEPS-R and the mSCOFF, the authors decided not to ask any questions about insulin restriction or any questions pertaining to T1D itself, because of their belief that such questions could be suggestive of maladaptive behaviors (Powers, Richter, Ackard, & Craft, 2016).

Some studies have compared eating disorder rates found through generic screens and diabetes-specific screens. All studies show higher rates in T1D than in those without diabetes regardless of the type of screen used. However, there is some indication that generic screens may risk inflating these rates, while diabetes-specific tools may be less likely to generate false positives (Young et al., 2013). Other works support the use of more widely used, generic eating disorder questionnaires (d'Emden et al., 2012) with the argument that the current diabetes-specific screening tools do not assess for the full spectrum of eating disorder eating thoughts and behaviors (d'Emden, McDermott, Gibbons, Harris, & Cotterill, 2015).

Rather than focusing on creating a screening questionnaire, Pinhas-Hamiel et al. (2013) used data mining to create a model for identifying insulin restriction and DEBs. They found that those patients who restrict insulin have not only higher A1cs but also more widely fluctuating A1cs than patients who do not restrict. Additionally, those with diabetes onset after 13.8 years and with shorter disease duration were more likely to restrict insulin. The authors recommend that these factors be considered as increasing the risk of developing disordered eating and insulin restriction.

Women with eating disorders can be quite ashamed about their struggle, resulting in DEBs being difficult to acknowledge and discuss. It is important that clinicians use sensitive, open-ended questions which can increase their understanding of the patient's situation without the risk of unintentionally "educating" the patient about these dangerous behaviors. Clinicians should also note that a positive response to a single, straightforward question like "Do you take less insulin than you should?" was shown to be associated with increased eating disorder symptoms and mortality risk in women with T1D (Goebel-Fabbri et al., 2008). The question is simple and quick, potentially opens the opportunity for discussion, and may be vague enough not to accidentally encourage insulin restriction for weight loss.

Suggestions for Treatment

Insulin restriction becomes a more significant problem in older adolescents, perhaps coinciding with decreased parental involvement in diabetes management. It becomes more common and potentially worse in severity and frequency throughout early adulthood. Once the pattern of frequent and habitual insulin restriction becomes entrenched, the cycle of negative feelings about body image, shape, and weight, chronically elevated blood sugars, depression, anxiety, shame, and poor diabetes self-care can be complex and difficult to treat. Indeed, diabetes health-care professionals often express anxiety about how to best work with this population and frustration over the relative lack of treatment resources (Tierney, Deaton, & Whitehead, 2009).

To date, few studies have examined treatment effectiveness for eating disorders in T1D. The earliest ones were case reports in which cognitive behavioral therapy (CBT) protocols were used and clinicians described eating disorder patients with T1D to be more difficult to treat than patients without diabetes (Peveler & Fairburn, 1989; Peveler, Fairburn, Boller, & Dunger, 1992). This was supported in later research examining inpatient treatment (average of 3 months), day hospital treatment (ranging 6–14 weeks), and outpatient CBT (16 sessions). When compared to patients without T1D, those with eating disorders and diabetes had higher treatment dropout rates, lower reported motivation to change, and lower rates of eating disorder remission (Colton et al., 2015; Custal et al., 2014).

It may be that because of their complexity, patients with T1D seem to require longer and more intensive eating disorder treatments. One study of residential treatment ranging from 3 to 12.3 weeks reported improvements in A1c and eating disorder symptoms and found that more robust improvements correlated with longer length of treatment (Dickens, Haynos, Nunnemaker, Platka-Bird, &

Dolores, 2015). Despite these important findings, all of the studies mentioned were limited by their small sample sizes (under 40 participants each) and the lack of patient follow-up after treatment ends. Takii et al. (2003) improved upon this by following patients for 3 years after discharge; however their findings are also limited by their treatment group of only nine T1D patients. These patients were originally treated in a specialty eating disorder inpatient setting for 2.25–5.75 months (average 4 months). They reported significant improvements in glucose, eating disorder symptoms, depression, and anxiety both at the end of inpatient treatment and after the 3-year follow-up period. In fact, 78% of the former inpatients no longer met criteria for a clinical or subclinical eating disorder at follow-up.

The research thus far seems to indicate that this is a more complicated population to treat and that treatments of great intensity and duration may be required. Clearly, more research with larger samples and more follow-up evaluations are needed in order to get clarity about treatment effectiveness.

What follows is an adaptation of clinical consensus guidelines for outpatient treatment of eating disorders in T1D. These were published prior to the treatment research mentioned above and are based on the agreement of expert clinicians rather than empirical support (Goebel-Fabbri et al., 2009). Goebel-Fabbri (2017) conducted qualitative interviews with women who were recovered from eating disorders in T1D. The goal was to learn what they identified as the most important and helpful aspects of their care. They had much to say not only about their eating disorders treatment itself but also about ways that their diabetes treatment may have put them at risk initially and alternatively aided their recovery from their eating disorder later on. Most of what they spoke about confirmed the treatment guidelines.

A multi-disciplinary team approach to treatment is considered the standard of care for both eating disorders and diabetes treatment. When designed to treat a patient with these two comorbidities, such a team should include an endocrinologist, a nurse educator, a nutritionist with eating disorder and/or diabetes training, and a psychologist or social worker to provide weekly individual therapy. A psychiatrist may also need to be added to the team for psychopharmacologic evaluation and treatment. Team members should communicate frequently to maintain congruent treatment goals. Patients may require a medical or psychiatric inpatient hospitalization until they are medically stable and appropriate for outpatient treatment. Early in the treatment, the endocrinologist or nurse educator needs to schedule monthly (or still more frequent) appointments in order to maintain medical stability. Monthly appointments with the nutritionist are also recommended. Laboratory tests (especially A1c and electrolytes) and weight checks should occur routinely at medical appointments, and results should be communicated back to all team members.

Intensive glycemic management of diabetes is not an appropriate *early* treatment goal for a person with T1D and an eating disorder. In fact, patients should be taught that lowering their A1c slowly is a goal designed for their safety and that going too quickly can cause “treatment-induced complications” (Gibbons & Freeman, 2014). The treatment team must be willing to collaboratively establish small goals that the patient feels are realistic. An essential first goal is the patient’s agreement to maintain medical safety. For example, this goal may be as small (but clinically meaningful) as agreeing to routinely take basal insulin doses for DKA prevention.

Helping patients to identify and anticipate possible treatment challenges can help to solidify the treatment relationship and possibly decrease the risk of treatment dropout. The first challenge most patients face is weight gain associated with improved blood glucose. If they have been routinely restricting insulin and are dehydrated at the start of treatment, patients need to be reassured that this weight gain is related to fluid retention or “insulin edema.” Patients are likely to report feeling fat, bloated, and uncomfortable and will need to be reassured that this is temporary. Because eating disorder patients are exquisitely sensitive to body shape and weight changes, this rapid weight gain which comes just as they are starting to engage in treatment and see blood glucose improvements can be frightening. In fact, they may reveal that this triggered relapse in their past. Once fluid levels have stabilized, patients’ ongoing concerns about weight must also be taken seriously by the treatment team. When patients attempt to lower their blood glucose ranges and experience unwanted weight gain unrelated to fluid, their frustrated attempts to lose the weight may again raise their risk of relapse.

Fear of hypoglycemia may also lead patients with diabetes to aim for elevated blood glucose. Some patients report that treating hypoglycemic reactions can trigger them into episodes of binge eating (Merwin et al., 2014, 2015). Other patients worry about taking in these extra calories and therefore fear having to treat hypoglycemia. It may be helpful to anticipate these concerns with patients. To reduce their risk of bingeing or overtreating, patients should be encouraged to use fast portion-controlled treatments for hypoglycemia like glucose gels or tablets, which may be less tempting to overeat.

Over the course of time and with greater medical stability, treatment goals can build toward increasing doses of insulin, more frequent blood glucose monitoring, achieving lower blood glucose ranges, and greater flexibility in meal planning. Risk of recurrent hypoglycemia and weight gain can be decreased by frequently reviewing blood glucose pattern with the patient and making insulin adjustments as needed. Frequent, ongoing communication and support can also help establish and reinforce realistic expectations for blood glucose improvements, maintain motivation, and decrease the risk of treatment dropout (Wolpert & Anderson, 2001).

Type 2 Diabetes and Eating Disorders

To date, less research has examined the prevalence and consequences of eating disorders in type 2 diabetes (T2D) than in T1D. Most studies have focused on the correlates of binge eating and/or binge eating disorder (BED) comorbid with T2D. BED is the most frequently observed eating disorder in this population with up to 40% of patients with T2D – men and women – reporting DEBs (Garcia-Mayor & Garcia, 2016). Findings are mixed regarding the association between A1c and binge eating symptoms (Herbozo, Flynn, Stevens, & Betancourt, 2015). Some studies have found no association between binge eating and/or BED and A1c (Crow, Kendall, Praus, & Thuras, 2001; Gorin et al., 2008), while others have found positive associations. Kenardy et al. (2001) reported that the frequency of binge eating predicted blood glucose levels after controlling for BMI and exercise level, while others (Mannucci et al., 2002) found a significant positive correlation between severity of binge eating symptoms and A1c values. Other research indicates that T2D patients with BED have higher A1cs, BMIs, triglyceride levels, and rates of hospitalization than patients without BED (Nicolau & Masmiquel, 2015). Examining this issue from another angle, a large follow-up study of a cohort of patients who had received eating disorder treatment reports that 16 years after treatment, one in every three patients treated for BED had developed T2D (Raevuori et al., 2015). Finally, disordered eating symptoms are associated with poor quality of life in T2D and present an impact that is unique from A1c, diabetes duration, and presence of diabetes complications (Cerrelli et al., 2005). The large-scale, longitudinal TODAY study also found a strong association between binge eating, symptoms of depression, and decreased quality of life in adolescents with T2DM (Wilfley et al., 2011).

Treatment

No research thus far has evaluated specific treatment of binge eating or BED within a T2D population. For this reason, what follows are suggestions about small adaptations that could be helpful to make to empirically supported treatments for BED in order to address the specific needs of patients with T2D. These ideas are rooted in clinical experience and have not been empirically evaluated at this time.

CBT and interpersonal therapy (Fairburn, 2013) are the two treatment approaches that have the most empirical support for treating binge eating and BED. Either approach can be successfully applied to these problems in T2D with some modifications that will be detailed below. As is the case in T1D, treatment should involve a multidisciplinary team approach – ideally one in which team members are well-versed in issues related to T2D, though this is often difficult to find (Gagnon, Aime, Belanger, & Markowitz, 2010).

Treatment begins with the recommendation to adopt a reliable and routine eating pattern in order to prevent the cycle wherein food restriction can trigger binge eating and can then reinforce the perceived need for restricting food again (Fairburn, 2013). Patients are encouraged to keep food records including the time of day, types and amounts of food consumed, context and feelings, and if the eating episode is defined as a binge or not. When integrated into T2D treatment, patients should also record what their blood sugar values are prior to and approximately 2 h after the meal, snack, or binge. This will help them to learn the impact that their eating patterns have on their diabetes management and may increase their motivation to change.

Medical providers should understand the struggle and shame involved in binge eating and take a sensitive and nonjudgmental approach, especially since treatment will often involve recommendations to lose weight. The patient may sometimes feel as if the medical and the psychological sides of the team are providing contradictory advice. Patients may interpret their doctor's weight loss recommendations to mean rigid dietary restriction as opposed to the routine eating plan recommended by the eating disorder specialists. This underscores the importance of clear communication between team members in order to emphasize both regular eating as well as an approach that involves moderate portions (neither restriction nor binge eating) for slow and sustainable weight loss.

Binge eating and BED treatments also emphasize identifying negative cognitions and healthier strategies for coping with painful affect (Fairburn, 2013). Eating disorder specialists should be ready to identify those thoughts and feelings that may be specific to diabetes. For example, patients may blame themselves for developing diabetes, may perceive diabetes complications as inevitable or even deserved, and may feel at fault for blood sugar and weight variations. These examples of diabetes-specific ideas can be readily integrated into cognitive restructuring exercises. Patients will also benefit from learning healthier coping skills to help them prevent binge eating during times of distress.

Medications for T2D can be divided into two broad categories: those associated with weight gain and those that are weight neutral or even associated with weight loss. Some T2D treatment experts are now recommending avoiding those medicines with the risk of weight gain if possible and starting treatment by using those that do not have this side effect profile (Hamdy & Carver, 2008). This may help reduce patient frustration, increase their sense of self-efficacy, and promote trust in their treaters.

Conclusions

While more is known about eating disorders in T1D than in T2D, much work is yet to be done. Neither group of patients have been studied using large randomized controlled treatment outcome research with long-term follow-up after treatment in order to examine relapse and remission rates. As such, the field lacks evidence-based treatments for these comorbid conditions. Moreover, most of the work in this area focuses on women. Little attention has been paid to eating disorders in men with diabetes. In both T1D and T2D, eating disorders present with a heightened risk of poor health outcomes and are associated with decreased quality of life. More research is needed in order to best address the needs of these complex patients.

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Chapter 23

Neurocognitive Functioning in Type 1 and Type 2 Diabetes Mellitus

Eelco van Duinkerken and Augustina M. A. Brands

Introduction

Neuropsychology, which is the study of the brain-behavior relationship, has traditionally focused on behavioral changes due to neurological disease, such as dementias, epilepsy, and brain trauma. Determining the effect of neurological disorders on memory, attention, planning, and visuospatial functions was core business for neuropsychologists (Lezak, 2012). Over the years the focus of neuropsychology has widened to include the brain-behavior relationship in non-neurological diseases. In this widened view, obesity and diabetes mellitus have a central role.

While little was known about diabetes itself, the first paper on cognitive difficulties in patients with diabetes was published as early as 1922 (Miles & Root, 1922). Miles and Root acknowledged that diabetes had a well-established effect on the central nervous system (CNS) and that many patients had complaints about poor memory and difficulty concentrating and focusing attention. They used neuropsychological tests that covered short-term and working memory, sustained attention, calculation, and psychomotor efficiency in 40 diabetic patients with a mean age of 46 and controls. Without an exception the patients with diabetes had poorer performance on all tests as compared with the controls, although the variation was wide within the diabetic group (Miles & Root, 1922). Their conclusion was therefore that "…undoubtedly very many diabetic individuals will be able to do as much light physical or mental work as is actually done by many normal men and women."

Observations that diabetes leads to CNS damage were also made in the 1950s (De Jong, 1950) and in the late 1960s when Reske-Nielsen and colleagues performed a series of postmortem studies finding evidence for atrophy, demyelination, and vascular lesions in patients with long-term type 1 or juvenile, diabetes mellitus (Reske-Nielsen, Lundbæk, & Rafaelsen, 1966; Reske-Nielsen & Lundbæk, 1968). It was not, however, until the development and wide availability of neuroimaging technologies that studies aimed at understanding the radiological and neurocognitive effects of diabetes really moved forward. These studies have helped us gaining a better understanding of the neurocognitive and CNS changes and ultimately also of the brain-behavior relationship in patients with diabetes. In this chapter the effects of both type 1 and

E. van Duinkerken (✉)
Department of Medical Psychology, Amsterdam University Medical Centers, Amsterdam, The Netherlands

Center for Epilepsy, Instituto Estadual do Cérebro Paulo Niemeyer, Rio de Janeiro, Brazil
e-mail: e.vanduinkerken@amsterdamumc.nl

A. M. A. Brands
Franciscus Gasthuis & Vlietland Hospital, Rotterdam, The Netherlands

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type 2 diabetes on neurocognitive functioning across the adult life span are discussed. Where necessary and helpful, we will use neuroimaging studies to highlight the brain-behavior relationship. Risk factors for neurocognitive problems in diabetes will be discussed, as well as the association between obesity and prediabetic stages and cognition and dementia and diabetes. Finally, the clinical implications of these neurocognitive decrements will be discussed.

Cognitive Functioning in Young- and Middle-Aged Adults with Type 1 Diabetes

Deficits in cognitive functioning in this population have been repeatedly reported by numerous studies. These cognitive decrements can be evident within the first 2 years after disease onset (Northam et al., 1998) and as early as 4 years of age (Patiño-Fernández et al., 2010). As patients continue to experience episodes of hypoglycemia and periods of hyperglycemia, one might expect these negatives effects of type 1 diabetes on childhood and adolescent cognitive functioning to worsen with increasing age. Reanalysis of the Diabetes Control and Complications Trial and its follow-up Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study of cognitive data of those who were adolescents when entering the study did not confirm such a continuous decline in cognitive functioning (Musen, Jacobson et al., 2008). A further detailed discussion of cognition in childhood type 1 diabetes is beyond the scope of this chapter.

Cross-sectional studies in adults with type 1 diabetes have shown decrements in cognitive functioning on various cognitive domains, including speed of information processing, attention, mental flexibility, and other executive functions. This wide variety is a result of differences in neuropsychological tests used, differences in patient and control characteristics, and differences in analytical methodologies. In 2005, Brands and colleagues published the first meta-analysis summarizing neurocognitive studies in type 1 diabetes (Brands, Biessels, de Haan, Kappelle, & Kessels, 2005). They included 33 studies published between 1980 and 2004 with a total of 660 patients. All participants were young- to middle-aged adults, suggesting that older adults, e.g., those over 65 years of age, were not represented in this meta-analysis. These patients were all over 18 years of age when included and had either an early-onset age (as defined as onset below 7 years) or a late-onset age (onset age 7 or higher). All studies included a matched control group.

As is shown in Fig. 23.1, the meta-analyses covered all major neuropsychological domains, including intelligence, learning and memory, attention, executive functioning, speed of information processing, language, and visual perception. Most domains were relatively homogenous across publications, which means that similar neuropsychological tests were used and conclusions can be drawn with more certainty. Only the domains of crystalized intelligence, cognitive flexibility, and psychomotor efficiency were relatively inhomogeneous, which results in a wider variation of the observed effect. The size of the effect is estimated by Cohen's δ. By definition a Cohen's δ of 0.2 is considered small, 0.5 medium, and 0.8 large (Cohen, 1988; Biessels, Deary, & Ryan, 2008). As is demonstrated in Fig. 23.1, type 1 diabetes has a global negative effect on cognitive function, but this effect is limited (Cohen's $\delta = 0.3$). Effects of similar size are found for fluid intelligence, speed of information processing, visual perception, and attentional measures, whereas somewhat larger effects were found for crystalized intelligence, cognitive flexibility, and psychomotor efficiency, with medium to large effect sizes. Although there is a global and statistically significant effect of type 1 diabetes on cognitive functioning in adults, the pattern characterizes itself by diminished processing speed and mental flexibility (Brands et al., 2005). This indicates that type 1 diabetes patients are less effective in rapidly and flexibly applying newly acquired information, which may be a problem in demanding situations. Another meta-analysis published in 2014 included 55 articles and showed similar results, a modest effect of type 1 diabetes on cognitive functioning (Tonoli et al., 2014).

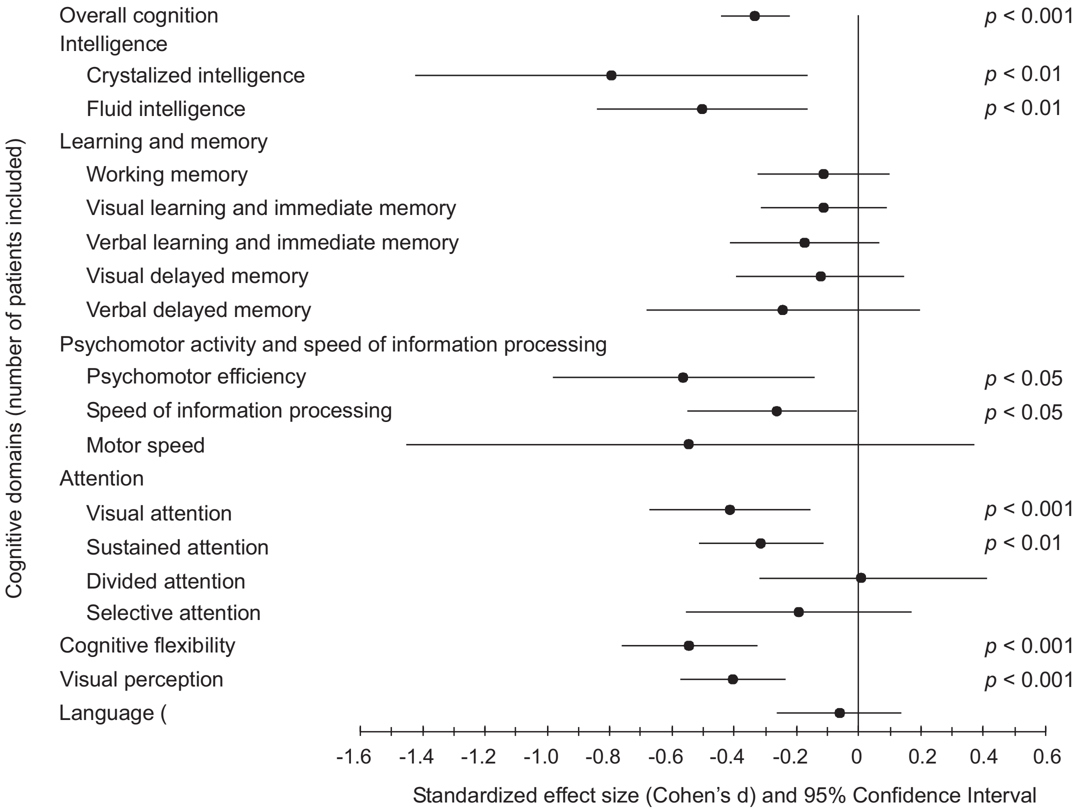

Fig. 23.1 Effect sizes in Cohen's δ with 95% confidence intervals for the cognitive domains in patients with type 1 diabetes compared with non-diabetes control subjects. (Original figure in Brands et al., (2005))

Little is known about the progression of these decrements over time. So far only two studies are published assessing changes with aging. By far the largest study is the DCCT/EDIC study in which patients were followed for at least 18 years (The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group, 2007). Of note is that this study did not include a non-diabetes control group, although the sample was large. The patients in this study did not show a notable or generalized decline in cognitive functioning. Rather, selective patients, i.e., those with HbA_{1c} values of 8.8% (73 mmol/mol) or higher, showed a marked decline on psychomotor efficiency and motor speed. Psychomotor efficiency decline was also seen in a smaller case-control study that followed the patients over a 7-year period (Ryan, Geckle, & Orchard, 2003).

Cognitive Decrements in Older Patients with Type 1 Diabetes

A limitation of both longitudinal studies is the relatively young age of the study population; there were all middle-aged adults. Diminished cognitive flexibility and mental processing speed are also found with normal aging (Harada, Natelson Love, & Triebel, 2013), and thus an interaction between type 1 diabetes and aging might be expected. This interaction is important as the life expectancy of patients with this disease is rapidly increasing. So far there is no evidence supporting an interaction between type 1 diabetes and aging. One study of 40 patients who were over 50 years of age at time of assessment lowers cognitive performance only on speed of information processing compared with non-diabetes controls (Brands et al., 2006). Importantly, the effect size was around Cohen's $\delta = 0.4$, indicating that the effect of type 1 diabetes on the brain did not increase. After 4 years, 36 patients were retested, and again there was no evidence of generalized decline (van Duinkerken, Brands et al., 2011). The study did show that patients with incident cardiovascular or severe hypoglycemic events had lower general cognition and speed of information processing scores, suggesting that specific groups may be susceptible of a disease by aging interaction.

Risk Factors of Long-Term Cognitive Decrements in Type 1 Diabetes

For a long time, it was considered that hypoglycemia was related to cognitive decrements found (Ryan, 2006). Acute hypoglycemia has a profound effect on cognitive functioning. This has been shown in many experimental studies under various degrees of hypoglycemia and applying different experimental tests, ranging from classical neuropsychological tests to experimental driving tests (Cox, Kovatchev, Anderson, Clarke, & Gonder-Frederick, 2010). Notwithstanding the debilitating effects of acute hypoglycemia on cognitive functions, more recent studies have failed to find an association between hypoglycemic events and neurocognitive deficits. Although this may be caused by the difficulty and variety of the definition of a hypoglycemic event, and by the uncertainty of autobiographical memory, the meta-analysis of Brands et al. failed to find an effect of hypoglycemia on cognition on all of the cognitive domains assessed (Brands et al., 2005).

The influential DCCT/EDIC also failed to observe an effect of hypoglycemia on cognitive decline, whereas hypoglycemic events were registered according to a standardized protocol (The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group, 2007). As said, this study did find an effect of high HbA_{1c} levels on cognitive decline, suggesting an effect of hyperglycemia, rather than hypoglycemia. A hyperglycemia effect was also supported by the other longitudinal study by Ryan and colleagues, who found a relation between psychomotor efficiency decline and the development of proliferative retinopathy and macrovascular complications (Ryan et al., 2003). Both micro- and macroangiopathy are strongly related to hyperglycemia. Later studies have used the presence of microvascular complications as a determinant of chronic hyperglycemia and indeed showed that those patients with complications had lower scores on general cognition, attention, and processing speed, with effect sizes up to Cohen's $\delta = 1.0$ (van Duinkerken et al., 2012). In this study, a group of patients without any microvascular complications was also included and also showed decrements in processing speed as compared with controls in the order of Cohen's $\delta = 0.4$. This suggests that cognitive deficits are already present in the absence of microvascular complications and provides additional evidence that chronic hyperglycemia affects the brain at an earlier stage.

It is not yet understood through which pathways hyperglycemia exerts its negative effects on the brain. Hyperglycemia itself leads to a cascade of reaction, such as an increased inflammatory response, deregulated hypothalamus-pituitary-adrenal axis (HPA-axis) functioning, and the formation of advanced glycation end products (Brownlee, 2001, 2005). It is known that, for example, both inflammation and HPA-axis deregulation are related to changes in cognition (Bruehl et al., 2009; Chung et al., 2015).

Cognition in Type 2 Diabetes

Over the past decades, there have been many studies trying to understand the relationship between type 2 diabetes and cognitive functioning. It has become increasingly clear that type 2 diabetes, just as type 1 diabetes, exerts a mild negative effect on cognitive functioning (Awad, Gagnon, & Messier, 2004).

A recent meta-analysis of 24 studies assessing cognitive functioning in more than 3300 patients with type 2 diabetes showed decrements in all cognitive domains that were measured. Effect sizes were largest for processing speed, executive functions, visual and verbal memory, and motor speed (Cohen's δ~0.3) (Palta, Schneider, Biessels, Touradji, & Hill-Briggs, 2014). For attention and concentration, the effect size was approximately 0.2 (Palta et al., 2014). Memory and learning performance is often found lower in patients with type 2 diabetes in comparison with controls. One systematic review identified 44% of the included studies reporting decrements in this domain (van den Berg, Kloppenborg, Kessels, Kappelle, & Biessels, 2009). Slowing of processing speed and mental efficiency seems, just as in type 1 diabetes, to be to core cognitive feature of type 2 diabetes, with up to 66% of studies reporting decrements in this domains (van den Berg et al., 2009). The effect sizes found in type 2 diabetic patients are roughly similar to the effect sizes found in type 1 diabetes, with the exception of memory and learning, which is not generally affected in type 1 diabetes patients.

This leads to the speculation that the negative effect of both types of diabetes may be relatively similar. Despite being an interesting question, there are not many studies that have actually compared cognitive performance between both patient groups. So far, one study, by Brands and colleagues, directly compared older type 1 diabetic patients with type 2 diabetes patients on cognition and MRI measures. They included 40 type 1 diabetes patients with a mean age of 61 years to 40 age-, sex-, and education-matched type 2 diabetic patients, on abstract reasoning, memory, information processing speed, attention and executive functions, and visuoconstruction (Brands et al., 2007a). Earlier reports had shown that both patient groups had poorer cognitive functioning compared with controls, mainly on measures of information processing speed (Brands et al., 2006; Brands, van den Berg, et al., 2007b). Combining both patient groups, there was an overall effect of group on cognitive functioning. Further statistical testing showed that patients with type 2 diabetes performed substantially worse on the visuoconstruction domain than their counterparts with type 1 diabetes. This is shown in Fig. 23.2. This is despite the large difference in disease duration, which was 34 years in the type 1 and 7 years in the type 2 diabetes group (Brands et al., 2007a). Groups did differ significantly on MRI measures of the brain, with the type 2 diabetes group having more deep white matter lesions and general cortical atrophy (Brands et al., 2007a). One criticism here is that the patients with type

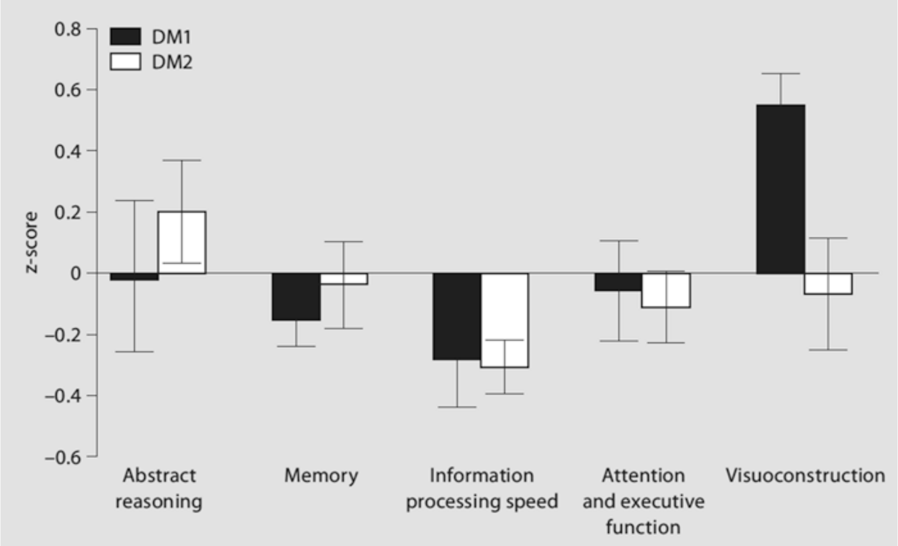

Fig. 23.2 Bar graph of neuropsychological domain scores for a group of type 1 diabetes patients (black bars) and type 2 diabetes patients (white bars). (Original figure in Brands et al., (2007a))

1 diabetes can be labeled as survivors. Despite that 70% of the 40 patients had microvascular complications, many have survived their type 1 diabetes for more than 40 years. Also, onset age in most patients was after the age of 7 years, whereas onset before this age is seen as particularly detrimental to cognitive performance. Such factors may have blunted the differences in performance between both patient groups.

Age of Onset Effects in Type 2 Diabetes

Both the meta-analysis by Palta and colleagues and the systematic review by van den Berg et al. showed a large variety in the magnitude of effect size as well as observed decrements between studies assessing type 2 diabetes patients. This is likely to reflect the heterogeneity of studies in age range, neuropsychological tests used, and inclusion of patients with risk factors than type 2 diabetes. The recent meta-analysis by Palta and colleagues, for example, included studies with patients being between 50 and 85 years of age with halve of the studies including patients over 65 years (Palta et al., 2014). An earlier onset of type 2 diabetes will inevitably lead to a longer time of exposure to metabolic derangement, and a higher risk of vascular complications, which can influence cognitive outcomes. Whether or not earlier onset age is indeed related to more profound cognitive decrements remains under investigation.

A study by Roy and colleagues included 82 type 2 diabetes patients between the age of 26% and 60 years (Roy et al., 2015). They showed that about 20% of their sample showed cognitive decrements. These decrements were weakly related to both higher glycosylated hemoglobin values and longer disease duration (Roy et al., 2015). A limitation of this study, though, is they only used the modified mini mental state examination and not more subtle neuropsychological tests. Moreover, no control subjects were included. It does, however, indicate that patients with type 2 diabetes early in life are sensitive to cognitive decrements and it might thus be hypothesized that mid-life onset type 2 diabetes has more detrimental effects on cognition than the late-life onset variant of the disease due to the longer duration of the disease.

This has effectively been shown by Roberts and colleagues. They included 1437 participants with a mean age of 80 years of whom 15.2% had diabetes and 74.3% had hypertension. Of those with diabetes, about one-third developed it during mid-life (i.e., before the age of 65 years). About 42% had hypertension during mid-life (Roberts et al., 2014). In that article, they showed that subjects with diabetes during mid-life were most susceptible to be diagnosed with mild cognitive impairment by expert physicians and that executive functions were particularly affected by mid-life diabetes (Roberts et al., 2014). Mid-life diabetes was also related to an increased prevalence of subcortical infarcts, lower hippocampal volume, and higher indices of global cortical atrophy (Roberts et al., 2014). Late-life onset diabetes, on the other hand, had no effects of cognition, the diagnosis of mild cognitive impairment, and was only related to higher cortical infarction load. Mid-life, but not late-life, hypertension had a similar detrimental effect of vascular measures of brain damage, such as infarctions, white matter lesion volume, and global cortical atrophy. Neither mid-life nor late-life hypertension had any effect on cognitive functioning in this sample. The mechanisms behind the effect of longer disease duration on cognitive functioning remain unclear and will likely involve many different factors. Factors of importance are (neuro)inflammation, with inflammation being related to both central obesity and high blood glucose levels, vascular damage, and other biochemical reactions related to chronic hyperglycemia, including formation of advanced glycated end products.

Does Cognitive Performance Decline over Time?

It might be reasoned that, if type 2 diabetes is related to cognitive decrements and some point in time, it may also cause a gradual decline in cognitive functioning. Although data on this is still somewhat contradictory, most studies seem to support the hypothesis of accelerated cognitive decline, at least in some patients. The Whitehall II study is a study exploring the relationship between socioeconomic status, stress, and cardiovascular disease. Between 1991 and 1993, 8637 participants between 39 and 64 years of age were screened for diabetes (Tuligenga et al., 2014). Participants received cognitive evaluation three times up to 2009, including tests for short-term verbal memory, inductive reasoning, and phonemic and semantic verbal fluency. In the analysis of the cognitive data, they included 4703 normoglycemic subjects, 648 participants with prediabetes according to the WHO/IDF criteria (Foundation, 2006), 115 newly diagnosed diabetes patients, and 187 patients with known diabetes (Tuligenga et al., 2014). Those with known diabetes had a 24% faster decline rate in their global cognitive score (mean of all test scores) than normoglycemic participants over 10 years: this was 29% for inductive reasoning and 45% for short-term memory (Tuligenga et al., 2014). It needs to be noted that the difference in decline rate was −0.11, −0.10, and −0.13 standard deviation, respectively. Albeit these rates were statistically significant, they are small and by no means are comparable to rates of decline seen in dementias. This is also unexpected as the mean age of the study sample was 54.4 years with an interquartile range of 50.3–60.3 years. It does however clearly show that even at an age of relatively stable cognitive functions, patients with type 2 diabetes show accelerated decline in cognitive functioning, suggesting it is related to accelerated cognitive aging.

The Maastricht study included 1290 subjects from the Netherlands who were over 40 years of age at baseline. Of those, 68 had diabetes at baseline who were on average 69 years of age, older than the participants from the Whitehall II study. Subjects were tested at baseline, 6 years and 12 years using three tests for verbal memory, processing speed, and executive functions (Spauwen, Köhler, Verhey, Stehouwer, & van Boxtel, 2013). Compared to control participants, those with diabetes at baseline showed accelerated decline on the tests of processing speed, on executive functions, and on the delayed recall trial of the verbal memory test (Spauwen et al., 2013). Unfortunately, only raw scores were reported without standard deviation, which makes it difficult to evaluate the effect size, but they seem small to moderate and comparable to those from the Whitehall II study. A limitation of both studies is that only several cognitive tests were used, whereas normally various tests measuring a part of the same domain, such as memory or executive functions, are used. This limits the possibility to generalize these results to the general population.

A case-control study in 68 type 2 diabetes patients performed a detailed neuropsychological evaluation twice in 4 years and compared change over time with 38 controls. At baseline both groups had an average age of approximately 65 years. Although patients performed slightly worse than controls on information processing speed and attention and executive functions at baseline and both groups showed a moderate decline in abstract reasoning and attention and executive functions over time, there was no evidence of accelerated decline on any cognitive domain in those patients with type 2 diabetes (Fig. 23.3) (van den Berg, Reijmer et al., 2010).

In addition to this, van den Berg and colleagues assessed cognitive functioning in a group of 596 subjects of 85 years for 5 consecutive years (van den Berg, de Craen, Biessels, Gussekloo, & Westendorp, 2006). Of these, 96 had diabetes at age 85 years. Figure 23.4 shows the change over time in performance for each cognitive test used. Patients with diabetes performed worse on the Letter-Digit Coding Test and Stroop Test at age 85. From the graphs it is evident that in both groups cognitive performance drops over the course of the follow-up period. However, diabetes was not associated with and accelerated decline in cognitive performance up until age 90 (van den Berg et al., 2006).

Although there seems to be a distinct discrepancy between the studies discussed here, taking a closer look, the results may not be very different at all. What all four studies show is that patients with

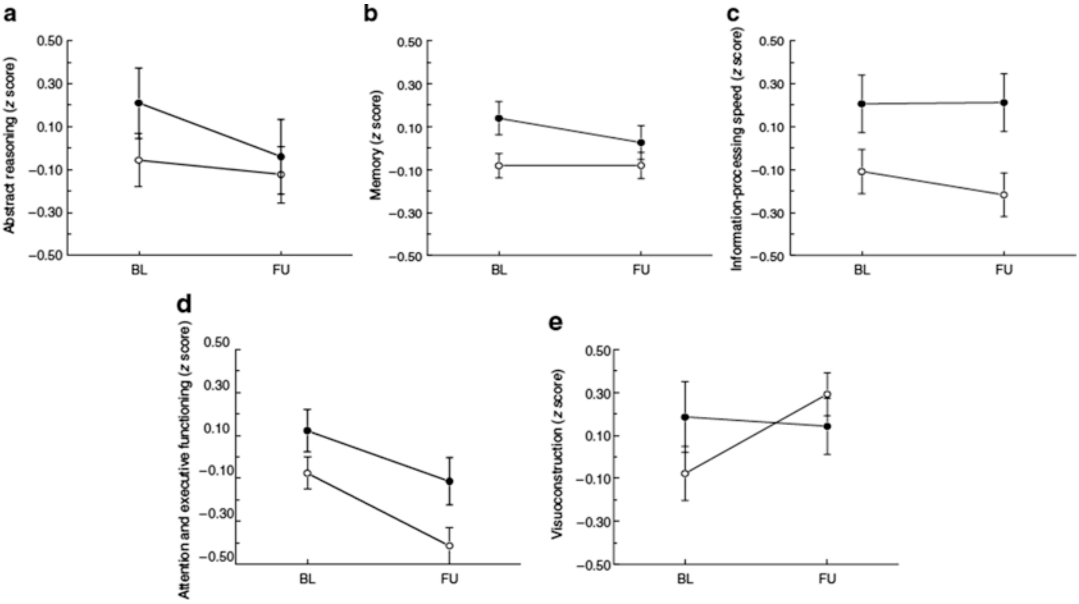

Fig. 23.3 Line graph of the various cognitive domains that were used to assess cognitive functioning in patients with type 2 diabetes (black dots) and controls (white dots) at baseline and at 4 years. (Original figure in van den Berg et al., (2010))

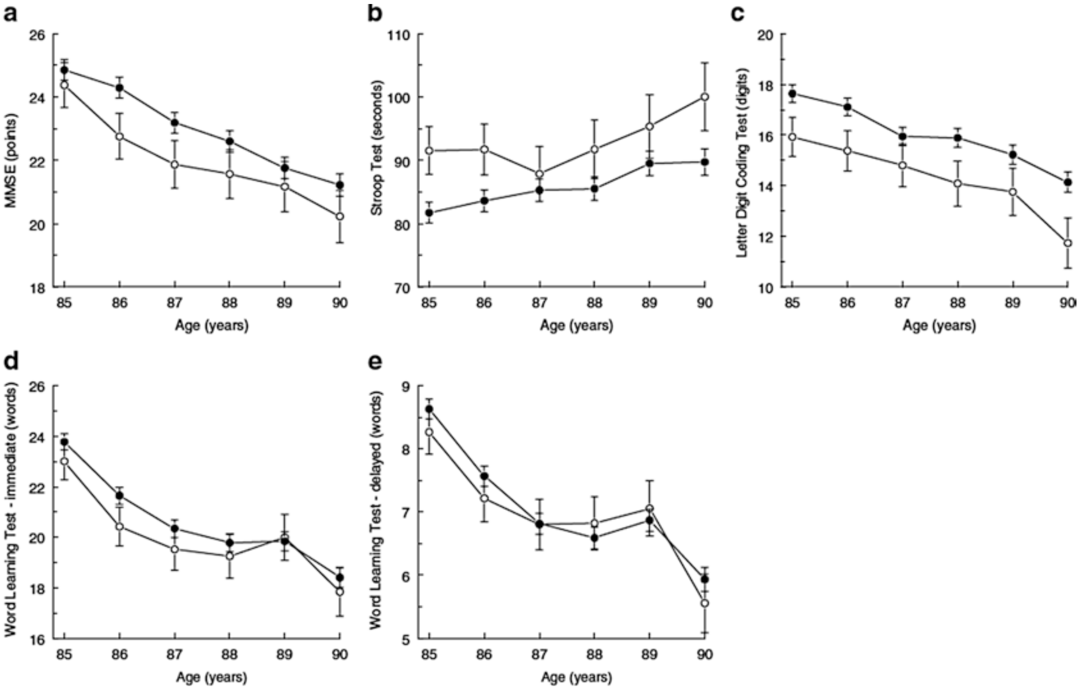

Fig. 23.4 Line graphs of annual performance of elderly patients with type 2 diabetes (black dots) and elderly controls (white dots) on various cognitive tests. (Original figure in van den Berg et al., (2006))

diabetes, despite their age, show cognitive decrements on tests that measure processing speed, attention, and executive functions. The Whitehall II and Maastricht study both show statistically significant accelerated decline in cognitive functions in the diabetes groups, but the differences with controls are relatively small and do not surpass more than 0.2 standard deviation. Taking a closer look at Fig. 23.3, one can see declines in cognitive performance of similar magnitudes on information processing speed and attention and executive functions. Especially the decline in information processing speed is not seen in the control group, suggesting that power rather than an absence of decline could be the result of the discrepancy. It shows that a closer look, not only taking into account p-values, helps clarifying seemingly contradictory results. Figure 23.4 from the Leiden 85+ study does not seem to suggest any different rates of decline in cognitive performance, suggesting that the effect of diabetes on cognition may be something that is more profound in younger patients relative to older patients.

Risk Factors for Cognitive Decrements in Type 2 Diabetes

Despite the potential protective effects of hypoglycemic medication, we still see cognitive decrements in patients with type 2 diabetes, which makes it important in understanding the risk factors in this patient population. Similar to type 1 diabetes, chronic hyperglycemic exposure has also been found to be related to poorer cognitive performance in type 2 diabetes patients (van den Berg et al., 2009). The ACCORD-MIND study has shown that retinopathy in type 2 diabetes patients is a proxy for future cognitive decline (Hugenschmidt et al., 2014). A study in elderly patients found that an improvement in HbA1c through a telemedicine intervention was related to delayed decline in global cognitive functioning, indicating that lowing the hyperglycemic burden can be beneficial for cognition (Luchsinger et al., 2011).

Hypertension, dyslipidemia, and obesity have also been linked to cognitive decrements in type 2 diabetes (van den Berg et al., 2009). These factors are part of the metabolic syndrome, a syndrome that has been shown to affect cognitive performance even before the development of type 2 diabetes (van den Berg et al., 2008). The effect of the metabolic syndrome on cognition is not uncontroversial, with some studies showing negative effects and other failing to find negative effects on cognition (Roriz-Filho et al., 2009). For example, in elderly patients with type 2 diabetes and the metabolic syndrome, a similar profile of cognitive decrements was found when comparing performance to that of controls (van den Berg et al., 2008). In the Leiden 85+ study, however, having the metabolic syndrome was related to decelerated cognitive decline over 5 years (van den Berg et al., 2007). This may have to do with the age of participants. As discussed before, mid-life diabetes and hypertension have been shown worse for cognitive performance than having those conditions only later in life. This may also be the case for the metabolic syndrome and its individual factors.

Macrovascular disease, such as cerebro- and cardiovascular events, in type 2 diabetes seems to be another risk factor for cognitive deficits, one that is less prominent in type 1 diabetes for obvious reasons. Patients with type 2 diabetes have a higher risk of having a stroke or a cardiovascular event. This may inevitably lead to cognitive deficits that are permanent in nature. A last factor of importance is depression. It is well-known now that patients with diabetes have a twofold higher risk of developing depressive symptoms and major depressive disorder (Snoek, Bremmer, & Hermanns, 2015). Depression in diabetes is more difficult to treat, has a higher recurrence rate (Snoek et al., 2015), and is associated with worsened glycemic control and higher incidence of micro- and macrovascular complications (Lin et al., 2010), cognitive decrements and dementia (Katon et al., 2015), and premature death (van Dooren et al., 2013). The large ACCORD-MIND study has shown that depression is a predictor of future cognitive decline. Having or having had depression is also part of the risk calculator for the development of dementia, created by Exalto and colleagues (Exalto et al., 2013), making depression a factor that needs to be taken into account in patients with type 2 diabetes (Sullivan et al., 2013).

Are Patients with Diabetes at Risk of Developing Dementia?

Over the years, there has been much attention for the relationship between diabetes, mainly type 2 diabetes, and dementia. This is a legitimate question as diabetes is related to cognitive decrements that slowly progress over time and is related to micro- and macrovascular disease. A meta-analysis by Cheng et al. from 2012 summarized 19 longitudinal studies including 6184 patients with diabetes and 38,530 subjects without diabetes (Cheng, Huang, Deng, & Wang, 2012). The follow-up time of these studies showed a wide range between 1 and 13 years. Overall, diabetes patients were at a slightly higher risk of developing mild cognitive impairment (relative risk, 1.21; 95% confidence interval, 1.02–1.45) and any dementia (relative risk, 1.51; 95% confidence interval, 1.31–1.74) over time (Cheng et al., 2012). When specifically calculating the risk to develop Alzheimer's disease, the most prevalent form of dementia, the relative risk values were only slightly elevated in diabetes patients relative to controls (relative risk, 1.46; 95% confidence interval, 1.20–1.77).

A substantially higher risk was found for the development of vascular dementia (relative risk, 2.48; 95% confidence interval, 2.08–2.96). An interesting note to these relative risk numbers is that of the 16 included studies that had Alzheimer's disease as their endpoint, 10 studies did not show an increased risk of developing Alzheimer's disease in diabetes patients. On the other hand, only two of the ten included studies with vascular dementia as endpoint could not objectify an elevated risk of vascular dementia development in diabetes patients. These numbers indicate that the relationship between diabetes and Alzheimer's disease is highly controversial.

A study by Roberts and colleagues showed that an increased risk of developing mild cognitive impairment later in life in diabetes patients was related to mid-life diabetes, but not late-life diabetes (odds ratio, 2.08; 95% confidence interval, 1.16–3.73, versus 1.17; 95% confidence interval, 0.74–1.84, respectively) (Roberts, Knopman et al. 2014). A recent study by Smolina and colleagues analyzed the medical records of 343,062 patients with type 1 diabetes and 1,855,141 patients with type 2 diabetes over the age of 30 years who were hospitalized between 1998 and 2011 (Smolina, Wotton, & Goldacre, 2015). Among patients with type 1 diabetes, 10,786 had any dementia (Alzheimer's disease, vascular and unspecified dementia). Compared to the reference group, type 1 diabetes patients had a relative risk of 1.65 (95% confidence interval, 1.61–1.68) to develop any dementia, which indicates a slightly higher risk. The risk of developing Alzheimer's disease was only marginally higher in type 1 diabetes (2.113 cases; relative risk, 1.10; 95% confidence interval, 1.05–1.15), but substantially higher for vascular dementia (3.885 cases; relative risk, 2.21; 95% confidence interval, 2.13–2.28).

For type 2 diabetes, the relative risk was slightly lower (any dementia, 60.127; relative risk, 1.37; 95% confidence interval, 1.35–1.38; Alzheimer's disease, 12.743; relative risk, 0.99; 95% confidence interval, 0.97–1.01; vascular dementia, 20.427; relative risk, 1.80; 95% confidence interval, 1.77–1.83). This study did not show a relationship between Alzheimer's disease and type 2 diabetes. Moreover, type 2 diabetes patients of 80 years of age and older had a significantly lower relative risk of developing Alzheimer's disease relative to the reference cohort (4.580 cases; relative risk, 0.87; 95% confidence interval, 0.84–0.91). This was also seen in admitted type 1 diabetes patients of this age category (483 cases; relative risk, 0.84; 95% confidence interval, 0.76–0.92). Regardless of age category, both types of diabetes were related to an increased risk of development of vascular dementia (Smolina et al., 2015).

Based on two 10-year follow-up cohort studies, Exalto and colleagues calculated the risk score calculator of dementia risk in type 2 diabetes patients. Besides age (increasing age leads to higher risk) and education (higher education is protective), six diabetes-specific factors or factors related to diabetes were included (Exalto et al., 2013). Having microvascular disease, diabetes foot, and cerebro- or cardiovascular disease lead to a higher risk of dementia development. Acute metabolic events, such as ketoacidosis or hypoglycemic coma, and having had depression also add to dementia risk (Exalto et al., 2013). Most of these factors are related to vascular incidents, and thus the calculator seems more a predictor of vascular dementia than of Alzheimer's disease. The lowest score is −1, which is associated with a 5.3% higher risk of dementia development. The highest scores (12–19) are related to a 73.3% increased risk of developing dementia.

Considering the link between diabetes and vascular disease, the higher risk of developing vascular dementia is intuitive. The mechanisms behind a possible relationship between diabetes and Alzheimer's disease are far less intuitive. Neuropathologically, there is almost no evidence in humans that diabetes is related to specific Alzheimer's disease pathology (i.e., neurofibrillary tangles and amyloid-beta depositions) (Guerrero-Berroa, Schmeidler, & Beeri, 2014). Early postmortem studies in type 1 diabetes mainly found vascular damage, such as white matter lesions, small infarcts, and micro-bleedings (Reske-Nielsen et al., 1966, Reske-Nielsen & Lundbæk, 1968). Postmortem studies in type 2 diabetes have also failed to find elevated levels of neurofibrillary tangles and amyloid depositions relative to controls and sometimes even found lower levels of these markers (Nelson et al., 2009; Sonnen, Larson, Brickell, et al., 2009; Ahtiluoto et al., 2010). Interestingly, one study showed that patients with dementia without diabetes had higher levels of amyloid-beta and F_2-isoprostanes (a marker of oxidative stress) in the brain, whereas dementia patients with diabetes had higher levels of microvascular infarcts and interleukin-6 (a proinflammatory marker), suggesting that, despite the diagnosis of dementia, there may be different pathophysiological mechanisms at work in patients with and without diabetes (Sonnen et al., 2009).

It is puzzling that an increased risk of Alzheimer's disease, as is found in some epidemiological studies, is not mirrored by a presence of Alzheimer pathology in the brain. One hypothesis to explain this discrepancy is that diabetic medication has neuroprotective properties (Guerrero-Berroa et al., 2014). Peripherally administered insulin in healthy elderly men was acutely related to better memory performance and lower levels of amyloid-beta deposition (Watson et al., 2003), whereas high amyloid-beta deposition is seen in Alzheimer's disease. In type 1 diabetes patients, higher concentrations of amyloid-beta (i.e., lower deposition) were found compared with controls, suggesting that chronic insulin administration may have a similar effect (Ouwens et al., 2014). In that sample, higher, but not above the clinical cutoff for Alzheimer's disease, concentrations of neurofibrillary tangles were observed in cerebrospinal fluid. Increases in this biomarker have been associated with hypertension in patients with Alzheimer's disease (Kester et al., 2010), suggesting a vascular link possibly related to this increase.

Antidiabetic medications that are often used in type 2 diabetes have also been suggested to be either neuroprotective or have direct effects on the brain. Metformin is one of the most common antidiabetic medications used in type 2 diabetes, and in patients with Alzheimer's disease and diabetes, the rate of cognitive decline was lower than in patients with Alzheimer's disease alone (Domínguez, Marschoff, González, Repetto, & Serra, 2012). Taking metformin or sulphonylureas has, in one study, also shown to lower the incidence of dementia in patients with type 2 diabetes (Hsu, Wahlqvist, Lee, & Tsai, 2011), although a second study revealed the opposite effect (Imfeld, Bodmer, Jick, & Meier, 2012).

Newer antidiabetic agents, such as glucagon-like peptide 1 (GLP-1) and dipeptidyl peptidase-4 (DPP-4) inhibitors, have also been shown to have effects directly in the brain and seem to work in a neuroprotective way (Patrone, Eriksson, & Lindholm, 2014). Although much remains unclear, antidiabetic drugs seem to be potent protectors against Alzheimer pathology in the brain, whereas the clear relationship between diabetes and vascular dementia seems linked to the vascular vulnerability of diabetes patients.

Magnitude of Cognitive Decrements

The magnitude of the differences in cognitive performance between patients with type 1 diabetes and controls is on average relatively small (Cohen's δ ~ 0.3). Although such an effect size is large enough to discriminate the patient group from the control group, it is by far not large enough to establish to

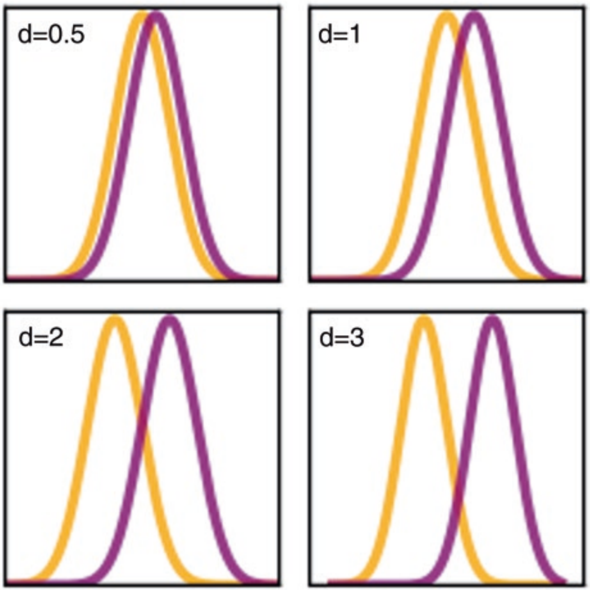

Fig. 23.5 Gaussian distributions of two groups with a between-group difference of Cohen's δ = 0.5, 1, 2, and 3. As can be seen, there is much overlap between the groups with a between-group effect size of 0.5 and 1, which makes it impossible to establish to which group a person belongs to. With larger between-group effect sizes, i.e., 2 or 3 or larger, it becomes easier to determine the group a participant belongs to based on the neuropsychological test scores. (Figure accessed from https://en.wikipedia.org/wiki/Effect_size)

what group a single subject belongs to, based on the neuropsychological test scores. Even with a magnitude of Cohen's δ = 1.0, which has been found in type 1 diabetes patients with proliferative retinopathy (van Duinkerken et al., 2012) and is considered a large effect size, and you should have no problem in detecting that there is a consistent cognitive difference, on average, between patients and controls, it would still be difficult to predict to what group a single subject belongs to (Fig. 23.5). This is important to recognize when evaluating cognitive performance in this group of patients.

Clinical Relevance of Cognitive Decrements in Type 1 and Type 2 Diabetes

The major question now is what is the clinical relevance of these cognitive decrements for patients with either type 1 or type 2 diabetes? It is beyond any doubt that a stroke or a cardiovascular event can lead to permanent and debilitating cognitive deficits. These are, however, not directly caused by a disturbance in glucose metabolism, but rather are a potential consequence of diabetes. The devastating effects of dementia on life are also beyond questioning. But what about those mild and moderate cognitive decrements that are found at a group level in almost every study in diabetes? How does that translate to the individual patient? The answers to those questions are not straightforward and leave room for individual interpretation.

As we have discussed above, the between-group effect sizes are not sufficiently large to determine with certainty to which group someone belongs to, but this is a purely research approach. However, even when a single patient scores up to 1 standard deviation below the score of people without diabetes of the same age, sex, and education level, it is not sufficient to be identified as having cognitive deficits. This pertains to methodological problems of neuropsychological tests (which are far from perfect), but also on the definition of a cognitive deficit, which is far from clear-cut (Lezak, 2012; Abramovitch, Mittelman, Tankersley, Abramowitz, & Schweiger, 2015).

Such methodological limitations are part of a discussion that neuropsychologists working in the field of medical neuropsychology need to participate in. The individual patient with cognitive complaints needs to be taken seriously. A neuropsychological evaluation can be helpful and insightful. In most cases, based on the currently available tests and norms, the evaluation will have a reassuring character. It will mostly show that no cognitive deficits are present. A potential danger is that the individual patient is not reassured as he or she keeps experiencing cognitive complaints. It is the role of the neuropsychologist to provide the patient with information about the profile of cognitive decrements in diabetes, about how extremes in glucose levels, either high or low, can influence our cognitive abilities on a daily basis. The professional needs to provide information on depression, stress, life events, and how they affect our cognition. Explaining that not finding any cognitive deficit on a neuropsychological evaluation does not mean that complaints are illegitimate is also very important.

Conclusions and Future Directions

To conclude, mild to modest cognitive decrements are found in patients with type 1 and type 2 diabetes. These decrements are mainly found in domains that involve mental flexibility and processing speed, although in type 2 diabetes, memory and executive functions decrements can also be observed. The risk factors for such decrements are mainly related to chronic hyperglycemic exposure. Diabetes is a clear risk factor for the development of vascular dementia, which may become a great concern given the rapid rise in diabetes incidence combined with the improvements in diabetes treatment and extension of the life expectancy. The effects of these cognitive decrements will differ from patient to patient, and it is important that, although the decrements are on average mild, individual patients' daily life's can suffer from these decrements.

Regarding future directions, it is clear that much research has already been done and more neuropsychological research will not help us improve the care of the individual patient. It is time to go back to the drawing table and see how the individual patients can be more central in cognitive research in diabetes. This is not only a problem in diabetes. Neuropsychology started as the science of cognitive functions in diseases with severe cognitive deficits, such as dementias (Lezak, 2012). Over the decades, interest in the neuropsychological effects of psychiatric and somatic disorders accumulated, but tests, norms, and definitions in neuropsychology are not yet adapted to this new field of neuropsychology (Abramovitch et al., 2015). This is not specific to diabetes though.

Specifically looking at diabetes, it is important that research take a deeper dive into the mechanisms that lead to cognitive decrements. Correlations with HbA1c or microvascular disease do not suffice anymore. We need a better understanding of how cognition is regulated on a molecular level. How do chronic inflammation, oxidative stress, and formation of advanced glycation end products relate to cognitive performance? What changes in the brain are mediators, lower perfusion, poorer white matter microstructure, etc.? But maybe the best question is not what is putting these patients in danger of cognitive decrements, but what is protecting these patients from developing more severe cognitive decrements. Continues insults of a misbalance in glucose metabolism lead, when untreated, to blindness, loss of limbs and kidneys, and premature death. Yet the brain seems to be largely unaffected. How is that possible? It seems the big challenge of the coming decades is not to figure out what is wrong with the brain, but rather to figure out what is protecting the brain.

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Chapter 24
Individual-Level Intervention Approaches

Frank J. Snoek and Juliane Menting

Psychosocial support is a key element of chronic care (Wagner, Austin, & von Korff, 1996), aiming for empowerment, well-being, and optimal clinical outcomes. In most settings, healthcare professionals (HCP) have contact with persons with diabetes (PWD) over a longer period of time, providing a unique opportunity to build trust and integrate psychological support in ongoing education and medical care. Face-to-face visits are scheduled to monitor metabolic control, screen for complications, and support the PWD in his/her self-management (American Diabetes Association, ADA, 2018; International Diabetes Federation, 2006). Visits may be supplemented and can sometimes be partly replaced by contact via email, telephone, or video consultations. Telemedicine is steadily growing, allowing for more frequent interaction between HCP and the PWD, synchronous or asynchronous. Rather than having to wait weeks or months for the next appointment, the PWD can ask questions in between clinic visits, submit blood glucose measurements, and receive feedback from the HCP (Duke et al., 2017). This way HCP and PWD can stay connected, and it allows for "in-time" advice and support. In their regular contacts and educational sessions, HCP can assist PWD to develop the necessary skills and build self-confidence for effective self-management, using motivational interviewing and behavior change techniques.

Talking about emotional health is an essential part of the diabetes consultation. In their contacts with PWD, physicians, diabetes nurse educators, and dieticians have the opportunity and responsibility to inquire about emotional problems and offer counseling to PWD where that is feasible. For PWD suffering from severe psychological or behavioral problems, a referral to a licensed social worker, clinical psychologist, or psychiatrist is warranted, preferably a member of the diabetes care team. When a PWD is referred for specialized psychological treatment, it is important to make sure there is close collaboration with the diabetes care team or a case manager to help integrate medical and psychological approaches. Given the complex interaction between emotional health and diabetes

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F. J. Snoek (✉)
Department of Medical Psychology, Amsterdam Public Health Research institute, Amsterdam University Medical Centers, Vrije Universiteit, Amsterdam, The Netherlands
e-mail: fj.snoek@amsterdamumc.nl

J. Menting
Department of Medical Psychology, Amsterdam Public Health (APH) Research Institute, VU University Medical Center, Amsterdam, The Netherlands

NIVEL, Netherlands Institute for Health Services Research, Utrecht, The Netherlands

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regulation, it may be necessary to adjust the medical treatment in order to help a PWD overcome certain barriers, e.g., extreme fear of hypoglycemia. Likewise, focus and intensity of psychological therapy may need to be adjusted to the capabilities of a patient with debilitating complications or comorbidities.

Recognizing and Responding to Emotional Distress

Diabetes professionals often work under time pressure and face increasing administrative tasks, leaving little room for an open conversation with the PWD. This may at least partly explain why psychological distress (e.g., depression, anxiety) is frequently missed by diabetes care professionals (Pouwer, Beekman, Lubach, & Snoek, 2006) leading to substantial under treatment of behavioral problems in PWD (Li et al., 2009; Peyrot et al., 2005). To promote timely detection and discussion of emotional distress by nonspecialized HCP, screening and monitoring has been advocated as part of routine diabetes care (Young-Hyman et al., 2016; IDF Task Force, 2006). Review and discussion of psychological functioning should be integral part of the consultation, with specific attention to the most vulnerable patients, e.g., those with long-standing poor diabetes control, complications, and previous episodes of psychological distress.

In this context, the use of well-validated practical assessment tools is recommended to help identify "caseness." Examples are the World Health Organization 5-item Well-Being Scale (WHO-5; Hajos et al., 2013), the 9-item Patient Health Questionnaire (PHQ-9; van Steenbergen-Weijenburg et al., 2010), the 20-item Problem Areas in Diabetes Scale (PAID; Polonsky et al., 1995; Snoek, Pouwer, Welch, & Polonsky, 2000), or the 17-item Diabetes Distress Scale (DD; Polonsky et al., 2005). Besides screening for psychological vulnerability, self-report questionnaires help to focus the conversation on patient-relevant topics and discuss barriers in self-management. Such an approach has shown to be feasible and effective in fostering time-limited, constructive conversations around psychological issues and help identify situations where actions are needed, e.g., adjustment of diabetes therapy (Snoek et al., 2012). Identified psychosocial problem areas may not always be directly related to the diabetes; in any case, it is relevant to know of the stresses experienced by the PWD in his/her personal or work life and if and how these stresses affect well-being, motivation, and diabetes self-management behaviors. Understanding the patient's context is always important and helpful to effectively tailor diabetes care to the changing individual needs of the PWD and promote adherence.

Talking about emotions and addressing psychological needs demands good communication skills and knowledge about common psychological issues experienced by PWD. Empathic communication on the part of the HCP is required, using open-ended questions, reflecting and paraphrasing to make sure that what is being said is understood. Responding constructively in a nonjudgmental way to the emotions expressed by the PWD will help to normalize negative emotions and make the PWD feel respected and "safe." It is important to recognize that being able to express one's emotions and being listened to empathically in and by itself offers relief and is therapeutic, often to the extent that the PWD has no need for further counseling. In some cases, further steps do need to be taken. Here, the "5 A's model" (originally developed by the National Cancer Institute to help people quit smoking, Fiore et al., 2008) can serve as a framework for the HCP to structure the process of problem-solving, where the A's stand for Ask, Advise, Assess, Assist, and Arrange. In case of a likely serious emotional problem, a referral (Arrange) to a mental health specialist is warranted; not all patients, however, immediately are ready to accept a referral and need time and encouragement before taking such a step. This may be related to the stigma around mental illness and the perception that not being able to resolve one's own psychological problems is a sign of "weakness." This then calls for further exploring the reasons underlying the reluctance (Ask, Assess) and assists the PWD in developing a more positive attitude toward accepting professional help. Having a mental health professional present in the diabetes clinic helps to normalize psychological counseling as part of diabetes care and lowers the threshold for making an appointment.

We should remind ourselves that the majority of PWD are coping effectively with their diabetes and doing well. Most PWD are not in need of professional psychological support. Should these people also be screened and monitored? Indeed, PWD who have shown to be resilient over time are at low risk of developing emotional problems. Yet, periodic monitoring and discussing well-being in PWD reporting to do well is useful. First and foremost, to validate the coping efforts and resilience of the PWD whose daily self-management in the face of other life stresses often stays unnoticed. Acknowledging the "hard work" of PWD helps to booster the person's confidence in maintaining the aspired behavioral changes and is conducive to the relationship. It also offers an opportunity to check for early signs of emotional distress and proactively discuss specific challenges the PWD may face in the near future (e.g., related to change of job) and discuss preventative strategies.

In summary, periodic monitoring and discussing of emotional well-being fosters constructive interactions with PWD in addition to improving detection of psychosocial problems, and subsequent well-being and patient satisfaction (Pouwer, Snoek, Ploeg, Adèr, & Heine, 2001; Snoek et al., MIND study Snoek et al., 2011, 2012). Having a monitoring procedure in place lays the foundation for effective psychosocial care for individuals with type 1 and type 2 diabetes and their significant others.

Psychological Counseling

Psychological interventions for people with a chronic somatic disease largely build on principles and evidence from psychotherapy practice for people without a medical condition, where cognitive behavioral therapy (CBT) is the mainstream approach. CBT is evidence-based and applicable to a wide range of problems and disorders. CBT fits well in the context of chronic illness and is the focus of this chapter.

CBT is focused on active problem-solving, with a prominent role for "cognitive restructuring," i.e., challenging negative beliefs about oneself and the world and changing them into positive, helpful thoughts with subsequent positive effects on feelings and behaviors. Reframing of negative thinking and behavioral activation are at the core of CBT, often combined with modules on stress management and assertiveness. In the past decade, CBT has further developed to incorporate elements of "mindfulness," where the emphasis is on accepting disruptive or unhelpful thoughts rather than changing them.

CBT in somatic patients, including diabetes, appears equally effective with respect to psychological outcomes, such as reduction of symptoms of depression and anxiety (Beltman, Voshaar, & Speckens, 2010). Epidemiological studies have shown that depression and anxiety are associated with poorer treatment adherence and worse diabetes outcomes relative to psychologically healthy PWD (Ciechanowski, Katon, Russo, & Hirsch, 2003; Gonzales et al., 2008; Peyrot et al., 2005). Overall, psychological therapies, most of which are based on CBT, have a small to moderate positive effect on short-term and medium-term glycemic control but not on long-term glycemic control (Uchendu & Blake, 2017). Improvements in psychological functioning do not always automatically and immediately translate into improved medical outcomes. As postulated by Detweiler-Bedell, Friedman, Leventhal, Miller, and Leventhal (2008), this may be explained by the fact that people with a chronic illness and psychological comorbidity are faced with perceived conflicting self-regulatory demands. For example, in CBT people are encouraged to improve their mood by engaging in pleasurable activities, such as eating out, while at the same time, they are advised to eat healthier and keep a low-fat diet. Similarly, advising patients to frequently check their blood glucose may be perceived as overly demanding and "depressogenic," conflicting with the goal to maintain well-being. CBT in diabetes should thus aim for optimal management of *comorbidity* rather than either mental or physical well-being, capitalizing on synergistic self-regularly demands such as physical activity and social interactions and adopting a positive attitude toward taking control and self-managing the diabetes.

CBT for Distress Living with and managing diabetes can be stressful and eventually lead to diabetes "burnout," a state of demoralization characterized by feelings of helplessness and hopelessness (Polonsky, 1999). It is well-known that emotional distress specifically related to diabetes – diabetes distress – is common among people with diabetes affecting 20 to 30% of the population. Diabetes distress is defined as the worries, anxieties, and frustrations people experience related to the disease and the treatment in the context of the daily lives of the PWD. Diabetes distress in itself is burdensome and has negative effects on self-management and subsequent diabetes outcomes. Distress and depression are not the same thing, but both are risk factors for the other (Snoek, Bremmer, & Hermanns, 2015). Other risk factors for elevated diabetes distress include female gender, prolonged poor glycemic control, complications, and comorbidities (Fisher et al., 2010; Snoek et al., 2012). From an adjustment (coping) perspective, facing the diagnosis of diabetes and onset of complications are particularly challenging events and may be regarded as "predictable crises" (Hamburg & Inoff, 1983) warranting special attention. In practice, coping difficulties can arise at any time, e.g., when the PWD is faced with additional life stresses, such as the loss of a loved one, family conflicts, or financial strains. This again underscores the importance of having a good understanding of the changing psychosocial context of the PWD, beyond conventional clinical diabetes parameters.

Educational and psychological interventions can help to alleviate diabetes distress, although programs specifically developed for people with diabetes distress are scarce. A structured group-based CBT program for PWD targeting diabetes distress and poor glycemic control (Snoek et al., 2008) showed a significant reduction of diabetes distress, but glycemic control (HbA1c) only improved in those with high diabetes distress and comorbid depression. Diabetes distress indeed has been found to mediate the relationship between reduced depression and improved glycemic control (Van Bastelaar et al., 2010). In their review and meta-analysis, Alam, Stuart, Lall, and Winkley (2009) studied the effects of psychological interventions on glycemic control and psychological status. The pooled effect size for psychological distress (13 included studies) was −0.56, 95% CI -1.00 to −0.13. Psychological interventions appear to reduce psychological distress; however, due to the high heterogeneity of measurement tools between trials, the results of the meta-analysis need to be interpreted with caution.

Chew, Vos, Metzendorf, Scholten, and Rutten (2017) conducted a Cochrane review of psychological interventions on diabetes distress in persons with type 2 diabetes (effect size −0.07, 95% CI −0.16 to 0.03). However, only 7 of the 24 included studies were conducted in PWD who actually reported elevated diabetes distress at baseline. Studies including PWD reporting low distress may suggest interventions are not effective, while in fact this is due to a floor effect. It follows that Fisher et al. (2013) found a larger reduction of diabetes distress in persons with higher baseline diabetes distress compared to those with lower distress in their Reducing Distress and Enhancing Effective Management (REDEEM) study. Here three behavioural approaches were tested against each other in non-clinically depressed persons diagnosed with type 2 diabetes: (1) a Computer Automated Self-Management program (CASM), (2) a Computer Automated Self-Management and Problem Solving Therapy (CAPS), and (3) a Lifestyle and Activities Education Program (LEAP-AHEAD). CASM is an automated web-based and telephony-based program aiming to improve self-management behaviors. CAPS incorporates a problem-solving program (CBT based) additional to the CASM elements. During the problem-solving therapy, PWD learn to reduce diabetes distress directly by adapting problem-solving techniques. LEAP-AHEAD is a minimal intervention consisting of web-delivered health risk appraisal and diabetes self-care practices. Diabetes distress was reduced equally in all three programs and showed an improvement in healthy eating, physical activity, and medication adherence after following the programs. It seems that diabetes distress is responsive to even minimal behavioral interventions.

In their DiaMind study, Van Son et al. (2013) investigated the effects of mindfulness-based cognitive therapy (MBCT) in PWD with emotional distress. The training is based on mindfulness-based stress reduction and mindfulness-based cognitive therapy according to the protocol of Segal, Williams, and Teasdale (2002) and combines meditation exercises with elements of CBT. During the treatment, PWD learn to regulate their attention by focussing on direct experiences and adopting an open attitude toward these experiences. The MBCT program was found to significantly reduce general perceived stress, depressive symptoms, and anxiety in comparison with a waitlist control group. Only in the subgroup of PWD with high diabetes distress at baseline was the intervention effective in reducing diabetes distress. As in the study of Fisher et al. (2013), this result could be attributed to a floor effect, and it seems important to tailor interventions for PWD with elevated diabetes distress.

CBT for Depression The high prevalence of comorbid depression in diabetes and its ramifications have received much attention in the past years. Two systematic reviews and meta-analyses showed that individual pharmacological and psychological treatment of major depression in PWD are both effective in reducing depressive symptoms (Van der Feltz-Cornelis et al., 2010; Baumeister, Hutter, & Bengel, 2012). Antidepressants often have side effects and are not always acceptable to patients. Moreover, psychological treatment, most often CBT, can be safely and effectively delivered face-to-face as well as online or combined (“blended”). Van Bastelaar, Pouwer, Cuijpers, Riper, and Snoek (2011) developed a web-based CBT depression program for PWD, based on Lewinsohn’s well-established 8-week Coping with Depression (CWD) course (Cuijpers, Munoz, Clarke, & Lewinsohn, 2009; Van Bastelaar, Cuijpers, Pouwer, Riper, & Snoek 2011). CWD helps participants acquire six basic skills: pleasant activities scheduling, cognitive restructuring, coping with worries, relaxation, communication, and assertiveness. The self-help CWD course was adapted to diabetes as an online guided depression treatment and tested in a RCT in a mixed sample of Dutch type 1 and type 2 diabetes patients with moderate to severe depression. Participants follow eight lessons chronologically and read text, watch videos modeling illustrative positive scenarios, engage in exercises, submit “homework,” and receive feedback by email from a coach (psychologist). Participants practice the principles of CBT in their daily lives to strengthen their skills. This online program was found to be twice as effective in reducing depression as the control group, even among those with major depressive disorder (MDD), general anxiety disorder (GAD), and/or high diabetes-related distress (Van Bastelaar et al., 2012). Nobis et al. (2015) developed a similar approach for type 1 and type 2 diabetes patients in primary care in Germany with an emphasis on problem-solving and optional modules on eating and sleep habits. They found large effects sizes with respect to reduction of depression and diabetes distress both at 2 months and 6 months follow-up (Ebert et al., 2017).

A review and meta-analysis of RCT’s looking at CBT, antidepressants, or “collaborative care” suggest that incorporating diabetes self-management education in CBT is the most effective approach when it comes to improving depression and glycemic control (Van der Feltz-Cornelis et al., 2010). Research clearly indicates that treatment of depression in diabetes requires an interdisciplinary approach. In primary care, a collaborative care model has been developed for persons with depression and a chronic illness, including type 2 diabetes and cardiovascular disease. Collaborative care is guideline-based and resource-efficient, delivered individually by trained nurse case managers with supervision from a primary care physician. Depression is monitored periodically using a screener (PHQ-9), and nurses offer behavioral counseling (e.g., goal setting, problem-solving) and stress management techniques as an integral part of care, with frequent (telephone) follow-ups. Depression treatment may include antidepressant medication and/or CBT and has shown to be effective in terms of reduction of depressive symptoms as well as improving cardiovascular and metabolic outcomes (Katon et al., 2010).

CBT for Chronic Fatigue In addition to CBT approaches for depression and distress, CBT for chronic fatigue in type 1 diabetes has been established and shown to be efficacious. Chronic fatigue presents in 40% of PWD who describe it as one of the most disabling symptoms of their disease (Goedendorp et al., 2014). Significantly higher scores on fatigue are found in people with type 1 diabetes than in the general population (Segerstedt, Lundqvist, & Eliasson, 2015). Chronic fatigue is indicated by a score of 35 or higher on the Checklist Individual Strength subscale fatigue severity

(Worm-Smeitink et al., 2017), in combination with a duration of fatigue of 6 months or longer. CBT for chronic fatigue in type 1 diabetes is based on a cognitive-behavioral model assuming that fatigue is triggered by diabetes and/or diabetes-related complications, while cognitions (thoughts) and behavior-related factors maintain the fatigue. These factors include sleep disturbances, physical inactivity, and low self-efficacy regarding fatigue and are modifiable.

Menting et al. (2015) developed the Dia-Fit program, a CBT approach for chronic fatigue in type 1 diabetes that addresses these maintaining factors. The aim of the intervention is to reduce fatigue severity and related functional impairments. Dia-Fit is delivered in a blended-care form, i.e., face-to-face sessions with a therapist are combined with a (guided) web-based program. During a 5-month period, PWD receive up to six modules, each aimed at one of the maintaining factors of fatigue: (1) regulation of a healthy sleep-wake pattern, (2) activity regulation and increasing the level of physical activity, (3) changing unhelpful beliefs about fatigue, (4) coping with pain, (5) the role of social support and interactions, and (6) coping with diabetes-related distress. As the treatment adopts a tailored approach, PWD only receive those modules that are of relevance to them. The sequence of the modules is flexible, i.e., the modules do not have to be followed one by one in consecutive order.

The effects of CBT for chronic fatigue in type 1 diabetes have been tested in a RCT (Menting et al., 2017). After CBT, PWD score significantly lower on fatigue severity and impairments in daily functioning, compared to a waitlist control group. In approximately three out of four PWD following CBT, a clinically significant decrease in fatigue is seen, compared to one out of four PWD in the control group. No significant changes have been found with respect to glycemic control, i.e., HbA1c values and glucose variability. More research investigating the long-term effects of CBT for fatigue is warranted.

Discussion

Diabetes is a psychologically demanding illness and HCP have a key role in offering personalized care and support to PWD and their family members. Evidence-based guidelines and clinical recommendations are available, but implementing psychosocial care pathways in busy clinics can be challenging. However, there are best practices to show that individual approaches to behavioral and psychological problems in PWD are acceptable, feasible, and effective. Still, more research is needed to increase the effectiveness of psychological care with regard to self-care behaviors and glycemic outcomes. Integrating behavioral and medical strategies demands a team effort, with close collaboration between diabetes care professionals and mental health specialists. Although few people would deny the importance of crossing the “soma-psyche” chasm, current healthcare systems operate in a way that complicates the integration of psychological services for PWD and funding is often problematic.

The collaborative care approach developed for persons with chronic illness and depression sets a good example for a patient-centered and efficient individual approach to diabetes and comorbid mental health problems. This model deserves further dissemination in primary care, not in the least because it offers an opportunity to expand reach, with a growing population of PWD and psychological comorbidities. Professional psychological support is scarce and can partly be replaced by applying new technologies such as Internet-based therapy and self-help apps that are economical and patient-friendly. However, not all PWD have access to the Internet or have difficulty adhering to the online programs, resulting in high attrition rates. More research is warranted in this area, with a special focus on integrating online support with face-to-face visits, diabetes technologies, and community services. Technology can support PWD but not fully replace skilled and compassionate diabetes professionals.

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Part IX
Social Level Factors for Adults

Chapter 25
The Role of Family and Peer Support in Diabetes

Joni S. Williams, Rebekah J. Walker, and Leonard E. Egede

Theory Behind Family and Peer Support in Adults with Diabetes

Social support has garnered significant attention as a contextual factor influencing and shaping individual behaviors, particularly in patients with diabetes (Miller & Dimatteo, 2013; Strom & Egede, 2012; Wysocki & Greco, 2006). Within the social ecological model of health behavior, social support serves as primarily an interpersonal sphere of influence. However, given the focus of the social ecological model on interactions across multiple spheres of influence, social support can serve as a mechanism for connecting individuals with the surrounding institutional/organizational, community, and policy environments. As such, healthy behaviors are maximized when environments support those behaviors. Therefore, efforts to educate individuals on healthy behavior necessary for good diabetes control, without ensuring supportive environments, may result in short-term or weak effects (Sallis, Owen, & Fisher, 2008). Thus, though self-management is often viewed as an individual responsibility, studies show significant declines after the interventions end, suggesting long-term behavior change requires supportive contexts surrounding the individual engaged in diabetes self-management (Norris, Lau, Smith, Schmid, & Engelgau, 2002; Sallis et al., 2008).

Social support is in fact a multifaceted experience, including both formal and informal associations that range from sources as varied as family members, friends, peers, healthcare professionals, and community organizations (Bardach, Tarasenko, & Schoenberg, 2011; Ford, Tilley, & McDonald, 1998; Strom & Egede, 2012; van Dam et al., 2004). As such, family and peer support is one specific type of social support, but can provide all four categories of social support established in the literature: emotional support, tangible support, informational support, and companionship support (Strom & Egede, 2012; van Dam et al., 2004; Ford et al., 1998; Taylor, 2011; Heaney & Israel, 2008; Krause, 1986; Wills, 1991; Uchino, 2004). Support has been hypothesized to influence physical and mental health through direct effects, and indirectly by serving as a protective factor for stressful situations (Miller & Dimatteo, 2013; Strom & Egede, 2012; Thoits, 1985; Uchino, 2004). Both satisfaction with and perception of support influence its relationship with health, and perceptions of the availability and

J. S. Williams · R. J. Walker · L. E. Egede (✉)
Department of Medicine, Division of General Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

Center for Advancing Population Science (CAPS), Medical College of Wisconsin, Milwaukee, WI, USA
e-mail: legede@mcw.edu

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type of support needed at stressful times can change the relationship (Ford et al., 1998; Strom & Egede, 2012). Given the complex nature of diabetes, and the considerable self-management required to achieve optimal outcomes, it is important to understand the factors influencing peer and family support, in addition to the evidence regarding its relationship with health in patients with diabetes.

Family and Peer Support in Patients with Type 1 Diabetes

Type 1 diabetes is not only a complex and challenging disease but requires individuals to develop self-management behaviors while transitioning through stages of life (Jaser, 2011; Shroff Pendley et al., 2002). As such it is important to understand the trajectory of support from the time of diagnosis to adulthood as the importance of peer and family support may change over time, and may be specific to particular disease management behaviors or particular situations (Shroff Pendley et al., 2002; Jaser, 2011). For instance, in childhood, family support plays an integral role in ensuring good metabolic control, and children who assumed greater responsibility of their diabetes care had worse metabolic control (LaGreca, Follansbee, & Skyler, 1990). However, as individuals age, self-management is increasingly managed by their own daily care. Simultaneously, as individuals age, social networks expand, and peer support becomes more influential (Shroff Pendley et al., 2002). As part of the natural developmental process, individuals gain autonomy and, if disease management is not handed over, may come to see support from family as negative (Shroff Pendley et al., 2002).

Family Support

Type 1 diabetes has been referred to as a "family disease" because family members are often involved in daily management tasks, such as meal planning (LaGreca & Bearman, 2002). By assessing factor structure of a diabetes social support questionnaire, Malik and Koot (2011) found five underlying constructs tied to family support: guidance and supervision, encouragement of self-care and exercise, support in critical situations, nourishment, and emotional support (Malik & Koot, 2011). In developing a scale to measure supportive family behaviors, La Greca and Bearman (2002) found items related to emotional support were more often reported as supportive, though additional items included support surrounding meals and blood glucose testing (LaGreca & Bearman, 2002). Items less likely to be reported as supportive surrounded dealing with insulin and exercise (LaGreca & Bearman, 2002). This may explain why in one study reporting of more family support was associated with reporting of more conflict surrounding diabetes care (Shroff Pendley et al., 2002). Some of the conflict may result from differences in the support individuals desire and the support their family provides (Shroff Pendley et al., 2002). For instance, the topics considered controversial differed by age group with ages 8–11, 11–15, and 17–19 indicating conflict was most often over food and blood glucose testing, but ages 15–17 indicating conflict was most often over exercise. As a result, the transfer of responsibilities can have a significant impact on the trajectory of diabetes management, glycemic control, healthcare utilization, and quality of life (Wysocki & Greco, 2006).

Differences in family support can vary, not only by age of the individual but also based on cultural factors (Jaser, 2011). For example, the term *familismo* represents the importance of family in Hispanic culture, including family involvement in diabetes management (Hsin, Greca, Valenzuela, Moine, & Delamater, 2010). In a study of Hispanic youth, Hsin et al., 2010, found that family support mediated the relationship between independent responsibility for self-management and treatment adherence (Hsin et al., 2010). In addition, recent immigrants (i.e., lower acculturation) had better adherence, and parents with higher education had better glycemic control (Hsin et al., 2010).

Peer Support

While support from family is generally more tangible, peers tend to provide more emotional support for individuals with type 1 diabetes (Bearman & La Greca, 2002; Shroff Pendley et al., 2002; Wysocki & Greco, 2006). Similar to family support, peer support can be both positive and negative. Particularly in adolescence, a decrease in self-management adherence was associated with an increase in choices consistent with meeting peer desires (Hains, Berlin, Davies, et al., 2006; Shroff Pendley et al., 2002; Wysocki & Greco, 2006). One reason is that peers may lack knowledge about diabetes and the necessary self-management, so while individuals perceive emotional support in the form of being “treated like everyone else,” peers may be encouraging nonadherence (Shroff Pendley et al., 2002). In addition, in a study of psychosocial adjustment in children with type 1 diabetes, Storch et al. (2004) found that youth with diabetes reported overall less positive peer support compared to those without a medical diagnosis (Storch et al., 2004). However, in an analysis of distress in patients with type 1 diabetes, peer support networks were specifically noted as a way to regulate negative emotions (Balfe et al., 2013). Peers, both in person and online, also provided those with diabetes with practical information and motivation to improve their diabetes control (Balfe et al., 2013).

In adults with type 1 diabetes, peer support continues to be important, though less research has been focused in this area (Joensen, Filges, & Willaing, 2016). Peer support in adults is hypothesized to provide assistance in self-management, social and emotional support, linkages to healthcare, and community resources (Joensen et al., 2016). Qualitative analyses found themes surrounding lack of peer support to focus on the feeling of being on one’s own, a lack of connection, and not feeling understood; whereas themes surrounding peer support included having a sense of sharing real-life experiences, mutual understanding, trust and confidence, and social participation by helping others (Joensen et al., 2016). For those with adult-onset type 1 diabetes, support in decision-making about self-care was identified as a critical factor (Jull, Witteman, Ferne, Yoganathan, & Stacey, 2016).

Relationship Between Family and Peer Support and Type 1 Diabetes Outcomes

Consistent with the general social support literature, family and peer support are generally associated with improved glycemic control, better self-care, and higher quality of life (Gillibrand & Stevenson, 2006; LaGreca & Bearman, 2002; Wysocki & Greco, 2006). The type and timing of support, however, are major factors that have not yet been fully examined in patients with type 1 diabetes.

Family Support and Outcomes

High levels of family support predicted adherence to self-care regime and lower perceptions of vulnerability to diabetes-related complications in individuals ages 16–25 diagnosed with type 1 diabetes (Gillibrand & Stevenson, 2006). However, high internal locus of control and high self-efficacy predicted respondents noting the benefits of adherence to self-care management outweighed the costs (Gillibrand & Stevenson, 2006). This suggests that family support should be a mechanism to facilitate high internal locus of control and self-efficacy, as support alone does not predict the multiple influences on decisions to follow self-care regimes. Investigation into support from both mothers and fathers shows that perception of parents being uninvolved is associated with poorer adherence (Jaser, 2011). Recent work specific to paternal support has found a distinct influence on improved adherence and quality of life (Jaser, 2011).

In addition to better adherence to self-care regimes, more supportive families were associated with better metabolic control in adolescents with type 1 diabetes (LaGreca & Bearman, 2002; Wysocki & Greco, 2006). Those with low A1c were more likely to describe parental roles in monitoring their diabetes as supportive, whereas those with high A1c were more likely to be annoyed and describe more conflict with their parents (Leonard, Garwich, & Adwan, 2006). In a multinational study of adolescents, perceptions of parents involved in their diabetes care were often seen as nagging, and this was associated with poor glycemic control (Jaser, 2011). Parental care and control were not associated with either glycemic control or quality of life in a study of adolescents with type 1 diabetes compared to those without (Graue, Wentzel-Larsen, Rokne Hanestad, & Sovik, 2005). In addition, parental conflict was associated with poorer adherence, lower glycemic control, and poorer quality of life (Graca Pereira, Berg-Cross, Almeida, & Cunha Machando, 2008; Jaser, 2011). While parental monitoring was associated with more knowledge, better adherence, and better glycemic control, the ability to provide monitoring was associated with the adolescent's willingness to share information (Jaser, 2011). Similarly, the relationship between support and outcomes is thought to be mediated by adherence, but more research is needed to understand the specific types that are most important (Miller & Dimatteo, 2013). Therefore, the importance of interventions focusing on improving communication and collaboration with family may have a major impact on how family support affects diabetes outcomes (Jaser, 2011).

Peer Support and Outcomes

Similar to family support, evidence regarding the relationship between peer support and diabetes outcomes is mixed, often due to the type of support perceived and given. For example, while global peer support was associated with both better self-care and glycemic control, diabetes-specific support was not associated with either (Doe, 2016). It was suggested that adolescents saw diabetes-specific support as nagging, rather than actual support (Doe, 2016). Additionally, while one study found that more peer influence was associated with increased blood sugar monitoring, there was no association with overall treatment adherence, and another study found peer support was not associated with metabolic control (Bearman & La Greca, 2002; Shroff Pendley et al., 2002). A number of studies have found that diet adherence is particularly susceptible to peer influence (Wysocki & Greco, 2006). Nondisclosure of diabetes diagnosis to friends was highly predictive of poor self-care behaviors in adolescents, suggesting the need to understand the reason for low support from peers (Wysocki & Greco, 2006). Overall, far less work has investigated the relationship between peer support and diabetes outcomes in patents with type 1 diabetes. Given peers provide support that is unique from family support, this is an important area for further study.

Peer and Family Support in Type 2 Diabetes

Type 2 diabetes is a chronic condition requiring management at both the patient and provider levels (Dale, Williams, & Bowyer, 2012; Nicklett, Heisler, Spencer, & Rosland, 2013; Strom & Egede, 2012). Medical management by providers, in collaboration with daily self-management and lifestyle and behavioral changes by patients—adherence to a healthier diet, increased physical activity, improved medication adherence, and enriched self-monitoring of blood glucose levels—is critical to achieving optimal outcomes, maintaining control in type 2 diabetes, and reducing the risk of developing adverse microvascular and macrovascular complications, poorer quality of life, and distressed and depressed moods (Dale et al., 2012; McEwen, Pasvogel, Gallegos, & Varrera, 2010; Nicklett et al., 2013;

Strom & Egede, 2012; van Dam et al., 2004). The need for a comprehensive approach to management in type 2 diabetes, particularly at the patient level, warrants the aid of formal and informal relationships that often occur as a result of individuals' personal social support networks (Kadirvelu, Sadasivan, & Ng, 2012; Strom & Egede, 2012; van Dam et al., 2004).

Social support has been considered a major component of management, sustainability, coping, and disease awareness in the care of patients with type 2 diabetes (Strom & Egede, 2012; van Dam et al., 2004; Zhang, Norris, Gregg, & Beckles, 2007). While the exact mechanism by which social support imparts its influence remains elusive (Kadirvelu et al., 2012), it has been shown to be valuable in guiding self-care and providing encouragement in order to achieve improved health outcomes (Stopford, Winkley, & Ismail, 2013; Strom & Egede, 2012). In addition, it has been instrumental in helping patients accept the diagnosis, adjust emotionally, and reduce undue stress associated with type 2 diabetes (Sacco & Yanover, 2006; Strom & Egede, 2012). The type, amount, and source of support needed by individuals, as well as satisfaction with the support, vary based on personal characteristics, factors, and circumstances. Nonetheless, for many, social support remains important in the management of type 2 diabetes (Strom & Egede, 2012).

Family Support

For patients diagnosed with type 2 diabetes, family support must be considered when managing care, especially given the challenges posed to individuals when trying to change behaviors alone (Kadirvelu et al., 2012). Family members are considered an important source of support; however, the type and amount of support from family members can positively or negatively influence self-management (Mayberry, Berg, Harper, & Obsorn, 2016; Strom & Egede, 2012). For example, positive support results when patients diagnosed with type 2 diabetes feel family members are well-informed about the condition and use that knowledge to promote appropriate self-care behaviors; whereas, negative support results when those affected by diabetes feel criticized for not adhering to a specified routine or not supported by the minor changes successfully adopted (Strom & Egede, 2012; Mayberry & Osborn, 2012; Kadirvelu et al., 2012). Depending on the need, however, family members can provide emotional support to increase feelings of value and worth; tangible support to satisfy subsistence, financial, and material needs; informational support to assist with problem solving, especially if also diagnosed with diabetes and well-controlled; and companionship support to encourage a sense of social acceptance (Strom & Egede, 2012). Because a diagnosis of diabetes affects the entire family, considerable attention should focus on the family dynamic and factors that may contribute to the success or failure of medical and self-management (Mayberry & Osborn, 2012; Rintala, Jaatinen, Paavilainen, & Astedt-Kurki, 2013).

Family members play a significant role in their relatives' adoption and maintenance of lifestyles and behaviors critical for achieving clinical and behavioral outcomes (Mayberry & Osborn, 2012; Rintala et al., 2013). They can either enable or hinder the behaviors and skills needed for self-managing care. Mayberry et al. suggest that instrumental support, or "observable actions that make it possible or easier for individuals to perform healthy behaviors," might be the most influential and impactful type of support a family member can offer to increase the likelihood of improved self-management by a loved one (Mayberry & Osborn, 2012). Kadirvelu et al. (2012) echo this sentiment, proposing that including family members in clinical care and research results in improved outcomes, but also advise that additional research assessing the role of family factors in diabetes-related research involving adults is warranted (Kadirvelu et al., 2012). In a review of social support from family members of patients with chronic diseases, including diabetes, family cohesion and family emphasis on self-reliance and personal achievement were associated with better outcomes, whereas critical, controlling, or distracting family responses were associated with negative outcomes (Rosland, Heisler, & Piette, 2012).

Peer Support

The use of peer support in the management of type 2 diabetes has become increasingly relevant in recent years as providers and researchers attempt to improve diabetes management and outcomes (Brownson & Heisler, 2009; Dale et al., 2012). Similar to family support, support from peers can be perceived as either positive or negative and can be perceived differently based on race and ethnicity, gender, and cultural background (Strom & Egede, 2012; van Dam et al., 2004). Peer support is based on a reciprocal relationship of exchanges of information and knowledge to improve health outcomes (Dale et al., 2012). For individuals diagnosed with type 2 diabetes, peer support results in (1) encouragement and assistance; (2) experiential knowledge, skills, and learned behaviors; and (3) actual examples of personal successes and failures in diabetes management. It can serve a unique role and complement other forms of support, contributing to access to clinical care, individualizing treatment, patient-centered goal setting, education and skills training, ongoing follow-up, and linkages to community resources (Brownson & Heisler, 2009). When perceived as positive, these shared experiences often result in enhanced problem-solving and goal-setting skills, empowerment, and self-efficacy, attributes shown to improve self-management, independently and, most profoundly, collaboratively (Dale et al., 2012). Most times, peer support relationships serve as a method of accountability, resulting in a mechanism by which goals are achieved and leading to a heightened sense of accomplishment and interpersonal competence (Dale et al., 2012; Strom & Egede, 2012). In addition, peer support can improve clinical care. When accompanied by a friend or family member, patients were more likely to understand primary care provider advice and discuss difficult topics with physicians (Rosland, Piette, Choi, & Heisler, 2011). In contrast, when peer support is perceived as negative or unwanted, it often results in increased stress and decreased adherence to a desired behavior or exchange (Strom & Egede, 2012; van Dam et al., 2004).

The approach to peer support in type 2 diabetes has taken different forms, being individual or group-based, in-person, or among online communities and occurring via various platforms such as telephone, web, email, and mobile devices (Dale et al., 2012), especially with the insurgence and advancement of new technologies. In addition, peer support can occur through community and healthcare organizations, in the form of community health workers, *promotores de salud*, or lay health advisers (Fisher et al., 2015). The type and amount of support offered and exchanged during the peer relationship can vary depending on the focus of the interaction, the preferred method of delivery, and the supportive need, whether for emotional and information support, tangible support, companionship support, or appraisal support (Brownson & Heisler, 2009; Dale et al., 2012; Strom & Egede, 2012). For example, in the management of type 2 diabetes, peers provide informational support by offering advice, guidance, and suggestions about how to better management and control type 2 diabetes and companionship support by encouraging involvement in social activities unrelated to the daily, and often daunting, routine of diabetes management (Strom & Egede, 2012; van Dam et al., 2004).

Relationship Between Family and Peer Support and Type 2 Diabetes Outcomes

Based on the current literature assessing the relationship between family and peer support in patients with type 2 diabetes, evidence suggests higher levels of social support influence more positive outcomes—improved clinical outcomes, reduced psychological symptoms, and better self-management and adoption of healthier behaviors (Stopford et al., 2013; Strom & Egede, 2012; van Dam et al., 2004). Findings by Tang, Brown, Funnell, and Anderson (2008), for example, suggest social support is important for a better quality of life and improved self-management in diabetes by incorporating multiple elements that differentially impact diabetes-related outcomes and behaviors (Tang et al., 2008). Additionally, Rosland et al. (2015) found that higher baseline social support was associated with greater improvements in glycemic control during a 6-month intervention trial (Rosland et al., 2015).

Despite this general consensus, however, additional research is justified as the evidence is limited, and the evidence that currently exists is inconsistent, subjective, and often, incomparable (Stopford et al., 2013). In addition, the exact mechanism of social support in the management of type 2 diabetes (i.e., direct versus indirect versus combined effort) remains unclear. Differences in the types, amounts, and sources of appropriate support are not standardized and vary depending on gender, race and ethnicity, and geographic location (Strom & Egede, 2012; van Dam et al., 2004). Furthermore, a uniform definition and framework or model of social support are lacking, resulting in heterogeneous interventions that lack a specific focus, diverge in desired outcomes and objectives, and demonstrate diverse results (Kadirvelu et al., 2012; van Dam et al., 2004). As these gaps in the social support literature continue to be identified and addressed, future research will begin to inform health policy and service delivery for patients with type 2 diabetes (Dale et al., 2012).

Family Support and Outcomes

Generally, the literature assessing the relationship between family support and outcomes is scarce. Despite this limitation, however, evidence favors an improvement in diabetes outcomes when family members are involved and included in disease management (Baig, Benitez, Quinn, & Burnet, 2015). Baig et al. (2015) advocate that primary management of diabetes occurs within personal family and social environments, where family members can provide support and actively share and participate in the care of a family member diagnosed with type 2 diabetes (Baig et al., 2015). They also propose that family cohesion and family functioning positively impact diabetes-related outcomes (Baig et al., 2015). Because a diabetes diagnosis affects not only the individual but also the family, it is important to be all inclusive (Rintala et al., 2013; Mayberry & Osborn, 2012). Family members should be taught ways to influence the patient positively and communicate effectively. In addition, information about anticipated and expected changes in routines and lifestyles must be expressed to both the patients and family members, especially since the diagnosis will affect the health of the entire family.

Family members often provide different types of support that can be perceived as either negative or positive (Baig et al., 2015; Mayberry et al., 2016; Strom & Egede, 2012). Perceived positive support leads to shared responsibility in disease management, shared decision-making, and adherence to recommended guidelines and behaviors, while negative support results in increased stress and obstructions in progress (Baig et al., 2015). Examples of positive support include preparing healthy meals, partnering on daily exercise regimens, assisting with insulin injections, and encouraging rest and relaxation to reduce stress and depressive symptomatology. On the contrary, continuing to prepare unhealthy meals, choosing not to attend medical appointments, providing negative feedback, and harassing patients about maintaining certain behaviors can all be harmful and perceived as negative support, hindering the disease management process. In patients with type 2 diabetes, negative support has been associated with decreased adherence to treatment plans and poorer glycemic control (Baig et al., 2015; Mayberry & Osborn, 2012).

The literature is inconsistent when considering patient outcomes by family involvement (Baig et al., 2015). Significant changes in clinical, behavioral, and psychosocial outcomes for the patients varied depending on a range of factors (study design, amount of family involvement, anticipated outcomes, etc.). In addition, family involvement and participation in clinical encounters and research varied (based on either personal choice or the design of the study); therefore, the impact on patient outcomes remains unpredictable (Baig et al., 2015). It is noteworthy to mention, however, that albeit limited evidence in the literature to validate the claims, family members often experienced and reported improvements in their personal knowledge, skills, and health as a result of participating in the care of a family member with type 2 diabetes (Baig et al., 2015).

Peer Support and Outcomes

In general, the effectiveness and impact of peer support on outcomes among adults with type 2 diabetes continue to be indeterminate. In a systematic review to assess the effect of peer support on diabetes outcomes among adults, Dale et al. (2012) conclude that the evidence is insufficient to determine the appropriate models and aspects of peer support that address individual patient needs (Dale et al., 2012).

While peer support seems to benefit some adults diagnosed with type 2 diabetes and lead to improved outcomes, it has not been effective in others. In a randomized study to assess the benefit of an online diabetes self-management program, Lorig et al. (2010) showed patients randomized to the online program had significantly improved (i.e., lower) A1c levels, increased patient activation, and self-efficacy compared to patients receiving usual care (Lorig et al., 2010). Similarly, in a randomized trial to compare reciprocal peer support and nurse case management for diabetes control, patients randomized to peer support had a significantly lower A1c at 6 months of follow-up compared to patients receiving nurse case management, who saw an increase in A1c levels from baseline at 6 months (Heisler, Vijan, Makki, & Piette, 2010). In both of these trials, no statistically significant differences between groups were observed in other clinical outcomes such as blood pressure control and self-care behavioral outcomes such as physical activity and diet adherence (Heisler et al., 2010; Lorig et al., 2010). Overall, current evidence—including randomized and non-randomized trials—assessing the relationship between peer support and diabetes continues to demonstrate mixed results in clinical outcomes (i.e., A1c, blood pressure, lipids/cholesterol), health behavior outcomes (i.e., physical activity, glucose monitoring, diet), empowerment outcomes (i.e., self-efficacy, knowledge, perceived barriers), and psychological outcomes (i.e., depression, distress) (Dale et al., 2012).

These findings suggest that peer support has the potential to be an effective strategy for improving diabetes outcomes; however, the current literature lacks sufficient and definitive evidence demonstrating better outcomes and self-management skills as a result of peer support. The reasons for the lack of consistency within the literature are not totally understood, but can be substantiated by a range of explanations including flawed study designs, inadequate sample sizes, and considerable variation in the populations of interest (Dale et al., 2012). Based on evidence from 14 evaluation and demonstration peer support projects in 9 countries, factors leading to success include attention to participant emotions and ongoing supervision (Fisher et al., 2015). Challenges include balancing quality control with maintaining key aspects of peer support, suggesting variation in implementation of programs may be the reason for conflicting results in the literature (Fisher et al., 2015).

Conclusions

Consistent with the ecological model noting the importance of taking influences at multiple levels into account, diabetes management for patients with type 1 and type 2 diabetes should engage support from multiple systems, including both family and peers (Kadirvelu et al., 2012; Mayberry et al., 2016; Rintala et al., 2013; Shroff Pendley et al., 2002). In a longitudinal analysis of patients with type 1 diabetes, those with combined family and peer support had better glycemic control, higher well-being, and less internalized symptoms (Oris et al., 2016). One particularly vulnerable time is in transition from adolescent care to adult care, as significant drop out rates occur (Cameron, 2006). Interventions aimed at family and peer support should consider how to engage social support in this transitional period and what additional support is needed to facilitate ongoing diabetes care. In type 2 diabetes, it has been postulated that positive family and peer support are associated with improved outcomes; however, the evidence is inconclusive (Baig et al., 2015; Dale et al., 2012; Stopford et al., 2013; van Dam et al., 2004). Given the heterogeneity of study designs, variations in sample sizes and proposed outcomes, and lack of a standardized definition for support, the evidence continues to be inconsistent (Baig et al., 2015; Kadirvelu et al., 2012; van Dam et al., 2004). In addition, differences in perceived support based on multiple characteristics have been identified in the literature (Strom & Egede, 2012; van Dam et al., 2004). Therefore, future interventions aimed at family and peer support should consider how to homogenize the use of support and consider specific population-based factors that should be considered to address sociodemographic and cultural factors.

Overall, while family and peer support has been investigated heavily in youth with type 1 diabetes, less focus has been given to its importance in adulthood. In a recent systematic review of the effect of peer support on diabetes outcomes in adults, only two studies included patients with type 1 diabetes along with adults with type 2 diabetes (Dale et al., 2012). The importance of practical help, emotional support, and cohesive social networks is necessary for improved adherence (Miller & Dimatteo, 2013). In addition, while family and peer support have tremendous potential to influence outcomes in patients with type 2 diabetes, additional research is needed to determine whether and how family and peer involvement in diabetes care and research can influence patient outcomes and impact policy (Baig et al., 2015; Dale et al., 2012; Kadirvelu et al., 2012). Finally, studies suggest the importance of family and peer support in outcomes such as glycemic control and quality of life, though more research is needed. As such, future studies should seek to understand the relative importance and utility of family and peer support in adults with type 1 and type 2 diabetes in order to design effective interventions using this important psychosocial factor.

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Chapter 26
Family Therapies for Adults with Diabetes

Paula M. Trief, Lawrence Fisher, and Rachel Hopkins

Families, Social Support, and Health

To understand the potential role of families in diabetes care and outcomes, one must look first to the literature on "social support." What do we mean by social support? In the most general sense, it is defined by the individual, i.e., one *feels* supported by others. This happens most commonly when you feel that others care for and nurture you (emotional support), provide companionship, provide help when you need it (instrumental or tangible support), and/or provide advice to help you solve your problems (informational support) (Taylor, 2011). Social support is measured directly by the size of one's social network (i.e., how many people you have in your life who will help and support you in these ways) and indirectly (i.e., do you feel supported by others?) (Heaney, Israel, Rimer, & Viswanath, 2008).

There is an extensive literature that demonstrates quite convincingly that social support is good for one's physical and mental health and overall well-being (Uchino, 2004). How might this work? One long-held theory is that social support serves as a "buffer" that protects us when we are under stress, thus mitigating the negative health effects of stress (Cohen & Wills, 1985; Thoits, 1985). Alternatively, the "direct effects" theory postulates that high levels of social support cause better health and recovery from illness (Thoits, 1985; Uchino, 2004), perhaps because social support has direct positive effects on the endocrine, cardiovascular, and immune systems (Herbert & Cohen, 1993; Kiecolt-Glaser et al., 1997; Kiecolt-Glaser & Newton, 2001), or encourages positive health habits (e.g., smoking cessation, more exercise) (Westmaas, Bontemps-Jones, & Bauer, 2010). In a study that looked at health behavior change within (married or cohabiting) couples, researchers found that both women and men were more likely to make a positive change (i.e., quit smoking, increase physical activity, lose weight) when their partner did so too, noting that the effect was even stronger than if the partner had been healthy consistently (Jackson, Steptoe, & Wardle, 2015). They suggested this may relate to enhanced motivation and modeling of health behavior change provided by the supportive partner.

P. M. Trief (✉) · R. Hopkins
State University of New York Upstate Medical University, Syracuse, NY, USA
e-mail: triefp@upstate.edu

L. Fisher
University of California, San Francisco, San Francisco, CA, USA

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Social Support and Diabetes

Studies of the impact of social support on diabetes outcomes have shown similar positive relationships, although conclusions are tenuous because most studies are cross-sectional, and thus cannot address causality. In general, greater social support has been found to relate to better glycemic control, adherence to diabetes self-care, quality of life, and, in two studies, lower mortality (Ciechanowski et al., 2010; Tang, Brown, Funnell, & Anderson, 2008; Zhang, Norris, Gregg, & Beckles, 2007). Strom and Egede (2012) systematically reviewed the literature on social support and type 2 diabetes (from 2000 to 2012) and, after thorough database searches, identified 37 papers relevant to this topic. Most were cross-sectional, but some were interventional, i.e., programs to enhance social support and assess the effect of doing so on diabetes-related outcomes. They found that most of the studies reported significant expected relationships between levels of perceived support and biomedical outcomes (A1c, lipids, blood pressure, mortality), psychosocial outcomes (depressive symptoms, well-being), and self-management (diet, exercise, blood glucose self-monitoring). While there were several studies that did not find this relationship, different study populations, definitions and measures of support, and study designs make comparisons challenging.

Two longitudinal studies are noteworthy. In one (type 2 diabetes patients, >60 years old), diabetes-related support significantly predicted adherence to diabetes self-care over 2 years of the study, although it did not predict decline in overall self-rated health (Nicklett & Liang, 2010). In another investigating non-depressed patients with diabetes, those whose general "relationship style" is to seek support (i.e., an "interactive relationship style") were found to have a decreased risk of mortality over 5 years when compared to a comparable group who are less likely to seek support (i.e., with an "independent relationship style") (Ciechanowski et al., 2010).

The Family as a Source of Support for Adults with Diabetes

Some of the uncertainty in this area may relate to the fact that in these studies, social support has been defined as support provided by a range of individuals: family members, spouses/partners, peers, neighborhoods, physicians, non-physician healthcare providers, and even through web-based interventions. In this chapter, we pay specific attention to the role of the family, since family, especially partner, relationships have been found to be important to health outcomes of adults with varied chronic illnesses (Cohen & Wills, 1985; Heaney et al., 2008; Uchino, 2004; Wortman & Conway, 1985). The social ecological theory of health promotion identifies the family as a key factor in one's health environment and provides a theoretical foundation for research in this area (Stokols, 1996).

Family, particularly partner support, can have a very powerful social influence on patient health, well-being, and disease outcomes. Adult partners engage in a unique kind of social relationship: it persists over time, it is emotionally intense, and it involves high levels of intimacy, creating a powerful, dynamic set of emotional ties. These ties create a structured social relationship that assumes a level of organization and complexity that goes beyond the individuals involved. Couples can create a shared social reality that has been linked to health and disease management (Dougherty & Campbell, 1988; Kleinman, Eisenberg, & Good, 1978), and this reality provides a vehicle for viewing and contrasting each partner's beliefs, values, and expectations about chronic disease and its treatment. Family beliefs, organization, and abilities have been linked with disease outcomes across chronic diseases, including adherence to treatment regimens, frequency of hospitalizations, use of health facilities, maintenance of weight loss, and post-illness recovery (Fisher et al., 1998). Coyne and Smith (1994) identified two broad partner interactional styles for coping with a chronic disease that can have effects on health outcomes. Joint "active engagement" in disease management was associated with constructive problem-solving, whereas “protective buffering” of one partner by the other (hiding concerns, denying worries, yielding to avoid overt disagreement) was associated with poor outcomes (Coyne & Smith, 1991).

In general, the following characteristics of partner relationships have demonstrated the most consistent associations with poor disease management: low cohesion, high conflict, too rigid or too permeable couple boundaries, low levels of structure or organization, distant or hostile affective or affiliative tone, high criticalness, and lack of clear and direct communication (Fisher, Ransom, Ted, Lipkin, & Weiss, 1992). Thus, it is important to view partner relationships as unique, insofar as they reflect far different levels of complexity, intensity, and meaning than other forms of social support.

For diabetes, a systematic review of the literature (2000–2011) on diabetes outcomes and family relationships, particularly adult couple relationships, lends support to the idea that family relationships affect patient diabetes outcomes (Rintala, Jaatinen, Paavilainen, & Astedt-Kurki, 2013). Studies have found that greater marital satisfaction relates to lower risk of developing metabolic syndrome (Troxel, Matthews, Gallo, & Kuller, 2005), better quality of life (Trief, Himes, Orendorff, & Weinstock, 2001; Trief, Wade, Britton, & Weinstock, 2002), and self-care regimen adherence (Trief, Ploutz-Snyder, Britton, & Weinstock, 2004). Non-supportive family behaviors or conflicts have been shown to relate to poorer medication adherence (Mayberry & Osborn, 2012), and greater marital stress relates to poorer glycemic control and prospectively predicts more depressive symptoms (Trief et al., 2006).

There are three important caveats to this summary that qualify the findings. First, differences among couples based on age and developmental level are rarely addressed. In a large ($N = 1228$) study of older Americans (two waves of the National Social Life, Health, and Aging Project), an increase in *negative* marital quality over time related to a higher likelihood of diabetes patients being in *good* glycemic control (Liu, Waite, & Shen, 2016), a counter-intuitive finding. This suggests that some conclusions may not apply to couples of different ages. Second, gender differences are rarely considered, i.e., in heterosexual couples, which partner has diabetes? Fisher et al. (2000) found that partners of diabetes patients had elevated depressive symptom scores, as high as those of patients. However, gender differences were noted. If the partner was male and the patient female, there was a greater discrepancy in depressive symptom scores than if the partner was female. Third, differences among couples based on culture and culturally based role expectations are often overlooked. For example, variations in cultural support for overt expressions of disagreement and conflict, assignment of well-defined household management roles, and support for shared decision making can strongly affect how couples approach the process of disease management (Fisher, Gudmundsdottir, et al., 2000; Fisher, Chesla, et al., 2000), yet culture is rarely considered. Gender and culture may also interact. In a sample of Korean Americans, men reported that their partners are their major source of support, while women look to others (Song et al., 2012).

In addition, all of these studies of adults with diabetes have focused on those with type 2 diabetes (T2D) [family issues for children with type 1 diabetes (T1D) are described in Chap. 9]. Although in some studies adults with T1D and T2D are both included in the sample studied, the relatively smaller number of participants with T1D makes it difficult to draw conclusions about their specific issues. For adults with T1D, living alone relates to higher diabetes distress and poorer self-care, especially for women with T1D, with social support having both direct and indirect effects (Joensen, Almdal, & Willaing, 2013); thus, relationships matter for adults with T1D. Qualitative work has suggested that adults with T1D face unique interpersonal challenges and potential sources of relationship conflict (Trief, Sandberg, Dimmock, Forken, & Weinstock, 2013). In addition, higher relationship satisfaction, and having an engaged, not overprotective, partner, has been associated with better self-care and glycemic control (Trief et al., 2015). However overall, studies of adults with T1D are lacking.

Family Interventions for Adults with Diabetes

Taken as a whole, these findings have led to calls for the development and testing of family-based interventions for adults with diabetes (Chesla, 2010; Delamater et al., 2001; Fisher et al., 1998; Fisher & Wiehs, 2000; Marrero et al., 2013; Rintala et al., 2013). This leads to the question: What should these interventions include? Positive support strategies have been defined, for example, as encouraging healthy eating (e.g., buying healthy foods, changing cooking preparations) and exercise (e.g., exercising together), reminding patients to take medications, and being emotionally supportive and sensitive to the patient's frustrations and fears (McEwen & Murdaugh, 2014; Mayberry, Harper, & Osborn, 2016). However, family members may also engage in "obstructive" (i.e., nagging, arguing) or "sabotaging" (i.e., undermining patient self-care) behaviors (Carter-Edwards, Skelly, Cagle, & Appel, 2004; Mayberry & Osborn, 2012, 2014; Stephens et al., 2013; Tang et al., 2008). Such behaviors have been associated with poorer self-care and glycemic control (Mayberry et al., 2016; Mayberry & Osborn, 2012, 2014). Thus, certain types of family involvement may lead to poorer diabetes outcomes. Family interventions, therefore, might aim to teach family members to be positively supportive and decrease obstructive behaviors (Mayberry et al., 2016; Trief et al., 2003). Clearly, there are a variety of strategies one might use to enhance disease management among adult couples in which one partner has diabetes.

In the following sections, we review the results of several family intervention trials that have targeted adults with T2D. Unfortunately, we did not identify any family intervention trials for adults with T1D, and this area is open for future research.

A systematic review of family interventions aimed at improving diabetes care (papers published between 1994 and 2014) identified 46 articles reporting on 26 unique studies (Baig, Benitez, Quinn, & Burnet, 2015). The studies were described as using family-based interventions to improve diabetes self-management and outcomes in adult patients with T2D. In many of these studies, family involvement was limited to encouraging family members to attend meetings and classes with the patient. And, no data were provided about the number of family members who did attend and how many sessions they attended. For example, in a study in which community health workers encouraged involvement of family members, the exact nature of their involvement or encouragement was not described (Gary et al., 2009). Therefore, although many of these studies reported positive outcomes for patients, one cannot attribute success specifically to family involvement.

In a few studies, family member participation was an integral part of the study design, with family participation more fully described. However, results are still difficult to attribute to family participation because of lack of adequate controls. Following are descriptions of those studies. We have organized them by study design. We hope this will help the reader understand the details of these studies and their strengths and limitations, to best assess the conclusions drawn from the data.

Nonexperimental Design: Single Group, Pre-post Measurement

In this design, an intervention is provided to a single group, and assessments occur before and after the intervention. In a program designed for an urban-dwelling, Native American population in the Midwest United States, the Family Education Diabetes Series used a community-based participatory research process to design a culturally relevant intervention (Mendenhall et al., 2010; Mendenhall, Seal, GreenCrow, LittleWalker, & BrownOwl, 2012). The resulting 6-month program included adult patients and their family (defined as spouses, parents, and/or children) and providers (physicians, nurses, dieticians, mental health personnel) in bi-weekly meetings that focused on diabetes self-management. Community activities, educational content, and community support were also provided. The education component included specific content about family relationships and social support. Compared to baseline, participants showed improvements in weight, blood pressure, and A1c (hemoglobin A1c, a measure of glycemic control over the past 2–3 months) at 3 months and 6 months. In qualitative evaluation of the program, communal support and a sense of accountability to the group felt by participants were key positive motivators described by the participants. No data regarding extent or type of family participation were provided.

A pilot study involving 36 Hispanic patients with T2D and their family members (defined as adults residing in the same household) had the express aim of focusing on family involvement and family centeredness, based on the Hispanic concept of *familismo,* with a group at risk for complications and poor adherence (Hu, Wallace, McCoy, & Amirehsani, 2014). The intervention was based in social cognitive theory and consisted of eight weekly educational group sessions for participants and family members. Family members participated in pre- and post-intervention assessments; 1-month post-intervention data were collected on participants only. Education sessions included discussion of "approaches to success through family support." Participants had statistically significant improvements in systolic blood pressure, diabetes self-efficacy, and Revised Summary of Diabetes Self-Care Activities (SDSCA) general diet score from pre- to immediate post-intervention and in SDSCA specific diet and blood glucose testing scores at 1-month follow-up. There was no statistically significant change in A1c. Family members also showed significant improvements in BMI and diabetes knowledge.

Both of these studies provide useful data about the feasibility, acceptability, and potential efficacy of the family-based interventions. And, the latter study included assessment of family members. However, the lack of control groups and randomization limits conclusions.

Quasi-experimental Design: Two Groups, Non-randomized

In this design, an intervention group is compared to a control group; in most cases the control group receives usual care only. In a study from Chile, a "family-oriented health center" was developed at an intervention clinic, while two comparable clinics were not modified and served as usual care controls (Garcia-Huidobro, Bittner, Brahm, & Puschel, 2011). During a 12-month intervention period, patients and family members participated in two interdisciplinary family meetings or home visits and were encouraged to attend multifamily group sessions. Interventionists reviewed family and other psychosocial factors that could interfere with patient blood glucose control. Participants also received at least one individual counseling session and one counseling session with their relatives, at which the importance of family support strategies was discussed. At 12 months, there were significant decreases in A1c in both the intervention and control clinic patients, with no statistically significant differences among the clinics. Since most of the intervention was implemented in the second 6 months of the year, the authors also looked at data from that later period and found a statistically significant reduction in A1c in the intervention clinic compared to one of the control clinics, but not the other. Unfortunately, only 34% of their patients received all of the intended intervention activities.

A non-randomized, community-based diabetes intervention trial was conducted at three Native American clinic sites in New Mexico, with two intervention clinics and one usual care control clinic (UC) (Gilliland, Azen, Perez, & Carter, 2002). In the two intervention clinics, one provided a family and friends (FF) intervention, in which patients were encouraged to invite family members and/or friends to group sessions, and the other provided a one-on-one (OO) intervention. There were no limiting criteria as to who would be considered a family member, nor did they track who, or how often, they participated. The FF and OO arms both received an intervention that consisted of five sessions, approximately 6 weeks apart, over a 10-month period. The same written materials were presented by a mentor in both the FF and OO sessions. In the FF arm, participants also engaged in activities designed to encourage social interaction and discussion about diabetes among members of the group, and the mentor led the participants through the written materials and encouraged discussion and sharing of stories. The FF participants also joined in physical activities as a group and shared a healthy meal. After 1 year, both intervention arms showed small, nonsignificant increases in A1c (0.4% in the combined intervention arms), while the UC arm showed a statistically significant increase in A1c of 1.2%. There were also statistically significant weight losses in both intervention arms. There were no significant differences between the FF and OO arms in A1c or weight change. The FF arm showed greater improvement in diastolic blood pressure than the OO arm. Thus, both interventions had better outcomes than usual care, but there were no meaningful differences between the outcomes of the participants in the FF arm (that included family/friends in group sessions) and the OO (individual intervention) arm. This study is stronger in that there was a comparison between an individual and a family/friend intervention and also comparison to usual care. However, lack of randomization is a significant concern, as the clinics may have differed in ways that could have affected results. Also, the two interventions varied in structure, with the FF arm receiving the intervention in groups and the OO arm receiving it individually, another confounding variable.

In these two studies, we find again that family involvement is feasible, yet results are generally not supportive of benefits derived from it. However, design concerns, including lack of randomization, lack of clear definition of how family was defined, and varying levels of participation, limit conclusions.

Experimental Design: Two Groups, Randomized

The Starr County Border Health Initiative was a prospective, randomized study of a culturally competent diabetes self-management education program for very low-income Mexican Americans living on the US-Mexico border (Brown, Garcia, Kouzekanani, & Hanis, 2002). Twelve weekly, 2-h education sessions, followed by 14 bi-weekly and then 3 monthly, 2-h support group sessions, offered a comprehensive review of diabetes self-management and included a session focused on family support and community resources. Participants were required to identify a family member or, if no family member was available, a close friend to accompany them to intervention sessions as a support person – although no data are given as to how many or how often family members participated. The control group consisted of individuals wait-listed for the intervention for 1 year while they received usual care. Statistically significant improvements were seen in the intervention group compared to the control group in diabetes knowledge, fasting blood glucose, and A1c.

A randomized controlled trial conducted in Taiwan compared family partnership intervention care (FPIC) to usual care (monthly outpatient visits) in patients with poorly controlled T2D (A1c >7% using oral meds only) (Kang et al., 2010). Involved family members could be a spouse, parent, significant other, or other cohabiting relative. FPIC emphasized family participation and support and consisted of three brief educational sessions attended by the patient and family member, 2-day-long group (multiple dyads) education sessions, a monthly 25–30-min dyad telephone discussion, and educational materials. Each patient/family member dyad also received an education plan based upon their specific needs as determined from their baseline assessments. The control group received usual care, which in Taiwan consists of monthly visits with the primary care provider. After 6 months, the authors found no significant differences between arms in A1c, lipids, or self-care behaviors. There were significant improvements in scores of family supportive behaviors and patients' knowledge and attitudes toward diabetes in the intervention group. It is possible that the lack of clinical differences was related to the fact that patients already had relatively well-controlled diabetes at baseline, and usual care in Taiwan is fairly intensive.

There is one study that explicitly incorporated some of the principles of family therapy, in that the intervention focused on relational aspects of family support. A randomized controlled trial in Ireland, described as a psychological family-based intervention, targeted people with persistently poorly controlled T2D (at least two out of their last three A1c measurements had been ≥8%). Patients recruited from a diabetes specialty clinic were randomly allocated to an intervention group or a control group (Keogh et al., 2007, 2011). Patients in the intervention group identified a family member (with a close relationship and regular contact with patient) to participate who was most involved in helping them with diabetes management. Seventy-five percent of the family members were spouses; the rest were their adult children. The intervention consisted of two 45-min sessions, delivered by a health psychologist, with the patient and family member in the patient's home, and a 15-min follow-up telephone call. The intervention was described as using health psychology techniques including elements of motivational interviewing (i.e., exchanging information, eliciting change talk, reducing resistance, building self-efficacy, problem-solving, and goal setting/action planning). The content targeted negative and/or inaccurate illness perceptions. The control group received usual diabetes care. At 6 months, the intervention group reported a 0.4% lower A1c. However, when they analyzed by baseline A1c, they found that the positive effect was only found in those with the poorest control at baseline (A1c ≥ 9.5%). In that subgroup, the intervention arm had a statistically significant 1.2% lower A1c than the control group. The intervention group also reported statistically significant improvements in beliefs about diabetes, psychological well-being, diet, exercise, and family support. While the authors concluded that inclusion of a family member was a key active ingredient in the success of the intervention, the lack of a patient-only intervention arm means one cannot draw a reliable conclusion about the role of family.

Baig et al. (2015), in their systematic review, noted the wide variation in study designs, reporting of results, and the degree of family involvement and concluded that, given the heterogeneity and lack of data specific to family involvement, no conclusions could be drawn about whether and how family involvement in diabetes interventions may affect outcomes in people with T2D. Taken as a whole, these studies indicate that family involvement is feasible and acceptable to patients and family members and that family interventions show the potential for improving patient outcomes when compared to usual care, though clearly results are mixed and inconclusive.

Any family intervention trial should be theoretically grounded and, importantly, provide a comparable individual intervention as a comparison group. If a family intervention is found to be superior to a usual care control group (as those cited), one can only conclude that the intervention was superior to no active intervention, not that family involvement itself was valuable (Campbell, 2002). Also, family should be clearly defined, and the nature of their involvement described.

We are aware of only one study that met these criteria, the Diabetes Support Project (DSP) (Trief et al., 2016). The DSP was a practical, randomized controlled trial in which adults with T2D in poor glycemic control (A1c ≥ 7.5%) were randomized to a couple intervention, a comparable individual patient intervention, or a patient-only diabetes education intervention (DE), all delivered via telephone to increase reach. Based on interdependence theory (Kelley & Thibaut, 1978; Rusbult & Van Lange, 2003), which holds that an intervention must look at the dyad and the interdependence of each partner with the other, the DSP couple-focused intervention was designed to promote "communal coping," shared problem-solving, and effective communication (Lewis et al., 2006). The individual call (IC) intervention was the same as the couple call (CC) intervention except that IC engaged individual patients, i.e., without partners. The difference between the content of the CC and IC interventions was that, in the CC arm, there were 2 (out of 12) calls that specifically focused on relationships and communication, while in IC these 2 calls addressed individual problem-solving instead. Of course, there were significant differences in process. In the CC intervention arm, partners were actively involved in all calls and homework. Both members of the couple were encouraged to use collaborative problem-solving techniques, provide mutual support for change, and work toward improved communication. In CC, each call engaged the partner by asking, for example, how (s)he could support the patient in making the identified behavior change and how the patient could understand and support the partner. Thus, in each CC call, the interventionist created an opportunity for a conversation between the partners that was encouraged and deepened by her prompts. It is also noteworthy that interventionists were selected for their expertise in working with couples, received additional training in doing so, and were supervised to competence to ensure that they had and used the necessary skills to be effective with couples.

Assessments occurred at 4 months (immediately post-intervention), 8 months, and 12 months. The participant sample (N = 280 couples) was mostly male (61.6%), middle-aged (56.8 ± 10.9 years), modestly diverse (30.4% self-described minority), in a long-term relationship (25.5 ± 14.8 years), and in very poor glycemic control (A1c mean = 9.1 ± 1.5%). Using intention-to-treat analyses, all groups showed improvement in A1c after 1 year (CC: −0.47%; IC: −0.52%; DE: −0.57%) with no significant differences between groups. However, preplanned subgroup analyses found that, for those in the middle A1c tertile (8.3–9.2%), only the couple intervention led to lower A1c and these gains were maintained for the 1-year study. In the top tertile (A1c ≥ 9.3%), all groups improved, and in the bottom tertile (A1c = 7.5–8.2%), none of the groups improved. In other behavioral intervention trials that report significant improvement in A1c, further analyses have shown that it was the data of the very high A1c group (e.g., >9.4%) that drove the significance and that the interventions did not benefit those with high, but not exceedingly high, A1c (Chamany et al., 2015; Keogh et al., 2011). In the DSP, the couple intervention did. Except for blood pressure, results of the other DSP medical outcomes (BMI, waist circumference) favored the couples arm too, though changes were clinically small. For psychosocial outcomes (diabetes distress, depressive symptoms, diabetes self-efficacy), positive changes were greater for the couple arm. This was reassuring, as results did not show that partner involvement led to greater distress or less self-efficacy, a concern about partner involvement that has been raised (Rook, August, Stephens, & Franks, 2011). Finally, participant satisfaction was extremely high for both intervention arms, but higher for the CC arm vs. IC and vs. DE.

These results are noteworthy as the DSP included the key elements of a trial to assess the value of family/partner intervention. Family was specifically described as "committed partner." The groups were randomized and by all measures equivalent at baseline. There was an individual intervention comparator arm, and the interventions were highly comparable, so that the added value of partner involvement could be assessed. The interventionists were trained and supervised to work well with couples. And, the couple intervention was targeted to specific communication, relationship, and social support skills that are hypothesized to be the mediators of patient behavior change. While the effect of the intervention on partners has not yet been reported, these data are forthcoming.

It is noteworthy that, other than the DSP, the family intervention trials described here were either done outside of the Unites States or, if in the United States, focused on ethnic minority patients. Why this is the case is unclear. Perhaps researchers see minority cultures as being more influenced by the potential impact of family members on patient outcomes. Or, since minority patients are at higher risk for poor outcomes, perhaps these researchers are interested in applying more resources from the patient's immediate social context.

We also note that only a few trials fall within the definition of "family therapy." Family therapy has been defined as "A type of psychotherapy designed to identify family patterns that contribute to a behavior disorder or mental illness and help family members break those habits. Family therapy involves discussion and problem-solving sessions with the family... In family therapy, the web of interpersonal relationships is examined and, ideally, communication is strengthened within the family" (medicinenet.com, n.d.). There are aspects of each study's interventions that fall within this definition, in that they commonly involve discussion and problem-solving sessions and a key goal is often to enhance communication. And, in a few studies, there is attention to the specific family dynamics, i.e., the "web of interpersonal relationships," that may be operating. But often in psychoeducational and behavioral trials, the specific and unique interactions within the family are not examined or addressed, as the need to develop a replicable, behavioral intervention may preclude the type of individual family focus that meets this criterion.

Discussion

As we and others have shown, the structure, function, beliefs, and expectations of family or couple relationships have powerful effects on the management of chronic disease and specifically the management of diabetes. Yet our review of recent studies indicates the paucity of clinical trials that take the unique aspects of family/couple relationships into account when developing interventions that capitalize on their strengths and influences on diabetes care (Trief et al., 2011). Most studies lack precision with respect to study design and the specificity of intervention goals. Given the potential of this line of research to enhance disease outcomes, we summarize the implications of these trends into three sets of potential challenges: challenges of definition, challenges of content, and challenges of study design.

Challenges of Definition

Interventions described as “family” or “social support” interventions rarely define the specific social unit that is targeted for intervention, and the intervention often includes partners, adult offspring and/or friends, and others in the community. Although each of these social units may affect disease management, each is also unique, with its own intrinsic social structures and roles. This general lack of precision in identifying the specific social target of an intervention fails to take advantage of unique characteristics and impacts of each relationship, thus change may not be maximized. This issue was recognized in the DSP in which the “couple” unit was self-defined and thus, while most dyads were married, also included other dyads. This pattern becomes more understandable when viewed historically. Disease has traditionally been viewed as occurring within individuals – individual people are defined as patients with a diagnosis. The biological processes that define disease occur within individuals. All others, in this light, are viewed uniformly as “others,” providing or not providing “social support.” Social support, then, is often viewed as a unitary construct regardless of how it is structured or from whom it is provided.

Because disease is viewed medically as a property of an individual, interventions tend to focus separately on those with the disease or on those in their general social world, sometimes in combination. It is rare that we see interventions that target the social unit of patient-partner relationships. This is important because, as we describe below, how an interventional target is defined has major implications for experimental design, evaluation, actual content of the intervention, and outcomes selected. We argue that there is a need to develop interventions that focus on specific kinds of relationships, with the couple or family being the most powerful. In the discussion below, we refer to “couple” interventions (for clarity), but these comments apply equally as well to those that might target a family member with another relationship with the patient, e.g., adult offspring.

Challenges of Content

In most of the “family intervention” studies reviewed above, the identification of well-defined couple skills or characteristics that were targeted for change was generally left unspecified. Typically, studies describe an intervention aimed at getting significant other(s) “involved” in some way, either through shared education, vaguely defined improved “support,” or assistance with use of community resources. But specificity is lacking, and it is rarely clear what the intervention is expected to change. In an early paper on couple-based interventions in diabetes, Fisher et al. (1998) suggested that interventions that target skill building for adult couples might center on disease-related communication (e.g., reduce criticalness and enhance clarity and directness), disease-related problem solving (e.g., how to reduce hypoglycemic episodes, plan for a night out or trip), or overprotectiveness and negative aspects of couple relationships (e.g., clarity of roles and boundaries – specifically who does what, when, and how regarding specific aspects of disease management). For example, how should a partner communicate concerns about a low or high blood glucose level without being perceived as intrusive or critical; how should a patient communicate a need for help without fearing that the partner will "take over"; and how should a couple manage a planned trip to visit family where eating and drinking together will be a major focus without running into conflict? Each of these examples focuses on specific, precise relationship skills and practices that could be addressed in a well-defined intervention. These types of discussions were incorporated into the couple intervention of the DSP; however, given the flexibility required to work with the unique issues of each couple, it is a challenge to standardize their exploration.

Challenges of Study Design

Targeting characteristics of couple relationships and patterns for change in diabetes interventions, in addition to focusing on the disease management behavior of individual patients and how the partner may support him/her, has major implications for how the intervention is evaluated. First, when the couple is the target of change, pre- and post-assessment must also include measures of the couple's relationship. These might include clarity of communication or level of criticalness, along with assessments of couple problem-solving skills. Such assessments were included in the DSP; however, standard measures of marital relationships and satisfaction do not always adequately assess the relevant constructs. In addition, partners are frequently the unassessed players in diabetes management, which can be problematic since the presence of diabetes in the family can have an impact on the physical health and emotional well-being of members of the family, including the partner (Barnard et al., 2016; Coyne et al., 1991; Polonsky, Fisher, Hessler, & Johnson, 2016). Therefore, it is important to assess independently how the intervention impacted the health and well-being of the partner and not focus exclusively on the outcomes of the person with diabetes. This challenge requires an expansion of measures employed to address each of the primary players and their relationship.

Second, couples display a variety of styles of relating – some are very close and share almost everything, whereas others foster a sense of independence and autonomy; some couples have rigid role structures concerning who is responsible for what, whereas others are more laissez-faire and flexible. These differences have major implications for how the intervention should be designed. Studies should not be designed with a one-size-fits-all strategy because the management styles within couples vary dramatically. Hence, interventions that allow partners to incorporate change within their unique relationship dynamics will likely have a better chance of success than those that ask all couples to do the same thing. Here again we see the tension between standardization that can ensure replicability and attention to unique relationship issues that can enhance efficacy. And, we note again the lack of studies that explored gender, age, and cultural differences that might impact intervention design, selection of assessment tools, and conclusions drawn.

Third, couple interventionists require a unique set of well-trained and well-supervised clinical skills. These should include a knowledge of couple and family dynamics; clinical skills for interviewing and intervening with couples, not just with individuals; and experience shifting perspectives noncritically from one partner to the other, as specific diabetes-related behavioral tasks and relationship dynamics are addressed. Investigators should not assume that research or clinical staff with experience working with individual patients can easily function well as couples interventionists. Unique skills are required.

Fourth, well-designed couple-focused interventions usually address one of the following two questions: does a couple-focused intervention lead to better outcomes for patients and partners than an intervention that includes only the adult with diabetes; and, within a couple-focused intervention, which behavioral change strategy or target yields the best outcomes? The first of these two questions requires a multiple-arm study design, with an arm for individual patients only, an arm for couples only, and an active control arm. To our knowledge, the DSP, described above, is the only couple intervention trial that included all three. The second question asks what the content of the couple-focused intervention should be for best outcomes. In this scenario, in one arm the intervention might work with couples on communication skills, while a second arm might focus on building specific problem-solving skills, to see which approach yields better results. Or, the study might compare a multi-couple group format with individual couples seen alone to see which type of intervention works best. Both approaches could also assess which type of intervention works best for which types of couples, e.g., those with low marital satisfaction and those that are highly disorganized, again addressing the idea that a one-size-fits-all strategy is less likely to be effective. Thus, adopting a couple approach to the development of clinical interventions mandates a different context for addressing primary study questions. This level of specificity and precision has not been achieved in the family and diabetes literature.

In summary, many questions remain in the domain of family/partner interventions for persons with diabetes: who should be involved (family member alone or with patient); which family member should be targeted (e.g., spouse, cohabiting family member, or in some cultures should there be a broader definition of family); what should the content be (disease specific or focused on the relationship); which outcomes are most important (patient medical/psychological outcomes vs. relationship change vs. partner outcomes); and what factors predict who would be most likely to benefit from a couples/family intervention?

Conclusions

Despite the long-standing recognition of the importance of social context in health and disease, a focus on family relationships as a setting for clinical intervention has been slow to develop. The literature strongly suggests that the family setting of disease management provides a productive target for intervention in ways that go well beyond interventions for individual patients, as close intimates interact intensely over varied situations and long time periods. While the social support literature provides a foundation for family involvement, it may be too broad to include family, particularly the couple relationship, in this domain of study, as doing so does not recognize the unique character and impact of family relationships.

In diabetes, systematic studies of intervention strategies to serve adults have been somewhat limited. This lack is most striking for adults with type 1 diabetes, but even studies for adults with type 2 diabetes are few and often poorly defined, although the direction is positive. Clearly, a focus on family/partners and the patient-partner relationship increases the complexity of study design, content, and evaluation, but these obstacles can be overcome resulting in well-designed trials that give us confidence in their conclusions. We therefore call for greater engagement with adult couples and family members in diabetes care to develop more effective programs of interventions to improve the health and well-being of both patients and their partners.

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Chapter 27
Enhancing Peer Support Interventions in Diabetes Care

Patrick Y. Tang and Edwin B. Fisher

As one of the most pressing health-care challenges of the twenty-first century, diabetes affects 450 million people, about 1 in 11 adults. An additional 193 million adults living with diabetes are undiagnosed (International Diabetes Federation, 2015). A disproportionate burden of diabetes falls on low- and middle-income countries, which have fewer health-care resources to deal with this public health crisis. These countries account for only 19% of global health care spending on diabetes despite having 75.4% of the diabetes population (International Diabetes Federation, 2015). In the absence of adequate care, people with diabetes tend to experience worse long-term outcomes, such as decreased function, complications, financial burden, lower quality of life, and increased mortality. This stark contrast underscores the necessity for economical and rapidly deployable strategies to help people with diabetes live healthier, happier lives.

Among the individual- and community-level strategies that have been implemented to improve care for people with diabetes, peer support from trained laypersons stands out as a versatile approach that has been effective and often cost-effective. Several reviews have found that peer support has significant impacts on diabetes knowledge, self-care behaviors, glycemic control, and emotional well-being (Fisher et al., 2017; Little, Wang, Castro, Jimenez, & Rosal, 2014; Palmas et al., 2015; Qi et al., 2015; Trump & Mendenhall, 2017). Peer support interventions are proving to be cost-effective by improving clinical status (Allen, Dennison Himmelfarb, Szanton, & Frick, 2014; Brown et al., 2012; Patil et al., 2016), reducing long-term complications (Prezio, Pagan, Shuval, & Culica, 2014; Ryabov, 2014), reducing excess health-care utilization (Fedder, Chang, Curry, & Nichols, 2003; Johansson, Keller, Sonnichsen, & Weitgasser, 2017), and improving the efficiency of care delivery (Kim et al., 2016). Born of pragmatism and necessity, peer support helps fill the gaps in diabetes care and strengthens the public health system.

Health-care systems around the world are increasingly tapping into peer support for diabetes care by partnering with community-based programs and integrating peer support into clinical care (Aswathy, Unnikrishnan, Kalra, & Leelamoni, 2013; Perry, Zulliger, & Rogers, 2014; Schneider, Okello, & Lehmann, 2016; Shah, Kaselitz, & Heisler, 2013; Zulu, Kinsman, Michelo, & Hurtig, 2014). The World Health Organization laid the foundations for peer support in primary care with the Alma Ata Declaration in 1978, defining primary care as a system that "relies, at local and referral levels, on physicians, nurses, midwives, auxiliaries and community workers as applicable, as well as traditional practitioners as needed, suitably trained socially and technically to work as a health team

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P. Y. Tang (✉) · E. B. Fisher
Peers for Progress, Department of Health Behavior, Gillings School of Global Public Health,
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
e-mail: ptang@unc.edu

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and to respond to the expressed health needs of the community" (World Health Organization, 1978). In the United States, the National Center for Chronic Disease Prevention and Health Promotion (CDC, 2015), the American Public Health Association (APHA, 2009), and the American Association of Diabetes Educators (Albright et al., 2009) have promulgated policy statements in favor of peer support. In 2010, the Affordable Care Act (2010; Islam et al., 2015) recognized the important contributions of community health workers for health promotion and prevention, outlining provisions to expand their utilization for chronic disease prevention and management.

Peer support has been widely studied for a host of health conditions, so its application to diabetes represents only a fraction of global research. Given the interoperability of peer support in chronic disease, we can draw important lessons from the greater body of peer support scholarship. This chapter summarizes the evidence for organized, intentional peer support in diabetes, recommendations for implementing high-quality programs, and implications for future research.

Defining Peer Support

Social support is a basic human need that is necessary for people to live healthier lives and manage complex health conditions. Loneliness, or a lack of social support, is as deadly as smoking a pack of cigarettes a day (Holt-Lunstad, Smith, & Layton, 2010). For persons with diabetes (PWD), social support can be an important factor in how well they are able to manage their diabetes, avoid complications, and avoid distress (Kadirvelu, Sadasivan, & Ng, 2012; Koetsenruijter et al., 2016). Peer supporters can make important contributions simply by "being there"; program participants often praise their peer supporters for "having their back." In addition to family members and health-care professionals, peers have a unique role to play in providing emotional and instrumental support to PWD (Brownson & Heisler, 2009).

Peer support refers to "support from a person who possesses experiential knowledge of a specific behavior or stressor and/or similar characteristics as the target population" (Dennis, 2003). In order for a peer supporter to be acceptable to PWD, they must have shared "peer identity." Peer identity is established by the recognition of shared experiences that the person receiving support *perceives to be valuable*. We often assume that peer identity is conferred by sharing a diagnosis and living in the same neighborhood, but people find many other things important besides diagnoses and where they live. Consider this from the perspective of the many other problems that frequently accompany diabetes. Would someone with diabetes, arthritis, high cholesterol, and hypertension need or want a single peer supporter that shares all of those conditions or four peer supporters, one for each condition? Further, consider things of importance outside of health and disease. What characteristics of a peer supporter would be valuable to a 70-year old with type 2 diabetes who is retired, recently widowed, and likes trout fishing? The nuances of peer identity may depend on what is important to the individual, perhaps their stage in life or recent life changes (widowhood, retirement), important interests (trout fishing), as well as their health concerns. On the other hand, some diseases are sufficiently unique that a peer supporter needs at least to be very familiar with them, if not share them. For instance, someone who has had type 1 diabetes since early adolescence is unlikely to accept peer support from someone who was diagnosed with type 2 diabetes in their 40s.

Peer support harnesses interpersonal relationships to activate intrapersonal change. In diabetes care, patient-level factors account for 95% of the variance in glycemic control, pointing to the importance of behavioral interventions for diabetes self-management education and support (C. P. Lynch & Egede, 2011; Tuerk, Mueller, & Egede, 2008). With appropriate training and supervision, peers apply a range of skills to offer support that is personalized, culturally competent, confidential, nonjudgmental, non-prescriptive, and person-centered. Peer supporters are often trained to use motivational interviewing or similar techniques to empower patients to eat healthier foods, exercise more, adhere to medications, reduce risk factors such as smoking and drinking alcohol, cope with stress, improve self-monitoring, solve problems, and utilize clinical and community resources (Ferguson, Lemay, Hargraves, Gorodetsky, & Calista, 2012; Richert, Webb, Morse, O'Toole, & Brownson, 2007; Sazlina, Browning, & Yasin, 2013; Tang, Funnell, Gillard, Nwankwo, & Heisler, 2011). Above all else, peers earn the trust of PWD over time and build relationships that catalyze behavior change.

People who provide peer support are known by a variety of names, such as community health workers, lay health advisors, *promotores de salud*, peer navigators, health ambassadors, and peer coaches. People working under these titles may perform a range of duties in addition to providing peer support and may work as volunteers or paid staff. Although personnel decisions will impact program design, no significant differences in program effectiveness have been reported between the various personnel that provide peer support (Qi et al., 2015). Even without high levels of formal education, natural helpers are found in every community, aiding community members to the best of their abilities with resources that are readily available. As natural helpers, people that provide peer support are driven by the desire to apply their personal experiences productively to help others. Additionally, peer support work serves as a point of entry into the health professions for people with limited formal education (Farrar, Morgan, Chuang, & Konrad, 2011).

It is important to note that peer support does not replace the role of health professionals. Instead, it complements and enhances health-care delivery by providing the emotional, social, and practical assistance necessary to manage diabetes and stay healthy (Brownson & Heisler, 2009; Collinsworth, Vulimiri, Schmidt, & Snead, 2013; Collinsworth, Vulimiri, Snead, & Walton, 2014). Numerous studies have stressed the importance of clearly defining a peer supporter's scope of practice to protect their unique role while simultaneously protecting patients, providers, and peer supporters themselves from unintended outcomes and liability (Findley et al., 2012; Shah et al., 2013). And although peer support does not challenge the role of health professionals, it disrupts the health-care system by expanding its boundaries and challenging us to rethink the organization of care (Mayer et al., 2016).

Standardization and Flexibility

Across the spectrum of peer support programs, relatively few are identical. Nevertheless, standardization of peer support is essential for quality assurance, quality improvement, and program dissemination. It is not clear, however, what features of programs should be the focus of standardization. In a 2007 World Health Organization meeting on peer support programs in diabetes (World Health Organization, 2008), representatives from over 20 countries reached consensus that (1) key aspects of peer support are generalizable across settings and (2) programs have to be tailored to different settings, populations, and problems. Accordingly, *Peers for Progress* has promoted a model of standardization by function, not content (Aro, Smith, & Dekker, 2008; Hawe, Shiell, & Riley, 2004). Selecting appropriate dimensions for standardization is important for evaluating the likelihood of program success and reasons for underperformance. In contrast to the more standardized content of diabetes education, the content of self-management support interventions needs to be tailored to specific populations and places. Therefore, imposing standards on specific program content would diminish a major strength by unnecessarily restraining program flexibility. Consider collaborative goal setting as part of primary care and self-management for diabetes. There might be a number of ways to achieve this – motivational interviewing (Miller & Rollnick, 2002), action planning (Bodenheimer & Handley, 2009), empowerment (Anderson & Funnell, 2005), etc. To test the specific contribution of one of these approaches, it would be important to standardize at the level of its procedures. On the other hand, if one were testing an approach to improve the quality of comprehensive diabetes management in primary care, one might be indifferent to the choice of collaborative approach, as long as some collaborative approaches were included.

Table 27.1 Four key functions of peer support

Assistance in daily management	Simple objectives like "exercising 150 min a week" or "eating more fruits and vegetables" sound pretty straightforward in the doctor's office, but often turn out to be difficult to put into practice. The peer supporter helps turn these into specific plans that fit in with people's lifestyles and circumstances. Peer supporters use their own experiences with diet, physical activity, and medication adherence in helping people figure out how to manage diabetes in their daily lives
Social and emotional support	Through empathetic listening and encouragement, peer supporters are an integral part of helping patients to cope with social or emotional barriers and to stay motivated to reach their goals
Linkages to clinical care and community resources	Peer supporters help bridge the gap between patients and health professionals, motivating patients to communicate and assert themselves in order to obtain regular and quality care, helping to identify local resources for buying affordable, healthy food, or to find safe, attractive places for physical activity
Ongoing support, extended over time	Diabetes and other chronic diseases are "for the rest of your life," and needs change as motivation diminishes or health problems emerge. Peer supporters keep patients engaged by providing proactive, flexible, and continual long-term follow-up

In standardization by function, key objectives or aims of the program are the focus. In the Robert Wood Johnson *Diabetes Initiative*, for example, programs were encouraged to address key functions of promoting self-management: individualized assessment, collaborative goal setting, teaching skills for self-management, ongoing follow-up and support, and continuity of clinical care (Fisher et al., 2005; Fisher, Brownson, O'Toole, Anwuri, & Shetty, 2007). Each program was free to determine how it would address these functions, after considering its setting, resources, and the needs and preferences of the people it served. Taking this approach to peer support has led to the identification of four key functions, with specific reference to diabetes, as outlined in Table 27.1 These provide a flexible framework for program development and quality improvement in a variety of populations and settings (Fisher, Earp, Maman, & Zolotor, 2010; Peers for Progress, 2014).

The Evidence for Peer Support

Studies have shown that peer support for diabetes improves outcomes (i.e., glycemic control, blood pressure, diabetes-related distress, depression) for people across the course of disease, across the lifespan, and in various populations (Dale, Williams, & Bowyer, 2012; Deng et al., 2016; Fisher et al., 2012; Hunt, Grant, & Appel, 2011; Qi et al., 2015). Through clinic-based programs and community-led initiatives, peer support may be effectively delivered through many settings. It can also be implemented through a wide range of modalities, such as one-on-one in-person, group-based, telephone, and digital health (Heisler, 2010).

In 2008, *Peers for Progress* funded 14 projects around the world to evaluate peer support in diabetes self-management (Boothroyd & Fisher, 2010). A 2012 paper in *Health Affairs* with global collaborators summarizes the initial findings from these projects (Fisher et al., 2012). In 2015, a supplement of the *Annals of Family Medicine* assembled outcomes reports from many of these funded projects (Fisher, et al., 2015). In aggregate, projects in the United States (five sites), Australia, China, and the United Kingdom showed the benefits of peer support across populations with and without health-care coverage, low-income and middle-class groups, retirees and those within the workforce, and ethnic minorities and majorities.

Peers for Progress conducted a systematic review of the literature on peer support for diabetes management and other complex, sustained health behaviors for managing chronic diseases, weight management, smoking cessation, etc. (Fisher, Ayala, et al., 2017). Of the 65 papers published between 2000 and 2011, 83.1% reported significant impacts of peer support, 61.5% reporting between-group differences and another 21.5% reporting significant within-group changes. The review also included 19 other reviews of peer support, among which a median of 64.5% of studies reviewed reported significant effects of peer support.

A third component of the review examined 30 papers reporting peer support for diabetes management published between 2000 and 2015. Among these, 86.7% reported significant impacts of peer support, with 56.7% reporting between-group differences and another 30.0% reporting significant within-group changes. Among 19 of these 30 reporting HbA1c data, average reduction was 0.76 points, far in excess of the half point that is generally seen as clinically meaningful. Finally, in examination of peer-based programs that did not show significant benefits, failures were often attributable to the absence of one or more of the four key functions described in Table 27.1 (Fisher, Ayala, et al., 2015).

Peer support programs can benefit peer supporters as well as the participants. In a program conducted with community-based peer coaches in San Francisco, the peer coaches became empowered to better manage their own diabetes (Goldman, Ghorob, Eyre, & Bodenheimer, 2013). Likewise, a program in China found that PWD that completed diabetes self-management education (DSME) and volunteered to serve as peer supporters were more likely to sustain improvements in self-care behaviors and metabolic control after 4 years compared to PWD that only completed the DSME but did not serve as peer supporters (Yin et al., 2015). The authors suggest that the volunteer effect, willingness to help others, mutual learning, and ongoing support were possible factors that contributed to the benefits that peer supporters experienced. In the field of mental health peer support, studies have found that providing peer support is associated with improvements in the intrapersonal, social, mental health, spiritual, and professional domains, as well as reductions in health-care utilization (case management, crisis services, inpatient hospitalizations) and public benefits (Ahmed, Hunter, Mabe, Tucker, & Buckley, 2015; Johnson et al., 2014).

Beyond individual-level outcomes, peer support also improves organizational- and systems-level outcomes. With its intrinsic patient-centeredness, peer support is a critical humanizing force in health care (Peers for Progress, 2014). The features of peer support that make it a humanizing force include the amount of time that peer supporters can devote to patients, shared experiences, and a keen understanding of the patient's culture, community, and circumstances. Effective and humanizing, peer support facilitates the right care at the right time at the right cost. By acting as a liaison between the PWD and the clinic, peer support improves patient perceptions of their providers while also improving providers' understanding of their patients' needs (Collinsworth et al., 2014). As patients get more out of their health-care services, they are more likely to trust their providers, follow providers' recommendations, miss fewer office appointments, and express satisfaction with clinical services (Heisler et al., 2009; Thom et al., 2015). Furthermore, timely referral to clinical services means that patients are more likely to engage in routine, preventive care, and appropriately utilize urgent care and emergency room visits.

Peer Support in Diabetes Self-Management Education and Support

In 2014, the American Association of Diabetes Educators published an update of its National Standards for Diabetes Self-Management (Haas et al. 2014), in which it made an important distinction between diabetes self-management education (DSME) and diabetes self-management support (DSMS). Recognizing the importance of both components in encouraging and maintaining diabetes self-care behaviors, the guidelines identified peer support as an important channel of delivering both DSME and DSMS.

Although this chapter deals primarily with peer support for DSMS, peer-led DSME also has a strong track record of success (Collinsworth et al., 2013). Peer-led DSME has been shown to be as effective as professionally led DSME at improving diabetes knowledge, attitudes, and health behaviors (Albright & Gregg, 2013; Gagliardino et al., 2013).

Some diabetes experts have challenged us to think about education as an ongoing process rather than a one-shot intervention (Peers for Progress, 2014). Withdrawing support after the completion of a DSME course represents a failure to capitalize on the gains made during DSME (Rao et al., 2015). Thus, DSMS approaches such as peer support are necessary to extend and enrich the process of diabetes education. Indeed, in the course of peer support programs for DSMS, peer supporters inevitably deliver some diabetes education, review and help clarify educational messages, help individuals figure out how to apply educational messages to their own circumstances, and then also provide ongoing support for continued self-management.

Peer Support in Diabetes Prevention

In addition to diabetes management, diabetes prevention provides important avenues for peer support and, more broadly, implementation of interventions by a variety of laypersons (Marrero, 2009). As background, substantial evidence shows that lifestyle interventions that focus on healthy diets and increased physical activity are effective in the prevention of diabetes, especially among high-risk individuals (Knowler et al., 2002; Pan et al., 1997; Tuomilehto et al., 2001; Yoon, Kwok, & Magkidis, 2013). In addition, economic analyses have shown that these interventions are cost-effective (Alouki, Delisle, Bermudez-Tamayo, & Johri, 2016).

The key factors in diabetes prevention are moderate physical activity, equivalent to about 30 minutes of brisk walking, 5 days a week, and modest weight loss of 5–10% of bodyweight (e.g., 10–20 pounds for someone starting at 200 pounds). In the diabetes prevention program (DPP) research study, an intensive lifestyle intervention focusing on these two objectives (150 minutes per week moderate physical activity, 7% loss of body weight) successfully reduced the incidence of type 2 diabetes by 58% over 3.2 years (Knowler et al., 2002) and by 34% over 10 years (Diabetes Prevention Program Research et al., 2009). The lifestyle intervention was structured around 16 core sessions delivered by trained lifestyle coaches and follow-up sessions focused on promoting physical activity. In follow-up studies, the critical components for success were identified to be (1) a goal-based behavioral intervention, (2) lifestyle coaches, (3) frequent contact, (4) tailoring strategies, (5) materials and strategies to address the needs of an ethnically diverse population, and (6) an extensive local and national network (Hoskin et al., 2014). Clearly, lifestyle coaching, frequent contact, and tailoring to the needs of individuals and to ethnically diverse groups are the kinds of program features that peer supporters can readily provide.

Many lifestyle interventions for diabetes prevention, such as that of the DPP, were originally delivered in clinical settings by health professionals such as nutritionists, exercise therapists, nurses, psychologists, social workers, and diabetes educators. However, many have now been translated to community-based settings, modified from individual- to group-based formats, and expanded to utilize laypersons in program delivery (Ackermann, Finch, Brizendine, Zhou, & Marrero, 2008; Chou, Burnet, Meltzer, & Huang, 2015; Finch, Kelly, Marrero, & Ackermann, 2009). Developmental studies have shown that deploying laypersons as DPP lifestyle coaches is both feasible and effective (Horowitz, Eckhardt, Talavera, Goytia, & Lorig, 2011; Morrow et al., 2016; Tabak et al., 2015; Whittemore, 2011). A systematic review found that weight loss was comparable in DPP interventions whether delivered by professional or lay educators (Ali, Echouffo-Tcheugui, & Williamson, 2012). That review recommended deploying more laypersons to reduce program costs without sacrificing intervention quality. Another systematic review of combined diet and physical activity promotion programs to prevent diabetes around the world found that 25% of programs utilized laypersons in program delivery (Balk et al., 2015).

The DPP intervention has been scaled up nationally through the Centers for Disease Control and Prevention's National Diabetes Prevention Program (NDPP) (Albright & Gregg, 2013). The NDPP provides a robust set of guidelines and resources for the implementation of DPP-based lifestyle interventions. Furthermore, by recognizing and promoting the training of laypersons to serve as lifestyle coaches, the NDPP has triggered substantial growth in the lay workforce for diabetes prevention (Diabetes Prevention Program Research, 2002).

A critical feature of the original DPP research study was that it tested the twin objectives of 7% weight loss and moderate physical activity, not any single approach to achieving them (Knowler et al., 2002). All the centers participating in the DPP drew upon a standard set of lifestyle intervention procedures, but they were also encouraged to adapt those protocols and add additional intervention strategies to meet the needs of their populations and settings. Thus, the DPP provided strong evidence for weight loss and physical activity that might be achieved through a variety of strategies.

Given the mandate for a variety of approaches to lifestyle modification for diabetes prevention, many programs have emerged, frequently involving peer supporters or community health workers. Based on this work, the US Community Preventive Services Task Force issued a report, *Diabetes Prevention: Interventions Engaging Community Health Workers (*Community Preventive Services Task Force, 2017*)* that "…recommends interventions engaging community health workers for diabetes prevention based on sufficient evidence of effectiveness in improving glycemic control and weight-related outcomes among people at increased risk for type 2 diabetes." The evidence on which this recommendation is based is summarized in Table 27.2, which shows that interventions implemented by community health workers (CHWs) led to significant benefits across a variety of measures related to both diabetes and cardiovascular risk. Most programs were group-based. Eight of the 22 studies also included individual CHW contacts along with the group meetings.

The DPP, the NDPP, and many other lifestyle interventions for diabetes prevention provide important opportunities for greater incorporation of trained laypersons, community health workers, and other peer supporters in key areas of health care. The contribution of peer support is made clear, for example, by qualitative studies showing that having a relationship with a trusted person motivates attendance and by a dose-response relationship between that attendance and weight loss (Ali et al., 2012). In addition, peer support is an important response to the challenge of reaching all those who might benefit from diabetes prevention and helping them to sustain healthy lifestyle changes.

Strategic Advantages of Peer Support

Peer support is especially beneficial for PWD with high needs and those that are hardly reached by conventional health-care services. Two meta-analyses have shown an association between higher baseline HbA1c and larger effect size (Palmas et al., 2015; Qi et al., 2015). Compared to usual care, peer support is an effective strategy for improving glycemic control for underserved, low-income, minority populations (Little et al., 2014; Lynch & Egede, 2011; Lynch, Liebman, Ventrelle, Avery, & Richardson, 2014). For example, a program for ethnic minority patients of safety-net clinics in San Francisco reported significantly greater reductions in HbA1c with peer support in addition to usual care, compared to usual care alone (Thom et al., 2013). These benefits of peer support were significantly greater for patients categorized as *low* on medication adherence and self-management at baseline (Moskowitz, Thom, Hessler, Ghorob, & Bodenheimer, 2013). Similarly, in support exchanged within dyads of US veterans with diabetes, improvements in blood glucose relative to controls were greatest among those with initially low levels of diabetes support or health literacy (Heisler, Vijan, Makki, & Piette, 2010). In an underserved Chicago population, a low intensity, home-based

Table 27.2 Summary of evidence for community health workers in diabetes prevention

Designs	Total = 22 studies
	Pre-post without comparison – 12
	Group randomized – 7
Sex and age	70% female
	19 studies: Ages 18–64
	2 studies: Ages ≤17
Mode	Group – 7
	Individual – 4
	Mostly group with individual – 8
Differences favoring community health worker interventions	
Weight lost (pounds)	Medians:
	Most suitable[a] – 3.7
	Least suitable – 2.8
	All – 3.0
BMI reduction	Medians:
	Most suitable – 0.6
	Least suitable – 0.5
	All – 0.5
Decreased waist circumference (inches)	Medians:
	Most suitable – 1.1
	Least suitable – 1.4
	All – 1.4
HbA1c reduction	Medians:
	Most suitable – 0.07
	Least suitable – 0.10
	All – 0.09
Fasting glucose (mg/dl)	Medians:
	Most suitable – 1.0
	Least suitable – 6.8
	All – 2.4
SBP reduction (mmHg)	Medians:
	Most suitable – 2.5
	Least suitable – 3.8
	All – 2.6

Source: Community Prevention Services Task Force, (2017). *Diabetes prevention: Interventions Engaging Community Health Workers*

[a] Most and least suitable refers to the suitability of designs. Most suitable was group RCT or pre-post with a comparison group

community health worker intervention was more effective at decreasing HbA1c among participants that had lower levels of diabetes self-care at baseline (Hughes, Yang, Ramanathan, & Benjamins, 2016). These are important observations: intervention worked across all individuals, but worked especially well relative to controls for individuals whose diabetes management was in most need of improvement (as suggested by various indicators). This pattern of peer support reaching and benefitting those whom we would expect are most difficult to reach and benefit was sustained in a systematic review of peer support programs across a variety of health conditions (Sokol & Fisher, 2016). Therefore, peer support is a viable strategy to address one of the major challenges in population health management: benefitting high need groups that experience disproportionate burdens and costs of care.

Peer support has also demonstrated strong potential to address diabetes and comorbidities (Fisher, Ayala, et al., 2015; Lynch et al., 2014). The co-occurrence of diabetes and depression is quite common;

PWD are twice as likely to be depressed as those without diabetes, and symptoms of depression are present among almost one-third of PWD (Roy & Lloyd, 2012). Psychological problems, from heightened distress to serious psychopathology, compromise self-management behaviors and exacerbate disease. Among PWD, depression is associated with poor glycemic control and decreased adherence to medical treatments (Fisher, Ayala, et al., 2015). Peer support directly mitigates depressive symptoms by providing social and emotional support through regular, affirming contacts. Even if recipients of peer support do not change their behaviors, they still experience emotional benefits from having someone to talk to (Liu et al., 2015). Additionally, peer support addresses diabetes and depression together by helping PWD overcome socioeconomic barriers and teaching common skills to cope with both conditions. Peer supporters can help identify safe places to exercise and ways of buying affordable food, as well as coach PWD to develop healthy coping skills when facing stressful situations and setbacks. For example, a CHW stress management intervention for US Latinos with type 2 diabetes found a dose-response relationship between attendance at stress management sessions and improvements in HbA1c and diabetes distress (Wagner et al., 2016).

In some cases, psychological improvements have been observed as a by-product of peer support programs designed principally for diabetes. With support from *Peers for Progress*, the PEARL project in Hong Kong examined the impacts of peer support on diabetes-related distress (Chan et al., 2014). This study found that peer support reduced distress and lowered hospitalization rates to normal among patients with high levels of depression, anxiety, and/or stress at baseline. In the control condition, these patients accounted for a disproportionate amount of hospital care. PEARL was designed to assist diabetes management, not to reduce emotional distress. Nevertheless, the peer support model was able to achieve substantial effects on distress and associated hospitalizations. Another example is the REACH program, a CHW diabetes lifestyle intervention for African Americans and Latinos with type 2 diabetes in Detroit (Spencer et al., 2013). Although the intervention was not intended to reduce symptoms of mental health problems, it was able to reduce diabetes-related distress by encouraging positive lifestyle changes and coping skills that could be applied to both diabetes and mental health.

Models of Peer Support in Diabetes Care

There are many effective models of peer support in diabetes care, offering a plethora of options for organizations looking to develop programs that meet the needs of their patient population according to their local resources. Modalities of delivering peer support were described in detail in a systematic review by Heisler and colleagues (Heisler, 2010). The most prevalent modalities of delivering peer support for diabetes are one-to-one in-person, in-person support groups, telephone-based, and digital health programs (e.g., computer-, mobile-, and web-based technologies). Each mode of delivery has strengths and drawbacks, but the important success factors are the quality, frequency, and longevity of contacts. Additionally, offering a variety of ways to receive peer support can promote sustained engagement by allowing PWD to access peer support according to their evolving needs and preferences.

In-person programs enable peer supporters to build rapport quickly, establish effective communication, gain an intimate understanding of patient living situations, and provide hands-on assistance with diabetes self-management. Basing peer support in clinical settings provides a number of advantages, such as regular communication between peer supporters and the clinical team and access to tracking tools and patient data. Clinic-based programs have the added benefit of building patient trust in the health-care system and encouraging routine medical care. However, clinics are not always the best settings for peer support, depending on organizational characteristics. An alternative is to locate peer support programs in community settings such as worksites, civic groups, faith-based organizations, or through home visits. The ability to expand DSMS to the places where people live, work, play, and worship is a characteristic strength of peer support. With endorsements and assistance from community leaders, community-based peer support programs can broadly disseminate diabetes education, rapidly recruit participants, align with community events, and promote collective action. Whether in clinical or community settings, face-to-face peer support poses challenges to accessibility. Arranging in-person meetings may be time-consuming and inconvenient, and regularly scheduled group interventions are prone to low attendance and dropout. To improve accessibility and meet the preferences of PWD, alternative delivery modes have grown substantially in recent years.

Telephone-based peer support (i.e., voice calls) has been widely utilized to deliver individual peer support (Safford et al., 2015; Small et al., 2013). Compared to face-to-face interventions, telephone-based programs are more feasible for PWD that have limited mobility, are geographically isolated or have transportation barriers, and/or prefer the convenience of communicating over the phone. Telephone-based peer support can be available on demand and accomplished outside of normal work hours. From a program perspective, peer supporters can conduct telephone calls with the aid of scripted prompts, and their calls can be recorded, both of which promote intervention fidelity and quality assurance. Finally, hand-offs to clinical and community resources can be made on the spot, providing the peer supporter with important sources of backup and ensuring that participants are not lost in referral. For example, when peer supporters recognize that callers are experiencing severe emotional distress or urgent medical situations, they can connect callers directly to the appropriate services.

Like telephone-based models, digital health interventions have gained favor for their convenience, accessibility, timeliness, and low cost (Aikens, Trivedi, Aron, & Piette, 2015; Ramadas, Quek, Chan, & Oldenburg, 2011; Rotheram-Borus et al., 2012). Computer-mediated environments enhance an individual's ability to interact with peers outside of their social network while increasing the convenience of obtaining personalized support (Lewinski & Fisher, 2015). Several digital health modalities have been studied for their potential to enhance, extend, and scale up peer support (Vorderstrasse, Lewinski, Melkus, & Johnson, 2016). These platforms can create environments for the exchange of organic and/or structured peer support; prompt timely outreach; facilitate communication between patients, peers, and providers; and collect and analyze patient data to deliver personalized messages and guide clinical decision-making (Aikens, Zivin, Trivedi, & Piette, 2014).

Online diabetes communities (e.g., forums, blogs, social media) are user-driven networks that facilitate the exchange of peer support and diabetes-related information. Peer support exchanged through online communities is largely informal and unstructured. These peer-to-peer relationships can drift in and out of digital modalities, where online connections lead to in-person contacts and vice versa. Although there have been few studies on the impact of digital engagement on diabetes outcomes, there is ample evidence that participating in online communities can improve feelings of support and connection, provide channels for self-expression and emotional coping, enhance diabetes and overall health knowledge (including translation of medical information to everyday language), and reinforce behavioral changes (Hilliard, Sparling, Hitchcock, Oser, & Hood, 2015; Kingod, Cleal, Wahlberg, & Husted, 2017). A recent qualitative review found that the type and richness of information exchanged in online communities is beyond the scope of what is provided in typical medical care (Kingod et al., 2017). Indeed, some PWD seek out online peer support to supplement medical care and address unmet needs, which implies that there is a gap in the medical system for meeting the whole health needs of PWD.

In recent years, mobile health apps for diabetes have grown at a remarkable pace. Two recent systematic reviews found that use of mobile health apps led to significant reductions in HbA1c (Bonoto et al., 2017; Wu et al., 2017). Mobile apps can directly support diabetes self-management through a combination of diabetes education, monitoring tools, patient-generated data, and personalized feedback to encourage self-management behaviors (Cotter, Durant, Agne, & Cherrington, 2014; Quinn et al., 2011). Reaching a high level of sophistication, these apps are able to provide guidance and support sensitive to each individual user. Consideration of fundamental aspects of social relationships points to the importance of sensitivity in creating meaningful bonds (Bowlby, 1988). With sufficient message variety and sophistication of algorithms guiding message delivery, apps can achieve a level of sensitivity that creates a real sense of support among users. Additionally, well-designed apps compare favorably to the four key functions of peer support and could be seen as providing a variety of peer support (Kowitt et al., 2017). Apps can also facilitate support from live peers. By translating the social features of online diabetes communities into mobile phone formats, apps can make peer support more timely, social, and responsive. In conjunction with live peer support, comprehensive diabetes apps are valuable tools that can address the routine tasks of daily self-management, leaving peer supporters free to troubleshoot more complex behavioral and socioeconomic issues. Furthermore, apps can collect patient-generated data that reveals insights into patient behaviors and needs that can be translated into higher-quality peer support.

Automated phone interventions, such as the Australian TLC (telephone-linked care) intervention, in which adults with type 2 diabetes received pre-recorded, automated, interactive voice messages that are directed by computer algorithms, have been effective at lowering HbA1c and improving mental health quality of life while showing excellent cost-effectiveness (Gordon et al., 2014; Williams et al., 2012). Surprisingly, program participants reported that they felt emotionally supported and that the program “had their backs,” opening the possibility that artificial systems can deliver user experiences that are similar to peer support provided by actual humans.

As illustrated in the examples above, digital health can extend peer support to more people and integrate the efficiencies of high tech with the humanizing force of personal contact (Lauckner & Hutchinson, 2016). In diabetes population health management, for example, those doing well with self-management might be offered an app to use at their discretion. Those whose clinical status is suboptimal but not considered poorly controlled might be offered an app and modest levels of peer support, perhaps using the peer support to introduce and promote the app. Those of greater clinical concern might be offered frequent peer support with optional use of an app to extend and enhance the peer support. Such integrated high-tech/soft-touch strategies might be able to reach entire populations of PWD while maximizing the efficiency of both peer supporters and clinical teams.

Across the many modalities of peer support – one-to-one in-person, support groups, telephone-based, and digital health – the four key functions of peer support can serve as a broad framework that can guide the development of interventions that are effective in achieving behavioral changes and improvements in clinical outcomes (Table 27.1).

Assistance in daily self-management is often a central focus of peer support interventions, as peer supporters are trained to deliver key health messages, encourage diabetes self-care behaviors, and teach skills such as problem-solving, goal-setting, action planning, and healthy coping. This key function is time-intensive and requires individual attention. Therefore, one-on-one modalities excel at providing support for daily self-management, along with some types of digital health apps. Nevertheless, group formats and online communities are valuable in presenting PWD with examples from other people’s experiences that may introduce them to new ideas, options, and solutions to their own self-management.

Social and emotional support appears to be ubiquitous as peer supporters can “be there” and provide encouragement through any modality. The classic view of social and emotional support rests upon the formation of authentic relationships and sense of connection. However, digital health is demonstrating that even short messages and automated responses can give participants a feeling of security and that someone “has their back.” Participation in support groups and online communities can increase feelings of connectedness and open up additional sources of encouragement. However, in the absence of thoughtful moderation, there is a risk that participants may be discouraged by judgmental people and adverse social comparisons.

Recommendations from a trusted source can be effective in linking PWD to clinical and community resources. A peer supporter alone may not know or remember all of the resources that could be relevant to a PWD, but crowdsourcing can generate a comprehensive list of resources. Certain digital health apps offer location-sensitive resource maps that can be useful for PWD and peer supporters alike. The critical step for linking PWD to resources is following up with them and reminding them of appointments – something that digital health does well. As mentioned earlier, telephone-based peer support is capable of making a direct connection with clinical and community resources following a call, though it is unclear whether this is a common practice.

Ongoing support for diabetes self-management is important for maintaining healthy behaviors and clinical improvements, especially as patient needs for support change over time. Proactive outreach, even for PWD that have stable clinical status, is needed to re-engage individuals that may once again benefit from peer support. Digital health stands out as the most cost-effective approach for providing a basic level of support over the long term. In addition, digital health apps can be programmed to alert programs when PWD may need a check-in from a live peer supporter.

Organization of Peer Support

The organization of peer support is vital to long-term sustainability and public health impact. In DSME and DSMS, integration of peer support into primary care systems is necessary to secure steady funding and effectively deploy peer supporters at scale. Researchers and policymakers have appealed for these steps to be taken, but progress is hampered by organizational inertia, lack of standardization, and the need for unequivocal cost-effectiveness data. For the moment, peer support in the United States is organized under both community health structures and formal health-care systems (Cherrington et al., 2008).

Team-Based Primary Care

In recent years, team-based primary care within the patient-centered medical home (PCMH) has gained traction for its capacity to coordinate and sustain peer support. The PCMH is an enhanced form of primary care that improves care quality and satisfaction and controls health-care costs by reducing intensive, hospital, and emergency care (Kangovi et al., 2014; Nielsen, Gibson, Buelt, Grundy, & Grumbach, 2015). One of its key objectives is to engage the health of the whole person from the perspective of his/her values, interests, family, and community. Its team-based approach maximizes the strengths of peer support, provides peer supporters with clinical backup and electronic data management systems, and provides a channel for reimbursement (Daaleman & Fisher, 2015; Findley, Matos, Hicks, Chang, & Reich, 2014; Herman, 2011; Mayer et al., 2016; Zahn, Matos, Findley, & Hicks, 2012).

In 2015, *Peers for Progress*, the Patient-Centered Primary Care Collaborative and the National Council of La Raza organized a conference to highlight models of integrated peer support in the PCMH and primary care (Zhong, Wang, Fisher, & Tanasugarn, 2015). A report highlights the themes that emerged from the conference, as well as ten model programs that were invited to share their findings and experiences. Conference participants unanimously agreed that PCMH and peer support are fundamentally aligned in their guiding values and principles. Key themes that emerged included the organization of peer support within PCMH, relationships with communities and clinical care, integration with behavioral health, integration of digital health, maintaining peerness and community ties, and financing and payment reform. The most notable theme was the idea that PCMH and peer support are both forces for health-care transformation. Just as primary care practices are required to undergo sweeping changes to achieve PCMH status, the integration of peer support also requires organizational redesign.

Team-based primary care offers a robust framework for the operation of peer support. Peer supporters can assist providers in conducting group visits, work with pharmacists to improve medication adherence, and team up with nurses for home health care. At Alivio Medical Center in Chicago, *Compañeros en Salud* organized under their own department was integrated into routine care across the clinic. Peer supporters can serve as extensions of the care coordination department, working closely with nurse care coordinators and social workers to provide navigation and individual counseling. At Vanguard Medical Group in New Jersey, a telephone-based health coaching and digital health intervention for patients with poorly controlled diabetes was organized under the care coordination department. That team-based environment was critical to the day-to-day operations and effectiveness of the health coaches.

Community Organizations

In many situations, health-care organizations recognize the need for peer support but lack the capacity to implement a program on their own. Instead of hiring peer supporters directly and taking responsibility for their training and supervision, health-care organizations can contract with community organizations that have experience and expertise in providing peer support services. For example, JASA, one of New York's largest and most trusted nonprofit agencies, employs community health navigators who are trained to deliver group programs and individual coaching for diabetes, hypertension, and other chronic conditions. JASA contracts with local medical centers to fund program services and serve its target populations.

A team at the University of Alabama at Birmingham co-led the development of ConnectionHealth with community groups. ConnectionHealth (www.connectionhealth.org) is a nonprofit organization that provides CHW services with a focus on diabetes self-management support and addressing the needs of those with frequent, avoidable emergency or hospital care. Using evidence-based training and diabetes management protocols, its CHWs can be rapidly deployed with reliable quality. ConnectionHealth is financed by contracts to provide services to patients of local providers, especially regarding reduction of costs of avoidable care through promotion of ambulatory care and connection to local resources. This provides one important model for long-term financial grounding of CHW and other peer support services.

To support the work of ConnectionHealth, the team at the University of Alabama at Birmingham also developed a digital health tool to integrate community-based CHWs with the primary health-care team (Cherrington et al., 2015). The digital health tool assists CHWs in their daily work, tracks patient progress toward self-management goals, and allows secure messaging with the health-care team. Additionally, the tool also contains a built-in reminder system and work list to help CHWs organize their activities and facilitate their work flow.

Credentialing and Quality Assurance

The NDPP provides a valuable model of how peer supporters and other laypersons can contribute to health care and prevention – they are a great fit for the role of lifestyle coaches. This form of task shifting aligns with the functions of peer support and capitalizes on the unique strengths of laypersons. Moreover, the NDPP's combination of standardized training, a national program model, local and national networks, flexibility for local tailoring, and a strong business case (Rehm, Marquez, Spurrell-Huss, Hollingsworth, & Parsons, 2017; Ruggiero, Castillo, Quinn, & Hochwert, 2012; Vojta, Koehler, Longjohn, Lever, & Caputo, 2013) provides an excellent model for scaling up peer support.

A common question raised about peer support is the approach to assuring quality of services and guarding against errors or bad advice. Accordingly, credentialing and formal training programs, such as degree-granting programs through postsecondary education, are gaining popularity as an approach to building a reliable peer support workforce. Just as with professional licensure and credentialing of other members of the health-care team, credentialing of CHWs will enhance the recognition and legitimacy of individuals as well as the field itself. However, there are concerns with this solution to quality assurance. These include the importance of maintaining the "peerness" of those providing peer support and the capacity of under-resourced organizations and individuals to pay for credentialing. Also, part of the vitality of the field rests on the continuum of peer support (Eng, Parker, & Harlan, 1997) that includes volunteers providing peer support a few hours a week or trained laypersons implementing the NDPP. Individuals that volunteer or work part time may face challenges or be disinterested in working through the requirements of formal credentialing, barriers that could limit recognized peer support to those at the professionalized end of the continuum.

The NDPP's approach to quality control demonstrates a useful model for credentialing large numbers of laypersons as part of scaling up a national program. Through the NDPP, the CDC certifies programs that meet standards for offering an evidence-based diabetes prevention program and requires periodic reviews and recertification. Part of this certification includes guidelines for the training and documentation of laypersons to implement the NDPP curriculum. Organizations that do not have the capacity to train lifestyle coaches on their own often help new hires obtain the 2-day training from an authorized third party. However, trained NDPP lifestyle coaches may only work in that capacity within approved NDPP organizations, and this qualification may not be used to as a credential for offering other lifestyle coaching directly to the public. Thus, the NDPP certifies *programs* rather than individuals. Program certification is a broadly applicable approach that may be an attractive option for under-resourced community health centers or voluntary organizations that could feasibly meet program quality standards but find it burdensome to manage the certification of volunteers and peer staff, many of whom may have little interest in completing lengthy and costly external requirements for individual certification.

The National Standards for Diabetes Self-Management Education and Support of the American Association of Diabetes Educators and the American Diabetes Association also encourage quality control by focusing on program characteristics such as training, supervision, and backup (Haas et al. 2014). In discussing quality control with respect to laypersons participating in DSME and DSMS, the Standards state:

> …lay health and community workers and peer counselors or educators may contribute to the provision of DSME instruction and provide DSMS if they have received training in diabetes management, the teaching of self-management skills, group facilitation, and emotional support. For these individuals, a system must be in place that ensures supervision of the services they provide by a diabetes educator or other health care professional and professional backup to address clinical problems or questions beyond their training (p. S147).

Quality control is necessary at both the program and individual levels to assure high-quality implementation of peer support with qualified peer staff. *Peers for Progress* has proposed model guidelines for accrediting peer support programs as a complement to individual credentialing (Center for Health Law and Policy Innovation at Harvard Law School, National Council of La Raza (NCLR), & Peers for Progress, 2015). The guidelines note that programs that are able to document the quality of their training, supervision, and services should qualify for financial support, without requiring the individual certification of peer staff in all cases. In settings where individual certification is time- and cost-prohibitive or, for example, individuals may be encouraged to become peer supporters as a step toward further career development in other roles in health care, program accreditation offers organizations the flexibility to employ a range of peer supporters and standards for deploying them effectively.

Implications for Future Research

The research agenda is expanding and becoming more innovative. Instead of asking "Does peer support work?", researchers are exploring how best to extend peer support while retaining its core effectiveness and person-centered features, what kinds of peer support work best in which settings, and how to integrate peer support effectively and efficiently in complex health systems (Fisher, Ballesteros, et al., 2015; Zhang, Yang, Sun, Fisher, & Sun, 2016). While there is ample evidence of the impact of peer support on PWDs and health-care systems, assessing community-level effects has proven difficult. Future research should include evaluation of how peer support may mobilize communities around diabetes and change cultures of health.

As exciting new technologies expand the reach and impact of peer support, it's important to resist the temptation to treat the technology platform as a "magic bullet" that obviates other approaches. No doubt there are applications of digital health that are beneficial when used on their own, without connection to clinical or other live support, but overemphasis on technology solutions at the expense of peer support would be a critical misstep in the direction of DSME and DSMS. We would do well to remind ourselves that these technologies are valuable for facilitating the delivery of peer support, making support more sensitive and personalized, and providing automated functions that decrease the workload for peer supporters. Research should explore further the boundary conditions of apps disconnected from other sources of support as well as the extent to which the development and improvement of such apps may be enhanced by understanding them as a variety of peer support, such as in terms of the four key functions detailed earlier in this chapter.

Current efforts are underway to develop and evaluate high-tech/soft-touch programs that seamlessly blend digital health and peer support. Important questions include "What kinds of patient data should be shared with peer supporters and how should it be presented?", "What constitutes meaningful use data?", "What sorts of automation are needed to prompt timely follow-up by peer supporters and clinical staff?", and "How can mobile apps tap into the potential of wearable technologies?"

The adoption of peer support represents a fundamental shift in the way that health care is delivered, from a top-down approach to a more collaborative patient-centered approach. Integrating peer support effectively into the primary care team challenges long-held views of the roles of patients, physicians, and other professionals, as well as needs of individuals and criteria of benefit. Accommodating peer support will require health-care systems to redesign their practices and push providers to learn to work collaboratively with peer supporters on the clinical team (Collinsworth et al., 2014). Despite the growing pains of care transformation, primary care networks, community health centers, and hospitals continue to adopt and expand peer support programs. However, until peer support becomes a part of routine care, health-care systems will continue to be missing a key piece of the puzzle to stem the tide of diabetes and improve the lives of those with the disease.

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Part X
Community Level Factors for Adults

Chapter 28
Demographic Influences and Health Disparities in Adults with Diabetes

Elizabeth L. Tung and Marshall H. Chin

Introduction

Diabetes burden and outcomes can differ substantially depending on peoples' demographic influences and where they live in the United States. A poor adult living in a poor neighborhood is five times more likely to have diabetes than a non-poor adult living in a non-poor neighborhood (Gaskin et al., 2014). A black man living in Baltimore, Maryland, is 50% more likely to die from diabetes than his white counterpart; that same black man is nearly 300% more likely to die from diabetes if he is living just 40 miles away in Washington D.C. (Rosenstock, Whitman, West, & Balkin, 2014). These differences in health between populations are called *health disparities* (US Department of Health and Human Services, 2010), and significant health disparities exist in the incidence, prevalence, and outcome of diabetes in the US population.

A rapidly expanding body of literature has documented that differences in health behavior that lead to or worsen health disparities largely depend on demographic influences, social and ecological conditions, and system-level factors—many of which are preventable in nature (Andersen, 1995; Andersen & Newman, 1973). In *Unequal Treatment*, the Institute of Medicine (IOM) emphasizes unacceptable causes of health disparities that stem from the health-care system, arguing that health-care contributions to health disparities should be systematically eliminated (Institute of Medicine, 2002). This landmark report defines *health-care disparities* as differences in treatment or access not justifiably explained by differences in clinical appropriateness or patient preference (Institute of Medicine, 2002). Recently, the US Department of Health and Human Services has called for an even broader view of what determines health, highlighting "the determinants of health not only at the individual level but also in broader society that lay bare the unacceptable" (Services, 2010). In addition, new health-care payment and delivery models, such as accountable care organizations (ACOs) and value-based purchasing, make health-care systems increasingly financially accountable for not just the care they provide but the health of their patients. Therefore, health-care institutions have strengthened their commitments to address the underlying social, economic, and ecological conditions that contribute to health disparities (Alley, Asomugha, Conway, & Sanghavi, 2016).

E. L. Tung (✉) · M. H. Chin
Department of Medicine, Section of General Internal Medicine, University of Chicago, Chicago, IL, USA
e-mail: eliztung@uchicago.edu

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In this chapter, we will review important demographic factors that contribute to health disparities among patients with type 1 and type 2 diabetes, including age, sex and gender, race and ethnicity, and socioeconomic status. For each demographic factor, we will review differences in the incidence and/or prevalence of diabetes, disease-related outcomes, health-care access, and health-care quality received. We will then expand our perspective from individual-level demographic factors to examine intersectionality of key demographic factors, spatial contexts, and the socioecological role of *place*. Finally, we will review system-level factors in health care and the community and current efforts to address the multilevel determinants of diabetes disparities.

Demographic Influences

Age

Rates of type 2 diabetes rise dramatically with advancing age. In the United States, the incidence of diabetes is threefold higher among older adults aged 45 years and older compared to younger adults (Centers for Disease Control and Prevention, 2015a). Concordantly, the American Diabetes Association (ADA) Standards of Medical Care in Diabetes recommends diabetes screening in all adults aged 45 years and older (Professional Practice Committee of the American Diabetes Association, 2015). In older adults, the incidence and prevalence rates of diabetes have risen dramatically over the past three decades (Centers for Disease Control and Prevention, 2015b). The overall growth in the US population is expected to continue (Black & Macinko, 2010; Huang, Basu, O'Grady, & Capretta, 2009; Polonsky, 2012), based in part on high incidence rates and demographic shifts in the aging population (Centers for Disease Control and Prevention, 2015b).

The high risk of type 2 diabetes among older adults can be attributed to a combination of pathophysiologic and environmental risk factors. First, type 2 diabetes is primarily mediated by *insulin resistance*, a condition under which the body's cells are resistant to insulin and unable to use it effectively (Kahn, 2003; Olefsky, Farquhar, & Reaven, 1973). This alters the way beta cells in the pancreas respond to insulin, leading to a state of *beta cell dysfunction* (Kahn, 2003). Both insulin resistance and beta cell dysfunction have been linked to aging (Chen, Bergman, Pacini, & Porte Jr., 1985; Noth & Mazzaferri, 1985). However, recent increases in type 2 diabetes across age groups, including children and adolescents, suggest environmental influences leading to higher glycemic load and rising obesity in the overall US population (American Diabetes Association, 2000; Polonsky, 2012).

Diabetic complications in adults with type 2 diabetes disproportionately affect older populations. A cohort study of over 70,000 older adults with type 2 diabetes found that advancing age and duration of diabetes independently predicted rates of diabetes complications and mortality (Huang et al., 2014). Advancing age was an independent risk factor for cardiovascular disease, while duration of diabetes was an independent risk factor for microvascular complications, such as diabetic eye disease (Huang et al., 2014; Professional Practice Committee of the American Diabetes Association, 2015). The interaction between advancing age and duration of diabetes also significantly predicted end-stage renal disease, eye disease, lower limb amputation, stroke, heart failure, and mortality (Huang et al., 2014).

Consequently, age-related disparities in diabetic complications are not as straightforward as comparing older and younger adult populations. Caring for older adults with diabetes is often complicated by significant variation in the clinical and functional status of patients. For instance, while one older person may have developed type 2 diabetes many years ago in the context of multiple comorbidities, another may be newly diagnosed with little risk of progression to overt complications within his or her anticipated life expectancy (Brown, Mangione, Saliba, & Sarkisian, 2003). One major development in

ADA guidelines over the past decade has been the recognition of different needs among geriatric populations with diabetes and recommendations to individualize care based on patient factors, such as life expectancy, frailty, comorbidities, and functional status (Brown et al., 2003; Professional Practice Committee of the American Diabetes Association, 2015). This development acknowledges, in part, the limitations of broad management guidelines in a highly heterogenous elderly population and the potential for individualized care to reduce disparities in not only diabetes-related morbidity but also quality of life.

Finally, prior literature has noted disparities in access to and quality of diabetes care among elderly populations. In a cross-sectional analysis of more than 9000 Medicare beneficiaries, investigators found that low-income elderly adults were less likely to receive routine diabetes care, including having a usual source of care and visiting an endocrinologist (McCall, Sauaia, Hamman, Reusch, & Barton, 2004). Other studies examining the quality of diabetes care among elderly populations have noted significant variability across clinical sites and provider type (Rosenblatt et al., 2001; Suwattee, Lynch, & Pendergrass, 2003). One study analyzed claims data for all primary care practices actively seeing Medicare patients in Alabama, Iowa, and Maryland and found that elderly patients with diabetes were not receiving optimal care. Investigators found no HbA1c measurement within the recommended period for 84% of patients, no ophthalmology visit for 54% of patients, and no cholesterol screening for 45% of patients with diabetes (Weiner et al., 1995).

Sex and Gender

The distribution of diabetes is relatively uniform between men and women in the US population. Rates of diabetes are slightly higher among men, with a rate of 6.6 per 100 population in men compared to 5.9 per 100 population in women (Centers for Disease Control and Prevention, 2015a). For both men and women, the incidence of diabetes has more than doubled over the past 30 years (Centers for Disease Control and Prevention, 2015a).

Although rates of diabetes are similar by sex, women may experience higher risk for severe complications due to diabetes. Compared to men, a longer duration of diabetes in women is associated with significantly higher rates of complications, including peripheral vascular disease and coronary heart disease fatality (Natarajan et al., 2005; Orchard et al., 1990). Women are also at risk for gestational diabetes, which is an independent risk factor for later development of type 2 diabetes (Chittleborough et al., 2010; Lee, Hiscock, Wein, Walker, & Permezel, 2007).

Interestingly, although women may experience more severe disease course than men, women traditionally have better access to health care. In *Out of Touch*, a report published by the Commonwealth Fund, women are almost twice as likely to have a regular doctor and three times as likely to have seen a physician in the prior year (Sandman, Simantov, & An, 2000). However, several studies have suggested that despite better access to care, women with diabetes may receive poorer quality of care compared to men. One cross-sectional study of 223 men and women with diabetes found that women in both younger and older age groups reported receiving poorer quality of care than their male counterparts (Unden et al., 2008). Similarly, a recent meta-analysis of prospective cohort studies noted that the excess risk of coronary heart disease fatality among women with diabetes may reflect treatment bias, noting that women were treated less aggressively than men (e.g., fewer women were prescribed a lipid-lowering agent) (Huxley, Barzi, & Woodward, 2006).

Among lesbian, gay, bisexual, and transgender (LGBT) adults, prior research has noted greater difficulty with accessing health care, cost-related barriers to care, and negative experiences with the health-care system (Macapagal, Bhatia, & Greene, 2016; Skopec & Long, 2015).

Race and Ethnicity

There are pervasive racial and ethnic disparities in the distribution of diabetes and related outcomes in the US population. Racial and ethnic minorities are nearly twice as likely to be affected by diabetes, with a rate of 9.5 per 100 population in blacks compared to 5.8 per 100 population in whites (Centers for Disease Control and Prevention, 2015a). The age-adjusted rates of diabetes have increased for all racial and ethnic groups since 1980 (Centers for Disease Control and Prevention, 2015a).

In addition to disparities in the distribution of diabetes by race, extensive research has documented disparities in the rate of complications and adverse outcomes. Data from the Dartmouth Atlas has reported that leg amputation, which is an uncommon but debilitating complication of diabetes, was almost four times more likely in black Medicare beneficiaries compared to white Medicare beneficiaries (Goodman, Brownlee, Chang, & Fisher, 2010). In other studies, rates of diabetic retinopathy and blindness were significantly higher among Hispanics and non-Hispanic blacks compared to non-Hispanic whites (Kuo et al., 2005; Osborn, de Groot, & Wagner, 2013). Interestingly, studies showed that Asians and Pacific Islanders had lower rates of leg amputation and cardiovascular events but higher rates of renal failure (Hsu et al., 2012). One longitudinal study of over 60,000 diabetic patients insured through the Kaiser Permanente Medical Care Program found that the incidence of renal failure was significantly higher for blacks, Asians, and Latinos compared to whites (Karter et al., 2002).

Recently, an effort to understand the reasons for racial and ethnic disparities has prompted a focus on differences in access to diabetes care and the receipt of preventive screening. One study using NHANES data from 2011 to 2012 found that the rate of undiagnosed diabetes was two times higher among non-Hispanic blacks and nearly three times higher among Hispanics and Latinos compared to non-Hispanic whites (Menke, Casagrande, Geiss, & Cowie, 2015), suggesting inadequate screening among minority groups. Recently, studies have also begun to document racial and ethnic disparities among Asian Americans, demonstrating lower rates of screening and nearly three times higher rates of undiagnosed diabetes compared to non-Hispanic whites (Menke et al., 2015; Tung, Baig, Huang, Laiteerapong, & Chua, 2016).

Other studies have focused on persistent gaps in the quality of care received by racial and ethnic minorities (Institute of Medicine, 2002). For instance, one large observational study examining over 300,000 Medicare managed care beneficiaries found that blacks were significantly less likely than whites to receive recommended diabetes care, such as diabetic eye exams (Schneider, Zaslavsky, & Epstein, 2002). Research examining racial discrimination in health care have also documented that patients who report a prior experience of racial discrimination are less likely to receive a diabetes-related primary care visit and HbA1c testing (Peek, Wagner, Tang, Baker, & Chin, 2011).

Socioeconomic Status

Socioeconomic status is a long-standing and potent determinant of diabetes disparities, including disparities by education and income.

Education

First, rates in diabetes differ dramatically by level of education. Among adults completing less than a high school education, the rate of diabetes is 12.9 per 100 population compared to 6.7 per 100 population among adults completing greater than a high school education (Centers for Disease Control and Prevention, 2015a). In contrast to disparities by age and sex, disparities by education have widened since the early 1990s for those completing less than a high school education (Centers for Disease Control and Prevention, 2015a).

One study examined almost 2500 adults with insulin-dependent diabetes mellitus and confirmed that glycemic control was poorest among those with the least education in both men and women (Chaturvedi, Stephenson, & Fuller, 1996). Complication rates were also lower among those with a college education compared to those with only a primary education, including macroalbuminuria, proliferative retinopathy, and prevalent heart disease (Chaturvedi et al., 1996). More recent studies have confirmed these findings (Bachmann et al., 2003).

To explain differences in diabetes prevalence and outcomes by educational attainment, the bulk of literature has examined differences in health literacy and health behaviors among patients with low educational attainment. *Health literacy*, a patient's ability to understand the basic health information required to make healthy decisions, is considered foundational to long-term diabetes care and self-management (Al Sayah, Majumdar, Williams, Robertson, & Johnson, 2013; Kim, Love, Quistberg, & Shea, 2004; Powell, Hill, & Clancy, 2007). Poor health literacy has been associated with poor knowledge about diabetes (Al Sayah et al., 2013; Powell et al., 2007) and, consequently, greater difficulty with complex diabetes self-management behaviors (Bains & Egede, 2011; McCleary-Jones, 2011; Wallace, Carlson, Malone, Joyner, & Dewalt, 2010). Diabetic patients with lower educational attainment have also been shown to have lower contact rates with their primary providers, poorer access to diabetes specialists, and lower utilization of preventive care (Bachmann et al., 2003; Van der Meer & Mackenbach, 1999).

Income

Low-income status has been associated with higher incidence and prevalence of diabetes. Having a household income below the federal poverty line (FPL) is associated with a prevalence rate of 10.6 per 100 population compared to 6.4 per 100 population for those having a household income ≥400% FPL (Beckles & Chou, 2013). Low-income status has also been associated with higher risk of diabetes-related mortality in the United States. One study showed that having a household income below FPL was associated with more than two times higher diabetes-related mortality (i.e., according to cause of death listed on death certificate) compared to those having a household income ≥400% FPL (Saydah & Lochner, 2010). There are limited data examining the impact of income status on type 1 diabetes; however, one study examining major complications in type 1 diabetes found that low-income level was associated with poorer glycemic control, as well as higher incidence of autonomic neuropathy and peripheral arterial disease (Secrest et al., 2011).

These disparities have been associated with limited access to and use of health-care services among low-income persons. One study examining patients with diabetes in Pittsburgh found that low-income status was negatively associated with receiving care from an endocrinologist, diabetologist, or diabetes clinic attending during the last year (Zgibor et al., 2000). Other studies have highlighted the relationship between low-income status and poor use of preventive services, limited physician availability, poor physical access to services, barriers to health-care insurance, and inability to pay out-of-pocket costs (Dorsey et al., 2007; Freeborn, Pope, Davis, & Mullooly, 1977; Kirby & Kaneda, 2005; Piette, Wagner, Potter, & Schillinger, 2004; Rabi et al., 2006; Simmons, Peng, Cecil, & Gatland, 1999; Zgibor et al., 2000).

Recently, researchers have also suggested that low-income status can have serious impacts on access to critical diabetes self-management resources (Berkowitz et al., 2014). For instance, prescription drug rationing and cost-related medication underuse are classic examples of how economic barriers can lead to poor diabetes control in high-poverty populations (Mojtabai & Olfson, 2003; Schectman, Nadkarni, & Voss, 2002). *Food insecurity*, defined as having limited or uncertain access to adequate and nutritious food (Ploeg et al., 2009), is another area of research that has gained increasing attention (Essien, Shahid, & Berkowitz, 2016). One study examining a nationally representative sample from the National Health and Nutrition Examination Survey found that 12% of adults with diabetes were food insecure, and food insecurity was independently associated with poor glycemic control (Berkowitz, Baggett, Wexler, Huskey, & Wee, 2013).

Other researchers have suggested that patients with low-income status receive poorer quality diabetes care (Grintsova, Maier, & Mielck, 2014). One study examining elderly Medicare patients found that dual-eligible Medicare/Medicaid patients, who received dual eligibility based on low-income status, were less likely to be referred to endocrinologists, receive annual HbA1c testing, have biennial ophthalmology exams, and have biennial lipid testing compared to standard Medicare patients (McCall et al., 2004).

The Role of Intersecting Demographic Influences

Although each demographic factor may have an independent effect on diabetes burden and outcomes, recent literature has highlighted the *intersectionality* of demographic factors—in effect, how multiple demographic factors interact and dynamically relate to one another (Fig. 28.1) (Diez Roux, 2016; Diez Roux & Mair, 2010). In clinical practice, this may seem matter-of-fact, as real-world patients seldom have one-dimensional problems and complaints: a patient with obesity also has chronic knee pain that limits physical activity. And so it is with demographic influences: intersecting rather than isolated demographic influences reflect the real-world nuance and complexity of health disparities.

Intersectionality also extends beyond individual patients to the communities and neighborhoods where patients live. This reflects “the need to consider not only individual characteristics but also characteristics of the groups and contexts to which individuals belong” (Diez Roux & Mair, 2010). Individual demographic influences are never isolated in vivo and also intersect at the community level. In Robert Sampson’s *Great American City*, he recognizes that there are dramatic differences and social inequalities between spatially defined regions and that inequalities are often bundled together. Most notably, regions with high levels of poverty are also more likely to be racially segregated

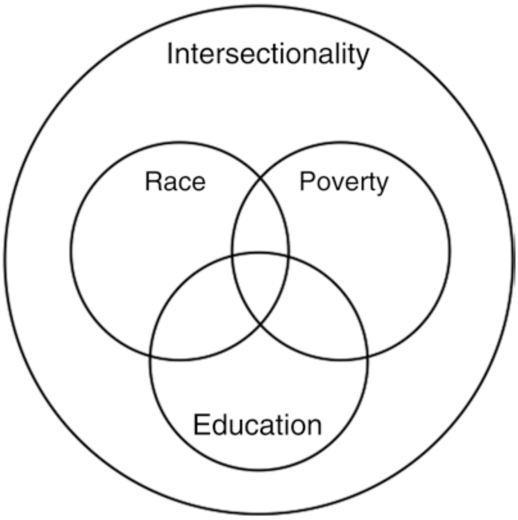

Fig. 28.1 Intersecting demographic influences

communities of color (Sampson, 2012). As such, demographic patterns are spatially organized and often predictable in nature.

For instance, a recent report from the Brookings Institution documented that blacks in the United States were five times more likely to live in a poor community, two times more likely to lack a high school diploma, and three times more likely to live in a non-working household compared to whites (Kneebone & Reeves, 2016). This phenomenon, referred to as *multidimensional disadvantage*, varied based on spatial context, such that differences by race widened in urban compared to suburban regions (Kneebone & Reeves, 2016). Spatial context can thus serve as an index for multidimensional disadvantage, thereby approximating intersectionality and downstream health disparities.

The Role of Place

Efforts to understand how demographic influences converge in real world spatial contexts are inextricably tied to the study of *place*. Broadly interpreted, place refers to the neighborhood-based attributes that influence a person's daily activities (Sampson, 2012), including personal health behaviors and use of medical services. Place is most commonly conceptualized within a *socioecological framework*, which expands behavior change influences beyond demographics to include their social and physical environments (Northridge, Sclar, & Biswas, 2003; Peek, Ferguson, Roberson, & Chin, 2014).

Examining place and its environmental influences on patient behavior has been a mainstay of health disparities research since the 1970s (Sampson, 2012). In the nation's largest attempt to understand the neighborhood health effects of concentrated poverty, *Moving to Opportunity* (MTO) was a longitudinal experiment that followed public housing residents in five major US cities over 15 years (Ludwig et al., 2011). At both 10- and 15-year follow-up assessments, people who were randomized at baseline with the opportunity to move from a neighborhood with high levels of poverty to a neighborhood with low levels of poverty were associated with a reduced risk of extreme obesity and diabetes (Ludwig et al., 2011). Although the overall findings of MTO have revealed a foggy picture of the mechanisms underlying neighborhood effects and health, it remains one of the first randomized experiments to suggest a causal relationship between neighborhood effects and diabetes (Sampson, 2012).

The study of place is often conceptualized from two perspectives: the built environment and the social environment. The *built environment* refers to the physical spaces or structures created by people for day-to-day use, including grocery stores, health-care facilities, and local businesses (Lee, Mikkelsen, Srikantharajah, & Cohen, 2008). The *social environment* refers to the immediate social setting in which people live, including interpersonal behaviors, cultures, and attitudes (e.g., social cohesion, crime, distrust of institutions) (Barnett & Casper, 2001).

The Built Environment

Health disparities research examining the built environment has predominantly focused on two dominant areas: the physical appearance of a neighborhood and access to built environment resources. A study of place and its impact on health disparities often hinges on the notion that disorder can be spatially and physically patterned. *Physical disorder* refers to the visual appearance of disorder and disorganization in neighborhoods, such as abandoned buildings, broken sidewalks, and the highly axiomatic broken window (Sampson, 2012).

Prior research examining physical disorder and diabetes has often focused on the impact of physical disorder on self-care behaviors, such as physical activity. For instance, walking is the most common form of physical activity in the United States; thus, the walkability of neighborhood sidewalks has been a chief focus of early research, particularly for low-income neighborhoods with less access to recreational facilities (Lovasi, Hutson, Guerra, & Neckerman, 2009; Saelens, Sallis, Black, & Chen, 2003). In one cross-sectional study of over 1000 urban-dwelling adults, investigators found that the absence of sidewalks and poor sidewalk quality were associated with both physical inactivity and obesity, with findings more pronounced among low-income adults (Boehmer, Hoehner, Deshpande, Brennan Ramirez, & Brownson, 2007). Other studies have investigated the impact of physical disorder on psychosocial stress. A recent study in Philadelphia measured dynamic stress responses to urban decay using ambulatory heart rate monitors and found that greening vacant lots led to a significant reduction in dynamic stress (South, Kondo, Cheney, & Branas, 2015).

Access to built environment resources has also been a mainstay of prior research, often focusing on the neighborhood food environment and healthful eating. A *food desert* is broadly defined as a geographic region with low spatial access to grocery stores (Kaplan, 2006; Ploeg et al., 2009). The US Department of Agriculture defines low access to food as living more than 1 mile from a supermarket and notes that approximately one third of people living in a low-income neighborhood have low access to nutritious food (Ploeg et al., 2009). Food deserts have been linked to diet-related diseases, including diabetes (Kaplan, 2006; Ploeg et al., 2009). More recently, policy experts have noted the disinclination of large, high-quality supermarkets to open in low-income communities of color, a discriminatory practice referred to as *supermarket or retail redlining* (Zhang & Debarchana, 2016).

Despite a general consensus to eliminate food deserts as policy, the evidence on food deserts has been mixed (Ploeg et al., 2009). One study examined a multiethnic cohort of 16,634 adults with diabetes in Northern California and found that the density of food vendors, both healthful and unhealthful, did not explain differences in BMI (Zhang et al., 2015). Another study analyzed data from the 2011 Los Angeles County Health Survey and found that the food environment was not a factor related to fruit and vegetable consumption, sugar-sweetened beverage consumption, or fast-food intake (Mejia, Lightstone, Basurto-Davila, Morales, & Sturm, 2015).

To explain these mixed findings, several studies have pointed to the behavioral economics literature, describing a complex relationship between access to resources, health consumerism, and health behavior. Drewnowski and colleagues demonstrated that only one in seven study participants reported shopping at the nearest food grocer; however, the price of supermarket was significantly associated with obesity rates, suggesting economic access as the principal driver of resource utilization and health status in the study sample (Drewnowski, Aggarwal, Hurvitz, Monsivais, & Moudon, 2012). Another study examined access to self-management resources in a high-poverty region and found that most people (98%) bypassed at least one major resource type to use resources farther than 1 mile from home. This "bypassing" behavior was significantly associated with a higher BMI (Tung, Peek, Makelarski, Escamilla, & Lindau, 2016). Similarly, a prior study examined "willingness to pay" for physical activity among socioeconomically vulnerable populations and found that people were willing to devote differing amounts of travel time and money to utilize physical activity resources (Herens, Ophem, Wagemakers, & Koelen, 2015).

The Social Environment

Increasingly, investigators are interested in the role of disruptive social conditions that influence diabetes prevention and control (Steve, Tung, Schlichtman, & Peek, 2016). According to Sampson, "Social disorder is commonly understood to mean public behavior that is considered threatening," such as public drunkenness, loitering in the streets, neighborhood crime, and interpersonal racism (Sampson, 2012). In this vein, *broken windows theory* hypothesizes a double meaning for physical disorder, arguing that persistently broken windows are mediated by social processes, such as crime (i.e., breaking windows), poor collective efficacy (i.e., failure to report broken windows), and concentrated disadvantage (i.e., failure to fix broken windows) (Sampson, 2012). In contrast, *collective efficacy* reflects the cohesion and trust in a neighborhood to support other residents and maintain shared expectations for social control (Sampson, 2012).

As such, early literature on the social environment and diabetes examines the role of social cohesion and collective efficacy to support sustained behavior change. Christine and colleagues examined a population-based cohort of older adults over 14 years and found that higher social cohesion was associated with lower type 2 diabetes risk but only in low-income and not high-income households (Christine et al., 2015). Another study examined collective efficacy and obesity-related behaviors in a community-based sample of African American adults and found that higher collective efficacy was associated with meeting recommended guidelines for fruit and vegetable intake in bivariate analyses; findings were only significant for fruit intake in final adjusted models (Halbert et al., 2014).

Additionally, patients living in chaotic social environments often experience high levels of psychosocial stress, which can impede the self-management and control of diabetes. Scholars have suggested that chronic psychosocial stress may trigger strong and frequent activation of stress response hormones (e.g., excess cortisol) (Burdette & Hill, 2008), resulting in poor metabolic control and related conditions (e.g., insulin resistance). One study examining over 3000 patients from the Kaiser Permanente Diabetes Study of Northern California (DISTANCE) found that higher neighborhood crime rates were associated with higher stress for African American and Latina women with diabetes (Tamayo et al., 2016). Another study examined interactions between Latina participants and a white interaction partner and documented an exacerbated stress response (i.e., measured cognitive, emotional, and cardiovascular responses) when participants learned that their interaction partner had biased racial and ethnic attitudes (Sawyer, Major, Casad, Townsend, & Mendes, 2012). Psychosocial stress can lead to adverse coping strategies (e.g., excess caloric intake, smoking), leading to downstream outcomes such as insulin resistance and poor diabetes control (Fowler-Brown et al., 2009; Wagner, Tennen, Feinn, & Finan, 2013; Williams & Mohammed, 2013).

Finally, recent studies suggest that competing social needs and priorities make it difficult for patients to prioritize health. In *Health Care's Blind Side*, a study conducted by the Robert Wood Johnson Foundation, 85% of physicians believed that unmet social needs, such as unemployment, poor educational opportunities, and homelessness, were directly leading to poorer health outcomes (Robert Wood Johnson Foundation, 2011). Similarly, patients with perceived safety concerns may have greater difficulty accessing resources that promote health, such as grocery stores and pharmacies (Tung, Peek, et al., 2016). One population-based study in California demonstrated that patients with type 2 diabetes who reported living in unsafe neighborhoods had greater difficulties with treatment adherence, including delays in filling prescribed medications (Billimek & Sorkin, 2012).

Overlapping Constructs and Shifting Relevance

In the real world, the relationship between intersectionality and place can be highly layered and complex (Fig. 28.2) (Tung, Cagney, Peek, & Chin, 2017). For instance, several studies have attempted to examine the role of intersecting demographic influences *and* neighborhood context in contributing to diabetes disparities. Gaskin and colleagues developed a race-place-poverty gradient to test its relationship with diabetes prevalence (Gaskin et al., 2014). Researchers found that adults living in poor neighborhoods had higher rates of diabetes than adults in non-poor neighborhoods. However, after combining individual-level and neighborhood level characteristics, living in poor neighborhoods only increased the odds of having diabetes for blacks and poor whites, but not for non-poor whites (Gaskin et al., 2014). In other words, living in a poor neighborhood had a similar effect on black adults regardless of individual-level poverty status. However, in contrast to poor whites, non-poor whites were able to mollify the harmful health effects of living in a poor neighborhood (Gaskin et al., 2014).

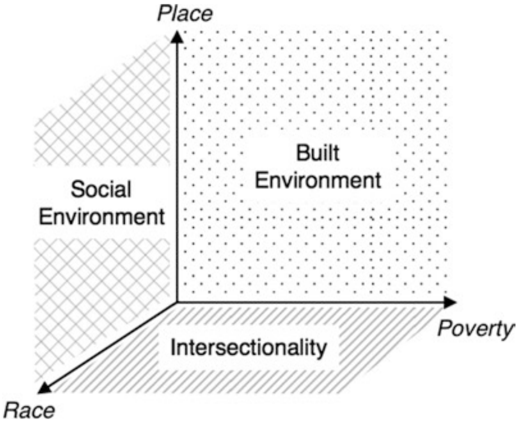

Fig. 28.2 Spatial context and disparities: intersecting demographic influences and place

In a different study, researchers focused on a racially integrated, low-income neighborhood in Southwest Baltimore and found that racial and ethnic disparities in diabetes prevalence substantially narrowed when participants were sampled in a socially and ecologically homogenous region (LaVeist, Pollack, Thorpe, Fesahazion, & Gaskin, 2011). In this particular neighborhood, the unique combination of individual and place-based characteristics, including socioeconomic status and environmental health risks, were more closely associated with diabetes prevalence than racial and ethnic composition.

These two similar but contradicting studies demonstrate the shifting relevance of isolated demographic factors, in this case, racial and ethnic status, depending on how those demographic factors intersect in a given spatial context. In the first study, the experience of place shifts depending on individual racial/ethnic and poverty status. In the latter study, the importance of racial/ethnic status diminishes in the context of an overriding place-based experience. Ultimately, these studies point to the intricate and highly layered real-world applications of mapping disparities to spatial contexts, as well as the critical importance of considering both constructs—intersectionality and place (Fig. 28.2).

Systems and Solutions

Strategies to address health disparities in health-care and clinical settings have often targeted individual behavior change and lifestyle intervention. For example, the Diabetes Prevention Program was a landmark clinical trial that randomly assigned participants to lifestyle intervention or metformin and showed that lifestyle intervention reduced the incidence of diabetes by 58%, a relative reduction of 27% compared to metformin (Knowler et al., 2002). The lifestyle intervention arm consisted of reducing weight by at least 7% and 150 minutes of physical activity per week. These individual behavioral interventions clearly have value.

However, a report by the Institute of Medicine (IOM) on health behavior research and policy noted that behavior change interventions often ignore the broader system-level factors that fundamentally shape and determine health behaviors (Institute of Medicine Committee on, Behavior: Research, & Policy, 2001; Paskett et al., 2016). For instance, a behavior change intervention that fails to account for the built environment resources available to a patient is unlikely to be sustainable, particularly for a patient with numerous competing priorities. Indeed, clinicians are all too familiar with implementing behavior change counseling in the office, only to find that 3 months later, a patient was unable to implement any changes due to financial limitations. Poor sensitivity to the multidimensional disadvantage that impedes healthy behavior may also erode a patient's self-efficacy and trust in the health-care system. As such, blunt behavior change interventions have often yielded mixed findings and have been difficult to scale and sustain over time (Peek, Ferguson et al., 2014; Peek, Cargill, & Huang, 2007).

Concordantly, policymakers have called for solutions that are broader than individual behavior change interventions—solutions should also address the community-level root causes and underlying socioeconomic conditions (e.g., lack of material resources), often captured by a holistic understanding of demographic influences and place. By targeting these root causes, behavior change solutions are more effective and easier for individuals to adopt into routine practices. Over the past 30 years, the US Department of Health and Human Services has strengthened its commitment to eradicating health disparities, calling for a broader view of what determines health, a "health in all policies" approach to organizing resources, and an effort to increase community capacity for health equity (US Department of Health and Human Services, 2010). This three-tier framework has recently set the stage for a demonstration approach, implemented by the Centers for Medicare and Medicaid Services, to address the underlying determinants of health through "Accountable Health Communities," which will be discussed in a later section.

Health-Care Approaches

Evidence-based road maps and best practices can inform health-care interventions to reduce disparities (Chin et al., 2012; National Academies of Sciences Engineering and Medicine, 2016). No magic solution exists. Instead, health-care organizations and providers must identify the root causes of identified disparities and tailor interventions to their patients, environment, and organizational context. Organizations must obtain buy-in from leadership and staff and create a culture in which achieving health equity is a strategic priority (Chin, 2016; Chin et al., 2012). Successful interventions frequently target multiple leverage points along the pathway of care and are culturally tailored. They use teams that closely monitor and follow patients and often incorporate community health workers. Successful interventions involve families and communities and employ interactive patient learning techniques rather than passive didactic teaching.

Provider and Clinical Staff Approaches

One promising approach tailors diabetes education to racial and ethnic backgrounds and offers culturally tailored shared decision-making and patient empowerment (Chin et al., 2012; Peek, Harmon, et al., 2012). Investigators developed an intervention that tailored diabetes lifestyle instruction to African American patients who were predominantly descendants of the "Great Migration" of blacks from the South (Peek, Harmon, et al., 2012). Dietary modifications involved food alternatives that aligned with cultural traditions, such as peach cobbler recipes that substituted sugars with healthier ingredients (Peek, Harmon, et al., 2012). Patients were taught to read food labels while shopping in the local supermarket. This intervention was associated with high patient satisfaction, improvement in diabetes self-care behaviors, and better glycemic control at 3 months (Peek, Harmon, et al., 2012). Although systematic reviews have generally reported consistently positive effects of cultural tailoring to address diabetes disparities among socially disadvantaged populations (Glazier, Bajcar, Kennie, & Willson, 2006; Peek et al., 2007), concerns about the scalability and sustainability of such interventions have often limited broader dissemination (Peek et al., 2007).

Another novel approach to tailoring diabetes education is “photovoice,” the process of empowering patients to document aspects of the built environment that influence their health (Baig et al., 2015). In a diabetes self-management pilot among Latino adults, investigators asked participants of a diabetes education course to take photographs of anything relevant to living with diabetes (Baig et al., 2015). Photographs stimulated discussion about diabetes self-management that were relevant and meaningfully tailored to participants’ lives. At 3 months, study participants had better glycemic control; and compared to study participants in the usual diabetes education group, those in the intervention group reported fewer days of consuming high fat foods and more days of participating in exercise (Baig et al., 2015).

Health-Care System Approaches

The Chronic Care Model (CCM) is a comprehensive systems framework that emphasizes tailoring care to patient contexts as a core principle of high-quality care (Coleman, Austin, Brach, & Wagner, 2009; Stellefson, Dipnarine, & Stopka, 2013). The CCM is comprised of six components, including organization of health care, self-management support, decision support, delivery system design, clinical information systems, and community resources (Stellefson et al., 2013). In a study assessing CCM-based interventions for managing diabetes in US primary care settings, investigators found that only 38% of CCM-based interventions implemented all six CCM components; however, even without full implementation, many interventions achieved improvement in diabetes care and outcomes, including patient empowerment, participation in self-management activities, receipt of annual eye and foot examinations, and better glycemic control (Stellefson et al., 2013). Similarly, an effectiveness study of CCM implementation among low-income patients from safety net clinics documented improvements in self-efficacy, patient experiences with chronic illness care, and self-management behaviors when clinical self-management support was tailored to consider specific attributes of a patient’s life (Schillinger, Handley, Wang, & Hammer, 2009).

The Patient Centered Medical Home (PCMH) is another widely popular model to redesign US primary care that emphasizes enhanced access to care, coordinated care, safety, and quality through whole-person oriented care (American College of Physicians, 2007). In one of the earliest and largest PCMH demonstration programs examining over 20,000 Medicare diabetic patients, investigators found improvements in diabetes quality performance 1 year after PCMH implementation (Bojadzievski & Gabbay, 2011). However, findings were mixed in a cohort of safety net clinics caring for more vulnerable populations (Gunter, Nocon, Gao, Casalino, & Chin, 2016). One community-based study in North Carolina redesigned practice-based diabetes care to emphasize case management, group visits, and patient registries and found significant improvements in documented self-management goals, aspirin use, and diabetic foot examinations over a 12-month period (Bray et al., 2005). Aligning payment and delivery system reform efforts to achieve health equity is attracting major national interest from policymakers and is critical for the sustainability of interventions (Chin, 2016; DeMeester et al., 2017).

Health Care-Community Linkages

More recent efforts have emphasized clinical linkages to community-based resources that address basic social and material needs (E. L. Tung & Peek, 2015). These linkages are critical for connecting health care to the health-enabling resources where people live (Fig. 28.3, bidirectional arrow). This reflects a socioeconomic determinants perspective, consistent with Thomas Friedan’s Health Impact

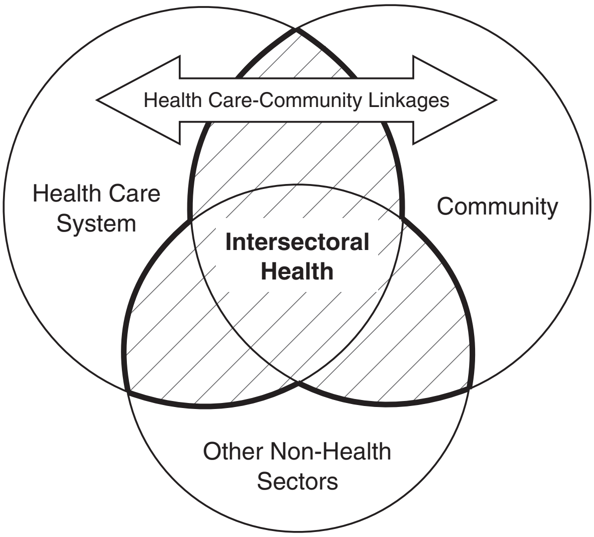

Fig. 28.3 System interventions to address diabetes disparities

Pyramid, suggesting that social and material resources are foundational to any sustained behavioral change (Frieden, 2010). For instance, a patient with diabetes may depend on local access to adequate and nutritious food to comply with a diabetic diet, a nearby gym with low-cost membership to exercise consistently, and safe transportation to attend clinical appointments as scheduled. Without access to these basic social and material resources, routine self-management behaviors can be extremely difficult to implement and sustain.

Community health workers and patient navigators have emerged as a prominent way to identify unaddressed needs and match patients to local resources that improve health (Kim et al., 2016; Peek, Ferguson, Bergeron, Maltby, & Chin, 2014). One longitudinal, quasi-experimental study enrolled Medicaid recipients in a "Community Connector Program" that used trained community health workers to screen adults for unmet needs and match them with home and community-based services, such as meal delivery programs and transportation services (Felix, Mays, Stewart, Cottoms, & Olson, 2011). On average, the program demonstrated nearly 25% lower annual Medicaid spending per participant enrolled in the program, totaling over $3.5 million in savings for 919 program participants enrolled over a 3-year period (Felix et al., 2011).

Researchers have also begun to consider electronic referrals to community resources as a practical and feasible way to address unmet health needs. CommunityRx is a multifaceted, community-engaged program that uses health IT to algorithmically connect patients to local resources (Lindau, Makelarski, et al., 2016; Lindau, Vickery, et al., 2016). The first component of the program, MAPSCorps (Meaningful, Active, Productive Science in Service to Community), employs local high school youths to conduct an annual census of all open and operating businesses and organizations on the South Side of Chicago (Lindau, Makelarski, et al., 2016; Lindau, Vickery, et al., 2016). The data collected by MAPSCorps is classified into condition-specific ontologies (i.e., formal categories constructed based on evidence and expert consensus) that subsequently power HealtheRx, an integrated health information technology platform that generates automated referrals based on conditions listed in a patient's electronic health record (Alley et al., 2016; Lindau, Makelarski, et al., 2016; Parekh, 2013). Preliminary analyses of this integrated referral system have demonstrated promising results, with more formal evaluations forthcoming (Alley et al., 2016).

An Accountable Care Organization (ACO) is a group of coordinated health organizations that collectively assumes responsibility for the cost of care, quality of care, and health of patients (Fisher & Shortell, 2010). ACOs link payment to the cost and quality of care, which in turn, incentivizes health care to favor community-based prevention strategies over costly treatments (Fisher & Shortell, 2010). Consequently, ACOs are highly invested in forming stronger health care-community linkages to address patient needs. One study interviewed leaders from 32 ACOs to assess how ACOs were addressing patients' nonmedical needs and found that the majority of ACOs did not coordinate health care-community linkages to nonmedical services (Fraze, Lewis, Rodriguez, & Fisher, 2016). However, 14 ACOs were "within or moving toward coordination," meaning nonmedical services were coordinated in some way (e.g., CHWs, care coordinators, vouchers for transportation) but remained fully distinct from the health-care system (Fraze et al., 2016). Interestingly, 2 ACOs were moving toward full integration of nonmedical services, in which nonmedical services (e.g., housing, transportation, food insecurity) played an integral role in the ACO, including voting membership on the ACO's board of directors (Fraze et al., 2016). This last evolutionary step moves the ACO beyond strictly health care-community linkages and into the era of intersectoral health (Shortell, 2013).

Intersectoral Health Approaches

Finally, there is increasing awareness that health occurs across all of life's sectors, whether it involves poor access to healthy foods at school, inadequate recreational options for physical activity near home, or more classically, poor health insurance coverage and inadequate access to medical services. Intersectoral health collaboration (also known as "cross-sector collaboration") has emerged as an important strategy to address socioeconomic determinants by enlisting a broad range of collaborators, including education, urban planning, housing, transportation, public health, health care, and others, to work together toward promoting health in communities (Mattessich & Rausch, 2013; Mattessich & Rausch, 2014). By taking into account the multiplicity of sectors involved in day-to-day life, healthy behaviors can be integrated into the social and ecological fabric, with less dependence on long-term or extraneous individual effort (Frieden, 2010).

In *Hidden Cities*, the World Health Organization (WHO) stresses the importance of intersectoral collaboration as a prerequisite for effective action against health inequity (World Health Organization, 2010). They define intersectoral health collaboration as "a recognized relationship between part or parts of the health sector with parts of another sector which has been formed to take action on an issue to achieve health outcomes (or intermediate health outcomes) in a way that is more effective, efficient or sustainable than could be achieved by the health sector acting alone" (World Health Organization, 2010, 2011). Intersectoral health can thus involve overlap between the health-care sector (e.g., primary care, hospitals), community sector (e.g., community-based nonprofits, local businesses), and other non-health sectors (e.g., transportation, education), or any combination thereof (Fig. 28.3, bolded outline).

The Robert Wood Johnson Foundation Commission to Build a Healthier America conducted a national survey of networks and associations involved in intersectoral health collaboration to assess the scope of collaboration and the key issues addressed by collaboration with non-health-care sectors (Mattessich & Rausch, 2013). The study found that of 661 respondents, 297 were engaged in successful cross-sector initiatives (Mattessich & Rausch, 2014). Collaborators reported successful collaboration to address several key issues, including access to health care; access to healthy food; opportunities for physical activity, promoting a culture of health and wellness in schools, workplaces, and neighborhoods; high-quality early child care and education; and health impact assessments for community development projects (Mattessich & Rausch, 2014).

Several early studies have specifically investigated the impact of comprehensive intersectoral health collaboration on reducing diabetes disparities. The "Improving Diabetes Care and Outcomes on the South Side of Chicago" (SSDP) program addresses the multiplicity of factors that drive diabetes disparities among racial and ethnic minorities in a high-poverty region (Chin, Goddu, Ferguson,

& Peek, 2014; Peek, Wilkes, et al., 2012). A key priority for the program has been to collaborate with stakeholders from diverse sectors to improve diabetes outcomes within the community. A novel feature within SSDP is FoodRx, a food prescription program that leverages intersectoral partnerships between a university research team, pharmacies, farmers' markets, and community-based health centers, to connect patients to locally available fresh food (Goddu, Roberson, Raffel, Chin, & Peek, 2015). Food prescriptions not only direct patients to sources of fresh food in their local neighborhoods but also provides nutritional education at each fresh food resource as well as monetary discounts (Goddu et al., 2015). Early anecdotal evidence suggests that FoodRx promoted cultural change in health centers participating in the program and also among community pharmacies and farmers' markets (Goddu et al., 2015).

The Centers for Medicare and Medicaid Services recently announced a large demonstration program to address the upstream determinants of health, called Accountable Health Communities (AHC). This three-track model includes screening for underlying health-related needs (e.g., housing, food insecurity, utilities, interpersonal safety, transportation difficulties), patient navigation of community resources and services that address those needs, and community capacity-building to ensure that communities have adequate capacity to address those needs (Alley et al., 2016). This demonstration program is among the first to systematically test the multilevel impact of addressing socioeconomic determinants by connecting patients to community resources.

Conclusions

Recognizing the multilevel impact of demographic, social, ecological, and structural influences is foundational to understanding health disparities among adults with type 1 and type 2 diabetes. Across categories of age, sex and gender, race and ethnicity, and socioeconomic status, there are pervasive disparities in the incidence, prevalence, and outcome of diabetes in the United States. An emphasis on the unacceptable causes of health disparities that stem from the health-care system has prompted scrutiny of demographic differences in health-care access and quality.

Recent policy shifts calling for a broader view of health have also prompted inquiry into causes of health disparities that stem from outside the health-care system and in the communities where patients live. Understanding a patient's spatial context is foundational to understanding the drivers of health disparities. *Intersectionality* describes how demographic influences converge and interact, often in a predictable pattern or spatial context; and *place* describes how the socioecological influences of a neighborhood can shape a person's health behaviors and outcomes. Together, these concepts can be highly layered and complex, pointing to the limitations of using isolated demographic influences to explain diabetes disparities in real-world scenarios.

Behavioral health solutions to diabetes disparities have often not fully included the social and economic contexts of individual patients; but recent efforts have galvanized strategies to address these very contexts. Health-care approaches have emphasized culturally tailored interventions, contextualized educational strategies, and comprehensive care management. Changes in health-care policy are starting to fortify linkages between the health-care system, community, and non-health sectors such as housing.

Disparities in diabetes risk and burden throughout the United States are complex and multilevel. Although many disparities are rooted in the physical, social, and system-based contexts in which people are embedded, health-care systems have been slow to adopt strategies that specifically target the multilevel root causes. However, research has documented early successes and a robust framework for action. The elimination of health disparities is more critical than ever. It remains our imperative to ensure that actions are taken so that diabetes disparities— between rich and poor, minority and non-minority, and urban and rural—diminish in the twenty-first century.

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Chapter 29
Medical Systems and Patient-Provider Relationships

Deborah J. Wiebe, Ashley C. Baker, and Jessica A. Marino

Medical Systems and Patient-Provider Relationships

Type 1 (T1D) and type 2 diabetes (T2D) are embedded within a web of social contexts that may facilitate or undermine the effectiveness of an individual's diabetes management (Marrero et al., 2013; Wiebe, Helgeson, & Berg, 2016). This social ecological perspective is particularly evident when one considers the role of patient-provider relationships and health-care systems in diabetes care. Current practice standards recommend that health care for diabetes be delivered through patient-centered care models where patients and families are partners with their medical team and health-care decisions are developed and modified through collaborative decisions that consider the patient's preferences and lifestyle needs. These standards place demands on both patients and providers. Patients and families have to assume responsibility for their illness, develop skills, and maintain motivation to complete often complex medical regimens and difficult-to-sustain lifestyle behaviors within the vicissitudes of daily life. Although there is clear evidence that diabetes can be managed and long-term complications can be prevented or delayed through intensive lifestyle and diabetes self-management behaviors (Diabetes Prevention Program Research Group, 2009; King, Peacock, & Donnelly, 1999; The Diabetes Control and Complications Trial Research Group, 1993), these illness management demands are challenging and often experienced as burdensome for patients and families. Providers (e.g., physicians, nurses, diabetes educators) need to make appropriate recommendations for medication, order and act upon relevant medical tests, educate and collaborate with patients to develop effective treatment goals, and provide ongoing support resources. Such patient-centered practices may be difficult to achieve within current health-care systems, given barriers such as time constraints, limited resources, and reimbursement policies that may support fee-for-service over quality care (Johnson & Marrero, 2016).

This chapter examines the crucial role of patients' relationships with health-care providers for effectively managing diabetes in adults, with a specific focus on patient-centered care. After summarizing how patient-centered care has been defined and the processes theorized to link patient-centered transactions to better diabetes management, we discuss four primary issues. We initially explore qualitative research to identify what patients with diabetes say they want from their interactions with providers. Observational research is then discussed to determine whether these desired aspects of

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D. J. Wiebe (✉) · A. C. Baker · J. A. Marino
Psychological Sciences and the Health Sciences Research Institute, University of California, Merced, CA, USA
e-mail: dwiebe@ucmerced.edu

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patient-centered interactions with providers are associated with improved diabetes outcomes (e.g., quality of life, diabetes self-management activities, glycemic control). Intervention studies are then reviewed to identify whether patient-centered interactions with health-care providers can be changed and whether doing so affects diabetes outcomes. Finally, we discuss the role of the health-care system in creating barriers to providing patient-centered care and new models of health-care delivery that may promote more effective patient-provider relationships to improve diabetes management.

Patient-Centered Care and the Patient-Provider Relationship

Medical care delivery has traditionally been paternalistic, with the physician as the driver and the patient as a passive passenger. However, it is increasingly recognized that the traditional health-care system is inadequate to the demands of chronic illnesses such as diabetes, where effective management is largely dependent on the patient's knowledge, attitudes, motivation, and ongoing self-care behaviors. The shift to a patient-centered approach gives patients reasonable control over their treatment options. This approach builds on the notion that decisions and goals that are autonomously chosen and personally meaningful are more likely to motivate and empower patients to carry out beneficial self-care behaviors.

The Institute of Medicine (USA) defines patient-centered care as "health care that establishes a partnership among practitioners, patients, and their families (when appropriate) to ensure that decisions respect patients' wants, needs, and preferences and that patients have the education and support they require to make decisions and participate in their own care" (IOM, 2001, p. 41). This patient-centered approach is argued to improve health outcomes and quality of life by addressing the needs of the whole person and not just the condition. The American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition (2015) recommend that diabetes self-management education and support be provided through "patient engagement, information sharing, psychosocial and behavioral support, integration with other therapies, and coordinated care" (Powers et al., 2015, p. 4). Such a patient-centered approach, which involves clear communication and effective collaboration, allows for greater consideration of the patient's real and perceived barriers to diabetes self-management. When implementing a patient-centered care approach, it is important to account for the patient's life, preferences, culture, needs, and capacity to form a partnership that encourages effective self-management so as to improve diabetes outcomes. It is noteworthy that patient-centered care has been specifically identified by the Institute of Medicine as a core objective for improving health care in the twenty-first century (IOM, 2001), is increasingly advocated by consumers (IAPO, 2007), and has been incorporated into the training and certification of health-care providers (USMLE, 2012).

What Do Patients Want from their Interactions with Health-Care Providers?

Understanding what patients with diabetes want from their health-care providers is a first step toward finding ways to improve patient-provider interactions and diabetes outcomes. Important insights have been gained by directly assessing patient's beliefs and preferences through in-depth interviews and focus groups (Beverly, Worley, Court, Prokopakis, & Ivanov, 2016). A limited number of qualitative studies have explored preferences for medical care among patients with diabetes. These studies have revealed that many patients with diabetes believe their personal health care can be improved through changes in aspects of providers' communication and greater provision of diabetes information at diagnosis and during ongoing treatment (Beverly, Wray, LaCoe, & Gabbay, 2014; Matthews, Peden, & Rowles, 2009; Murphy, Chuma, Mathews, Steyn, & Levitt, 2015; Peek et al., 2009; Pooley, Gerrard, Hollis, Morton, & Astbury, 2001; Ritholz, Beverly, Brooks, Abrahamson, & Weinger, 2014; Wilkinson, Whitehead, & Ritchie, 2014).

Several qualitative studies indicate that patients desire more adequate explanations about their diagnosis and subsequent treatment from their providers (Matthews et al., 2009; Murphy et al., 2015). In-depth interviews with five women with diabetes revealed considerable knowledge gaps that may be related to inadequate patient-provider communication (Matthews et al., 2009). All five women discussed receiving minimal information at diagnosis, and none of the women knew their HbA1C level or the recommended level at the time of the interview. Through interviews with patients with T2D and hypertension, Murphy and colleagues (2015) additionally found that patients who reported receiving inadequate explanations had high levels of stress and uncertainty. In 12 out of 22 participants, this was linked to misconceptions about diabetes, including that diabetes is a "death sentence." In both studies, most patients lacked the knowledge to carry out beneficial self-care behaviors but reported wanting more detailed information from their health-care provider to be able to properly manage their condition. This problem was compounded by patients' perceptions of provider indifference and communication patterns that restricted patients from asking questions.

Most studies found a common desire for provider communication styles that foster a nonjudgmental environment. For example, Ritholz et al. (2014) interviewed patients with T2D to identify perceived barriers and facilitators to better patient-provider communication. Patients' reluctance to participate often stemmed from a fear of being judged or shamed by their provider. Participants viewed accusatory language as a barrier and viewed open and honest communication that created feelings of trust and acceptance as a facilitator to better self-care. A second study that assessed perceived barriers to shared decision-making in an African-American sample found similar results in that patients wanted a provider with strong interpersonal skills (Peek et al., 2009). Patients desired an environment in which they could share their feelings, have their health concerns validated, and receive informational and emotional support while playing a role in their health decisions. Patients who had experienced poor interactions with their provider, such as perceiving rude and impatient communication, reported a negative impact on their motivation to participate in discussions and felt their self-care was impeded (Murphy et al., 2015).

In a systematic review, Wilkinson and colleagues (2014) identified several patient-provider factors that influenced diabetes self-management. Patients wanted respectful communication that took their own feelings and values into consideration, and they wanted their opinions acknowledged for treatment options. Provider issues involving quality and consistency of care were also identified. Patients preferred to be treated as individuals, with high-quality treatment tailored to their lifestyle. They also favored appointments with the same health-care provider over time. Other studies have echoed patients' and physicians' desire for continuity in care, noting that new physicians likely know little of the patient's personal history and that trusting partnerships are hard to build when treatment is fragmented between multiple parties (Pooley et al., 2001).

Matthews and colleagues (2009) found additional areas for improvement in provider communication. Patients explained that being lectured or "fussed at" by their provider for poor management had an opposite effect on their desire to adhere to treatment. Perceptions of providers' aggressive warnings, indifferent demeanor, and lack of encouragement were experienced as barriers to improved diabetes self-care. Evaluations of older patients' views also highlighted the importance of considering quality of life when deciding on treatments (Beverly et al., 2014). Patients reported that they value working relationships with their provider and considerations of quality of life in their diabetes care and prefer an honest provider who listens to their concerns.

Summary

This selected review of qualitative studies supports that individuals with diabetes want effective communication with a consistent provider that is informative, open, honest, supportive, and founded on trust and that encourages the development of a partnership. These studies are consistent with the patient-centered care model and enhance our understanding of what a diverse group of patients want from their interactions with health-care providers.

Are Patient-Provider Relationships Associated with Diabetes Management?

Observational studies have examined which aspects of patient-provider interactions are associated with better quality of life, diabetes self-management behaviors, and clinical outcomes (e.g., glycemic control). Most of these are cross-sectional surveys that measure patients' perceptions of their interactions with providers. It is well understood that a crucial component of providers' interactions with patients involves clear and comprehensive communication about diabetes and its treatment. Bundesmann and Kaplowitz (2011) conducted a telephone survey with a large sample of patients with T2D, asking them whether they recalled discussing with their providers various self-care activities that are recommended in practice guidelines (e.g., glucose monitoring, foot care, retina screenings, etc.) when they were initially diagnosed. Recollection of more diabetes-specific communication was strongly associated with patients' engagement in self-care activities, more than doubling the odds of engaging in blood glucose monitoring and foot care and increasing physical activity.

Although this confirms patients' needs for comprehensive diabetes education, such education is generally considered insufficient to motivate and sustain patients' diabetes self-care activities, raising the question of what additional features of patient-provider interactions are necessary. Researchers have generally studied two broad and multifaceted aspects of the interaction. First, studies have examined patient perceptions of general interpersonal processes, measuring the extent to which providers are attentive, listen to the patient's concerns, convey respect and compassion, and/or provide support. Second, studies have measured the extent to which patients perceive that they are actively engaged in a partnership with their provider through collaborative goal-setting, autonomy-supportive communication, and participatory decision-making. Below we review the literature examining how these two broad dimensions of patient-provider interactions are associated with quality of life, diabetes self-management behaviors, and clinical outcomes.

Interpersonal Processes in Patient-Provider Relationships

In a large survey of ethnically diverse adults with diabetes, Piette, Schillinger, Potter, and Heisler (2003) found patients' perceptions of providers' diabetes-specific communication (e.g., recommendations for foot care, exercise, diet) and general communication style (e.g., conveying care and compassion, providing emotional support, eliciting patient preferences and concerns) were independently associated with better self-care activities. Aikens, Bingham, and Piette (2005) tested these same constructs in multivariate models predicting a variety of outcomes. Diabetes-specific communication, but not general communication, was associated with better self-management behaviors (i.e., medication-taking, glucose testing, eating, exercise) and glycemic control. In contrast, general but not diabetes-specific communication was associated with better quality of life.

More recently, Linetzky, Jian, Curtis, Funnell, and Polonsky (2016) examined which of the multiple aspects of patient-provider interactions were associated with diabetes outcomes. Patients with T2D rated their provider on six domains from the Interpersonal Processes of Care Survey (Stewart, Nápoles-Springer, Gregorich, & Santoyo-Olsson, 2007): *Hurried Communication* (i.e., spoke quickly, ignored or discouraged input, appeared distracted and unengaged); *Elicited Concerns* (i.e., heard and took concerns seriously); *Explained Results* (i.e., explained test results and consequences of taking or not taking prescribed medications); *Patient-Centered Decision-Making* (i.e., asked about treatment preferences); *Compassionate Respect* (i.e., expressed concern about feelings); and *Discrimination* (i.e., made assumptions about education, treated differently because of race/ethnicity). In structural equation models examining all domains simultaneously, hurried communication was associated with more negative outcomes for diabetes distress, adherence, and glycemic control. Higher-perceived discrimination and lower explained results also independently predicted higher distress and poorer adherence.

Using the same scale, Polonsky et al. (2017) identified that patient perceptions of good provider communication quality were comprised of four factors including high levels of *Encouraging Communication* (e.g., reassurance that good self-care will control diabetes), *Collaboration* (e.g., developing a treatment plan that fits into daily life), *Recommending other Resources* (e.g., referrals to dietician, educator, counselor), and low levels of *Discouraging Communication* (e.g., blaming T2D on the patient's lifestyle). Patients' recollections of good communication qualities at the time of diagnosis were associated with better self-care activities and lower diabetes distress. These studies confirm the importance of interpersonal processes in patient-provider relationships and demonstrate the complexity and multifaceted nature of which interpersonal aspects are related to effective diabetes care.

Active Partnership Building Processes in Patient-Provider Relationships

In addition to these general interpersonal aspects of good patient-provider communication, patient-centered care includes a focus on engaging patients as active participants in treatment goal-setting and decision-making. Providers who use more patient-centered communication do tend to have more actively engaged patients. For example, Moran and colleagues (2008) audio-recorded routine consults of patients with diabetes and coded physicians' patient-centered communication (e.g., provider encouraged patients to discuss opinions and communicate feelings) and patients' active engagement in the consult (e.g., patient expressed own views, asked questions). Although physicians did not routinely display high levels of patient-centered communication, doing so was associated with more actively engaged patients. It is generally theorized that such active patient engagement is beneficial for diabetes management because it results in a more informed, intrinsically motivated, and empowered patient who, in turn, will more effectively self-manage his or her diabetes.

In a large survey study of older adults with T2D, Heisler et al. (2002) assessed patient perceptions of physicians' participatory decision-making style (e.g., offered choices and considered preferences when making treatment recommendations) as well as of their general communication of diabetes information. Participatory decision-making and communicating diabetes information were each associated with better self-management behaviors when analyzed individually. When modeled together, however, ratings of provider diabetes communications remained a predictor of self-management behaviors, while participatory decision-making did not. Although this suggests that patient active engagement is not a necessary component, a follow-up study suggested physician communication of diabetes information was sufficient primarily for easier aspects of diabetes self-care (e.g., foot care, medication) but that actively involving patients in diabetes goals and treatment plans was necessary for aspects that demand behaviorally complex lifestyle modifications (e.g., exercise, diet, blood glucose monitoring, Heisler, Cole, Weir, Kerr, & Hayward, 2007).

The large multinational DAWN study of patients with T1D or T2D revealed that patients' reports of higher collaboration with their providers were related to better ratings on all patient-reported outcomes, including diabetes-related distress, lifestyle and medication adherence, and perceived diabetes control (Rubin, Peyrot, & Siminerio, 2006). Heisler and colleagues (2003) examined patient-provider collaboration by measuring the level of concordance between patient and provider reports of treatment goals. Although concordance rates were generally low, higher concordance was associated with higher self-efficacy beliefs and better diabetes self-management behaviors. In a longitudinal study, Lafata et al. (2013) found collaborative goal-setting with physicians was linked to subsequent improvements in glycemic control through patient perceptions of higher self-competence as well as trust in their physician. This relatively unusual longitudinal design is important because it precludes a reverse causality explanation that patient-provider collaboration is simply easier when diabetes management is going well. Together, such findings suggest active collaboration between patients and providers may be beneficial by promoting shared goals, trust in the provider, and confidence in one's ability to manage diabetes.

A fairly robust literature indicates that patient perceptions of autonomy support from providers may also be an important aspect of patient-centered care that promotes better diabetes outcomes. Autonomy support involves activating patients by eliciting patient perspectives, providing treatment choices, and supporting patient self-initiation, which together are theorized to promote patient autonomous motivation and self-competence. In a series of studies involving both cross-sectional and longitudinal approaches with T1D and T2D patients, Williams and colleagues have demonstrated the importance of autonomy support in patient-provider interactions (Williams et al., 2009; Williams, Freedman, & Deci, 1998; Williams, McGregor, King, Nelson, & Glasgow, 2005; Williams, McGregor, Zeldman, Freedman, & Deci, 2004). For example, Williams, Zeldman, Freedman, and Deci (2004) found that perceptions of autonomy support were associated with improvements in glycemic control across 1 year among patients with T2D, and this association was mediated by increases in patients' autonomous motivation, perceived competence, and diabetes self-management behaviors. More recent studies demonstrated perceived autonomy support from providers predicted lower depressive symptoms (Williams et al., 2005), improved cholesterol profiles (Williams et al., 2009), and better quality of life in patients with diabetes (Lee & Lin, 2010). Autonomy support has also been found to be associated with greater patient-provider congruence in perceived treatment goals (Heisler et al., 2003) and higher patient satisfaction and trust in the provider (Lee & Lin, 2010).

Although these findings indicate that actively engaged patients who experience collaborative and autonomy-supportive relationships with providers display better diabetes outcomes, it is important to note that patients' preferences for involvement may vary widely. Some patients may want involvement primarily in being comprehensively informed, some may want to express their ideas and feelings, while others may want final decision-making authority. For example, in a large sample of adults with T2D, patients strongly preferred full information but had lower preferences for decisional control in their interactions with providers, with lower preferences for decisional control especially found among those who were older and less educated (Lee & Lin, 2010). Furthermore, Lee and Lin (2010) found that preferences for involvement in care moderated associations between perceived autonomy support from providers and increases in patient satisfaction, trust in provider, and quality of life across the subsequent year. In all cases, perceived autonomy support from providers was less strongly associated with the outcomes when patients had lower preferences for involvement in care. There is also evidence that providers vary in their preferences for patients' involvement in care. Jahng, Martin, Golin, and DiMatteo (2005) assessed both patients' and physicians' preferences for patient involvement in care. Congruence on preferences for patient involvement in care was correlated with higher patient satisfaction with medical care, adherence, and perceptions of health. Such studies highlight the complex nature of patient-physician interactions and the careful considerations that must be involved when evaluating and promoting patient-centered care.

Summary

These observational studies generally support the notion that patients display better outcomes when they experience more comprehensive communications about diabetes and treatments, perceive high-quality relationships with providers, and feel empowered to participate in treatment decisions. However, it remains unclear whether specific aspects of patient-provider relationships are most important and clear conclusions are hampered by ongoing research limitations. Patient-centered communication is a complex multidimensional construct, and there is great heterogeneity in how it has been conceptualized and measured across studies. In addition, most measures have focused on patients' *perceptions* of relationships with their providers, despite the fact that patients and providers often differ in their perceptions of the medical encounter and these perceptions may not match objective measures of the interactions (Stuckey et al., 2015). Cross-sectional research dominates these observational designs, undermining our ability to make causal inferences. It is unclear, for example, whether patient-centered communication improves diabetes management, whether effective relationships are challenged when diabetes management is not going well, or whether both relationships and diabetes management reflect covariation with a third variable (e.g., health literacy). Finally, mechanisms theorized to underlie associations are rarely tested, resulting in a limited understanding of the processes through which patient-centered care may affect diabetes outcomes.

Do Interventions on Patient-Provider Relationships Improve Diabetes Management?

Interventions to promote more patient-centered care in medical consultations have been developed and are important not only for establishing more compelling evidence of the causal influences of patient-provider relationships on diabetes outcomes but also for clarifying the most important aspects of patients' interactions with their providers. Numerous intervention approaches have been developed. Many have focused on empowering *patients* to change the nature of their relationships with providers by taking a more active role in medical consultations. Others have focused on educating *providers* to provide more patient-centered care or have altered aspects of the *health-care environment* to reduce barriers to providing patient-centered care within the very real constraints of ongoing medical practice. This heterogeneity makes it challenging to evaluate the literature but provides additional information about the most effective approaches for translating the existing evidence base into clinical care.

A fairly large literature has now emerged evaluating whether such interventions are feasible or beneficial in general medical practice. Numerous high-quality systematic and meta-analytic reviews have examined randomized controlled trials aimed at altering patient-centered aspects of care in either general medical populations that include patients with and without diabetes (e.g., (Dwamena et al., 2012; Griffin et al., 2004; Kelley, Kraft-Todd, Schapira, Kossowsky, & Riess, 2014; McMillan et al., 2013; Rathert, Wyrwich, & Boren, 2012) or in populations comprised exclusively of patients with diabetes (e.g., Dambha-Miller, Cooper, Simmons, Kinmonth, & Griffin, 2016; Mieziene, Sinkariova, & Jankauskiene, 2014; Schoenthaler & Cuffee, 2013; Van Dam, Van Der Horst, Van Den Borne, Ryckman, & Crebolder, 2003). These reviews converge on several consistent findings. First, it is possible to alter aspects of patient-provider relationships through interventions that target either the patient or members of the health-care team. Second, interventions usually demonstrate improvements on intermediate outcomes involving patient satisfaction and empowerment but less consistently affect self-care behaviors and physical health outcomes. Third, part of this inconsistency may reflect that not all interventions are equally effective. Interventions that target patients appear to be more effective than interventions that target providers, and interventions that include additional illness-specific educational information are more effective than those that do not. Below we summarize randomized controlled trials that have been conducted specifically for patients with diabetes.

Interventions to empower patients with diabetes have been conducted by teaching patients how to actively engage with providers or by providing empowerment-based diabetes self-management education and support. Greenfield et al. (1988) taught patients with T2D how to negotiate with their provider, ask questions, and overcome embarrassment. Audiotapes of the consultation revealed intervention patients were more actively engaged in the consult (e.g., asked more questions, received more information) and displayed improvements in glycemic control and activities of daily life compared to controls. Using a similar intervention, Williams et al. (2005) found that poorly controlled patients with T2D responded to the intervention with more active engagement. All patients displayed improvements in glycemic control, with no differences between intervention and control groups. However, levels of active engagement documented in audiotaped interactions of the medical consultation were correlated with subsequent improvements in glycemic control in both groups. Patient empowerment education (e.g., focusing on collaborative goal-setting, problem-solving and coping skills, and self-motivation) delivered in individual or group settings has also been found to increase patient satisfaction, with care as well as aspects of empowerment (e.g., self-efficacy beliefs, self-motivation, knowledge), and to improve glycemic control (Anderson et al., 1995, 2009; Deakin, Cade, Williams, & Greenwood, 2006). Improvements in self-management behaviors have been less consistently documented, but these studies as a whole provide compelling evidence for the importance of interventions to empower patients to actively engage with their health-care providers.

Interventions targeting providers have been conducted by training members of the health-care team to be more patient-centered in their interactions with patients or by altering aspects of the health-care environment to support such interactions. Interventions to teach providers how to conduct patient-centered consultations improved some aspects of the medical consult (e.g., increases in patient-initiated discussions, higher levels of physician communication), but only inconsistently improved patient satisfaction with care, and had no effects on self-care behaviors or glycemic control (Kinmonth, Woodcock, Griffin, Spiegal, & Campbell, 1998; Pill, Stott, Rollnick, & Rees, 1998). Some interventions have trained members of the health-care team in motivational interviewing techniques aimed at developing a working relationship with the patient that enhances patient motivation and reduces ambivalence for behavior change. Although there are examples of the benefits of motivational interviewing for patients with diabetes (Channon et al., 2007; West, Gore, DiLillo, Greene, & Bursac, 2007), a meta-analysis of randomized controlled trials testing motivational interviewing with patients with diabetes failed to support its effectiveness at improving glycemic control relative to controls (Jones et al., 2014). Interventions providing decision aids or other tools to facilitate physicians' patient-centered care activities (e.g., problem-solving and collaborative goal-setting education; plan of care tools; reminders of and feedback on compliance with clinical guidelines) have been more effective. These interventions consistently improved quality of care, patient knowledge, satisfaction, and/or empowerment beliefs, and all but one also improved self-care behaviors or glycemic control (Branda et al., 2013; Olivarius et al., 2001; Piette, Weinberger, Kraemer, & Mcphee, 2001; Rocco, Scher, Basberg, Yalamanchi, & Baker-Genaw, 2011).

Multifaceted interventions targeting both patient and provider have also emerged, often teaching patients empowerment-based diabetes education, teaching members of the health-care team in patient-centered communication, and providing tools or health system supports to enhance patient-centered interactions (e.g., interactive computer technology generated reports provided to patient and provider; clinical information system supports; consistent access to a diabetes educator). Patients in these varied interventions have displayed improvements in delivery of evidence-based medical care and patient-centered procedures (Glasgow et al., 2004), perceptions of provider autonomy support (Zoffmann & Lauritzen, 2006), and targeted self-care behaviors (Christian, 2008; Piatt et al., 2006; Zoffmann & Lauritzen, 2006) relative to controls. In some but not all of these intervention studies, improvements in glycemic control or indices of cardiovascular risk were also evidenced (Christian, 2008; Piatt et al., 2006;

Zoffmann & Lauritzen, 2006). It is difficult to isolate the source of effects given the multifaceted nature of these interventions. However, in a secondary analysis of Glasgow et al. (2004), Williams and colleagues (2007) demonstrated that increases in perceived autonomy support from providers mediated improvements in glycemic control across 1 year, regardless of intervention group.

There have been calls to incorporate theory more consistently into interventions to promote patient-centered consultations and improve diabetes outcomes. Dambha-Miller et al. (2016) conducted a recent meta-analysis of interventions on patient-centered consultations to improve cardiovascular risk factors (e.g., weight, blood pressure, cholesterol, HbA1c) in patients with T2D. Seven randomized control trials were identified that targeted one or more specific features of patient-centered care (e.g., exploring the disease and illness experience, realistic goal-setting, understanding the whole person, enhancing the relationship, etc.). The analysis coded whether the intervention was theoretically based and whether the targeted patient-centered feature was actually altered by the intervention. Only three studies provided a theoretical rationale for how the intervention translated into clinical outcomes. Five studies demonstrated the intervention altered some patient-centered aspect of the consultation, but no trial tested whether this underlying process was associated with outcomes. No overall difference between intervention and usual care groups was found for HbA1c or other cardiovascular risk outcomes. However, when only interventions that demonstrated an effect on the targeted patient-centered variable were examined, improvements in clinical outcomes were consistently found. This finding supports the need for better incorporation of theory in interventions to elucidate the mechanisms that underlie potential benefits of patient-centered care.

Summary

Findings from these intervention studies confirm both qualitative and observational research suggesting that patients' more comprehensive understanding of their illness and its treatments is necessary but insufficient for optimal diabetes care. Interventions that promote relationships built on trust, respect, and support, that consider the patient's life context, and that actively support the patient as an active and autonomous partner in treatment decisions have been developed and appear helpful for intermediate outcomes (e.g., satisfaction with care), especially when targeted at the patient or multifaceted aspects of the health-care environment. The multifaceted interventions are particularly impressive in that they were conducted in the context of ongoing clinical care, targeted underserved and poorly controlled Hispanic (Christian, 2008) or African-American (Piatt et al., 2006) patients with T2D, and examined the maintenance of effects across several years (e.g., Piatt et al., 2010). At the same time, there are ongoing problems with this body of research. Interventions most consistently improve intermediate outcomes and less consistently reveal effects on diabetes self-care activities and clinical outcomes relative to controls. Understanding the sources of these inconsistencies is hampered by the study of different patient-centered constructs, the lack of standard measures of these constructs, and the underutilization of theory to guide interventions and test mediation processes.

Systems of Health-Care Delivery and Patient-Provider Relationships

Patient-provider relationships are embedded within the context of the broader health-care system, which may constrain or facilitate the development of collaborative patient-provider partnerships and the delivery of patient-centered care. The DAWN2 study surveyed 4785 health-care professionals worldwide to understand provider perspectives on health-care delivery for people with diabetes (Holt et al., 2013; Stuckey et al., 2015). Despite major technological advances and the availability of improved medical treatments, the majority of providers believed that the current health-care system is poorly equipped to manage and treat patients with diabetes. Providers valued and expressed a strong desire to deliver patient-centered care but identified health-care system barriers to doing so. These included insufficient time to understand patients' concerns or provide support during medical consults; uncoordinated care resulting from limited collaboration and communication among members of multidisciplinary health-care teams; limited resources to provide ongoing diabetes self-management education and support; and a lack of training and resources to support the psychosocial needs of people with diabetes (Holt et al., 2013; Stuckey et al., 2015). Providers desired more education and training to strengthen their capacity to provide effective patient-centered care but also believed that shifts in the provision of health care for people with diabetes are necessary. The traditional acute care model characterized by episodic face-to-face visits with a physician expert was perceived as inadequate to support the ongoing self-management requirements of a chronic illness such as diabetes.

A number of innovations in health-care delivery are now underway to treat patients with diabetes and other chronic conditions more effectively. A central feature of these innovations is the development of collaborative patient-provider relationships that empower patients and families to be active participants in their health care. For example, the *chronic care model* is a broad-ranging organizational approach to improving care for patients with chronic diseases in primary care settings, where most diabetes care for adults occurs. This model identifies six essential elements to deliver more effective care for people with chronic diseases such as diabetes: (a) self-management education and support, where patients with diabetes and their families receive ongoing education and support to develop the skills and confidence necessary to self-manage their illness; (b) a coordinated health-care team that works together to support the patient's self-management; (c) decision-support systems to ensure that evidence-based practice is integrated into routine care; (d) computer systems to remind providers of evidence-based practice guidelines, provide feedback on their patients' illness measures, and create registries to proactively plan for innovative care; (e) organizational and reimbursement policies that support evidence-based chronic illness care; and (f) access to community resources to support prevention and self-management efforts (Bodenheimer, Wagner, & Grumbach, 2002a).

Although this model has not been fully tested, there is some evidence to support its utility (see Stellefson, Dipnarine, & Stopka, 2013 for review). Initial demonstration projects suggested that innovations based on this model could improve clinical care while decreasing costs (Bodenheimer, Wagner, & Grumbach, 2002b), and the multifaceted randomized controlled trials described above – which targeted patients, providers, and aspects of the health-care system in a manner consistent with the chronic care model – revealed improvements in health-care delivery and some patient outcomes (Glasgow et al., 2004; Piatt et al., 2006).

A closely related model, the *patient-centered medical home (PCMH)*, has gained prominence as an effective system for delivering patient-centered care within primary care settings. Basic components of the PCMH include connection with a personal physician embedded within a coordinated health-care team; a patient-centered orientation to the whole person; care that is coordinated across all aspects of the health-care system and the patient's community; enhanced access through flexible scheduling and ongoing communications with providers (e.g., secure email or telephone); and a systems approach to quality and safety (Ackroyd & Wexler, 2014; Bojadzievski & Gabbay, 2011; Jackson et al., 2013).

As with the chronic care model, initial demonstration projects have been encouraging (Bojadzievski & Gabbay, 2011), and there is evidence that some aspects of the PCMH model are individually associated with improved levels of glycemic control (Tricco et al., 2012). Ackroyd and Wexler (2014) reviewed the existing literature and concluded that the most consistent evidence is in improved patient and provider satisfaction. Improvements in a variety of other outcomes (e.g., quality of life, glycemic control, cardiovascular risk factors) were modest but may be meaningful when spread across many patients at the population level. Individually or in combination, the most effective components included diabetes self-management education, team changes to promote coordinated care management, and the use of electronic patient registries to support care strategies.

Summary

It is widely recognized that traditional models of health care may undermine the development of effective patient-provider relationships and the delivery of patient-centered care. New models of health-care delivery, such as the chronic care model and the patient-centered medical home, have been developed, and initial demonstration projects support their potential to improve the delivery of effective diabetes health care. The demonstrated effects thus far appear most apparent for patient satisfaction, an important outcome, but less so for clinical outcomes such as glycemic control. It is also not clear whether enhanced patient-provider relationships are an important part of the processes through which health-care innovations may influence diabetes outcomes. Given the early stages of these demonstration projects and the variety of ways in which the components of alternative models of care have been implemented, such findings are not definitive but provide optimism for future patient-centered care.

Conclusions and Implications

Diabetes occurs in a complex interpersonal context that can facilitate or undermine its effective management (Wiebe et al., 2016). Patient-provider relationships and the surrounding health-care system are crucial components of a patient's social context. The types of interactions that patients have with their health-care providers have been found to be associated with patient satisfaction, self-confidence, motivation, diabetes knowledge, quality of life, psychosocial adjustment, medication adherence, self-management and lifestyle behaviors, and physical health outcomes. Understanding the characteristics of patient-provider relationships that are most central and amenable to change is, thus, a high priority for enhancing patient quality of life and improving self-management and clinical outcomes.

We are beginning to understand the broad features of patient-provider interactions that are most important. Qualitative research indicates that patients desire interactions that convey clear and comprehensive information about diabetes and its treatment; that are characterized by understanding, respect, and support; and that engage them as active partners in health-care decisions. These characteristics – clear diabetes communication, high relationship quality, and collaborative partnerships – have been found to be associated with important outcomes in observational survey research, and interventions to alter these features of patient-provider interactions are often associated with improved outcomes. It is notable that these characteristics map well onto the patient-centered care model and have been consistently evident across three distinct literatures. Although problems with each of these literatures were noted, these findings are encouraging and hold promise for improving the lives and health of patients with diabetes.

Although there is consistency in the broad relationship features that are most salient, patient-centered care is a complex multidimensional construct, and studies vary greatly on which dimensions of patient-centered relationships are examined and analyzed. Some studies measure a single dimension, others measure multiple dimensions, but relatively few include a full assessment of all the dimensions that have been identified under the umbrella of patient-centered communication. This incomplete assessment makes it difficult to interpret inconsistent findings and to understand which aspects of patient-centered care should be included in assessments and interventions. Problems with incomplete assessments are compounded by evidence that different relationship dimensions may be associated with different outcomes. For example, good relationship quality may be most important for improving quality of life (Aikens et al., 2005), diabetes communications that enhance patient knowledge may be sufficient for easier diabetes self-care activities, and active involvement in treatment decisions may be necessary to maintain more difficult lifestyle behaviors (Heisler et al., 2007). In a review of the general medical literature, Michie, Miles, and Weinman (2003) argued that providers' elicitation of patients' preferences is distinct from their activation of patients' motivation to complete preferred treatment regimens. Both characteristics fall under the rubric of patient empowerment, and both were associated with better adherence. However, only activation was associated with physical health outcomes.

Heterogeneity in the measurement of patient-provider relationships and patient-centered communication has also hampered research progress (Epstein et al., 2005). Measures of patient-provider relationships or aspects of patient-centered communications have varied greatly, with different studies often using different measures to assess similar constructs. Such heterogeneity makes consistent findings more impressive but creates problems when comparing findings across studies or interpreting inconsistent effects. Studies have also most consistently measured patients' *perceptions* of their physician without validating whether these perceptions relate to actual interpersonal interactions. Although patients' perceptions may have the most proximal influence on their attitudes and behaviors, understanding the features of patient-provider transactions that shape these perceptions is necessary to develop valid measures, as well as efficient and effective interventions. A high priority for future research is the continued development of the scope and valid measurement of the patient-centered construct as it relates to patient-provider interactions.

Intervention research provides important evidence for the role of patient-centered communication in enhancing patient-provider relationships and improving diabetes outcomes. Some of the most compelling efforts have targeted patients or aspects of the health-care system to empower patients' more active involvement in care. Nevertheless, studies as a whole show mixed support with evidence more consistently present for outcomes such as quality of health-care delivery and patient satisfaction, than for self-management behaviors and physical health outcomes. Future efforts may benefit from greater incorporation of theory into intervention development and evaluation (Dambha-Miller et al., 2016). Theories thus far have often been at the level of broad descriptive frameworks. These have served an important purpose and advanced an impressive body of research, but we may be at a point when theoretical advances are possible and necessary.

Patient-centered care and health-care innovations such as the PCMH focus on delivering diabetes care through a coordinated health-care team that engages both patients and their families. However, most research has focused solely on the patient with diabetes and their physician provider, with little systematic exploration of other salient partners in the patient's social context. Patients' perceptions of physicians do not directly map onto perceptions of other health-care clinicians, and perceptions of physicians versus other providers may be differentially associated with outcomes (Shafran-Tikva & Kluger, 2017). There is also little research examining how family members interact with health-care providers and systems, despite findings that providers view families as an important resource in their interactions with patients (Holt et al., 2013), that patients and family members may have different perspectives on interactions with health-care providers (Croom et al., 2010), and that families play a central role in diabetes self-management and outcomes (Wiebe et al., 2016). Future research and interventions may benefit from broadening the scope to include family and other members of the health-care team.

High-quality patient-provider relationships that are grounded on principles of patient-centered care and supported by health-care system innovations hold great promise for enhancing patients' quality of life and diabetes self-management and outcomes. Significant progress has been made in understanding the types of relationships that activate patients' self-management and improve diabetes outcomes and the health-care system innovations that may be necessary to support patients, families, and providers.

We are now poised to continue the development of approaches that utilize this important social context to improve quality of life and promote better diabetes management and clinical outcomes for patient with diabetes.

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Chapter 30
Type 2 Diabetes Prevention in Adults

Ronald T. Ackermann

Significance of Type 2 Diabetes Development in Adults

Diabetes is a considerable threat to population health, spares no segment of our society, and disproportionately affects the poor, the aged, and racial and ethnic minorities (CDC, 2017; Narayan, Boyle, Thompson, Sorensen, & Williamson, 2003). Although modern medicine enables most individuals with a diagnosis of diabetes to live full lives, realizing this goal requires those individuals to overcome sources of worry and self-doubt and to commit considerable energy toward the execution of multiple daily behaviors, such as self-monitoring of blood glucose, timely medication-taking, and careful attention to physical activity and dietary choices. For many who live with diabetes, intensive management adds psychological distress and adverse effects such as hypoglycemia or weight gain (ADA, 2018; Huang, Brown, Ewigman, Foley, & Meltzer, 2007). Undoubtedly, a life with diabetes greatly shapes the quality of life and well-being of all who are affected. Eliminating this burden for tens of millions of additional Americans who will develop diabetes in the next decade requires an unwavering dedication to achieve a goal of primary prevention.

The US Centers for Disease Control and Prevention (CDC) estimates that about 1.9 million more Americans develop diabetes each year, with a vast majority developing type 2 diabetes (CDC, 2017). This is important, because the development of type 2 diabetes is the culmination of a progression from less severe and identifiable stages of abnormal glucose metabolism, collectively referred to as prediabetes. The rate of this progression can vary from months to many years, during which time high-risk individuals can be identified and targeted for more intensive interventions to prevent or delay progression to type 2 diabetes. The purpose of this chapter is to review what is currently known about the primary prevention of type 2 diabetes, including the role of behavioral intervention programs, which currently offer the strongest research-proven solution for achieving this goal.

R. T. Ackermann (✉)
Northwestern University Feinberg School of Medicine, Chicago, IL, USA
e-mail: r.ackermann@northwestern.edu

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Research that Type 2 Diabetes Is Preventable

Extensive past research underscores the potential for individual behavior change to prevent or delay type 2 diabetes among adults with prediabetes (Balk et al., 2015; Gillies et al., 2007, 2012; Stevens et al., 2015). The US Diabetes Prevention Program (DPP) and subsequent translational research studies have demonstrated that intensive lifestyle interventions focused on helping individuals achieve 5–10% weight loss and at least 150 min per week of moderate physical activity can slow the rate of developing type 2 diabetes by about half (Ali, Echouffo-Tcheugui, & Williamson, 2012; Knowler et al., 2002). There also is a graded relationship between the percentage of weight loss achieved and the subsequent extent of diabetes risk reduction. In the DPP, every 1 kg of additional weight loss resulted in about a 16% additional reduction in the rate of diabetes development (Hamman et al., 2006). In this context, a 5 kg weight loss for a 100 kg person (or about 5% weight loss from baseline) is associated with about a 58% reduction in the rate of type 2 diabetes development, whereas a 10 kg (about 10% weight loss) would translate to about a 83% reduction. Lifestyle interventions also improve health-related quality of life for people with prediabetes (Florez et al., 2012), enable some of those people to reduce their need for medications (Ratner et al., 2005), and may lower future healthcare expenditures (Ackermann et al., 2006; Herman et al., 2005; Li et al., 2015; Zhuo et al., 2012). Unfortunately, despite the passage of many years since the DPP trial was published in 2002, most people at high risk for developing diabetes still have not been offered an intensive lifestyle intervention (CDC, 2013). This gap separates millions of high-risk Americans from the most evidence-based solution currently known to prevent type 2 diabetes.

Opportunities and Challenges for Diabetes Prevention in the Real World

Considering the striking increases in type 2 diabetes across our entire population over the past few decades, it is easy to conclude that key features of our environment, quite simply, are geared to promote diabetes development, rather than prevention. Workplace automation, computer workstations, mass transit, decreases in neighborhood walkability, fast food, and food processing are only a handful of secular trends over the past 50 years that likely contribute to this trend. Superimposed on this changing environment, type 2 diabetes development is accelerated by genes, aging, increasing body mass, unhealthful behavior, other health conditions, and sometimes the treatments for those other conditions (Hsueh, 2003). A quintessential question is whether diabetes prevention efforts should focus on ways to reverse what are potentially harmful aspects of our environment or to support individuals to engage in healthier lifestyle behaviors while continuing to live in the environment that now exists. Realistically, a complete solution for type 2 diabetes prevention likely will require a multipronged approach emphasizing high-level approaches, such as policy, systems, and environmental change, as well as more focused intervention programs supporting individual behavioral changes and attempts to elevate our social demand for healthy foods and activity-friendly worksites and communities.

Policy, Systems, and Environment Change in Diabetes Prevention

Policy, systems, and environmental change seem to strike most directly at the heart of the diabetes epidemic. Conceptually, these levers offer a potential to reshape the entire fabric of the dietary and activity patterns for our entire population. Unfortunately, altering our food or physical environment requires time, resources, and high social and political will. In reality, most people can live comfortably with very little physical activity, and all people must eat calories to survive. People also value the autonomy to choose what they wish to eat and drink, particularly if there is not very direct evidence that a specific substance or toxin is the cause of most cases of type 2 diabetes. Broad efforts to limit population intake of calorie dense foods and beverages, such as through the taxation of sugared beverages, have failed to muster enough public support and subsequent political will needed to overcome industry and even community resistance. Unlike in areas such as tobacco control, where policy efforts have successfully targeted compounds and products that are not needed for human health and where an individual's choice to smoke impacts the health of others who are near them, similar solutions to curtail the development of type 2 diabetes are not as forthcoming. What this means is that policy solutions for diabetes prevention, for the time being, are likely to be implemented in ways that are incomplete and incremental.

When policy, systems, and environment changes are made incrementally, they still enable individuals to continue an existing behavior that is more familiar and less healthy. For example, individuals still must choose whether to use a new walking path or to drink water as an alternative if the cost of a sugared beverage has been increased by a tax. Though policy solutions may ultimately provide the most complete solution for restructuring our environment to prevent rather than promote type 2 diabetes, the actual passage and subsequent "ripening" of those policies may be many years away. This may be too late for those who are at very high risk for developing type 2 diabetes today.

Individual Behavioral Change Programs in Diabetes Prevention

Ideally, participation in healthy lifestyle behaviors that are protective against type 2 diabetes would be normative and pervasive in our population. Unfortunately, this is not the case. Over the past 50 years, average daily calorie intake by Americans has increased dramatically and average daily energy expenditure has decreased by about 300 kcal. Until these behavioral trends revert, we will continue to face alarmingly high rates of type 2 diabetes development. In this context, any individual person wishing to reduce their risk of developing diabetes will face the challenge of attempting behavioral changes in the context of a generally unsupportive social and physical environment. An important question is how best to support these attempts to result in sustained and meaningful behavioral changes that can prevent or delay type 2 diabetes.

Before people make purposeful attempts at behavioral changes that run countercurrent to what society as a whole supports, they must be both informed and activated to make a change. When advised about the risks of their current behavioral patterns, individuals often do not adopt the most "rational" behaviors that should lead them toward better health. However, they do value being informed and knowing "what they need to do," even if they do not always choose to do it. Healthy behavioral changes are difficult to adopt and maintain when social influences and the environment that surrounds all of us are more supportive of less healthful behaviors. However, if people remain unaware of the relationships between daily behavior and their personal health, we should not expect them to suddenly attempt a healthy change.

Many researchers and other stakeholders who are interested in areas of health promotion still assume incorrectly that most of the public has a sufficient understanding of how type 2 diabetes develops and the benefits of healthy behavior change as a means to successfully prevent it. Reality seems quite the opposite. Recent reports show that only about 11% of Americans who have prediabetes are aware they have this high-risk condition (CDC, 2013). In addition, among the 89% who are unaware, only about 1 in 20 of them reports success in achieving the behavioral goals that have been shown as protective against diabetes prevention: participating in 150 min of moderate physical activity and achieving ≥7% weight loss in the past year (Gopalan, Lorincz, Wirtalla, Marcus, & Long, 2015). By contrast, among people who report they have been told they have prediabetes, almost twice as many (1 in 11 people) report having attempted and achieved those two steps (Gopalan et al., 2015). These findings suggest that risk awareness is not alone sufficient for people to adopt behaviors that lead to diabetes prevention, but it may be an important motivator for attempting action. At a minimum, adults should be fully aware of how their current behaviors increase their individual risk for type 2 diabetes, as well as the actions they can take to prevent developing it.

Many individuals who are informed and aware of a behavior-related health risk will cycle naturally through phases of increased motivation, goal setting, and even behavioral attempts. When these individuals are provided only brief coaching and simple tools to track their progress, as many as 15% may successfully reach goals for modest weight loss and moderate physical activity (Ackermann et al., 2011, 2015). Unfortunately, these behaviors often do not become habitual or sustained without more intensive forms of ongoing, long-term support. More resource-intensive and longitudinal intervention programs result in a two- to threefold increase in the probability an individual will successfully achieve and maintain meaningful behavioral changes (Balk et al., 2015; Leblanc, O'Connor, Whitlock, Patnode, & Kapka, 2011). Intensive programs work by concentrating additional resources on forms of support that advance an individual's motivational readiness, goal setting, skill-building, and mastery, which are needed when attempting a behavior that is new and is not necessarily supported by family, peers, or the environment.

Research evidence is strongest for intervention programs that focus on goals and support for both diet and physical activity behaviors and those that incorporate the behavioral approaches of goal setting, self-monitoring, self-regulation, stimulus control, and problem-solving (Venditti & Kramer, 2012). More effective programs also involve at least 8–26 h of intervention contact time delivered during 12–26 sessions that are offered over the first 12–18 months (Leblanc et al., 2011). This level of contact defines a minimum necessary "dose" of intervention exposure. Moreover, because each session typically involves a human facilitator or "coach," the more intensive contact also builds a critical element of "supportive accountability"(Mohr, Cuijpers, & Lehman, 2011). Accountability toward a behavior exists when an individual has an expectation that he/she may be called upon to justify his/her actions or inactions to another person (Mohr et al., 2011). Accountability requires real or perceived social interactions with another human (i.e., a coach) who the patient views as trustworthy and possessing suitable expertise. This relationship may be established in person, by telephone, or via an electronic channel (Leblanc et al., 2011). These elements should be considered "essential components" of an effective intensive diabetes prevention program. Though attempts should be made to preserve these core components to maximize the effect of any intensive program, there is a tremendous need to diversify formats and delivery channels to engage and support different segments of our population in ways that are attractive, fun, accessible, and culturally salient.

Challenges and Strategies for the Spread of Intensive Diabetes Prevention Programs

If we know that more intensive behavioral support resources are critical to successful diabetes prevention, an important question is why those resources are not being created and offered on every street corner. One possible answer is simply that there is not a sufficient "market" or consumer demand to encourage the commercial sector to develop and offer enough programs. Although the population that should use such a program is quite large, almost none of these individuals feel ill or have symptoms attributable to prediabetes. This may limit any sense of urgency by those individuals to seek out and pay fees to access programs that provide support for the difficult task of improving lifestyle behaviors.

However, evidence-based lifestyle intervention programs offered in community or clinical settings require costs to administer them – about $424 per person per year (Li et al., 2015). Regardless of whether the organization offering such a program is a commercial entity or a public agency, it must at least recover those intervention delivery costs to remain in operation. If these costs were recovered from individual participants by charging a fee to access the program, the resultant cost would be similar to what many millions of consumers currently pay for commercial weight loss programs such as Weight Watchers (Tsai & Wadden, 2005). Although enrollment in commercial weight loss programs is striking (Marrero et al., 2016), it still represents only a very small fraction of the total population at risk for type 2 diabetes development.

Most people who might conceivably benefit have never enrolled in or paid fees for such a program. Reasons for this could of course include nonfinancial reasons, such as lack of knowledge, a dislike for the format or location, or a variety of other reasons. However, program fees do impose a barrier for many individuals, particularly the elderly and low-income groups that are often at the highest risks for developing diabetes. Even an employed adult who understands he is at risk for diabetes and believes he has control over behaviors that can reduce his risk may not rush to spend limited marginal income for a program to support him in the difficult task of behavioral changes to address a condition that is not causing any immediate symptoms. The inability or unwillingness of high-risk individuals to spend their own resources to secure the support of an intensive diabetes prevention program is indeed a key barrier to reaching a very large population with this evidence-based treatment.

In order to expand the implementation of intensive diabetes prevention programs and their subsequent engagement of a large population of individuals at risk for type 2 diabetes, not only must programs be packaged in more diverse formats and delivery channels, but the costs incurred by individuals to access these programs must be minimal. One common strategy to address this challenge has been to seek public subsidies or other sources of payment for diabetes prevention programs from third parties, such as employers or health insurers. Though this approach lessens the financial burden on individual program participants, it does not necessarily allow the programs to be more accessible in other ways, such as in people's homes, in worksites or schools, or through social media channels.

The average adult in the USA spends about 2300 h per year working, 1000 h in front of a television, 515 h in household activities, 240 h communicating and socializing, 140 h on a computer or playing games, 80 h in civic or religious activities, 115 h in sport or recreational activities, and about 1 h at a doctor's office (BLS, 2016). Intuitively, workplace settings, household settings (television viewing, computer use, and other household activities), and social and civic settings offer the greatest opportunities for exposing individuals to information, resources, and social influences that encourage and support increased physical activity or healthier eating habits. To engage diverse individuals, programs offered through these different channels must also be continually engaging to the individual and culturally salient while continuing to provide the "essential components" of evidence-based diabetes prevention interventions.

Scope and Drivers of Recent Expansion of Community Intervention Programs

One rapidly evolving channel for delivery of evidence-based diabetes prevention programs is via community organizations. Communities are vital channels for diabetes prevention because they define where we work, learn, recreate, and interact with others. Recent action in community implementation of diabetes prevention programs has been motivated by Affordable Care Act provisions that require Medicare, Medicaid, and most commercial health plans to provide full coverage for evidence-based preventive services given an A or B rating by the US Preventive Services Task Force (DHHS, 2010;

NCSL, 2010). In August 2014, the Task Force issued a "B" rating and recommended that all overweight or obese adults with one or more cardiovascular risk factors be offered resource-intensive lifestyle interventions for weight loss, giving specific examples for how the recommendation could be satisfied by linking patients to intensive programs delivered outside of the clinical practice setting (LeFevre & Force, 2014). As one example, YMCA of the USA (YUSA) partnered with UnitedHealth Group, CDC, and others in 2010 to implement an adapted version of the Diabetes Prevention Program (DPP) intensive lifestyle intervention, supported by payments from employers and private health insurers, on a national scale (CDC, 2016; Vojta, Koehler, Longjohn, Lever, & Caputo, 2013). As of October 2017, YUSA reported having offered the YMCA's DPP to more than 55,000 people in nearly 1700 locations in 47 states (YMCA, 2017).

Complementing YUSA's rollout of the DPP, the CDC hosts the National Diabetes Prevention Program (NDPP), offering tools and resources for bolstering community and workforce capacity to deliver DPP (CDC, 2016). As of October 2017, the NDPP registry of recognized DPP delivery organizations listed 26 nationally accessible online programs and 1369 additional non-YMCA organizations delivering programs in all 50 states (CDC, 2015). CDC reports that over 60 health plans now provide some amount of coverage for the NDPP, with the goal of providing an intensive lifestyle intervention program for enrollees who have prediabetes as well as other cardiometabolic risk factors. In March 2016, the US Department of Health and Human Services also announced that Medicare would pay for NDPP interventions for patients with prediabetes (CMS, 2016), a policy that launched nationally in April 2018 and is likely to encourage similar policies by Medicaid and other health payers nationally.

Several commercial programs also have entered contracts with employers or health plans to offer a behavioral weight management resource that fulfills the Task Force directive. One example is Weight Watchers International, which offers both face-to-face and online behavioral weight loss solutions for overweight and obese adults with or without CVD risk factors; Weight Watchers reports 25,000 meetings each week in the USA (Marrero et al., 2016). Another example, Omada Health's "Prevent" program, provides eHealth and mHealth delivered behavioral and social support for overweight and obese adults with prediabetes, dyslipidemia, or hypertension. The combined growth of these evidence-based intensive programs has greatly amplified the reach of diabetes prevention programming in local communities and workplace settings throughout the USA. In addition to maximizing population engagement via these different delivery channels, these efforts all aim to minimize intervention costs while maintaining fidelity to the essential components of an effective behavioral prevention program.

Indeed, a predominant driver of the overall cost of delivering effective diabetes prevention programs is the cost of the intervention workforce. Behavioral programs typically deliver intervention content and provide supportive accountability via the use of trained facilitators or "coaches." Since these individuals are typically paid by an hourly wage, the amount of "human" coaching often becomes the largest cost of a behavioral intervention program. Other costs may include printed or electronic educational and self-monitoring tools and other resources such as weight scales and often a physical space (i.e., except in the case of a virtual delivery model). One way to reach individuals with diabetes prevention programming through an engaging delivery channel that may reduce costs is via remote or mobile technologies. Mobile health technologies offer an alternative and perhaps less costly way to provide supportive accountability by reducing the need for face-to-face visits with human coaches. However, with current technology limitations, it is likely that some individualized coaching from a human is still necessary to develop the trusting relationship and sense of accountability that helps drive behavioral changes in the context of a coaching intervention. This human involvement may become minimized but still adds some cost to offering an effective intervention program. Importantly, most technologies also have costs, such as hardware, software licensing, IT maintenance, data storage, and assuring data security, which will contribute to the overall cost of a program. In this context, health IT offers another opportunity, but not a complete solution, for population level diabetes prevention.

Finding a Complete Solution

Efforts to diversify delivery channels as a means to expand engagement in diabetes prevention programs while lowering costs can also be combined with third-party payment strategies to reduce both overall and individual participant costs to access a program. Although diversification of funding sources and reductions in the incremental costs of delivering diabetes prevention programs to each additional participant are essential to encourage the widest implementation of programs and highest individual participation level, the total population-level impact of delivering individual intervention programs as the predominant approach for diabetes prevention will remain limited by the total costs and by incomplete adoption. If all 160 million overweight or obese American adults did elect to take part in an intensive lifestyle intervention that cost $424 per person, the added annual expenditure would total $67.8 billion per year. Even if the individual intervention cost were cut by half, the total expenditure still would exceed $33 billion annually. It is probably just as unrealistic to assume that third parties will fund this large of an expense for an individual behavioral change program as it is to assume somehow that all people at risk will participate.

These realities underscore how population level diabetes prevention simply is not achievable through a singular intervention strategy. Individuals differ in their preferred channels for receiving health information and are likely not equally receptive to the same intervention. As certain as we can be that not all individuals will go to a YMCA or to Weight Watchers to prevent their diabetes, we also cannot assume that a television program, social media platform, or a better iPhone application will reach all individuals. Because each individual person at risk for developing diabetes may engage with programs or support systems offered via some but not all of these different channels, efforts to maximize the full population-wide reach of diabetes prevention efforts will require an intense focus on diversification of both intervention formats and delivery channels in ways that still preserve fidelity to the “essential” components that make behavioral programs effective. In concert with these diverse strategies for delivering evidence-based behavioral intervention content at the lowest cost possible, it also will be essential that broader population-wide efforts continue slowly to expand knowledge, risk awareness, and social and environmental changes that will not only enable motivated individuals to successfully adopt healthier behaviors but to slowly establish them as the new societal norm. Until this happens, we will continue to have much work ahead of us to achieve the elusive goal of primary prevention of type 2 diabetes.

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Part XI
Policy Level Factors for Adults

Chapter 31
Impact of Health Insurance Policy on Diabetes Management

Rebecca Myerson, Tianyi Lu, Anne Peters, Steven Fox, and Elbert Huang

As the prevalence of diabetes and prediabetes continues to climb, population-level measures to prevent diabetes and improve diabetes management are urgently needed (Bullard, 2018; Huang, Basu, O'Grady, & Capretta, 2009; Selvin & Ali, 2017). Although effective prevention and management interventions are available to reduce the diabetes health burden, widespread population-level implementation of these strategies is not achievable without the involvement of payers and policymakers (Baxter et al., 2016; Diabetes Prevention Program Research Group, 2012; UK Prospective Diabetes Study group, 1998a, 1998b).

In this chapter, we argue that insurance policy can play a key role in managing diabetes burden at the population level. We summarize some of the available evidence linking the availability of affordable insurance covering diabetes care to changes in prevention, diagnosis, and treatment of diabetes. We also comment on the possibly different effects for patients with Type 1 (T1D) vs. Type 2 diabetes (T2D) and summarize some of the evidence on new payment models in Medicare that can affect diabetes management.

Prevention of Type 2 Diabetes

As of April 1, 2018, all Medicare beneficiaries with prediabetes are eligible to receive a version of the Diabetes Prevention Program (DPP) lifestyle intervention called the Medicare Diabetes Prevention Program (Centers for Medicare and Medicaid Services, 2018). This intervention aims to

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R. Myerson (✉)
Department of Population Health Sciences, University of Wisconsin Madison,
Madison, WI, USA
e-mail: rmyerson@wisc.edu

T. Lu · S. Fox
Department of Pharmaceutical and Health Economics, University of Southern California,
Los Angeles, CA, USA

A. Peters
Department of Medicine, University of Southern California, Los Angeles, CA, USA

E. Huang
Department of Medicine, University of Chicago, Chicago, IL, USA

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prevent development of diabetes in overweight or obese people with prediabetes through a series of courses and exercise materials designed to achieve and maintain a loss of 7% of body weight. The policy decision was ultimately based on a CMS innovation project that found that the intensive lifestyle intervention saved money. This innovation project was in fact the culmination of a long history of clinical trials and translational studies that are briefly reviewed below.

The original Diabetes Prevention Program trial, in individuals selected to be at particularly high risk for progression to T2D, found that intensive lifestyle intervention reduced the incidence of T2D by 58% over an average follow-up of 2.8 years, and the reduction in diabetes incidence remained significant even after 10 years (Diabetes Prevention Program Research Group, 2002, 2009). This resembled findings from similar international studies (Pan et al., 1997; Tuomilehto et al., 2001). Cost-effectiveness analyses of the DPP data found the intervention to be highly cost-effective, meaning that the intervention's up-front costs were offset by subsequent benefits such as reductions in need for medical care and improvements in quality of life (Diabetes Prevention Program Research Group, 2009; Herman, 2015).

Subsequently, the DPP program was adapted to community settings. The YMCA trial findings, in particular, were crucial to the Medicare coverage decision. In 2013, the YMCA of the USA received an award from the Centers for Medicare and Medicaid Services (CMS) to deliver the program in 17 participating YMCAs across the nation. The program was coordinated and taught by trained YMCA lifestyle coaches. An evaluation of this program compared both health spending and medical utilization between participants and a matched control group of nonparticipants using Medicare claims data. The weighted average quarterly saving of Medicare spending per member per quarter was $278, with the strongest effect in the first three quarters after enrollment. The YMCA program was also associated with significant decreases in inpatient admissions and emergency department (ED) visits (Alva, Hoerger, Jeyaraman, Amico, & Rojas-Smith, 2017).

Another community-based version of the DPP, for Medicaid enrollees in Minnesota with prediabetes, We Can Prevent Diabetes (WCPD), was also found to be cost-effective for that low-income population at high risk for diabetes. This program provided financial incentives for participation and weight loss. The incremental cost-effectiveness ratio was estimated to be $14,011 per QALY, which is considered highly cost-effective by commonly accepted standards (Gilmer et al., 2018). Some private insurers also provide coverage for diabetes prevention programs based on this body of evidence.

Diagnosis

In the USA, almost one-quarter of all diabetes cases are undiagnosed (7.2 million) (National Center for Chronic Disease Prevention and Health Promotion, 2017). Timely diagnosis of diabetes improves health outcomes by increasing access to diabetes management. First, diagnosis leads to increases in doctor visits to manage diabetes (Myerson, Colantonio, Safford, & Huang, 2018). Timely initiation of doctor visits, in turn, is associated with improved health outcomes for patients with diabetes. For example, a large, longitudinal study showed that patients who initiated management of diabetes while still at a relatively low fasting plasma glucose (<140 mg/dl [<7.8 mmol/l]) subsequently had a significantly lower risk of any diabetes-related complications, diabetes-related death, all-cause mortality, myocardial infarction, peripheral vascular disease, and microvascular disease (Colagiuri, Cull, & Holman, 2002).

Insurance status is significantly associated with the risk of delayed diagnoses. By some estimates, people with diabetes who lack health insurance are twice as likely to be undiagnosed as diabetes patients with health insurance (Wilper et al., 2009). However, it is difficult to ascertain the *causal* impact of health insurance on diabetes diagnosis and treatment by simply comparing people with versus without insurance, since there may also be many other unmeasured differences between individuals with or without insurance that could also affect those outcomes (Levy & Meltzer, 2008). To address that issue, other studies have exploited random or quasi-random changes in policy to further assess the causal relationship between access to insurance and diabetes diagnosis and care. The evidence presented here on the impacts of insurance policy on diagnosis and treatment draws from those experimental and quasi-experimental studies.

Increases in access to health insurance have been associated with increases in diabetes diagnosis. In 2008, Oregon expanded access to Medicaid insurance among eligible nondisabled low-income adults using a random lottery. This Medicaid coverage expansion significantly increased the absolute probability of a diabetes diagnosis by 3.8 percentage points (Baicker et al., 2013). Other studies examine the effects of expanding Medicaid insurance to low-income adults under the Affordable Care Act (ACA), which occurred in some states but not others. The ACA originally required that all states expand Medicaid eligibility to all adults with incomes below 138% of the federal poverty level, but a US Supreme Court decision made expansion voluntary for the states. Ultimately, many states opted out, creating quasi-experimental variation in the implementation of Medicaid expansion. States that expanded Medicaid under the ACA showed a 23% increase in the number of Medicaid-enrolled patients with newly identified diabetes, compared with 0.4% in states that did not expand Medicaid (Kaufman, Chen, Fonseca, & McPhaul, 2015).

The additional increase in diabetes diagnosis in Medicaid expansion states was further corroborated by similarly large increases in the use of metformin (the first-line medication for people with new onset T2D) among patients eligible for Medicaid. Indeed, metformin accounted for more than 40% of the additional increase in antidiabetic medications filled using Medicaid insurance in states that expanded Medicaid under the ACA (Myerson, Lu, Tonnu-Mihara, & Huang, 2018).

Changes in patient cost sharing for diagnostic tests mandated under the ACA could also pave the way to timely diagnosis of diabetes. Section 2713 of the ACA requires that health insurance issuers "not impose any cost sharing requirements for evidence-based items or services that have in effect a rating of A or B in the current recommendations of the US Preventive Services Task Force" (USPSTF). As of October 2015, the USPSTF recommends diabetes screening (evidence grade B) for all overweight or obese adults between the ages of 40 and 70 (Selph et al., 2015). That recommendation is currently under review, and recommended screening may soon be expanded to younger ages. A recent study estimated that 76 million Americans were newly eligible for expanded preventive services coverage under the ACA (Burke & Simmons, 2014). An estimated 2.3 million out of the 4.6 million people aged 18–64 with undiagnosed diabetes in 2009–2010 could have gained access to diabetes screening without cost sharing due to this policy (Myerson & Laiteerapong, 2016).

Medication Use

In addition to lifestyle modifications, medications are also often necessary for the management of diabetes. The UK Prospective Diabetes Study found that newly diagnosed patients with diabetes assigned to control their blood glucose intensively with diet and medication (sulphonylurea or insulin) to reduce the fasting glucose level to less than 6 mmol/L rather than conventional policy designed to treat for symptoms of diabetes and/or target a fasting glucose level of <15 mmol experienced improved glycemic control (7.0% vs. 7.9%) and experienced significantly lower risk of diabetes-related end points, diabetes-related mortality, and all-cause mortality over 10 years (UK Prospective Diabetes Study group, 1998b). In hypertensive patients with diabetes, tight blood pressure control is recommended given research from the UK Prospective Diabetes Study and other studies showing substantial declines in the risk of all diabetes-related end points, deaths related to diabetes, stroke, and microvascular end points (Association, 2018; Sarafidis, Lazaridis, Ruiz-Hurtado, & Ruilope, 2017; Turner et al., 1998).

The cost of diabetes medications has rapidly escalated, raising concerns about affordability (Greene & Riggs, 2015; Squires et al., 2018). Newer medications, including more sophisticated insulin formulations, are particularly costly. The number of antidiabetic drug classes has tripled since the early 1990s, and the mean expenditure per patient for newer insulin analogues, noninsulin injectables, and newer oral antidiabetic medications was almost double that for the comparable older medications. In the period 2002–2013, insulin's mean price rose 197% – growth faster than that of any other drug class used to treat diabetes. Estimated insulin spending per patient more than tripled, from $231.48 in 2002 to $736.09 in 2013 (Hirsch, 2016; Hua et al., 2016).

Gaining insurance may facilitate uptake of costly diabetes medications by reducing out of pocket costs. Below, we summarize literature linking changes in the availability of Medicaid insurance, Medicare Part D insurance, and cost sharing in private insurance with variations in diabetes prescription fills.

Medicaid

Medicaid expansions under the Affordable Care Act (ACA) were associated with increases in fills for antidiabetic drugs (Myerson et al., 2018). During 2014 and 2015, states with Medicaid expansions experienced an additional 40% increase in diabetes prescriptions filled using Medicaid insurance, compared to non-expansion states. The Oregon health insurance experiment also found large effects of Medicaid coverage expansions on the use of diabetes medication: Medicaid coverage increased use of diabetes medications by an additional 5.4 percentage points, representing more than an 80% increase above the control group rate (Baicker et al., 2013).

About a third of the increase in Medicaid diabetes prescription fills after ACA Medicaid expansions constituted costly newer classes of drugs, including both rapid- and longer-acting insulin analogues, extended release metformin, and various second-line oral medications: dipeptidyl peptidase [DPP]-4 inhibitors, GLP-1 agonists, and SGLT-2 inhibitors. This represented an increase in use of these newer drugs overall, compared with uninsured patients: prior to the eligibility expansions, 15% of diabetes prescriptions filled using cash were for these newer medications, compared with more than 30% of prescriptions filled using insurance (Myerson et al., 2018). Long-acting- and rapid-acting insulin analogues accounted for more than two-thirds of the increased use of newer drugs in this study, which included data through 2015. Costly newer antidiabetic drugs will likely be increasingly recommended due to the accumulating evidence of their benefits for patients with established cardiovascular disease, heart failure, or chronic kidney disease.

A comparison across drug classes indicated that fills of antidiabetic drugs increased more than any other prescription drug class after Medicaid eligibility expansions under the ACA (Ghosh, Simon, & Sommers, 2017). People with diabetes who gained Medicaid coverage also benefited from larger absolute reductions in out-of-pocket spending (over $300) than people without a chronic condition who gained Medicaid coverage ($152) (Mulcahy, Eibner, & Finegold, 2016).

Although much of the research in this field focuses on Medicaid, which is available for adults and children depending on the state, the availability of public coverage (via the Children's Health Insurance Program (CHIP)) is clearly relevant for children. Enrollment in CHIP is associated with fewer unmet health-care needs and higher use of prescription drugs for children with special health-care needs such as diabetes Clemans-Cope, Kenney, Waidmann, Huntress, & Anderson, 2015; Zickafoose, Smith, & Dye, 2015).

Medicare Part D

Medicare Part D, implemented in January of 2006, expanded uptake of antidiabetic medications among Medicare beneficiaries by providing new options for prescription drug coverage. Enrollment in Medicare Part D was associated with increases in the number of monthly antidiabetic medication prescriptions by 44% among Medicare enrollees with no previous drug coverage and by 13% among Medicare enrollees who previously had a $150 quarterly benefit cap (Zhang, Donohue, Lave, O'Donnell, & Newhouse, 2009).

The coverage provided by Medicare Part D is not uniform across different patient use profiles. As an individual patient's prescription costs increase beyond a moderate threshold, coverage for medications decreases (the Part D coverage gap) and then increases again (the catastrophic coverage phase). Overall, 26% of Medicare Advantage beneficiaries with diabetes from two large California health plans reached their Part D coverage gap, and 2% reached the catastrophic coverage phase (Schmittdiel et al., 2009). This structure appears to affect utilization of medications for patients with diabetes. Having a Medicare Part D coverage gap was associated with lower total drug cost, higher out-of-pocket spending, and worse medication adherence among Medicare beneficiaries with diabetes (Fung et al., 2010). This coverage gap is gradually being closed as part of the ACA.

Private Insurance

Patients' use of antidiabetic agents is highly sensitive to changes in cost sharing in private insurance markets as well, with a doubling of patients' co-payments associated with a 25% reduction in their use of antidiabetic agents (Goldman et al., 2004). A review of the literature indicated that increased cost sharing in prescription drug plans is broadly associated with lower rates of drug treatment, worse adherence, and more frequent discontinuity of therapy across multiple settings (Goldman, Joyce, & Zheng, 2007).

Hospitalization Related to Diabetes

Effective diabetes management decreases the risk of subsequent diabetes-related hospitalizations (CDC Diabetes Cost-effectiveness Group, 2002; Jha, Aubert, Yao, Teagarden, & Epstein, 2012). Thus, diabetes-related hospitalizations are sometimes tracked as an indirect, population-level measure of diabetes management (Bindman et al., 1995; Davies et al., 2009; National Center for Chronic Disease Prevention and Health Promotion, 2017). A number of studies have examined whether changes in insurance policy are linked to declines in diabetes-related hospitalizations.

The evidence linking Medicaid insurance expansion to declines in diabetes hospitalizations is mixed. One study linked expansion of eligibility for Medicaid under the ACA to declines in diabetes-related hospital discharges by about 4 per 100,000 population (Freedman, Nikpay, Carroll, & Simon, 2017). Similarly, Wisconsin also saw declines in hospitalization related to diabetes after expanding access to a Medicaid-like public insurance in 2008–2009 (DeLeire, Dague, Leininger, Voskuil, & Friedsam, 2013). In contrast, the Oregon Health Insurance Experiment found that Medicaid insurance did not significantly change rates of hospitalization for diabetes, or other ambulatory care-sensitive conditions, during the first year (Finkelstein et al., 2012). Studies with longer follow-up found that Medicaid coverage actually increased emergency department visits, but diabetes visits were not reported separately (Finkelstein, Taubman, Allen, Wright, & Baicker, 2016; Taubman, Allen, Wright, Baicker, & Finkelstein, 2014).

Evidence from Medicare Part D indicated that expansions in access were linked with declines in hospital visits related to uncontrolled diabetes among older adults (Afendulis, He, Zaslavsky, & Chernew, 2011; Lipska et al., 2014). Massachusetts health-care reform, which increased coverage using multiple policy tools, was likewise associated with declines in preventable admissions that resulted from long-term diabetes complications, after adjusting for other patient risk factors. The main benefit was seen among diabetes patients who had fewer or no previous complications or comorbidities. For those patients, access to outpatient care was associated with a decline in preventable admissions (Kolstad & Kowalski, 2012).

Relevance of these Issues for Patients with Different Types of Diabetes

Thus far, we have discussed the relevance of insurance policy for prevention, detection, and management of diabetes overall. Yet, specific policy issues may have different relevance for patients with T1D vs. T2D or for diabetes that is or is not insulin-requiring (i.e., T1D and insulin-requiring T2D). In this section, we briefly review some of the key differences.

Gaps in insurance status are associated with clinically important diagnostic delays for not only T2D but also for T1D, exemplified by the prevalence of life-threatening diabetic ketoacidosis at the time of diagnosis. In a Colorado study of newly diagnosed T1D patients under age 18, the odds ratio for presenting in diabetic ketoacidosis was 0.37 for patients with private insurance, and 0.67 for patients with government insurance, as compared with uninsured patients (Rewers, Dong, Slover, Klingensmith, & Rewers, 2015). Conversely, diabetes prevention initiatives are most relevant for averting new onset T2D but not T1D, because while T2D can often be prevented, T1D is not currently considered preventable.

Treatment needs also differ between patients who do or do not require insulin and also for patients with T1D vs. T2D. Those differences shape the impact of gaps in insurance coverage on the health of these different patient groups. Insurance is particularly crucial for affordability in insulin-requiring patients, because the cost of insulin has escalated more quickly than the cost of other diabetes drugs (Hirsch, 2016; Hua et al., 2016). Additionally, proper (and safe) management of insulin-dependent diabetes requires patients to have access to testing and/or glucose monitoring devices, so that they can readily monitor their blood glucose (American Diabetes Association, 2018; Beran & Yudkin, 2010). Given the high cost of these supplies, it seems plausible that out-of-pocket cost reductions provided by insurance could increase patients' compliance with self-monitoring of blood glucose (Chiang, Kirkman, Laffel, & Peters, 2014; Rogers, Lee, Tipirneni, Banerjee, & Kim, 2018; Silverstein et al., 2005). Increases in insurance coverage for diabetes testing supplies and glucose monitors are associated with increases in their use (Li, Zhang, & Narayan, 2008; Li, Zhang, Barker, & Hartsfield, 2010; Soumerai, Mah, Zhang, et al., 2004) and may also improve overall glucose control (Bowker, Mitchell, Majumdar, Toth, & Johnson, 2004).

Accordingly, interruptions in health insurance coverage appear to have more severe impacts on health for patients with T1D in the short run. One study of 168,612 working age adults with T1D found that 24% experienced an interruption in their private health coverage during a mean follow-up duration of 2.6 years. Patients with T1D who experienced interruptions in coverage had a 3.6% relative increase in their glycated hemoglobin, and their use of acute care services increased fivefold (Rogers et al., 2018). These changes in health outcomes could result from the disruptions in the access to medication, devices, and testing supplies that patients with insulin-dependent diabetes require. In contrast, gaining insurance coverage for 2 years had no detectable effect on health for patients with diabetes overall, most of whom have T2D (Baicker et al., 2013).

A key limitation is that these studies document short-run effects. The extent to which insurance coverage improves glycemic management and prevents complications for T1D and T2D patients in the long run remains unclear. This is a key gap in knowledge because prevention of complications can result in substantial savings for the health-care system (Baxter et al., 2016; McEwan, Bennett, Bolin, Evans, & Bergenheim, 2018; Parekh et al., 2018).

New Payment Models for Medicare Patients

A number of new payment models are being tested or implemented that could affect diabetes care for patients with Medicare insurance. In this section, we review a number of these payment models and the available evidence regarding their impacts on diabetes care.

Value-Based Insurance Design

Value-based insurance design is a type of insurance design under which patient cost sharing for services is determined based on the service's value (Choudhry et al., 2010). This approach often reduces patients' cost sharing for diabetes medications, which may in turn improve adherence to diabetes treatment. For example, a value-based co-pay reduction implemented by ActiveHealth Management was associated with reductions in diabetes medication nonadherence by 14% (Chernew et al., 2008). Another large commercial insurer eliminated generic and insulin co-payment (reducing them from $15 to $0) among other cost sharing reductions. Patients exposed to this change had a significantly higher diabetes treatment initiation rate (2.3% vs 1.6%) and lower discontinuation rates (16.0% vs 24.3% for newly treated patients, and 26.0% vs 29.8% for those on continuing treatment) (Chang, Liberman, Coulen, Berger, & Brennan, 2010). In contrast, another value-based insurance program, in a large global pharmaceutical company, reduced patient cost sharing for prescription drugs for diabetes but found no increase in adherence or fills (Gibson et al., 2011).

Starting in 2017, a value-based insurance design model is being applied within 12 Medicare Advantage Plans, private HMO-style plans which provide an alternative to traditional Medicare coverage. As part of the initiative, these plans may offer alternate benefit designs that reduce cost sharing or offer additional services for enrollees in certain clinical categories such as those with diabetes. This pilot initiative will continue until 2021, with additional plans added to the pilot over time (Centers for Medicare & Medicaid Services, 2018). Given the large fraction of Medicare patients with T2D and prediabetes, and the potential for a successful approach to significantly reduce morbidity and mortality, the observed health outcomes for diabetes patients in those pilot plans should strongly influence future use of this insurance model.

Accountable Care Organizations

Under an Accountable Care Organization (ACO) structure, Medicare ACO providers receive a portion of the savings that accrued to Medicare if the costs of care for their attributed beneficiary population fall sufficiently below a set benchmark. The proportion of savings gained by providers is further linked to their performance on quality metrics that emphasize care coordination and prevention; these include measures specific to diabetes (Centers for Medicare and Medicaid Services, 2017). Thus, ACO providers are incentivized to reduce costs while maintaining quality of care for patients with diabetes.

Evidence on the impact of ACO contracts on diabetes care is somewhat mixed. The first year of the Pioneer ACO program was associated with significant increases in preventive services for beneficiaries with diabetes, although not with changes in combined hospitalizations for diabetes or cardiovascular disease (McWilliams, Chernew, Landon, & Schwartz, 2015). In contrast, a subsequent study of ACO providers in 2013 found no links between the program and use of preventive services among beneficiaries with diabetes (McWilliams, Hatfield, Chernew, Landon, & Schwartz, 2016). Subsequent studies also found that the ACO program was not associated with a decline in hospitalizations for ambulatory care-sensitive conditions such as diabetes (McWilliams, Chernew, & Landon, 2017). Yet, quality of care for patients with diabetes may have improved in other ways: for example, ACO providers reported higher mean scores than other providers on timely care and clinical communication (Nyweide et al., 2015).

Comprehensive Primary Care Initiative

In October 2012, Medicare collaborated with 39 other public and private payers to design and execute a 4-year test of a new model primary care financing and delivery model in seven regions across the USA. The Comprehensive Primary Care Initiative aimed to both improve the quality of primary care and reduce costs. The program provided support to selected primary care practices in three key ways: (1) paying a non-visit-based care management fee per beneficiary per month, (2) offering providers the opportunity to earn shared savings, and (3) delivering data feedback and learning support. First, the initiative included risk-stratified care management. Care management fees were distributed to practices in the initiative based on the patient's hierarchical condition category (HCC) ranking at the time the patient was firstly attributed to the practice (i.e., higher fees were paid to providers caring for patients with more comorbid conditions). Second, initiative practices that met targets for improved quality were also eligible for shared savings beginning in the second year of the initiative. The goal of this fee structure was to encourage primary care providers to engage in quality improvement activities, such as improving control of glycated hemoglobin for patients with diabetes. Third, the practices received practice-level feedback on Medicare FFS expenditures, service use, patient experience, and practice approaches to help them identify areas of performance success and weakness (Ayanian & Hamel, 2016; Dale et al., 2016).

During the first 2 years of the Comprehensive Primary Care Initiative, practices participating in the program did not exhibit an improvement in their quality of care or in reported patient experience, nor were there any significant changes within the overall cohort in total Medicare spending, emergency department visits, or hospitalizations. Among high-risk patients with diabetes, patients in practices participating in the initiative were more likely to receive four recommended tests: glycosylated hemoglobin, fasting lipids, urinary protein, and retinal eye examination (Dale et al., 2016). However, 4 years after implementation of the initiative, those effects on recommended testing among high-risk patients with diabetes were no longer statistically significant, while other findings remained largely unchanged (Peikes et al., 2018).

The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA)

In 2015, Congress enacted the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), to establish a two-track performance-based payment system.

The first track is the Merit-Based Incentive Payment System (MIPS) for physicians primarily reimbursed via Medicare fee-for-service. Physicians in that system are subject to quality reporting requirements to receive bonuses or penalties related to their performances. Performance will be evaluated based on quality of care, resource use, meaningful use of electronic health records (EHRs), and clinical practice improvement. These performance measures include activities closely related to diabetes care, such as glycemic management services, as well as both chronic and preventative care management for empaneled patients. The second track is for physicians participating in certain alternative payment models (APMs). Qualified APMs must make use of certified electronic health records, report required quality measures, and bear more than nominal downside financial performance risks. Physicians in this track are provided significant financial incentives based on quality measures comparable to those used in MIPS.

Data on the performance of the MACRA programs is not yet available. In a nationwide survey of internal medicine physicians, the majority believed that the MIPS quality measures will ultimately improve the value of patient care. At the same time, 60% of the physicians reported being not at all or only slightly familiar with MACRA's requirements (Liao, Shea, Weissman, & Navathe, 2018). Other physicians have concerns about the complexity and high-risk sharing involved in MACRA (Casalino, 2017; Liao et al., 2018; Wynne, 2016).

Conclusions

Diabetes and prediabetes affect a large and increasing fraction of the US population, imposing a significant morbidity and mortality burden. Proven programs and medication regimens exist that can improve health and cost outcomes by preventing progression of prediabetes to diabetes. For example, the Diabetes Prevention Program and other insurance-reimbursed programs that adopted a lifestyle modification emphasis, such as the Medicare's YMCA demonstration, and Minnesota Medicaid's "We Can Prevent Diabetes" initiative yielded health benefits that made the programs cost-effective or even cost saving. Insurance coverage for such interventions has just become more widespread in 2018, and the impact of this change in coverage on program uptake is not yet known.

Increases in insurance coverage, such as those achieved by expanding Medicaid eligibility to include non-disabled adults, improve the rate and timeliness of diabetes diagnosis. Diabetes diagnosis rates should further improve given the ACA mandate to cover preventative services recommended by the USPSTF without any patient cost sharing, including testing for elevated blood glucose. Similarly, gaining insurance coverage and reducing patient co-pays both significantly increase the fraction of diabetes patients who initiate and adhere to an appropriately comprehensive medication regimen. This finding has been replicated using data from Medicare Part D, Medicaid, and employer-based health coverage.

The evidence on the impacts of access to insurance on diabetes-related hospitalizations is more mixed. Analysis of ACA-supported Medicaid expansions, a similar Wisconsin expansion, and Massachusetts health insurance expansions found significant reductions in diabetes-related hospitalizations associated with these policies. In contrast, the Oregon Health Insurance Experiment did not show any decline in diabetes-related hospitalizations, and all-cause emergency department utilization increased. Other evidence suggests that health insurance coverage is most likely to improve diabetes control and reduce acute care utilization for patients with insulin-dependent diabetes. Therefore, the population-level effects of insurance on hospitalization may depend on what proportion of the patients with diabetes in a population are insulin-dependent, among other factors.

These findings are timely given recent changes in private health insurance markets. The ACA included measures to improve access to private insurance among people with diabetes. Starting on January 1, 2014, all individual and small group market health plans created after March 23, 2010 were required to provide coverage for medications as an essential benefit. Plans were also no longer permitted to take diabetes status (or other health conditions) into account in calculating premium prices or in deciding whether to accept an applicant. However, new rules promulgated in 2018 has increased access to short-term, limited-duration insurance and association health plans which will be exempt from these requirements (Katie, 2018, Keith, 2018). Ultimately, this may adversely impact patient adherence to optimal diabetes management regimens.

Finally, we found that the evidence on insurance policies that change provider reimbursement is still accumulating. Value-based insurance programs that reduce patient co-pays for highly effective treatments may improve medication initiation and adherence. A large Medicare Advantage pilot of this program is in progress, and more data may be available soon. Accountable Care Organization structures do not appear to consistently improve diabetes care or reduce hospitalizations for ambulatory care- sensitive conditions such as diabetes. The Medicare Comprehensive Primary Care Initiative, which offered financial incentives for primary care management of diabetes patients, also showed no persistent improvements in diabetes care or changes in related hospitalizations. Meanwhile, data are not yet available on the changes in outcomes associated with Medicare's new Merit-Based Incentive Payment System and Alternative Payment Models. Only time will tell if those incentives improve quality of care or health outcomes for patients with diabetes.

What can we conclude from this literature about the impact of insurance design on care outcomes for patients with or at risk for diabetes? First, recent expansions in insurance coverage for diabetes prevention lifestyle programs for people with prediabetes should improve health, if they sufficiently increase program uptake. Second, expanding access to insurance coverage and reducing co-pays for diabetes medicines and testing supplies will increase diagnosis and treatment of diabetes, including blood glucose monitoring and use of medications. Third, provider-side financial incentives to improve diabetes care have not yet been shown to persistently improve diabetes management, but several large investigations in progress may soon provide additional evidence.

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Part XII
Conclusions for Adult Populations

Chapter 32
Summary and Implications for Clinical Practice and Research in Adult Populations

David G. Marrero and Alan M. Delamater

Diabetes has been recognized for over 5000 years. For generations, the ability to effectively treat it was virtually nonexistent. Fortunately, over the past few decades, there has been a virtual explosion of advances that have significantly changed the ability to control the disease. These include the discovery and production of insulin, the growth of a wide array of pharmacologic treatments, and the increasing use of advanced technologies that enable us to assess the adequacy of therapy and make appropriate therapeutic decisions. For example, the introduction of using glycosylated hemoglobin A1c, systems that enable patients to measure their glucose at home, and the continuing rise of continuous glucose monitoring have significantly improved therapeutic strategies and patients' ability to self-manage their condition. In addition, the role of education in achieving more optimal outcomes is now widely recognized and routinely integrated into routine care.

In many respects, we are living in the Golden Age of diabetes therapy where achieving a normal lifespan is more the norm than the anomaly of past generations. There remains, however, a need to more critically address the mental health issues that are inherent with a chronic condition that demands substantial effort by both those who are affiliated by diabetes and their significant others who share in the treatment burden. With the myriad of advances in diabetes treatment is a concomitant increase in personal decision-making and the potential to increase both the physical and emotional burden for patients. It is increasingly evident that diabetes is associated with both short- and long-term consequences that can significantly impact health and emotional well-being. In this regard, the chapters in Parts VII–XI of this book have attempted to address the many issues that are inherent in managing diabetes as we seek to develop a greater understanding and a more optimal approach to its management. We have engaged experts in several domains of diabetes to reflect on the critical issues that still demand our attention and conjecture on what research is needed to drive both the research and clinical fields forward. In this chapter, we review the summaries and implications suggested by these authors for the future of research and clinical practice for type 1 diabetes (T1D) and type 2 diabetes (T2D) in adults.

In Chap. 18, Chertman, Neuman, and Vendrame provided an update on our current understanding of strategies for diabetes medical management. They illuminate a growing concern: that diabetes has become a global emergency in the adult population with T2D and is closely tied to the increasing prevalence of obesity. Indeed, they point that a new term "diabesity" has been used to indicate the

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D. G. Marrero
Center for Border Health Disparities, University of Arizona, Tuscon, AZ, USA

A. M. Delamater (✉)
Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA
e-mail: adelamater@med.miami.edu

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combination and relationship of diabetes and obesity. Importantly, they emphasize that the combined occurrence of obesity and diabetes is closely linked to adverse cardiovascular events. As a result, there is a growing emphasis on developing new drugs able to target the cardiovascular system that are not limited to controlling glucose levels. In this context, they stress that it is crucial that patients acquire awareness of diabetes and its complications. They point out that many persons do not understand that diabetes and obesity are prime contributors to cardiac events, which remain a leading cause of death among those with T2D. Of concern clinically, macrovascular events associated with the disease are often ignored. This is often the case with persons from ethnic minorities and low social economic status. As a result, there continues to be increased morbidity and mortality for both T1D and T2D. They emphasize that it is imperative that we invest in education to increase awareness in both individuals and communities about the links between diabetes and obesity to cardiovascular disease and encourage and support behavioral changes. Achieving this aim will help improve both life expectancy and quality of life of patients with diabetes.

This theme is continued in Chap. 19 by Venditti, Emery, and Kolko, who reviewed biobehavioral factors related to the development and course of T2D and cardiometabolic impairment in adults. As was the case in Chap. 18, the critical role of weight, diet, physical activity, and other lifestyle behaviors was discussed. They reviewed many of the empirical findings from the past decade that highlight the importance and significance of biobehavioral factors associated with the natural history of cardiometabolic impairment and the onset and course of T2D. Their review suggests that if we are to combat the dual epidemics of obesity and T2D, a research agenda that integrates a more comprehensive biobehavioral, social-ecological, and healthy aging framework is needed.

They argue that such a framework will require innovative studies concerning the role of diet composition, eating habits and patterns, physical activity and inactivity, and variability in behavioral phenotypes over the lifespan in relation to biomarkers inclusive of lipid, glucose, and insulin physiology, inflammatory processes, and the gut microbiome. Such integration will aid in the development of effective preventive and disease management approaches. Moreover, they suggest that to be optimally effective, it will also be necessary to understand the impact of other behavioral lifestyle factors such as sleep, cigarette smoking, alcohol use, and psychosocial stress. They suggest that current research in these areas, in association with neuroendocrine, cardiometabolic, immune function, and functional quality of life outcomes, widens the scope of diabetes-relevant inquiry and further highlights the critical importance of social-ecological and lifespan research approaches.

In Chap. 20, Hoogendoorn, Shapira, Roy, Kane, and Gonzalez address an area of recent, but growing awareness that with increasing therapeutic options, there is also increased potential to impact patients' perceptions of distress and quality of life. These factors are often included in a category termed "Patient Reported Outcomes" (PROs). PROs are broadly defined as "a measurement based on a report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else" (US FDA, 2006). Thus, PROs can describe many related but distinct concepts including emotional and psychological well-being, health-related quality of life (HRQOL), and diabetes distress, which involves perceptions of treatment burden including social and healthcare provider relationships.

The authors point out that there is a growing trend for patient-centered care in which providers are viewing biological processes in the context of the individual's psychosocial and cultural environment. In this context, PROs have emerged as valid, reliable, and meaningful constructs reflecting aspects of a patient's health and well-being that are not fully captured by physiological measures alone. Moreover, they argue that measuring PROs becomes particularly important for guiding care recommendations and informing shared decision-making among physicians and their patients. They point out that using PROs requires careful selection of measurement tools. They note that while the FDA has stimulated the use of PROs as outcome measures for new drugs and devices, they have also shown concern about psychometric properties and standardization of various PRO measures (US FDA, 2006; Brown, Kennedy, Runge, & Close, 2016) and have suggested a four-stage process for PRO instrument development and modification. They also note that "retrospective reports of these constructs in study designs that attempt to relate these reports to distal outcomes (e.g., A1c) and crudely measured exposures (e.g., complications, yes/no) are limited in their ability to shed light on what is surely a bidirectional and dynamic process."

Based on these observations, they argue that several adjustments to measurement practices seem warranted. They suggest that investigators who are either constructing or revising measures should consider the wording of items, so that emotional responses are more clearly captured rather than cognitive or behavioral aspects related to an emotional response. Qualitative studies could also help identify current omissions to constructs to help identify additional domains not currently assessed by available measures.

One issue of concern is when assessing HRQOL, agreement on conceptualization of HRQOL remains unclear, with some definitions focusing more on life satisfaction/well-being and others focusing more on overall life quality. Future work will need to further tease apart conceptual and measurement overlap between health and HRQOL. They strongly suggest that to get a full picture of the impact of diabetes, HRQOL should considered as equally important as measures of glycemic control and self-care.

Finally, they suggest that as health professionals increase their assessment of PROs, it will be important to better understand the underlying biopsychosocial and cultural mechanisms linking PROs to objective measures of behavior and health (Young-Hyman et al., 2016). A greater understanding of the cultural and ecological processes that influence patient's behavior in complex health and social systems will be essential to move us toward a patient-centered model of diabetes care.

In Chap. 21, Blevins, Gonzalez, and Wagner continue the discussion of PROs by reviewing evidence that support the importance of depression and anxiety in diabetes care. The importance of the role that depression and anxiety play in diabetes self-management has been recognized by the American Diabetes Association's release of a position statement on the psychosocial care of individuals living with diabetes (Young-Hyman et al., 2016). The recommendations to providers include consideration of routine annual screening of all patients with diabetes for depression and screening for anxiety disorders in those exhibiting anxiety-related symptoms. They do point out, however, that currently there is no direct evidence supporting that depression screening programs without integrated enhancements in depression care are effective in improving depression outcomes. This lack of evidence has resulted in some investigators cautioning against routine screening in diabetes and arguing that depression screening could unintentionally harm patients who do not derive benefit from treatment but who experience side effects and expose patients to distressing information related to being misidentified through a false-positive result. Moreover, critics argue that screening can be expensive and can reduce availability of mental health services that are often scarce (Thombs & Ziegelstein, 2014).

These observations lead the authors to recommend that providers should consider screening for problems related to depression and anxiety and should appreciate the importance of coordinating these efforts with systems that can provide subsequent assessment, treatment, and follow-up. To control for the issue of potential false positives, they suggest that readily usable instruments with strong psychometric properties should be utilized, especially in the presence of symptoms reported in response to assessments of well-being that should be part of routine care for diabetes (Young-Hyman et al., 2016; Young-Hyman & Davis, 2010).

With regard to future research and clinical applications, the authors argue that depression and anxiety should be considered in terms of the context of diabetes treatment and self-management and in the broader, health systems, socioeconomic, cultural, historical, and political contexts that are relevant to understanding and developing interventions to address their root causes at multiple levels (e.g., targeting the individual, family, healthcare team, local community). They do point out that much of the available evidence is limited by small sample sizes and methodologically limited studies. Thus, they suggest that a greater investment will be necessary in high-quality studies that evaluate approaches to care that can be translated into real-world practice. Such studies should include a better understanding of the intersection of diabetes and mental health and identifying common precursors that may at least partially explain the co-occurrence of depression and anxiety, including both genetics and contextual factors. Elucidating the contextual, psychological, behavioral, and/or biological pathways through which mental health problems influence, and are influenced by, diabetes could inform the development of treatments with greater impact.

In Chap. 22, Goebel-Fabbri addresses an issue that is not well studied yet often observed clinically in persons with diabetes – eating disorders. What has been done tends to focus patients with T1D. She points out that neither T1D nor T2D cohorts have been studied using large randomized controlled treatment outcome research or long-term follow-up after treatment in order to examine relapse and remission rates. As a result, there is a lack of evidence-based treatments for these comorbid conditions. Moreover, most of the work in this area focuses on women. Little attention has been paid to eating disorders in men with diabetes. In both T1D and T2D, the presence of eating disorders increase risk of poor health outcomes and are associated with decreased quality of life. Clearly more research is needed in order to develop effective strategies to meet the needs of these complex patients.

In Chap. 23, van Duinkerken and Brands discuss the relationship of diabetes to neurocognitive functioning. They highlight the growing evidence that mild to modest cognitive decrements are often observed in patients with T1D and T2D. These decrements are mainly associated with domains that involve mental flexibility and processing speed, although in T2D, memory and executive function decrements have also been observed. Of clinical importance, chronic hyperglycemic exposure is seen as a prime risk factor to such decrements. Moreover, diabetes is a clear risk factor for the development of vascular dementia. They suggest that this may become a growing concern given the rapid rise in diabetes incidence combined with the improvements in diabetes treatment and extension of the life expectancy. They are clear to state that the research shows that cognitive decrements differ among patients and that while often mild, individual patients' daily lives can suffer from these decrements.

When considering what future research in this area is needed, they argue that "much research has already been done and more neuropsychological research will not help us improve the care of the individual patient. It is time to go back to the drawing table and see how the individual patients can be more central in cognitive research in diabetes." They suggest that research try to go beyond correlations with HbA1c or microvascular disease and elucidate the mechanisms that lead to cognitive decrements. This perspective gives rise to several intriguing questions. For example, how is cognition regulated on a molecular level? How does chronic inflammation, oxidative stress, and formation of advanced glycation end products relate to cognitive performance? What changes in the brain are mediators (e.g., lower perfusion, poorer white matter microstructure, etc.)? They note that while glucosuria often leads to the serious complications associated with diabetes, the brain seems to be largely unaffected. They suggest that perhaps the ultimate research challenge will not be to figure out what is wrong with the brain, but rather to figure out what is protecting it from the degeneration observed in other systems with diabetes.

In Chap. 24, Snoek and Menting turn the discussion to intervention approaches, reviewing those done at the individual level. They emphasize that healthcare professionals play a key role in offering personalized care and support the person with diabetes and their family members. Also, while there are evidence-based guidelines and clinical recommendations available, implementing psychosocial care pathways in busy clinics can be challenging. However, there are best practices to show that individual approaches to behavioral and psychological problems in people with diabetes are acceptable, feasible, and effective. Integrating behavioral and medical strategies, however, demands a team effort, with close collaboration between diabetes care professionals and mental health specialists. In this regard, they note that current healthcare systems operate in a way that complicates the integration of psychological services and funding is often problematic.

They offer and describe the collaborative care approach developed for persons with chronic illness and depression as a good example for a patient-centered and efficient individual approach to diabetes and comorbid mental health problems. More research is needed to increase the effectiveness of psychological care with regard to self-care behaviors and glycemic outcomes. Moreover, since professional psychological support is often scarce, they suggest that greater attention in future research be paid to the use of new technologies such as Internet-based therapy and self-help apps that are economical and patient-friendly. They do caution that there are limitations to the application of technological approaches such as access to the Internet or difficulty adhering to the online programs, resulting in high attrition rates. More research is warranted in this area, with a special focus on integrating online support with face-to-face visits, diabetes technologies, and community services.

In Chap. 25, Williams, Walker, and Egede expand the discussion of therapeutic approaches to the role of family and peer support. Noting the expanding circles of influence in the ecological model, they posit that diabetes management for patients with diabetes should engage support from multiple systems, including both family and peers (Kadirvelu, Sadasivan, Ng, 2012; Mayberry, Berg, Harper, & Obsorn, 2016; Rintala, Jaatinen, Paavilainen, and Astedt-Kurki, 2013). They review research that demonstrates that in a longitudinal analysis of patients with T1D, those with combined family and peer support had better glycemic control, higher well-being, and less internalized symptoms (Oris et al., 2016). They describe the critical role that family and peer support plays in the transition from adolescent care to adult care (Cameron, 2006). They also note that while family and peer support has been investigated heavily in youth with T1D, less focus has been given to its importance in adulthood.

They do note, however, that while in T2D, it has been suggested that positive family and peer support are associated with improved outcomes, the scientific evidence is inconclusive (Baig, Benitez, Quinn, & Burnet, 2015; Dale, Williams, and Bowyer, 2012); Stopford, Winkley, & Ismail, 2013; van Dam et al., 2004). They suggest that due to the heterogeneity of study designs, variations in sample sizes and proposed outcomes, and lack of a standardized definition for support, the evidence continues to be inconsistent. Therefore, future interventions aimed at family and peer support should consider how to homogenize the use of support and consider specific population-based factors that should be considered to address sociodemographic and cultural factors.

Additional research is needed to determine whether and how family and peer involvement in diabetes care and research can influence patient outcomes and impact policy. Finally, they argue that "future studies should seek to understand the relative importance and utility of family and peer support in adults with T1D and T2D in order to design effective interventions using this important psychosocial factor."

In Chap. 26, Trief, Fisher, and Hopkins expand on challenges for research and clinical applications in family therapies for adults with diabetes. Underlying this discussion is the belief that the structure, function, beliefs, and expectations of family or couple relationships have powerful effects on the management of diabetes. This is tempered, however, by the limited number of clinical trials that account for the unique aspects of family/couple relationships when developing interventions that capitalize on their strengths and influences on diabetes care (Trief et al., 2011). They argue that most studies lack precision with respect to study design and the specificity of intervention goals. To address this deficit, they define various challenges of definition, content, and study design.

With regard to challenges of definition, the authors suggest that social support is often viewed as a unitary construct regardless of how it is structured or from whom it is provided. They note that interventions described as focusing on "family" or "social support" rarely define the specific social unit that is targeted for intervention, and the intervention often includes partners, adult offspring and/or friends, and others in the community. This general lack of precision in identifying the specific social target of an intervention fails to take advantage of unique characteristics and impacts of each relationship; thus, change may not be maximized. They posit that how an interventional target is defined can significantly impact experimental design, evaluation, actual content of the intervention, and outcomes selected.

When considering challenges of content, in most of the "family intervention" studies they reviewed, the identification of well-defined couple skills or characteristics that were targeted for change were generally left unspecified. It is rarely clear what the intervention is expected to change. This makes it difficult or impossible to design effective interventions that target skill-building for adult couples that they might focus on – specifically who does what, when, and how regarding specific aspects of disease management.

In challenges of study design, the authors argue that "Targeting characteristics of couple relationships and patterns for change in diabetes interventions, in addition to focusing on the disease management behavior of individual patients and how the partner may support him/her, has major implications for how the intervention is evaluated." Several examples of how differences in definitions can impact decisions about measurement. For example, it is important to assess independently how the intervention impacted the health and well-being of the partner, and not focus exclusively on the outcomes of the person with diabetes. This challenge requires an expansion of measures employed to address each of the primary players and their relationship. They also point out that "couple interventionists require a unique set of well-trained and well-supervised clinical skills. These should include a knowledge of couple and family dynamics, clinical skills for interviewing and intervening with couples, not just with individuals, and experience shifting perspectives non-critically from one partner to the other, as specific diabetes-related behavioral tasks and relationship dynamics are addressed."

They argue that interventions that focus on specific kinds of relationships, with the couple or family being the most powerful, need to be developed. This will require that many issues be addressed including who should be involved; which family member should be targeted; what should the content be; which outcomes are most important; and what factors predict who would be most likely to benefit from a couples/family intervention.

In Chap. 27, Tang and Fisher expand the discussion on the utility of social support to consider best strategies for enhancing peer support. They argue that the adoption of peer support represents a fundamental shift in the way that healthcare is delivered, from a top-down approach to a more collaborative patient-centered approach. They view the current state of research as moving away from "Does peer support work?" to "studies exploring how best to extend peer support, while retaining its core effectiveness and person-centered features, what kinds of peer support work best in which settings, and how to integrate peer support effectively and efficiently in complex health systems" (Fisher, et al., 2015; Zhang, Yang, Sun, Fisher, & Sun, 2016). They note that despite ample evidence that peer support has positive impacts on both persons with diabetes and healthcare systems, less is known about community-level effects. They argue that future research should include evaluation of how peer support may mobilize communities around diabetes and change cultures of health.

They also discuss the potential role of using technologies to expand the reach and impact of peer support. They argue that it is important to recognize the limits to such approaches, noting that "overemphasis on technology solutions at the expense of peer support would be a critical misstep….We would do well to remind ourselves that these technologies are valuable for facilitating the delivery of peer support, making support more sensitive and personalized, and providing automated functions that decrease the workload for peer supporters." In this regard, they suggest that research should explore the boundary conditions of apps disconnected from other sources of support, and the extent to which the development and improvement of such apps may be enhanced by understanding them as a variety of peer support. They conclude by suggesting that integrating peer support into healthcare will "require healthcare systems to redesign their practices and push providers to learn to work collaboratively with peer supporters on the clinical team (Collinsworth, Vulimiri, Snead, & Walton, 2014)."

In Chap. 28, Tung and Chin clearly embrace the ecological model that forms a foundation for this book by discussing the multilevel impact of demographic, social, ecological, and structural influences in understanding health disparities among adults with T1D and T2D. They point out that across categories of age, sex and gender, race and ethnicity, and socioeconomic status, there are pervasive and, in some cases, growing, disparities in the incidence, prevalence, and outcome of diabetes in the United States.

They discuss that recent policy shifts calling for a broader view of health have also stimulated inquiry into causes of health disparities that stem from outside the healthcare system and in the communities where patients live. Understanding a patient's spatial context is foundational to understanding the drivers of health disparities. They discuss *Intersectionality,* which describes how demographic influences converge and interact, often in a predictable pattern or spatial context; and *place* describes how the socioecological influences of a neighborhood can shape a person's health behaviors and outcomes. Together, these concepts can be highly layered and complex, pointing to the limitations of using isolated demographic influences to explain diabetes disparities in real-world scenarios.

Importantly, they discuss how behavioral health solutions to diabetes disparities have historically not fully included the social and economic contexts of individual patients. Recent efforts, however, have implemented strategies to address these contexts by emphasizing culturally tailored interventions, contextualized educational strategies, and comprehensive care management. Moreover, changes in healthcare policy are starting to strengthen the linkages between the healthcare system, community, and non-health factors.

Clearly, there are complex and multilevel factors that contribute to disparities in diabetes risk and burden throughout the United States. Moreover, as the demographics of the United States continue to shift, with rapid growth in minority populations, this burden is likely to grow. Thus, the elimination of health disparities is more critical than ever. Fortunately, increasing research findings point to early successes and are beginning to establish a dynamic framework for change. It remains our imperative to ensure that actions are taken so that diabetes disparities – between rich and poor, minority and nonminority, and urban and rural – diminish into the twenty-first century.

In Chap. 29, Wiebe, Baker, and Marino expand into the outer rings of the ecological model by discussing the relationship of medical systems and patient-provider relationships. They provide a review of qualitative studies that suggest that persons with diabetes want effective communication with a consistent provider that is informative, open, honest, supportive, and founded on trust and that encourages the development of a partnership.

Researchers have largely focused on two broad aspects of the patient-provider interaction. The first is patient perceptions of interpersonal processes, which usually measures provider attentiveness, receptivity to the patient's concerns, and convey respect and compassion, and/or provide support. Second is the patient's perception of being actively engaged in a partnership with their provider through collaborative goal setting, autonomy-supportive communication, and participatory decision-making. The types of interactions that patients have with their healthcare providers have been found to be associated with patient satisfaction, self-confidence, motivation, diabetes knowledge, quality of life, psychosocial adjustment, medication adherence, self-management and lifestyle behaviors, and physical health outcomes. Understanding the characteristics of patient-provider relationships that are most central and amenable to change is, thus, a high priority for enhancing patient quality of life and improving self-management and clinical outcomes.

However, it is not clear which specific aspects of patient-provider relationships are most important and conclusions from this research are hard to draw due to research limitations. These include heterogeneity in how patient-centered communication is conceptualized and measured across studies. In addition, most measures have focused on patients' *perceptions* of relationships with their providers, despite the fact that patients and providers often differ in their perceptions of the medical encounter and these perceptions may not match objective measures of the interactions (Stuckey et al., 2015). Cross-sectional research dominates these observational designs, undermining our ability to make causal inferences.

Findings from intervention studies support both qualitative and observational research suggesting that patients' more comprehensive understanding of their illness and its treatments is necessary but insufficient for optimal diabetes care. Moreover, interventions tend to improve intermediate outcomes and not reliably diabetes self-care activities and clinical outcomes. Understanding the sources of these inconsistencies is hampered by the use of different patient-centered constructs, a lack of standard measures, and the relative lack of theory to guide interventions and test mediation processes.

Despite these limitations, greater understanding of the broad features of patient-provider interactions that are most important is emerging. Qualitative research indicates that patients desire interactions that convey clear and comprehensive information about diabetes and its treatment; that are characterized by understanding, respect, and support; and that engage them as active partners in healthcare decisions. These characteristics are associated with improved outcomes in both observational survey and intervention research.

Studies do vary significantly, however, on which dimensions of patient-centered relationships are examined and analyzed. This variability in assessment makes it difficult to interpret inconsistent findings and to understand which aspects of patient-centered care should be included in assessments and interventions. Future efforts may benefit from greater incorporation of theory into intervention development and evaluation. The authors point out that theories applied thus far have often been at the level of broad descriptive frameworks. “These have served an important purpose and advanced an impressive body of research, but we may be at a point when theoretical advances are possible and necessary.”

In Chap. 30, Ackermann moves away from persons with extant diabetes and considers the issue of the primary prevention of T2D. This focuses on the policy ring of the ecological model by emphasizing issue of how best to scale the strong evidence of an effective strategy to prevent or delay the onset of T2D in persons with increased factors. The author points out that attempts to diversify delivery channels to expand engagement in diabetes prevention programs while lowering costs can also be combined with third-party payment strategies. This can help to reduce both overall and individual participant costs. He also point out, however, that the total population-level impact of delivering individual intervention programs as the predominant approach for diabetes prevention is still limited by the total costs and by incomplete adoption of programs. Indeed, several efforts have been attempted to scale the most effective approach to diabetes prevention: a lifestyle intervention that attempts to promote modest weight loss and increased physical activity. A key issue is the sheer number of persons who have the primary risk factor, which is excess weight or obesity. The author notes that the large financial cost makes universal participation extremely unlikely.

These realities underscore how population-level diabetes prevention simply is not achievable through a singular intervention strategy. A contributing factor is that previous attempts at scaling have demonstrated that all at-risk individuals differ in their preferred method for receiving health information and are likely not equally receptive to the same intervention. The author notes that each individual person at risk for developing diabetes may engage with programs or support systems offered by some but not all different channels. As a result, efforts to maximize the full population-wide reach of diabetes prevention efforts will require an intense focus on diversification of intervention formats and delivery channels that still preserve fidelity to “essential” components that make behavioral programs effective. In concert with these diverse strategies for delivering evidence-based behavioral intervention content at the lowest cost, he points out that “it also will be essential that broader population-wide efforts continue slowly to expand knowledge, risk awareness, and social and environmental changes that will not only enable motivated individuals to successfully adopt healthier behaviors but to slowly establish them as the new societal norm.” In essence, it will require a cultural change if we are to effectively stem the epidemic of T2D.

In the final chapter of this section on adults, Myerson, Lu, Peters, Fox, and Huang expand on the outer ring of the ecological model – policy – by discussing the impact of health insurance policy on diabetes management**.** Diabetes and prediabetes affect an increasingly large percentage of Americans which is dramatically increasing the fiscal and social burdens associated with the disease. As a result, there is increasing availability to programs and medication regimens that promise to improve health and cost outcomes by preventing progression of prediabetes to diabetes. The authors illustrate this by reviews of insurance-reimbursed programs that adopted a lifestyle modification emphasis, such as the Medicare’s YMCA demonstration and Minnesota Medicaid’s ‘We Can Prevent Diabetes’ initiative. These efforts produced health benefits and demonstrated cost-effectiveness or even cost saving. As a result, insurance coverage for such interventions has just become more widespread in 2018; however, the impact of this change in coverage on program uptake is not yet known.

The authors note: “Increases in insurance coverage, such as those achieved by expanding Medicaid eligibility to include non-disabled adults, improve the rate and timeliness of diabetes diagnosis. Diabetes diagnosis rates should further improve given the ACA mandate to cover preventative services recommended by the USPSTF without any patient cost-sharing, including testing for elevated blood glucose. Similarly, gaining insurance coverage and reducing patient co-pays both significantly increase the fraction of diabetes patients who initiate and adhere to an appropriately comprehensive medication regimen.”

While coverage changes are promising, the evidence is mixed on access to insurance on diabetes-related hospitalizations. Analysis of ACA-supported Medicaid expansions, a similar Wisconsin expansion, and Massachusetts health insurance expansions found significant reductions in diabetes-related hospitalizations associated with these policies. This is in contrast to the Oregon Health Insurance Experiment that did not show any decline in diabetes-related hospitalizations, and all-cause emergency department utilization increased. The authors conclude that “the population-level effects of insurance on hospitalization may depend on what proportion of the patients with diabetes in a population are insulin-dependent, among other factors.”

Changes in the private health insurance market may have a significant impact on patient adherence to optimal diabetes management. The ACA improved access to private insurance among people with diabetes. Plans were not permitted to take diabetes status into account in calculating premium prices or in deciding whether to accept an applicant. The new rules implemented in 2018 will increase access to short-term, limited-duration insurance and association health plans which will be exempt from these requirements (Keith, 2018). As a result, it is likely that patient with diabetes will have a more difficult time accessing or adhering to optimal diabetes management regimens.

After reviewing the different changes in insurance plans, the authors concluded that “First, recent expansions in insurance coverage for diabetes prevention lifestyle programs for people with pre-diabetes should improve health, if they sufficiently increase program uptake. Second, expanding access to insurance coverage and reducing co-pays for diabetes medicines and testing supplies will increase diagnosis and treatment of diabetes, including blood glucose monitoring and use of medications. Third, provider-side financial incentives to improve diabetes care have not yet been shown to persistently improve diabetes management, but several large investigations in progress may soon provide additional evidence.”

Conclusions

Diabetes demands active involvement of the patient, a unique treatment dilemma among chronic illnesses. Because diabetes is largely a self-managed disease, outcomes are largely based on the patient’s behavior. The chapters in this section of the book clearly illuminate that a more ecological approach is needed to achieve optimal outcomes. Considering the *context* in which a person responds to the demands of their socioeconomic environment, understanding the myriad of factors that influence decisions, and communicating a patient-specific treatment plan are necessary to affect behavioral change and improve outcomes.

This requires that we consider that the individual level – both psychological and biological aspects – operates within the context of family, friends, and small groups which are, in turn, embedded within several layers of larger contexts. Indeed, diabetes is a prime example of this fundamental interaction of individual characteristics with contextual factors. Diabetes care requires a truly collaborative approach where patients and clinicians relate as equals and both appreciate and integrate the rich and varied contextual factors that influence all of health decisions. In this context, it is important to keep in mind that the choices affecting the health and well-being of a person with diabetes are ultimately made by that person in the context of his or her daily life. As long as the individual has been fully supported, the consequences of these choices belong to the person as well.

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