



Outpatient Diabetes Management and the Chronic Care Model

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Joel Rodriguez-Saldana

Introduction: The Ongoing Story of Diabetes Clinics

In the 1960s, diabetes was considered a common disease, even when being much less common than today; the average practitioner treated 15 or 16 known patients, and hospital clinics admitted approximately 1000 patients each year [1, 2]. The first diabetes clinics were established in North America and Europe in the years following the discovery of insulin with the main objective of teaching patients the technique and principles of its use; only in Britain, 500 had been established in 1973, even in isolated geographical entities [1, 3]. Hospital surveys showed that diabetes was controlled by diet and insulin, early diabetic complications and patient education were overlooked by physicians, and diabetic management by nursing, administrative, and dietetic staff was considered ineffective [4]. Successful clinics prevailing until today were the ones that had the vision, ability, and resources to institute comprehensive diabetic services which coordinated the activities of medical, nursing, and dietetic staffs to deliver multidisciplinary outpatient care, “special services” (dietetic, foot, eye, pregnancy, children, and adolescents), and diabetes education programs as essential components of their services [4–7]. These programs showed marked improvements in all areas of diabetes care, including diagnosis, assessment, hypoglycemia prevention, diet, and referrals [4]. In the majority of hospitals, patients with diabetes admitted to hospitals were seen mostly by specialists, but the sharp rise in the prevalence of type 2 diabetes made this unpractical [8]. Hospital diabetes programs including telephone support for patients, screening by nurses, and a mixture of outpatient and inpatient services showed reductions in emergency room visits, decreases in the

incidence of acute complications (ketoacidosis, hypoglycemia) and amputations, lower rates of broken appointments and complaints, and higher levels of patient and professional satisfaction [9, 10]. Most of the other hospitals told a different story: once referred, patients were supposed to be treated for life, doomed to take time out of work and travel, and wait to be seen by a different physician at almost every visit at the diabetes clinic; this approach of fleeting consultations was – and still is – unrewarding from every perspective [1]. Even when the estimated incidence of diabetes was 1.2–1.3% in England, diabetic clinics had such a large load that they became unable to devote sufficient time to difficult cases; medical manpower to deal with the growing workload was (and currently more than ever) met with increasing use of junior staff, resulting in large dropout rates, lack of adherence, high levels of patient dissatisfaction, and abysmal levels of quality of care [1, 2]. Taking into account that the average diabetic required seven to ten clinical visits every year, hospital demands meant establishing huge diabetic clinics with dissatisfaction and depersonalization for patients and staff [1]. In Germany and other countries, hospital diabetes management was paternalistic; patients were admitted to stabilize blood glucose control, and the lack of self-care support had many consequences: glycosuria was preferred to prevent hypoglycemia, the routine therapy was one or two injections of medium-acting insulin per day, self-monitoring and changes in insulin dosage were not allowed, and education was conceived as “obedience training” to follow rigid dietary prescriptions consisting of six to seven meals with fixed amounts of carbohydrates, proteins and fats, and prohibition of sugar [11]. This approach was never assessed, but acute and late complications were evident and frequent [11]. Hospital wards overflowed with patients with diabetes routinely assigned to hospital beds in hallways, timely access to appropriate medical advice was poor, hospital resources were largely devoted to episodic care for acutely and severely ill patients, there was low supervision by specialists, and rates of acute complications were very high [8, 9]. Inpatient hospital care represented >80% of the direct costs of diabetes and was related to higher

J. Rodriguez-Saldana (✉)
Multidisciplinary Centre of Diabetes, Mexico City, Mexico

risks of cardiovascular complications and renal disease [12]. On the other hand, understaffing and low resources to outpatient facilities were associated with an excess in hospital admissions and direct costs [13]. With the increasing rates of diabetes in recent decades, the amount of patients admitted to hospitals continues to rise [14]. They are more likely to die in the hospital, to occupy more bed days, and to incur in higher costs than people without diabetes [14]. Health systems, unable or unwilling to reinforce multidisciplinary outpatient management, can only expect to see increases in the financial and health burden of preventable hospitalizations [15]. The title of an article by Simmons and Wenzel is accurate: in many cases, diabetes inpatients are a case of lose, lose, lose [14]. The aim of diabetes care should be enabling patients to lead normal lives, with good metabolic control and free from complications. For many patients across the world, such an ideal is still far away [13].

Lessons Learned and Still Unlearned

Failure of clinics established at hospitals, which rapidly became overwhelmed, increased the role of primary health-care professionals in the shared care of diabetes management. General physicians became increasingly aware of the importance of tailoring management to patient's lifestyles, their expectation to be actively involved in their treatment, and their unwillingness to continue accepting medical advice without questioning [8]. General practitioners in the United Kingdom were among the first to see that they could manage many aspects of diabetes in their own practice. Albeit the pace to provide ambulatory diabetes care was initially slow, many innovative schemes were described and initiated [16]. Combination of need and opportunity prompted the creation of "small clinics of general practice" where groups of general physicians were organized to assist groups of 80 to 100 patients to stop the flow of patient to hospital-based clinics devoted to difficult cases [2, 18, 19]. Pioneering reports from Wilkes, Thorn, Russell, Hill, Singh, and colleagues showed that:

1. Diabetes could be looked after by the family doctor [1].
2. General practice seemed the proper place to look after many diabetics, allowing general practitioners to become increasingly competent in diabetes care [2].
3. Coordinating and sharing "the diabetic workload" with hospital clinics raised community awareness about diabetes, allowing family physicians to deal with problems for which they were trained [17].
4. "Diabetes care delivered by organized general physicians achieved similar levels of metabolic control to the ones reached in hospital clinics" [18].

To summarize, increases in the number of patients with type 2 diabetes, longer life expectancy, and sophistication of treatment produced overcrowding and inadequacies of delivery in hospital-based diabetes care [20, 21]. Increasingly low rates of access to hospital or university clinics and unsuccessful indices of performance occurred, even in countries with large and comparatively smaller populations of patients [20, 21]. Home and Walford reflected that "though some activities required the expertise and resources only available in hospitals, most of them did not require them, as long as general physicians had access to blood glucose monitoring, dietetic, chiropody and nurse educational services [20]." The need to reappraise the role of diabetes clinics was recognized by Thorn and Russell since 1973, but it was also essential to increase the access to effective diabetes management, because only a small proportion of patients attended hospital and outpatient clinics [20, 21]. Since 1986, it was acknowledged that the huge amount of people with diabetes in the community made it unrealistic to treat them in specialist outpatient clinics [21].

Transforming Diabetes Care

Suboptimal diabetes care was associated with high hospital admission rates and poor diagnostic differentiation between patients with mild and severe metabolic problems. Planning of diabetes services needed to be broader beyond those available in most centers, but surveys at facilities demonstrated (and continue to show) large discrepancies with recommended national and international guidelines [22]. A survey carried out by the Medical Advisory Committee (MAC) in Britain showed a scarcity of diabetes clinics or even examination rooms, resulting in lack of referrals; a variety of deficiencies in access to professional services, including obstetricians, ophthalmologists, dietitians, chiropodists, and nurses; a scarcity in the availability of resources to measure glucose and A1c; and absent or inadequate facilities to deliver diabetes education [23]. Nineteen recommendations were endorsed by the MAC; a follow-up report 10 years later showed significant improvements in all the previously described deficiencies, albeit there was still room for improvement [24]. Even when resources were insufficient, reorganization and integration of services produced great improvements in healthcare standards. From its inception in the 1970s, the concept of diabetes centers evolved to a number of "different breeds in the 1990s" [25]. Dunn and colleagues identified four priority areas to be considered for implementation of the Diabetes Control and Complications Trial (DCCT) in Australia: (1) allocation and effective use of resources, (2) standards of care and quality assurance, (3) training and continuing education, and (4) research and evaluation [25].

Effectiveness of Diabetes Outpatient Management: The Evidence

Diabetes centers evolved from traditional hospitalization of new patients; hospital admission to start insulin was occasionally used, but ambulatory care became the norm. The main objective of diabetes management became preventing or delaying the physical and social consequences of the disorder [19]. Early reports showed that transforming traditional to modern management methods was feasible, acceptable, and effective and produced significant improvements in A1c levels without associated increases in the frequency of hypoglycemia [24]. Recent emphasis

on issues of cost-effectiveness came to realize that diabetes is a disorder that rarely warrants hospitalization; awareness to these facts reinforced the concept of diabetes ambulatory care [25]. Nevertheless and despite demonstrations of cost-effectiveness of ambulatory management, funding of ambulatory services remained (and continues to be) in huge disadvantage with hospital care [25]. The 1980s witnessed the emergence of multiple initiatives devoted to shift the focus of diabetes management from hospitals to outpatient clinics in Europe, North America, and Australia. Table 20.1 shows examples of outpatient diabetes programs manually collected or identified in a PubMed search from 1980 thru 2018.

Table 20.1 Experiences of outpatient diabetes management across the world

Year, country, and reference	Objectives	Type of study, patients, health professionals, and intervention	Results
1988, United States [26]	Comparative effectiveness of community diabetes care and education on clinical outcomes	Prospective, randomized study 261 patients treated by 61 primary care physicians from 1980 until 1985 from four large and four small communities randomly selected Intervention: four group sessions delivered by paramedical personnel Five-year follow-up	Patients receiving the intervention showed significant changes in healthcare practices, including increases in the use of multiple injections of insulin and self-monitoring of blood glucose Decrease in hospitalizations related to diabetes, probably representing changes in healthcare practices rather than changes in health status A1c levels unchanged
1988, Germany [27]	Efficacy of a structured treatment and education program on the selection of pharmacological therapy, A1c levels, triglycerides, and body weight	Prospective randomized study 114 patients with type 2 diabetes, 65 in the intervention group and 49 in the control group from five general practices Intervention: preparatory course for physicians and assistants; four group monthly education sessions delivered by paramedical personnel	A1c levels remained unchanged in the intervention group; significant decreases in triglycerides and weight loss The percentage of patients receiving sulfonylureas decreased from 68% to 38%
1993, Germany [28]	Feasibility and efficacy of a structured treatment and teaching program in routine primary healthcare	Observational study of a random sample of 17 physicians and their office staffs Intervention: remunerations to physicians and office staff upon completion of a postgraduate training course 179 patients with type 2 diabetes Four 90–120-minute sessions for groups of 4–10 patients, partly based on the Grady Memorial diabetes medical and education program [10] and previously assessed in a controlled trial [27] Program delivered by the office staff	Acceptance by physicians Significant decreases in A1c levels from 8.11% to 7.47%, body weight (mean 2.8 kg), use, and proportion of patients treated with oral antidiabetics
1994, United States [29]	Follow-up of a structured treatment and education program on the selection of pharmacological therapy, A1c levels, triglycerides, and body weight	Prospective, randomized study 440 patients with type 2 diabetes, 61 in the intervention group and 355 in the control group Ten-year follow-up 1981–1991	Positive changes in diabetes care and education Nonsignificant increases in A1c and total cholesterol, significant increases in HDL cholesterol, significant decreases in hospital admissions, and small increases in the proportion of patients receiving formal diabetes education The majority of patients with type 2 diabetes managed on diet alone had never seen a dietitian Nonsignificant changes in ophthalmologic examinations Less patients managed with insulin

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Table 20.1 (continued)

Year, country, and reference	Objectives	Type of study, patients, health professionals, and intervention	Results
1997, United States [30]	Effectiveness and safety of intensive insulin therapy (IIT) on outpatient, endocrine-based, multidisciplinary practice in patients with type 1 and type 2 diabetes	Longitudinal cohort study, 14-year duration 780 patients, 209 receiving long-term comprehensive treatment including cardiac screening with exercise treadmill tests, noninvasive thallium scan, and cardiology referrals if necessary 571 declined continuing care	Patients with prolonged exposure to comprehensive therapy had significant reductions in overall and cardiac mortality and lower incidence of renal failure Lower comorbidity scores associated with higher survival Two thirds of the patients declined receiving multidisciplinary, intensive care
1998, United Kingdom [31]	Changes in the proportion of patients with diabetes receiving treatment in primary and secondary care over 5 years	Longitudinal study, 1990–1995 Seven general practices, five of them with organized diabetes programs A diabetes review was defined as a contact with a general physician or nurse including examination for at least three potential complications or risk factors	The proportion of patients treated in general practice doubled from 17% in 1990 to 35% in 1995 Patients treated in secondary practice fell from 35% in 1990 to 30% in 1995 Patients treated both in general and secondary practice fell from 6% to 2% Newly diagnosed and treated patients in general practice also increased Albeit theoretically greater activity in primary care would increase the pressure on hospital services, this study showed that this had not occurred
1998, United Kingdom [32]	Effect of training about a patient-centered intervention for general practitioners and nurses on outcomes	Randomized controlled trial 29 general practices receiving training about patient-centered care 252 type 2 diabetic patients Duration: 2 years	High initial levels of professional adoption by professionals Persistence after 2 years: 19% No significant biochemical or functional improvements
1999, Poland [33]	Effect of a disease management program on A1c and fasting blood glucose, the appropriateness of treatment modalities, and timing of therapeutic choices	Pilot prospective study in outpatient clinics, 18-month duration 88 randomly selected patients with type 1 diabetes 132 randomly selected patients with type 2 diabetes 177 pregnant women with type 1 diabetes, 81 receiving the structured program, 74 non-recipients 155 infants from these 2 groups	Patients with type 1 diabetes had significant decreases in A1c, fasting, and postprandial blood glucose, without severe hypoglycemia Body mass changes were nonsignificant Patients with type 2 diabetes had significant decreases in A1c, fasting, and postprandial blood glucose, without severe hypoglycemia Body mass decrease was significant Pregnant women not receiving the structured program had higher rates of hyperglycemia, preeclampsia, ketoacidosis, polyhydramnios, and cesarean sections Higher APGAR scores in infants from recipients of the structured program
2001, United States [34]	Effectiveness of a comprehensive diabetes management program including risk stratification and social marketing on clinical outcomes and patient satisfaction	Prospective trial, 12 months Two outpatient primary care clinics from a managed care organization 370 patients in the intervention group, 193 with available information at 12 months 623 patients in the control group	Significant improvements in glycemic control: Patients at low risk (A1c <7.0%) increased by 51.1% Patients at moderate risk (A1c 7.0–8.0%) increased by 2.5% Patients at high risk (A1c ≥8.0%) decreased by 58.3% and 97.4% had changes in therapy Patients with blood pressure <140/90 mm Hg increased from 38.9% at baseline to 66.8%; 63.0% of patients with blood readings >130/85 mmHg at baseline had changes in medication Patients receiving lipid profile tests increased from 66% at baseline to 100% Patients with LDL >130 mg/dl decreased from 25.4% at baseline to 20.2% 76.7% of patients at the highest risk of nephropathy had a change in medications Patients receiving dilated eye examinations increased from 53.9% to 80.3% Foot examinations increased from 0% to 100.0% 100% of patients and providers were satisfied with the program Patients in the control group remained essentially unchanged

Table 20.1 (continued)

Year, country, and reference	Objectives	Type of study, patients, health professionals, and intervention	Results
2001, Denmark [35]	Effectiveness of a multifaceted intervention for general practitioners on 6-year mortality, morbidity, and risk factors of patients with type 2 diabetes	Open controlled trial randomization of practices to structured personal care or routine care 311 Danish practices, 474 general practitioners 243 in intervention group 231 in comparison group 459 patients randomized to structured care 415 patients randomized to routine care Regular follow-up and individualized goal setting supported by prompting of doctors, clinical guidelines, feedback, and continuing medical education	Equal rates of nonfatal outcomes and mortality in both groups Findings in the intervention group: significantly lower fasting plasma glucose, A1c levels, systolic blood pressure, and cholesterol levels More frequent use of metformin, doctors arranged more follow-up visits, referred fewer patients to hospital clinics, and set more optimistic goals Individualized goals, education, and surveillance in primary care for at least 6 years may bring risk factors of patients with type 2 diabetes to a level that has been shown to reduce diabetic complications without weight gain
2001, Netherlands [36]	Comparative effectiveness of a disease management model to a shared care model for diabetes	Observational non-randomized trial In the traditional care model, patients were seen by endocrinologists at outpatient clinics In the disease management model, patients were seen by nurse specialists delivering direct, organized, and coordinated care with specialists and other providers in general practice 22 general practitioners accepted the shared care model and 29 continued using the traditional model 74 patients agreed to participate in the shared care model and 47 patients continued using the traditional model	No differences were found between groups in quality of life, knowledge of diabetes, patient satisfaction, or consultation with caregivers Glycemic control improved in patients receiving shared care and deteriorated in patients receiving traditional care Factors influencing implementation of the shared care model: project management, commitment, power, and structure
2002, United States [37]	Effectiveness of community-based diabetes care models and use of a diabetes electronic management system (DEMS)	Observational study Three primary care practice sites Implementation of planned care and DEMS with 16 primary care providers	Planned care showed improvements in A1c, cholesterol, microalbuminuria, and tobacco advice DEMS was associated with improvements in all indicators including microalbuminuria, retinal examination, foot examinations, and self-management support The way in which healthcare services are organized and delivered can improve documentation of clinical practice, adherence to performance measures, and metabolic outcomes
2003, United States [38]	Effectiveness of diabetes care directed by nurses and supervised by a diabetologist to meet the American Diabetes Association process and outcome measures versus usual care	Randomized observational trial 504 patients from 2 county clinics: 252 receiving nurse-directed diabetes care 252 patients receiving usual care as controls	Patients under nurse-directed diabetes care received almost all process measures significantly more frequently than control patients A1c levels fell 3.5% by comparison to a 1.5% decrease in patients under usual care After 1 year under nurse-directed care, A1c levels decreased to 7.1%, and the median value fell from 8.3% to 6.6%
2003, United Kingdom [39]	Effectiveness of specialist diabetes clinics receiving patients from primary and secondary care	Observational prospective study, 2-year duration 19 specialist clinics 2415 patients referred to 19 specialist diabetes clinics led by GPs with a special interest in diabetes, to alleviate increasing waiting times for secondary care Training based on 2-day workshops for GPs, follow-up workshops, and case reviews Multidisciplinary support from specialist nurses, podiatrists, dietitians, and retinal screening cameras	Significant increases in overall patient attendance Significant reductions in hospital attendance Main benefits: geographical accessibility, availability in community setting, short waiting times at most clinics, and continuity of staff Reservations included lack of strategic planning in the location of clinics, long waiting times in some of them, and poor communication for referrals Advantages: convenience to patients, acceptability, and increased capacity of physicians

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Year, country, and reference	Objectives	Type of study, patients, health professionals, and intervention	Results
2004, United States [40]	Effectiveness of community-based, nurse case management and peer education to improve diabetes care, patient knowledge, and satisfaction and reduce health adverse beliefs in undeserved patients	Prospective study, 1-year duration 153 patients from 6 community clinics 76 non-randomized patients from the same clinics with A1c values $\geq 9.0\%$ as controls	Patients in the intervention group had significant improvements in A1c, total cholesterol, LDL cholesterol, and diastolic blood pressure Nonsignificant changes among patients in the control group
2004, France [41]	Impact of a local adaptation of a structured program on primary care to encourage intensive treatment of diabetes as routine practice	Prospective, randomized, controlled trial in a suburban and semirural area, 12-month Follow-up allocation of all the general physicians from a suburban and semirural area, 35 in the intervention group, 32 in the control group 192 patients in the intervention group 148 patients in the control group Three-day training and follow-up of physicians in the intervention group	Patients in the intervention group were managed more adequately according to guidelines and referrals Significant decreases in A1c in the intervention group (0.86%) No significant differences in other clinical outcomes, incremental costs from the intervention No significant changes in quality of life
2008, South Africa [42]	Effectiveness of a nurse-led protocol and education-based system on diabetes management in a rural setting	Prospective non-comparative intervention 326 patients, 96% with type 2 diabetes Two rural nurses received 12-month training from a diabetes specialist One weekly hospital diabetes clinic and 14 monthly diabetes clinics established in peripheral clinics Cornerstones of the system: patient education, drug dose titration, and clinical outcomes	High levels of acceptance by patients and staff 980 patients enrolled within 9 months Significant decreases of A1c from $11.1 \pm 4.2\%$ to $8.7 \pm 2.6\%$ at 6 months Patients with baseline A1c $>10.0\%$ showed a mean 5.8% fall Diabetes education was associated with significant A1c improvements Rates of hypoglycemia did not increase
2010, United States [43]	Effectiveness of systems-based care in an undeserved population to reduce disparity in care for cultural, ethnic, commercial, and socioeconomic minorities	Implementation of disease registry and management system in four community health centers from a suburban practice network	Community health center patients meeting guidelines showed significant improvements in clinical outcomes except percentage of patients with A1c $>9.0\%$ Despite improvements, statistically significant discrepancies persisted between community health clinics and suburban practices in percentage of patients with A1c $<7.0\%$, LDL <100 , retinopathy, and microalbuminuria screening Community health centers lagged in all comparisons
2010, United States [44]	Comparative effectiveness of nurse-directed diabetes management between a non-integrated model in which patients were removed from primary care clinics and followed by supervision from an endocrinologist versus an integrated model in which patients were seen by nurses under the supervision of primary care physicians	Observational study, 9–12 months 387 patients randomly assigned to the non-integrated model 178 patients were referred to the integrated model	25% of the patients in the non-integrated model were using insulin (mostly bedtime), and 75% of the patients in the integrated model were using intensified insulin regimens A1c decreased 1.9% in the non-integrated model and 3.9% in the integrated model In the integrated model: 90% of patients met blood pressure goals, 96% met LDL goals, and 47% met the three goals of treatment (A1c, blood pressure, LDL)

Table 20.1 (continued)

Year, country, and reference	Objectives	Type of study, patients, health professionals, and intervention	Results
2010, Mexico [45]	Effectiveness of structured diabetes management on the quality of primary diabetes care	Seven-year statewide diabetes Training, feedback, and reminders to general physicians, nurses, and health professionals to implement 43 outpatient multidisciplinary diabetes clinics at urban and rural health centers Organizational arrangements to reduce waiting times, avoid rotation of staff, and increase time for baseline and follow-up visits Statewide diabetes registry 4393 patients	After five visits, significant increases in the percentage of recorded process indicators were documented in the diabetes registry, including body mass index, blood pressure, A1c, total cholesterol, and foot examination Outcome measures showed significant decreases in A1c and fasting blood glucose Nonsignificant changes in systolic/diastolic blood pressure and lipoprotein levels
2011, Netherlands [46]	Effectiveness of structured diabetes care from the perspective of patients and healthcare professionals in routine practice	Quasi-experimental study, 4-year duration Comparison of structured care (SC) and usual care (UC) SC including organizational components: multidisciplinary cooperation, clear task division, and cooperation between general practitioners, diabetes specialist nurse, and dietitians UC based on clinical guidelines and included three general checks and one extensive check per year, performed by GPs, nurses, or assistants Questionnaires were sent to healthcare professionals and patients in the SC and the UC group	No differences between SC and UC in yearly and three monthly checks More patients in the SC group received diabetes education by diabetes specialist nurses All practices in the SC used the diabetes registry GPs in the SC were significantly more satisfied than GPs in the UC group More patients in the SC group reported contact with GPs, nurses, assistant, and dietitians, received adequate education about diet and foot care, and knew their blood glucose level One year after SC finished, the effects of structured care were still visible
2013, Denmark [47]	Follow-up of study referenced as [34]	Observational study 1381 patients aged ≥ 40 years and newly diagnosed with type 2 diabetes from national registries 19-year follow-up	Group differences in risk factors from the 6-year follow-up had leveled out Lower rates of microalbuminuria and triglycerides in the intervention group Similar rates in all-cause mortality between the intervention and control group Prompting, feedback, clinical guidelines, continuing medical education, individualization of goal setting, and drug treatment may safely be applied to treat patients with newly diagnosed type 2 diabetes to lower the risk of complications
2013, United Kingdom [48]	Effectiveness of integrated, structured primary diabetes care in partnership with specialists. A challenging vision for two reasons: It challenged the secondary care status quo It would mean a shift of resources within the health economy	Consistent messages tailored and delivered to primary and secondary care providers to persuade them about the need and benefits of change Two phases of implementation: establishment of community diabetes teams changing the secondary care model and establishment of six "super-clinics": pregnancy, renal dialysis, insulin pumps, acute type 1 diabetes, type 1 education, adolescents	Significant improvements of care; 85% of patients discharged from secondary care; estimated savings: £59,940.00 per year 108 patients receiving appropriate treatment in the "super-six" clinic 2996 patients received DESMOND education training 287 clinicians received training Relationships with clinicians and other staff consistently positive Patient feedback overwhelmingly positive

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Table 20.1 (continued)

Year, country, and reference	Objectives	Type of study, patients, health professionals, and intervention	Results
2013, Australia [49]	Effectiveness on patient outcomes of an integrated primary/specialist model for community care for complex Type 2 diabetes management compared with outcomes for usual care at a tertiary hospital for diabetes outpatients	Prospective, open controlled trial in a primary and tertiary care setting 330 patients with type 2 diabetes ≥ 18 years old allocated to an intervention (community-based care by general practitioner with advanced skills and endocrinologist partnership) or to usual care in the hospital diabetes outpatient department	Patients in the intervention group showed a 0.8% decrease in A1c, increased from 21% to 42% achieving the A1c target (7.0%), experienced significant improvements in blood pressure and total cholesterol, and achieved significantly higher combined A1c, blood pressure, and LDL cholesterol targets by comparison to the usual care group Community-based, integrated models of complex diabetes care delivered by general practitioners with advanced skills produce clinical and process benefits compared with tertiary diabetes outpatient clinics
2015, United States [50]	Comparative effectiveness of in-clinic health coaching by medical assistants on diabetes and cardiovascular risk factor control versus usual care	Randomized controlled trial 441 patients from 2 primary care clinics Health coaching delivered by three medical assistants who received 40 hours of training and were embedded as part of the care team at the two clinics Patients randomized to usual care had access to any resources available at the clinics except for health coaching Primary outcome: a composite measure of A1c, systolic blood pressure, and LDL cholesterol Secondary outcome: meeting all three goals	Participants in the coaching arm were more likely to achieve goals for one or more uncontrolled conditions at baseline and more likely to achieve control of all conditions Almost twice of the people in the health coaching group achieved the A1c goal and were more likely to achieve LDL cholesterol goals Nonsignificant changes in systolic blood pressure Health coaching by medical assistants has the potential to alleviate nationwide deficiencies in diabetes control in an environment of deepening primary care clinician shortage
2015, Australia [51]	Effectiveness of an integrated model of care for patients with complex type 2 diabetes on potentially preventable hospitalizations	Prospective controlled trial, 36 months duration Multidisciplinary, community-based, integrated primary-secondary diabetes care compared to usual care at a hospital diabetes outpatient clinic 327 patients, 206 of them hospitalized	Compared with the usual care group, patients in the integrated model of care group were nearly half as likely to be hospitalized for a potentially preventable diabetes-related diagnosis after 24 months, even adjusting for age, sex, education, and A1c concentration Integrated diabetes care models reduce hospitalizations
2016, United States [52]	Association between patient-centered care (PCC), diabetes self-care, glycemic control, and quality of life (QOL)	Two adult primary care clinics 615 patients	PCC was significantly associated with QOL, medication adherence, general diet, specific diet, blood sugar testing, and foot care, but was not significantly associated with glycemic control Focusing care around the patient may need to expand throughout the healthcare system before changes in outcomes occur
2017, United Kingdom [53]	Comparative effectiveness of enhanced diabetes primary care with more expensive integrated specialist-community diabetes services	Eight primary care practices and eight matching neighboring practices Enhanced practices had primary care physicians and nurses with an interest in diabetes who attended monthly diabetes education meetings and provided care plans and audits Control practices provided integrated primary-specialist care services	No significant differences were noted between enhanced and primary-specialist services Enhanced primary diabetes care has similar outcomes to that provided by more expensive primary-specialist care
2017, Brazil [54]	Effectiveness of a structured intervention to improve type 2 diabetes management in primary care in a defined region	Comparative observational study 230,448 patients, 124,779 in the intervention group and 105,669 in the control group 61 family strategy team professionals (FHS) from two cities 29 in the intervention group and 32 in the control group One awareness-raising workshop with heads of municipal health departments of the selected cities, with extensive participation of FHS health professionals Constitution of local management teams, reorganization, and local action plans to improve diabetes care Delivery of three training sessions for FHS professionals	Significant differences in staffing the intervention group, including deficiencies in physicians and nurses By comparison with the intervention group, the control group showed better outcomes including: multidisciplinary management, adherence to treatment referrals, diagnostic tests, and educational activities This complex intervention had no detectable impact despite an enormous investment in money and manpower

Outpatient Management of Type 1 Diabetes

Traditional models for type 1 diabetes are organized around a specialist with a multidisciplinary team to deal with education, nutrition, and psychosocial adjustment [55]. A limited number of patients with type 1 diabetes are treated by primary physicians, but even in developed countries, availability and geographical distribution of specialists are real obstacles to refer all these patients to diabetologists [56–58]. Even in the United States, it was estimated that in 2014 the shortage of adult and pediatric endocrinologists was of 1500 and 100, respectively, and that the gap for adult endocrinologists would expand to 2700 [58]. Models of primary care for type 1 diabetes are scarce, but innovative strategies have been conceived and implemented. Based on experiences collected as one of the participating centers in the DCCT, in 1988 the International Diabetes Center organized a team comprising three family physicians, four endocrinologists, a clinical epidemiologist, three nurse specialists, and a dietitian and developed Staged Diabetes Management (SDM), a systematic approach to support clinical decision-making including clinical pathways or DecisionPaths to start, adjust, maintain, or change therapies [55, 59]. Initial experiences with SDM in the United States demonstrated its feasibility and its capacity to standardize clinical practice, reduce clinical inertia, and establish criteria for referral [59]. International dissemination of Staged Diabetes Management has confirmed its feasibility and effectiveness [33, 41, 45].

Challenges of Comorbidity and Multi-morbidity in Diabetes Management

Treating chronic diseases like diabetes is often complicated by the coexistence of multiple medical conditions and of social and psychological deterrents; currently, the most common chronic condition among adults is multi-morbidity [60, 61], in the words of Kate Lorig, “the Disease of the 21st Century [62].” The contribution of multi-morbidity to the global burden of disease is already huge, but projections are of great concern: it is estimated that during the last 15 years of life, one half of the newborns in industrialized countries will suffer multi-morbidity and its consequences, including poor quality of life, psychological distress, worsening functional capacity, longer hospital stays, higher costs of care, and higher mortality [63–67]. MM also affects processes of care resulting in complex self-care needs; multiple organiza-

tional problems; polypharmacy; increased use of emergency facilities; difficulties to apply clinical guidelines; fragmented, costly, and ineffective care; and higher mortality rates [66–71]. Multi-morbidity is important for diabetes management because besides its long-time recognized association with metabolic and cardiovascular risk factors, the frequency of nondiabetes-related (or non-apparently related) comorbidities is starting to be recognized. Negative outcomes associated with multi-morbidity partly result from the fact that healthcare delivery is organized and designed for patients with single diseases [63]. Fortin and colleagues state that “clinical practice is still based on a single disease paradigm which is not appropriate for patients with complex and overlapping health problems [66]”. To make matters worse, most clinical trials exclude patients with comorbidity, therefore limiting generalization of research results [71]. Diabetes management clearly applies to these statements: until recently, clinical guidelines failed to recognize the importance of comorbidity, and it has been demonstrated that this is a limiting factor to their implementation [63]. Research about the epidemiology of multi-morbidity, its consequences, and its effects on the process of care is still very limited [71–75].

Definitions and Magnitude

Multi-morbidity (MM) was originally defined by Feinstein in 1970 as “the coexistence of two or more diseases, pathological conditions or clinical entities in the same patient” [76], while comorbidity (CM) is defined as the presence of one index disease and at least one other chronic condition in the same person [77]. MM and CM have become some of the greatest challenges and an additional pressure on healthcare systems. They represent an additional burden on the acute care model which impedes in many cases, even recognizing the main complaint in a hurried visit. Increased effectiveness of healthcare interventions have delayed death by managing (not curing) diseases but have also led to a marked increase in the coexistence of separate diseases in individuals [78]. In less than three decades, the frequency of chronic diseases and associated patterns of comorbidity and multi-morbidity have escalated for several reasons: (1) lowered diagnostic thresholds, (2) new diagnoses, and (3) true increases of some diseases, such as diabetes [78, 79]. Table 20.2 confirms the steady increase in the worldwide prevalence of comorbidity (two or more diseases) in every age group, associated disease patterns, and outcomes.

Table 20.2 Epidemiology of multi-morbidity and comorbidity

Authors, year, and reference	Country	Number	Age group	Prevalence of multi-morbidity (MM) by age groups and additional results
Schellevis et al. [80]	Netherlands	23,534	65 years and older	15%
van den Akker et al. [81]	Netherlands	60,857	Five age groups 0–19 20–39 40–59 60–79 ≥80 years	Highest rates of comorbidity for osteoarthritis and diabetes General prevalence of MM: 29.7%; by age group, males (M) and females (F) 0–19 years: 10.7% and 9.2% 20–39 years: 16% (M) and 18.8% (F) 40–59 years: 33.6% (M) and 35.9 (F) 60–79 years: 60.9% (M) and 64.9% (F) ≥80 years: 74.2% (M) and 79.9% (F) The number of prevalent diseases increased from less than one below 30 years to more than three at 80 years and older
Menotti et al. [82]	Finland (F), Italy (I), Netherlands (N)	F: 716 I: 682 N: 887	65–84 years	10–15%
Westert et al. [83]	Netherlands	13,806	16 years and older	Number of chronic conditions: 1: 80.7% ≥2: 19.3% ≥3: 3.3% Diabetes prevalence: 4.4% Most prevalent comorbid patterns: Lung disease + musculoskeletal disease + neurological disease In addition to being the most common condition, musculoskeletal disease was the most likely to occur in all disease clusters
Woolf et al. [84]	USA	1,217,103	65 years and older	Prevalence of MM: 65% Inpatient admissions for ambulatory care-sensitive conditions and hospitalizations for preventable complications increased with the number of chronic conditions
Beasley et al. [85]	USA	572	Adults	Prevalence of MM: 26% An average of 3.2 problems are managed at each clinical encounter
Fortin et al. [86]	Canada	980	Three age groups 18–44 45–64 65 years and older	Prevalence of MM by age group 18–44 years: 69.3% 45–64 years: 92.8% 65 and older: 98.7% Cumulative index rating scale increases significantly with age
Naughton et al. [87]	Ireland	271,518	70 years and older	2 conditions: 27% 3 conditions: 19% ≥4 conditions: 14% Consistent patterns of disease by age groups
Kadam et al. [88]	UK	9439	50 years and older	1 morbidity: 19% 2–3 morbidities: 36% 4–5 morbidities: 22% ≥6 morbidities: 23% Increasing strength of association between poor physical function and increasing severity of multi-morbidity

Britt et al. [89]	Australia	9156	Five age groups <25 25–44 45–64 65–74 75 years and older	Prevalence of MM <25 years: 2.6% 25–44 years: 14.7% 45–64 years: 46.5% 65–74 years: 74.6% 75 years and older: 83.2% The most common combination was arthritis/chronic back pain + vascular disease
Schramm et al. [90]	Netherlands	Three population studies, two general practitioner registries, one hospital discharge registry, one nursing home registry	55 years and older	Prevalence of MM: Nursing homes: 82% General practice: 72% General population: 56% Hospital setting: 22% Large differences in type of MM between settings
Smith et al. [91]	Ireland	267	45–64 years old	Prevalence of MM: 34.4% Median number of conditions: 4 Mean number of medications: 7.5 Mean number of medical visits per patient: 11.3 in the 12 previous months
Nagel et al. [92]	Germany	13,781	50–75 years old	Prevalence of MM: 67.3% Low educational level was significantly associated with higher prevalence of MM
Marengoni et al. [93, 94]	Sweden	1099	77–100 years old	Prevalence of MM: 55% Median number of diseases among persons with MM: 3 Diabetes was the 12th most prevalent chronic disease occurring independently of CM; when it occurs, it is more frequently associated with hypertension and heart failure Age, gender, and education are independently associated with MM Cardiovascular disease prevalence is not different by age or gender Higher proportion of mental disorders in the oldest old Co-occurrence of diseases exists beyond chance, which clinicians need to take into account in their daily practice; some pathological mechanisms behind identified clusters are well known; others need clarification
Loza et al. [95]	Spain	2192	Adults with MM including rheumatic disease (RhD)	General prevalence of MM: 30% Prevalence of MM including a RhD: 17% MM is associated with impaired daily functioning and lower quality of life Having a RhD worsens the outcomes
Uijen et al. [96]	Netherlands	13,584	Seven age groups, 0 to more than 75 years old	Prevalence of MM, four or more chronic diseases 45–64 years: 7.0% 65–74 years: 30% ≥55% Older age, female sex, and low socioeconomic class associated with higher prevalence of MM

(continued)

Table 20.2 (continued)

Authors, year, and reference	Country	Number	Age group	Prevalence of multi-morbidity (MM) by age groups and additional results
Lee et al. [97]	USA	11,113	65 years and older	Prevalence of MM: 23% Chronic diseases frequently co-occurring: Diabetes: 19.4% Coronary artery disease: 15.9% Congestive heart failure: 4.8% Geriatric syndromes: Falls: 23.2% Urinary incontinence: 25.0% Co-occurrence of chronic diseases and geriatric syndromes is very common
Mimas et al. [98]	Greece	20,299	Two age groups: <65 years 65 years and older	Prevalence of MM: <65 years: 7.78% 65 years and older: 11.52%
Glynn et al. [99]	Ireland	3309	50 years and older	Prevalence of MM: 66.2% Healthcare utilization and costs significantly higher in patients with MM Each additional chronic condition is associated with increases in primary care visits, hospital outpatient visits, hospital admissions, and total health costs
Steinman et al. [100]	USA	1.9 million men, 39,000 women	65 years and older	Mean number of chronic conditions: Men: 5.5 ± 2.6 Women: 5.1 ± 2.6 Disease burden increased with advancing age Most common triplet in men: hypertension, hyperlipidemia, and coronary artery disease Most common triplet in women: hypertension, hyperlipidemia, and arthritis Diabetes more frequently associated with hypertension and hyperlipidemia
Barnett et al. [101]	Scotland	1,751,841	Five age groups, 16 years and older	Prevalence of MM: 23.2% The absolute number of people with MM was higher in people younger than 65 years Onset of MM occurred 10–15 years earlier in people living in the most deprived areas and particularly associated with mental health disorders
Paulsen et al. [102]	Denmark	37,651	Patients with hypertension, 25–79 years old	Prevalence of comorbidities: Diabetes: 26.2% Cardiovascular disease: 19.0% Other serious comorbidities, including cancer and mental disorders: 25.7%
Prados-Torres et al. [103]	Spain	275,682	Three age groups 15–44 years 45–64 years ≥65 years	Prevalence of MM 15–44 years: 13% 45–64 years: 43% ≥65 years: 67% Five clinically consistent patterns of MM: Cardio-metabolic Psychiatric Mechanical-obesity-thyroidal Psycho-geriatric Depressive

Streit et al. [104]	Switzerland	1002	50–80 years old Assessment of comorbidity with the Charlson index Quality assessment of preventive care and cardiovascular preventive care with 37 indicators from the RAND's Quality Tools	Prevalence of MM: 67.5% Mean Charlson index: 1.8 31.1% of patients had an index of 0 1.4% of patients had an index >8. Quality of care was not associated with higher numbers of comorbidities
Koller et al. [105]	Germany	115,203	65 years and older Five-year follow-up	Prevalence of MM ^a : 57.62% Patients with MM and older than 75 years had higher risk of becoming care dependent than non-multi-morbid people after the first year
van Oostrom et al. [106, 107]	Netherlands	32,583	55 years and older Time trends 2001–2011 in the prevalence of chronic diseases and multi-morbidity	General prevalence of MM: 26% 15% had two diseases 7% had three diseases 3% had four diseases 1% had five or more diseases MM patients received more medical visits, telephone consultations, home visits, diagnostic tests, or minor surgical procedures
Déruaz-Luyet et al. [108]	Switzerland	888	18 years and older; average: 73 years Assessment of clustering of chronic diseases	MM increased from 12.7% to 16.2% in the general practice and from 14.3% to 17.5% on self-reports Aging of population explained part of these trends Four clusters of chronic conditions identified 1 Cardiovascular risk factors and conditions 2 Metabolic and age-related conditions including diabetes, obesity, atherosclerosis, hypertension, neuropathy, osteoarthritis, hearing complaints, and urinary incontinence 3 Alcohol- and tobacco-related conditions 4 Pain, musculoskeletal, and psychological conditions
Nogueira de Carvalho et al. [109]	Brazil	60,202	≥ 18 years old Prevalence of self-reported MM according to socioeconomic and demographic characteristics	Prevalence of MM: 23.6% Two chronic diseases: 52.8% Three chronic diseases: 25.8% Four chronic diseases: 12.2% Five or more: 9.3% Higher rates in women, people older than 60 years, with low educational level, living in urban areas and unemployed

^aIn the study of Koller et al., multi-morbidity was defined as the coexistence of three or more chronic conditions

Multi-morbidity in Diabetes: The Elephant in the Medical Office

Comorbidity and multi-morbidity are extremely frequent among patients with diabetes; its association with cardiovascular risk factors has been recognized for a long time. From this perspective, Piette and Kerr proposed a framework to consider ways by which associated chronic conditions could influence diabetes medical care, self-management, and outcomes [110]. They classified comorbidities in three groups, (1) clinical dominant conditions, (2) concordant versus discordant chronic conditions, and (3) symptomatic versus asymptomatic chronic conditions, and recognized, in the first place, the preeminence of diseases like cancer, end-stage renal failure, or severe cognitive impairment in the realities of diabetes care and even on life expectancy.

Comorbidities in the second group are very common and compete for time in the medical visit and for resources from patients and their families; some of them are inextricably related to the outcomes of diabetes care (hypertension, dyslipidemia), and others are related from their emotional outcomes (depression, stress) or through recently explained pathogenic mechanisms (musculoskeletal diseases). The third group includes chronic conditions which should be managed regardless of being symptoms, worsening, or recurrence [110]. Most reports about diabetes and chronic disease are about associations with single medical disorders or clusters of chronic conditions, in denial of the unifying role of diabetes in the pathogenesis of apparently disparate disorders within the cardiovascular, musculoskeletal, or digestive systems. The study of comorbidity in patients with diabetes is a recent topic and is summarized in Table 20.3.

Table 20.3 Comorbidity in patients with diabetes

Year, author, and reference	Country	Patients	Prevalence of MM and comments
Kerr et al. [111]	United States	1901 diabetes patients who responded to a survey	40% of respondents had at least one microvascular comorbidity 79% had at least one macrovascular comorbidity 61% had at least one nondiabetes comorbidity including arthritis (55%), cancer (14%), and lung disease (10%) Patients with a greater number of comorbidities placed lower priority to diabetes and had worse diabetes self-management scores Type and severity of comorbid conditions, not just the comorbidity count, influence diabetes self-management Patients with comorbidities need additional support to accomplish self-management activities
Ose et al. [112]	Germany	3546 patients with type 2 diabetes	Participation in a diabetes management program, the number of comorbidities, and the interaction between management and comorbidities have a significant impact on quality of life Structured diabetes management may help to counteract the negative effect of comorbidity
Zhang et al. [113]	Australia	17,095 patients with diabetes, 65 years and older	80% of patients had four or more comorbid conditions Only 1.0% had no comorbidity 18.7% were receiving medications for chronic obstructive pulmonary disease or asthma 17.5% were receiving nonsteroidal anti-inflammatory drugs 7.1% had cancer 4.4% were receiving medications for dementia Low utilization of preventive diabetes care services in patients with comorbidity Competing health demands and patients' preferences are very influential in diabetes management
Wermeling et al. [114]	Netherlands	2086 well-controlled patients with type 2 diabetes, including A1c, systolic blood pressure, and total cholesterol	Compared to patients without comorbidities, patients with type 2 diabetes and comorbidities had much lower health status despite good diabetes control Physical limitations and functional impairment are decisive Physicians may take into account patients' health status and integrate the impact of comorbidities into diabetes care
Luijckx et al. [115]	Netherlands	712	Prevalence of "any type" of comorbidity: 84.6% 70.6% had one or more discordant comorbid disorders, mostly musculoskeletal and mental, chronic functional somatic symptoms, and deafness 27.2% had three or more comorbid diseases At the date of diabetes diagnosis, patients had between 1.5 and 2.1 comorbidity clusters Diabetes management in general practice is complex in terms of chronic comorbidity "Straightforward" patients without comorbidities are extremely rare" Diabetes management demands management of comorbidities, including discordant diseases Validity of clinical guidelines is questionable if they do not consider comorbidity A patient-centered approach can be of added value

Table 20.3 (continued)

Year, author, and reference	Country	Patients	Prevalence of MM and comments
Pentakota et al. [116]	United States	42,826 patients with new-onset diabetes	Prevalence of comorbidity: 80% Prevalence of discordant illness: 30.1% Prevalence of both concordant and discordant illnesses: 25.5% Prevalence of concordant illness: 13% Prevalence of a dominant illness different to diabetes: 12% Comorbidity from concordant illnesses is associated with increased visit frequency and higher levels of receiving recommended diabetes care Patients with discordant illnesses had decreased diabetes care and patients with dominant illnesses received markedly decreased diabetes care
Teljeur et al. [117]	Ireland	424 patients with type 2 diabetes treated in general practice	Prevalence of comorbidity: 90% 25% of the patients had four or more additional chronic conditions, the most common: Hypertension: 66% Heart disease: 25% Arthritis: 16% Comorbidity significantly increased the number of medical visits and polypharmacy The variety of conditions emphasizes the complexity of diabetes management and the importance of maintaining a generalist and multidisciplinary approach
Alonso-Morán et al. [118]	Spain	126,889 patients with type 2 diabetes	87.6% of men and 92% of women with type 2 diabetes had at least another chronic condition 1.7% of men and 1.9% of women with type 2 diabetes had ten or more chronic conditions By comparison, 54.2% of men and 57% of women without diabetes had at least another chronic condition Ten morbidity clusters were identified in patients with diabetes, the most common related to cardiovascular risk factors and heart disease Patients with diabetes are at higher risk of peripheral vascular disease, heart failure, hypertension, and chronic renal disease
Sancho-Mestre et al. [119]	Spain	491,854 patients with diabetes identified and selected through clinical codes	70% of patients suffered from more than two comorbidities, the most common Hypertension: 68.4% Dyslipidemia: 53.3% Mental disorders: 25.0% Osteoarticular disease: 24.5% Cardiovascular disease: 14.4% Pharmaceutical expenditures increased according to the number of comorbidities
Bralic Lang et al. [120]	Croatia	10,264 patients from 449 primary care practices	77.7% patients had comorbidity The most common Cardiovascular diseases: 69.7% Endocrine and metabolic: 30.1% Musculoskeletal: 14.0% As the number of comorbidities increase, patients were less likely to achieve A1c levels Despite limited time, general physicians are able to deliver proper treatment of patients with type 2 diabetes and comorbidities Comorbidity increases clinical inertia and treatment fragmentation by different physicians, institutions, and therapies
Petrosyan et al. [121]	Canada	861,354 adults with diabetes Compliance with three quality measures according with type of comorbidity	Prevalence of comorbidity: 86% Diabetes-concordant conditions: 20.7% Diabetes discordant: 15.6% Patients with diabetes-concordant and diabetes-discordant conditions: 49.8% Receipt of all recommended monitoring tests in diabetes is higher in patients with diabetes-concordant and diabetes-discordant conditions (30.2%) and lower in patients with diabetes-discordant conditions (19.6%) Hospitalization for diabetes complications is lower in patients with concordant conditions Meeting goals for A1c does not necessarily prevent hospitalizations for diabetes, especially in patients with comorbidities Other factors, including self-monitoring of blood glucose, glycemic control, lifestyle changes, patient education, and drug therapy, are more important

Multi-morbidity in Patients with Diabetes: How Can It Be Explained?

The results of studies described in Tables 20.2 and 20.3 confirm the increasing prevalence of co-morbidity and multi-morbidity. In people with diabetes, the prevalence more than doubles the observed rates in people without diabetes, partly explained by the long-time recognized aggregation of cardiovascular risk factors. The concept of multi-morbidity started with a uni-level approach: to the simple counting of co-occurring diseases [122]. Patients are usually managed for each individual disease according to specific guidelines and by different physicians [123]. The logical limitations of this approach have encouraged a shift to integrated, albeit limited, approaches to meet the needs of individual patients [123]. The current view and classification of human disease dates to the late nineteenth century and derive from the observational correlation between pathological analysis and clinical syndromes [124]. Over the years, attention to the interactions of multiple, apparently unrelated diseases occurring at different levels led to a vertical dimension which attempts to clarify the complex interactions of multi-morbidity at the cellular, organizational, and community (even the emotional) levels [117]. In a brilliant essay, Aron addressed the additional burden imposed by multi-morbidity on diabetes self-management and the conflicts and potential risks of glycemic control [122]. A new, holistic view suggests that common linked pathophysiological pathways underlie the development of diseases in a non-organ-specific manner and that multiple diseases within one person, regardless of symptoms or organ system, are not necessarily caused by independent mechanisms [123]. Taking into account the highly internal organization of the cell, it would be possible to improve the single gene-one disease approach by developing a conceptual framework to link all genetic disorders with the complete list of disease genes, resulting in a global view of the “diseasome,” the combined set of all known disease/gene associations [125]. In the “human disease network,” nodes represent diseases, and two diseases are connected if they share at least one gene in which mutations are associated with both diseases [125]. The existence of intricate molecular links between subcellular components and disease genes raises the possibility that diseases may not be as independent of each other as physicians traditionally consider them to be and that diseases form networks in which two of them are connected if they share at least one gene [126]. Diabetes management at one level ignores its complexity, clearly illustrated by its unique aggregation of concordant and discordant conditions... clinicians must think in multiple dimensions! [122].

Addressing Comorbidity in Clinical Practice

Several instruments have been devised to measure comorbidity [127], but the most widely used is the Charlson

Comorbidity Index (CCI) [128]. Developed by Mary E. Charlson and colleagues, the CCI assigns a weight of 1 to 10 for a variety of diseases, including diabetes without organ damage [129]. Six diseases have weights of 2, one disease has a weight of 3, and two diseases have weights of 6, in order to calculate the relative risk of 1-year mortality by summing the weights of each condition [129]. Index scores range from 0 to 10, although higher scores are possible for severely ill patients [129]. The CCI has been used to estimate prognosis of comorbidities in a variety of disciplines, from dermatology to oncology, and its power to predict morbidity, mortality, costs, and hospitalizations has been validated and compared with other measures [130]. Its use continues to extend, and it has become available in several versions of online calculators.

Comorbidity is usually managed by different specialists (“as many as necessary”), using independent clinical guidelines. This approach is ineffective and conflicting, increases the demand of professional services and costs, and may even pose risks for the patients. Current disease-oriented guidelines do not account the interactions between different diseases and are designed to manage single chronic conditions [131]. Innovative approaches have been proposed to address the challenge of comorbidity, such as the Adriane principles, a tool to support decision-making during consultations in primary care that involve patients [132, 133]. The Adriane principles were designed as a process aimed to foster an innovative concept in medical decision making for patients with multimorbidity in primary care [132]. This approach establishes realistic goals at the center and three core principles: (1) individualized management, (2) prioritization of patients’ preferences, and (3) interactive assessment [132, 133]. The effectiveness of implementing the Adriane principles in comorbidity management remains to be demonstrated.

Challenges of Multi-morbidity in Diabetes Management

Multiple diseases have an additive effect: comorbidity or multi-morbidity has negative effects on mental status and quality of life and increases the frequency of medical visits and the risk of death [67, 134]. Models of integrated, simplified care of comorbidities involving chronic physical disease and mental disorders can decrease disabilities and are associated with significant reductions in total healthcare costs and hospital costs [68, 135]. The challenge to deliver patient-centered care for people with comorbidities is to provide the right care for the right person at the right time, but current medical structures do not support multidimensional care and encourage treating only disease-specific outcomes [136]. The number and type of comorbid diseases have multiple consequences in patients with diabetes, create competing

demands, and promote clinical inertia [137, 138], negatively influencing glycemic and cardiovascular risk control [139, 140]. Comorbidity should be screened at baseline and follow-up visits. The evidence about effective interventions in the management of patients with multi-morbidity is still limited, and remaining uncertainties prevail, despite its high prevalence and impact on patients and healthcare systems [141, 142]. The last two decades have witnessed a steady increase of knowledge about comorbidity in medicine, which has become a challenge for researchers, clinicians, and health policy makers. The current narrow focus on single diseases should be replaced with a holistic view and approach to established patterns of comorbidity and multi-morbidity [143, 144]. Only a radical rethinking of health systems will facilitate the transition and challenges multi-morbidity and its associated disability [145].

The Chronic Care Model and Diabetes

Usual medical care often fails to meet the needs of patients with chronic diseases, even in advanced countries [146]. Meeting the complex needs of patients with chronic illness or disability is the single greatest challenge facing organized medical practice, and usual care is not doing the job [147]. Most of the patients with diabetes either have no access to medical care or receive inadequate treatment [148]. To improve care for patients with chronic diseases, the negative evidence continuing to accumulate about the inefficacy of usual care and the positive evidence about the benefits of innovations in ambulatory care have encouraged new paradigms. Based on their work at Group Health Cooperative of Puget Sound, Washington, literature reviews, and suggestions of an advisory panel, two decades ago, Wagner and colleagues developed a model to improve chronic illness care, a guide to be used to develop effective chronic care by incorporating successful interventions [147]. The chronic care model (CCM) is based on the reality that in chronic diseases, the outcomes are largely dependent on the efforts, resources, and support of patients and their families [149]. The success of treatment requires that patients are well informed about their disease, the place where they can receive treatment, and to have greater control over their treatment [150]. The CCM is not a quick and easy fix or an abstract theory; it is a multidimensional solution to a complex problem, a concrete guide to improve clinical practice [148]. Care for chronic noncommunicable diseases (NCDs) is a global problem; the CCM is a tool to deliver integrated management for NCDs within the context of primary care and provides practical guidance for healthcare program managers, policy makers, and stakeholders to plan and deliver high-quality services for people with NCDs [151].

Taking into account that chronic illness care is largely performed within the primary care setting, the CCM has

become a major component [147, 152]. The CCM assumes that medical care is centered in the interaction of patients and practice teams, with support from the community and organization of healthcare inside and outside the health system [153]. By comparison to usual care, in which isolated physicians give orders to patients, chronic disease management involves collaboration from a group of clinicians from diverse disciplines (nurse case managers, physicians, pharmacists, social workers, dietitians, lay health workers) who communicate regularly and participate in the care of a defined group of patients. Chronic care occurs in three overlapping scenarios: (1) the community, (2) the health system, and (3) the healthcare organization, taking into account that coordination and performance may help or obstruct optimal chronic care. Essential ingredients are research, performance measurement, and quality improvement. The “six pillars of the chronic care edifice” include (1) community resources and policies, (2) healthcare organizations, (3) self-management support, (4) delivery systems design, (5) decision support, and (6) clinical information systems [148, 154, 155]. A systematic review showed that primary care practices are able to implement the CCM and incorporating most or all of its elements is associated with improved quality of care and outcomes in various chronic diseases including diabetes [156].

Glasgow and colleagues developed two scales or surveys to assess the CCM: the Assessment of Chronic Illness Care (ACIC) and the Patient Assessment of Chronic Illness Care [157, 158]. The PACIC and PACIC+ (PACIC extended with six additional multidisciplinary team functioning items to improve content validity) are reliable instruments to measure the chronic care management experiences of patients with diabetes [159, 160]. The PACIC has been translated to other languages [160] and validated in several countries [159, 161, 162] (Fig. 20.1).

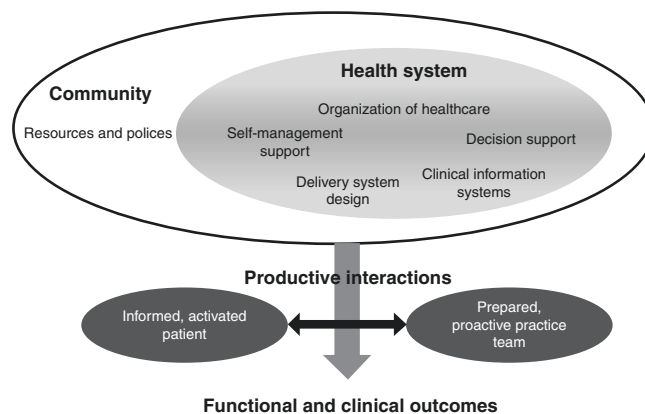


Fig. 20.1 The chronic care model

The CCM in Diabetes

In many ways, diabetes care is the prototype for the CCM and became an emblematic clinical scenario to assess its effectiveness, and increasing evidence shows that the CCM provides a framework for optimal diabetes care [156]. Table 20.4 summarizes the results of interventions implementing the CCM since 2001.

To summarize, diabetes represents an ideal clinical setting to implement the CCM. After two decades of being conceived, however, the amount of studies and, most importantly, the number of health organizations and national health systems who have implemented the CCM are still scarce. Beyond endorsement from international agencies [151] and with remarkable exceptions [172], most of the

studies and interventions to implement the CCM have occurred in developed countries; adaptations to preexisting models are the rule, instead of studies devoted to implement the CCM “as it is [173].” Most of the studies cited in Table 20.4 continue to appear in systematic reviews, not only because of importance but also because of scarcity of new trials [174, 175]. Available studies show limitations, including non-blinding of participants, brief follow-up, absence of self-report measures for behavior change, small sample size, inadequate training of health professionals, and absence of registries and electronic medical records [176]. Despite these challenges, in less than 20 years, a large amount of experience using the CCM has accumulated worldwide, in every age group and for multiple diseases. More evidence about the effectiveness of the CCM in diabetes management is essential.

Table 20.4 The chronic care model (CCM) in diabetes management

Year, country, and reference	Patients and intervention	Results	Comments
2001, United States [163]	Randomized controlled trial 57 primary care practices serving ≈500,000 people Patients with diabetes ≥30 years attending chronic care clinics at 3–6-month intervals. Components of the CCM: Baseline assessment Individual visits with primary care physicians, nurses, clinical pharmacists, one-group peer support session	Patients receiving the intervention were more likely to receive preventive procedures, foot and retinal examinations, and medication reviews, at no significant differences Rates of participation in diabetes education were significantly higher Nonsignificant differences on physical function, depression measures, days confined in bed, and patient satisfaction Mean A1c levels were equally higher in the two groups, and cholesterol levels were equally lower Chronic care clinic patients visited primary care more frequently; the increase was associated with significant reductions in specialty, emergency room visits, and hospital admissions	Redesign of care including delegation of roles within the practice team, involvement of other disciplines, organization of visits and follow-up, and integration of psychoeducational interventions plays an important role in success
2006, United States [164–166]	Multilevel, cluster design, randomized controlled trial 19 hospitals 166 primary care clinics 1400 academic physicians 90,000 patients with diabetes Implementation of the six elements of the CCM Delivery of diabetes self-management (DSMT) training Stepped approach	Over 4 years, the number of CCM-recognized programs grew from 3 to 21 Significant differences in A1c among patients receiving DSMT in hospital programs versus primary care 2–3 greater proportion of patients received SMDT at primary care offices versus patients referred to hospital-based programs	The CCM is an effective framework to support DSMT With reliable clinical information systems, educators are able to demonstrate the benefits of DSMT on A1c levels Improvements in program and patient outcomes can be sustained, financially self-supporting
2007, United States [167]	Controlled pre- and post-intervention study, 1-year duration 1170 patients with type 2 diabetes 613 assigned to chronic care 557 assigned to usual care	Patients in both groups had improvements in A1c, blood pressure, and lipoprotein levels Participants in the intervention group had a 2.1% greater reduction in cardiovascular risk	Collaborative interventions using the CCM lower cardiovascular risk factors in patients with diabetes

Table 20.4 (continued)

Year, country, and reference	Patients and intervention	Results	Comments
2007, United States [168]	Observational study 30 small, independent primary care practices 90 clinicians, including 60 physicians, 17 nurses, and 13 assistants who completed a questionnaire assessing the use of the CCM 886 patients with diabetes	Use of the CCM was significantly associated with lower A1c levels and ratios of total cholesterol to high-density lipoproteins Every unit increase in the use of the CCM was associated with a 30% A1c reduction and a 0.17% reduction in the lipid ratio	Clinicians in small independent primary care are able to incorporate elements of the CCM in their practice, associated with higher levels of process and intermediate outcomes of diabetes care
2009, 2010, Belgium [169, 170]	Four-year evaluation of a project based on the CCM Implementation based on the ACIC survey Implementation: First stage: 2300 patients with type 2 diabetes Follow-up: 4174 patients	Overall ACIC scores improved from 1.45 at baseline to 5.5 at the end of the study Mean A1c and total cholesterol significantly improved in the intervention group Assessment of long-term complications was insufficient Crucial steps for strengthening primary care included a local steering group, appointment of program managers, and willingness of well-trained and motivated care providers Important barriers include complexity of the intervention, lack of quality data, inadequate information technology, lack of commitment, and unsustainable funding	Adapting the CCM in primary diabetes care has opportunities and bottlenecks Further improvements are required to deliver the CCM components Albeit remarkable improvements were achieved, primary care providers lack the opportunities and resources to take full responsibility for chronic care
2010, United States [171]	Intervention trial 25 practices, 4 physicians per practice Implementation of the CCM measured through staff and clinical management surveys, chart audits, and patient questionnaires	Overall low levels of implementation Sites with higher levels of CCM implementation showed improvements in diabetes assessment and treatment Physical activity counseling for persons with overweight and obesity was associated with CCM implementation, except for people with diabetes	Modest levels of CCM implementation in unsupported primary care is associated with improvements in diabetes care and higher rates of behavioral counseling
2015, Philippines [172]	Observational study Two primary healthcare units in semirural and rural municipalities Adaptation and implementation of the CCM Assessment of chronic illness care (PACIC) and glycemic control	Significant improvements in A1c, glycemic control, and PACIC scores	In resource-limited settings, the CCM improves the quality of primary diabetes care as measured with the PACIC and A1c
2017 Italy [173]	Population-based cohort study 8486 patients exposed to the CCM versus 8486 non-exposed patients Four-year duration	Significant improvements for adherence to clinical guidelines, reduced risk of cardiovascular complications, and protective effects for neurological complications, cardio-cerebrovascular complications, and mortality	Implementation of the CCM-improved diabetes management and reduced cardiovascular outcomes

Diabetes as a Complex Disease

Zimmerman, Lindberg, and Plsek described three kinds of problems in the world: simple, complicated, and complex [177]. Simple problems are clearly defined, with straightforward solutions. Complicated problems don't have straightforward solutions but can be dissected into groups of simple problems. Complex problems have multiple components,

commonly not initially perceived and appear during the process of solution. To address complex problems, expertise is important but not sufficient; uncertainty and risk are trademarks. Diabetes management is a complex task. Complexities of diabetic control were recognized five decades ago by Franklin Williams and colleagues, who described the degree in which a variety of continuing intervening factors including (1) biological, (2) psychological, (3) appropriateness

Table 20.5 Main factors affecting outpatient diabetes management

Practice factors	Organizational factors
Partners with interest in diabetes	Diabetes registry
Practice nurses with interest in diabetes	Recall system
Number of practice nurses	Structured diabetes care
Computerized practice	Attachment to diabetes nurses or health visitors
Practice workload	Access to chiropractors
Practice motivation	Access to optometrists
Diabetes education in the general practice	Access to dietitians
Patient factors	Patients self-monitoring
Self-monitoring of patients	Delivery of diabetes education
Frequency of attendance	Diabetes clinical guidelines
Social deprivation	

Modified from Kunthi [179]

(and timeliness referring to clinical inertia) of medical recommendations, (4) adequacy of diabetes education (from a pedagogic to an andragogic approach in adults), (5) patient's resources (cognitive, socioeconomic, motivation, health literacy), and (6) family and social support, converge to achieve the lifetime challenge of day-to-day control [178]. Despite these arguments, reductionist approaches abound and prevail in diabetes management.

To illustrate the complexities of diabetes management, Khunti identified 54 factors associated with effective delivery of care: 23 were practice-related, 14 were patient-related, and 20 were organizational [179]. Table 20.5 summarizes the highest-ranked factors among the 54 original, based on 5 assessment methods: literature review, brainstorming, focus groups, and key informants – general physicians, nurses, and patients.

Countless efforts have failed and continue to fail from denial of this reality. Recognition of complexities of diabetes care starts by identifying the three components of successful diabetes management: (1) patient activation, (2) self-care, (3) support. Each one is essential to achieve the desired outcomes; all of them are directly related to the crucial role and responsibility of people with diabetes and their families. Self-care and support are associated to the capacity to deliver multidisciplinary, patient-centered care, including diabetes self-care education and support. The absence of any one of these components leads to clinical failure, waste of economic resources, and overall dissatisfaction from patients, their families, payers, and providers.

Patient Activation and Its Measurement

Patients unable or unwilling to move in the right direction are very unlikely to achieve the goals of treatment established by evidence-based medicine, even in the best professional environments. Ideally, therefore, it would be desired

to explore or assess the level of patient activation. Based on her experience about the unwillingness of health systems to accommodate with her needs as a patient, in 2004 Hibbard and colleagues devised the Patient Activation Measure (PAM), a tool for gauging the capacity of patients to advocate for themselves as they proceed through a medical experience [180]. The original scale had 22 items, which assessed patient self-reported knowledge, skill, and confidence for self-management of one's health or chronic condition [181]. On further analysis, the PAM was reduced to a 13-item measure which has been translated to other languages and validated in the assessment of a variety of chronic conditions [182–185]. Patient activation has been significantly related to health outcomes, in patients with chronic diseases, including diabetes [186, 187]. The PAM has become the gold standard to understand the role of people with chronic conditions in their own health and is likely to be the focus of the next generation of interventions to support informed consumer choices [188].

Self-Care Management

In 1980, Donnell Etwiler recognized the increased demand of sustained care for chronic disease management, the importance of medical teams, and the main evolution in their development: to include the patients [189]! Don reflected that this had come about not only from the chronic nature of many diseases but also by the number of daily tasks that (patients) are frequently required to carry out. He also stated that to address the health needs of people with diabetes requires developing comprehensive healthcare teams including physicians, health professionals, patients, family members, and involving the community [189]. Self-care was recognized as an essential component of all the pioneering models of diabetes management [5, 6, 10, 11], and a variety of interventions including “teaching machines” (combinations of printed text and still pictures) were proposed since the 1960s [190]. Early efforts were based on prescriptive, pedagogic approaches in which patients were to “be instructed to report” with their physicians; other health professionals were discarded [191]. The consistent failure of traditional diabetes education programs to improve patient self-care, documented since the 1970s, encouraged exploration of innovative approaches [192]. Lorig and Wagner stressed the importance of collaborative relationships between patients and health professionals and the need to share complementary knowledge and authority in the health-care process, with health services as organizers and financial supporters of these new roles [149, 193]. Many patients are overwhelmed by the multiple, continuous, annoying demands and unpredictable results of diabetes management [194]. Facilitating strategies include asking questions, identifica-

tion of “sticking points” of self-care, goal setting, action planning for change, involvement of family and friends, follow-up, problem-solving, and nourishment of coping skills [194, 195]. Diabetes self-management and support education (DSMSE) has become essential in structured diabetes care and is brilliantly addressed in Chap. 26 of this book. Self-management interventions in people with diabetes receiving self-care management, especially delivered in compact programs with sessions closely grouped together, have shown advantages in glycemic control compared to interventions with an educational approach [196, 197]. Self-management training has higher medium-term efficacy than didactic diabetes education [198]. Self-management is highly dependent from collaborating forces at four levels, according to the ecological model of self-care by Fisher and colleagues: (1) personal factors, reflecting the physical and mental status of patients; (2) immediate relations, with family members and friends, at school and work; (3) health systems; and (4) social determinants of health [199]. After more than three decades, “inclusion of patients” is increasingly recognized but at the same time denied in the real world. The importance of self-care is an undeniable component of success. Integrating DSMSE in routine diabetes care is the essence of person-centered care [200]. “Although the achievement of evidence-based clinical goals reduces the risk of morbidity and mortality in type 2 diabetes, delivery of community practices and referral centers often falls short of these goals [201].” Multiple misconceptions and barriers to integrate self-management support into clinical practice include (1) “we’re already doing this”; (2) inability, disinterest, and disdain to address skill deficits; and (3) the need for organizational change [202]. “By comparison to other therapies, DSMSE appears to be the Cinderella of diabetes management...but with greater collaboration, leadership and direction, Cinderella really can become the belle of the ball [200].”

Support

Besides new medicines, main challenges in diabetes outpatient management include (1) recognizing and addressing its complexities; (2) developing, implementing, and sustaining improvements in healthcare systems; and (3) broadening the definition of the “office,” reminding that a year has 8760 hours and, in the best possible situation, patients have a very limited amount of time at physician’s offices [203]. Essential components of structured diabetes outpatient management include (1) targeting patients at high risk, including intensively reducing A1c levels $\geq 9.0\%$, blood pressure $\geq 160/95$ mmHg, and foot care in patients at high risk of foot ulcers [204, 205]; (2) diabetes registries for data collection, reporting, support, and quality improvement [205–209]; (3) local physician champions with specific interest in diabe-

tes and chronic care management, the responsible to coordinate the implementation of the patient-centered medical home [205, 206]; (4) team management involving primary care providers, nurse practitioners, dietitians, and “physician extenders” [210–212]; and (5) health coaching to make sure that patients understand the care plan involving “knowing their numbers,” shared decision-making, promoting behavior change, and medication adherence [213]. Health coaching has greatly evolved as an important resource in diabetes self-management and care [214]. Diabetes health coaching improves glycemic control, reduces distress, and increases medication concordance and adherence [215, 216]. Diabetes coaching models comprise (1) personal case management and monitoring; (2) diabetes self-management education and support; (3) behavior modification, goal setting, and reinforcement; and (4) general psychosocial support [214]. Technology has leveraged to facilitate each component of diabetes coaching; its rate of development surpasses advances achieved in other major areas of research [217]. Understanding, development, and implementation of effective interventions for patient support, including diabetes coaching, has become a major challenge and, at the same time, a huge opportunity to link the advances of evidence-based medicine with everyday clinical practice.

Conclusions

Establishing the best evidence is not the same as implementing the best practice though the former does provide a basis for the latter.
Philip Davies [218]

Randomized controlled trials, meta-analysis, and systematic reviews have confirmed that unstructured community care is associated with poorer follow-up, worse glycemic control, and greater mortality [176]. This is the case of health systems reluctant and resistant to change the acute care approach in diabetes management like Mexico, where three decades of ill-devised, unstructured, short range, and low resource efforts have not been able to improve clinical outcomes or to reduce diabetes morbidity and mortality [219, 220]. By comparison, worldwide experiences accumulated over three decades have documented the effectiveness of diabetes care in primary practice to reduce risk factors, improve the process of care, decrease referrals to specialized care, and increase the number of consultations when complex, multifaceted interventions and organizational interventions that facilitate structured and regular review of patients are established, in addition to patient education and with support of nurses and health professionals [26–48, 221]. The results of randomized controlled trials have demonstrated that achieving the goals of metabolic control by lowering glucose, blood pressure, and LDL cholesterol reduces the risk of

microvascular and macrovascular diabetes complications [222]. Nevertheless, most diabetic patients do not meet these recommended goals; prevailing and persistent structure and process deficiencies in primary care impede the achievement of outcomes. Studies of the level of diabetes care provided “in the real world” and especially in primary care where the vast majority of patients are seen continue to show that performance levels are highly suboptimal from what is recommended [223]. Challenges of diabetes translation, starting with the urgency to change healthcare systems, were described by Anderson since 1991, but a large proportion of persons with diabetes worldwide continue to be treated “as usual [224].” Establishing effective, sustainable, long-term outpatient diabetes management programs is one of the greatest challenges in this era.

Multiple-Choice Questions

1. Initial experience of hospital diabetes clinics in Europe showed that:
 - (a) It was absolutely feasible to treat all patients with diabetes.
 - (b) Every patient could receive treatment from highly trained specialists.
 - (c) Nurses and dietitians were not required.
 - (d) Physicians were the most important elements of success.
 - (e) Clinics became overwhelmed, resulting in long waiting times and dissatisfaction.
2. Successful clinics are the ones:
 - (a) With the most qualified medical specialists
 - (b) Who had the vision and were able to offer comprehensive services
 - (c) Charging the highest fees for their services
 - (d) In which patients could be admitted to an hospital
 - (e) Having access to the newest medications
3. Diabetes management from a paternalistic approach:
 - (a) Is essential to make patients follow physicians’ orders
 - (b) Has been shown to reduce the risk of acute complications
 - (c) Reduces the risk of chronic complications
 - (d) Has received high levels of satisfaction from patients and their families
 - (e) Has never been assessed and is associated with acute and late complications
4. Planning of diabetes services:
 - (a) Needs to be broader beyond those available in most centers
 - (b) Requires procuring for new medications
 - (c) Must be based on the expertise of specialists
 - (d) Occurs exclusively at the medical office
 - (e) Is not important, patients may attend whenever they want
5. Implementation of a model based on the DCCT in clinical practice requires all the following except:
 - (a) Allocation and effective use of resources
 - (b) Standards of care and quality assurance
 - (c) Training and continuing education
 - (d) Research and evaluation
 - (e) Recognition that patients are unable to self-manage
6. Outpatient diabetes management:
 - (a) Is feasible, acceptable, and effective
 - (b) Produces significant improvements in A1c
 - (c) Does not increase the frequency of hypoglycemia
 - (d) Is not inferior to management in hospital clinics
 - (e) All of the above
7. Comorbidity:
 - (a) Should be treated by different specialists
 - (b) Is very uncommon
 - (c) Has no impact on diabetes management
 - (d) Is increasingly frequent, “the disease of the twentieth century”
 - (e) Is never been more important than diabetes
8. Compared with people without diabetes, the prevalence of comorbidity in patients with diabetes:
 - (a) Is very rare
 - (b) Is lower
 - (c) Is equal
 - (d) Is slightly higher
 - (e) Is more than double
9. The chronic care model:
 - (a) Recognizes that outcomes are largely dependent on patients and their families
 - (b) Depends on the availability of all the necessary medications
 - (c) Recognizes the preeminence of physicians in all the decisions of management
 - (d) Involves fragmentation of services
 - (e) Is important but very expensive and complicated
10. Diabetes management:
 - (a) Is simple and straightforward
 - (b) Is complex but outcomes are certain
 - (c) Is complex and outcomes are uncertain
 - (d) Depends exclusively on physicians’ expertise
 - (e) Is independent of patients’ resources

Correct Answers

1. (e) Clinics became overwhelmed, resulting in long waiting times and dissatisfaction.
2. (b) Who had the vision and were able to offer comprehensive services

3. (e) Has never been assessed and is associated with acute and late complications
4. (a) Needs to be broader beyond those available in most centers
5. (e) Recognition that patients are unable to self-manage
6. (e) All of the above
7. (d) Is increasingly frequent, “the disease of the twentieth century”
8. (e) Is more than double
9. (a) Recognizes that outcomes are largely dependent on patients and their families
10. (c) Is complex and outcomes are uncertain

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