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PSYCHOSOCIAL ASPECTS (KK HOOD AND S JASER, SECTION EDITORS)

A Review of Adolescent Adherence in Type 1 Diabetes and the Untapped Potential of Diabetes Providers to Improve Outcomes

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Abstract Only 21 % of adolescents with type 1 diabetes (T1D) meet glycemic goals set forth by the American Diabetes Association. Adherence to therapy is a particular concern in this population, and the association between poor adherence and worsening glycemic control indicates that there is a critical need to improve adherence to therapy in adolescents with T1D. In this article, we review barriers to adherence in adolescents with T1D and discuss interventions aimed at improving adherence to therapy and glycemic control. Interventions include technology-based applications, family-based therapies, motivational interviewing, and others. Notably, less than 10 % of the interventions reviewed are provider-led, clinic-based interventions, and few have focused on regimen-related aspects of adherence. This article also outlines the importance of provider communication and the role of providers in facilitating adherence behaviors in adolescents with T1D. Finally, we suggest future directions of research to improve adherence to therapy in adolescents with T1D.

Keywords Type 1 diabetes · Adolescents · Adherence · Providers

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Introduction

Only 21 % of adolescents with type 1 diabetes (T1D) meet American Diabetes Association guidelines for target hemoglobin A1c (a surrogate for disease control) [1••, 2]. As glycemic control is typically at its worst in adolescence, this window is a critical opportunity to improve control and minimize the multiorgan complications (e.g., kidney disease, eye disease, cardiovascular disease, and neuropathy) associated with chronic hyperglycemia [1••, 3]. Adolescence is a period of marked change, including the hormonal and psychosocial changes associated with puberty and emerging young adulthood. While the hormonal changes of adolescence can lead to insulin resistance, there are several other factors (psychosocial, regimen-related, and communication-related) that drive poor glycemic control seen in adolescents. Understanding and targeting the reasons behind the poor control seen in adolescence are requisite steps to improve glycemic control in this population.

The association between glycemic control and adherence to therapy suggests that to improve glycemic control, adherence to therapy must be improved (as adherence increases, A1c decreases, effect size −0.28 with 95 % confidence interval (CI) −0.24 to −0.32) [4]. Adherence can be loosely defined as "the degree to which patients follow the recommendations of their health professionals" [5]. In T1D, these recommendations include checking and logging blood sugars four to six times per day, counting carbohydrates, giving meal, snack, and long-acting insulin, monitoring blood sugar trends, adjusting insulin therapy as needed, attending routine clinic visits, and communicating with providers as necessary between visits [2]. While these specific tasks may change as diabetes technology advances, data suggest that adherence to therapy continues to be a problem even with advanced technologies. For example, research shows that youths with T1D

rarely use continuous glucose monitoring (CGM), a technology associated with improved glycemic control and reduction of hypoglycemia when worn regularly [6]. These findings demonstrate that even as diabetes therapies change, poor adherence remains an important problem.

Measuring adherence to therapy in T1D is difficult because adherence is defined by the several recommendations outlined above and individuals may exhibit varying levels of adherence to the different recommendations; fortunately, studies have shown that blood glucose monitoring frequency (BGMF) may be one of the best markers of adherence to therapy [7••]. While other measures of adherence rely primarily on self-report, BGMF provides an objective way to monitor adherence to therapy. Additionally, BGMF has a strong association with change in glycemic control (even when controlling for covariates such as age, ethnicity, gender, and insulin delivery method) [7••, 8]. As would be expected given the poor glycemic control seen in adolescence, data also show that adherence to therapy (measured with BGMF) worsens during adolescence [7••]. This finding reinforces the concept that to improve glycemic control in this age group, adherence to therapy must be improved.

In this article, we review barriers to adherence in adolescents with T1D, discuss interventions to improve adherence behaviors, outline the role of providers in improving adherence, and finally suggest future areas of research to improve adherence to therapy.

Barriers to Adherence in Adolescents with T1D

Many of the barriers to and facilitators of treatment adherence in pediatric diabetes are psychosocial in nature. Family functioning is a well-established factor contributing to adherence in youth with T1D. Parent-child relationships characterized by warmth and support for diabetes management are associated with better adherence to treatment [9–12]. While there is a natural shift in responsibility for diabetes management as children enter adolescence, declines in parental oversight have been associated with worsening adherence [13]. Parental monitoring in particular has emerged as a strong predictor of adolescents' adherence to their recommended diabetes treatment regimen [9, 10, 14–16]. More recently, studies have examined the influence of fathers on adherence in pediatric diabetes, finding that fathers' helpfulness and amount of involvement are related to better treatment adherence and quality of life in children [17]. However, the perceptions of involvement are important; parental involvement has been related to better adjustment and adherence when the adolescent enjoyed and needed it [10], whereas involvement that is perceived as intrusive, rather than collaborative, is associated with lower adherence and suboptimal glycemic control [18–20].

Less attention has been given to the role of peers in adherence to diabetes care. For example, one study found that family provided more support for diabetes care, but peers provided more emotional support for diabetes [21]. A more recent review on peer influences in adolescents with diabetes concluded that there is no strong evidence for peer support on adherence in this population [22]. Another study followed adolescents during their transition from high school to college and found that peer support and peer conflict were not significantly associated with glycemic control; however, there were some limitations in patient follow-up during the study [23]. The role of peers during the transition into adulthood and their effect on adherence are still unclear; therefore, additional investigation into their role in this transition period is warranted.

Additional psychosocial barriers to adherence include a high prevalence of mood, anxiety, and eating disorders in adolescents with T1D. While adolescence is a high risk period for depression and other mood disorders in the general population, a recent study examined adolescents 10 years after diagnosis with T1D and found much higher rates of psychiatric morbidity than what was reported in the community [24, 25]. A post hoc analysis also found higher rates of DSM-IV diagnoses in those with poor glycemic control compared to those with good control [25]. Similarly, symptoms of depression, anxiety, and other mood disorders (without formal diagnoses of depression and anxiety) also increase the risk of poor adherence to therapy [26, 27]. Further, eating disorders and disordered eating behavior have been reported at significantly higher rates in adolescents with T1D as compared to the general population, and these have a negative impact on adherence through omission of insulin for weight loss [28]. Eating disorders and disordered eating behavior are seen at higher rates in females with T1D (as compared to males with T1D); however, there is evidence that these behaviors are becoming more common in males with T1D implying that this may be a barrier to adherence in both males and females with T1D [28].

Barriers to care such as problems communicating with providers and cost of care also pose challenges to adherence to therapy. Using the SEARCH cohort of youth with T1D, Valenzuela et al. found that 48 % of families with children with T1D reported that "getting information" was a barrier to care, 43 % reported that communication with health care providers was a barrier, and 48 % reported that cost of care was a barrier [29••]. Communication with health care providers referred to providers listening to patients, spending enough time with patients, and explaining concepts appropriately. Getting information referred to providers discussing questions/concerns and answering patient questions. Nearly half of families with T1D felt that they were unable to effectively communicate with their providers or did not receive the information that they needed, making this a significant barrier to adherence to therapy [29••].

Finally, regimen-associated barriers to adherence also challenge families/adolescent patients. Burdick et al. showed that 65 % of insulin pump-wearing patients miss one or more meal doses of insulin per week and that two missed meal doses of insulin per week increase A1c 0.5 %, a clinically significant amount [30]. The most common reason for not giving a meal bolus of insulin was forgetting to give the insulin, but additional details of this alarming statistic are not known [30]. Specifically, are meals and snacks at certain times of day more easily forgotten, and are blood glucose checks at certain times of day more challenging to remember or act upon? For example, a study using ecological momentary assessment to measure BGM and insulin administration found that morning time was associated with worse adherence [31]. Assessing and intervening on these regimen-associated barriers are important future areas of investigation (see "Future Directions" section below).

Clearly, multiple barriers to adherence in adolescents with T1D exist, including psychosocial, communication, cost, and regimen-associated barriers. To improve adherence in adolescents with T1D, interventions need to target these barriers with the goal of minimizing barriers and improving adherence behaviors.

Interventions to Improve Adherence to Therapy in Youth with T1D

It is not surprising that several interventions have targeted adherence to therapy in pediatric patients with the goal of improving glycemic control given the association between adherence to therapy and glycemic control. Hood et al. conducted a meta-analysis of adherence promoting interventions in pediatric patients with T1D using intervention studies from 1994 to 2009. The analysis examined the ability of the interventions to improve glycemic control (difference in effect size in intervention and control groups when comparing glycemic control before and after the interventions) [32]. This study demonstrated essentially no improvement comparing pre- versus post-intervention in the intervention versus control group (effect size of 0.11 95 % CI −0.01–0.23) [32]. These interventions varied in their approach and included individual and family-based interventions, utilized behavioral family system therapy, problem-solving, coping skills, diabetes video games, blood glucose downloads, telephone case management, and educational interventions. Interestingly, the authors found that interventions that were multicomponent in nature that targeted more than direct behavioral processes had a larger effect (their example was a coping skill intervention by Grey and colleagues that may have improved general coping skills, in addition to diabetes coping skills, with an effect size of 0.49 [33]). No comparisons were made examining gender or other demographic variables with respect to effect size. The small effect of these interventions is concerning in that, as a whole, multiple different types of adherence promoting interventions had very little effect on glycemic control.

One intervention that has recently been gaining more attention is motivational interviewing (MI). In MI the interviewer and patient engage in a collaborative conversation, empowering and motivating the patient to make goals to change behavior [34]. A meta-analysis examining the effects of MI in pediatric chronic care conditions found that across several different chronic diseases, the overall effect size of MI interventions on pediatric health behavior change was small/moderate g=0.282 (95 % CI 0.242–0.323) [35•]. Interestingly, of the studies analyzed, the largest effect size was found in T1D (g=0.914). However, of the four T1D studies two had a negative or non-significant effect size, and two had very large effect sizes, suggesting that these results should be interpreted cautiously [35•]. Additionally, an MI intervention targeting providers (see "The Role of Providers" section below) was not effective in improving glycemic control, suggesting that either the intervention itself (web-based modules, and day long training sessions focusing on certain aspects of MI) or the method of implementation may have a limited impact on glycemic control [36]. Powell and colleagues recently published an article reviewing MI in pediatric T1D [37]. They concluded that to be successful, MI needs to be taught and delivered in a uniform way and that MI interventions should focus on components of diabetes care rather than diabetes outcomes alone. While pediatric MI studies have had mixed results thus far, this intervention may hold promise when applied more uniformly and when targeting adherence behaviors, as Powell and colleagues suggest.

Ongoing pilot studies trialing adherence-promoting interventions may offer promising new directions. One study evaluates the effect of positive affect on adherence in T1D—specifically, whether inducing positive affect amongst adolescents increases their motivation to complete diabetes-related tasks. The pilot study found an association between adolescents' level of positive affect and adherence (measured through the Self-Care inventory, self-reported glucose monitoring, and meter downloads) [38]. High retention in the study suggests that families are engaged by the positive psychology approach, and further/follow-up studies are indicated.

Another pilot study employed a cognitive-behavioral intervention for adolescents to reduce worry/distress that occurred with completing diabetes adherence behaviors around friends. This study was not powered to achieve statistical significance, and no change was seen between levels of worry and distress pre, post, and 1 month after the intervention [39]. However, this study demonstrates another original strategy to improve adherence behaviors in adolescents with T1D. It is difficult to know whether employing this strategy in a larger sample size would demonstrate an improvement in adolescent worry and

distress or whether it would improve worry/distress in certain populations of adolescents, thereby improving adherence.

A less-studied component of adherence is the relation between adherence and health care utilization and costs. A 2003 study investigated the effect of Care Ambassadors (CA), non-medically trained research staff that monitored appointments and helped schedule/reschedule appointments, on glycemic control, significant hypoglycemia, and ER visits/hospitalization [40]. The authors found that those in the CA and the CA+ group (which involved a CA plus a psychoeducational intervention) had significantly improved clinic visit attendance compared to those receiving the standard of care (no CA or psychoeducational intervention) ($P<0.001$). Additionally, in the CA+ group, there was a decrease in ED visits and rate of hospitalization, an increased likelihood of improving glycemic control amongst "high-risk patients," and decreased hypoglycemia [40].

Limitations of this study include a homogeneous patient population and no true cost outcome measurement, making it difficult to determine whether a full-time CA who can monitor clinic attendance and perform the psychoeducational intervention is really a cost-saving resource. A follow-up study involving CA failed to show improvement in glycemic control when comparing the intervention groups to the standard of care group [41]. While CA may help facilitate appointments and reduce hypoglycemia and ER visits, their effect on glycemic control is unclear.

Other innovative approaches to improving adherence behaviors in adolescents with T1D include use of technology, specifically cell phones. Eighty-eight percent of American teens aged 13–17 have access to cell phones, and 90 % of teen cell phone users text message [42]. Additionally, research from the Pew Research Center shows that while there are some racial disparities in cell phone ownership, the majority of teens (including White, non-Hispanic black, and Hispanic teens) own cell phones and use text messaging, allowing cell phone/text messaging interventions to reach a broad patient population [42, 43]. Additionally, a report published in April of 2015 found that a majority of adult smart phone users (62 %) used their smart phone to access health-related information in the past year [44]. However, recent text messaging interventions targeting youth with T1D have had mixed results. A pilot study that used text messages to encourage and remind youth about diabetes-related tasks reported stable glycemic control in their intervention group (compared to worsening control in the non-text messaging historical control group) [45]. Another pilot study developed a text message-based system to remind participants to check blood sugars (with email reminders sent to a control group) with notably decreased participation in both the intervention and control groups after the initial month of the study and no change in glycemic control (although no change was expected given small sample size in this pilot study) [46]. While using text messaging to communicate with patients is certainly a new and exciting area, there is doubt about the long-term efficacy of text messaging interventions, given the above data and concerns regarding changing technologies, cell phone use during the summer vs. school year, cell phone use during school hours, caregiver and peer involvement, and lack of novelty over time [47•]. It is likely that text-messaging interventions will be most effective when they incorporate other approaches (e.g., positive psychology, coping skills training).

While these are promising new areas of adherence research, it is important to consider not only the effect of the actual interventions studied, but also *who* provided the intervention in question. Figure 1 depicts the interventions discussed in this section (in addition to other recent interventions) separated by the group that delivered the intervention [33, 36, 38–41, 45, 46, 48–71]. The majority of the interventions are automated (e.g., text message-based intervention) or are provided by research staff, nurses, PhD-trained psychologists, or therapists. While some clinics are very fortunate to have these types of resources, other smaller or more rural clinics would not benefit from these interventions without recruiting additional personnel or further adapting already strained resources. For example, a recent study that surveyed pediatric endocrinologists around the world found that only 40 % of centers studied had a psychologist as a member of the diabetes treatment team [72•]. It is therefore necessary to consider the feasibility of these interventions and consider developing interventions that may be able to target a larger patient population (see "The Role of Providers" and "Future Directions" sections).

The Role of Providers

One area that has been less studied in the adherence field is the role of providers (physicians, nurse practitioners, and physicians assistants), and how providers can impact adherence and, therefore, glycemic control. Of note, other types of providers such as nurses/certified diabetes educators play a large role in providing diabetes care. However, the American Diabetes Association recommends quarterly provider (physician, nurse practitioner, physician assistant) visits for those with poor glycemic control (and at least twice yearly in those meeting glycemic targets) [2]. Given this frequency of visits, interventions that utilize these providers may be an effective way to improve adherence amongst adolescents with T1D.

Notably, less than 10 % of the recent interventions reviewed in this paper aimed at improving adherence or that used adherence as an outcome measure (or with components to improve adherence in the intervention) had a routine clinic visit-based provider component (see Fig. 1). Two of the four studies reviewed in this paper that did utilize providers (1) had a nurse practitioner deliver a behavioral intervention outside

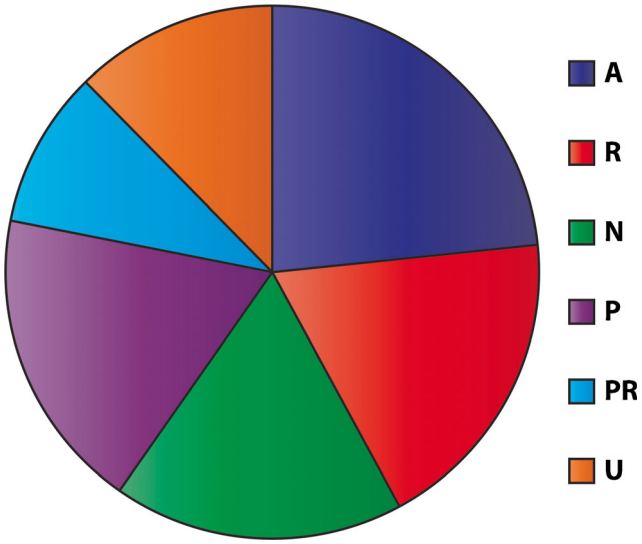

Fig. 1 Intervention studies (n=32) in youth with diabetes that have components to improve adherence in the intervention- and/or adherence-based outcome measures, separated by who delivered the intervention. A minority of recent intervention studies with adherence-based components in adolescents with diabetes are performed by providers. *A* automated [45, 46, 48–53]; *R* research staff [38, 40, 41, 54–57]; *N* nurse, diabetes educator, social worker, and dietician [58–65]; *P* PhD-trained psychologist, graduate student therapist, and therapist [39, 56, 57, 60, 61, 63, 65–67]; *PR* provider (nurse practitioner or physician) [33, 36, 51, 64]; *U* unable to determine who provided the intervention [68–71]

of routine office visits (which may not be possible in a busy practice) or (2) asked the nurse practitioner to review blood sugars (part of a telemedicine intervention) [33, 51]. The remaining two studies integrated their intervention into outpatient care delivered by different members of the health care team (including providers) [36, 64]. One of these studies employed guided self-determination (life skills) to improve glycemic control, with no significant improvements in adherence or glycemic control in the intervention versus control groups [64]. The other study (the DEPICTED study) utilized an MI-based intervention to improve glycemic control. There was no difference between the intervention and standard of care arms at 1 year (end of study) in hemoglobin A1c (primary outcome) when compared to baseline nor was there a difference in adherence as measured by the quality of life inventory [36]. It is possible that this type of intervention did not work because of the difficulties in teaching providers MI, in consistently employing the intervention over the year of the study or that this intervention does not work uniformly in all patients with T1D. This study illustrates a type of provider-based intervention that may not be effective in improving patient adherence. It is important that only 4 of the 32 studies reviewed in this paper utilized providers in their intervention, and only 2 of those were targeting clinic visits. Clearly, very few studies in youth with diabetes have investigated what providers can do to impact adherence behaviors during routine office visits.

Provider communication may be an important target for adherence-promoting interventions amongst adolescents with T1D. A 2009 meta-analysis by Zolnierek examining (1) physician communication and its effect on patient adherence and (2) whether communication training amongst physicians improves patient adherence showed the importance of physicians/providers and their effect on patient adherence [5]. Specifically, this study found that the odds of a patient adhering to therapy were much higher when the physician was a "good communicator" (odds ratio 2.16, 95 % CI 1.91–2.35). Interestingly, this relationship was even stronger when the provider was a pediatrician (pediatrician r=0.25 vs. non-pediatrician r=0.18). The authors suggest that this may be because unlike adult providers, pediatricians must communicate with both parents and patients and therefore must communicate effectively with two different groups who may require varying levels of detail and explanation. Finally, this meta-analysis also found that the odds of a patient adhering to therapy were higher (1.62) if the physician had received specific training in communication skills [5]. Clearly, patient adherence is closely tied and positively associated with provider communication; therefore, focusing on provider communication specifically within the field of T1D will be very important, as these data suggest that providers have the ability to influence and improve patient adherence to medical therapy.

It is important to note that Zolnierek's meta-analysis was not specific to diabetes patients and the heterogeneity amongst the studies may make it difficult to broadly apply findings to specific patient populations. However, the overall finding that physician communication is associated with improved patient adherence is very important and warrants investigation in pediatric diabetes patients. This finding is also in line with the recent study by Valenzuela and colleagues, which demonstrated that amongst the SEARCH cohort of youth with T1D, a prominent barrier to care reported by patients and their families was provider communication (43 % of patients/families) [29••]. Taken together, these studies suggest that there is significant room for improvement in provider-patient communication and that improving communication may promote patient adherence. Interestingly, the concept that providers must be able to understand and effectively communicate with their patients may also be gaining national attention. The Association of American Medical Colleges (AAMC) is changing the Medical College Admission Test (which is required for admission to medical school) to include a section on social and behavioral sciences [73]. The AAMC hopes that this will help inform future physicians on social and health care issues that will prepare them to become better physicians. Changing the way providers are trained, and requiring that providers understand the social- and health-related issues of their patients, is an important and necessary step toward improving provider communication and ultimately adherence.

Notably, the need for provider-based interventions, specifically those improving provider communication, is gaining attention within some pediatric settings. In some institutions, providers receive ongoing communication training to facilitate their ability to assist families in their management of chronic disease [74]. While this communication training is not specific to diabetes providers, the approach to improving provider communication has potential to benefit patients with diabetes. Linking these interventions to outcomes in adherence will also be of particular importance.

Thus far, relatively few provider-based interventions aimed at improving adolescent adherence to therapy have been trialed. However, evidence suggests that providers, especially pediatric providers, may be uniquely positioned to improve adherence to therapy in their patients with T1D, making this an important new avenue for research.

Future Directions

Improving glycemic control in adolescents with T1D starts with improving adherence to therapy. Unfortunately, interventions thus far have had very modest effects on glycemic control. The effect of these interventions on adherence is difficult to determine, as studies use different measures to assess adherence, and this range of measures makes it challenging to compare adherence across studies. A minority of studies examined frequency of blood glucose monitoring (an excellent proxy for adherence), and some of these studies relied on patient report of BGMF rather than meter download (which can be unreliable) [7••, 75]. Additionally, it can be challenging to assess which interventions are truly aimed at improving adherence to therapy, as different studies use different terminology for adherence (adherence, compliance, self-management, and self-efficacy are all used synonymously). Moving forward research aimed at improving adherence to therapy should use similar terminology and measures of adherence (BGMF) to allow for clear understanding of the effect of the intervention in question.

Several of the interventions reviewed in this article require resources that may not be available to all patients. Therefore, focus should be given to provider-based interventions to allow providers to influence adherence behaviors in their patients. In addition to improving provider communication, there may be other methods for providers to impact their patients' adherence to therapy. In a 2001 study, for example, adolescents completed a computerized assessment of health behaviors (focusing on activity and nutrition) prior to office clinic visits and set goals for behavioral change based on problem areas identified in the assessment [76]. Providers were then able to counsel on the health assessment and goals created during routine clinic visits. The study demonstrated that areas targeted by adolescents improved at subsequent clinic visits [76]. Although this study did not involve patients with T1D, time-saving strategies such as this may allow providers to quickly and effectively assess and target barriers to adherence in adolescents with T1D.

Another future direction involves investigating specific regimen-associated barriers to adherence, defined as barriers directly related to adhering to the prescribed diabetes regimen of blood glucose monitoring and administration of meal, snack, and basal insulin (see Table 1). Also, included in this table is provider communication, as patients must be able to effectively communicate with their providers to understand and follow their diabetes regimens. Learning how patients understand and follow provider recommendations, and focusing on the specific barriers that they face, may allow providers to intervene and improve specific aspects of diabetes care during routine quarterly clinic visits. In this way, providers may be able to improve the adherence and, therefore, glycemic control of adolescents with T1D.

An important consideration regarding provider-directed interventions is the pressure that providers are under to see more and more patients. Given limited provider time (15–30 min

Table 1 Future studies

Barrier to adherence	Next steps
-Forget meal or snack insulin doses	-Explore timing of meal dose insulin
-Difficult to plan or follow regimen	-Question providers about how they teach patients to give meal dose insulin
-Difficult to administer insulin and/or eat meals at the right time	-Trial pre-meal insulin administration
-Forget to check and record blood sugars	-Determine availability of meters, strips, log books -Review/re-educate about logging blood sugars, monitoring trends -Assess technologies available (pump alarms, cell phones, etc.)
-Difficult to administer correct insulin dose or to adjust dose based on blood sugar	-Assess carbohydrate counting and diabetes numeracy during provider visits
-Difficult to communicate with provider	-Investigate communication resources/training available to providers -Explore targeted interventions to improve communication
-Forget to obtain refills, unable to obtain refills	-Investigate how often families run out of supplies and whether financial constraints play a major role in this -Explore means to help pediatric patients remember to obtain refills

per patient) and busy pediatric practices, provider-directed interventions will need to demonstrate not only improved patient adherence to therapy and glycemic control but also decreased health care costs. Specifically, examining provider interventions as a function of ED visits and rates of hospitalization to show decreased health care costs both in the short and long term will be a necessary part of this research.

Conclusions

Adherence to therapy in adolescents with T1D is a challenging problem necessitating a multifaceted approach. In addition to the ongoing research in adolescent adherence to therapy in T1D, specific attention needs to be given to the role of providers and their ability to affect change, especially related to regimen-related barriers. As technology becomes more advanced, providers may play an even larger role in promoting adherence. Giving providers the tools to assess and impact their patients' barriers to adherence holds promise as a strategy that may be universally used by providers to improve adherence and, therefore, glycemic control in youth with T1D.

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Compliance with Ethics Guidelines

Conflict of Interest Karishma A. Datye, Daniel J. Moore, William E. Russell, and Sarah S. Jaser declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This is a review article and therefore does not contain any unpublished original studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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