Psychosocial Needs for Newly Diagnosed Youth with Type 1 Diabetes and Their Families

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Abstract

Purpose of Review To synthesize findings from studies published within the last 5 to 10 years and recruiting families of children with new-onset type 1 diabetes (T1D).

Recent Findings Children can establish glycated hemoglobin (HbA1c) trajectories in the new-onset period that may persist for up to a decade. Demographic factors, family conflict, and diabetic ketoacidosis at the time of diagnosis may be risk factors for sub-optimal child HbA1c, while new immune modulating therapies and a treatment approach that combines advanced technologies and remote patient monitoring may improve child HbA1c. Nonetheless, recent trials in the new-onset period have largely overlooked how treatments may impact families' psychosocial functioning and longitudinal observational studies have been limited.

Summary The new-onset period of T1D is an important time for research and clinical intervention, though gaps exist specific to families' psychosocial needs. Filling these gaps is essential to inform clinical management and standard of care guidelines and improve outcomes.

Keywords New-onset · Diabetes · Treatment · Adult · Pediatrics

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Introduction

Type 1 diabetes mellitus (T1D) is the third most common chronic medical condition in youth [1]. In the USA, there are nearly 18,000 youth diagnosed with T1D annually [2, 3]; worldwide, the incidence rate may be as high as 98,200 youth [4], and recent reports suggest a rising incidence of T1D in youth associated with the SARS CoV-2 pandemic [5–7]. Parents and youth experience many challenges in the months following a T1D diagnosis, a period sometimes referred to as the "Honeymoon Period" or Partial Clinical Remission and defined by their glycemic levels and insulin dose requirements [8]. For instance, parents and children must quickly learn new and complex self-management behaviors, including carbohydrate counting, glucose monitoring, and insulin administration [9]. They may experience distress, anger, and grief related to the diagnosis and its associated disruption to their family patterns, lifestyle, or routines [10]. Moreover, because of waning endogenous insulin levels, youth may be vulnerable to rapid glucose changes, which can complicate their self-management and ability to achieve an optimal glycated hemoglobin (HbA1c) level [8]. Within the last 5 to 10 years, new studies have been

published to expand what we know about physiology in the new-onset period, the effectiveness of diabetes education and treatment strategies, and family psychosocial adjustment in the new-onset period. Our purpose in this review is to synthesize the results of these new studies to inform clinical management and future directions of research especially with respect to the psychosocial needs of families of children with new-onset T1D.

Trajectories of HbA1c

Current national and international clinical care guidelines recommend that the youth with T1D maintain an HbA1c level ≤ 7.0% or as low as safely possible [9, 11]. This recommendation balances the potential increased risk of severe hypoglycemia with the known risk reduction for diabetes-related complications that can be achieved with tighter glycemic levels as established by the results of the Diabetes Control and Complications Trial (DCCT) [12, 13]. In a series of recent studies, researchers have sought to track the natural history of the new-onset period in youth with T1D with respect to their HbA1c levels. The largest study, the New Onset (NeOn) Study, recruited 1,048 youth with new-onset T1D from seven pediatric diabetes centers across the USA [14, 15]. Eligible youth were within three months of their diabetes diagnosis when recruited. Study data included clinical characteristics (e.g., regimen, acute complications), laboratory measures (e.g., HbA1c, C-peptide), and demographics collected from the electronic health record during youth's routine diabetes clinic visits. Results suggested that youth achieved their lowest HbA1c levels between 3–6 months post-diagnosis followed by a gradual increase in HbA1c levels out to 36 months Moreover, out to 36 months post-diagnosis, only 30% of youth achieved an HbA1c level below 7.5%, and there was a sixfold increase in the percentage of youth developing diabetic ketoacidosis (DKA) in years 2 and 3 post-diagnosis compared to year 1 (excluding DKA at the time of diagnosis) [14]. Sherr et al. [16••] examined HbA1c trajectories post-diagnosis from youth recruited into three international T1D registries: Australasian Diabetes Data Network, German/Austrian Prospective Diabetes Follow-Up Registry, and US T1D Exchange. Data collected in these registries were both prospective and retrospective (pre-enrollment). The authors found that the same five trajectories of glycemic control (i.e., low stable, intermediate stable, high stable, target increase, and high increase) occurred across all registries, with patterns emerging in the new-onset period and persisting out to 10 years post-diagnosis. Ethnic minorities were underrepresented in the low stable and intermediate stable trajectories, and older youth were over-represented in the high increase group, which was characterized by an above-target

HbA1c at baseline and progressively increasing glycemia [17]. Prahalad et al. [18] tracked HbA1c levels in 261 youth (mean age 9.6 ± 4.0 years) with new-onset T1D in a single center in the USA. Again, results suggested a median time to nadir in youth HbA1c at about 5 months post-diagnosis with progressively increasing levels out to 18 months post-diagnosis. The researchers also noted associations between youth demographics and their HbA1c nadir or trajectory like the findings from Sherr et al. [16••]. Specifically, Prahalad et al. [18] found that children under 6 years old had the highest HbA1c nadir, the youth with public insurance showed a faster rise in HbA1c than youth with private insurance, and the youth from a minority background showed a faster rise in HbA1c than youth from a non-Hispanic White background. Finally, the Treatment Adherence and Control in Kids: A Longitudinal Evaluation (TACKLE-T1D) study [19•], a smaller, prospective longitudinal cohort study, tracked HbA1c levels in one hundred six 5 to 9-year-olds with T1D recruited from two pediatric diabetes clinics in the USA. This study is unique because in addition to replicating previous findings demonstrating overall increasing HbA1c levels in children across the new-onset period, researchers identified four distinct trajectories of HbA1c in children, namely, low and high stable and intermediate and high increasing HbA1c trajectories. Further, this study collected psychosocial data from parents at baseline and, in a series of logistic regressions, determined that, compared to a low stable trajectory, increasing parent-reported hypoglycemia fear was associated with decreased odds of children following a high stable or intermediate increasing trajectory, while increasing parent-reported diabetes-specific conflict was associated with increased odds of children following a high stable or intermediate increasing HbA1c trajectory. While the results of this small prospective, cohort study will require replication in a larger sample of families, at this preliminary stage, they suggest that in the new-onset period, families may experience heightened hypoglycemia fear especially if their child's HbA1c levels appear within target. These results also identify diabetes-specific family conflict as a possible early risk factor for suboptimal child HbA1c levels [19•].

Preservation of Residual β-Cell Function

Partial remission (aka, Honeymoon) is a period characterized by near-normal glucose levels and low insulin dose requirements theoretically due to β-cell preservation, endogenous insulin production, and reduced peripheral insulin resistance [8]. Indeed, data from a prospective observational study of persons of varying ages and with varying durations of T1D suggest that one-third of persons experience functional insulin secretion for 3 years or greater post-diagnosis, although persons diagnosed in adulthood may demonstrate

C-peptide production with greater frequency and at higher levels than persons diagnosed in childhood [20]. There are several recent studies that demonstrate potential long-term benefits to preserving residual β-cell function in persons with T1D. For instance, Rickels et al. [21] demonstrated that among adults with T1D, those with detectable C-peptide levels on a mixed meal tolerance test demonstrated functional β-cell responses to hyperglycemia and α-cell responses to hypoglycemia, while those with the highest C-peptide levels demonstrated lower mean glucose and higher time in range. Similarly, in a recent re-analysis of data from the DCCT/EDIC clinical trial, researchers found evidence of an association between preserved residual β-cell function and clinically significant, long-lasting reductions in the incidence of severe hypoglycemic events [22].

Considering the potential value of preserving endogenous insulin production, researchers have tested multiple immune modulating therapies to preserve residual β-cell function in randomized controlled trials, either in persons at risk for T1D or in persons with new-onset T1D. To target persons at risk for T1D, in a large randomized controlled trial, researchers recruited first- and second-degree relatives of persons with T1D (median age at enrollment = 8.2 years [IQR: 5.7–12.1 years]) and compared oral insulin therapy to a placebo [23]. While the overall results of the trial suggested no beneficial effects of oral insulin therapy, secondary analyses suggested a significant protective effect in the use of oral insulin therapy among persons with mIAA autoantibodies [23]. For persons with new-onset T1D, the results of an open-label randomized, controlled trial comparing teplizumab at the time of diagnosis to a placebo demonstrated a slower decline of β-cell function among persons receiving the teplizumab at both 2 and 7 years post-diagnosis [24, 25]. Similarly, in a 2-year, three-arm randomized, double-blind, placebo-controlled trial, comparing low-dose murine anti-thymocyte globulin (ATG) alone and low-dose ATG plus granulocyte colony-stimulating factor (ATG/GCSF) to a placebo in 89 youth with new-onset T1D [26•, 27], researchers found that at both 1 and 2 years post-diagnosis, the youth receiving low-dose ATG had a slower decline of β-cell loss compared to placebo and youth in both the low-dose ATG alone and ATG/GCSF groups had lower HbA1c levels than youth in the placebo group, suggesting that they experienced a longer partial remission period [26•, 27].

In addition to studying immune modulating therapies, a few recent clinical studies have explored other strategies. For instance, in a prospective observational study, researchers studied the beneficial impact of physical activity [28•]. This study included 125 youth, 54 of whom the researchers identified as physically active based on International Society of Pediatric and Adolescent Diabetes guidelines [29]. At the end of 2 years, the data demonstrated that the physically active youth had lower HbA1c levels and lower daily insulin requirements than their less active counterparts, suggesting that the physical activity could also help to prolong partial remission time and/or increase insulin sensitivity [28•]. In a single-center pilot study, researchers tested the effect of probiotic supplementation in youth with new-onset T1D [30]. This trial recruited 90 youth (ages 2–12 years) and randomized them to receive either a high dose multi-strain probiotic plus standard diabetes treatment (intervention) or standard diabetes treatment only (control). After 3 months of treatment, researchers found that the youth in the intervention arm experienced a greater reduction in daily insulin requirements (0.3 U/Kg/day versus 0.1 U/Kg/day) than the youth in the control group. Moreover, they determined that the number of children who achieved partial remission over the study period was more than three times higher for the intervention group compared to the control group (26.6% versus 8.8%) [30]. Finally, in a randomized clinical trial, researchers explored whether tighter glycemic control during the new-onset period of T1D could help to preserve residual β-cell function [31]. This trial randomized 68 youth with new-onset T1D (mean age 13.3 ± 5.7 years) to either sensor-augmented insulin pump therapy (SAP) or usual care. While the overall trial results revealed no differences in C-peptide levels and HbA1c for youth receiving SAP versus usual care at 1 year post-diagnosis [31], in follow-up sensitivity analyses, researchers discovered a significance difference in HbA1c levels at both 1 and 2 years post-diagnosis among youth with more frequent SAP use compared to less frequent SAP use. There are at least two ongoing clinical trials registered in ClinicalTrials.gov (NCT04233034 and NCT02871089) that are evaluating the effect of tight glycemic control during the new-onset period on preservation of endogenous insulin production, which may provide a different route of treatment.

In sum, several trials have offered promising results suggesting that immune modulating therapies and other strategies may help to improve children's medical outcomes in the new-onset period. However, a notable gap in these trials is an examination of whether these treatments also offer any psychosocial benefits. Because the youth in partial remission tend to experience more optimal glycemic levels with reduced self-care burden, it is possible that there could be secondary psychosocial benefits for some of these treatments, including reduced diabetes distress, hypoglycemia fear, and diabetes-specific family conflict. In contrast, for treatments that require greater attention to diabetes self-care and maintenance of tighter glycemic control in the new-onset period, it is possible that families might experience higher levels of distress, fear, and conflict. Therefore, as an important next step, we need future clinical trials to include an assessment of families' psychosocial outcomes so that it may be possible to obtain a more comprehensive understanding of treatment impacts in the new-onset period of T1D.

DKA at Time of Diagnosis

There is evidence that between 28 and 47% of youth with new-onset T1D present in DKA at the time of diagnosis [32–34] and potentially even higher frequencies in some populations in the time of the SARS CoV-2 pandemic [35, 36]. This is alarming because DKA at the time of diagnosis associates with persistently higher HbA1c levels and a greater rate of change (trending toward less optimal levels) in HbA1c in youth, even when controlling for sociodemographic factors and continuous glucose monitor (CGM) use [32, 37, 38]. However, several recent studies have also looked to see if there are neurocognitive sequelae associated with DKA at the time of diagnosis. For instance, in a recent large, prospective study of children with T1D (ages 4–10 years old), researchers found that children with moderate/severe DKA at diagnosis had a lower full-scale IQ (Cohen's $d = -0.47$) and lower measures of memory ($d = -0.41$) and attention ($d = -0.52$) than children with no/mild DKA at diagnosis [39]. A large, cross-sectional study recruiting 392 children with DKA at diagnosis and comparing them to 376 children with T1D and no history of DKA found a deficit for item-color recall ($\beta = -0.08$, $p = 0.04$) in children with DKA at diagnosis [40]. Likewise, a smaller cross-sectional study that included siblings without T1D as controls found a deficit for spatial memory ($d = 0.64$, $p = 0.01$) in children with DKA at time of diagnosis [41]. Overall, the results suggest DKA at diagnosis is a risk factor for suboptimal HbA1c levels in youth and could be a risk factor for neurocognitive problems in youth, though there is a need for more research in this area. In addition, future research should consider including family psychosocial measures as covariates in updated models relating DKA at the time of diagnosis to future HbA1c levels and trajectories in youth. It may also be important to include psychosocial measures in future neurocognitive studies, as it is possible that the families of children experiencing negative neurocognitive effects of DKA at diagnosis could be vulnerable to symptoms of depression or anxiety which could also impact their health and well-being.

Diabetes Education

To date, consensus guidelines influence the typical content of new-onset diabetes education, and there remains a gap in knowledge regarding the overall efficacy of new-onset diabetes education or the specific components of new-onset diabetes education (e.g., content, presentation style, or mode of delivery) that predict HbA1c levels in

the new-onset period. However, recently researchers have explored ways to innovate diabetes education through different delivery approaches. For instance, within the last 5 years, two studies have added to the growing body of evidence suggesting that it is feasible to deliver new-onset T1D education in the outpatient setting without compromising children's glycemic levels [42, 43]. Additionally, one small clinical trial examined the feasibility and initial effectiveness of web-based delivery of new-onset T1D education [44]. The trial included 16 parent-youth dyads recruited from a single center within 48 h of diagnosis. Half of parent-youth dyads received standard group-based diabetes education, and half of parent-youth dyads received the web-based program. The results showed that parent-youth dyads in both groups demonstrated a statistically significant change in diabetes knowledge after education, suggesting initial effectiveness for the web-based education program [44]. Undeniably, the transition of new-onset diabetes education to more natural settings such as families' homes should remain a central focus of research going forward due to changes in health care reimbursement in the USA and recent impacts from the SARS CoV-2 pandemic. However, the impact of different educational approaches on families' psychosocial outcomes is currently unknown and should be a direction for future research.

Treatment Approaches: Advanced Technologies and Remote Patient Monitoring

In recent studies, there is emerging evidence that early initiation of an insulin pump or CGM may help to improve HbA1c levels [45–47] and decrease parents' use of hypoglycemia avoidance behaviors [48] in youth with new-onset T1D. Thus, the 4 T Program: Teamwork, Targets, Technology, and Tight Control [49, 50••] may offer a way to innovate diabetes treatment in the new-onset period. In the 4 T Program, youth with new-onset T1D initiate CGM within the first of month of diabetes. Then, following CGM start, families participate in frequent follow-up visits with their diabetes team via telephone calls and telehealth to review their glucose data, receive insulin dose adjustments, and, if needed, receive psychotherapy for symptoms of distress or depression up to 12 months post-diagnosis. In a pilot study that included 135 youth with new-onset T1D, researchers found that HbA1c levels in their 4 T participants were 0.54%, 0.52%, and 0.58% lower than historical controls at 6, 9, and 12 months post-diagnosis, respectively. They also found that between 4 and 12 months post-diagnosis, youth in 4 T experienced a lower average rise in HbA1c compared to historical controls (1.32% vs 1.47%) and that at 12 months

post-diagnosis, a greater percentage of youth in 4 T met a HbA1c target < 7.5% compared to historical controls (66% versus 43%, respectively) [50••]. Finally, there was initial evidence of high acceptability for starting CGM close to the time of diagnosis among parents [51]. In short, these results suggest that early CGM initiation and the 4 T model of frequent follow-up, tailored education and psychotherapy, and tight glycemic targets may help youth to achieve more optimal glucose levels in the new-onset period. In the future, it will also be interesting to learn how successful this approach was with respect to meeting families' psychosocial needs in the new-onset period.

Psychosocial Well-being in the New-Onset Period

Although there is an established body of literature examining the psychosocial functioning of families of youth with T1D in the new-onset period, many of these studies were published a decade ago or more, and daily diabetes treatment has changed with the addition of new insulin analogs exhibiting different onset/duration of action, and with the widespread uptake of insulin pumps, CGM, and hybrid closed loop insulin delivery systems in youth. Thus, new studies provide an important update to this literature and the opportunity to observe how youth and families may be adjusting in the new-onset period of T1D given these recent advances in therapy. In a recent prospective, longitudinal study of 54 adolescents with new-onset T1D, McGill et al. [52] found that 17% had elevated depressive symptoms at 1 month post-diagnosis, which is comparable to rates for youth with established T1D and higher than rates in youth without T1D [53]. Moreover, this study found that youth reporting elevated depressive symptoms at 1 month post-diagnosis had a higher risk of reporting elevated depressive symptoms at 6 and 12 months post-diagnosis and had a higher HbA1c level at 6 months post-diagnosis than youth who did not report elevated depressive symptoms at 1 month post-diagnosis.

The TACKLE-T1D study prospectively examined the psychosocial functioning of families of children who were diagnosed with T1D between 5 and 9 years old. The researchers conducting TACKLE-T1D targeted families of 5 to 9-year-olds with new-onset T1D specifically because this age group has the second highest incidence rate of T1D [54]. Additionally, because existing studies often excluded these families, there was limited information available regarding their psychosocial functioning and adjustment in the new-onset period of T1D. Researchers recruited 128 families from two pediatric diabetes centers in the USA and followed them for up to 30 months conducting study assessments every 3 months. In a series of separate reports, researchers revealed that 26% of parents reported elevated depressive symptoms at baseline (~ 4.6 months post-diagnosis) and 19% reported elevated depressive symptoms 12 months later [55]. Additionally, compared to parents who did not report elevated depressive symptoms at baseline, parents reporting elevated depressive symptoms had higher levels of hypoglycemia worry up to 18 months post baseline [56] and higher levels of diabetes distress up to 24 months post baseline [57], suggesting that early parent depressive symptoms could be a risk factor for on-going challenges with adjustment. Interestingly, in this same sample, researchers looked at the occurrence of stressful life events in the first 16 months of T1D [58]. They found that more than half of families reported the occurrence of at least one stressful life event, such as income changes, job or school changes, additional family health changes, or changes in parents' marital status in addition to their child's diabetes diagnosis. Further, they found significant associations between stressful life events and parents' baseline depressive symptoms ($r = 0.197$, $p < 0.05$), perceptions of family conflict ($r = 0.225$, $p < 0.01$), and use suboptimal coping strategies ($r = 0.239$, $p < 0.01$), suggesting that parental psychosocial difficulties at diagnosis could also increase risk for general life stressors in the new-onset period.

Finally, the results of one small mixed methods study are noteworthy because this study found that parents of children with new-onset T1D want to receive assistance in managing symptoms of anxiety, depression, and diabetes distress as part of new-onset diabetes education as well as learn strategies to reduce the impact of diabetes burn-out after 6 months post-diagnosis [59].

Limitations

Our goal in this review was to synthesize the findings of recent studies of families of youth newly diagnosed with T1D to inform our understanding of the psychosocial needs of this patient group. A priori, we chose to focus primarily on studies published within the last 5 to 10 years to enhance the relevance and timeliness of our review, although we include a few older studies to provide context. Nonetheless, we recognize that this tightly focused publication window may have excluded some other relevant studies. We recognize that our review may be limited because some recent studies in youth with new-onset T1D had limited racial/ethnic diversity and/or limited socioeconomic diversity. We recognize that our review may be limited because some recent studies in youth with new-onset T1D used cross-sectional or retrospective designs. Finally, we recognize that our review may be limited because many recent studies in youth with new-onset T1D did not specifically report on family

psychosocial outcomes, leading us to identify that this as an important gap to fill in future research.

Conclusions

The new-onset period of T1D is an important period for research and clinical intervention. Based on the results of studies reviewed here, youth with T1D experience established HbA1c trajectories in the new-onset period that persist for up to a decade beyond diagnosis [16••, 60]. Moreover, the occurrence of DKA at diagnosis can present as a risk factor for less optimal glycemic levels [32, 37, 38] and neurocognitive problems in youth [39–41]. While there are a few promising new immune modulating therapies to preserve β-cell functioning and improve HbA1c levels in youth with new-onset T1D, to date, the scope of these trials has not included family psychosocial variables [24, 25, 26•, 27]. Likewise, we have limited information exploring the psychosocial experiences of families who attempt to preserve β-cell function by maintaining very tight glycemic targets in the new-onset period [31, 61]. Therefore, to address these gaps, we need future clinical trials to include families' psychosocial variables when testing therapies for youth with new-onset T1D.

We also need future studies to assess for families' psychosocial outcomes when piloting new diabetes education programs and testing new behavioral treatments in the new-onset period as these studies could directly inform standard of care. For instance, it would be important to find out how different implementation strategies for new-onset diabetes education might relate to families' psychosocial adjustment and whether there is an implementation strategy that predicts both optimal glycemic levels and quality of life. In relation to increasing uptake of insulin pumps and CGM in youth with new-onset T1D, we need studies exploring the psychosocial effects of these devices as well as the efficacy of new adjunctive therapies to promote optimal use.

Finally, existing research demonstrates that the new-onset period of T1D is dynamic, suggesting a cross-sectional design may not be sufficient. Also, some of variables that might relate to families' early psychosocial adjustment, such as DKA at diagnosis, pre-existing depression/anxiety, and additional life stressors, would be difficult to study in a clinical trial. Thus, to continue to expand our understanding of the psychosocial needs of families in the new-onset period, we require well-designed, longitudinal observational studies that include families from diverse backgrounds and incorporate relevant biomarkers (e.g., C-peptide), and consider differences in child age and developmental status that might impact families' psychosocial needs. Indeed, data on the psychosocial adjustment and functioning of families for all research in the new-onset period are essential to inform

clinical management and standard of care guidelines and improve outcomes.

Declarations

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Papers of particular interest, published recently, have been highlighted as:
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●● Of major importance

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