



# Improving Clinical Outcomes in Newly Diagnosed Pediatric Type 1 Diabetes: Teamwork, Targets, Technology, and Tight Control—The 4T Study

## OPEN ACCESS

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Many youth with type 1 diabetes (T1D) do not achieve hemoglobin A1c (HbA1c) targets. The mean HbA1c of youth in the USA is higher than much of the developed world. Mean HbA1c in other nations has been successfully modified following benchmarking and quality improvement methods. In this review, we describe the novel 4T approach—teamwork, targets, technology, and tight control—to diabetes management in youth with new-onset T1D. In this program, the diabetes care team (physicians, nurse practitioners, certified diabetes educators, dietitians, social workers, psychologists, and exercise physiologists) work closely to deliver diabetes education from diagnosis. Part of the education curriculum involves early integration of technology, specifically continuous glucose monitoring (CGM), and developing a curriculum around using the CGM to maintain tight control and optimize quality of life.

**Keywords:** type 1 diabetes, pediatrics, insulin pump, continuous glucose monitoring, hemoglobin A1c

## INTRODUCTION

The Diabetes Control and Complications Trial (DCCT) firmly established the efficacy of intensive diabetes management to reduce vascular complications of type 1 diabetes (T1D) (1, 2). Despite results from the DCCT, most youth do not meet glycemic targets (3). For example, based on the T1D Exchange (T1DX) registry, the mean hemoglobin A1c (HbA1c) in 17-year-old Americans in 2010–2012 is similar to the conventional arm of the DCCT (9%) (1, 2, 4), whereas in the DPV registry in Germany and Austria, the mean HbA1c is 8.2% (5). Current care for children, adolescents, and young adults with T1D has failed to make meaningful progress in lowering HbA1c despite advances in diabetes technology (6–8) [insulin pumps, continuous glucose monitoring (CGM), and now automated insulin delivery systems, analog insulins (both basal and bolus), and refinements in care delivery, among others] (9).

There have been efforts to modify care delivery to improve outcomes in individuals with T1D. For example, in the DPV registry in Germany and Austria, HbA1c decreased from 9 to 8.2% from 1995 to 2010 on the basis of benchmarking and quality improvement methods (10, 11). The comparison of 2015 HbA1c data between the T1DX and DPV shows about a 1% gap in people 3–21 years of age (12). Similarly, numerous other countries with similar economic status to the USA have reported reductions in HbA1c, leaving the mean HbA1c in American youth with T1D among the highest worldwide (3). While these countries have dramatically different health-care systems, all are in developed countries such as the USA. In contrast, the international SWEET registry reports the mean HbA1c in individual clinics in many developing countries such as India, Nepal, and Mexico are in the 8–9.5% range, suggesting that even in resource-poor situations, better glucose control than the USA can be achieved (13). Therefore, other countries have effectively implemented the DCCT message of intensive glucose control, leaving the USA as an outlier in achieved pediatric HbA1c (14–16). In fact, pediatric HbA1c in the T1DX was higher in the 2017 data than in 2010–2012 data (17). From literature describing efforts to decrease HbA1c (10, 18), common themes emerge as potentially critical contributors to success in HbA1c management (9, 19, 20). These include (1) a unified and consistent team approach; (2) communicating clear glucose targets to youth and their families; (3) flexibility in supporting youth and families; and (4) timely detection of increasing glucose trends followed by rapid intensification of therapy to regain target control.

Moreover, a practical and sustainable approach to improving long-term outcomes is to focus on youth with new-onset T1D. A recent study has shown that an individual's long-term glycemic track is set by 5 years post-diabetes diagnosis (21), and we have previously shown that HbA1c rises between 5 and 6 months post-diabetes diagnosis and levels at 12–18 months (22). Taken together, these studies suggest that interventions early in the course of diabetes can have long-term impact on glycemic outcomes. Additional rationale to focus on newly diagnosed youth includes the following: a fresh start to deliver diabetes education and establishing diabetes care habits instead of reteaching and breaking old habits, both for youth and providers; greater efficiency in the use of resources to maintain rather than regain tight control; and the opportunity to capitalize on the tighter control that commonly occurs post-T1D diagnosis. In this review, we will describe the 4T (teamwork, targets, technology, and tight control) approach to improving outcomes in youth with T1D.

## THE 4T APPROACH

Increased frequency of blood glucose monitoring has been shown to improve HbA1c (23). Glucometers provide an intermittent trend of glucoses, but CGM, which measures 96–288 glucose values per day, also provides glucose trends. Given the benefit of CGM, the cornerstone of the 4T approach is to start youth on CGM technology within the first month of diagnosis to allow for tighter control of glucoses in the new-onset period.

Initiation of CGM so early in the course of T1D requires highly coordinated teamwork to provide the education needed for youth and families to manage not only diabetes but also the large volume of data provided by the CGM. Using technology and creating an education curriculum centered on the data provided by CGM can allow for tighter targets during the honeymoon period and beyond. The main principle behind the 4T approach is that using a CGM is not sufficient. The data must be frequently reviewed and dose adjustments or additional education should be provided to maintain glucoses in the target range. To prevent overburdening the care team with data analysis, clinical decision support tools are necessary to automate data analysis and facilitate population health management.

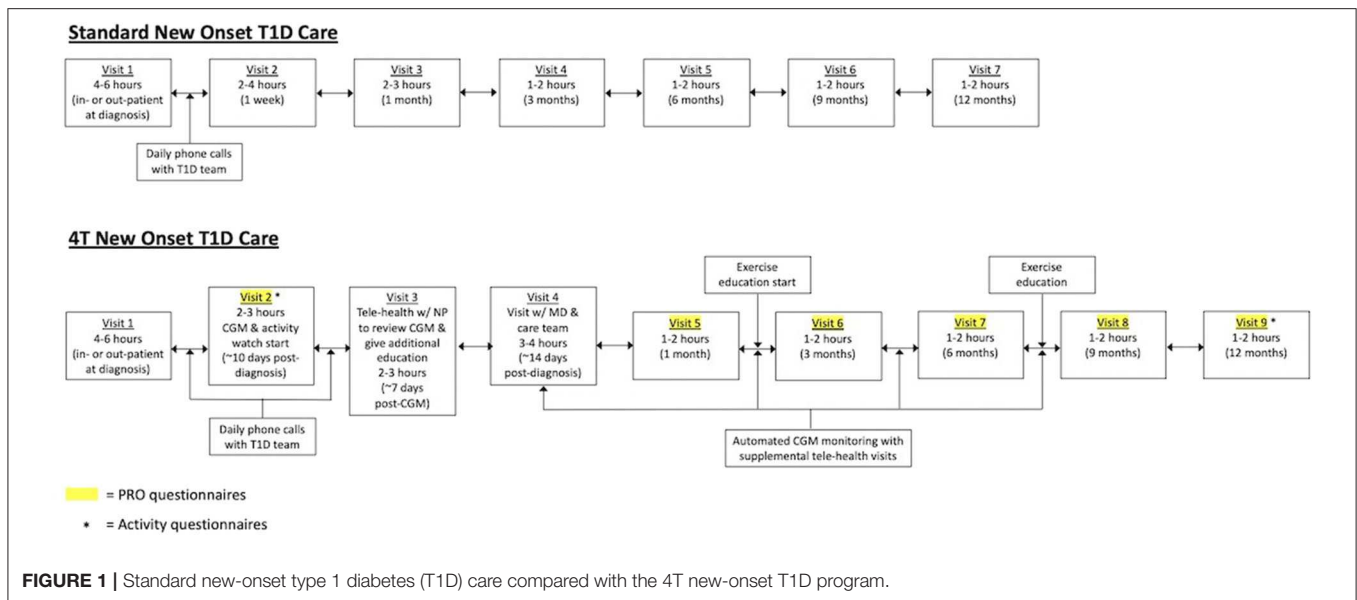
## 4T Protocol

Historically, our new-onset care involved a 4- to 6-h diabetes education visit with the care team [physician, certified diabetes educator (CDE), and registered dietician]. Patients received daily phone calls from the care team for dose adjustments until the recent onset visit, which occurred at 1 week post-diagnosis. There was another follow-up visit at 1 month post-diagnosis followed by routine follow-up every 3 months. Patients could start on diabetes technology at various time points in this process.

In the 4T program (**Figure 1**), we are revising our new-onset program to provide more touchpoints between patients with newly diagnosed T1D and the care team. In addition, technology, in the form of a Dexcom G6 CGM, is introduced in the first month post-diagnosis. Following routine new-onset education, all patients with newly diagnosed T1D are offered the opportunity to initiate CGM within the first month of diagnosis. Individuals who choose to participate in this study will receive CGM through the study for 1 year. CGM initiation will occur at an additional visit that is typically 10 days post-diagnosis. Patients will continue to receive daily phone calls from the diabetes care team until a telehealth education visit with a nurse practitioner, which typically occurs 1 week after the CGM start. Patients then have subsequent follow-ups at 2 weeks post-diagnosis, 1 month post-diagnosis, and then every 3 months. In addition, individuals can elect to be part of a remote monitoring arm in which CGM data are reviewed by the care team weekly following CGM initiation. The care team will reach out to families through secure messaging, phone calls, and telehealth visits to provide education and dose adjustments between visits. All patients are started on a multidose injection (MDI) regimen at diagnosis. However, there are no restrictions on adding other pieces of diabetes technology including insulin pumps or hybrid closed-loop systems. At approximately, 1 month post-diagnosis, patients can also elect to be part of an exercise intervention. Patient-reported outcomes (PROs) will be obtained at visits 2 and 5–9.

## Technology

Recent advances in diabetes technology place us in the third era of glucose monitoring (urine, blood, and now interstitial fluid with CGM systems). Compared with self-monitoring of blood glucose (SMBG), CGM has the advantages of providing readings as frequently as every 5 min (up to 288 readings per day) with fewer finger pricks as well as providing the rate and direction of



glucose change. Rates of CGM use in pediatrics as reported by the T1DX have increased from 4% (2013) to 14% (2015) to 31% (2017) (24–26), similar to what is observed worldwide (24, 26). Retrospective studies examining the use of CGM in the first year of diabetes diagnosis have demonstrated improvements in glycemic control (27, 28). However, in these studies, the timing of CGM initiation has been variable, and many of the youth started after the rise in HbA1c observed between 5 and 6 months post-diagnosis. Initiation of CGM in the first month of diabetes diagnosis can allow for more frequent insulin dose adjustments in between visits and education around tighter targets. In a pilot study, our team initiated 40 youth on CGM in the first month of diagnosis and demonstrated a high persistence of use with a low incidence of hypoglycemia in participants (29).

In the past year, CGM systems have been approved for use in insulin dosing (non-adjunctive use) and for factory calibration, allowing it to be a true substitute for SMBG. These features combined with the increased number of readings, rates and directions of change, alerts, and remote data sharing have promise for improving glycemic control in youth with T1D. The remote data sharing feature of CGM can allow for remote monitoring not just by a youth's caregiver but also the youth's care team. We have previously developed a system for transmitting data from an individual's CGM into our electronic health record (EHR) using Apple HealthKit on iOS devices [Figure 2; (30)]. This system meets criteria set forth by the US Health Information Portability and Accountability Act (HIPAA). With the use of this feature, CGM data can be reviewed by the diabetes care team, securely, to perform dose adjustments in between clinic visits. Dose adjustments are performed using a secure patient messaging platform embedded in the EHR or via secure telehealth, also embedded in the EHR. Given the large number of individuals in any clinic population, population health management tools need to be developed to allow for the frequent review of a large volume of data. Unfortunately, the increased

use of CGM in pediatric T1D care has not been fully utilized in how education is provided, targets are defined, or glucose data are used in between quarterly clinic visits.

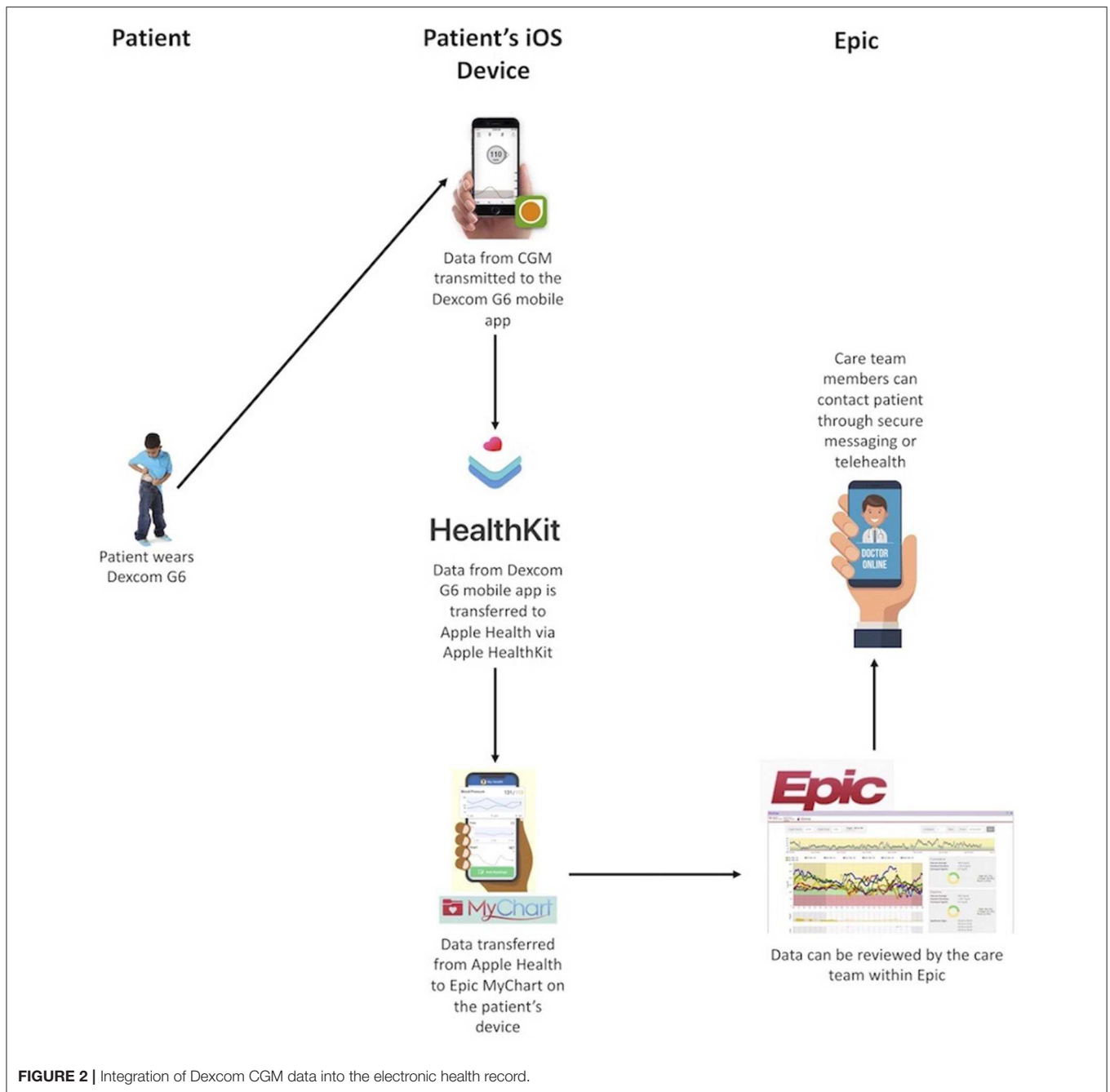
Other technologies can also change diabetes care delivery. Internet access, including smart phone usage, is becoming nearly ubiquitous, even in the developing world (31). The high penetrance of internet access can allow for remote care delivery through telehealth.

Standard of care for individuals with T1D is at least four visits per year with a HbA1c measurement at each visit. Children who attend quarterly visits were more likely to have improved HbA1c than those attending fewer visits per year (32). Data suggest that children who were further from their diabetes center had fewer visits per year and a higher HbA1c (33). In our practice, we have youth who drive several hundred miles for care, which makes clinical visits burdensome and expensive. Telehealth provided to an individual's home allows for face-to-face care without parents missing work, children missing school, or traveling. Telehealth can also be utilized for group education classes to reinforce diabetes learnings. Because telehealth visits do not require dedicated clinic space or ancillary staff, visit times can be more flexible to meet the needs of youth and their caregivers.

Technology has the potential to improve care delivery to people with T1D. However, the limiting resource is the time of the care team. Modern data analysis and visualization tools allow for the design of decision-support tools that translate the analysis of CGM data to allow for efficient population-health management with existing staff.

## Teamwork

Care for youth with T1D requires a coordinated effort by a team consisting of pediatric endocrinologists, CDEs, nurses, registered dietitians, social workers, psychologists, and exercise physiologists. Both the American Diabetes Association (ADA)



(34) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) (35) advocate for a team-based approach to diabetes management. The team-based approach starts in the new-onset period, with education provided to the family by physicians, diabetes educators, and registered dietitians. Initiation of CGM requires a highly integrated team effort to not only provide basic diabetes education but also to provide education on using CGM for improved diabetes care. The role of the diabetes care team does not end in the new-onset period and should be ongoing. Thus, access to these care team members should be available at each follow-up visit.

In addition to education, T1D is associated with psychosocial comorbidities. In a systematic review, one third of youth with T1D experienced diabetes distress, which is the emotional distress that is associated with the burden of diabetes self-management (36). Diabetes distress is associated with poorer clinical outcomes. Given the importance of mental health to the care of children and young adults with T1D, mental health support, through psychologists and social workers, should be made available to help with diabetes management. PROs have been an established means of screening for psychosocial issues as recommended by the ADA guidelines.

**TABLE 1** | PROs incorporated into the 4T program.

Topic	Construct measured/relevant points
<b>Youth and parent outcomes—diabetes distress</b>	
Diabetes distress (Diabetes Distress Scale) Fisher et al. (37)	The DDS-2 (2 item youth survey) and DDS-P (20 item parent survey) are commonly used measures to understand distress symptoms related to diabetes. Validated and used in >25 publications. The DDS-2 will be given to those above 11 years old. DDS-P will be given to all parents. The surveys take 5 min to complete.
<b>Youth-only outcomes</b>	
Diabetes technology attitudes Naranjo et al. (38)	Subjective questions about attitudes related to diabetes technologies and devices. Predictive of outcomes and interacts with diabetes distress. Has 6 items; 2 min to complete.
PROMIS Global Health (7-item Global Health) Forrest et al. (39)	This survey was developed by the PROMIS team and measures aspects of physical and mental health; 7 items and 3 min to complete. We have found it to be sensitive to picking up general quality of life changes.
CGM Benefits and Burden Scale Messer et al. (40)	This survey is a 16-item survey that evaluates perceived benefits (8 items) and burden (8 items) specific to CGM use.

PROs, patient-reported outcomes.

In the 4T program, all youth in the clinic will receive early psychoeducation that describes symptoms of common psychological concerns in youth with T1D (e.g., distress and depression). This will be administered as part of standard teaching visits. All youth will be screened regularly (visits 2, 4, 5, 6, and 7), and therapeutic services can be offered when there are positive screens on the PROs (Table 1). Several examples of the interventions delivered as part of the 4T program include the Guiding Adolescents Through E-Psychotherapy (GATE) program, a five-session web-delivered cognitive behavioral therapy (CBT) program that is tailored to diabetes-specific concerns and designed to address topics that are most salient in these youths' lives. CBT is a gold-standard psychotherapy treatment for depression and the type of psychotherapy treatment that pediatric youth are most likely to receive in the community (41, 42). Not all youth will be able to attend weekly psychotherapy sessions; therefore, psychotherapy will be delivered via telehealth. Previous literature has shown this to be effective (43–45).

## Targets

Advice and teaching on glucose targets should be updated in response to existing diabetes technology, specifically the availability of CGM systems that provide real-time glucose data every 5 minutes, trend arrows, and alarms to notify youth and parents (remotely, if desired) when thresholds are crossed. A previous study has demonstrated the acceptability of CGM to both parents and youth soon after diagnosis via a “CGM at Diagnosis” protocol with 55 newly diagnosed pediatric youth (46). An important finding of the CGM group (vs. no-CGM control group) was the benefit of three times

**TABLE 2** | Glucose targets from NICE, ISPAD, and ADA (49–51).

	NICE Goal A1c (49) ≤48 mmol/mol (≤6.5%)	ISPAD Goal A1c (50) <53 mmol/mol (<7.0%)	ADA Goal A1c (51) <58 mmol/mol (<7.5%)
Pre-meal	4.0–7.0 mmol/l (70–126 mg/dl)	4.0–7.2 mmol/l (70–130 mg/dl)	5.0–7.2 mmol/l (90–130 mg/dl)
Post-meal	5.0–9.0 mmol/l (90–162 mg/dl)	5.0–10.0 mmol/l (90–180 mg/dl)	
Pre-bed	4.0–7.0 mmol/l (70–126 mg/dl)	4.4–7.8 mmol/l (80–140 mg/dl)	5.0–8.3 mmol/l (90–150 mg/dl)

NICE, National Institute for Health and Care Excellence; ISPAD, International Society for Pediatric and Adolescent Diabetes; ADA, American Diabetes Association.

less hypoglycemia, and parents reported more confidence in managing hypoglycemia when they used CGM in the first 6 months after diagnosis (47). Therefore, CGM provides a safety net to allow for tighter glucose targets especially after new onset and has psychosocial benefits. Glucose targets, however, have not been adapted to aim for tighter control, a missed opportunity to lower HbA1c, although data are clear on the effectiveness of clear target setting (48). Three sets of HbA1c and related glucose targets have been published [Table 2; (51–53)]. The 4T approach involves educating families on the association of glucose data with specific HbA1c targets (50). Initial targets after diagnosis will be an HbA1c of 6.5%, and this target should be adapted and individualized to each family per guideline recommendations but in a standardized manner with a team approach. Recent data indicate that glucose time-in-range (TIR) can also be a useful metric for families that correlate with HbA1c (49). Unlike HbA1c, which is measured quarterly, TIR (and mean CGM glucose) can be determined between clinic visits and provide guidance on glucose control and insulin dosing (54, 55). Moreover, we will emphasize education to differentiate between hypoglycemia as a clinical alert of hypoglycemia (stage 1, 70–54 mg/dl) and clinically important or serious hypoglycemia (stage 2, <54 mg/dl) or seizure/coma (stage 3) (55). Each youth and family will receive HbA1c, mean glucose, TIR, and hypoglycemia targets to guide care. Simple metrics for education include aiming for a mean CGM glucose of 150 mg/dl, 70% of time spent between 70 and 180 mg/dl, <4% of time below 70 mg/dl, and <1% of time below 54 mg/dl or the shorthand phrasing: 150/70/4/1. Families will be provided education on interpreting CGM data and performing basic insulin dose adjustments.

## Tight Control

Frequent review of data and dose adjustments are central to maintaining tight control. Unfortunately, only a minority of youth or caregivers review diabetes device data on a regular basis (56). Typically, the diabetes care team reviews glucoses every 3 months at patient visits. This interval may be too long to optimize glycemic control, especially in a growing child and one who is recently diagnosed. Several CGM systems offer the ability to share data remotely through mobile apps. This ability can be used by diabetes care teams to perform remote data review and dose adjustments for youth with T1D in between clinic visits rather



than relying on HbA1c values, which reflect 3 months of glucose control (57, 58). This creates the opportunity to intervene in response to problematic trends as soon as they arise, rather than only when clinical care occurs at 3-month intervals. Given the volume of data, performing routine reviews for all youth can be burdensome to the diabetes care team. As a result, tools should be developed to facilitate population health management.

Recent applications of machine learning and decision support have shown great promise for informing clinical decisions, but not (59) to developing personalized disease management recommendations for youth with T1D (59–61). We have developed a system that aims to identify deviations and opportunities at shorter intervals to notify the clinical team for the possible need for insulin adjustments. The system is designed with equal emphasis on algorithmic analysis of CGM data and on facilitating a systematic, coordinated approach by the care team. The algorithms identify youth with deteriorating control and generate alerts. The systematic, coordinated approach ensures that care team members can (1) consistently see data for a small cohort of “their” youth; (2) quickly review data for all other youth for whom there has been an alert; and (3) maximize efficiency by only reviewing data that have not already been reviewed by someone else or contacting a patient that has been recently contacted. This will allow care team members to prioritize data review of individuals who require additional interventions to maintain tight control, thereby decreasing the burden on care team members.

## Exercise in Youth With New-Onset Type 1 Diabetes

Regular physical activity is important to promote well-being, psychological development, and overall health (62–64). However, it is also recognized that many individuals with T1D are not engaging in the recommended daily levels of physical activity (65). Youth living with T1D and health-care professionals have identified “exercising safely” as one of the most challenging aspects of diabetes, and many choose not to partake in activity because of the associated risks. Matson et al. (66) reported that newly diagnosed adults with T1D spent on average a quarter less time in moderate-to-vigorous physical activity (MVPA) per day than did adults without T1D. Similarly, for children who develop T1D under the age of 7, the rates of physical activity are significantly lower than in those without T1D (67). These lower rates of activity may also be due to factors including patient fear of hypoglycemia and primary caregiver restrictions (68).

For youth with T1D, many factors need to be taken into consideration before engaging in physical activity such as starting glucose level, timing and intensity of activity, insulin dosing, carbohydrate supplementation, exercise time of day, individual fitness, and prior episodes of hypoglycemia (69–71). It is essential for clinicians and health-care practitioners to encourage regular physical activity; however, this requires a more in-depth understanding of strategies to better manage glycemia during exercise (66, 70). Clinical guidelines, consensus, and position statements on exercise provide some structured approaches to assist clinicians in forming individualized exercise management

plans for youth with T1D (53, 70, 72). To reduce exercise-associated hypoglycemia, some strategies include reducing the basal insulin dose pre-exercise, reducing prandial insulin for the meal before exercise, and/or increasing carbohydrate feeding (53). Overall, more vigilant and frequent monitoring of blood glucose around exercise is recommended for safety.

In an attempt to achieve tighter glucose targets in the 4T study, an additional focus will include exercise education. The teaching materials will be generated using current international findings and published research. The aim is to provide this education material to youth and their families in the first 12 months of diabetes duration, as this is where the rise in HbA1c has been previously documented.

## Preliminary Outcomes

Since July 2018 and as of December 2019, we have had 90 youth initiate CGM in the new-onset period. Of those 90 youth, 65 of them have been in this program for at least 6 months. Although the median HbA1c at diabetes onset was higher relative to our previous cohort from 2014 to 2016, the nadir was lower. At 6 months post-diabetes diagnosis, unadjusted the HbA1c was 0.54% lower in the new-onset CGM cohort compared with our historic controls (73).

Of the 65 participants, 30 were enrolled in a remote monitoring study, facilitated through an internal grant, whereby participants were provided an iOS device if they did not have one of their own. We integrated their data into our EHR (Figure 2). Data were reviewed weekly by a member of the diabetes care team and youth and/or caregivers were contacted for insulin dose adjustments and/or education. On average, these youth had 15 data reviews between clinic visits with an average of five dose changes per patient (74). Efforts to streamline this process are ongoing so that it can be scaled to a larger population without increasing burden on the diabetes care team.

## CONCLUSIONS

Despite the results of the DCCT, many youth with T1D do not meet glycemic targets. With benchmarking and quality improvement efforts, clinics have managed to lower HbA1c closer to the ISPAD target of 7%, but few have achieved this target. Although technology has helped to ease some of the burden related to T1D, it has not led to significant improvements in glycemic control. Some of the challenges lie in the fact that youth with T1D received education in the pre-CGM days when targets were not as tight to prevent severe hypoglycemia. CGM technology allows for tighter targets because there are alerts to prevent clinically significant hypoglycemia. In addition, automated insulin delivery systems in which CGM is an integral component use the CGM to suspend insulin for suspected hypoglycemia. Despite advances in technology, education has not evolved to promote tighter targets.

The 4T approach discussed in this review develops diabetes education and a management program centered around the use of technology, specifically CGM, in the new-onset period. The new-onset period was chosen because it offers the opportunity to provide education to youth with T1D and their caregivers,

which is consistent with modern diabetes care. Initiation of CGM in the new-onset period requires a coordinated team effort by physicians, diabetes educators, nutritionists, social workers, exercise physiologists, and psychologists. Once CGM is initiated, education can focus around consistent targets to achieve tight control. Technology can also allow for remote monitoring of CGM data, and the development of population health tools can make CGM review between clinic visits the standard of care for all youth. With the advent of telehealth, care can be delivered by virtual teleconference, further decreasing the burden of diabetes care by decreasing travel to diabetes clinic.

Psychosocial support is an integral part of this program. Although CGM has the opportunity to decrease the burden of diabetes care and improve glycemic control, it should not come at a cost to quality of life. Thus, an important piece of the 4T program is to monitor PROs while also making psychosocial support a key element of diabetes care.

In conclusion, the 4T program aims to achieve tighter glucose control after T1D diagnosis and maintain it as the clinical remission phase wanes while optimizing quality of life. Moreover,

in the future, automated insulin delivery systems promise tighter glucose control with less hypoglycemia and lower burden of care for youth with T1D and their families (75–78). Therefore, early integration and attention to the adoption of diabetes technology and psychosocial outcomes will be increasingly important to fully realize the potential of optimal T1D care.

## AUTHOR CONTRIBUTIONS

PP, AA, DZ, DS, MD, KH, and DM contributed to the concept and design of the study. MD performed the statistical analysis. PP wrote the first draft of the manuscript. All authors contributed to manuscript revision and approved the submitted manuscript.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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