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

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ABSTRACT

Many teenagers and youths with type 1 diabetes (T1D) do not meet their haemoglobin A1c (HbA1c) goals. In India, the average HbA1c of young people is greater than in much of the industrialised world. Other countries' mean HbA1c levels have been effectively changed using benchmarking and quality improvement techniques. We present the revolutionary 4T strategy to diabetes care in kids with new-onset T1D in this review, which includes teamwork, targets, technology, and tight control.The diabetes care team (physicians, nurse practitioners, certified diabetes educators, dieticians, social workers, psychologists, and exercise physiologists) collaborate closely in this approach to provide diabetes education beginning with diagnosis. Early integration of technology, notably continuous glucose monitoring (CGM), and establishing a curriculum around using the CGM to maintain tight control and maximisethe quality of life are both parts of the education curriculum.

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

INTRODUCTION

The Diabetes Control and Complications Trial (DCCT) has proved that aggressive diabetes treatment can help people with type 1 diabetes (T1D) avoid vascular complications [1, 2]. Despite the DCCT findings, the majority of young people do not fulfill glycemic objectives [3]. According to the T1D Exchange (T1DX) registry, the mean haemoglobin A1c (HbA1c) among 17-year-old Indians in 2010–2012 was identical to the conventional arm of the DCCT (9 percent) [1, 2, 4], whereas the mean HbA1c in the DPV registry in Germany and Austria was 8.2 percent [5].Despite advances in diabetes technology [6–8] [insulin pumps, continuous glucose monitoring (CGM), and now automated insulin delivery systems, analogue insulins (both basal and bolus), and refinements in care delivery, among others], current care for children, adolescents, and young adults with T1D have failed to make meaningful progress in lowering HbA1c. [9].

There have been attempts to change the way care is delivered in order to improve outcomes for people with T1D. For example, using benchmarking and quality

improvement methodologies, HbA1c reduced from 9 to 8.2% in the DPV registry in Germany and Austria from 1995 to 2010. [10, 11]. When comparing 2015 HbA1c data from the T1DX to the DPV, there is around a 1% difference in adults aged 3 to 21. [12]. Similarly, multiple other nations with similar economic circumstances to India have recorded decreases in HbA1c, leaving the mean HbA1c in Indian kids with T1D among the highest in the world [3].While these countries' health-care systems are vastly varied, they are all developed countries, such as the United States. The international SWEET registry, on the other hand, reports that the mean HbA1c in individual clinics in many developing countries, including India, Nepal, and Mexico, is in the 8–9.5% range, implying that even in resource-poor situations, better glucose control than the United States can be achieved [13]. As a result, other countries have successfully followed the DCCT message of aggressive glucose management, leaving the United States as an anomaly in terms of HbA1c reached in children [14–16].In fact, paediatric HbA1c levels in the T1DX were greater in 2017 than they were in 2010–2012. [17]. Common elements appear as potentially essential contributions to success in HbA1c control from literature detailing efforts to reduce HbA1c [10, 18]. [9, 19, 20]. These include [1]a united and consistent team approach; [2] clearly conveying glucose targets to children and their families; [3] flexibility in assisting youth and families; and [4] immediate detection of rising glucose trends followed by the rapid acceleration of medication to re-establish target control.

Furthermore, focusing on youth with new-onset T1D is a viable and long-term approach to improving long-term outcomes. A recent study found that 5 years after diabetes diagnosis, an individual's long-term glycemic path is defined [21], and we have previously demonstrated that HbA1c levels rise between 5 and 6 months after diabetes diagnosis and levels at 12–18 months [22]. These findings imply that early therapies in the course of diabetes can have a long-term impact on glycemic outcomes.A fresh start to deliver diabetes education and establish diabetes care habits rather than 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 capitalise on the tighter control that commonly occurs post-T1D diagnosis are all additional reasons to focus on newly diagnosed youth. The 4T (teamwork, targets, technology, and tight control) strategy to improve outcomes in youth with T1D will be described in this review.

THE 4TAPPROACH

HbA1c levels have been demonstrated to improve with increased blood glucose monitoring frequency [23]. Glucometers offer an intermittent glucose trend, while CGM provides glucose trends as well, measuring 96–288 glucose values every day. Given the benefits of CGM, the 4T approach's cornerstone is to start young people on CGM technology during the first month of diagnosis, allowing for better glucose management during the new-onset phase.

CGM initiation so early in the course of T1D necessitates a well-coordinated team effort to provide the education needed for kids and families to handle not only diabetes but also the vast amount of data presented by the CGM. Using technology and developing an education curriculum based on CGM data might help you hit your goals throughout the honeymoon period and beyond. The 4T method is based on the idea that employing a CGM alone is insufficient. To keep glucose levels in the target range, the data should be evaluated on a regular basis, and dose modifications or more education should be offered. Clinical decision support systems are required to

automate data analysis and facilitate community health management in order to avoid overburdening the care team with data analysis.

4T PROTOCOL

Previously, a 4- to 6-hour diabetes education visit with the care team [physician, certified diabetes educator (CDE), and registered dietitian] was required for new-onset diabetes. Until the recent onset visit, which occurred at 1 week post-diagnosis, patients got daily phone calls from the care team for dose changes. A month after the diagnosis, there was another follow-up visit, followed by standard follow-up every three months. Patients could begin using diabetic technologies at any stage during the process.

We are changing our new-onset programme under the 4T programme (Figure 1) to create more touchpoints between newly diagnosed T1D patients and the care team. In addition, technology is introduced in the first month after diagnosis in the form of a Dexcom G6 CGM. Following standard new-onset instruction, all newly diagnosed T1D patients are given the option to start CGM within the first month of diagnosis. Participants will receive CGM for a year if they want to participate in this trial. CGM introduction will take place at a follow-up appointment, usually 10 days after the diagnosis.Patients will continue to get daily phone calls from the diabetes care team until they have a telehealth education visit with a nurse practitioner, which usually takes place 1 week after they start using the CGM. Patients are then followed up with every two weeks, one month, and three months after their diagnosis. Individuals can also choose to be part of a remote monitoring arm, in which CGM data is evaluated weekly by the care team after CGM beginning. To provide education and dose changes between visits, the care team will contact families via encrypted messaging, phone conversations, and telehealth visits.At the time of diagnosis, all patients are started on a multidose injection (MDI) protocol. There are no limits on adding other diabetes equipment, such as insulin pumps or hybrid closed-loop systems, to the system. Patients might also choose to participate in an exercise intervention one month after their diagnosis. At visits 2 and 5–9, patient-reported outcomes (PROs) will be collected.

TECHNOLOGY

We are now in the third era of glucose monitoring, thanks to recent improvements in diabetes technology (urine, blood, and now interstitial fluid with CGM systems). CGM provides several advantages over self-monitoring of blood glucose (SMBG), including the ability to provide readings as frequently as every 5 minutes (up to 288 readings per day) with fewer finger pricks and the ability to provide the pace and direction of glucose change. According to the T1DX, rates of CGM use in paediatrics have climbed from 4% (2013) to 14% (2015) to 31% (2017) [24–26], which is similar to what is seen globally [24, 26]. Glycemic control has improved in retrospective studies investigating the use of CGM in the first year after diabetes diagnosis (27, 28).

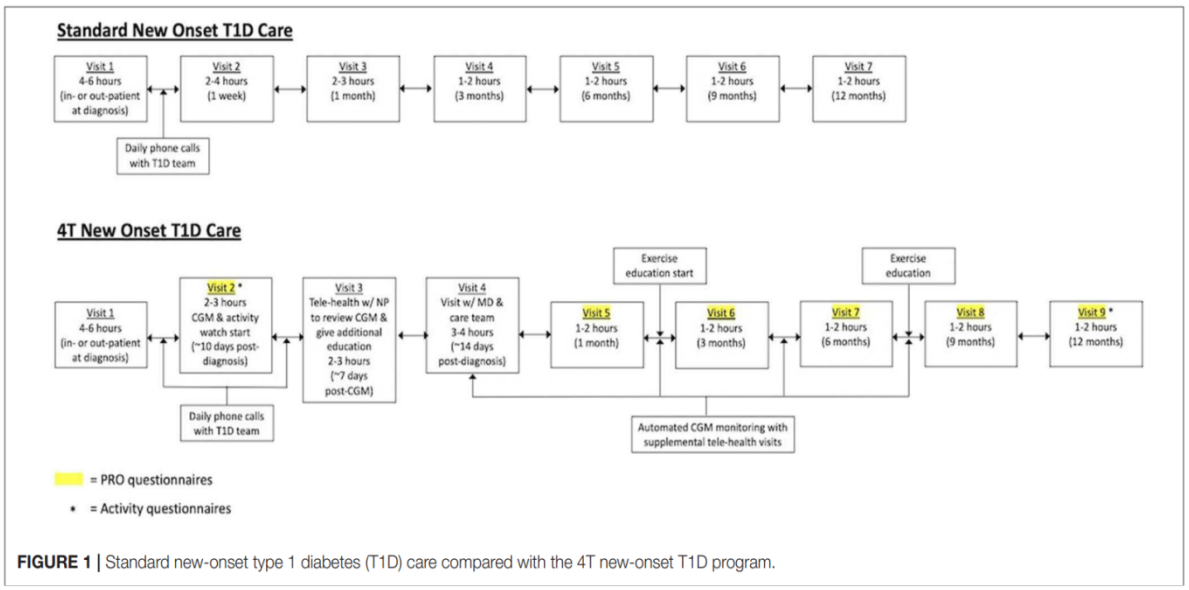

FIGURE 1 | Standard new-onset type 1 diabetes (T1D) care compared with the 4T new-onset T1D program.

However, the date of CGM commencement was inconsistent in these trials, with many of the kids starting after a rise in HbA1c between 5 and 6 months following diagnosis. When CGM is started within the first month of receiving a diabetes diagnosis, it allows for more frequent insulin dose adjustments between visits and education about tighter objectives. In a pilot trial, our team started 40 young people on CGM during the first month of diagnosis and found that they had a high rate of utilisation and a low risk of hypoglycemia [29].

CGM devices have been certified for usage in insulin dosage (non-adjunctive use) and factory calibration in the last year, allowing them to be a real replacement for SMBG. These characteristics, when paired with the increased number of readings, rates and directions of change, warnings, and remote data sharing, have the potential to improve glycemic management in children and adolescents with T1D. CGM's remote data sharing capability allows not only the youngster's caregiver, but also the youth's care team, to monitor the youth remotely.We previously established a system that used Apple HealthKit on iOS devices to transmit data from an individual's CGM into our electronic health record (EHR) Figure 2; [30]. This system complies with the US Health Information Portability and Accountability Act's requirements (HIPAA). CGM data can be securely analysed by the diabetic care team to make dose adjustments in between clinic visits using this function. Dose modifications are made utilising a secure patient messaging platform integrated into the EHR or secure telehealth, which is also integrated into the EHR.Given the enormous number of people in any clinic, population health management solutions must be designed to enable for regular reviews of vast amounts of data. Unfortunately, the rising use of CGM in paediatric T1D management has not been properly exploited in terms of teaching, target definition, or glucose data utilisation between quarterly clinic appointments.

Other technologies have the potential to revolutionise the way diabetes care is delivered. Even in underdeveloped countries, Internet access, including smart phone use, is becoming almost universal [31] Because of the widespread availability of internet connectivity, telehealth can be used to provide remote care.

Individuals with T1D should have at least four visits each year, with each visit including a HbA1c measurement. Children who had quarterly visits had a higher chance of improving their HbA1c than those who had fewer visits each year [32]. According to the data, children who lived further away from their diabetes centre had fewer annual visits and a higher HbA1c [33]. In our practise, we have adolescents who travel hundreds of miles for care, making clinical visits time-consuming and costly.Face-to-face care can be delivered to an individual's home without the need for parents to leave work, children to miss school, or for them to travel.

Telehealth can also be used to supplement diabetes teaching in group settings. Visit times can be more flexible to accommodate the requirements of adolescents and their carers because telehealth visits do not require dedicated clinic space or ancillary employees.
Technology has the ability to help persons with T1D receive better care. The time of the care team, on the other hand, is a finite resource. Modern data analysis and visualisation techniques enable the development of decision-support tools that translate CGM data analysis into efficient population-health management with existing personnel.

TEAMWORK

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

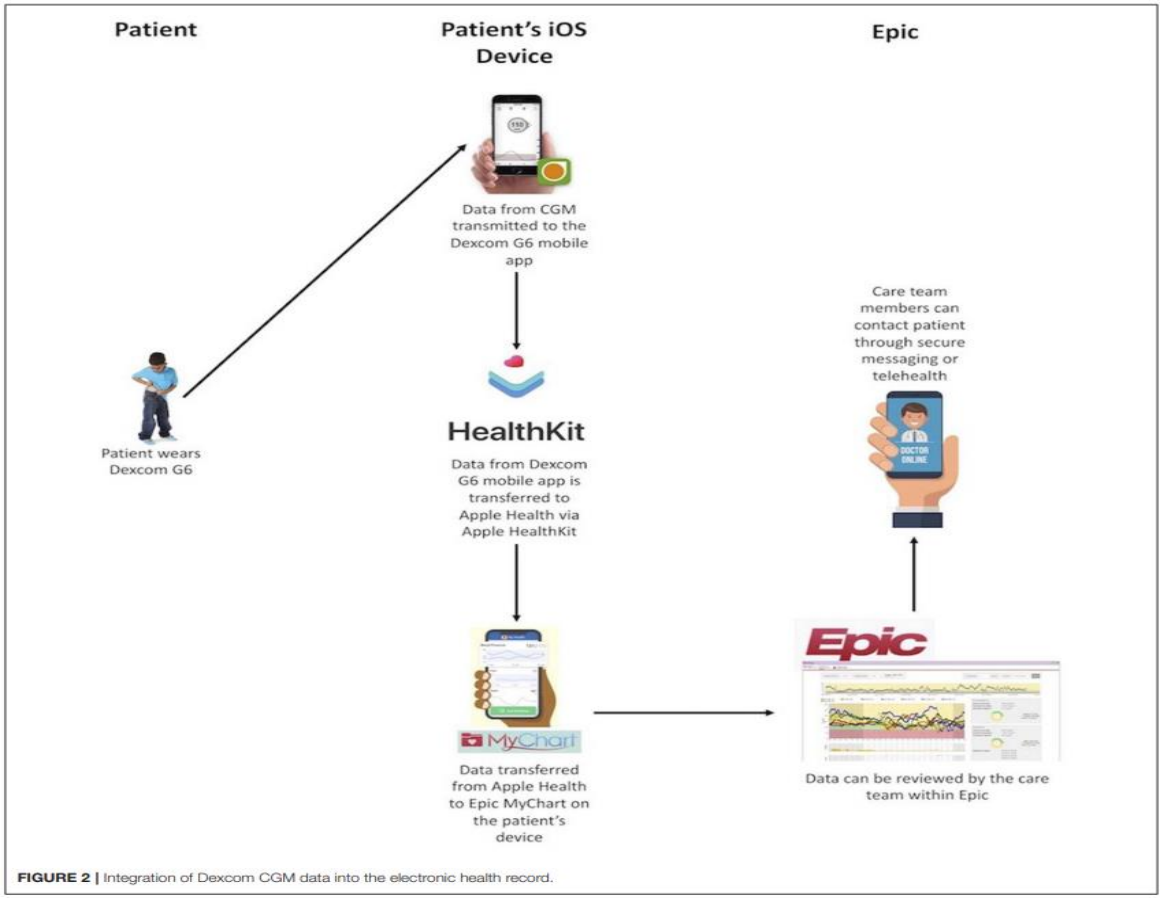

FIGURE 2 | Integration of Dexcom CGM data into the electronic health record.

[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 begins with family education delivered by physicians, diabetes educators, and registered dieticians during the new-onset phase. CGM implementation necessitates a well-coordinated team effort that includes not only basic diabetes education but also teaching on how to use CGM to improve diabetic care. The diabetes care team's involvement does not cease with the new-onset period and should continue. As a result, each follow-up visit should include access to these members of the care team.
T1D is linked to psychosocial comorbidities in addition to schooling. According to a systematic review, one-third of young people with T1D report diabetes distress, which is emotional anguish caused by the burden of diabetes self-management [36]. Diabetes discomfort is linked to a worsening of clinical outcomes. Given the importance of mental health in the care of children and young people with T1D, mental health support should be made available through psychologists and social workers to assist with diabetes management. PROs have long been

used to screen for psychological disorders, as recommended by the American Psychiatric Association.

TABLE 1 | PROs incorporated into the 4T program.

Topic	Construct measured/relevant points
Youth and parent outcomes—diabetes distress	
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.
Youth-only outcomes	
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.

All youth in the clinic will receive early psychoeducation in the 4T programme, which will describe signs of typical psychological difficulties in T1D youth (e.g., distress and depression). This will be given out as part of routine teacher visits. All youth will be examined on a regular basis [visits 2, 4, 5, 6, and 7] and therapeutic treatments will be available if the PROs are positive (Table 1). The Guiding Adolescents Through E- Psychotherapy (GATE) programme, a five-session web-delivered cognitive behavioural therapy (CBT) programme tailored to diabetes-specific concerns and designed to address topics that are most important in these youths' lives, is one example of the interventions delivered as part of the 4T programme.CBT is a gold-standard psychotherapy treatment for depression, and it is the most used type of psychotherapy treatment for paediatric kids in the community [41, 42]. Because not all youth will be able to attend weekly psychotherapy sessions, telemedicine will be used to give psychotherapy. This has been proved to be successful in the past [43–45].

TARGETS

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 should be updated in response to existing diabetes technology, particularly 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. Using a "CGM at Diagnosis" procedure with 55 newly diagnosed paediatric kids, a previous study proved the acceptability of CGM to both parents and adolescents shortly after diagnosis [46]. The CGM group had 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 than the no-CGM control group, and parents reported better confidence in managing hypoglycemia when they utilised CGM in the first six months following diagnosis [47].As a result, CGM acts as a safety net, allowing for tighter glucose targets, particularly after initial onset, as well as providing psychosocial benefits. Although data on the effectiveness of unambiguous target setting is obvious, glucose objectives have not been altered to aim for tighter control, a missed chance to lower HbA1c [48]. Table 2; [51–53] Three sets of HbA1c and related glucose goals have been published. The 4T method entails informing families about the relationship between glucose measurements and specified HbA1c targets [50]. An HbA1c of 6.5 percent will be the initial aim after diagnosis, and this target should be adapted and personalised to each family according to guideline recommendations, but in a uniform manner with a team approach.According to new research, glucose time-in-range (TIR) can also be a beneficial indicator for families with HbA1c [49]. TIR (and mean CGM glucose) may be estimated between clinic visits, unlike HbA1c, which is done weekly, and can provide advise on glucose control and insulin administration [54, 55]. Furthermore, we will stress education to distinguish between hypoglycemia as a clinical alert (stage 1, 70–54 mg/dl) and clinically relevant or dangerous hypoglycemia (stage 2, <54 mg/dl) or seizure/coma (stage 3) hypoglycemia [55]To assist care, each teen and family will be given HbA1c, mean glucose, TIR, and hypoglycemia targets. Aiming for a mean CGM glucose of 150 mg/dl, 70 percent 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, are simple education measures. Families will receive training on how to interpret CGM data and make simple insulin dose adjustments.

TIGHT CONTROL

Maintaining tight control necessitates frequent data evaluation and dose modifications. Regrettably, just a small percentage of children and their caregivers evaluate diabetic device data on a frequent basis [56]. Glucose levels are usually checked every three months at patient visits by the diabetes care team. This interval may be too long to achieve optimal glycemic control, particularly in a growing child who has recently been diagnosed. Several CGM systems allow data to be shared remotely via mobile apps. Instead of depending on HbA1c results, which indicate three months of glucose management, diabetic care teams can use this capability to undertake remote data review and dose modifications for kids with T1D in between clinic visits [57, 58].This allows for early intervention in response to harmful tendencies rather than waiting until clinical care is provided every three months. Routine reviews for all adolescents can be taxing for the diabetes care team due to the volume of data. As a result, instruments to aid population health management should be developed.

Machine learning and decision support technologies have shown considerable potential in guiding clinical decisions, but not in producing individualised disease management

recommendations for kids with T1D [59–61]. We've created a system that identifies aberrations and opportunities at shorter intervals, alerting the clinical team to the possibility of insulin adjustments. The system is built to facilitate a systematic, coordinated approach by the care team as well as algorithmic analysis of CGM data. The algorithms detect when a child's control is weakening and send out alerts.The systematic, coordinated approach ensures that care team members can [1] see data for a small cohort of "their" youth on a regular basis; [2] quickly review data for all other youth for whom an alert has been issued; and [3]maximise efficiency by only reviewing data that has not been reviewed by someone else or contacting a patient who has recently been contacted. This will enable care team members to prioritise data review of individuals who require further actions in order to maintain tight control, reducing their workload.

EXERCISE IN YOUTH WITH NEW-ONSET TYPE 1 DIABETES

Regular physical activity is vital for overall health, well-being, and psychological development [62–64]. However, it is also acknowledged that many people with T1D do not get the necessary amount of physical activity on a regular basis [65]. "Exercising safely," according to T1D youth and health-care experts, is one of the most difficult elements of diabetes, and many people avoid physical activity because of the hazards. According to Matson et al. [66], newly diagnosed persons with T1D spend a quarter less time per day in moderate-to-vigorous physical activity (MVPA) than adults without T1D.Similarly, children who develop T1D before the age of seven have significantly lower levels of physical activity than children who do not have T1D. [67]. These reduced rates of activity could be attributable to a variety of circumstances, including patient fear of hypoglycemia and constraints imposed by primary caregivers [68].

Before engaging in physical activity, numerous factors must be considered for kids with T1D, including starting glucose level, activity timing and intensity, insulin dose, carbohydrate supplementation, exercise time of day, individual fitness, and prior episodes of hypoglycemia [69–71]. Encouragement of regular physical activity is critical for doctors and health-care practitioners; yet, this necessitates a deeper understanding of techniques to better regulate glycemia during exercise [66, 70]. Clinical recommendations, consensus statements, and position statements on exercise equip doctors with some systematic techniques to help them develop tailored exercise management regimens for children and adolescents with T1D. [53, 70, 72].Some options for minimising exercise-related hypoglycemia include lowering the basal insulin dose prior to exercise, lowering prandial insulin during the meal prior to exercise, and/or boosting carbohydrate feeding [53]. Overall, increased vigilance and regular blood glucose monitoring around exercise are recommended for safety.

PRELIMINARY OUTCOMES

We've had 90 youth start CGM in the new-onset period forone and half years. Sixty-five of the 90 youth have been in the programme for at least six months. Although the median HbA1c at diabetes onset was greater in this cohort than in the preceding one from 2014 to 2016, the nadir was lower. Unadjusted HbA1c was 0.54 percent lower in the new-onset CGM cohort at 6 months post-diabetes diagnosis compared to our historic controls [73].

Thirty of the 65 individuals were engaged in a remote monitoring research, which was made possible by an internal grant, and in which participants were given an iOS device if they did not already have one. We included their information into our EHR (Figure 2). A member of the diabetes care team analysed the data weekly, and adolescents and/or caregivers were called for insulin dose modifications and/or education. Between clinic appointments, these kids had 15 data evaluations on average, with an average of five dose modifications per child [74]. Efforts are still being made to streamline this procedure so that it can be scaled to a broader population without putting more strain on the diabetes care team.

CONCLUSIONS

Despite the DCCT findings, many young people with T1D fail to attain their glycemic objectives. Clinics have been able to lower HbA1c closer to the ISPAD target of 7% through benchmarking and quality improvement efforts, although few have achieved this goal. Although technology has helped to alleviate some of the burdens associated with T1D, it has not resulted in major glycemic control improvements. Some of the difficulties stem from the fact that kids with T1D were educated before to the advent of CGM, when targets for preventing severe hypoglycemia were less stringent.Because there are alarms to prevent clinically serious hypoglycemia, CGM technology enables for more precise targeting. In addition, automated insulin administration systems that include a CGM use the CGM to suspend insulin if hypoglycemia is suspected. Despite technological advancements, education has not progressed to encourage more stringent goals.

In the new-onset period, the 4T strategy presented in this review develops diabetes education and a management programme focusing on the use of technology, notably CGM. The new-onset time was chosen because it allows for teaching of kids with T1D and their carers, which is in line with current diabetic treatment. Physicians, diabetes educators, nutritionists, social workers, exercise physiologists, and psychologists must work together to start CGM during the new-onset period.Following the implementation of CGM, education can be centred on achieving consistent targets in order to ensure tight control. Remote monitoring of CGM data is also possible with technology, and the development of population health technologies could make CGM review between clinic visits the standard of care for all young people. With the introduction of telehealth, care can now be delivered by virtual teleconference, reducing the burden of diabetes care even more by reducing travel to the diabetic clinic.

This programme includes psychosocial support as a key component. CGM has the potential to reduce the burden of diabetes treatment while also improving glucose control, but it should not come at the expense of quality of life. As a result, monitoring PROs is an important part of the 4T programme, as is making psychological support a fundamental component of diabetic management.

Finally, the 4T programme attempts to improve glucose control after T1D diagnosis and sustain it after the clinical remission phase ends, all while improving quality of life. Furthermore, automated insulin administration devices for kids with T1D and their families in the future promise tighter glucose control with fewer hypoglycemia and a lower burden of care [75–78]. To fully exploit the potential of optimal T1D care, early integration and attention to diabetes technology uptake and psychosocial outcomes will become increasingly critical.

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