Title: Intermittently scanned continuous glucose monitoring is associated with high satisfaction but increased HbA1c and weight in well-controlled youth with type 1 diabetes

Running title: high acceptance, worse HbA1c in youth on isCGM

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ABSTRACT

Objective: We undertook a 24-month prospective observational single-center real-world trial to study impact of access to intermittently scanned continuous glucose monitoring (isCGM) on quality of life (QOL) and glycemic control of youth with type 1 diabetes (T1D).

Methods: Between September 2016 and November 2017, 138 children and adolescents with T1D were recruited. Demographic, metabolic, and QOL data were collected during 24 months of routine follow-up. Primary endpoint was evolution of QOL, with secondary outcomes change in HbA1c, occurrence of acute diabetes complications, and school absenteeism.

Results: Ninety-two percent of participants found isCGM more user-friendly than capillary finger-stick tests and had high treatment satisfaction, without change in diabetes-specific QOL. HbA1c significantly increased from 7.2% (7.0–7.3) (55 mmol/mol [53–56]) at baseline to 7.6% (7.4–7.8) (60 mmol/mol [57–62]) at 12 months ($P<0.0001$) and was unchanged up to 24 months. Overall increase was mainly driven by children with baseline HbA1c $<7.0\%$ (<53 mmol/mol). Additionally, BMI adjusted for age was higher at study end. In year before isCGM, 228 days per 100 patient-years of school absenteeism were reported, which dramatically decreased to 13 days per 100 patient-years ($P=0.016$) after 24 months. Parents of children also reported less work absenteeism ($P=0.011$).

Conclusion: Use of isCGM by T1D pediatrics is associated with high treatment satisfaction and less days of school absence. However, increased HbA1c and weight may reflect a looser lifestyle, with less attention to diet and more avoidance of hypoglycemia. Intensive education specifically focusing on these points may mitigate these issues.

Keywords: type 1 diabetes mellitus, children, intermittently scanned continuous glucose monitoring, quality of life, absenteeism

INTRODUCTION

Management of type 1 diabetes (T1D) is a task performed around the clock that can form a challenge for children, adolescents, and their parents, often characterized by a worsening in glycemic control during adolescence.^{1,2} Suboptimal diabetes control early in life is a risk factor for developing microvascular and macrovascular complications later in life.³ In addition, the negative impact of struggling with diabetes management on mental well-being and quality of daily living should not be put aside as this can lead to depression or even suicide.^{4,5} The use of diabetes technology has the hope of lessening the burden of diabetes management and improve outcomes in youth. Since the introduction of continuous glucose monitoring (CGM), self-management of type 1 diabetes (T1D) has changed dramatically. The availability to visualize day-to-day trends, hypoglycemic events, time in range, and the generation of an informative one page ambulatory glucose profile can enhance individualized diabetes care and day-to-day changes in insulin therapy.⁶ CGM has been recognized as a benefit in the adult population with favorable results on hypoglycemia risk, quality of life, and hospitalization rate.^{7–10} However, results in the pediatric age group are less certain.^{8,11,12}

From 2014 onwards, intermittently scanned CGM (isCGM) (Freestyle Libre, Abbott Diabetes Care, Witney, UK) was introduced, and has been approved for use in children older than 4 years of age in January 2016. This device differs from CGM by the need for active “scanning” of the sensor, absence of alarms for hypo- and hyperglycemia in the first version, no need for calibration, and a sensor lifespan of 14 days.¹³ To date, only few studies report isCGM use of longer than 6 months with a follow-up of maximum 12 months.^{14–16} These observational studies show mixed results for glycemic outcomes, and quality of life was not always part of the assessment.¹⁴ Additionally, the effect on diabetes-related absence days from school has not been studied before. Thus, it remains unclear whether the long-term use of isCGM has a benefit in an unselected population in real-world settings.

Therefore we wanted to provide an answer to the question whether 24-month use of isCGM in an unselected real-world cohort of youth living with T1D had an impact on quality of life, diabetes control, acute complication risk, and absence from school.

METHODS

Study design and participants

Youth with T1D were consecutively recruited between September 2016 and November 2017 for this single-center prospective observational real-world cohort study (FUTURE trial, Flash glucose monitoring study for diabetes, ClinicalTrials.gov: NCT02898714). Recruitment took place at University

Hospitals Leuven. All children and adolescents who were planned to start isCGM were proposed to participate and included in the study after signed informed consent of at least one of the parents and informed assent of the person with T1D. The decision to use isCGM was made prior to and independently of their entrance to the study, and was based on preferences of the patients and their parents. Beforehand, we estimated that about 70% of youth with T1D (n=190/272) would be willing to use isCGM. For the current analysis, only data from people who were diagnosed with T1D more than three months before start of isCGM were used.

Data were collected during routine clinical follow-up and from validated questionnaires that were presented to the participants at defined time points.

Outcomes

Primary outcome was defined as evolution over time of quality of life between baseline and 24 months after start of isCGM. Secondary outcomes were change in acute diabetes complications (hypoglycemia and/or ketoacidosis), school absenteeism, work absenteeism of parents, HbA1c, proportion of participants with HbA1c <7%, <7.5%, and <8.5% (<53 mmol/mol, <58 mmol/mol, 69 mmol/mol), total daily insulin dose, BMI, reasons to discontinue isCGM, and monitoring complaints.

Device and diabetes management

In Belgium, people with T1D treated for their diabetes in specialist centers by multidisciplinary teams lead by endocrinologists are free to choose which reimbursed device they use for diabetes management. On August 1, 2016, the first version of the FreeStyle Libre flash glucose monitoring system (Abbott Diabetes Care, Witney, UK) became fully reimbursed for youth with T1D in Belgium. If they chose to switch to isCGM, they were trained individually or in group during two to three hours by experienced diabetes educator nurses as part of the standard of care.

Children and their parents were trained in setting up the device, inserting the sensor on the back of the upper arm, scanning the sensor with the reader, interpreting trend arrows and glucose sensor reports, uploading glucose sensor data using the designated diabetes management software, entering extra information in the reader (e.g. carbohydrate intake, insulin dosing, exercise), and understanding when a confirmatory capillary glucose test was recommended.

After the training session, the device was immediately unblinded. They received instructions to scan frequently (at least four times daily), to adapt insulin dose on the basis of the actual value, and to take associated trend arrows into account. During every routine diabetes consultation, isCGM data were uploaded and relevant reports were generated using the designated software. These reports were thoroughly reviewed together with the multidisciplinary team and, if necessary, treatment adaptations were proposed.

Data Collection

Pre-specified clinical data were collected from the electronic medical records from 12 months before until 24 months after start of isCGM. BMI was converted to standard deviation scores (SDS).¹⁷

For the primary outcome, different questionnaires were presented to participants at baseline, 6, 12, and 24 months. All questionnaires (Diabetes Quality of Life for Youth [DQOLY]¹⁸ and Hypoglycemia Fear Survey [HFS] for children¹⁹) were validated in both Belgian languages (Dutch and French) and in English, and presented to participants and their parents in their mother tongue or the language they understood best. After 6, 12, and 24 months, participants were asked how satisfied they were with the new device on a 10-point Likert-scale ranging from 0 (“not at all satisfied”) to 10 (“very satisfied, could not be better”), and they could indicate if they found isCGM less convenient, similar, or more convenient than finger-stick testing. Additionally, comments on the use of isCGM were gathered and grouped for qualitative research purposes.

At baseline, after 6, 12, and 24 months, children/parents were asked to report on how many diabetes-related events the children experienced, how many days the children missed school due to their diabetes, and how many days their parents were absent from work due to the diabetes of their child, all in the previous 6 months prior to the routine clinic visits (Supplementary Table 1). Patient-reported medical interventions, emergency room admissions, and hospitalizations for (symptoms of) acute diabetes complications (hypoglycemia/ketoacidosis/ketosis) were validated using hospital records. Hospitalizations for ketoacidosis at diagnosis of type 1 diabetes were excluded.

Reports of isCGM data were generated using the designated diabetes management software (FreeStyle Libre software version 1.0 and LibreView) and used to determine scan frequency.

Ethics

The protocol was approved by the coordinating institutional review board (Ethics Committee University Hospitals Leuven). The study was executed in line with Good Clinical Practice guidelines of the Declaration of Helsinki in its latest form.

Statistical analysis

Post-hoc, the total population was grouped based on clinically relevant parameters for subgroup analyses: quantiles of mean scan frequency over the 24-month follow-up period (<9 times per day and ≥9 times per day), two age-groups (≤12 years and >12 years), and clinically relevant subgroups of baseline HbA1c (<7.0% and ≥7.0%, <7.5% and ≥7.5%, and <8.5% and ≥8.5% [<53 and ≥ 53 mmol/mol, <58 and ≥ 58 mmol/mol, <69 and ≥ 69 mmol/mol]). The number of people in different subgroups at the different time points is shown in Supplementary Table 2.

We used a linear mixed model to evaluate DQOLY (satisfaction, impact, and worry subscales), HFS (behavior and worry subscales), HbA1c, insulin dose per day, and BMI with an unstructured covariance matrix for four repeated measurements within the same patient. By using a linear mixed model, cases with missing data still contributed to the analyses (see Supplementary Table 3 for number of missing cases per outcome). Differences in HbA1c between the two scan frequency groups were analyzed using Mann-Whitney U test. Pearson's correlation coefficient was used to analyze the relationship between scan frequency and HbA1c. The McNemar's test was used to evaluate the evolution of proportion of participants (with HbA1c <7% and <7.5% [<53 and <58 mmol/mol], with school/work absenteeism, needing help from third parties due to hypoglycemia, having hypoglycemic comas, and with admissions due to hypoglycemia/ketoacidosis).

Differences in days of school/work absenteeism, number of times help from third parties was needed, number of hypoglycemic comas, and number of days of hospitalizations for hypoglycemia/ketoacidosis per 100 patient-years were assessed with the Wilcoxon signed-rank test.

All tests were performed with SPSS software for Windows (IBM SPSS Statistics version 26, Armonk, USA) and conducted at the 0.05 significance level. Data are shown as mean with SD, or least-squares mean with 95% CI for results from the linear mixed model, unless otherwise stated.

RESULTS

Participants

A total of 138 children and adolescents with T1D since >3 months were included (Table 1). One hundred thirty-four (97%) and 122 (88%) participants used isCGM for at least 12 and 24 months, respectively. Of sixteen (11.6%) children who stopped participating in the study, 9 (6.5%) were lost to follow-up, and 7 (5.1%) stopped using isCGM (Supplementary Figure 1). Two participants stopped using isCGM because they preferred finger stick tests ($n=2/7$, 28.6%). Other reasons were mentioned only once: incidence of a severe hypoglycemic event, switch to real-time CGM, allergic reaction on sensor, sensor values were confronting, and the sensor was too visible ($n=1/7$, 14.3% for each reason). On average, children scanned 9.3 ± 5.7 times per day over 24 months.

Quality of life

The DQOLY satisfaction subscale was significantly improved after 12 months (68.8 [67.4–70.3] at baseline vs 71.2 [69.8–72.7] at 12 months, $P<0.0001$), but dropped slightly by 24 months (70.2 [68.8–71.5], $P=0.055$ vs baseline). DQOLY impact and worry, and HFS behavior and worry subscales did not change significantly over 24 months (Table 2). However, there was a trend towards higher HFS-behavior scores and lower HFS-worry scores, which was also present in the subgroup analyses (Table 2 and Supplementary Table 4).

When evaluating quality of life changes based on age, both those ≤ 12 years and those >12 years of age had higher scores for DQOLY satisfaction at 6 months. Those ≤ 12 years of age could keep the higher scores until 24 months, while youth >12 years of age could not. Improvements in DQOLY subscales were maintained for children who scanned <9 times per day, while those with a scan frequency of ≥ 9 times per day only showed an improvement in DQOLY satisfaction at 6 and 12 months when compared to baseline. For the subgroup analysis based on baseline HbA1c, each subgroup had higher DQOLY satisfaction up to 12 months (Supplementary Table 4).

Overall, participants self-reported high satisfaction with the device (8.2 ± 1.4 , 8.3 ± 1.2 , and 8.0 ± 1.4 at 6, 12, and 24 months respectively on scale from 0 to 10) and they agreed almost unanimously that isCGM was more convenient than finger-stick tests ($n=93/97$ [95.9%], $n=90/92$ [97.8%], and $n=71/77$ [92.2%] after 6, 12, and 24 months, respectively)

Change in acute diabetes complications and school absenteeism

The number of participants admitted to emergency room or hospital because of hypoglycemia decreased, although not reaching statistical significance ($p=0.453$). The same was observed for other acute hypoglycemic events. On the other hand, more hospitalizations due to diabetic ketoacidosis were observed, but this change was also not significant (Table 3).

In the year before use of isCGM, 228 days per 100 patient-years of school absence were reported. After 24 months, this significantly decreased to 13 days per 100 patient-years ($P=0.016$). Parents of children also reported less days off work, from 149 days per 100 patient-years before to 18 days per 100 patient-years after 24 months of isCGM use ($P=0.011$) (Table 3).

Change in HbA1c

The proportion of children with HbA1c $<7.5\%$ (<58 mmol/mol) was 66.7% ($n=92/138$) at baseline and was stable up to 6 months ($n=93/137$, 67.9%; $P=0.851$). Between 6 and 12 months, it significantly decreased to 54.5% ($n=73/134$; $P=0.003$ vs 6 months, $P=0.006$ vs baseline) and from 12 months onward it remained stable until 24 months ($n=72/122$, 59.0% after 24 months; $P=0.701$ vs 12 months, $P=0.019$ vs baseline).

The same was seen for the proportion of children with HbA1c <7.0% (<53 mmol/mol), which decreased from 47.8% (n=64/138) at baseline to 27.6% (n=37/134) after 12 months ($P<0.0001$) and was stable thereafter (n=38/122, 31.1% at 24 months; $P=0.851$ vs 12 months, $P=0.001$ vs baseline).

HbA1c significantly increased from baseline to 12 months (7.2% [7.0–7.3], 55 mmol/mol [53–56] at baseline vs 7.6% [7.4–7.8], 60 mmol/mol [57–62] at 12 months; $P<0.0001$) and was sustained until 24 months (7.6% [7.4–7.8], 60 mmol/mol [57–62], $P<0.0001$ vs baseline) (Figure 1a).

This overall increase was mainly driven by the group of children with baseline HbA1c <7.0% (<53 mmol/mol). Their HbA1c rose from 6.3% (6.2–6.4) (45 mmol/mol [44–46]) to 6.9% (6.7–7.1) (52 mmol/mol [50–54]) over 24 months ($P<0.0001$), whereas those with baseline HbA1c $\geq 7\%$ (≥ 53 mmol/mol) remained stable (7.9% [7.7–8.1], 63 mmol/mol [61–65] vs 8.1% [7.8–8.4], 65 mmol/mol [62–68] over 24 months; $P=0.086$) (Figure 1b). See Supplementary Figure 2 for evolution of HbA1c for subgroups with baseline HbA1c <7.5% (<58 mmol/mol) and <8.5% (<69 mmol/mol).

Youth >12 years of age had worse diabetes control than children ≤ 12 years of age. However, they showed the same evolution of HbA1c over 24 months of isCGM use (Figure 1c).

During the first 12 months, children who scanned <9 times and who scanned ≥ 9 times per day showed the same increase in HbA1c. However, between 12 and 24 months, those scanning ≥ 9 times per day showed a slight decrease (7.5% [7.2–7.7], 58 mmol/mol [55–61] at 12 months vs 7.2% [7.0–7.4], 55 mmol/mol [53–57] at 24 months; $P=0.006$), while those who scanned <9 times per day remained stable (7.8% [7.5–8.1], 62 mmol/mol [58–65] at 12 months vs 7.8% [7.5–8.2], 62 mmol/mol [58–66] at 24 months; $P=0.651$) (Figure 1d). The difference in HbA1c between the two groups at 24 months was significantly different ($P=0.005$), whereas this was not the case at the other follow-up moments.

The mean change in HbA1c ($0.4\pm 0.8\%$, 5 ± 8 mmol/mol) was not correlated with mean scan frequency during 24 months ($r=-0.14$, $P=0.137$).

Change in insulin dose and BMI

Prescribed insulin doses increased over the study period. Overall daily insulin dose increased by 4.9 units (1.7–8.0) ($P=0.003$), daily basal dose increased by 2.4 units (1.3–3.4) ($P<0.0001$), and daily bolus dose increased by 3.2 units (0.8–5.7) ($P=0.011$). However, when assessed as units per kilogram bodyweight, it decreased non-significantly over 24 months (Supplementary table 5).

BMI increased with 1.8 kg/m^2 (1.4–2.1) during 24 months ($P<0.0001$). BMI adjusted for age increased by 0.13 SDS (0.02–0.24) ($P=0.026$).

Self-reported adverse events and complaints with isCGM

Although users were very satisfied with the system, 64% (n=88/138) of participants reported 349 negative user experiences with the device.

Comments were mainly regarding the frequent sensor loss (n=50/138 [36%], 31% of comments) and accuracy (n=52/138 [38%], 27% of comments). Other comments were related to wearing comfort and pain (n=28/138 [20%], 12% of comments), skin irritation or allergy (n=23/138 [17%], 10% of comments), technical issues (n=21/138 [15%], 9% of comments), and visibility on the upper arm (n=12/138 [9%], 5% of comments).

DISCUSSION

This study shows that isCGM in a real-world pediatric population increases self-reported treatment satisfaction, without changing overall diabetes-related quality of life, and is well accepted by the children and their parents. With use of isCGM, less days off school for the children with T1D and less days off work for their parents could be achieved. However, there was no impact on acute hypoglycemia complications and diabetes-related hospitalizations. On the other hand, metabolic control worsened with an increase in HbA1c and BMI for the total population.

Since August 2016, isCGM is fully reimbursed in Belgium for children with T1D from 4 years of age onward. Full reimbursement was already implemented for adults with T1D one month earlier. This made it possible to study the use of isCGM in our pediatric population without the burden of financial constraints, which is often a reason to discontinue diabetes devices.²⁰ Here, only 5% decided to stop the use of isCGM, which is lower than in other populations where reimbursement was not provided.^{14,16,21}

Patient-reported outcome measures (PROMs) are more and more recognized as important endpoints in clinical studies evaluating new interventions in the management of diabetes. They provide us with qualitative information regarding the impact on daily life, and are powerful tools to inform patients, clinicians, and policy-makers.²² This study incorporated several PROMs, such as diabetes-specific quality of life questionnaires, satisfaction scales, and the potential to point out complaints about isCGM. When considering isCGM in an unselected population, these PROMs should be combined to allow for a complete evaluation. To start with, our population perceived their quality of life as good, with high satisfaction with life, moderate impact of diabetes on their quality of daily living, and relatively low worries about diabetes.²³ This did not change when isCGM was introduced, with even higher satisfaction on the DQOLY questionnaire up to 12 months. This is in line with results from isCGM

use among adults with T1D.²⁴ This suggests that, when studying an unselected population of people with T1D, quality of life scores will be relatively high, which makes it rather difficult to show any improvement. Another important quality of life factor is fear of hypoglycemia, as it presents a major psychological barrier to achieving optimal glycemic control.²⁵ Although, changes were not significantly different for HFS-behavior and HFS-worry, there was a recurring trend towards increasing behavior and decreasing worry scores. This could indicate that with isCGM, they were able to intervene earlier on upcoming lows with a decrease in fear. However, through the visualization of all glucose values, more hypoglycemic events may have come to light which previously remained undetected or unrecognized,²⁶ prompting children and parents to take more defensive actions to prevent hypoglycemia.

As T1D is a chronic disease and life-long therapy is needed, it is important for technology to be user-friendly without debilitating effects on quality of daily living, which in turn allows for high device uptake. As observed in other studies,²⁷⁻²⁹ device acceptance was high as seen by unambiguous scores on system utilization and self-reported satisfaction. They preferred isCGM over capillary glucose tests, however, more than half of participants reported problems with the device. By gathering device complaints, healthcare practitioners can inform future isCGM users to keep the frequently reported problems into mind, which in turn may result in less frustrations when problems arise. In the present study, the most frequently reported problems were due to early sensor loss and perceived low accuracy. There are several arguments for the latter. First, the delay in glucose concentration variation between the blood and the interstitial fluid causes a lag time of 5-15 minutes and is inherent to glucose sensors.³⁰ Further, when the glucose is rapidly changing, the lag time will be more prominent.³¹ And last, sensor accuracy is lower during the first 24 hours after insertion³² as a consequence of tissue trauma and a compromised skin barrier, which may lead to inflammation.³³ To avoid a distrust in sensor values, it remains important to explain the concept of lag time and advise people when a confirmatory capillary glucose test is warranted. Other frequently reported issues were pain and skin irritation/allergy due to the sensor or adhesive patch. Seventeen percent reported the development of skin reactions and is in line with other reported incidences in children.^{16,21}

To the best of our knowledge, this is the first long-term study assessing changes in school and work absence after initiation of CGM in children. For the children as well as for the parents, we observed a continuing decrease in absence days from school and work, representing an important advantage on both individual and societal level. Previous studies have reported higher levels of absenteeism for children with T1D compared to their healthy peers and siblings,³⁴⁻³⁹ which is associated with poorer school results even after controlling for demographic and socioeconomic characteristics.^{37,38,40} Studies pointed out that lower educational achievements may subsequently impact labor market

opportunities leading to a higher likelihood to be unemployed after school with lower income and a higher chance of early retirement.^{37,40,41} It should be kept in mind that these studies looked at individuals who spent their childhood in the 20th century, thus without the availability of modern diabetes technology. Therefore, new long-term studies are needed to understand the impact of CGM on participation in society, as being able to manage diabetes in a timely manner may positively impact educational results by a reduction in cognitive deficits. Furthermore, a child spends between 8-10 hours per day at school. It is therefore crucial that school personnel provides the support the child needs to manage diabetes effectively. Diabetes management training for school personnel is part of the standard of care when a child is diagnosed with T1D in Belgium and many other Western countries.⁴² However, deficiencies to support diabetes self-care in the young contribute to poor glycemic control and subsequent poorer educational attainment.⁴³ The ever-growing list of technological innovations to be used in the management of diabetes does not make it easier for school personnel to oversee diabetes self-management.⁴⁴ Differences between capillary glucose values and sensor readings should be explained to school personnel to avoid wrong treatment decisions due to a poor knowledge of the device, complemented with frequent updates when new information is available.⁴⁵

This single-center unselected pediatric population was well-controlled at baseline with mean HbA1c of 7.2% (55 mmol/mol), which is better than what has been reported for other studies assessing impact of isCGM,^{14–16,28,46,47} for general populations followed through diabetes registries,^{48–51} and even for the whole Belgian pediatric population.⁵² We are the first to follow a population up to 24 months after isCGM initiation. Unfortunately, after initiating isCGM, HbA1c increased and reached a plateau at 7.6% (60 mmol/mol) after 12 months. Studies with poorly controlled subjects observed a modest decrease in HbA1c after 2 to 3 months.^{14,28,46,47} Only one of these studies followed the study population for a longer period of time, here HbA1c was not different after 12 months of isCGM use than at baseline.¹⁴ Our results are different from the study of Bolinder *et al.* where adults with mean HbA1c of 6.7% (50 mmol/mol) were randomized to isCGM or capillary glucose tests for 6 months. They observed no change in HbA1c for their well-controlled population.⁵³ We observed a simultaneous increase in BMI and no decrease in prescribed insulin doses. Together with a trend towards higher scores on the behavior subscale of the HFS questionnaire, this would suggest that HbA1c increased as a consequence of more defensive snacking to prevent hypoglycemia. Due to the easiness of measuring glucose with isCGM, lower glucose levels are noticed much faster than with capillary glucose tests.⁵³ Additionally, isCGM also provides trend arrows upon scanning. It is our clinical experience that when a downward trend arrow is shown with normoglycemic levels, too quickly this is seen as a state that needs correction. So, earlier awareness can result in people treating hypoglycemia at a higher glucose level

than they would have previously done without ample reduction in carbohydrate intake, thereby increasing subsequent glucose values. There is also the risk of wrong sensor readings, because isCGM sensors have been shown to have lower accuracy in the hypoglycemic range and when glucose is fluctuating.^{31,32,54} In addition, it has been reported that pressure-induced sensor attenuation can cause false low measurements,⁵⁵ especially seen at night, and thus hyperglycemia due to unnecessary carbohydrate intake. Therefore, making treatment decisions based on isCGM values is not allowed under these circumstances.⁵⁶ All these factors only came to the attention of clinicians during the first year of the study. Hence, proposed diabetes treatment changes at standard diabetes consultations did not yet take these caveats into account, contributing to the increase in HbA1c and BMI with possibly hyperglycemia, during the first 12 months. Data is emerging about the possible negative impact of hyperglycemia on cognitive function in youth with T1D.⁵⁷ Therefore, continued efforts are needed to improve education about the use of isCGM with a focus on timely and adapted treatment changes based on the sensor glucose level, trend arrows, and the understanding when confirmatory capillary glucose tests are necessary.

Even though the landscape of glucose monitoring technology changes rapidly as seen by the high turnover rate and the development of even more complex and automated systems, we believe that the results from this study are still relevant for tomorrow's diabetes management. Namely, it will be a long time before every child with T1D will be able to use complex devices like closed-loop systems, because of the high cost and lack of availability through reimbursement programs. In this regard, isCGM (specifically FreeStyle Libre) will remain an important player, due to its cheaper price, ease of use, and higher penetrance in the CGM market. When considering a high glucose test frequency, isCGM is even more economical than capillary glucose tests.⁵⁸ At the end of 2018, the second-generation FreeStyle Libre was selectively launched in Europe. It adds optional real-time alarms for hypo- and hyperglycemia (only an indication if glucose is high or low), is said to be more accurate than the previous generation, and the allergen isobornyl acrylate is removed from the adhesive patch.^{59,60} However, in 2020 still the majority of people use the first-generation FreeStyle Libre. It remains to be evaluated what the added benefit of these optional alarms will be on an isCGM system. Nonetheless, education will continue to be an important aspect to achieve optimal diabetes control while using glucose monitoring technology.

Our study has limitations, like the fact that we did not have a control group and that severe hypoglycemic events prior to initiation could only be recorded by recall. However, all hospitalizations for hypoglycemia and ketoacidosis were validated using the hospital records of the participants. Further, we only report on outcomes of one pediatric center, so it is not known if this team or its patient population is representative of other centers across the country. Next, we only assessed quality

of life changes among the children, but it is also important to question the parents about the impact of isCGM on their lives. The most important limitation lies in the fact that we were not able to assess changes in time spent in different glycemic ranges, which would also be of interest to look for associations between time in ranges and the decrease in school absence days.

Despite these limitations, of which some are inherent to an observational study, we provide valuable data on the real-life unrestricted use of isCGM in a well-controlled pediatric population with T1D. It is namely associated with high treatment satisfaction and less days of absence from school. However, metabolic control was worse after 24 months with also an increase in BMI. Thus, regular education on how to cope with trend arrows, lag time, and sensor errors will be imperative to teach children, parents, and school personnel to apply effective diabetes management.

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TABLES

Table 1. Baseline characteristics

Total number of participants	138
Gender	
Girls	75 (54.3%)
Boys	63 (45.7%)
Age (years)	
Mean	12.9 (3.1)
4 to 6	5 (3.6%)
7 to 12	49 (35.5%)
13 to 18	84 (60.9%)
Height (m), (inches)	1.58 (0.2), 62.2 (7.1)
Weight (kg), (lbs)	51.0 (16.7), 112.4 (36.8)
BMI (kg/m ²)	19.8 (3.5)
Education level parents	
Higher [†]	76 (55.1%)
No higher	25 (18.1%)
Unknown	37 (26.8%)
Years since type 1 diabetes diagnosis	5.4 (3.9)
Baseline HbA1c (%), (mmol/mol)	7.2 (1.1), 55 (11)
Insulin administration method	
Insulin pump therapy	27 (19.6%)
Multiple daily insulin injections	111 (80.4%)
Insulin, total daily dose (units/kg)	
Overall	0.91 (0.32)
Basal	0.32 (0.14)
Bolus	0.58 (0.22)
Insulin, total daily dose (units)	
Overall	48.2 (26.3)
Basal	17.4 (10.5)
Bolus	30.5 (17.1)
Impaired awareness of hypoglycemia	12 (8.7%)

Data are n (%) or mean (SD). [†]At least one of the two parents graduated from university or college.

Table 2. Quality of life scores before and after initiation of intermittently scanned continuous glucose monitoring

	baseline	6 months	12 months	24 months
DQOLY				
Satisfaction	68.8 (67.4 – 70.3)	71.9 (70.3 – 73.4)***	71.2 (69.8 – 72.7)***	70.2 (68.8 – 71.5)
Impact	52.1 (50.1 – 54.0)	50.5 (48.8 – 52.1)*	50.8 (49.0 – 52.7)	50.3 (48.4 – 52.1)
Worry	18.8 (17.6 – 20.0)	18.4 (17.1 – 19.7)	18.6 (17.4 – 19.8)	18.1 (17.0 – 19.2)
HFS for children				
Behavior	16.1 (15.1 – 17.2)	16.4 (15.3 – 17.4)	16.4 (15.4 – 17.4)	17.0 (15.9 – 18.2)
Worry	14.7 (13.2 – 16.1)	14.7 (13.1 – 16.3)	13.5 (12.2 – 14.8)	14.1 (12.8 – 15.4)

Data are least-squares mean (95% confidence interval). DQOLY=Diabetes Quality of Life for Youth, HFS=Hypoglycemia Fear Survey. * $P<0.05$, ** $P<0.01$, *** $P<0.001$ for the comparison with the baseline score.

DQOLY satisfaction score ranges from 17 to 85; high scores indicate much more satisfied. DQOLY impact score ranges from 23 to 115; high scores indicate high impact of diabetes on life. DQOLY worry score ranges from 13 to 65; high scores indicate many worries about diabetes. HFS behavior score ranges from 0 to 40; high scores indicate frequent hypoglycemia avoidant behaviors. HFS worry score ranges from 0 to 60; high scores indicate many worries related to hypoglycemia.

Table 3. Diabetes-related acute complications and school absenteeism before and after initiation of intermittently scanned continuous glucose monitoring

	baseline	6 months	12 months	24 months
People with				
Hospitalizations due to hypoglycemia and/or ketoacidosis ^{†‡}	9 (6.5%)	..	3 (2.2%)	8 (6.6%)
Hospitalizations due to hypoglycemia [‡]	7 (5.1%)	..	2 (1.5%)	1 (0.8%)
Hospitalizations due to ketoacidosis ^{†‡}	2 (1.4%)	..	1 (0.7%)	7 (5.7%)
Help from third parties due to hypoglycemia [§]	19 (13.8%)	13 (9.5%)	12 (9.0%)	16 (13.1%)
Hypoglycemic comas [§]	3 (2.2%)	0 (0%)	1 (0.7%)	1 (0.8%)
School absenteeism [§]	19 (13.8%)	13 (9.5%)	9 (6.7%)	6 (4.9%)
Work absenteeism by parents [§]	27 (19.6%)	25 (18.2%)	15 (11.2%)	10 (8.2%)
Number per 100 patient-years of				
Help from third parties due to hypoglycemia [‡]	65.2	..	37.3	59.0
Hypoglycemic comas [‡]	5.8	..	0.7	1.6
Days per 100 patient-years of				
Hospitalizations due to hypoglycemia and/or ketoacidosis ^{†‡}	18.8	..	7.1*	26.4
Hospitalizations due to hypoglycemia [‡]	2.9	..	0.4*	5.7
Hospitalizations due to ketoacidosis ^{†‡}	15.9	..	6.7	20.7
School absenteeism [‡]	227.5	..	65.2	13.1*
Work absenteeism by parents [‡]	149.3	..	87.3	18.0*

Data are n (% of total population) or n. Patient-reported hospital admissions were validated by clinicians.

[†]Hospitalizations for ketoacidosis at diagnosis of type 1 diabetes were excluded. [‡]Numbers represent period of 12 months before start, 12 months, and 24 months follow-up. [§]Numbers represent period of 6 months before each time point.

* $P < 0.05$ for the comparison with the baseline score.

FIGURE LEGENDS

Figure 1. HbA_{1c} from baseline to 24 months after initiation of intermittently scanned continuous glucose monitoring for the total population, groups based on baseline HbA_{1c}, age, and scan frequency

Data points represent least-squares mean (95% confidence interval) of HbA_{1c} measurements in percent (upper number) and mmol/mol (lower number) per time point for (A) the total population, (B) as a function of baseline HbA_{1c}, (C) as a function of age, and (D) as a function mean scan frequency over 24 months.

*** $P < 0.001$, ** $P < 0.01$, and * $P < 0.05$ for the comparisons versus baseline HbA_{1c}.