Optimization of Insulin Regimen and Glucose Outcomes with Short-Term Real-Time Continuous Glucose Monitoring in Adult Type 1 Diabetes Patients with Suboptimal Control on Multiple Daily Injections: The Adult DIACCOR Study

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Optimization of Insulin Regimen and Glucose Outcomes with Short-Term Real-Time Continuous Glucose Monitoring (RT-CGM) in Type 1 Diabetic Children with Sub-Optimal Glucose Control on Multiple Daily Injections: The Pediatric DIACCOR Study

Short title: Pediatric DIACCOR Study

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Abstract:

Background: The impact of 7-day real-time continuous glucose monitoring (RT-CGM) on type 1 diabetes (T1D) management remains unknown in youths with suboptimal control by multiple daily injections (MDI). The DIACCOR Study aimed to describe treatment decisions and glucose outcomes after a short-term RT-CGM sequence in real-life conditions.

Methods: This French multicenter longitudinal observational study included T1D youths with HbA1c >7.5% or a history of severe hypoglycemia (SH) or recurrent documented hypoglycemia. A sensor was inserted at the study-inclusion visit, and one of three predefined treatment changes was proposed by the investigator within 7–15 days: INT= MDI intensification, CSII= switch to continuous insulin infusion, or ER= educational reinforcement with no change in insulin regimen and a 4-month follow-up visit (M4) was scheduled.

Results: A total of 229 children (12.2±3.5 years old) were recruited by 74 pediatricians; 12.8% had a history of SH, 22.2% had recurrent hypoglycemia. Baseline HbA1c was 8.7±1.5% (>7.5% in 82.8%). Overall, 139 (79.4%), 19 (10.9%), and 17 patients (9.7%) were, respectively, included in the INT, CSII, and ER subgroups. At M4, the global incidence of SH and recurrent hypoglycemia dropped (3.4% vs. 12.8% and 6.0% vs. 22.2%, respectively) as well as the incidence of ketoacidosis (2.1% vs. 8.1%) or ketosis (6.9% vs. 11.4%). The HbA1c decrease was significant overall and in the INT subgroup (adjusted difference -0.29%, p=0.009). The satisfaction rate was ≥93.0% among children.

Conclusion: In a real-life setting, a 1-week RT-CGM can promote treatment optimization in youths with uncontrolled T1D resulting mostly in less acute events. CGM acceptance may improve with new-generation sensors.

Key words: type 1 diabetes, continuous glucose monitoring (CGM), multiple daily injections (MDI), continuous subcutaneous insulin infusion (CSII), pediatrics, hypogl

1. Introduction

Most of the cases of type 1 diabetes (T1D) are diagnosed in children and adolescents. T1D management in children has unique characteristics, as food intake and physical activity are quite unpredictable in toddlers while hormonal changes in growing children may alter insulin sensitivity and diabetes management. Although insulin analogs, insulin pumps, and insulin bolus calculators have been helpful with these issues, optimal glucose control often remains very difficult to achieve in youths. Nevertheless, chronic hyperglycemia can ultimately lead to micro- and macrovascular complications [1] as well as to cognitive impairment [2] and there is also concern about the long-term consequences of hypoglycemia and mostly severe hypoglycemia (SH). In fact, when SH events occur before the age of 6 years, subtle changes in cognitive performances can be observed at young adult age [3].

Adequate glucose control can be reached in children with T1D with either multiple daily insulin injections (MDI) or continuous subcutaneous insulin infusion (CSII), which usually leads to better glucose control, as was reported in the SWEET registry (16,570 children worldwide) [4] in which 44.4% of the children were treated with CSII. In France, CSII cost is entirely covered by the national health insurance. However, some patients or their family remain reluctant to use CSII treatment. Pump rejection has been reported in young patients for mainly social/psychological reasons, while pump discontinuation was associated with previous poor glucose control [5].

It was clearly shown in adults that the use of long-term real-time continuous glucose monitoring (RT-CGM) helps to identify glucose profiles and results in HbA1c lowering, improvement in glucose variability, and reduction in the incidence of hypoglycemia events. Unlike in adults, early trials using CGM, such as the JDRF study, failed to show a benefit of RT-CGM in children or teens [6]. However, only 30% (in the 15–24-year-old group) to 50% (in the 8–14-year-old group) of the young patients from the JDRF study used the sensor more than 6 days per week, whereas it was shown that CGM efficacy is clearly related to adherence

[7]. This points out the difficulty of wearing a glucose sensor on a long-term basis in youths even with the newest devices: in the T1D Exchange Registry, 26% of the 18–25-year-olds were CGM users compared with 40–48% in the older age groups [8]. Nevertheless, the effect of CGM in a pediatric population can be the same as in an adult population provided the wearing of the sensor is long enough, as was shown in the SWITCH study (mean wearing of the sensor: 80% of the time, 73% in youths) [9].

The role of short-term diagnostic CGM in helping patients to optimize their insulin regimen has not been examined in a large dedicated study. Only two studies reported some treatment changes [10] or treatment intensification [11] after a short-term CGM course in children. One study reported the effect of advice on bolus timing / use of active insulin after a 3-day masked CGM course in youths [12]. Thus, we designed the DIACCOR Study, which was a national multicenter study aiming to look in real-life conditions at the impact of short-term (7-day) RT-CGM on the insulin treatment strategy and more specifically on the decision for either MDI intensification or switching from MDI to CSII or educational reinforcement. Since the pediatric population differs from adults, with the parents being very much involved in therapeutic decisions and with a strong interaction between the family and the pediatrician, we designed a specific pediatric study and report the results here.

2. Patients and Methods

2.1.Design of the study

DIACCOR was a French multicenter longitudinal observational study including an adult study [13] and the present pediatric study. Investigators were diabetes-specialized pediatricians and were selected out of a national list of physicians with experience in the use of CSII and CGM, whatever their practice (university hospital or non-university hospital). Pediatricians who accepted to participate enrolled the first three consecutive patients (up to 10

patients) who fulfilled inclusion criteria. Enrolment was competitive up to 150 patients (three to 10 per center) over 8 months and each patient was followed up for 4 months.

2.2.Inclusion and exclusion criteria

Patients ≤ 18 years old could be included if they had uncontrolled type 1 diabetes defined by either an HbA1c value >7.5% and/or a history of SH more than once per year and/or recurrent (>4 per week) documented hypoglycemia (<60 mg/dl) events. SH definition was the one used by the ISPAD. Since any type of hypoglycemia in a child requires assistance, SH in children was defined by the loss of consciousness or the presence of seizures. Diabetes had to be treated with insulin injections (at least twice daily) and patients and their parents had to agree to using a 7-day CGM; they had to be able to fill out a satisfaction questionnaire. Exclusion criteria included patients on CSII, current participation in a clinical trial, and patients who could not complete a 7-day CGM.

2.3.Visits

No specific visit was necessary for the study: Patients were followed up as usual and data were recorded at the study-inclusion visit (M0) and at the follow-up visit 4 months later (M4). Patients (and their parents) agreed to insert a sensor at both M0 and M4. Sensors used were either Enlite® sensors (with a Medtronic pump as monitor) or Dexcom G4® sensors (with an Animas pump as monitor) according to the physician's decision. A nurse employed by VitalAire France, a homecare provider, instructed the family on sensor use (insertion, calibration, display interpretation including trends) and was in charge of potential technical issues, as we previously reported [14]. There was no alarm setting. The patients and their parents also filled out a satisfaction questionnaire both at M0 and M4 either in the waiting room or at home right after the visit; questionnaires were returned with a prepaid envelope. An additional visit (M+), 7–15 days after M0 and the first CGM period, could be planned to

interpret data and change the treatment for one of three predefined choices according to the pediatrician, the youth, and the parents' shared decision.

2.4.Treatment change

A decision to change treatment was based on several items according to the investigator's evaluation. Eleven main items were given to the investigators to help them identify issues in CGM data. These items were subsequently summarized into five pre-specified categories: hyperglycemia, asymptomatic nocturnal hypoglycemia, glucose variability (including succession of hyperglycemia/hypoglycemia and Somogyi effect), inadequate insulin dosing, and dawn phenomenon. After the baseline CGM, treatment decision was made "in real-life conditions" with the youth and his/her parents, and the patients were included in one of the three predefined subgroups: (a) the INT subgroup was MDI intensification including increases in insulin dosing and/or in the number of daily injections and/or carbohydrate counting initiation or reinforcement; (b) the CSII subgroup included patients who switched to CSII; (c)in the ER subgroup, only educational reinforcement was performed including diet modifications, recommendations for the prevention and correction of hypoglycemia, changes in bolus timing, and intensification of blood glucose monitoring without any change in the insulin regimen. The decision of the inclusion in one of the subgroups was based on the youth's, his/her parents', and the pediatrician's shared decision.

2.5.Funding of the study

The promotor of the study was VitalAire France, which did not have any role in data interpretation. Logistical issues were managed by GECEM, a contract research organization. For each patient, at least one of the parents gave informed consent and was given an information letter. The study did not change the physician–patient relationship as all the included patients fulfilled French recommendations for diagnostic CGM and no specific treatment change occurred. The usual real-life treatment decision was simply given the

predefined term of “INT” or “CSII” or “ER” decision. Therefore, there was no need to sign a written consent form. The agreement of the CCTIRS and of the CNIL (agencies for the security and confidentiality of data management) was obtained (Number DR-2014-338).

2.6. Statistical analysis

Population sets for this study were total population with all included patients and per protocol population including patients with available baseline CGM data. Statistical analyses were conducted using SAS® software, version 9.1 (SAS Institute, Cary NC, USA). Unless otherwise specified, results are expressed for quantitative data as means ± SD; missing data were excluded. Percentages were determined using the number of responses as the denominators. For the determination of the HbA1c development between inclusion and follow-up visit according to treatment strategy, an analysis of covariance model (ANCOVA) was used allowing for adjustment of initial HbA1c values between the groups. The probability of type 1 error (α) was set at 0.05.

3. Results

3.1. Population of the study

A total of 229 children and adolescents were included in the study by 74 physicians from September 2014 to October 2015. Clinical data were available for 211 patients (92.1%) and the initial CGM was performed on 183 patients (79.9%) (Figure 1). The therapeutic decision was available for 175 patients (76.4%). Demographic characteristics are shown in Table 1. Age ranged from 3 to 18 years. Comorbidities were present in 18 children, the most frequent being autoimmune thyroiditis (*n*=8) and asthma (*n*=3). Among the participating children, seven (3.8%) were in preschool, 48 (26.4%) in elementary school, 76 (41.8%) in junior high school, 42 (23.1%) in high school, and nine (4.9%) in other situations (apprentice or special school).

Among the 110 children (60.1%) who practiced sport outside of school, 70 (38.3%) spent more than 2 h per week in physical activity and 43 (23.5%) were involved in competitions. The mean HbA1c value at study inclusion was 8.7% ± 1.5%; 82.8% of the children had an HbA1c level >7.5%. Among the children, 12.8% had experienced SH events during the 6 months before study inclusion and 22.2% had recurrent mild hypoglycemia. Diabetic ketoacidosis (DKA) and isolated ketosis had occurred in 8.1% and 11.4%, respectively, of the patients in the previous 6 months.

At M0, diabetes treatment included 3.7 ± 1.0 daily times of injection; 158 children (85.8%) had at least three daily times of injections, 16 (9.1%) counted carbohydrates and 64 (35.0%) occasionally used additional rapid insulin injections. The daily frequency of self-monitoring of blood glucose (SMBG) was 4.3 ± 1.6 with almost 72% of the children testing four times or more per day. Only two patients did not use insulin pens but syringes for injections and all but nine patients (4.9%) used a long-acting analogue as basal insulin.

3.2.CGM data

Sensors were either Enlite® sensors in 62.1% of the children or Dexcom G4® sensors in 37.9%. The mean duration of wearing the diagnostic sensor was 7.7 ± 2.1 days (median 7.0 days, range 1–19). Most of the patients (86.3%) had a dedicated visit (M+) to interpret the CGM data. The most frequent issue revealed by the CGM among the 11 suggested items was postprandial hyperglycemia that was found in 62.8% of the patients (Table 2). When the five prespecified items were considered, hyperglycemia was present in 82.2% of the children, inadequate insulin dosing in 63.9%, asymptomatic nocturnal hypoglycemia in 23.3%, glucose variability in 21.7%, and dawn phenomenon was detected in 18.9% of the patients.

3.3.Treatment strategy after CGM

The therapeutic decision was available for 175 patients, but full data were available only for 168 patients. Changes in insulin doses or regimen were proposed to 158 patients (94.0%).

Among them, 139 patients (82.7%) were included in the INT subgroup and 19 patients (11.3%) in the CSII subgroup. Intensification of the insulin regimen in patients on MDI consisted mainly in additional daily injections (≥4 daily in 91.4%) and carbohydrate counting was implemented/reinforced in 11.7% of them. Educational reinforcement without change in insulin regimen occurred in 10 children (6.0%) (ER subgroup).

The therapeutic decisions according to baseline characteristics and CGM data in the three predefined groups are shown in Table 3 and Table 4, respectively. SH or recurrent hypoglycemia history appeared to be more frequent in the CSII subgroup (61.1%) compared with the INT subgroup (30.5%) or ER subgroup (23.6%). The decision for CSII initiation was taken mostly in the presence of chronic hyperglycemia (72%), glucose variability (44.4%), and inadequate insulin dosing (38.9%). The frequency of practicing four or more SMBG tests per day at M0 appeared higher in the 19 children for whom CSII was initiated compared with the 139 children with MDI intensification and the 17 children with no change (83.3%, 71.4%, and 62.5%, respectively). CSII was initiated less often in children who were physically active outside of school (31.6% vs. 68.4%) and a switch to CSII occurred in only one child out of the 70 children physically active more than 2 h per week outside of school.

3.4.Follow-up at 4 months

Among the 183 patients who had the initial CGM, 145 (79.2%) had an M4 visit and 142 (77.6%) a second CGM. M4 was done 161.8 ± 76.2 days after M0 (median: 140 days). During this period, 14 unscheduled hospitalizations occurred in 13 patients, eight times for diabetes-related events (two ketoacidosis, two hypoglycemia, four uncontrolled diabetes). At M4, a dramatic decrease in asymptomatic nocturnal hypoglycemia was observed (11.1% vs. 23.3% at M0) while the frequency of nocturnal hyperglycemia slightly increased (43.6% vs. 37.8%) (Table 2). Compared with the 6 months before study inclusion, there was a dramatic drop in the percentage of children experiencing SH (3.4% vs. 12.8%) or frequent mild

hypoglycemia (6.0% vs. 22.2%) between M0 and M4. The same trend was observed for the percentage of children who experienced DKA and mild ketosis (2.1% vs. 8.1% and 6.9% vs. 11.4%, respectively).

The mean HbA1c level decreased from 8.7 ± 1.5% at M0 to 8.4 ± 1.4% at M4 (p<0.001). After adjustment to baseline HbA1c values in the INT subgroup (8.7 ± 1.4%), CSII subgroup (8.6 ± 2.0%), and ER subgroup (8.4 ± 1.2%), we found that the HbA1c reduction was significant in the INT subgroup (-0.29%, p=0.009), but not in the CSII or the ER subgroups (-0.48% and -0.42%, p=0.10 and p=0.24, respectively).

Children were satisfied or very satisfied with wearing the sensor, with 93.0%, 100%, and 100% of satisfaction expressed by the children of the INT, CSII, and ER subgroups, respectively. Furthermore, 54.5%, 54.5%, and 50.0% of the children (and 35.1%, 25.0%, and 16.7% of their parents, respectively) from the INT, CSII, and ER subgroups, respectively, wished they could wear a sensor on a long-term basis.

4. Discussion

While the usefulness of sensor-augmented MDI therapy has been widely demonstrated in T1D, specific issues exist in the pediatric population with potential negative effects of CGM [15]. Interferences of CGM on the quality of life could be a cause for the poor adherence of sensor wear in youth that has been consistently reported. Since adherence is necessary for CGM success, this could be the reason why most of the studies could not show CGM benefits in youths. Nevertheless, the impact on children with uncontrolled T1D on MDI, their parents, and the pediatrician of short-term diagnostic RT-CGM in decision-making had not been considered before this study.

At inclusion in the study, the HbA1c value was consistent with other pediatric studies. In theT1D Exchange Clinic Registry [16], the mean HbA1c value at enrollment (2010–2012)

was 8.3% for 6–12-year-old children and 8.7% for 13–17-year-old teens (*n*=4,061 and 3,213, respectively). The mean HbA1c value in our population aged 12.2 ± 3.5 years seems comparatively slightly higher (8.7% ± 1.5%), but we selected the children. One specificity of our study is that we selected children with SH and/or uncontrolled diabetes and this translates into SH and DKA reports at M0 (12.8% and 8.1%, respectively) much higher than those in the T1D Exchange Clinic Registry (2–5% in different age groups and 3%, respectively). This selection in diagnostic CGM indication, combined with an "issue guide" provided to the investigator for issue identification, probably played a role in decision-making on the basis of data analysis by the specialist.

The first CGM led to changes in all of the children who were accordingly allocated to one of the three predefined groups. Overall, 82.7% of the youths were allocated to the MDI intensification group (even if most of them injected at least three times daily at M0) that included the implementation/intensification of carbohydrate counting. RT-CGM probably provided a lot more information about glucose patterns to the pediatricians and to the families compared with self-monitoring of blood glucose. Asymptomatic NH was quite frequent at M0 (23.3%), while Ahmet et al. [17] reported an even higher prevalence of 52% asymptomatic NH in children using CGM when using the same glucose threshold. A more than 50% drop in asymptomatic NH occurred between M0 and M4, whereas, simultaneously, there was an increase in nocturnal hyperglycemia of about "only" 15%. This suggests that parents and children learned from the CGM data analysis and probably reduced most often the dose of basal insulin in adequate proportions in children on MDI, while this was considered by the pediatrician in the basal rate setting for children included in the CSII subgroup.

The numbers of children in the CSII and ER subgroups were too small to allow for comparisons per subgroups. This is also probably the reason why the adjusted drops in

HbA1c in the CSII and ER subgroups (-0.48% and -0.42%, respectively) were not significant while the decrease in the MDI subgroup (-0.29%) was highly significant (p=0.009).

The trend in the ER subgroup, in the absence of major change in the treatment, suggests that an issue such as abnormal eating behavior [18] and/or overcorrection of hypoglycemia and/or inappropriate bolus timing was identified with the short-term CGM sequence and fixed with educational reinforcement.

One of the main reasons for changing treatment was the succession of hyper- and hypoglycemia. Glycemic variability could play an important role in the development of complications in T1D and it appears to be more frequent in youths [19]. It was shown that sensor-augmented pump (SAP) therapy improved glucose variability in children compared with MDI [20]. A 1-month CGM use could be helpful in decreasing glucose variability and improving endothelial function [21]. In our study, pediatricians observed a slight decrease in the prevalence of glucose variability on the second CGM compared with the first one. It is impossible to conclude that glucose variability was improved by the 1e-week CGM, but it could have helped. Glucose variability was one of the main reasons that was put forward for switching patients to CSII.

CSII was initiated in 19 patients (10.9%) after the first CGM. CSII was shown to improve glucose variability (with a similar HbA1c level) and treatment satisfaction in young patients in transition from pediatric to adult care [22]. Furthermore, families who participated in clinical studies evaluating MDI versus CSII usually chose to continue with CSII after the study was completed even when no benefit could be shown with CSII [23]. SAP therapy was also shown to be more effective than sensor-augmented MDI therapy in children in terms of both glucose mean values and glucose variability. Interestingly, only one of the very active youths (>2 h per week of physical activity outside of school) had CSII initiation although the adaptation of the insulin dose with a pump was shown to improve post-exercise glucose

control after moderate-to-vigorous exercise in children [24]. Binek et al. [25] reported that "difficulties in doing sport" is given as a motive for pump discontinuation in 70% of the children who quit CSII. It is likely that frequent physical activity is one of the reasons for CSII refusal and this should be systematically discussed with the youth and the family.

Regarding sensor wear, it appears that children and teens had very high degrees of satisfaction with CGM. It is probable that most often, parents were worried about this new technology and even if no alarms were set in this study, it was reported that, often, parents have negative emotions against CGM with sleep disturbances, although they recognize the role of CGM in glucose control improvement [26]. Things could change with new generations of sensors featuring improved accuracy and no need for confirmatory SMBG [27], such as the FreeStyle Libre® that has been positively rated by both children (boys and girls) ≥4 years old and their parents [28].

There are limitations to our study. This was a real-life study and thus there was no control group. Furthermore, even if HbA1c variation could be statistically evaluated after adjustment to the baseline value, the difference between the 6-month retrospective frequency of SH or recurrent mild hypoglycemia or ketosis and the 4-month prospective incidence of these issues between M0 and M4 did not allow for any statistical comparison. Finally, the patients included in this study might not reflect all T1D children on MDI as almost three fourths of them had a daily SMBG frequency of ≥4 and they were, moreover, followed up by specialists with experience in both CSII and CGM. Nevertheless, these patients were consecutive patients followed up by pediatricians in different settings and real-life conditions.

This study confirms the two mains indications of retrospective CGM as defined in the French position statement [29]: HbA1c levels above target and patients unaware of—or suspected of—having frequent/severe hypoglycemia. Miscellaneous indications also include brittle diabetes, help with determining carbohydrate counting parameters, and physical activity. It

was also shown that retrospective CGM helps in deciding changes in treatment and results in improvement during subsequent CGM recordings [30]. Our study suggests that for the few T1D children and/or parents who refuse to use a sensor on a long-term basis, a short-term use could be very beneficial.

5. Conclusion

This is the first real-life large study including children with uncontrolled T1D showing that diagnostic RT-CGM helps with treatment strategy by identifying control issues such as glucose variability and by giving tips for diabetes management and insulin treatment intensification. Diagnostic CGM induced changes in treatment and sometimes in CSII initiation. HbA1c improved significantly with MDI intensification and these trends were observed in the few children who switched to CSII or even those without major changes in treatment but with educational reinforcement. Overall, the incidence of SH and DKA dropped dramatically. The indications for diagnostic RT-CGM are not the same as for continuous CGM, but it could help youths who do not want to wear permanent CGM.

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Appendix: The Pediatric DIACCOR Study Group.

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Table 1: Demographic parameters at study inclusion
Unless otherwise specified, values are expressed as mean ± SD

	Total population (*n*=211)	**Per protocol population (*n*=183)**
Male/female, %	55.2 / 44.8	58.8 / 43.2
Age (years)	12.2 ± 3.5	12.3 ± 3.4
Duration of diabetes (years)	4.82 ± 3.58	4.76 ± 3.49
Weight (kg)	47.6 ± 16.6	48.5 ± 16.2
Height (cm)	150.6 ± 21.0	151.6 ± 20.8
HbA1c, % ≤ 7.5% / > 7.5% ; %	8.7 ± 1.5 17.2 / 82.8	8.7 ± 1.5 16.5/ 83.5
Daily SMBG tests < 4 daily / ≥4 daily, %		4.3 ± 1.6 28.2 / 71.8
At least 1 comorbidity, %	8.5	8.7
DKA during the previous 6 months, Yes, %	8.1	8.7
Isolated ketosis during the previous 6 months, Yes, %	11.4	10.9
SH during the previous 6 months, Yes, %	12.8	12.6
>4 documented mild hypoglycemia episodes per week, Yes, %	22.2	22.5

SMBG: self-monitoring of blood glucose, DKA: diabetic ketoacidosis, SH: severe hypoglycemia

Table 2: Results of the inclusion (M0) and 4-month follow-up (M4) CGM data analysis.

Data are expressed as the percentage of patients for whom the parameter was reported by the investigator in the CGM data analysis

	M0	**M4**
Postprandial hyperglycemia	62.8	56.4
Elevated 24-h mean glucose value	50.0	48.7
Inadequate prandial bolus	48.9	41.9
Nocturnal hyperglycemia	37.8	43.6
Asymptomatic nocturnal hypoglycemia	23.3	11.1
Succession of “hypers” and “hypos”	19.4	17.9
Dawn phenomenon	18.9	15.4
Preprandial hyperglycemia	18.3	17.1
Missed injections	15.6	18.8
Too short action of basal insulin	13.9	8.5
Inadequate dosing for exercise	8.3	6.0
Others	15.6	14.5

CGM: continuous glucose monitoring.

Table 3: Treatment management according to baseline characteristics

	MDI intensification (n=139)	CSII initiation (*n*=19)	Educational reinforcement (*n*= 17)
HbA1c (*n*=168)			
<7.0% (*n*=8)	7 (5.3%)	1 (5.6%)	0
7.0-8.0% (*n*=48)	33 (24.9%)	8 (44.4%)	7 (41.2%)
>8.0% (*n*=112)	93 (69.8%)	9 (50.0%)	10 (58.8%)
SH history (*n*=175)			
Yes (*n*=23)	14 (10.1%)	6 (31.6%)	3 (17.6%)
No (*n*=152)	125 (89.9%)	13 (68.4%)	14 (82.4%)
>4 mild hypo/week (*n*=163)			
Yes (*n*=37)	28 (21.5%)	6 (37.5%)	3 (17.6%)
No (*n*=126)	102 (78.5%)	10 (62.5%)	14 (82.4%)
SH OR >4 mild hypo/week (*n*=55)	40 (30.5%)	11 (61.1%)	4 (23.6%)
No SH AND ≤ 4 mild hypo/week (*n*=111)	91 (69.5%)	7 (38.9%)	13 (76.4%)

CSII: continuous subcutaneous insulin infusion; SH: severe hypoglycemia, NH: nocturnal hypoglycemia; hypo: hypoglycemia

Table 4: Treatment management according to CGM findings

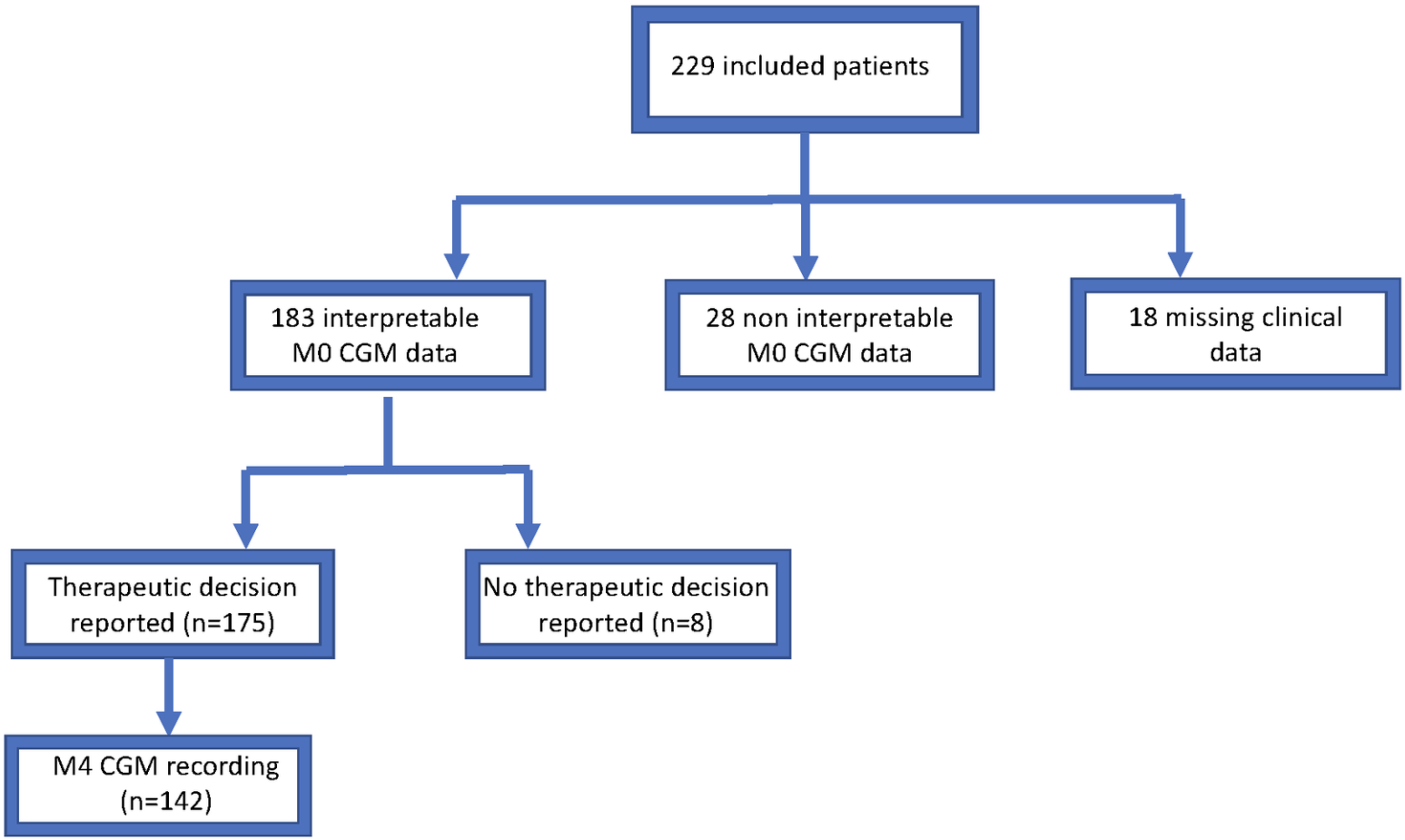
	MDI intensification (*n*=139)	CSII initiation (*n*=19)	Educational reinforcement (*n*= 17)
Hyperglycemia			
Yes (*n*=144)	120 (86.9%)	13 (72.2%)	11 (64.7%)
No (*n*=29)	18 (13.1%)	5 (27.8%)	6 (35.3%)
Nocturnal recurrent “hyper”			
Yes (*n*=66)	54 (39.1%)	7 (38.9%)	5 (29.4%)
No (*n*=107)	84 (60.9%)	11 (61.1%)	12 (70.6%)
Asymptomatic NH			
Yes (*n*=41)	33 (23.9%)	4 (22.2%)	4 (23.6%)
No (*n*=132)	105 (76.1%)	14 (77.8%)	13 (76.4%)
Glucose variability including Somogyi effect			
Yes (*n*=39)	27 (19.6%)	8 (44.4%)	4 (23.6%)
No (*n*=134)	111 (80.4%)	10 (55.6%)	13 (76.4%)
Inadequate insulin dosing			
Yes (*n*=112)	96 (69.6%)	7 (38.9%)	9 (52.9%)
No (*n*=61)	42 (30.4%)	11 (61.1%)	8 (47.1%)
Dawn phenomenon			
Yes (*n*=32)	26 (18.8%)	3 (16.7%)	3 (17.6%)
No (*n*=141)	112 (81.2%)	15 (83.3%)	14 (82.4%)

CSII: continuous subcutaneous insulin infusion; SH: severe hypoglycemia; NH: nocturnal hypoglycemia; hyper: hyperglycemia; hypo: hypoglycemia

Figure 1: Pediatric DIACCOR patient flow chart

CGM: Continuous Glucose Monitoring

M0: Inclusion, M4: 4 months


229 included patients
183 interpretable M0 CGM data
28 non interpretable M0 CGM data
18 missing clinical data
Therapeutic decision reported (n=175)
No therapeutic decision reported (n=8)
M4 CGM recording (n=142)