Glycemic Outcome Associated With Insulin Pump and Glucose Sensor Use in Children and Adolescents With Type 1 Diabetes: Data From the International Pediatric Registry SWEET

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OBJECTIVE

Insulin delivery methods, glucose-monitoring modalities, and related outcomes were examined in a large, international, diverse cohort of children and adolescents with type 1 diabetes from the Better Control in Pediatric and Adolescent Diabetes: Working to Create Centers of Reference (SWEET) registry.

RESEARCH DESIGN AND METHODS

Participants with type 1 diabetes of ≥1 year duration, aged ≤18 years, and who had documented pump or sensor usage during the period August 2017–July 2019 were stratified into four categories: injections–no sensor (reference); injections + sensor; pump–no sensor; and pump + sensor. HbA_{1c} and proportion of patients with diabetic ketoacidosis (DKA) or severe hypoglycemia (SH) were analyzed; linear and logistic regression models adjusted for demographics, region, and gross domestic product per capita were applied.

RESULTS

Data of 25,654 participants were analyzed. The proportions of participants (adjusted HbA_{1c} data) by study group were as follows: injections–no sensor group, 37.44% (8.72%; 95% CI 8.68–8.75); injections + sensor group, 14.98% (8.30%; 95% CI 8.25–8.35); pump–no sensor group, 17.22% (8.07%; 95% CI 8.03–8.12); and pump + sensor group, 30.35% (7.81%; 95% CI 7.77–7.84). HbA_{1c} was lower in all categories of participants who used a pump and/or sensor compared with the injections–no sensor treatment method ($P < 0.001$). The proportion of DKA episodes was lower in participants in the pump + sensor (1.98%; 95% CI 1.64–2.48; $P < 0.001$) and the pump–no sensor (2.02%; 95% CI 1.64–2.48; $P < 0.05$) groups when compared with those in the injections–no sensor group (2.91%; 95% CI 2.59–3.31). The proportion of participants experiencing SH was lower in pump–no sensor group (1.10%; 95% CI 0.85–1.43; $P < 0.001$) but higher in the injections + sensor group (4.25%; 95% CI 3.65–4.95; $P < 0.001$) compared with the injections–no sensor group (2.35%; 95% CI 2.04–2.71).

CONCLUSIONS

Lower HbA_{1c} and fewer DKA episodes were observed in participants using either a pump or continuous glucose monitoring (CGM) or both. Pump use was associated with a lower rate of SH. Across SWEET centers, use of pumps and CGM is increasing. The concomitant use of pump and CGM was associated with an additive benefit.

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**A full list of contributing centers for the SWEET Study Group can be found in the supplementary material online.*

The Diabetes Control and Complications Trial (DCCT) established the importance of attaining optimal glycemic control in participants with type 1 diabetes to delay and potentially avoid long-term diabetes complications (1). Advances in pharmacology with newer insulin analogs and technology, including insulin delivery via pump and continuous glucose monitoring (CGM), offer greater options and flexibility for diabetes management. Improved therapies to manage diabetes are increasingly being used to achieve hemoglobin A_{1c} (HbA_{1c}) targets and also to avoid acute complications of severe hypoglycemia (SH) and diabetic ketoacidosis (DKA). Selection of treatment modality may depend on clinical indications, patient personal preferences, variable costs, or reimbursement models.

Although the efficacy and safety of different insulin analogs, pumps, and sensors have been established in clinical trials and meta-analyses (2–5), data from different registry-based studies have shown that only a minority of youths are able to achieve the recommended HbA_{1c} targets despite the increasing use of such technology (6–8). Data from the T1D Exchange registry in the U.S. suggest that the concomitant use of pumps and sensors may have an additive beneficial effect on HbA_{1c} levels respective to when they are used separately, both in adult and pediatric populations (7). This contrasts with findings from a prospective, real-world, single-center, 3-year study suggesting that glycemic outcomes in adults are more influenced by the use of CGM than by the insulin-delivery method (9).

In pediatric populations, use of pumps and CGM vary across health care delivery contexts internationally, and substantial differences have been observed in HbA_{1c} outcomes. In some countries these outcomes are well established (10,11). Insulin delivery method and CGM use varies widely depending on the geographic area and especially the characteristics of the different health care systems. Accordingly, the evaluation of clinical outcomes and treatment modalities in international multicenter registries is essential to determine the impact of diabetes technology on the achievement of glycemic targets and the occurrence of SH and DKA worldwide. In this study, we examined the association between different treatment modalities and clinical outcomes in a large, diverse, international cohort of children and adolescents with type 1 diabetes from the Better Control in Pediatric and Adolescent Diabetes: Working to Create Centers of Reference (SWEET) registry.

RESEARCH DESIGN AND METHODS

SWEET is a multinational network of centers providing care for children, adolescents, and young adults with diabetes. Its mission is to harmonize diabetes care to optimize clinical outcomes and thereby establish standards of care in pediatric diabetes worldwide (12). The centers participating in the SWEET registry submit a set of standardized data to the Institute of Epidemiology and Medical Biometry, Ulm University, in Ulm, Germany, biannually either through the Diabetes Patienten Verlaufskodocumentation (DPV)-for-SWEET software (https://sweet.zibmt.uni-ulm.de/software.php) developed at Ulm University, from national registries, or through local clinical electronic health records. Data plausibility is validated by the team at Ulm University; if inconsistent or missing data are present, a request for correction is sent to the corresponding submitting center. All contributing centers fulfill current regulatory data protection security and ethics compliance. SWEET centers are present in five geographic hubs: Europe, Asia/Middle East/Africa, Australia/New Zealand, North America, and South America.

As of October 2019, the SWEET database contained information on 66,421 participants from 101 centers worldwide. For the final analysis of this study, 25,654 participants with type 1 diabetes who were aged $\leq$18 years and had diabetes duration $\geq$1 year with documented pump or sensor status during August 2017–July 2019 were included (Fig. 1). For each participant, data were aggregated for the 2-year observation period.

Age, sex, diabetes duration, age at diabetes onset, number of self-monitoring blood glucose (SMBG) tests, total daily insulin dose per kilogram of body weight, type of insulin administration (pump or injections), type of glucose monitoring (CGM: yes/no), HbA_{1c}, number of SH episodes, and number of hospitalizations due to DKA were documented in the SWEET database. Each participant was assigned to their corresponding geographic SWEET region, gross domestic product (GDP)-per-capita, and GDP–health expenditure-per-capita of the corresponding country. GDP-per-capita data were based on World Bank data indicators from 2018 (13) and expressed in current U.S. dollars; GDP health expenditure was based on data from 2016 (14) and also expressed in current U.S. dollars. In addition, centers were grouped in clusters according to health system similarities, geographic area, and reimbursement policies.

HbA_{1c} was measured locally and standardized to the DCCT reference of 20–42 mmol/mol (4%–6%) (1,15). Participants were defined as insulin pump or CGM users when they were using the respective device at least at one visit during the observation period. Both real-time CGM and intermittent CGM were considered within the CGM category. SH and DKA were defined according to International Society of Pediatric and Adolescent Diabetes (ISPAD) Clinical Consensus Guidelines (16,17) and expressed in proportion of episodes during the entire observation period.

Participants were categorized into four groups depending on the insulin delivery method and the use of CGM: *1*) injections–no sensor; *2*) injections + sensor; *3*) pump–no sensor; and *4*) pump + sensor. For the participants in the pump + sensor category, the proportion of participants using a sensor-augmented pump was also estimated. The category sensor-augmented pump was defined as any pump that integrates CGM data and incorporates any kind of automation, such as insulin suspension on low, before low, or hybrid closed loop. Because of the small sample of participants in this group, no additional analysis was performed. Use of each category was analyzed according to the following age groups: <5 years, 5–10 years, and 10–18 years.

For each of the four categories, mean HbA_{1c} and the proportion of participants achieving both the former ISPAD HbA_{1c} target of <7.5% (<58 mmol/mol) (18) and the current ISPAD HbA_{1c} target of <7.0% (<53 mmol/mol) (19) was calculated. The percentages of SH and DKA episodes (percentage of participants

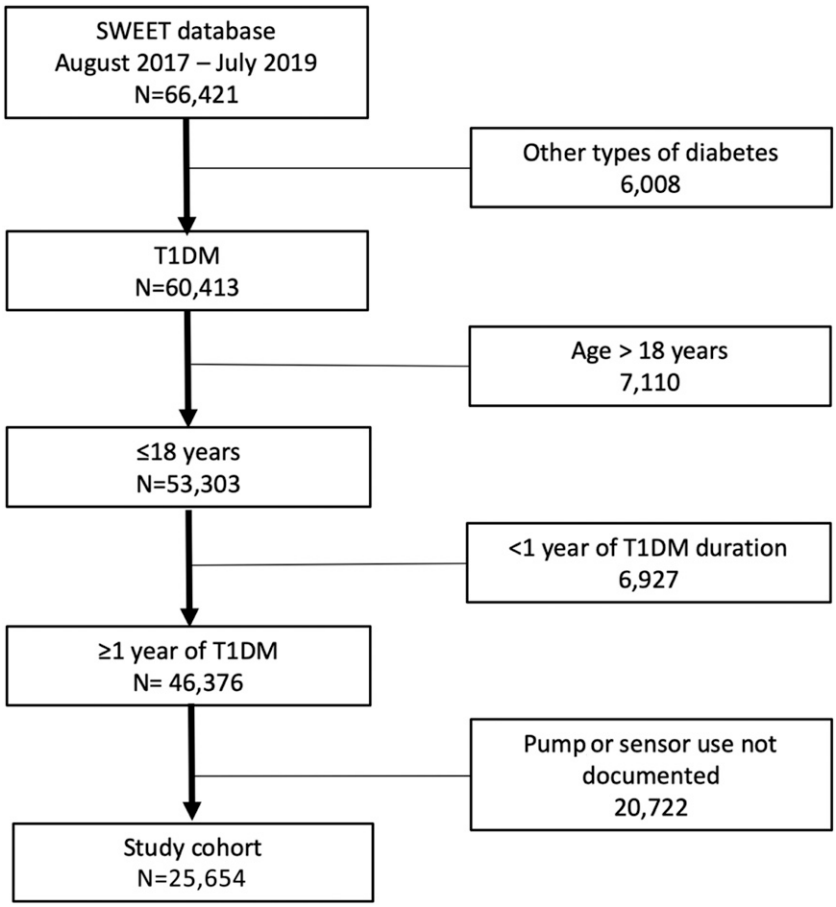

Figure 1—Flowchart for selection of the study population from the SWEET registry. T1DM, type 1 diabetes mellitus.

having one episode of DKA or SH during the 2-year aggregated period) were determined for each treatment category. HbA_{1c} and percentages of DKA and SH episodes were calculated for participants in different age groups: <12 years, 12–16 years, and >16 years.

Statistical Analysis

Continuous variables were described as median, quartile 1 (Q1) and quartile 3 (Q3). Categorical variables were presented as percentages. The Kruskal-Wallis test was used to compare continuous variables and χ^2 test to compare binary variables. To adjust for multiple testing, *P* values were corrected by the Bonferroni-Holm method. To examine the potential differences, the injections–no sensor group was used as the reference for establishing comparisons. HbA_{1c} (continuous variable) and proportion of SH and DKA episodes (binary variable) were adjusted, respectively, using linear and logistic regression models. The following models were applied: model 1 was adjusted for age at onset, sex, and diabetes duration. Model 2 was additionally adjusted for region to account for variations among regions. Model 3 was adjusted for demographics and GDP per capita. In model 4, demographics and GDP health expenditure per capita data were used. In addition, an adjusted sex-specific comparisons regression model for HbA_{1c} <7.0% (<53 mmol/mol), proportion of DKA episodes, and proportion of SH episodes between the reference group and the rest of the treatment modality categories was used.

Results were presented as means with 95% CIs. To adjust for multiple group comparisons, Turkey-Kramer test was used. Two-sided *P* values <0.05 were defined as statistically significant. All analyses were performed with SAS, version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Unadjusted Results

The final study population comprised 25,654 people with type 1 diabetes from 101 centers participating in the pediatric diabetes network SWEET (median age, 13.80 [Q1; Q3: 10.60; 16.40] years; males, 51.41%; diabetes duration, 5.18 [Q1; Q3: 2.99; 8.25] years). The distribution of treatment modality was as follows: injections–no sensor, 37.44%; injections + sensor, 14.98%; pump–no sensor, 17.22%; and pump + sensor 30.35%. Among those participants using a pump + sensor, 8.0% were using a sensor-augmented pump.

The pump + sensor modality was the most frequently used in the age group <5 years. For the age groups 5–9.9 years and 10–18 years, the most frequently used modality was injections–no sensor, followed by pump + sensor. For all age groups, the injections + sensor modality was the least common except for the age group 10–18 years, in which it was the pump–no sensor modality (Fig. 2).

Demographic features across treatment modality groups are described in Table 1. Across these groups, significant differences were observed in sex, age, age at diabetes onset, diabetes duration, number of SMBG tests, insulin requirements, GDP per capita, health investment on GDP per capita, and region distribution ($P < 0.001$).

The distribution of study population origins was as follows: Europe (50%), North America (26%), Asia/Middle East/Asia (15%), Australia/New Zealand (6%), and South America (3%). The use of different treatment modalities varied across centers and regions. Grouping the countries on the basis of similar health care systems showed differences in the distribution of different treatment modalities (Supplementary Table 1). The GDP per capita and health investment on GDP for participants using technology components (i.e., pump with or without sensor and injections + sensor) were higher than for those using injections–no sensor.

In the whole cohort, 37% of participants attained HbA_{1c} <7.5% (58 mmol/mol) and 21% achieved HbA_{1c} <7.0% (53 mmol/mol). The proportion of

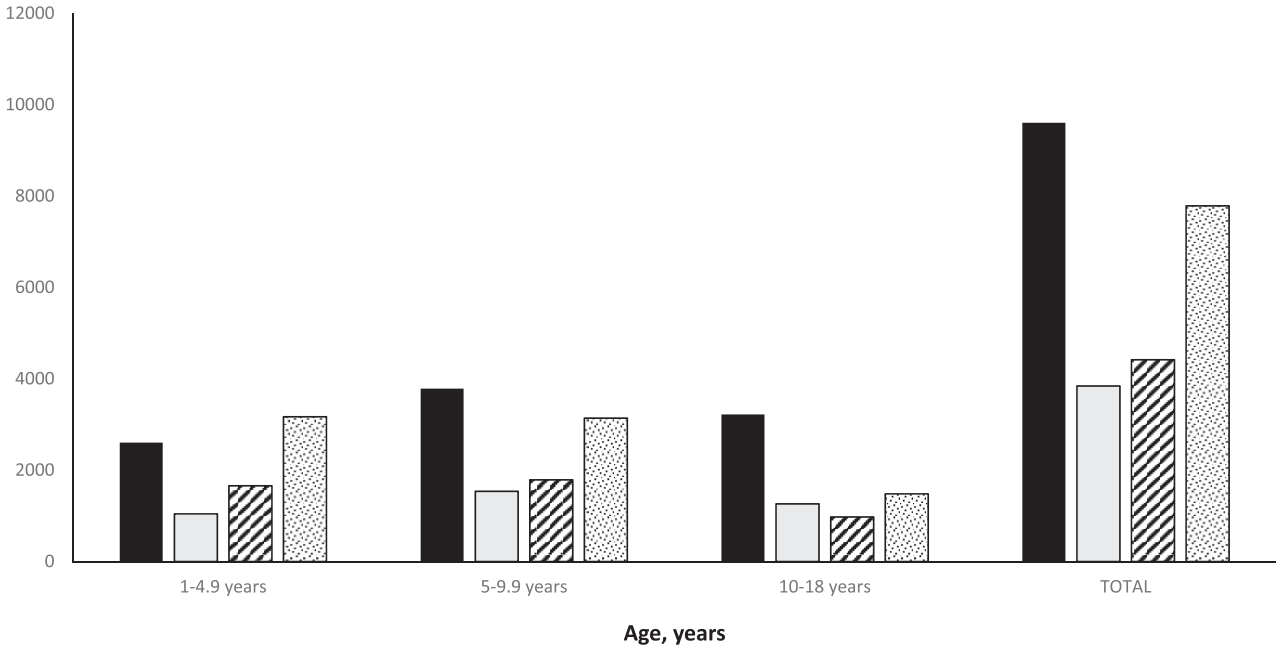

Figure 2—The distribution of treatment modality by age group. Each bar represents a treatment modality. Black bars denote injection-no sensor group; light grey bars denote injection+sensor group; striped bars denote pump-no sensor group; white bars with dots represent pump+sensor group. Data are number of patients.

participants achieving both targets was significantly higher in those groups using technology. The HbA_{1c} target <7.5% (<58 mmol/mol) was achieved by 44% of participants aged <12 years, 34% of those aged 12–16 years, and 31% of those aged >16 years. The HbA_{1c} target <7.0% (<53 mmol/mol) was achieved by 27% of participants aged <12 years, 20% of those aged 12–16 years, and 18% of participants >16 years.

Differences among participants with technology components and the reference group for unadjusted values of HbA_{1c}, DKA, and SH episodes were found when the participants were stratified by age groups (Supplementary Table 2).

Adjusted Results

The results for linear and logistic regression analyses are shown in Table 2. Adjusted for demographics (model 1), HbA_{1c} was significantly lower for all treatment modality groups when compared with the reference group. Even after adjustment for demographics and region (model 2); demographics, region, and GDP per capita (model 3); and demographics, region, and GDP–health per capita (model 4), similar results were found.

The proportion of DKA episodes was significantly lower only in participants using a pump (with or without sensor) when compared with the reference group (Table 2), although the significance varied across the different models. The proportion of SH episodes was significantly lower only in the pump–no sensor group, compared with the reference group. The proportion of SH events was significantly higher in the injections + sensor group. No differences were found in terms of SH between the with pump + sensor group and the injections–no sensor group. These results did not vary after adjusting for the different models.

Sex-Specific Analyses

Odds ratios (ORs) for the proportions of DKA hospitalizations, SH episodes, and participants with HbA_{1c} <7.0% (<53 mmol/mol) were calculated for boys and girls separately in subsequent comparisons between the reference group and the rest of treatment modalities (Supplementary Fig. 1). The ORs of boys and girls were similar for all three comparisons with the reference, except for the proportion of participants with HbA_{1c} <7.0% (<53 mmol/mol) in the pump–no sensor group (Supplementary Fig. 1*B*) and in the pump + sensor group (Supplementary Fig. 1*C*), where the ORs were higher for girls.

CONCLUSIONS

This study comprised a large, diverse, international cohort of children and adolescents with type 1 diabetes and demonstrated that the management of type 1 diabetes has diversified, and the use of insulin pumps and CGM is increasing. Although the most frequently used combination during the study was still injections and SBGM, our study shows that >60% of participants were using at least one technological component for diabetes management (CGM or pump). Those using a pump and CGM concomitantly were observed to be more likely to achieve glycemic targets.

The increasing use of technology is consistent with data described by other registry-based studies. We report 48% of all participants younger than 18 years used insulin pumps, compared with 44% reported in a 2016 SWEET study (20). The DPV registry recently reported that Germany and Austria have pump therapy rates of 39% in participants younger than 20 years, with a net increase of 52% occurring during the period 1995–2017 (21). Scandinavian registries show a higher use of pumps (22,23), whereas lower uptake has been observed in the England and Wales registry (24) and in Ireland (25).

Our study showed 45% of participants used CGM. This proportion is

Table 1—Demographics across treatment modality groups (unadjusted results)

	Total no.	Injections–no sensor (reference group; $n = 9,606$)	Injections + sensor group ($n = 3843$)	Pump–no sensor group ($n = 4418$)	Pump + sensor group ($n = 7787$)
Male sex (%)	25,654	51.37	54.49	49.82	50.78
Age, years	25,654	14.10 (10.80; 16.60)	13.70 (10.50; 16.30)	14.50 (11.40; 17.00)	13.10 (9.90; 15.80)
Age at onset, years	25,654	7.90 (4.60; 11.00)	7.90 (4.70; 11.00)	6.30 (3.50; 9.50)	6.00 (3.30; 9.20)
Diabetes duration, years	25,654	4.61 (2.60; 7.51)	4.25 (2.42; 7.28)	6.59 (3.98; 9.66)	5.58 (3.41; 8.62)
SMBG, number/day	22,073	4.00 (2.00; 5.00)	3.80 (2.00; 5.00)	5.05 (4.00; 7.14)	4.10 (2.50; 6.00)
Daily insulin dose, units/kg	23,684	0.90 (0.70; 1.00)	0.84 (0.66; 1.01)	0.82 (0.68; 0.97)	0.80 (0.67; 0.95)
GDP per capita, USD	25,654	15,424 (3,238; 42,491)	41,966 (23,146; 57,305)	46,211 (23,079; 60,726)	54,112 (34,318; 62,641)
Health investment on GDP per capita, USD	25,654	696 (80; 3,274)	3,274 (1,195; 3,992)	3,274 (918; 4,862)	3,534 (2,034; 8,078)
Region (%)					
Europe	12,840	39	59	68	48
Asia/Middle East/Africa	3,890	36	5	4	1
Australia/New Zealand	1,646	3	10	3	10
North America	6,590	15	25	24	40
South America	688	7	1	1	1
HbA_{1c} <58 mmol/mol (<7.5%), (%)	25,253	26.32	39.68*	45.78*	44.11*
HbA_{1c} <53 mmol/mol (<7%), (%)	25,253	14.58	24.08*	27.89*	26.47*
Participants <12 years age with HbA_{1c} <58 mmol/mol (<7.5%), (%)	8,811	28.59	46.17*	58.80*	54.17*
Participants <12 years old with HbA_{1c} <53 mmol/mol (<7%), (%)	8,811	15.26	29.88*	38.56*	33.66*
Participants 12–16 years old with HbA_{1c} <58 mmol/mol (<7.5%), (%)	8,901	24.96	36.12*	44.70*	39.09*
Participants 12–16 years old with HbA_{1c} <53 mmol/mol (<7%), (%)	8,901	14.25	20.96*	25.93*	23.04*
Participants >16 years old with HbA_{1c} <58 mmol/mol (<7.5%), (%)	7,541	25.36	35.82*	36.03*	33.82*
Participants >16 years old with HbA_{1c} <53 mmol/mol (<7%), (%)	7,541	14.25	20.99*	21.04*	19.49*

Data are given as median with quartiles (Q1; Q3) unless otherwise stated. Binary variables are expressed as percentages. *Significantly different from the reference group at $P < 0.001$.

slightly higher than 2017 data reported by the T1D Exchange registry (26) and significantly higher than reported by DPV registry (21). We note that the period of the studies (2017–2019) coincided with increasing access to and reimbursement for CGM in European countries, especially in the pediatric population. In a previous SWEET study (27), we reported that the vast majority of European countries had recently started CGM reimbursement, contrasting with Sweden and Slovenia, where CGM has been reimbursed for more than a decade. In parallel, the reimbursement of intermittent scanning CGM rose substantially during the period 2017–2019 across Europe, where funding for this technology became available in >30 countries. The U.S. has also increased CGM use in the pediatric population with improved insurance coverage (26,28). In the present study, we did not distinguish between the type of CGM (i.e., real-time or intermittent scanning CGM), but we speculate that the increase in CGM use among European centers is based primarily on a growing use of intermittent scanning CGM, whereas in North America, it is based on real-time CGM.

The majority of participants using a pump, with or without CGM, were affiliated with European or North American centers included in the SWEET database, whereas those using injections alone without CGM were more often located in Europe and Asia/Middle East/Africa centers. Interestingly, when we grouped countries on the basis of similarities in health care systems, we observed differences in the use of treatment modalities, with a higher

Table 2—HbA_{1c} linear regression model and DKA and SH logistic models

	Injections–no sensor (reference group)	Injections + sensor group	Pump–no sensor group	Pump + sensor group
HbA_{1c} by model				
1				
HbA_{1c} (mmol/mol)	72.7 (72.4–73.1)	65.3 (64.7–65.9)**	62.8 (62.3–63.3)**	62.6 (62.2–63.0)**
HbA_{1c} (%)	8.80 (8.77–8.84)	8.12 (8.07–8.18)	7.89 (7.84–7.94)	7.88 (7.84–7.91)
2				
HbA_{1c} (mmol/mol)	71.6 (71.2–72.1)	66.7 (66.1–67.2)**	65.1 (64.6–65.6)**	62.1 (61.8–62.5)**
HbA_{1c} (%)	8.69 (8.66–8.69)	8.25 (8.20–8.30)	8.10 (8.06–8.15)	7.83 (7.80–7.87)
3				
HbA_{1c} (mmol/mol)	71.9 (71.5–72.3)	67.1 (66.5–67.6)**	64.8 (64.3–65.3)**	61.7 (61.3–62.1)**
HbA_{1c} (%)	8.73 (8.69–8.76)	8.29 (8.24–8.34)	8.08 (8.03–8.12)	7.80 (7.76–7.83)
4				
HbA_{1c} (mmol/mol)	71.8 (71.4–72.2)	67.2 (66.7–67.8)**	64.7 (64.2–65.2)**	61.8 (61.4–62.2)**
HbA_{1c} (%)	8.72 (8.68–8.75)	8.30 (8.25–8.35)	8.07 (8.03–8.12)	7.81 (7.77–7.84)
DKA by model (%)				
1	3.49 (3.14–3.69)	3.09 (2.59–3.69)	2.05 (1.68–2.50)**	2.67 (2.33–3.05)*
2	2.89 (2.54–3.29)	2.87 (2.54–3.29)	2.08 (1.69–2.55)*	2.08 (1.79–2.42)**
3	2.92 (2.58–3.35)	2.84 (2.36–3.42)	2.03 (1.65–2.50)*	1.99 (1.70–2.32)**
4	2.91 (2.59–3.31)	2.87 (2.34–3.45)	2.02 (1.64–2.48)*	1.98 (1.64–2.48)**
SH by model (%)				
1	2.19 (1.91–2.50)	4.78 (4.15–5.52)**	1.18 (1.12–1.53)**	2.56 (2.23–2.93)
2	2.37 (2.06–2.73)	4.58 (3.95–5.31)**	1.13 (0.97–1.47)**	2.31 (2.00–2.68)
3	2.22 (1.92–2.56)	4.06 (3.48–4.73)**	1.11 (0.86–1.45)**	2.24 (1.93–2.60)
4	2.35 (2.04–2.71)	4.25 (3.65–4.95)**	1.10 (0.85–1.43)**	2.17 (1.86–2.52)

Linear regression model was applied for HbA_{1c} and logistic models were used for DKA and SH. Adjusted means with 95% CIs are shown for linear models. Logistic model estimates with 95% CIs: model 1 was adjusted for demographics (sex, age at onset, and diabetes duration); model 2 was adjusted for demographics and region; model 3 was adjusted for demographics, region, and GDP per capita; and model 4 was adjusted for demographics, region, and health investment on GDP per capita. *Significantly different from the reference group at $P < 0.05$. **Significantly different from the reference group at $P < 0.01$.

proportion of concomitant use of pump and CGM in participants belonging to centers in the U.S., Australia/Canada/New Zealand and Northern Europe/Slovenia. It is noteworthy that treatment modality distribution varied between the Southern/Eastern Europe and Northern Europe/Slovenia centers, with a greater use of pumps, with or without sensor, in participants in Northern Europe/Slovenia and a higher proportion of injections and CGM use in participants in the Southern/Eastern Europe group. Among participants in Asia/Middle East/Africa and South America, most used insulin injections without CGM. This reflects that access to diabetes device technology is likely related to more favorable reimbursement policies (27–30) and how robust the economy is in these countries. Nevertheless, SWEET is a network of reference centers and perhaps these data may not reflect, accordingly, the reality of pump and CGM access in each country.

We noted the treatment modality varied across the different age groups. In those younger than 5 years, the most frequently used modality was the concomitant use of pump and sensor. This may be related to the hypoglycemia vulnerability in younger children and the care burden experienced by parents and caregivers in the day-to-day management of diabetes (31). Such management is consistent with current recommendations of ISPAD (32). Interestingly, among those children aged 5–18 years, the concomitant use of pump and sensor was the second most used treatment modality after the injections without a sensor. To our knowledge, this observation has not yet been described and highlights that diabetes management is evolving, with a focus on technology.

The percentage of participants attaining the previous ISPAD target of HbA_{1c} <7.5% contrasts to that published in individual countries. The percentage is higher than in Wales, the U.S., England, and Norway; similar to Denmark; and lower than the percentages reported for Austria, Germany, and Sweden (33). This demonstrates the diversity of SWEET centers. This finding is consistent with a recent description of two contemporary diabetes cohorts from T1D Exchange and DPV, which showed large discrepancies in glycemic control between these registries, although the trajectories in life span of HbA_{1c} may describe a similar pattern (34). Despite the increased use of technology, in this study we observed a similar percentage of participants attaining the former ISPAD HbA_{1c} target as reported by SWEET researchers previously (35). Our study is first registry-based study, to our knowledge, to provide data describing the proportion of participants attaining the current ISPAD target <7.0%. As anticipated, participants younger than 12 years had higher rates of achieving both former and current ISPAD HbA_{1c} targets than did participants aged 12–16 years and those older than 16 years.

Furthermore, we found that the group with more technology components (i.e., who used injections with sensor and a pump with or without sensor) had the lowest HbA_{1c} when compared with the group using no technology (i.e., injections–no sensor). Those differences persisted when the

participants were categorized by age groups. Interestingly, our finding that HbA_{1c} in the group of pump–no sensor was slightly lower than in those in the injection + sensor group, suggests a greater impact of the pump on HbA_{1c} as compared with the CGM in this cohort. This is in contrast to observations from 2018 by DeSalvo et al. (11), who described in a registry-based study that participants using injections and a sensor had lower HbA_{1c} than participants using a pump and SMBG tests. In a recent prospective clinical trial (9), researchers found that injections and sensor modality may be equivalent to sensor-augmented pumps and superior to the pump and SBGM modality. In many countries, CGM is more accessible than pumps. This may confound results because pump treatment might be selectively used for candidates more likely to achieve better results. Nevertheless, the pump effect on the lower HbA_{1c} should be interpreted with caution. HbA_{1c} alone does not reflect glycemic excursions or time spent in hypoglycemia. Those using CGM may have reduced hypoglycemia frequency, which may result in a higher HbA_{1c}.

Some studies have found that socioeconomic background, minority status, and parental level of education may influence not only the access but also the outcomes of pump and CGM users (36–37). In our study, we were unable to account for those variables, but the adjustment of the HbA_{1c} variable by economic in-country parameters, GDP, and GDP per capita showed no differences with respect to the unadjusted analyses.

Hospitalizations due to DKA were less frequent in pump users, independent of sensor use. In a previous multinational, registry-based study with a large number of pediatric participants, pump use was not significantly associated with DKA (39). A more recent study from the T1D Exchange registry found that pump use was associated with a lower rate of DKA (7). Our results are also aligned with contemporary observations that in participants using pump therapy, the proportion of hospitalizations due to DKA is lower than for those whose diabetes is managed with multiple daily injections (40). These findings differ from first follow-up studies focused on pump therapy that described a higher risk of DKA with this treatment modality (41). The inclusion of structured education programs and a tailored selection of the best candidates for pump therapy may explain the change (42). The effect of CGM on preventing DKA seems to be additive to the effect of pump therapy, with the lowest DKA rate observed in the combined pump and sensor group. The impact of CGM on DKA is currently not sufficiently described, although observational studies from the U.S. and Germany suggest fewer DKA episodes in CGM users than in nonusers (7,37) and among those with early initiation of CGM within the first year of new-onset diabetes diagnosis (43).

An unexpected finding in our study was that, when compared with the modality of injections without a sensor, only the group of pump–no sensor had a lower incidence of SH. We expected an association between CGM use and lower incidence of hypoglycemia. The association of pump therapy and lower rates of SH has been well established separately in the T1D Exchange and DPV registries (7,40). In addition, in the present study, the injection + sensor group had a considerably higher frequency of SH episodes than in the injections no–sensor group. We can hypothesize that residual confounding, either due to the 2-year period of aggregated data we assigned the treatment category on the basis of last documented visit, or preferential use of sensors in patients at risk for SH (indication bias) may explain these findings. Another potential reason for an increased incidence of SH with CGM use may relate to the user's or caregiver's ability to view changes in sensor glucose levels in real time and be alerted when the glucose levels are high or rising rapidly. For patients or families who are strongly motivated to maintain normoglycemia, especially avoiding postprandial glucose excursions, this may lead to an assertive or premature response, resulting in a potential over-bolus of insulin. In a survey-based study of adolescents, responders stated that when the CGM device showed two arrows up, they increased their correction bolus by 140% on average (44). This self-management behavior should be discussed as part of initial and ongoing quality CGM education. The absence of alerts in some CGM models also may be influencing this observation. Interestingly, we observed differences in SH episodes for the different age groups only in the injection-sensor category, with a higher proportion of SH in the 12–16 years and >16 years age groups. These results should be interpreted with caution because the number of observed events is low and results are unadjusted.

We did not observe a sex effect on clinical outcomes related to the different treatment modalities, except for a slightly higher probability of attaining HbA_{1c} <7.0% (<53 mmol/mol) among girls who used a pump (with or without sensor) compared with girls who did not use this treatment. To our knowledge, no studies on different treatment modalities related outcomes focused on sex have been performed in a pediatric population.

A limitation in our analyses is that we were not able to describe the proportion of participants within the category of pump + sensor that were using advanced features of the system (e.g., hybrid closed loop), because the sample size was inadequate to establish comparisons as a single group. This information may be underreported in the SWEET database. To our knowledge, studies performed by other registry networks have not incorporated this information either. Another study limitation was that we were unable to provide time-in-range data, because this parameter was not recorded during the study period. We recognize that the categorization of participants according to health care–based country groups, type of center, or geographic hub may present concerns because health care and reimbursement policies, although similar among several countries or centers, are not completely identical to establish unequivocal and objective clusters.

Despite these limitations, our study has several strengths. We report on the global distribution of technology based on data from a very large number of participants followed in many centers from a variety of countries around the world. In addition, the adjusted models incorporated socioeconomic parameters such as GDP and GDP health investment to decrease potential geographic bias.

In conclusion, we found that children and adolescents in SWEET centers who use a pump or/and sensor to manage

diabetes have a lower HbA_{1c} and fewer episodes of DKA. Also, pump users experience a lower rate of SH episodes. Our findings show a major evolution in technology use over the past 10 years and a progressive improvement in the attaining of glycemic targets globally.

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