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ORIGINAL ARTICLE

Continuous glucose monitoring and glycemic control among youth with type 1 diabetes: International comparison from the T1D Exchange and DPV Initiative

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Background: To assess the change in rates of pediatric real-time or intermittent scanning continuous glucose monitoring (CGM) use over the past 5 years, and how it impacts glycemic control, data from two registries were compared: the US-based type 1 diabetes Exchange Registry (T1DX) and the German/Austrian DPV (Prospective Diabetes Follow-Up Registry).

Methods: Registry participants aged <18 years with T1D duration ≥ 1 year encompassed 29 007 individuals in 2011 and 29 150 participants in 2016. Demographic data, CGM use and hemoglobin A1c (HbA1c) were obtained from medical records.

Results: CGM use increased from 2011 to 2016 in both registries across all age groups, regardless of gender, ethnic minority status or insulin delivery method. The increase in CGM use was most pronounced in the youngest patients, and usage rates remain lowest for adolescent patients in 2016. For both registries in 2016, mean HbA1c was lower among CGM users regardless of insulin delivery method compared to pump only ($P < 0.001$) and injection only ($P < 0.001$), and CGM users were more likely to achieve glycemic target of HbA1c <7.5% (56% vs 43% for DPV and 30% vs 15% for T1DX, $P < 0.001$). T1DX participants had a higher mean HbA1c compared with DPV despite whether they were CGM users or non-users; however, the difference was less pronounced in CGM users ($P < 0.001$).

Conclusions: Pediatric CGM use increased in both registries and was associated with lower mean HbA1c regardless of insulin delivery modality.

KEYWORDS

continuous glucose monitoring, longitudinal analysis, type 1 diabetes

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ABBREVIATIONS: CGM, continuous glucose monitoring; DPV, Prospective Diabetes Follow-Up Registry; HbA1c, hemoglobin A1c; T1DX, T1D Exchange Registry

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1 | INTRODUCTION

The goal of diabetes management in children and adolescents with type 1 diabetes (T1D) is to achieve tight glycemic control to prevent acute and chronic complications; however, youth often fail to meet hemoglobin A1c (HbA1c) targets.^{1,2} Growing evidence shows the benefit of continuous glucose monitoring (CGM) as a basis for improving glycemic control in those who wear the CGM device almost daily.³⁻⁵

Although the potential benefits of CGM are well known to clinicians, the actual rates of CGM device use in T1D youth in prior studies have been low. In an earlier study of the T1D Exchange Registry (T1DX), only 6% of children <13 years and 4% of adolescents 13 to <18 years were using CGM.⁶ Previously, DPV (Prospective Diabetes Follow-Up Registry) data were used to compare pump and injection users.⁷ In the DPV registry, rates of CGM use were even lower; however, reimbursement by health insurance for CGM in Germany and Austria recently started in summer of 2016. The JDRF (Juvenile Diabetes Research Foundation International) CGM randomized controlled trial published in 2008³ highlighted the challenge of CGM use in adolescents and young adults.

After 6 months, only 30% of the adolescents and young adults (15-24 years) were using CGM 6 or more days per week compared to 83% of adults aged 25 years or older. However, among those who were using CGM on a daily or near-daily basis, improvement in glycemic control was similar, independent of age group.

Over the past 10 years, the accuracy⁸ and usability of CGM devices has improved considerably, which may be accompanied by an increase in CGM use, and associated improvement in glycemic control. To assess this, we analyzed data from the US T1DX and German/Austrian DPV registries to assess the increase in CGM use over the past 5 years, compare current CGM use between registries, and compare glycemic control (HbA1c %) between current CGM users and non-users.

2 | METHODS

We analyzed T1DX Registry and DPV Initiative participants aged <18 years with T1D duration ≥ 1 year in 2011 and again in 2016. This encompassed 29 007 individuals in 2011 ($N = 11 608$ from T1DX and $N = 17 399$ from DPV) and 29 150 participants in 2016 ($N = 8186$ from

TABLE 1 Participant characteristics and diabetes management data in 2011 vs 2016 for each registry

	DPV		P-value	T1DX		P-value
	2011 (N = 17 399)	2016 (N = 20 964)		2011 (N = 11 608)	2016 (N = 8186)	
Gender (male)	52%	52%	0.6	51%	52%	0.4
Age (y), mean \pm SD	12 \pm 4	12 \pm 4	<0.001	12 \pm 4	13 \pm 4	<0.001
<6	6%	5%		6%	5%	
6 to <13	34%	32%		46%	37%	
13 to <18	60%	64%		48%	58%	
Duration of diabetes (y), mean \pm SD	5 \pm 3	5 \pm 3	<0.001	5 \pm 4	7 \pm 4	<0.001
HbA1c, % (mmol/mol), mean \pm SD	7.9 \pm 1.4 (63 \pm 15)	7.8 \pm 1.3 (62 \pm 14)	<0.001	8.5 \pm 1.5 (70 \pm 16)	8.8 \pm 1.6 (72 \pm 18)	<0.001
Percentage of subjects with HbA1c <7.5% (<58 mmol/mol)	43%	46%	<0.001	22%	19%	<0.001
Ethnic minority status	20%	23%	<0.001	22%	22%	0.8
Pump use	43%	56%	<0.001	56%	64%	<0.001
Overall CGM use	4%	19%	<0.001	3%	22%	<0.001
CGM use by age (y)						
<6	6%	28%	<0.001	4%	45%	<0.001
6 to <12	4%	23%	<0.001	4%	27%	<0.001
12 to <18	3%	16%	<0.001	3%	17%	<0.001
CGM use by gender						
Male	4%	18%	<0.001	3%	21%	<0.001
Female	4%	19%	<0.001	3%	22%	<0.001
CGM use by ethnicity						
Minority status: yes	3%	14%	<0.001	2%	12%	<0.001
Minority status: no	4%	20%	<0.001	4%	25%	<0.001
CGM use by insulin delivery method						
Injections	3%	14%	<0.001	1%	9%	<0.001
Pump	5%	22%	<0.001	5%	29%	<0.001

72 T1DX sites and $N = 20\,964$ from 309 DPV sites). Demographic data, CGM use (either real-time or intermittent “flash” CGM), insulin modality (injections or insulin pump) and the most recent HbA1c value were obtained from clinic medical records. Definitions of migration background or ethnic minority status for each registry were as described previously⁹ (DPV: patient or at least one parent born outside of Austria/Germany, T1DX: any race/ethnicity other than non-Hispanic white). Sites for the DPV and T1DX are listed in S1 (Supporting Information).

Logistic and linear regression modeling were used to compare demographic and clinical characteristics in 2011 vs 2016 within each registry. Differences in CGM use between registries was assessed separately for 2011 and 2016 time points in a logistic regression model stratified by age group and adjusted for gender, minority status and diabetes duration. The interaction between CGM use and registry on mean HbA1c in 2016 was assessed in a linear regression model adjusted for age, gender, and minority status. Separate statistical tests were performed comparing T1DX vs DPV in CGM users and non-

users for each age group. The interaction between insulin delivery method and CGM use on mean HbA1c within each registry was assessed in linear regression models adjusted for age, gender and minority status. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina). All P -values are two-sided. A priori, in view of the large sample size and multiple comparisons, only P -values <0.01 were considered statistically significant.

3 | RESULTS

Demographic and clinical characteristics for both T1DX and DPV registries in 2011 vs 2016 are displayed in Table 1. In the last 5 years, CGM use increased from 4% to 19% for the DPV Initiative ($P < 0.001$) and from 3% to 22% in the T1DX Registry ($P < 0.001$). CGM use increased for all age groups in both registries, and was most pronounced in the youngest patients (1 to <6 years) with an increase from 6% to 28% for DPV and 4% to 45% for T1DX. Although CGM

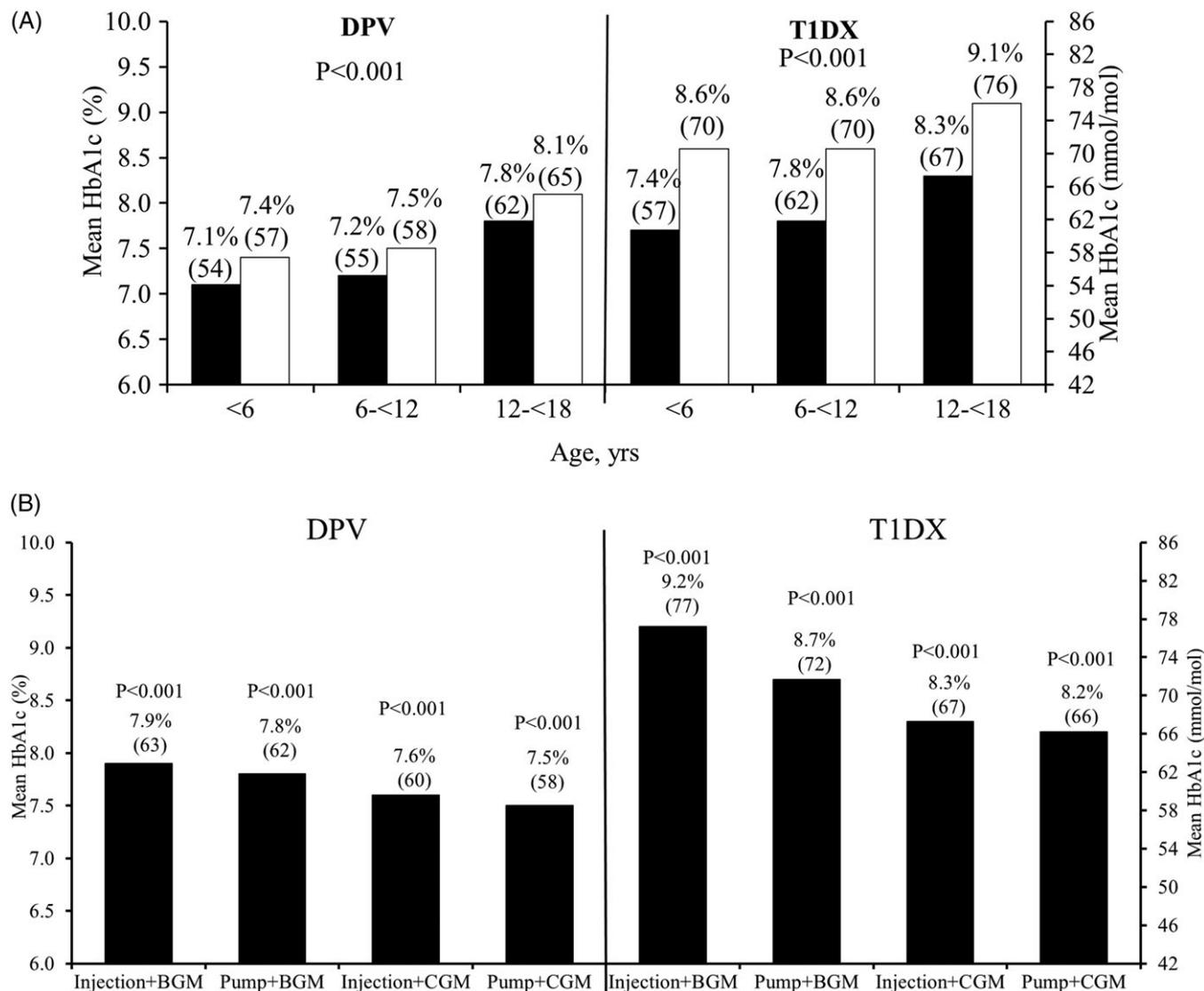


FIGURE 1 (A) Mean HbA1c in 2016 for each registry stratified by CGM use and age group. Solid black bar represents CGM users. Solid white bar represents non-CGM users. (B) Mean HbA1c by insulin delivery method and CGM use within each registry in 2016. BGM, blood glucose monitoring; CGM, continuous glucose monitoring or intermittent flash glucose monitoring. * P -values compared with the reference group of pump + CGM

use increased significantly from 2011, adolescent patients (13 to <18 years) had the lowest rates of CGM use in 2016 (DPV: 3% in 2011, 16% in 2016; T1DX: 3% in 2011, 17% in 2016). For both registries, CGM use increased from 2011 to 2016 regardless of gender or ethnic minority status, as well as for both pump and injection users. Notably, insulin pump use increased for both T1DX and DPV registries between 2011 and 2016, with usage rates exceeding 50% in DPV and 60% in T1DX in 2016.

After adjustment for gender, ethnic/minority status and diabetes duration, CGM use was similar between registries in 2011 for patients aged 1 to <6 years ($P = 0.20$) and 6 to <12 years ($P = 0.94$) with higher CGM use in T1DX compared to DPV for 12 to <18 years ($P = 0.005$). In 2016, higher CGM use was observed in T1DX compared with DPV among 1 to <6 and 6 to <13 years (both adjusted $P < 0.001$). There were no significant differences in CGM use between registries for 13 to <18-year-old age groups (adjusted $P = 0.15$).

In 2011, CGM use was not associated with a difference in HbA1c among DPV participants (7.9% vs 7.9% [63 vs 63 mmol/mol], $P = 0.55$); however, in 2016 mean HbA1c was lower in CGM users (7.6% vs 7.9% [60 vs 63 mmol/mol], $P < 0.001$). For T1DX CGM users, lower mean HbA1c compared to non-users was seen in both 2011 (7.9% vs 8.6% [63 vs 70 mmol/mol], $P < 0.001$) and 2016 (8.1% vs 9.0% [65 vs 75 mmol/mol], $P < 0.001$).

Mean HbA1c in DPV vs T1DX according to CGM use and age group for the more recent 2016 data is shown in Figure 1. T1DX participants had a higher mean HbA1c compared with DPV despite whether they were CGM users or non-users. However, the difference between mean HbA1c in DPV vs T1DX was less pronounced in CGM users ($P < 0.001$) (Figure 1). In 2016, mean HbA1c was lower among CGM users regardless of insulin delivery method compared to pump only ($P < 0.001$) and injection only ($P < 0.001$) in both T1DX and DPV registries (Figure 1B). Additionally, CGM users were more likely to achieve glycemic targets (HbA1c < 7.5% [<58 mmol/mol]) for both DPV (56% vs 43%, $P < 0.001$) and T1DX (30% vs 15%, $P < 0.001$) registries in 2016.

4 | DISCUSSION

Utilization of CGM in pediatric T1D management provides opportunity to improve glycemic control if consistent CGM use can be achieved in this population. In this study, CGM use was associated with lower mean HbA1c across all ages and regardless of insulin delivery modality for both registries. Additionally, a higher percentage of CGM users compared to non-users achieved a glycemic target of <7.5% (<58 mmol/mol) in both registries. The cross-sectional nature of our study does not preclude the possibility that those with lower HbA1c were more likely to initiate CGM; however, our findings align with results from controlled trials showing improved glycemic control with CGM use compared to SMBG only.³⁻⁵ Other limitations to our study include: data on CGM brand and consistency of use by patients were not available, and we did not differentiate between real-time CGM vs flash glucose monitoring in this analysis. Additionally, the difference in ethnic minority

definitions between the DPV and T1DX Registries limits the ability to compare across continents.

Improvement in CGM technology over the last 10 years, as well as growing evidence for clinical efficacy of CGM, has been associated with increased CGM use in both the DPV Initiative and T1DX Registry. Increased rates of CGM use were evident across all age ranges, but especially in the youngest children where CGM usage rates increased dramatically. As penetrance of this technology is lowest in adolescents, a group noted to have the highest mean HbA1c; strategies to engage this cohort of youth in adoption and long-term use of CGM are needed. Additionally, reimbursement practices for CGM remains quite complex and varies across countries, states, regions and insurance companies, so advocacy efforts for insurance coverage are needed especially in the United States where coverage by Medicaid programs varies greatly across states.

A majority of pediatric patients are now utilizing insulin pumps for diabetes management in both DPV and T1DX registries in 2016. CGM use has increased over the last 5 years, still less than half of pediatric patients are utilizing these devices. This is especially concerning in light of the challenges in achieving glycemic targets (HbA1c < 7.5% [<58 mmol/mol]) in pediatrics. Further analysis is needed to determine the reasons for low frequency of CGM use including whether reimbursement or cost of CGM may be a barrier to use. Robust clinical protocols, quality improvement and research efforts to optimize real-time CGM use are essential to ensuring durability of CGM use, facilitating automation of insulin delivery and improving glycemic outcomes.⁹

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Conflict of interest

D.J.D. is funded by the Helmsley Charitable Trust and has consulted for Dexcom and Insulet. K.M.M. and J.M.H. have no conflict of interest to report. D.M.M. is funded by the NIH (including 1P30DK116074), JDRF, NSF, and the Helmsley Charitable Trust. He is on an advisory board for Insulet, has consulted for Abbott Diabetes Care and the Helmsley Charitable Trust, and his institution has received research support or materials from Medtronic, Dexcom, Insulet, Bigfoot Biomedical, Type Zero, and Roche. S.E.H. has no conflict of interest to report. M.A.C. is funded by the NIH (including 1R01DK100779, 1DP3DK108211, 1R21HD081502, 1U01DK106984, and 1UG1HD090849), Helmsley Charitable Trust, and Jaeb Center for Health Research. He is on an advisory board for Glooko and Aegle Palette, has consulted for Eli Lilly and Medtronic, and his institution has received material support for research from Abbott Diabetes Care. E.L., J.L.S. and R.W.H. have no conflict of interest to report.

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Author contributions

D.J.D. researched data and wrote/edited the manuscript. J.M.H. researched data, performed statistical analyses and wrote/edited the manuscript. K.M.M., D.M.M., S.H.E., M.A.C., E.L., J.L.S., M.T. and R.W.H. researched data, contributed to data interpretation, and reviewed/edited the manuscript. All authors reviewed and approved the final version of the manuscript. R.W.H. is the guarantor of this work.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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