Diabetes Ther (2023) 14:593–610
https://doi.org/10.1007/s13300-023-01366-9

ORIGINAL RESEARCH

Improvements in Glycemic Outcomes in 4738 Children, Adolescents, and Adults with Type 1 Diabetes Initiating a Tubeless Insulin Management System

Grazia Aleppo · Daniel J. DeSalvo · Felipe Lauand · Lauren M. Huyett · Albert Chang · Todd Vienneau · Trang T. Ly

Received: September 28, 2022 / Accepted: January 9, 2023 / Published online: February 10, 2023

ABSTRACT

Introduction: Despite recent advances in diabetes technology, most people living with type 1 diabetes mellitus (T1D) are unable to meet glycemic targets. Real-world evidence can provide insight into outcomes achieved with specific treatment devices when used in clinical practice. The aim of this study was to analyze real-world outcomes collected from a large cohort of people living with T1D and initiating treatment with the Omnipod DASH System.

Methods: In this retrospective observational study, real-world outcomes were analyzed from a database of information collected from people with T1D initiating the Omnipod DASH System. Information in the database was either taken directly from the patient's medical record or self-reported if medical records were unavailable. The primary outcome was change in glycated hemoglobin (HbA1c) from baseline (before initiation) to 3 months after initiation. Secondary outcomes were changes in total daily dose of insulin (TDD) and self-reported frequency of hypoglycemic events (< 70 mg/dL). Results are separated for the adult (≥ 18 years, $N = 3341$) and pediatric (< 18 years, $N = 1397$) cohorts.

Results: The change in HbA1c from baseline was $-0.9 \pm 1.6\%$ (-10 ± 18 mmol/mol; $p < 0.0001$) in adults and $-0.9 \pm 2.0\%$ (-10 ± 22 mmol/mol; $p < 0.0001$) in the pediatric cohort. For those previously using multiple daily injections, HbA1c decreased by $-1.0 \pm 1.7\%$ (-11 ± 19 mmol/mol) in adults and $-1.0 \pm 2.1\%$ (-11 ± 23 mmol/mol) in the pediatric cohort (both $p < 0.0001$). Hypoglycemic events decreased in adults from 2.9 to 1.3 episodes per week (-1.6 ± 3.2 events/week; $p < 0.0001$), and in the pediatric cohort from 2.8 to 1.5 episodes per week (-1.3 ± 2.7 events/week; $p < 0.0001$). In adults, TDD decreased by 19.9% ($p < 0.0001$), and it remained stable in the pediatric cohort ($p > 0.05$).

Conclusions: Real-world outcomes from this large cohort of people initiating therapy with the Omnipod DASH System showed significant

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13300-023-01366-9.

G. Aleppo
Division of Endocrinology, Metabolism and Molecular Medicine, Feinberg School of Medicine, Northwestern University, 645 North Michigan Ave, Suite 530, Chicago, IL 60611, USA

D. J. DeSalvo
Baylor College of Medicine, 1 Moursund St., Houston, TX 77030, USA

F. Lauand · L. M. Huyett (✉) · A. Chang · T. Vienneau · T. T. Ly
Insulet Corporation, 100 Nagog Park, Acton, MA 01720, USA
e-mail: lhuyett@insulet.com

improvement in HbA1c and a substantial reduction in hypoglycemic events after 3 months of use.

Keywords: CSII; HbA1c; Insulin pumps; Insulin therapy; Real-world outcomes; Type 1 diabetes

Key Summary Points

Why carry out this study?
The Omnipod DASH Insulin Management System, a tubeless insulin pump, was first cleared in the United States by the FDA in 2018, and has since become available in multiple additional countries; yet, there are no published data available on the clinical outcomes achieved with this system.
The aim of the present study was to address this gap in evidence by analyzing real-world outcomes of a large group of people living with type 1 diabetes mellitus and initiating treatment with the Omnipod DASH System.
What was learned from this study?
After 3 months of use of the Omnipod DASH System, HbA1c was reduced and patients reported a lower frequency of hypoglycemic events.
Total daily dose of insulin decreased among adults using the Omnipod DASH System.
Overall, these real-world outcomes provide positive evidence to support the use of Omnipod DASH as an option for people of all ages living with type 1 diabetes mellitus.

INTRODUCTION

Type 1 diabetes mellitus (T1D) affects people of all ages worldwide; in fact, its prevalence appears to be increasing [1–3]. Despite growing awareness among researchers and healthcare providers of the pressing need to improve glycemic outcomes among people with diabetes, national registry data show that most people with T1D are unable to meet the recommended consensus targets for glycated hemoglobin (HbA1c) [4]. Consequently, they may experience an increased risk for complications, deteriorations in quality of life, and increased financial burden [5–8]. Of note is the emerging body of evidence highlighting the impact of T1D on those diagnosed at a young age, including an increased risk for cardiovascular disease [9], deteriorations in neurocognitive health [10, 11], and an overall decreased life span [12]. Thus, the ability to improve glycemic outcomes is a high priority for people of all ages with T1D, underscoring the need for innovative insulin treatment modalities that can enable them to be successful in meeting their individual treatment goals throughout their lifespan.

In recent years, many new diabetes management devices have entered the market, including insulin pumps and continuous glucose monitoring systems (CGM). Insulin pump therapy is increasingly being recommended by professional societies as a treatment option for people with T1D [13–16], and, in particular, is the preferred method of insulin administration for very young children [17]. Even so, multiple daily injections (MDI) remain a commonly used therapy in the United States (US) and worldwide [4]. Although all insulin pumps ultimately perform the same function of continuous subcutaneous insulin infusion (CSII), each device has unique characteristics that may affect the user's perceptions, experience, and the outcomes achieved [18–23].

The Omnipod® Insulin Management System ('Omnipod System') and Omnipod DASH® Insulin Management System ('Omnipod DASH System,' Insulet Corp., Acton, MA) are the only full-featured insulin pumps currently available in the US that do not involve external tubing to deliver insulin [24]. Rather, these pumps are worn directly on the body, with the cannula automatically inserted just beneath the pump. The user delivers boluses and adjusts basal delivery using a wireless handheld device.

Released in 2018, the Omnipod DASH System incorporates additional unique features different from the earlier Omnipod System, including a color touchscreen handheld device, Bluetooth® communication, fractional insulin-to-carbohydrate ratios (0.1 g carb/unit (U) increments versus 1 g carb/U increments), and the option to set a basal rate of 0 U/h (e.g., for very insulin sensitive patients or those in the honeymoon phase) [25]. The Omnipod DASH also contains an optional Pod site map, which allows users to record and track current and recent Pod site locations. This can help users remember to rotate infusion sites and may be particularly useful for providing continuity in situations in which multiple caregivers in different households or other settings (e.g., grandparents, separated parents, school) are involved in a child's treatment.

Studies have shown that the earlier Omnipod System may improve glycemic outcomes in both T1D and type 2 diabetes (T2D) [26–33]; however, no study to date has presented clinical outcomes specifically for the newer Omnipod DASH System. While the insulin delivery mechanism (Pod) has not changed, some of the differing features of the Omnipod DASH System may affect how users interact with the system and how their insulin therapy is managed. Notably, the interface of the Omnipod DASH System was designed with a focus on user experience, which may enhance user interaction and persistence in using the system [34]. As Omnipod DASH will be the primary device used going forward, including through the expansion of availability in additional countries, it is crucial to understand the outcomes patients have with this specific device in the real world.

The aim of the present study was to address this gap in evidence using a large database of real-world outcomes collected from new Omnipod DASH users across the US. Outcomes were analyzed in pediatric and adult cohorts of people with T1D before (baseline) and 90 days after (follow-up) initiation of the Omnipod DASH System. It was hypothesized that HbA1c, total daily dose of insulin (TDD), and frequency of hypoglycemic events would all decrease significantly following Omnipod DASH initiation.

METHODS

Study Design

This retrospective observational study evaluated a large database of real-world outcomes, including HbA1c, TDD, and self-reported frequency of hypoglycemic events, collected between July 2018 and March 2021 from people living with T1D in the US and initiating treatment with the Omnipod DASH System. This study used the same database and methodology as a previously published analysis in people living with T2D and initiating the Omnipod and Omnipod DASH Systems [35]. The dataset was collected as part of standard procedures for training and providing ongoing support to new users by US Insulet clinical staff with certification in diabetes education (CDCES certification). Analyses were performed separately in the adult ($\geq$ 18 years (y)) and pediatric ($<$ 18 y) cohorts to consider differences in clinical characteristics and care between adults and children with T1D [36].

Outcome Measures

The primary outcome was change in HbA1c, and secondary outcomes included change in TDD and self-reported frequency of hypoglycemic events ($<$ 70 mg/dL) per week from before Omnipod DASH initiation (baseline) to 90 days post-initiation (follow-up).

Omnipod DASH Insulin Management System

The Omnipod DASH System comprises two components: a small, waterproof (IP28), adhesive insulin pump called the "Pod", which holds up to 200 U of U-100 rapid-acting insulin and is worn directly on the body for up to 72 h, and the personal diabetes manager (PDM), a smartphone-like touchscreen device used for wirelessly programming the Pod with insulin delivery instructions, delivering boluses, and monitoring Pod status [25, 34].

Study Procedures

This study was a retrospective analysis of an existing patient information dataset routinely collected by clinical service managers (CSMs) for Insulet Corporation across the US as part of standard Omnipod initiation procedures. CSMs include certified diabetes educators, registered dieticians, and registered nurses who work with and support patients, caregivers, and healthcare professionals using Omnipod.

During the initial meeting, CSMs trained patients on the use of Omnipod DASH for insulin therapy per standard practice, supported the implementation of pump settings prescribed by the healthcare provider, and collected baseline data, including demographic information, prior therapy, baseline HbA1c levels, TDD, and frequency of hypoglycemic events. These outcomes were taken directly from the patient's medical record or were self-reported if medical records were unavailable. Frequency of hypoglycemic events was typically collected based on the patient's estimate of the number of events < 70 mg/dL over the past few weeks.

As part of a standard follow-up session, CSMs called or met with patients as close to 90 days post-initiation as practical and collected updated information on each outcome, which were taken from medical records if available or otherwise were self-reported. During the COVID-19 pandemic, rises in telemedicine and decreases in safe access to clinical laboratories led to shifts in standard clinical practice across the US, with the potential for increased use of an estimated HbA1c from CGM data (Glucose Management Indicator, GMI) in place of a laboratory test [37–39]. For this reason, during the affected period (March 2020 onward), GMI may have been provided in place of a laboratory HbA1c in some cases. However, CSMs were instructed to denote this within the data record, and upon review, only 0.8% of entries in this study may have used GMI; thus, the impact on the results is expected to be minimal. All patient data collected by CSMs were entered into an encrypted, password-protected electronic database which anonymized and aggregated results.

Study Participants

Inclusion criteria were people of all ages with T1D who initiated the Omnipod DASH System and had both baseline and follow-up data on HbA1c in the database. No patients were excluded based on missing data from other fields (e.g., prior treatment modality, TDD, hypoglycemic events) to maintain a broad study population inclusive of as many users with primary outcome data as possible. The study protocol for this retrospective analysis was submitted to the Western Institutional Review Board (submission number 2623242–44579044), which granted a waiver of authorization for the use and disclosure of protected health information and granted human subjects research exemption under 45CFR§46.104(d)(4). The study protocol was in agreement with the Helsinki Declaration of 1964 and its later amendments.

Statistical Analyses

Paired *t*-tests were used to evaluate changes in HbA1c, TDD, and frequency of hypoglycemic events from baseline to 90 days after Omnipod DASH initiation, similar to previously described methods [35]. Bonferroni correction was used to account for multiple comparisons. Analyses were performed for each age cohort overall and stratified by age group (pediatric cohort: < 2, 2–5, 6–12, 13-17 y; adult cohort: 18–25, 26–49, 50–64 and ≥ 65 y), prior therapy (MDI or CSII), and baseline HbA1c range (< 6% [< 42 mmol/mol], 6% to < 7% [42 to < 53 mmol/mol], 7% to < 8% [53 to < 64 mmol/mol], 8% to < 9% [64 to < 75 mmol/mol], 9% to < 10% [75 to < 86 mmol/mol], and ≥ 10% [≥ 86 mmol/mol]). Additionally, the proportion of each cohort moving between HbA1c categories was evaluated. Pearson's chi-squared test was used to evaluate the overall difference between HbA1c range distributions at baseline and follow-up, with post-hoc binomial testing to assess significant changes for each category.

RESULTS

Baseline characteristics

Table 1 shows baseline characteristics of the study population. A total of 4738 Omnipod DASH users had HbA1c data available in the database at both baseline and follow-up: 1397 in the pediatric and 3341 in the adult cohort. Within the pediatric cohort, 78.6% switched from MDI and 9.5% from a CSII device other than Omnipod DASH (11.9% unknown). Among the adult cohort, 61.3% switched from MDI and 21.5% from a CSII device other than Omnipod DASH (17.2% unknown).

Baseline characteristics stratified into more granular age groups are shown in Supplementary Material Table S1. The study population contained representation across all age groups: within the pediatric cohort, 1.5%, 15.1%, 51.7%, and 31.7% were aged < 2y , 2–5 y, 6–12 y, and 13–17 y, respectively. Within the adult cohort, 15.7%, 46.9%, 24.1%, and 13.3% were aged 18–25 y, 26–49 y, 50–64 y, and ≥ 65 y, respectively.

Primary Outcome: HbA1c

Table 2 shows the primary outcome results overall and stratified by prior therapy and by baseline HbA1c. The change in HbA1c in the pediatric cohort was (mean ± SD) − 0.9 ± 2.0% (− 10 ± 22 mmol/mol; $p < 0.0001$), from 8.6 ± 2.1%

Table 1 Baseline characteristics

	Age < 18 years	Age ≥ 18 years	Total
N (%)	1397 (29.5)	3341 (70.5)	4738
Age (y)	10.2 ± 4.2	43.8 ± 16.4	33.9 ± 20.7
Female[a] (%)	48.3	58.8	55.7
Duration of diabetes[a] (y)	2.4 ± 2.8	16.7 ± 14.5	10.7 ± 13.2
Prior treatment, *n* (%)			
MDI (%)	1098 (78.6)	2048 (61.3)	3146 (66.4)
CSII (%)	133 (9.5)	719 (21.5)	852 (18.0)
Unknown[b]	166 (11.9)	574 (17.2)	740 (15.6)
HbA1c (%)	8.6 ± 2.1	8.5 ± 2.0	8.5 ± 2.0
HbA1c (mmol/mol)	70 ± 23	69 ± 22	69 ± 22
TDD of insulin[a] (U/d)	32.6 ± 24.4	62.3 ± 40.9	54.0 ± 39.4
Hypoglycemic events[a] (*n*/week)	2.8 ± 2.8	2.9 ± 3.4	2.9 ± 3.3

Values are mean ± SD unless otherwise indicated

[a]Due to missing data, gender was available for $n = 4737$ patients in total; duration of diabetes was available for $n = 2656$ patients in total; TDD was available for $n = 3152$ patients in total; and hypoglycemic events were available for $n = 2375$ patients in total

[b]The group with an unknown prior treatment was missing the data from their record that would allow the determination of the product used

CSII continuous subcutaneous insulin infusion, *HbA1c* glycated hemoglobin, *MDI* multiple daily injections, *TDD* total daily dose of insulin, *U* units, *y* years

Table 2 Change in HbA1c overall and stratified by prior therapy and by baseline HbA1c

	Age < 18 years					Age ≥ 18 years				
	n	Baseline HbA1c (% (mmol/mol))	Follow-up HbA1c (% (mmol/mol))	Change in HbA1c (% (mmol/mol))	*p* value[a]	*n*	Baseline HbA1c (% (mmol/mol))	Follow-up HbA1c (% (mmol/mol))	Change in HbA1c (% (mmol/mol))	*p* value[a]
Overall	1397	8.6 ± 2.1	7.7 ± 1.3	− 0.9 ± 2.0	< 0.0001	3341	8.5 ± 2.0	7.6 ± 1.3	− 0.9 ± 1.6	< 0.0001
		(70 ± 23)	(61 ± 14)	(−10 ± 22)			(69 ± 22)	(60 ± 14)	(− 10 ± 18)	
Prior therapy										
MDI	1098	8.6 ± 2.2	7.6 ± 1.3	− 1.0 ± 2.1	< 0.0001	2048	8.6 ± 2.1	7.7 ± 1.4	− 1.0 ± 1.7	< 0.0001
		(70 ± 24)	(60 ± 14)	(− 11 ± 23)			(70 ± 23)	(61 ± 15)	(− 11 ± 19)	
CSII	133	8.5 ± 1.6	8.1 ± 1.4	− 0.4 ± 1.3	> 0.05	719	8.0 ± 1.5	7.4 ± 1.1	− 0.6 ± 1.2	< 0.0001
		(69 ± 18)	(65 ± 15)	(−4 ± 14)			(64 ± 16)	(57 ± 12)	(−7 ± 13)	
Baseline HbA1c, % (mmol/mol)										
< 6	58	5.7 ± 0.3	6.1 ± 0.6	0.4 ± 0.6	0.0003	137	5.6 ± 0.3	5.8 ± 0.6	0.3 ± 0.6	0.0001
(< 42)		(39 ± 3)	(43 ± 7)	(4 ± 7)			(38 ± 3)	(40 ± 7)	(3 ± 7)	
6 to < 7	210	6.5 ± 0.3	6.8 ± 0.9	0.3 ± 0.9	0.0001	536	6.5 ± 0.3	6.6 ± 0.6	0.0 ± 0.6	> 0.05
(42 to < 53)		(48 ± 3)	(51 ± 10)	(3 ± 10)			(48 ± 3)	(49 ± 7)	(0 ± 7)	
7 to < 8	356	7.4 ± 0.3	7.4 ± 0.9	0.0 ± 0.8	> 0.05	878	7.4 ± 0.3	7.2 ± 0.7	− 0.3 ± 0.7	< 0.0001
(53 to < 64)		(57 ± 3)	(57 ± 10)	(0 ± 9)			(57 ± 3)	(55 ± 8)	(− 3 ± 8)	
8 to < 9	318	8.4 ± 0.3	7.9 ± 0.9	− 0.5 ± 0.9	< 0.0001	706	8.4 ± 0.3	7.8 ± 0.8	− 0.6 ± 0.9	< 0.0001
(64 to < 75)		(68 ± 3)	(63 ± 10)	(− 6 ± 10)			(68 ± 3)	(62 ± 9)	(− 7 ± 10)	
9 to < 10	172	9.4 ± 0.3	8.2 ± 1.1	− 1.2 ± 1.1	< 0.0001	432	9.4 ± 0.3	8.3 ± 1.0	− 1.1 ± 1.0	< 0.0001
(75 to < 86)		(79 ± 3)	(66 ± 12)	(− 13 ± 12)			(79 ± 3)	(67 ± 11)	(− 12 ± 11)	

Table 2 continued

	Age < 18 years					Age ≥ 18 years				
	n	Baseline HbA1c (% (mmol/mol))	Follow-up HbA1c (% (mmol/mol))	Change in HbA1c (% (mmol/mol))	*p* value[a]	*n*	Baseline HbA1c (% (mmol/mol))	Follow-up HbA1c (% (mmol/mol))	Change in HbA1c (% (mmol/mol))	*p* value[a]
≥ 10 (≥ 86)	283	11.9 ± 1.8 (107 ± 20)	8.4 ± 1.7 (68 ± 19)	− 3.5 ± 2.6 (− 38 ± 28)	< 0.0001	652	11.7 ± 1.6 (104 ± 18)	8.8 ± 1.7 (73 ± 19)	− 2.9 ± 2.1 (− 32 ± 23)	< 0.0001

Values are mean ± SD

[a]Significant differences between baseline and follow-up HbA1c were determined using paired *t*-tests adjusted for multiple comparisons using Bonferroni correction

CSII continuous subcutaneous insulin infusion, *HbA1c* glycated hemoglobin, *MDI* multiple daily injections

(70 ± 23 mmol/mol) at baseline to 7.7 ± 1.3% (61 ± 14 mmol/mol) at follow-up. A significant decrease in HbA1c was observed in prior MDI users (− 1.0 ± 2.1% [− 11 ± 23 mmol/mol], $n = 1098$; $p < 0.0001$) but not in the smaller group of prior CSII users (− 0.4 ± 1.3% [− 4 ± 14 mmol/mol], $n = 133$; $p > 0.05$). When stratifying by baseline HbA1c, decreases were seen in the groups with baseline HbA1c ≥ 8% (≥ 64 mmol/mol), which represents 55.3% of the cohort. Changes in HbA1c ranged from a small but significant increase of 0.4 ± 0.6% (4 ± 7 mmol/mol) in those < 6% (< 42 mmol/mol) at baseline ($p = 0.0003$) to a decrease of as much as − 3.5 ± 2.6% (− 38 ± 28 mmol/mol) in those ≥ 10% (≥ 86 mmol/mol) at baseline ($p < 0.0001$).

Within the adult cohort, the change in HbA1c was − 0.9 ± 1.6% (− 10 ± 18 mmol/mol; $p < 0.0001$), from 8.5 ± 2.0% (69 ± 22 mmol/mol) at baseline to 7.6 ± 1.3% (60 ± 14 mmol/mol) at follow-up. The decrease in HbA1c levels was − 1.0 ± 1.7% (− 11 ± 19 mmol/mol) in those previously on MDI and − 0.6 ± 1.2% (− 7 ± 13 mmol/mol) in those previously on another CSII device (both $p < 0.0001$). When stratifying by baseline HbA1c, a significant mean decrease was observed in the groups with baseline HbA1c ≥ 7% (≥ 53 mmol/mol), which represents 79.9% of the cohort. Changes in HbA1c ranged from a small but significant increase of 0.3 ± 0.6% (3 ± 7 mmol/mol) in those < 6% (< 42 mmol/mol) at baseline ($p = 0.0001$) to a decrease of as much as − 2.9 ± 2.1% (− 32 ± 23 mmol/mol) in those ≥ 10% (≥ 86 mmol/mol) at baseline ($p < 0.0001$).

Figure 1a shows results stratified into more granular age groups across the entire study population (numerical results in Supplementary Material Table S2). A significant decrease in HbA1c was seen in all groups aged 2 y and above, while the change was not significant in the small group of those aged < 2 y (− 1.0 ± 2.1% [− 11 ± 23 mmol/mol], $n = 21$; $p > 0.05$).

Supplementary Material Fig. S1 shows the percentage of the population within each HbA1c category at baseline and follow-up. In the pediatric cohort, the proportion in each of

Table 3 Change in TDD overall and stratified by prior therapy and by baseline HbA1c

	Age < 18 years						Age ≥ 18 years					
	n	Baseline TDD (U/d)	Follow-up TDD (U/d)	Change in TDD (U/d)	Change in TDD (%)	*p* value[a]	*n*	Baseline TDD (U/d)	Follow-up TDD (U/d)	Change in TDD (U/d)	Change in TDD (%)	*p* value[a]
Overall	872	32.6 ± 24.4	31.4 ± 21.7	− 1.2 ± 12.1	− 3.7	> 0.05	2280	62.3 ± 40.9	49.8 ± 30.7	− 12.4 ± 28.7	− 19.9	< 0.0001
Prior therapy												
MDI	674	30.9 ± 23.1	30.1 ± 20.6	− 0.9 ± 12.2	− 2.9	> 0.05	1430	62.8 ± 41.4	48.8 ± 27.7	− 13.9 ± 26.2	− 22.1	< 0.0001
CSII	92	40.5 ± 27.7	37.5 ± 22.7	− 3.0 ± 11.9	− 7.4	> 0.05	470	56.2 ± 37.6	49.5 ± 38.7	− 6.7 ± 36.8	− 11.9	0.015
Baseline HbA1c, % (mmol/mol)												
< 6 (< 42)	36	28.1 ± 18.8	25.5 ± 17.3	− 2.6 ± 17.6	− 9.3	> 0.05	97	43.1 ± 40.9	35.6 ± 20.8	− 7.5 ± 26.8	− 17.4	> 0.05
6 to < 7 (42 to < 53)	124	30.6 ± 19.9	30.9 ± 19.2	0.3 ± 11.8	+ 1.0	> 0.05	375	52.9 ± 34.0	44.0 ± 23.5	− 8.9 ± 21.4	− 16.8	< 0.0001
7 to < 8 (53 to < 64)	213	32.3 ± 23.6	30.5 ± 19.7	− 1.8 ± 11.2	− 5.6	> 0.05	608	57.2 ± 31.6	47.8 ± 34.9	− 9.4 ± 31.5	− 16.4	< 0.0001
8 to < 9 (64 to < 75)	210	31.6 ± 23.7	30.5 ± 22.2	− 1.1 ± 10.3	− 3.5	> 0.05	476	65.1 ± 40.6	52.7 ± 30.8	− 12.5 ± 21.1	− 19.2	< 0.0001
9 to < 10 (75 to < 86)	105	32.3 ± 27.3	31.2 ± 22.9	− 1.1 ± 13.1	− 3.4	> 0.05	284	73.3 ± 44.8	56.1 ± 30.5	− 17.2 ± 30.8	− 23.5	< 0.0001
≥ 10 (≥ 86)	184	36.3 ± 27.8	35.1 ± 24.7	− 1.2 ± 13.2	− 3.3	> 0.05	440	71.3 ± 50.0	53.7 ± 29.9	− 17.6 ± 34.6	− 24.7	< 0.0001

Values are mean ± SD

[a]Significant differences between baseline and follow-up TDD were determined using paired *t*-tests adjusted for multiple comparisons using Bonferroni correction

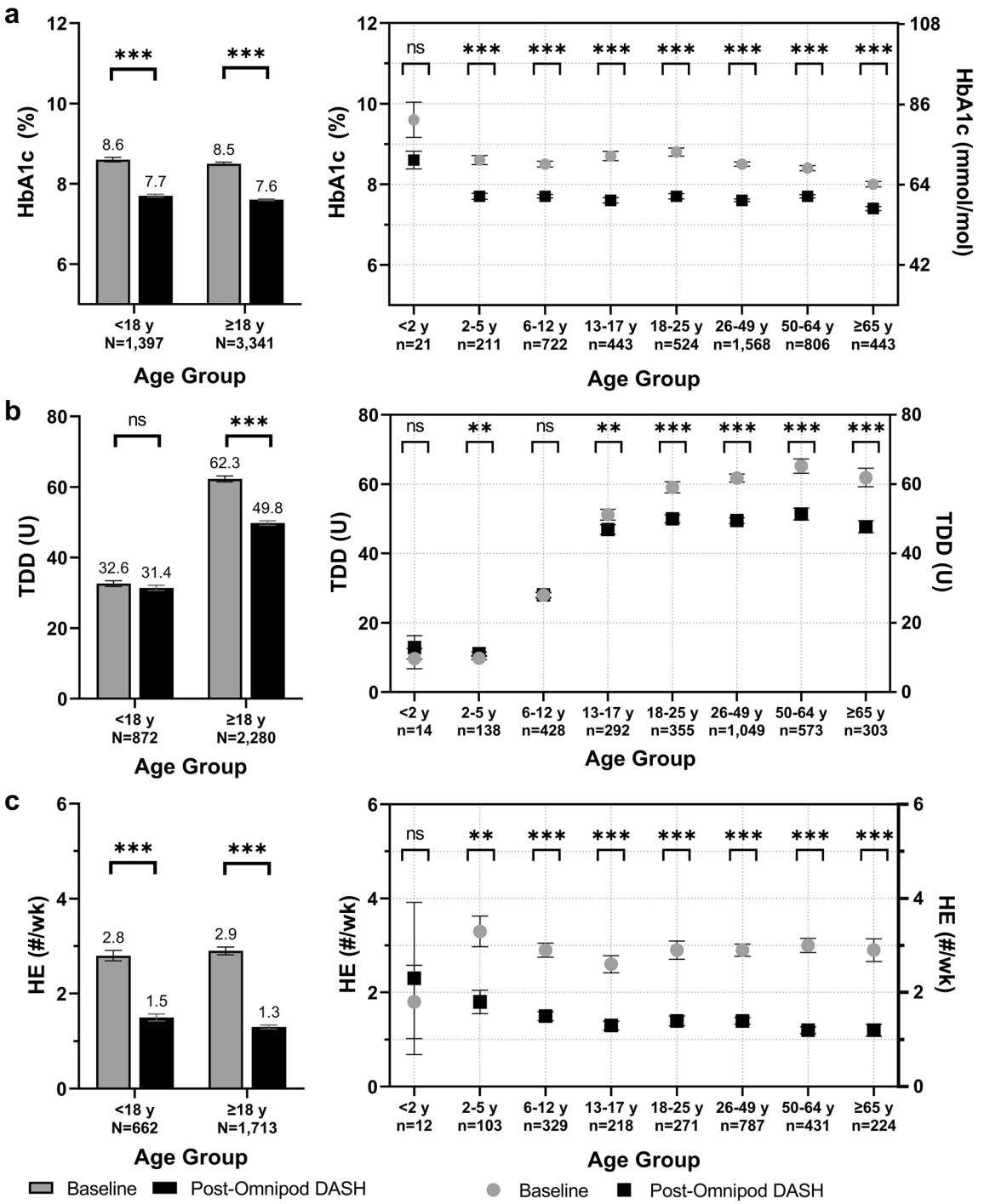

Fig. 1 Results for mean **a** HbA1c, **b** TDD, and **c** hypoglycemic events (HE) at baseline (*gray bars*, *gray circles*) and at follow-up (*black bars*, *black squares*) overall for each cohort (*left panels*) and stratified by age group (*right panels*). Error bars show the standard error of the mean. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, *ns*, not significant with $p > 0.05$

Table 4 Change in hypoglycemic events overall and stratified by prior therapy and by baseline HbA1c

	Age < 18 years					Age ≥ 18 years				
	n	Baseline hypoglycemic events (*n*/week)	Follow-up hypoglycemic events (*n*/week)	Change in hypoglycemic events (*n*/week)	*p* value[a]	*n*	Baseline hypoglycemic events (*n*/week)	Follow-up hypoglycemic events (*n*/week)	Change in hypoglycemic events (*n*/week)	*p* value[a]
Overall	662	2.8 ± 2.8	1.5 ± 1.9	− 1.3 ± 2.7	< 0.0001	1713	2.9 ± 3.4	1.3 ± 1.8	− 1.6 ± 3.2	< 0.0001
Prior therapy										
MDI	524	2.9 ± 2.8	1.5 ± 1.9	− 1.4 ± 2.8	< 0.0001	1,068	2.9 ± 3.4	1.2 ± 1.6	− 1.7 ± 3.1	< 0.0001
CSII	66	2.2 ± 1.8	1.3 ± 1.5	− 0.8 ± 2.0	> 0.05	375	3.3 ± 3.8	1.6 ± 2.4	− 1.7 ± 3.5	< 0.0001
Baseline HbA1c, % (mmol/mol)										
< 6 (< 42)	25	4.4 ± 3.9	1.8 ± 2.1	− 2.7 ± 3.2	0.048	72	4.6 ± 3.9	1.9 ± 3.0	− 2.7 ± 3.3	< 0.0001
6 to < 7 (42 to < 53)	101	4.0 ± 3.6	1.6 ± 1.9	− 2.4 ± 3.2	< 0.0001	287	4.0 ± 4.1	1.8 ± 2.5	− 2.1 ± 3.9	< 0.0001
7 to < 8 (53 to < 64)	165	2.9 ± 2.4	1.4 ± 1.6	− 1.4 ± 2.1	< 0.0001	463	3.2 ± 3.4	1.4 ± 1.8	− 1.8 ± 3.2	< 0.0001
8 to < 9 (64 to < 75)	157	2.9 ± 2.7	1.7 ± 1.9	− 1.2 ± 2.3	< 0.0001	354	2.9 ± 3.6	1.3 ± 1.4	− 1.6 ± 3.3	< 0.0001
9 to < 10 (75 to < 86)	73	2.5 ± 2.8	1.8 ± 3.1	− 0.7 ± 3.7	> 0.05	225	2.3 ± 2.6	1.0 ± 1.5	− 1.3 ± 2.6	< 0.0001
≥ 10 (≥ 86)	141	1.7 ± 1.9	1.1 ± 1.3	− 0.6 ± 2.0	> 0.05	312	1.7 ± 2.6	0.9 ± 1.2	− 0.8 ± 2.5	< 0.0001

Values are mean ± SD

[a]Significant differences between baseline and follow-up hypoglycemic events were determined using paired *t*-tests adjusted for multiple comparisons using Bonferroni correction

CSII continuous subcutaneous insulin infusion, *HbA1c* hemoglobin A1c, *MDI* multiple daily injections, *y* years

the categories < 7% increased (< 6% and 6 to < 7% [< 42 mmol/mol and 42 to < 53 mmol/mol], $p = 0.0071$ and $p < 0.0001$, respectively). The percentage of the pediatric cohort achieving an HbA1c < 7% (< 53 mmol/mol) increased from 19.2% at baseline to 29.8% at follow-up. In adults, the proportion in both the < 6% and 6 to < 7% (< 42 mmol/mol and 42 to < 53 mmol/mol) categories also increased (both $p < 0.0001$). The percentage of adults achieving an HbA1c < 7% (< 53 mmol/mol) increased from 20.1% at baseline to 32.4% at follow-up. Approximately one-third of the pediatric cohort (32.6%) presented with an HbA1c of ≥ 9% (≥ 75 mmol/mol) at baseline, decreasing to 14.7% at follow-up. Similarly, in the adult cohort, this percentage decreased from 32.4% to 13.6%. In both age groups, decreases were seen in the proportion of patients within both the 9 to < 10% and ≥ 10% (75 to < 86 mmol/mol and ≥ 86 mmol/mol) categories (all $p < 0.0001$).

Secondary Outcome: Total Daily Dose of Insulin

Results for the secondary outcome of TDD are shown in Table 3. In the pediatric cohort, TDD remained unchanged overall (-1.2 ± 12.1 U/day; $p > 0.05$), as well as when stratifying by prior therapy or baseline HbA1c. When stratifying into more granular age groups, mean TDD at baseline ranged from 9.7 ± 11.0 U/day in ages < 2 y to 51.2 ± 27.1 U/day in ages 13–17 y (Fig. 1b, numerical results in Supplementary Material Table S2). There was a relatively small but significant increase in TDD in children 2–5 y of age (1.3 ± 3.6 U/day; $p = 0.0067$) and a decrease in TDD in adolescents aged 13–17 y (-4.3 ± 16.0 U/day; $p = 0.0012$).

In the adult cohort, there was a significant decrease in TDD of -12.4 ± 28.7 U/day overall (62.3 ± 40.9 U/day vs. 49.8 ± 30.7 U/day; $p < 0.0001$), corresponding to a 19.9% decrease. A change was observed for both prior MDI (−22.1%; $p < 0.0001$) and prior CSII (−11.9%; $p = 0.015$) users. Significant reductions in mean TDD were also seen across all groups stratified by baseline HbA1c except the group with the lowest HbA1c at baseline (< 6% [< 42 mmol/mol]). Stratified analyses revealed a decrease in TDD across all adult age subgroups (Fig. 1b, Supplementary Material Table S2).

Secondary Outcome: Frequency of Hypoglycemic Events

Results for the secondary outcome of self-reported frequency of hypoglycemic events are shown in Table 4. In the pediatric cohort, there was a significant decrease from 2.8 ± 2.8 to 1.5 ± 1.9 events/week (-1.3 ± 2.7 events/week; $p < 0.0001$). An improvement was seen in those switching from MDI (-1.4 ± 2.8 events/week, $n = 524$; $p < 0.0001$), while the decrease was not significant in the smaller group of users switching from other CSII devices (-0.8 ± 2.0 events/week, $n = 66$; $p > 0.05$). Notably, a decrease in hypoglycemic event frequency was seen in all groups with baseline HbA1c < 9% (< 75 mmol/mol), which includes the groups that did not experience an improvement in HbA1c (Supplementary Material Fig. S2). In particular, the frequency of events in the lowest-baseline HbA1c group (< 6% [< 42 mmol/mol]) decreased from 4.4 ± 3.9 events/week at baseline to 1.8 ± 2.1 events/week at follow-up ($p = 0.048$).

When examining the more granular age cohorts, a reduction in hypoglycemic events was seen in all age groups aged 2 y and above. In the small group of users aged < 2 y ($n = 12$), no change was seen (Fig. 1c, numerical results in Supplementary Material Table S2). While not statistically different, the numerical increase in mean at follow-up was due to one outlier, as shown by the median, which was 0.5 events/week both at baseline and follow-up.

In the adult cohort, there was a significant decrease in hypoglycemic events reported, from 2.9 ± 3.4 to 1.3 ± 1.8 events/week (-1.6 ± 3.2 events/week; $p < 0.0001$). A mean decrease was seen across all adult age subgroups studied (Fig. 1c, Supplementary Material Table S2). Likewise, the change in frequency of

hypoglycemic events was seen regardless of prior therapy. A decrease in hypoglycemic event frequency was seen in all baseline HbA1c groups, including the groups with baseline HbA1c < 7% (< 53 mmol/mol), which are the groups that did not see a decrease in HbA1c (Supplementary Material Fig. S3). In particular, the frequency of events in the lowest baseline HbA1c group (< 6% [< 42 mmol/mol]) decreased from 4.6 ± 3.9 events/week at baseline to 1.9 ± 3.0 events/week at follow-up ($p < 0.0001$).

DISCUSSION

In this first report of clinical outcomes with the Omnipod DASH System, results from a large database of real-world outcomes from people aged < 2 to ≥ 65 y living with T1D in the US revealed a significant decrease in HbA1c of − 0.9% in both pediatric and adult cohorts after 90 days of use. Importantly, this improvement in HbA1c was achieved with a concomitant decrease in the amount of insulin used in adults and with a reduction in hypoglycemic events in both age cohorts. Although a small but significant increase in HbA1c was seen in the groups with the lowest values at baseline, the mean HbA1c remained below the recommended target of 7% (53 mmol/mol) at follow-up [40]. Further, these groups with low HbA1c at baseline did see a benefit in the reduction of hypoglycemic events at follow-up. Overall, the mean frequency of hypoglycemic events per week in each cohort was approximately halved, from 2.8 to 1.5 events/week in the pediatric cohort and from 2.9 to 1.3 events/week in adults. These real-world findings can help inform clinicians when choosing a treatment modality for their patients with T1D regardless of age.

Several studies of varying size and design have suggested that better clinical outcomes are achieved with CSII versus MDI [41–50]. Yet, many people today are still using MDI therapy, whether by choice, due to low awareness of alternatives, or due to obstacles to accessing CSII therapy [4]. The findings of the present study further support the conclusion that CSII results in improved clinical outcomes versus MDI in adults and children and is consistent with previous findings with the earlier Omnipod System [29]. It is not surprising that children transitioning from another CSII device did not have a significant improvement in HbA1c, as they may have already received the glycemic benefit of CSII when initiating their prior device. Additionally, the number of children in this subgroup was relatively low, at only 9.5% of the total group, making it challenging to detect any differences.

Conversely, a benefit of switching to Omnipod DASH was seen in adults previously using other CSII devices, namely traditional tubed pumps. This outcome is somewhat unexpected, as a previous observational, retrospective study designed to assess differences among pump models in adults with T1D reported overall HbA1c improvements for up to 10 y which did not differ between pump makes, including a comparison of the Omnipod System versus tubed pumps [28]. Another retrospective study found a significant improvement in adults transitioning from another CSII device to the Omnipod System [29], while one other did not [27]. These varying results suggest that there are likely a multitude of factors that can affect this outcome, including prior CSII device success and the user's reasons for switching. The much larger sample size of the present study and the inclusion of users from many centers across the US resulted in a diverse population which revealed a significant improvement for prior CSII users. Whether specific features of the Omnipod DASH System—such as features that may help with better insulin absorption, i.e., the flexibility to use different infusion sites on arms, legs, etc. due to the tubeless design, and/or the Pod site tracker, which could promote increased site rotation—may have also contributed to these more favorable results remains speculative and requires further study [25, 34].

Previous studies in adults initiating the Omnipod System over similar or longer time frames have suggested that benefits may only be seen in those with high HbA1c at baseline. In a retrospective, observational study, Brown et al. found improved HbA1c in those initiating the Omnipod System in comparison to a matched cohort of adults who maintained MDI therapy

[26]; however, this improvement was primarily driven by those with a high HbA1c (≥ 9% [≥ 75 mmol/mol]) at baseline. A similar trend was observed in another study, which evaluated outcomes up to 1 y of use [27]. Overall, this trend is expected, as a greater treatment effect in those with higher HbA1c at baseline is typically seen across various therapeutic interventions in people living with diabetes; however, both studies were limited by a smaller sample size, and they did not stratify into additional baseline HbA1c groups. In the present study, significant improvements in HbA1c were found for groups down to ≥ 8% (≥ 64 mmol/mol) at baseline in the pediatric cohort and ≥ 7% (≥ 53 mmol/mol) at baseline in the adult cohort. Notably, despite people with T1D in the US having overall higher HbA1c levels than reported for Europe [51–53], the mean HbA1c levels in Omnipod DASH users aged > 2 y were reduced to similar levels to those reported for adult pump users in European registries by the end of the study [30, 52]. Our results showed a significant reduction of hypoglycemia for the groups with lower HbA1c at baseline, which may be the more relevant outcome for this group in terms of increasing safety from short-term risks.

Additionally, improvements in HbA1c occurred with a concomitant decrease in the amount of insulin used in adults with HbA1c > 6% (> 42 mmol/mol) at baseline. These findings are in accordance with previous studies that report a significant reduction in TDD when switching to a tubeless pump from prior tubed pump or MDI therapy [29, 54, 55]. Conversely, TDD in the pediatric cohort remained unchanged after 3 months of Omnipod System use, potentially due to the variability of insulin needs in this age group.

There are several potential reasons that adults initiating the Omnipod DASH System would experience reductions in TDD compared to their prior therapy. Notably, prior MDI users may benefit from receiving smaller, more precise insulin amounts throughout the day rather than large doses [56, 57], which could lead to improved absorption and insulin delivery only when it is needed, thus lowering the TDD. Many tubed pump users report disconnecting their pumps without suspending the flow of insulin [58, 59], which can waste insulin and result in an inflated TDD value not observed when initiating a tubeless pump for these users. Lastly, more frequent infusion site rotation, which may be facilitated by the tubeless design, may reduce the risk of lipohypertrophy and improve insulin absorption with this system compared to MDI or tubed pump therapy [60].

Comparatively fewer studies are available assessing outcomes with the Omnipod System in young children; and of those that exist, outcomes are not presented separately for clinically distinct age groups (e.g., < 2 y, 2–5 y, 6–12 y, and 13–17 y) [29–31]. For example, in a retrospective European real-world study from the Diabetes-Patienten-Verlaufsdokumentation (DPV) registry, a favorable effect of the Omnipod System in terms of acute complications (diabetic ketoacidosis and severe hypoglycemia) was reported in year 3 vs. MDI users from the same study centers; however, although the median age was 12.3 y, results are presented combined across all ages [31]. Outcomes for young children are of particular interest, as they tend to require very low volumes of insulin, and at times even require a basal rate of 0 U/h for periods of time to avoid over-delivery. As a result, insulin pumps that can be used across all ages and diabetes types must be able to accommodate a wide range of insulin doses. The present study provides evidence for outcomes achieved in these age groups using low volume doses of insulin, down to a mean of 11.1 ± 5.8 U/day in children 2–5 y of age and 12.9 ± 12.6 U/day in children < 2 y. These results support the safety and effectiveness of Omnipod DASH when applied in real-world clinical settings, including in young children down to age < 2 y.

A major strength of the present study is its large sample size, allowing investigation into smaller subgroups stratified by age and baseline HbA1c while still allowing enough power to detect differences within these groups. Also, data were collected in a real-world, observational setting in a broad population with very few restrictions in terms of inclusion in the study. This may enhance the likelihood that

results can be applied to clinical practice in various environments.

Still, there are several limitations of this study which must be recognized. This is a retrospective, observational, nonblinded, nonrandomized study, which presents potential limitations inherent to the design, such as a selection bias in who is initiating Omnipod DASH and the ability to only report associations rather than causal effects. While efforts were made to obtain values from medical records when possible, some results were self-reported, which must be considered when interpreting the results. Further, additional details of treatment and medical history, such as concurrent CGM use, were not available. Finally, while the 3-month follow-up period provides an assessment of the initial outcomes with the system, it is possible the observed improvements are a result of initiating new equipment in patients' diabetes management. Although another study with the earlier Omnipod System showed improvements up to 1 y of use [27], more long-term data are needed to assess the durability of these benefits.

CONCLUSIONS

In this first report of clinical outcomes from people living with T1D and initiating therapy with the Omnipod DASH System, we address a gap in evidence to provide healthcare providers, people living with diabetes, and other stakeholders with an understanding of outcomes achieved with real-world device use. In this large population of ~ 4800 users, there was a significant change in HbA1c of − 0.9% (− 10 mmol/mol) after 90 days of use in both the pediatric and adult cohorts. In adults, the decrease in HbA1c was achieved with a concomitant decrease in the amount of insulin used, while doses remained similar from baseline to follow-up for the pediatric group. A substantial reduction in hypoglycemic events was seen across age groups and was an important benefit for those who started the system with an HbA1c that was already meeting the recommended target. These real-world outcomes provide positive evidence to support the use of Omnipod DASH by people of all ages living with T1D.

ACKNOWLEDGEMENTS

The authors thank the Omnipod DASH users whose data were included in this study. The authors appreciate the efforts of Steve Lowen, PhD, of Insulet Corporation for providing advice on the data analysis, and Irene Hadjiyianni, PhD, for the critical review of the manuscript.

Funding. Funding for this work and the journal's Rapid Service Fee was provided by Insulet Corporation.

Medical Writing, Editorial, and Other Assistance. Andreas Festa, MD, provided writing and administrative support throughout the publication process and received payment from Insulet Corporation for this support. Editorial support of the manuscript was provided by Jodi Bernstein, PhD MPH RD, of Jodi Bernstein Medical Writing (Toronto, Canada), who received payment from Insulet Corporation.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. TV and TTL contributed to the conception of the work. LMH, TV, and TTL contributed to the design of the work, and FL and LMH contributed to the acquisition of data for the work. AC, FL, LMH, and TTL contributed to the analysis of the data, and GA, DJD, FL, LMH, TV, and TTL contributed to the interpretation of data. FL and LMH drafted the manuscript, and all authors critically reviewed the manuscript for important intellectual content. All authors approved of the final manuscript.

Prior Presentation. The primary results were presented in part at the 14th International

Conference on Advanced Technologies and Treatments for Diabetes in June 2021, the 57th Annual Meeting of the European Association for the Study of Diabetes in September 2021, and the 47th Annual Conference of the International Society for Pediatric and Adolescent Diabetes in October 2021 (all virtual meetings). Additionally, the results were encored at the American Pharmacists Association 2022 Annual Meeting in San Antonio, Texas in March 2022.

Disclosures. GA has served as independent consultant for Bayer, Dexcom, and Insulet, and her institution has received research support from Dexcom, Eli Lilly, Fractyl, EMMES, Insulet, Tandem Diabetes, and Welldoc separate from this work. DJD has served as an independent consultant for Dexcom and Insulet, and his institution has received research support from Insulet separate from this work. FL was a full-time employee of Insulet Corporation at the time the study was conducted and is currently a full-time employee of Sanofi. LMH, AC, TV, and TTL are full-time employees of Insulet Corporation and are shareholders of stock in Insulet Corporation.

Compliance with Ethics Guidelines. The study protocol was submitted to the Western Institutional Review Board (submission number 2623242–44579044), which granted a waiver of authorization for use and disclosure of protected health information and granted human subjects research exemption under 45CFR§46.104(d)(4). The study protocol was in agreement with the Helsinki Declaration of 1964 and its later amendments.

Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available.

REFERENCES

1. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271–81.

2. Tuomilehto J. The emerging global epidemic of type 1 diabetes. Curr Diab Rep. 2013;13(6):795–804.

3. Lawrence JM, Divers J, Isom S, Saydah S, Imperatore G, Pihoker C, et al. Trends in prevalence of type 1 and type 2 diabetes in children and adolescents in the US, 2001–2017. JAMA. 2021;326(8):717–27.

4. Foster NC, Beck RW, Miller KM, Clements MA, Rickels MR, DiMeglio LA, et al. State of type 1 diabetes management and outcomes from the T1D exchange in 2016–2018. Diabetes Technol Ther. 2019;21(2):66–72.

5. Mauras N, Mazaika P, Buckingham B, Weinzimer S, White NH, Tsalikian E, et al. Longitudinal assessment of neuroanatomical and cognitive differences in young children with type 1 diabetes: association with hyperglycemia. Diabetes. 2015;64(5):1770–9.

6. Herman WH, Braffett BH, Kuo S, Lee JM, Brandle M, Jacobson AM, et al. What are the clinical, quality-of-life, and cost consequences of 30 years of excellent vs. poor glycemic control in type 1 diabetes? J Diabetes Complications. 2018;32(10):911–5.

7. Baxter M, Hudson R, Mahon J, Bartlett C, Samyshkin Y, Alexiou D, et al. Estimating the impact of better management of glycaemic control in adults with type 1 and type 2 diabetes on the number of clinical complications and the associated financial benefit. Diabet Med. 2016;33(11):1575–81.

8. Diabetes Control Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, Cleary P,

Crofford O, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. New England J Med. 1993;329(14):977–86.

9. Rawshani A, Rawshani A, Franzen S, Eliasson B, Svensson AM, Miftaraj M, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. N Engl J Med. 2017;376(15):1407–18.

10. Mauras N, Buckingham B, White NH, Tsalikian E, Weinzimer SA, Jo B, et al. Impact of type 1 diabetes in the developing brain in children: a longitudinal study. Diabetes Care. 2021;44(4):983–92.

11. Jaser SS, Jordan LC. Brain health in children with type 1 diabetes: risk and protective factors. Curr Diab Rep. 2021;21(4):12.

12. Rawshani A, Sattar N, Franzen S, Rawshani A, Hattersley AT, Svensson AM, et al. Excess mortality and cardiovascular disease in young adults with type 1 diabetes in relation to age at onset: a nationwide, register-based cohort study. Lancet. 2018;392(10146):477–86.

13. American Diabetes Association Professional Practice Committee. 7. Diabetes technology: standards of medical care in diabetes—2022. Diabetes Care. 2021;45(Suppl 1):S97–S112.

14. Peters AL, Ahmann AJ, Battelino T, Evert A, Hirsch IB, Murad MH, et al. Diabetes technology—continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2016;101(11):3922–37.

15. Holt RIG, DeVries JH, Hess-Fischl A, Hirsch IB, Kirkman MS, Klupa T, et al. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2021;64(12):2609–52.

16. Grunberger G, Bailey TS, Cohen AJ, Flood TM, Handelsman Y, Hellman R, et al. Statement by the American Association of Clinical Endocrinologists Consensus Panel on Insulin Pump Management. Endocr Pract. 2010;16(5):746–62.

17. Sundberg F, Barnard K, Cato A, de Beaufort C, DiMeglio LA, Dooley G, et al. ISPAD guidelines. Managing diabetes in preschool children. Pediatr Diabetes. 2017;18(7):499–517.

18. Messer LH, Tanenbaum ML, Cook PF, Wong JJ, Hanes SJ, Driscoll KA, et al. Cost, hassle, and on-body experience: barriers to diabetes device use in adolescents and potential intervention targets. Diabetes Technol Ther. 2020;22(10):760–7.

19. Perez-Nieves M, Garey C, Fan L, McAuliffe-Fogarty AH. Insulin pump therapy—patient and provider perceptions. Diabetes. 2018;67(Suppl 1):981–P.

20. Taleb N, Messier V, Ott-Braschi S, Ardilouze JL, Rabasa-Lhoret R. Perceptions and experiences of adult patients with type 1 diabetes using continuous subcutaneous insulin infusion therapy: results of an online survey. Diabetes Res Clin Pract. 2018;144:42–50.

21. Tanenbaum ML, Adams RN, Hanes SJ, Barley RC, Miller KM, Mulvaney SA, et al. Optimal use of diabetes devices: clinician perspectives on barriers and adherence to device use. J Diabetes Sci Technol. 2017;11(3):484–92.

22. Reidy C, Bracher M, Foster C, Vassilev I, Rogers A. The process of incorporating insulin pumps into the everyday lives of people with type 1 diabetes: a critical interpretive synthesis. Health Expect. 2018;21(4):714–29.

23. Commissariat PV, Boyle CT, Miller KM, Mantravadi MG, DeSalvo DJ, Tamborlane WV, et al. Insulin pump use in young children with type 1 diabetes: sociodemographic factors and parent-reported barriers. Diabetes Technol Ther. 2017;19(6):363–9.

24. Zisser HC. The OmniPod Insulin Management System: the latest innovation in insulin pump therapy. Diabetes Ther. 2010;1(1):10–24.

25. Ly TT, Layne JE, Huyett LM, Nazzaro D, O'Connor JB. Novel bluetooth-enabled tubeless insulin pump: innovating pump therapy for patients in the digital age. J Diabetes Sci Technol. 2019;13(1):20–6.

26. Brown RE, Vienneau T, Aronson R. Canadian real-world outcomes of omnipod initiation in people with type 1 diabetes (COPPER study): evidence from the LMC Diabetes Registry. Diabet Med. 2020;38(6):e14420.

27. Mehta SN, Tinsley LJ, Kruger D, Bode B, Layne JE, Huyett LM, et al. Improved glycemic control following transition to tubeless insulin pump therapy in adults with type 1 diabetes. Clinical Diabetes. 2021;39(1):72–9.

28. Leelarathna L, Roberts SA, Hindle A, Markakis K, Alam T, Chapman A, et al. Comparison of different insulin pump makes under routine care conditions in adults with type 1 diabetes. Diabet Med. 2017;34(10):1372–9.

29. Layne JE, Parkin CG, Zisser H. Efficacy of the omnipod insulin management system on glycemic control in patients with type 1 diabetes previously treated with multiple daily injections or continuous subcutaneous insulin infusion. J Diabetes Sci Technol. 2016;10(5):1130–5.

30. Danne T, Schwandt A, Biester T, Heidtmann B, Rami-Merhar B, Haberland H, et al. Long-term study of tubeless insulin pump therapy compared to multiple daily injections in youth with type 1 diabetes: Data from the German/Austrian DPV Registry. Pediatr Diabetes. 2018;19(5):979–84.

31. Biester T, Schwandt A, Heidtmann B, Rami-Merhar B, Haak T, Festa A, et al. Declining frequency of acute complications associated with tubeless insulin pump use: data from 2,911 patients in the German/Austrian Diabetes Patienten Verlaufsdokumentation Registry. Diabetes Technol Ther. 2021;23(8):527–36.

32. Carlson AL, Huyett LM, Jantz J, Chang A, Vienneau T, Ly TT. Improved glycemic control in 3,592 adults with type 2 diabetes mellitus initiating a tubeless insulin management system. Diabetes Res Clin Pract. 2021;174: 108735.

33. Layne JE, Parkin CG, Zisser H. Efficacy of a tubeless patch pump in patients with type 2 diabetes previously treated with multiple daily injections. J Diabetes Sci Technol. 2017;11(1):178–9.

34. Pillalamarri SS, Huyett LM, Abdel-Malek A. Novel bluetooth-enabled tubeless insulin pump: a user experience design approach for a connected digital diabetes management platform. J Diabetes Sci Technol. 2018;12(6):1132–42.

35. Carlson AL, Huyett LM, Jantz J, Chang A, Vienneau T, Ly TT. Improved glycemic control in 3,592 adults with type 2 diabetes mellitus initiating a tubeless insulin management system. Diabetes Res Clin Pract. 2021;174:108735.

36. Sherr JL. Closing the loop on managing youth with type 1 diabetes: children are not just small adults. Diabetes Care. 2018;41(8):1572–8.

37. Bergenstal RM, Beck RW, Close KL, Grunberger G, Sacks DB, Kowalski A, et al. Glucose management indicator (GMI): a new term for estimating A1C from continuous glucose monitoring. Diabetes Care. 2018;41(11):2275–80.

38. Lee JM, Carlson E, Albanese-O'Neill A, Demeterco-Berggren C, Corathers SD, Vendrame F, et al. Adoption of telemedicine for type 1 diabetes care during the COVID-19 pandemic. Diabetes Technol Ther. 2021;23(9):642–51.

39. Garg SK, Rodbard D, Hirsch IB, Forlenza GP. Managing new-onset type 1 diabetes during the COVID-19 pandemic: challenges and opportunities. Diabetes Technol Ther. 2020;22(6):431–9.

40. American Diabetes Association Professional Practice Committee. 6. Glycemic targets: standards of medical care in diabetes—2022. Diabetes Care. 2021;45(Suppl 1):S83–S96.

41. Bode BW, Steed RD, Davidson PC. Reduction in severe hypoglycemia with long-term continuous subcutaneous insulin infusion in type I diabetes. Diabetes Care. 1996;19(4):324–7.

42. Pickup JC, Kidd J, Burmiston S, Yemane N. Determinants of glycaemic control in type 1 diabetes during intensified therapy with multiple daily insulin injections or continuous subcutaneous insulin infusion: importance of blood glucose variability. Diabetes Metab Res Rev. 2006;22(3): 232–7.

43. Sherr J, Tamborlane WV. Past, present, and future of insulin pump therapy: better shot at diabetes control. Mt Sinai J Med. 2008;75(4):352–61.

44. Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabet Med. 2008;25(7):765–74.

45. Jeitler K, Horvath K, Berghold A, Gratzer TW, Neeser K, Pieber TR, et al. Continuous subcutaneous insulin infusion versus multiple daily insulin injections in patients with diabetes mellitus: systematic review and meta-analysis. Diabetologia. 2008;51(6):941–51.

46. Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J. Continuous subcutaneous insulin infusion (CSII) versus multiple insulin injections for type 1 diabetes mellitus. Cochrane Database Syst Rev. 2010(1):CD005103.

47. Pickup JC. Management of diabetes mellitus: is the pump mightier than the pen? Nat Rev Endocrinol. 2012;8(7):425–33.

48. Steineck I, Cederholm J, Eliasson B, Rawshani A, Eeg-Olofsson K, Svensson AM, et al. Insulin pump therapy, multiple daily injections, and cardiovascular mortality in 18,168 people with type 1 diabetes: observational study. BMJ. 2015;350: h3234.

49. Rosenlund S, Hansen TW, Andersen S, Rossing P. Effect of 4 years subcutaneous insulin infusion treatment on albuminuria, kidney function and HbA1c compared with multiple daily injections: a longitudinal follow-up study. Diabet Med. 2015;32(11):1445–52.

50. Beato-Vibora P, Yeoh E, Rogers H, Hopkins D, Amiel SA, Choudhary P. Sustained benefit of continuous subcutaneous insulin infusion on glycaemic control and hypoglycaemia in adults with type 1 diabetes. Diabet Med. 2015;32(11):1453–9.

51. Albanese-O'Neill A, Grimsmann JM, Svensson AM, Miller KM, Raile K, Akesson K, et al. Changes in HbA1c between 2011 and 2017 in Germany/Austria, Sweden, and the United States: a lifespan perspective. Diabetes Technol Ther. 2022;24(1):32–41.

52. Hermann JM, Miller KM, Hofer SE, Clements MA, Karges W, Foster NC, et al. The transatlantic HbA1c gap: differences in glycaemic control across the lifespan between people included in the US T1D Exchange Registry and those included in the German/Austrian DPV Registry. Diabet Med. 2020;37(5):848–55.

53. Sherr JL, Hermann JM, Campbell F, Foster NC, Hofer SE, Allgrove J, et al. Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries. Diabetologia. 2016;59(1):87–91.

54. Pickup J, Mattock M, Kerry S. Glycaemic control with continuous subcutaneous insulin infusion compared with intensive insulin injections in patients with type 1 diabetes: meta-analysis of randomised controlled trials. BMJ. 2002;324(7339):705.

55. Paldus B, Lee MH, O'Neal DN. Insulin pumps in general practice. Aust Prescr. 2018;41(6):186–90.

56. McAdams BH, Rizvi AA. An overview of insulin pumps and glucose sensors for the generalist. J Clin Med. 2016;5(1):5.

57. Berget C, Messer LH, Forlenza GP. A clinical overview of insulin pump therapy for the management of diabetes: past, present, and future of intensive therapy. Diabetes Spectr. 2019;32(3):194–204.

58. Klonoff DC, Reyes JS. Insulin pump safety meeting: summary report. J Diabetes Sci Technol. 2009;3(2):396–402.

59. Zhang Y, Jones PL, Klonoff DC. Second insulin pump safety meeting: summary report. J Diabetes Sci Technol. 2010;4(2):488–93.

60. Gradel AKJ, Porsgaard T, Lykkesfeldt J, Seested T, Gram-Nielsen S, Kristensen NR, et al. Factors affecting the absorption of subcutaneously administered insulin: effect on variability. J Diabetes Res. 2018;2018:1205121.