



## Research: Epidemiology

# The Transatlantic HbA<sub>1c</sub> 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

J. M. Hermann<sup>1,2</sup> , K. M. Miller<sup>3</sup>, S. E. Hofer<sup>4</sup>, M. A. Clements<sup>5</sup>, W. Karges<sup>6</sup>, N. C. Foster<sup>3</sup>, E. Fröhlich-Reiterer<sup>7</sup>, M. R. Rickels<sup>8</sup>, J. Rosenbauer<sup>2,9</sup>, D. J. DeSalvo<sup>10</sup>, R. W. Holl<sup>1,2</sup> and D. M. Maahs<sup>11,12</sup>  for the T1D Exchange Clinic Network and the DPV initiative

<sup>1</sup>University of Ulm, Institute of Epidemiology and Medical Biometry, ZIBMT, Ulm, Germany, <sup>2</sup>German Centre for Diabetes Research, Munich-Neuherberg, Germany, <sup>3</sup>Jaeb Centre for Health Research, Tampa, FL, USA, <sup>4</sup>Department of Paediatrics, Medical University of Innsbruck, Innsbruck, Austria, <sup>5</sup>Children's Mercy Hospital, Kansas City, MO, USA, <sup>6</sup>Division of Endocrinology and Diabetes, RWTH Aachen University, Aachen, Germany, <sup>7</sup>Department of Pediatrics, Medical University of Graz, Graz, Austria, <sup>8</sup>Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, <sup>9</sup>German Diabetes Centre, Institute for Biometrics and Epidemiology, Leibniz Centre for Diabetes Research at Düsseldorf University, Düsseldorf, Germany, <sup>10</sup>Baylor College of Medicine, Houston, TX, USA, <sup>11</sup>Stanford University, Palo Alto, CA, USA and <sup>12</sup>Stanford Diabetes Research Centre, Stanford, CA, USA

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## Abstract

**Aim** To compare HbA<sub>1c</sub> levels across the lifespan in people with type 1 diabetes in the USA with those in Germany/Austria, and to examine potential differences in HbA<sub>1c</sub> levels between sexes, insulin delivery methods and minority status.

**Methods** Data were extracted from the US T1D Exchange Registry ( $n=18\,381$  participants from 73 sites) and from the German/Austrian Prospective Diabetes Follow-up Registry, the DPV ( $n=32\,643$  participants from 362 sites). Mean HbA<sub>1c</sub> was calculated for each year of age for individuals aged  $\leq 25$  years, and at 2-year age intervals for individuals aged  $>25$  years. Curves for mean HbA<sub>1c</sub> by age were estimated using locally weighted scatterplot smoothing. HbA<sub>1c</sub> differences between registries, sexes, insulin delivery methods, and minority status were assessed by age group using multiple linear regression.

**Results** In both registries, mean HbA<sub>1c</sub> increased by  $\sim 11$  mmol/mol (1.0%) between the ages of 9 and 18 years, although at quite different absolute levels: from 66 mmol/mol (8.2%) to 77 mmol/mol (9.2%) in the T1D Exchange Registry, and from 56 mmol/mol (7.3%) to 66 mmol/mol (8.2%) in the DPV. Sex differences were observed in the DPV only. In the T1D Exchange Registry, injection users had higher mean HbA<sub>1c</sub> than pump users across the lifespan, whereas in the DPV higher HbA<sub>1c</sub> levels in injection users were observed in the age groups 6 to  $<12$  years, 12 to  $<18$  years, and 30 to  $<50$  years ( $P < 0.001$ ). Minority status was significantly associated with higher HbA<sub>1c</sub> in most age groups in both registries.

**Conclusions** Significant differences in HbA<sub>1c</sub> were noted between the USA and Germany/Austria, with disparities more pronounced in early childhood through to young adulthood. Further studies should identify causes for these disparities.

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## Introduction

For individuals with type 1 diabetes, optimal glycaemic control is essential to reduce the risk of acute and long-term complications. Treatment guidelines from the International Society for Paediatric and Adolescent Diabetes (ISPAD) as well as from the American Diabetes Association (ADA), the

Correspondence to: Julia M. Hermann. E-mail: julia.hermann@uni-ulm.de  
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**What's new?**

- Data from the T1D Exchange Registry (T1DX) have shown that only few individuals with type 1 diabetes meet HbA<sub>1c</sub> targets, and that glycaemic control has worsened in adolescents over recent years.
- Although a similar increase in HbA<sub>1c</sub> on reaching adolescence was observed, young people in the German/Austrian DPV registry had HbA<sub>1c</sub> levels that were ~11 mmol/mol (1.0%) lower compared with young people included in the T1DX.
- Comparison of the two contemporary diabetes cohorts showed large discrepancies in glycaemic control between developed Western countries, and highlights the need for increased efforts to improve care and particularly to lower HbA<sub>1c</sub> in young people with type 1 diabetes, especially those included in the T1DX.

German Diabetes Association (DDG), the Austrian Diabetes Association (ÖDG) and the Austrian working group for paediatric endocrinology and diabetology (APEDÖ) set target HbA<sub>1c</sub> levels of < 53 or 58 mmol/mol (7.0% or 7.5%) [1–4]. However, studies from various regions of the world have demonstrated that individuals with type 1 diabetes, especially adolescents and young adults, often do not meet HbA<sub>1c</sub> targets [5–8].

The T1D Exchange Registry (T1DX) in the USA and the Prospective Diabetes Follow-up Registry, the DPV, in Germany and Austria are two well-established consortia of diabetes centres that document treatment and outcome of individuals across all ages, thus allowing cross-sectional comparison of HbA<sub>1c</sub> patterns across the lifespan between registries. These data provide a contemporary picture of glycaemic control by age in two high-income Western regions. A recent analysis from the T1DX has reported an

increase in mean HbA<sub>1c</sub> in the paediatric population with type 1 diabetes from 2010–2012 to 2016–2018 and has highlighted the need to lower HbA<sub>1c</sub> in the USA [9]. International comparisons give insights into diabetes care and outcomes in other countries.

In the present study, we aimed to compare HbA<sub>1c</sub> across the lifespan between people included in the T1DX and those included in the DPV, and to examine differences in the HbA<sub>1c</sub> patterns between sexes, between individuals with and without ethnic minority status/migration background, and between insulin pump and injection users.

**Participants and methods**

The analysis cohort included 51 024 individuals of all ages with type 1 diabetes for at least 1 year. The T1DX cohort included 18 381 individuals from 73 paediatric and adult endocrinology clinics in 34 US states, and the DPV cohort included 32 643 individuals from 362 specialized diabetes centres in Germany and Austria. Detailed information on the two registries can be found in Miller *et al.* [6] and Schwandt *et al.* [8].

Demographic and clinical data were obtained from medical records. We analysed the most recent HbA<sub>1c</sub> value between 1 April 2015 and 1 July 2016, with all values having been mathematically standardized to the Diabetes Control and Complications Trial (DCCT) reference range of 21–43 mmol/mol (4.1–6.1%) using the multiple-of-the-mean transformation method [10]. For both registries, mean HbA<sub>1c</sub> was calculated for each year of age for individuals aged ≤25 years and, due to the lower sample size, at 2-year age intervals for individuals aged >25 years; individuals aged <3 years [T1DX, *n*=28 (0.2%); DPV, *n*=94 (0.3%)] were combined into one group, as were those aged ≥75 years [T1DX, *n*=139 (0.8%); DPV, *n*=636 (*n*=1.9%)]. Minority status was defined based on race/ethnicity for the T1DX (majority: non-Hispanic white, minority: black non-Hispanic, Hispanic or

**Table 1** Participant characteristics

	DPV ( <i>n</i> =32 643)	T1DX ( <i>n</i> =18 381)	<i>P</i> *
Age, years	15 (12, 20)	17 (13, 33)	<0.001
Duration of diabetes, years	7 (4, 11)	9 (6, 17)	<0.001
Diagnosis year ≥2010, <i>n</i> (%)	15 700 (48)	5132 (28)	<0.001
Male sex, <i>n</i> (%)	17 127 (52)	9125 (50)	<0.001
Obesity, <i>n</i> (%)	4347 (14)	3472 (20)	<0.001
Minority status*, <i>n</i> (%)	5598 (17)	2991 (17)	0.316
HbA <sub>1c</sub>			<0.001
mmol/mol	62 ± 16	69 ± 18	
%	7.8 ± 1.5	8.5 ± 1.7	
Total daily insulin dose per kg bodyweight	0.80 (0.62, 1.00)	0.75 (0.58, 0.94)	<0.001
Pump use, <i>n</i> (%)	14 759 (49)	11 340 (63)	<0.001
CGM use, <i>n</i> (%)	2103 (6)	3516 (20)	<0.001

CGM, continuous glucose monitoring; T1DX, T1D Exchange Registry.

Data are presented as median (interquartile range), percentage, or mean ± SD. \**P* values are obtained from Wilcoxon or chi-squared test and are adjusted for multiple testing using the Bonferroni–Holm method. \*Minority status: based on ethnicity (non-Hispanic white vs other ethnicities) for T1DX and migration background for DPV.

Latino, other race/ethnicity), and on migration background for the DPV (minority: the individual or at least one parent born outside of Germany or Austria, majority: the individual and parents born in Germany or Austria).

### Statistical methods

Characteristics of the study cohorts are given by registry (Table 1) and stratified by registry and age group (<6 years, 6 to <12 years, 12 to <18 years, 18 to <30 years, 30 to <50 years, ≥50 years; Table 2) as median (lower, upper quartile) and mean ± SD for asymmetrically and symmetrically distributed continuous variables, respectively, or as percentages. Unadjusted comparisons of cohort characteristics between registries were performed using Wilcoxon tests for continuous variables and chi-squared tests for percentages.

Curves of mean HbA<sub>1c</sub> by age were estimated using locally weighted scatterplot smoothing. The optimal smoothing parameter was selected using the corrected Akaike information criterion. Respective curves of mean HbA<sub>1c</sub> by age were estimated for boys/men and girls/women and for pump users and injection users.

Differences in HbA<sub>1c</sub> levels between the registries were assessed using a linear regression model stratified by age group and adjusted for sex, duration of type 1 diabetes, obesity, pump use and continuous glucose monitoring (CGM) use. Results are presented as adjusted mean differences between the T1DX and DPV with corresponding 95% CIs. Additional linear regression models were used to assess the difference in HbA<sub>1c</sub> within registries between sexes (adjusted for duration of diabetes, obesity, minority status, pump use and CGM use), between injection and pump users (adjusted for sex, duration of diabetes, obesity, minority status and CGM use), and between minority and non-minority status (adjusted for sex, duration of diabetes, obesity, pump use and CGM use).

The percentage of individuals achieving HbA<sub>1c</sub> levels <58 mmol/mol (7.5%) and <53 mmol/mol (7.0%) was tabulated by registry. The ISPAD, ADA and DDG HbA<sub>1c</sub> target for children and adolescents aged <18 years was <58 mmol/mol (7.5%) for the time period analysed [1–3], whereas the Austrian APEDÖ recommended an HbA<sub>1c</sub> target of <53 mmol/mol (7.0%) [4]. The ADA set an HbA<sub>1c</sub> target of <53 mmol/mol (7.0%) for adults, whereas the DDG recommended the same target HbA<sub>1c</sub> for adults as for children [<58 mmol/mol (7.5%)].

All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA). Two-sided *P* values <0.05 were considered statistically significant. The Bonferroni–Holm method was applied to adjust *P* values for multiple comparisons.

### Ethics

Data collection was approved by the institutional review boards at the clinics participating in the T1DX or DPV

**Table 2** Participant characteristics by age group

	<6 years		6 to <12 years		12 to <18 years		18 to <30 years		30 to <50 years		≥50 years	
	DPV	T1DX	DPV	T1DX	DPV	T1DX	DPV	T1DX	DPV	T1DX	DPV	T1DX
<i>n</i>	1127	463	6837	2736	13 658	6486	4593	3721	2548	2437	3880	2538
Duration of diabetes, years	2 (1, 3)	2 (2, 3)	4 (2, 6)	5 (4, 7)	6 (4, 9)	7 (5, 10)	9 (6, 14)	12 (8, 16)	17 (8, 26)	23 (15, 31)	24 (13, 37)	34 (22, 45)
Diagnosis year ≥2010, <i>n</i> (%)	1127 (100)	463 (100)	5364 (79)	1769 (65)	7000 (51)	2299 (35)	1232 (27)	437 (12)	515 (20)	110 (5)	462 (12)	54 (2)
Male sex, <i>n</i> (%)	600 (53)	243 (52)	3565 (52)	1448 (53)	7144 (52)	3311 (51)	2437 (53)	1843 (50)	1303 (51)	1077 (44)	2078 (54)	1203 (47)
BMIz (WHO), BMI*	0.86 ± 1.14	0.90 ± 1.10	0.68 ± 1.01	0.81 ± 1.16	0.62 ± 1.05	0.93 ± 1.08	24.5 ± 4.5	26.2 ± 6.2	26.6 ± 5.4	28.4 ± 5.9	27.3 ± 5.5	27.8 ± 7.5
Obesity, <i>n</i> (%)	150 (14)	66 (14)	781 (12)	401 (15)	1470 (11)	1170 (18)	466 (11)	619 (18)	532 (22)	635 (31)	948 (26)	581 (28)
Total daily insulin dose per kg body weight	0.66 (0.54, 0.79)	0.70 (0.58, 0.81)	0.73 (0.60, 0.89)	0.78 (0.66, 0.92)	0.91 (0.73, 1.11)	0.90 (0.75, 1.07)	0.84 (0.66, 1.04)	0.72 (0.59, 0.87)	0.56 (0.42, 0.73)	0.57 (0.47, 0.71)	0.54 (0.40, 0.71)	0.50 (0.40, 0.66)
Pump use, <i>n</i> (%)	999 (89)	296 (65)	4280 (63)	1771 (66)	6245 (46)	3986 (63)	1756 (42)	2150 (59)	780 (46)	1563 (65)	699 (29)	1574 (63)
CGM use, <i>n</i> (%)	153 (14)	162 (36)	619 (9)	589 (22)	786 (6)	860 (14)	207 (5)	566 (16)	141 (6)	703 (30)	197 (5)	636 (26)
HbA <sub>1c</sub> mmol/mol	57 ± 9	66 ± 12	58 ± 11	68 ± 13	65 ± 17	75 ± 19	65 ± 19	71 ± 21	61 ± 17	61 ± 15	58 ± 14	60 ± 13
%	7.3 ± 0.9	8.2 ± 1.1	7.5 ± 1.0	8.4 ± 1.2	8.1 ± 1.5	9.0 ± 1.8	8.1 ± 1.7	8.7 ± 1.9	7.8 ± 1.5	7.7 ± 1.3	7.4 ± 1.3	7.6 ± 1.1
HbA <sub>1c</sub> <58 mmol/mol (7.5%), <i>n</i> (%)	670 (59)	118 (26)	3840 (41)	600 (22)	5367 (39)	1099 (16)	1895 (41)	1015 (27)	1281 (50)	1167 (48)	2285 (59)	1234 (49)
HbA <sub>1c</sub> <53 mmol/mol (7.0%), <i>n</i> (%)	397 (35)	42 (9)	2313 (26)	218 (8)	3086 (23)	430 (7)	1187 (26)	556 (15)	842 (33)	702 (29)	1585 (41)	683 (27)

T1DX, T1D Exchange Registry.

Data are presented as median (interquartile range), percentage, or mean ± SD. \*BMIz (WHO) for participants aged <18 years, BMI for participants aged ≥18 years.

and by the ethics committee at Ulm University. Informed consent from the participants was obtained according to the requirements of the institutional review boards.

## Results

Participant characteristics by registry are shown in Table 1. The median (lower, upper quartile) age was 15 (12, 20) years in the DPV and 17 (13, 33) years in the T1DX, and the median duration of diabetes was 7 (4, 11) and 9 (6, 17) years, respectively. Participant characteristics by age group (Table 2) revealed longer duration of type 1 diabetes in the T1DX than in the DPV in all age groups (all  $P < 0.001$ ) except for the age group  $<6$  years ( $P=0.662$ ). In the T1DX, use of insulin pump therapy ranged between 59% (18 to  $<30$  years) and 66% (6 to  $<12$  years), whereas in the DPV pump use was most frequent in the youngest age group (89%) and least frequent in adults aged  $\geq 50$  years (29%). CGM use was higher in the T1DX compared with the DPV in all age groups (all  $P < 0.001$ ).

In both registries, mean HbA<sub>1c</sub> increased by  $\sim 11$  mmol/mol (1.0%) between ages 9 and 18 years, although at quite different absolute levels: from 66 mmol/mol (8.2%) to 77 mmol/mol (9.2%) in the T1DX, and from 56 mmol/mol (7.3%) to 66 mmol/mol (8.2%) in the DPV. HbA<sub>1c</sub> decreased in young adults, with a steeper slope in the T1DX, followed by plateaus at similar levels between the ages of 30 and 50 years. Beyond age 50 years, HbA<sub>1c</sub> gradually declined in both registries, although the decline was steeper in the DPV (Fig. 1). HbA<sub>1c</sub> was significantly lower (all  $P < 0.02$ ) in the DPV compared with the T1DX in all age groups except for the age group 30 to  $<50$  years (adjusted  $P=0.198$ ; Table 3).

## Differences between sexes

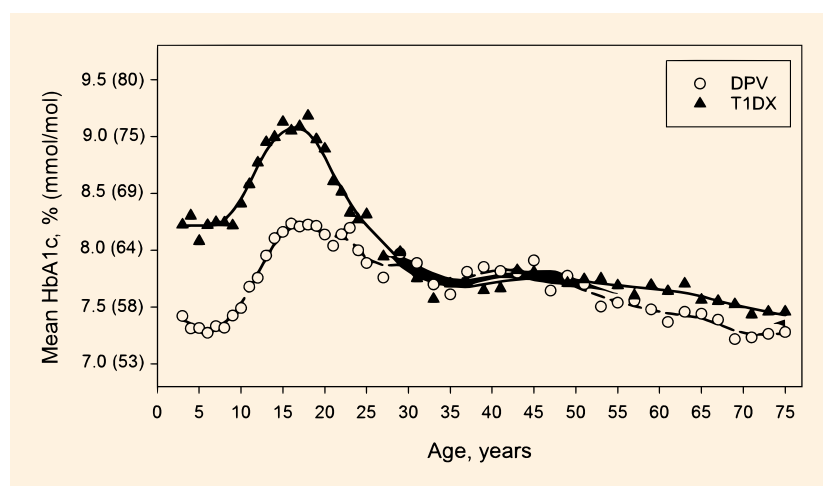
In the T1DX, no significant sex differences were observed (data not shown). In the DPV, HbA<sub>1c</sub> was higher in women than in men in the age group 18 to  $<30$  years [adjusted mean difference 2 mmol/mol (95% CI 0, 3) or 0.1% (95% CI 0.0, 0.3);  $P=0.006$ ] as well as in individuals aged  $\geq 50$  years [adjusted mean difference 2 mmol/mol (95% CI 1, 3) or 0.2% (95% CI 0.1, 0.3%);  $P=0.002$ ].

## Differences between pump and injection users

In the T1DX, mean HbA<sub>1c</sub> was higher in injection users than in pump users across the lifespan (Fig. 2a). The differences in mean HbA<sub>1c</sub> were significant for all age groups between 6 and  $<50$  years after adjustment for sex, duration of diabetes, obesity, minority status and CGM use (Table 3). In the DPV, the largest difference in mean HbA<sub>1c</sub> between pump and injection users was observed in adults aged  $<50$  years (Fig. 2b). Adjusted linear regression revealed significantly higher HbA<sub>1c</sub> in injection vs pump users in the age groups 6 to  $<12$  years, 12 to  $<18$  years, and 30 to  $<50$  years, but there were no differences in HbA<sub>1c</sub> between treatment regimens in the other age groups (Table 3).

## Differences between minority and non-minority status

In the T1DX, individuals with ethnic minority status had higher adjusted mean HbA<sub>1c</sub> than non-Hispanic white individuals in all age groups except for the age group  $<6$  years (all  $P < 0.001$ ; Table 3). In the DPV, significant differences between individuals with and without migration background were found for adolescents and adults aged 6 to  $<30$  years and  $\geq 50$  years (Table 3).



**FIGURE 1** Mean most recent HbA<sub>1c</sub> by age (1-year intervals for individuals aged  $\leq 25$  years, 2-year intervals for individuals aged  $> 25$  years). Solid and dashed lines represent locally weighted scatterplot smoothing curves for the T1D Exchange Registry (T1DX) and the German/Austrian Prospective Diabetes Follow-up Registry (DPV), respectively. Grey areas represent corresponding 95% CIs.

**Table 3** Adjusted differences in mean HbA<sub>1c</sub> (%) by age group

Age group	T1DX vs DPV		T1DX Injection vs pump		DPV Injection vs pump		T1DX Minority: yes vs no		DPV Minority: yes vs no	
	Adjusted <sup>†</sup> difference (95% CI)	P <sup>§</sup>	Adjusted <sup>†</sup> difference (95% CI)	P <sup>§</sup>	Adjusted <sup>†</sup> difference (95% CI)	P <sup>§</sup>	Adjusted <sup>†</sup> difference (95% CI)	P <sup>§</sup>	Adjusted <sup>†</sup> difference (95% CI)	P <sup>§</sup>
<6 years	10 (9, 11) mmol/mol 0.9 (0.9, 1.0)%	<0.001	1 (-1, 4) mmol/mol 0.1 (-0.1, 0.4)%	0.321	-1 (-2, 1) mmol/mol -0.1 (-0.2, 0.1)%	0.458	2 (-1, 5) mmol/mol 0.2 (-0.1, 0.4)%	0.204	1 (0, 2) mmol/mol 0.1 (0.0, 0.2)%	0.080
6 to <12 years	10 (10, 11) mmol/mol 1.0 (0.9, 1.0)%	<0.001	4 (3, 5) mmol/mol 0.3 (0.2, 0.4)%	<0.001	1 (1, 2) mmol/mol 0.1 (0.1, 0.2)%	<0.001	4 (2, 5) mmol/mol 0.3 (0.2, 0.4)%	<0.001	1 (1, 2) mmol/mol 0.1 (0.1, 0.2)%	<0.001
12 to <18 years	11 (10, 11) mmol/mol 1.0 (0.9, 1.0)%	<0.001	6 (5, 7) mmol/mol 0.6 (0.5, 0.7)%	<0.001	1 (1, 2) mmol/mol 0.1 (0.1, 0.2)%	<0.001	6 (4, 7) mmol/mol 0.5 (0.4, 0.6)%	<0.001	2 (2, 3) mmol/mol 0.2 (0.2, 0.3)%	<0.001
18 to <30 years	7 (6, 8) mmol/mol 0.6 (0.5, 0.7)%	<0.001	5 (4, 7) mmol/mol 0.5 (0.3, 0.6)%	<0.001	1 (0, 2) mmol/mol 0.1 (0.0, 0.2)%	0.131	6 (5, 8) mmol/mol 0.6 (0.4, 0.8)%	<0.001	2 (0, 3) mmol/mol 0.2 (0.0, 0.3)%	0.032
30 to <50 years	-1 (-2, 0) mmol/mol -0.1 (-0.2, 0.0)%	0.198	2 (1, 4) mmol/mol 0.2 (0.1, 0.3)%	0.007	4 (2, 5) mmol/mol 0.3 (0.2, 0.5)%	<0.001	5 (3, 7) mmol/mol 0.4 (0.3, 0.6)%	<0.001	2 (-4, 8) mmol/mol 0.2 (-0.3, 0.7)%	0.455
≥50 years	1 (0, 2) mmol/mol 0.1 (0.0, 0.2)%	0.025	1 (0, 2) mmol/mol 0.1 (0.0, 0.2)%	0.256	0 (-2, 1) mmol/mol 0.0 (-0.1, 0.1)%	0.662	7 (4, 9) mmol/mol 0.6 (0.4, 0.8)%	<0.001	6 (2, 10) mmol/mol 0.5 (0.1, 0.9)%	0.007

CGM, continuous glucose monitoring; T1DX, T1D Exchange Registry.

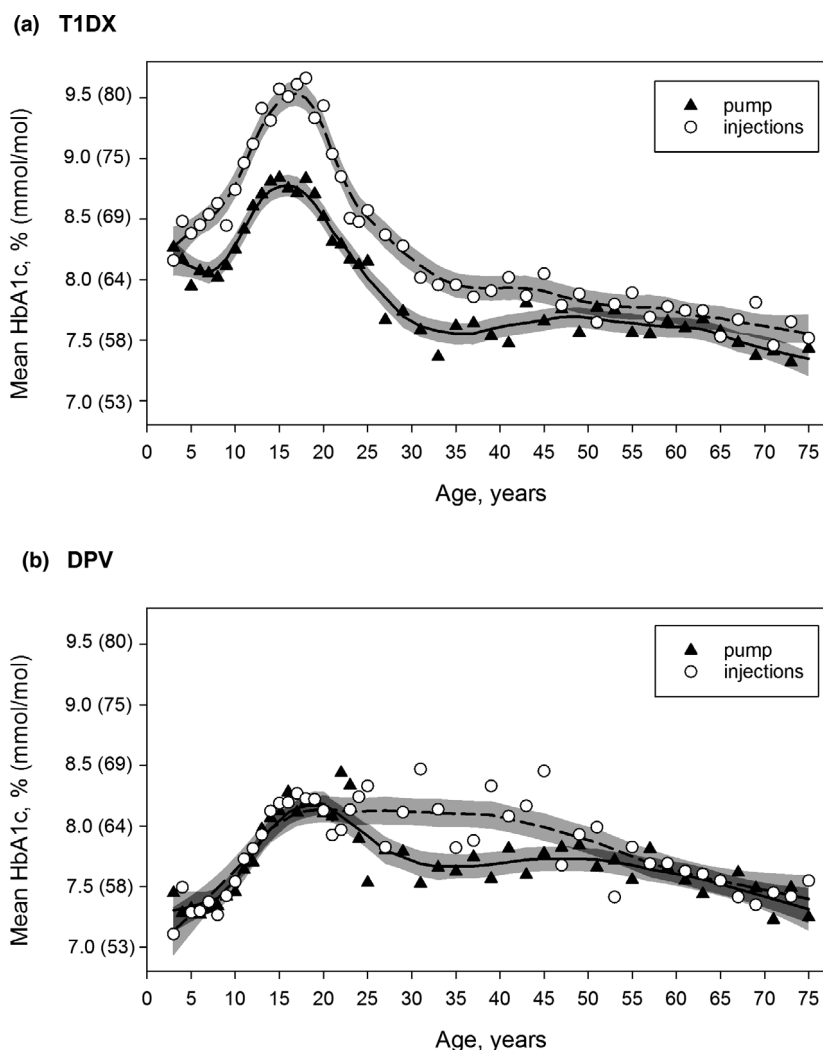
Difference in HbA<sub>1c</sub> given as estimated mean with 95% CI.

\*Adjusted for duration of type 1 diabetes, sex, obesity, insulin delivery method (injections vs pump use), CGM use, and minority status.

†Adjusted for duration of diabetes, sex, obesity, CGM use and minority status.

‡Adjusted for duration of diabetes, sex, obesity, insulin delivery method (injections vs pump use) and CGM use.

§P values adjusted for multiple testing.



**FIGURE 2** Mean most recent HbA<sub>1c</sub> by age (1-year intervals for individuals aged  $\leq 25$  years, 2-year intervals for individuals aged  $> 25$  years) in (a) Type 1 Diabetes Exchange Registry (T1DX) and (b) German/Austrian Prospective Diabetes Follow-up Registry (DPV). Solid and dashed lines represent locally weighted scatterplot smoothing curves for pump and injections users, respectively. Grey areas represent corresponding 95% CIs.

### Percentage of individuals achieving HbA<sub>1c</sub> targets

Among individuals in the DPV aged  $< 6$  years, 6 to  $< 12$  years and 12 to  $< 18$  years, 59%, 41% and 39%, respectively, achieved the ISPAD HbA<sub>1c</sub> target of  $< 58$  mmol/mol (7.5%); the respective percentages in the T1DX were lower (26%, 22% and 16%). In all three adult age groups, the percentage of individuals with HbA<sub>1c</sub> values  $< 58$  mmol/mol (7.5%) or  $< 53$  mmol/mol (7.0%) was higher in the DPV than in the T1DX (Table 2).

### Discussion

In this cross-sectional lifespan comparison, significant differences in HbA<sub>1c</sub> were noted between two diabetes registries, with disparities more pronounced in early childhood through to young adulthood. The difference in HbA<sub>1c</sub> levels between

pump and injection users was larger in the USA than in Germany and Austria, whereas differences in HbA<sub>1c</sub> levels between the sexes were found in Germany and Austria only. The higher HbA<sub>1c</sub> in young people in the USA compared to Germany/Austria may be related to systemic differences in access to medical care, diabetes education, provider prescribing practices, regulatory approval and insurance coverage of advanced technologies; as well as differences in patient self-management including adherence to treatment regimen, eating patterns, nutrient content of meals or snacks, and level of physical activity [11–14]. The high percentage of insulin pump use in the adult participants in the T1DX is in part attributable to the fact that the adults who receive their care at specialized diabetes clinics are more likely to be offered and interested in diabetes technology. This may not be representative of pump use in the general adult population with type 1 diabetes in the USA.



In both the USA and Europe, quarterly follow-up of people receiving type 1 diabetes care is recommended. A DPV study in individuals with type 1 diabetes aged <20 years reported a mean  $\pm$  SD of  $4.8 \pm 2.5$  visits per year [15]. In adults, the median HbA<sub>1c</sub> testing frequency was 8 (5; 9) times per 2 years, with 64% of the individuals being categorized as undergoing 'frequent' HbA<sub>1c</sub> testing (at least seven HbA<sub>1c</sub> measurements per 2 years) [16]. Transition from paediatric to adult care is a crucial time, however, and is often associated with deterioration of metabolic control [17–19]. In a T1DX survey of young adults aged 18 to <30 years who had already transitioned to adult care, 21% of the respondents reported a gap of >6 months between paediatric and adult diabetes care [17]. A DPV study even indicated that 60% of individuals with type 1 diabetes transitioning from paediatric to adult care had a period of >1 year between the last paediatric care visit and the first adult care visit [18].

Limitations of the present study are that the methods of data collection differ between the two registries and that HbA<sub>1c</sub> was not measured in a central laboratory. Nevertheless, all the HbA<sub>1c</sub> values were DCCT-standardized. In addition, a previous joint T1DX and DPV analysis in the paediatric population showed that differences in HbA<sub>1c</sub> were not attributable to differences in laboratory methods [20]. The DPV database comprises 70–90% of all potential paediatric individuals with type 1 diabetes in Germany and Austria, whereas it is not population-based for adults. All individuals in Germany and Austria are covered by statutory (90%) or private health (10%) insurance [21]. The T1DX includes a sample of specialized diabetes clinics in the USA, and uninsured individuals are probably under-represented in the cohort [6]; therefore, it is possible that HbA<sub>1c</sub> levels in the USA are underestimated, especially in adults, who are more likely to visit general practitioners/primary care settings to obtain prescriptions for diabetes treatment supply. Another limitation of this cross-sectional study is that it did not account for the period of pump or injection use, which could diminish the ability to detect differences in HbA<sub>1c</sub> between the insulin delivery methods. As the US concept of race/ethnicity is not transferable to Germany, minority status based on race/ethnicity for the T1DX and migration background for the DPV was used instead. Although the two definitions do not capture the same minority groups, previous comparisons between young people in the T1DX vs the DPV found minority status to be associated with worse glycaemic control [6,22]. In adults, however, migration background might be under-reported in the DPV database, and it represents a very heterogeneous group of individuals (e.g. older adults of German ancestry who were expelled after the end of World War II from various Eastern and Central European territories that had been occupied or annexed by Nazi Germany, or migrant workers mainly from Southern Europe who moved to Germany in the 1950s to 1970s).

Despite these limitations, the data provide a contemporary picture of glycaemic control across the lifespan in two large

cohorts. Both cohorts report a consistent elevation in HbA<sub>1c</sub> with adolescence, but HbA<sub>1c</sub> was  $\sim 11$  mmol/mol (1.0%) higher at all ages in the T1DX as compared to the DPV in paediatric care, whereas HbA<sub>1c</sub> is more similar in the two registries after the age of 30 years. It is concerning that, unlike HbA<sub>1c</sub> levels in young people in the DPV, HbA<sub>1c</sub> in those in the T1DX has not improved since the report of 2010–2012 data [9,22]. Further research to determine the causes of health outcome-related disparities between registries is critical to inform the design of quality improvement interventions, clinical trials of new treatment approaches, and innovative technologies/therapeutics to improve glycaemic control and patient-centred outcomes on both continents.

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### References

- 1 Rewers MJ, Pillay K, de Beaufort C, Craig ME, Hanas R, Acerini CL *et al.* ISPAD Clinical Practice Consensus Guidelines 2014. Assessment and monitoring of glycemic control in children and adolescents with diabetes. *Pediatr Diabetes* 2014; 15 (Suppl. 20): 102–114.
- 2 American Diabetes Association (ADA). Standards of Medical Care in Diabetes - 2017, 6. Glycemic Targets. *Diabetes Care* 2017; 40 (Suppl 1): S48–S56.
- 3 Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften. *S3-Leitlinie: Therapie des Typ-1-Diabetes. 2. Auflage*,

2018. Available at <https://www.awmf.org/leitlinien/detail/ll/057-013.html> Last accessed 07 October 2019.
- 4 Rami-Merhar B, Frohlich-Reiterer E, Hofer SE. Diabetes in the youth. *Wien Klin Wochenschr* 2016; 128: S119–123.
  - 5 Charalampopoulos D, Hermann JM, Svensson J, Skriverhaug T, Maahs DM, Akesson K *et al.* Exploring Variation in Glycemic Control Across and Within Eight High-Income Countries: A Cross-sectional Analysis of 64,666 Children and Adolescents With Type 1 Diabetes. *Diabetes Care* 2018; 6: 1180–1187.
  - 6 Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA *et al.* Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. *Diabetes Care* 2015; 6: 971–978.
  - 7 Haynes A, Hermann JM, Miller KM, Hofer SE, Jones TW, Beck RW *et al.* Severe hypoglycemia rates are not associated with HbA<sub>1c</sub>: a cross-sectional analysis of 3 contemporary pediatric diabetes registry databases. *Pediatr Diabetes* 2017; 7: 643–650.
  - 8 Schwandt A, Hermann JM, Rosenbauer J, Boettcher C, Dunstheimer D, Grulich-Henn J *et al.* Longitudinal Trajectories of Metabolic Control From Childhood to Young Adulthood in Type 1 Diabetes From a Large German/Austrian Registry: A Group-Based Modeling Approach. *Diabetes Care* 2017; 3: 309–316.
  - 9 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: 66–72.
  - 10 Rosenbauer J, Dost A, Karges B, Hungele A, Stahl A, Bachle C *et al.* Improved metabolic control in children and adolescents with type 1 diabetes: a trend analysis using prospective multicenter data from Germany and Austria. *Diabetes Care* 2012; 1: 80–86.
  - 11 Lyons SK, Hermann JM, Miller KM, Hofer SE, Foster NC, Rami-Merhar BM *et al.* Use of Adjuvant Pharmacotherapy in Type 1 Diabetes: International Comparison of 49,367 Individuals in the Diabetes Prospective Follow-up and T1D Exchange Registries. *Diabetes Care* 2017; dc170403.
  - 12 Weinstock RS, Schutz-Fuhrmann I, Connor CG, Hermann JM, Maahs DM, Schutt M *et al.* Type 1 diabetes in older adults: Comparing treatments and chronic complications in the United States T1D Exchange and the German/Austrian DPV registries. *Diabetes Res Clin Pract* 2016; 122: 28–37.
  - 13 Simmons JH, Chen V, Miller KM, McGill JB, Bergenstal RM, Goland RS *et al.* Differences in the management of type 1 diabetes among adults under excellent control compared with those under poor control in the T1D Exchange Clinic Registry. *Diabetes Care* 2013; 11: 3573–3577.
  - 14 McCarthy MM, Grey M. Type 1 Diabetes Self-Management From Emerging Adulthood Through Older Adulthood. *Diabetes Care* 2018; 41(8): 1608–1614.
  - 15 Karges B, Schwandt A, Heidtmann B, Kordonouri O, Binder E, Schierloh U *et al.* Association of Insulin Pump Therapy vs Insulin Injection Therapy With Severe Hypoglycemia, Ketoacidosis, and Glycemic Control Among Children, Adolescents, and Young Adults With Type 1 Diabetes. *JAMA* 2017; 14: 1358–1366.
  - 16 Schwandt A, Best F, Biester T, Grunerbel A, Kopp F, Krakow D *et al.* Both the frequency of HbA<sub>1c</sub> testing and the frequency of self-monitoring of blood glucose predict metabolic control: A multicentre analysis of 15 199 adult type 1 diabetes patients from Germany and Austria. *Diabetes Metab Res Rev* 2017; 33: 7: <https://doi.org/10.1002/dmrr.2908>. Epub 2017 Jun 14.
  - 17 Garvey KC, Foster NC, Agarwal S, DiMeglio LA, Anderson BJ, Corathers SD *et al.* Health Care Transition Preparation and Experiences in a U.S. National Sample of Young Adults With Type 1 Diabetes. *Diabetes Care* 2017; 3: 317–324.
  - 18 Kapellen TM, Muther S, Schwandt A, Grulich-Henn J, Schenk B, Schwab KO *et al.* Transition to adult diabetes care in Germany-High risk for acute complications and declining metabolic control during the transition phase. *Pediatr Diabetes* 2018; <https://doi.org/10.1111/pedi.12687>. [Epub ahead of print].
  - 19 Campbell F, Biggs K, Aldiss SK, O'Neill PM, Clowes M, McDonagh J *et al.* Transition of care for adolescents from paediatric services to adult health services. *Cochrane Database Syst Rev* 2016; 4: CD009794.
  - 20 Maahs DM, Hermann JM, DuBose SN, Miller KM, Heidtmann B, DiMeglio LA *et al.* Contrasting the clinical care and outcomes of 2,622 children with type 1 diabetes less than 6 years of age in the United States T1D Exchange and German/Austrian DPV registries. *Diabetologia* 2014; 8: 1578–1585.
  - 21 European Commission, Directorate-General for Economic and Financial Affairs, Economic Policy Committee, Ageing Working Group. Germany. Health Care & Long-Term Care Systems. An excerpt from the Joint Report on Health Care and Long-Term Care Systems & Fiscal Sustainability. Institutional Paper 37, 2016. Available at [https://ec.europa.eu/info/sites/info/files/file\\_import/joint-report\\_de\\_en\\_2.pdf](https://ec.europa.eu/info/sites/info/files/file_import/joint-report_de_en_2.pdf) Last accessed 07 October 2019.
  - 22 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; 1: 87–91.