Current State of Type 1 Diabetes Treatment in the U.S.: Updated Data From the T1D Exchange Clinic Registry

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To examine the overall state of metabolic control and current use of advanced diabetes technologies in the U.S., we report recent data collected on individuals with type 1 diabetes participating in the T1D Exchange clinic registry. Data from 16,061 participants updated between 1 September 2013 and 1 December 2014 were compared with registry enrollment data collected from 1 September 2010 to 1 August 2012. Mean hemoglobin A_{1c} (HbA_{1c}) was assessed by year of age from <4 to >75 years. The overall average HbA_{1c} was 8.2% (66 mmol/mol) at enrollment and 8.4% (68 mmol/mol) at the most recent update. During childhood, mean HbA_{1c} decreased from 8.3% (67 mmol/mol) in 2–4-year-olds to 8.1% (65 mmol/mol) at 7 years of age, followed by an increase to 9.2% (77 mmol/mol) in 19-year-olds. Subsequently, mean HbA_{1c} values decline gradually until ~30 years of age, plateauing at 7.5–7.8% (58–62 mmol/mol) beyond age 30 until a modest drop in HbA_{1c} below 7.5% (58 mmol/mol) in those 65 years of age. Severe hypoglycemia (SH) and diabetic ketoacidosis (DKA) remain all too common complications of treatment, especially in older (SH) and younger patients (DKA). Insulin pump use increased slightly from enrollment (58–62%), and use of continuous glucose monitoring (CGM) did not change (7%). Although the T1D Exchange registry findings are not population based and could be biased, it is clear that there remains considerable room for improving outcomes of treatment of type 1 diabetes across all age-groups. Barriers to more effective use of current treatments need to be addressed and new therapies are needed to achieve optimal metabolic control in people with type 1 diabetes.

Results of the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) follow-up study of the DCCT cohort have demonstrated that most people with type 1 diabetes should be treated intensively to achieve hemoglobin A_{1c} (HbA_{1c}) levels as close to normal as possible and as early in the course of the disease as possible to prevent and delay the late micro- and macrovascular complications of the disease (1). Most recently, the DCCT/EDIC study group reported that all-cause mortality also was reduced over 30 years of follow-up during DCCT/EDIC in the original DCCT intensive treatment group compared with the original conventional treatment group (2). Consequently, the American Diabetes Association (ADA) treatment guidelines indicate that adults with type 1 diabetes should aim at target HbA_{1c} levels <7.0% (53 mmol/mol) unless there is a reason, such as recurrent severe hypoglycemia (SH), to set a higher target, whereas the target is set slightly higher in children and adolescents at <7.5% (58 mmol/mol) by both the ADA and the International Society for Pediatric and Adolescent Diabetes (ISPAD) (3,4).

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Compared with treatment methods used in the DCCT 20–30 years ago, rapid- and long-acting insulin analogs, improved insulin pumps and blood glucose meters, continuous glucose monitoring (CGM) devices, and integrated sensor-augmented insulin pump systems with automatic threshold suspend capabilities have provided clinicians and patients with new tools to achieve target HbA_{1c} levels more readily and safely (5). Whether and to what extent these advances in diabetes technology have been translated into better glycemic control in patients with type 1 diabetes in the U.S. has not been established due, in part, to the lack of a broad-based, large-scale, multisite registry that covered patients at all ages across the life span. Supported by a grant by the Helmsley Charitable Trust, the T1D Exchange Clinic Network was established to fill this gap. Leading adult and pediatric diabetes treatment centers with a wide geographical distribution throughout the U.S. (Supplementary Fig. 1) are participating in the T1D Exchange Clinic Network, with the Jaeb Center for Health Research in Tampa, FL serving as the coordinating center. The first initiative of the T1D Exchange Clinic Network was the establishment of the T1D Exchange clinic registry.

Initially, 25,833 participants who ranged in age from 2 to 95 years were enrolled into the registry between September 2010 and August 2012. A comprehensive set of baseline clinical, laboratory, and demographic data were obtained for each participant at registry enrollment and the core data have been updated annually. The data collected at baseline have provided a number of particularly notable findings (Supplementary Table 1), including showing that most adults and children with type 1 diabetes were not achieving HbA_{1c} goals set by the ADA and ISPAD (6–8); that there was a relationship between increased frequency of blood glucose testing and lower HbA_{1c} levels (9); that ethnic/racial and socioeconomic factors played a role in differences in metabolic control and use of insulin pumps in youth with type 1 diabetes (10); that diabetic ketoacidosis (DKA) occurred less frequently in insulin pump users than injection users (11,12); and that CGM was being used by only a small proportion of adults and children with type 1 diabetes (13).

In this article we report the results of the most recent follow-up data for registry participants—data that have allowed us to prospectively assess trends in outcomes over time. We examine the current state of metabolic control and use of advanced diabetes technologies and whether cross-sectional changes have occurred over time, as well as assess the current frequencies of SH and DKA by participant self-report.

METHODS

The T1D Exchange Clinic Network currently includes 76 U.S.-based pediatric and adult endocrinology practices in 33 states. Seventeen of the centers primarily care for adult patients, 38 primarily care for pediatric patients, and 21 care for both; 58 are institution based, 17 are community based, and 1 is in a managed care setting. During the initial registry enrollment period, 25,833 individuals with type 1 diabetes (14,593 $<$18 years old and 11,240 $\geq$18 years old) were enrolled. Details on the eligibility criteria, informed consent process, and baseline data collection have been reported previously (14). Core enrollment data are updated annually from medical records of all participants who had at least one clinic visit in the prior year. New modules concerning issues not addressed at enrollment have been designed for subsets of participants during annual updates.

This report includes data from 16,061 participants for whom an annual update was completed between 1 September 2013 and 1 December 2014 who had an available HbA_{1c} value associated with the office visit used for the medical record update. Participants with a history of pancreas or islet cell transplantation and those pregnant at the time of the most recent annual update were excluded. This report also includes the responses to a detailed questionnaire directed at specific aspects of diabetes management completed by a subset of 2,561 participants who chose to complete an electronic questionnaire during 2013. For the 16,061 with an annual update, clinical characteristics and diabetes management at the time of the most recent annual update were tabulated according to age-group. Use of an insulin pump and CGM were obtained from clinic medical records, and the frequency of self-monitoring of blood glucose (SMBG) was from the meter download at the clinic visit (available for 10,555 [66%] participants). Due to the variability and incompleteness of medical record recording of SH and DKA, the occurrence of these events during the prior 3 months was based on self-report data obtained from the subset of participants/caregivers who completed the web-based questionnaire. SH was defined as a participant-reported event that resulted in loss of consciousness or seizure. DKA was defined as participant-reported DKA diagnosed by a doctor that required treatment in a health care facility. Cross-sectional comparisons of data collected at enrollment were compared with the most recent update data for the 13,848 of the 16,061 participants who already had diabetes for at least 1 year at the time of initial registry enrollment. Cross-sectional comparisons of the occurrences of DKA and SH at enrollment versus recent update were not performed due to differences in the way in which events were collected between the two time points. In order to assess HbA_{1c} over the life span, participants were grouped by year of age at the time of the most recent HbA_{1c} value available (87% measured with an in-clinic point of care device, 11% local laboratory, and 2% unknown), and a mean HbA_{1c} was computed for that age using data from each of the 16,061 participants with a recent update. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

At the time of the most recent update, the 16,061 participants ranged in age from 2.7 to 93.9 years old, duration of type 1 diabetes ranged from 1.5 to 83.1 years, and 50% were female and 83% non-Hispanic white. Socioeconomic factors and clinical and diabetes management characteristics of the cohort stratified by age-group are shown in Table 1. Among participants with diabetes duration of $\geq$1 year at the time of registry enrollment, those with a recent update had a slightly lower HbA_{1c} at enrollment compared with those who did not have an update, particularly in participants $>$13 years of age (Supplementary Table 2).

Metabolic Control

Compared with the overall average HbA_{1c} of 8.2 $\pm$1.4% (66 $\pm$ 15.3 mmol/mol) at enrollment, the average HbA_{1c} was 8.4 $\pm$1.6% (68 $\pm$ 17.5 mmol/mol) at the most recent update, with the worsening over time largely being limited to the 13–25-year-olds (Table 2).

Table 1—Participant characteristics

	Overall	2–5 years old	6–12 years old	13–17 years old	18–25 years old	26–49 years old	≥50 years old
	n = 16,061	*n* = 236	*n* = 3,313	*n* = 4,914	*n* = 2,867	*n* = 2,606	*n* = 2,125
Demographic and clinical characteristics							
Race/ethnicity, *n* (%)							
White non-Hispanic	13,310 (83)	179 (76)	2,610 (79)	3,823 (78)	2,357 (82)	2,327 (89)	2,014 (95)
Black non-Hispanic	740 (5)	16 (7)	164 (5)	292 (6)	124 (4)	89 (3)	55 (3)
Hispanic or Latino	1,294 (8)	25 (11)	336 (10)	540 (11)	263 (9)	106 (4)	24 (1)
Other	699 (4)	16 (7)	194 (6)	255 (5)	121 (4)	81 (3)	32 (2)
Annual household income, *n* (%)‡							
<$50,000	3,540 (30)	76 (38)	823 (32)	1,045 (29)	514 (28)	652 (30)	430 (27)
$50,000 to <$100,000	4,299 (36)	77 (39)	934 (36)	1,246 (34)	639 (35)	814 (38)	589 (37)
≥$100,000	4,116 (34)	45 (23)	845 (32)	1,324 (37)	653 (36)	693 (32)	556 (35)
Education level, *n* (%)‡							
Less than Bachelor's degree	6,459 (49)	98 (44)	1,415 (46)	2,153 (46)	1,229 (91)	937 (38)	927 (47)
Bachelor's degree	3,959 (29)	60 (27)	926 (30)	1,324 (29)	120 (9)	993 (40)	536 (27)
Master's, professional, or doctorate	3,072 (22)	64 (28)	786 (25)	1,146 (25)	5 (<1)	554 (23)	517 (26)
Insurance status, *n* (%)							
Private	11,226 (77)	153 (70)	2,263 (73)	3,378 (75)	1,816 (77)	2,068 (85)	1,548 (76)
Other	3,254 (22)	64 (29)	822 (27)	1,096 (24)	507 (22)	321 (13)	444 (22)
None	149 (1)	1 (<1)	13 (<1)	24 (<1)	26 (1)	53 (2)	32 (2)
Duration of diabetes, mean ± SD	13.3 ± 11.9	3.1 ± 0.8	5.5 ± 2.3	7.6 ± 3.6	11.1 ± 4.9	27.7 ± 10.1	32.6 ± 14.8
Duration group, *n* (%)							
1 to <5 years	3,766 (23)	232 (98)	1,630 (49)	1,433 (29)	314 (11)	120 (5)	37 (2)
5 to <10 years	5,027 (31)	4 (2)	1,517 (46)	2,154 (44)	962 (34)	269 (10)	121 (6)
10 to <20 years	4,095 (25)		166 (5)	1,327 (27)	1,481 (52)	794 (30)	327 (15)
20 to <30 years	1,382 (9)				110 (4)	847 (33)	425 (20)
30 to <40 years	949 (6)					477 (18)	472 (22)
≥40 years	842 (5)					99 (4)	743 (35)
BMI *z* score, mean ± SD	0.4 ± 1.1	0.8 ± 0.9	0.6 ± 1.1	0.8 ± 1.0	0.2 ± 1.3	0.1 ± 1.1	−0.1 ± 0.9
BMI group, *n* (%)*							
Underweight/normal weight	7,863 (54)	136 (59)	2,257 (69)	2,885 (59)	1,443 (55)	639 (32)	503 (32)
Overweight	4,120 (28)	53 (23)	651 (20)	1,237 (25)	837 (31)	729 (37)	613 (39)
Obese	2,633 (18)	42 (18)	388 (12)	745 (15)	389 (15)	610 (31)	459 (29)
Diabetes management							
Pump use, *n* (%)	9,530 (60)	146 (63)	2,131 (65)	2,810 (58)	1,555 (55)	1,625 (63)	1,263 (60)
CGM use, *n* (%)	1,703 (11)	31 (13)	263 (8)	249 (5)	193 (7)	590 (23)	377 (18)
SMBG, mean ± SD#	4.7 ± 2.7	7.4 ± 2.9	6.2 ± 2.6	4.2 ± 2.3	3.5 ± 2.4	4.3 ± 2.7	4.8 ± 2.7
0–3 times per day	3,630 (34)	3 (2)	253 (11)	1,316 (39)	994 (55)	689 (41)	375 (30)
4–6 times per day	4,781 (45)	63 (37)	1,174 (50)	1,575 (47)	625 (35)	712 (43)	632 (51)
6–9 times per day	1,566 (15)	75 (44)	627 (27)	360 (11)	124 (7)	193 (12)	187 (15)
≥10 times per day	578 (5)	28 (17)	286 (12)	87 (3)	48 (3)	73 (4)	56 (4)
Downloading of meter at home, *n* (%)§							
≥1 time per month	298 (12)	6 (13)	92 (17)	73 (16)	40 (9)	49 (7)	38 (9)
Never	1,671 (65)	33 (70)	277 (52)	252 (55)	310 (69)	506 (77)	293 (71)
Noninsulin medications for blood glucose control, *n* (%)							
Metformin	515 (3)	0	12 (<1)	121 (2)	100 (3)	168 (6)	114 (5)
GLP-1 agonist	116 (<1)	0	0	2 (<1)	18 (<1)	64 (2)	32 (2)
DPP-4*i*	12 (<1)	0	0	0	0	9 (<1)	3 (<1)
SGLT2*i*	14 (<1)	0	0	0	0	9 (<1)	5 (<1)
Pramlintide	128 (<1)	0	1 (<1)	2 (<1)	11 (<1)	61 (2)	53 (2)
Other‖	30 (<1)	0	0	0	1 (<1)	12 (<1)	17 (<1)

‡Income data missing for 4,106 participants, education data missing for 2,271 participants, and insurance data missing for 1,432 participants. Education level is the parents' highest education level for participants <18 years of age and is the participants' education level for participants >18 years of age. *Underweight/normal weight defined as <85th BMI percentile adjusted for age and sex for participants <20 years of age and BMI <25 for adults ≥20 years of age. Overweight defined as 85th to <95th BMI percentile for participants <20 years of age and BMI 25 to <30 for adults ≥20 years of age. Obese defined as ≥95th BMI percentile for participants <20 years of age and BMI ≥30 for adults ≥20 years of age. #SMBG from meter download was available for 10,555 participants. §Only available for a subset of participants who completed an electronic questionnaire asking about insulin and device use; *n* = 2,561 (*n* = 47 for 2–5 years, 534 for 6–12 years, 455 for 13–17 years, 451 for 18–25 years, 661 for 26–49 years, and 413 for ≥50 years). ‖Includes thiazolidinediones and sulfonylureas.

As shown in Fig. 1, the mean of the most recent HbA_{1c} levels varied considerably with age. During childhood, mean HbA_{1c} levels decreased from 8.3% (67 mmol/mol) in 2–4-year-olds to 8.1% (65 mmol/mol) at 7 years of age, followed by an increase to 9.2% (77 mmol/mol) in 19-year-olds. Subsequently, mean HbA_{1c} values showed a gradual decline until ~30 years of age, plateauing at a level of 7.5–7.8% (58–62 mmol/mol) beyond age 30 until a modest drop in HbA_{1c} below 7.5% (58 mmol/mol) after 65 years of age. The ADA HbA_{1c} goal of <7.5% (58 mmol/mol) was achieved by only a small percentage of children and adolescents <18 years of age (17–23%), and even fewer 18–25-year-olds (14%) met the ADA goal for adults of <7.0% (53 mmol/mol); this percentage increased to ~30% in older adults (Fig. 2).

As previously reported, across all age-groups, HbA_{1c} was highest among non-Hispanic black participants, participants with lower annual household income, and those who performed SMBG less than four times per day (Table 3). On average, participants using an insulin pump or continuous glucose monitor tended to have lower HbA_{1c} values (Table 3).

Utilization of Diabetes Technologies, Insulin, and Other Glucose-Lowering Agents

An insulin pump was being used by 60% of participants, ranging from a low of 55% in 18–25-year-olds to 65% in 6–12-year-olds. In a cross-sectional comparison of enrollment with most recent update, the greatest relative increase in pump use was in pediatric participants likely due to an increase in mean diabetes duration, whereas pump use did not change in 18–25-year-olds and increased only slightly in older participants (Tables 1 and 2).

Across all age-groups, the use of CGM was more frequent at most recent update compared with enrollment and the frequency of SMBG by meter download did not change from enrollment; on both occasions, the frequency of SMBG was highest but CGM use was lowest in pediatric patients. Nearly two-thirds of patients/families reported never downloading SMBG data.

Insulin aspart was being used in pumps slightly more frequently than insulin lispro (Supplementary Table 3). Among injection users, lispro was the most common rapid-acting insulin being used and glargine the most common long-acting insulin (Supplementary Table 3). Use of glucose-lowering agents as adjuncts to insulin treatment of type 1 diabetes was uncommon across all age-groups. Metformin was the most common noninsulin glucose-lowering drug being used but only by 6% of those ≥26 years of age. No other noninsulin drug was being used by >2% of those ≥26 years of age or by >1% of younger participants.

SH and DKA

Among the subset of 2,561 participants who completed the participant questionnaire, 6% reported having had a seizure or loss of consciousness due to hypoglycemia in the prior 3 months, with the highest occurrence being among those who were 50 years old or older. An increase in frequency of SH with increasing age and duration of diabetes was also observed on enrollment (12). Insulin pump use was associated with a lower frequency of SH. Participants across all age-groups who

Table 2—Comparison of enrollment and most current registry data*

	Overall	Age at most current registry data					
		2–5 years old	6–12 years old	13–17 years old	18–25 years old	26–49 years old	≥50 years old
	Enrollment/ Current	Enrollment/ Current	Enrollment/ Current	Enrollment/ Current	Enrollment/ Current	Enrollment/ Current	Enrollment/ Current
n	13,848	522/54	4,061/2,347	3,213/4,065	1,686/2,717	2,553/2,557	1,810/2,108
Age, mean	23.6/26.4	4.1/4.9	9.6/10.0	14.7/15.1	20.4/20.6	37.4/37.3	60.0/61.1
Duration, mean	11.7/15.0	1.9/4.2	4.2/6.5	6.4/8.5	10.1/11.6	20.3/22.0	30.1/32.9
Pump use, %	58/62	50/69	58/68	57/61	56/56	61/64	58/61
CGM use, %	7/11	4/15	4/8	3/5	5/7	15/23	15/18
CGM device type, %							
Medtronic	53/39	—	60/21	62/41	47/38	52/41	51/43
Dexcom	45/61	—	34/79	34/59	52/62	47/59	48/57
Abbott	2/0	—	5/0	3/0	0/0	<1/0	<1/0
HbA_{1c}, mean, % (mmol/mol)	8.2/8.4 (66/68)	8.2/8.2 (66/66)	8.3/8.5 (67/69)	8.7/9.0 (72/75)	8.3/8.7 (67/72)	7.7/7.7 (61/61)	7.6/7.6 (60/60)
HbA_{1c} <7.5% (58 mmol/mol)	32/29	24/22	24/20	21/16	31/25	50/48	49/50
HbA_{1c} <7.0% (53 mmol/mol)	17/15	10/7	9/7	9/6	17/13	30/29	29/29
SMBG per day, mean#	5.1/4.7	7.1/7.1	6.0/6.2	4.3/4.3	4.0/3.5	4.7/4.5	5.0/5.0
Downloading of meter at home ≥1 times per month, %§	12/11	20/20	20/15	10/14	5/9	8/8	13/9

Severe hypoglycemia and DKA frequencies were not compared due to changes in how the data were collected. Dash (—) indicates *n* <20.
*Enrollment data were collected from 1 September 2010 to 1 August 2012. Current data were collected from 1 September 2013 to 1 December 2014. There are less participants in the younger age-groups for the current update data due to aging over time and they are included in the older age-groups. #Available for 5,787 participants with a meter download in the medical record at enrollment and most recent clinic visit. §Available for 2,124 participants who completed the participant questionnaire and did not respond "Don't know."

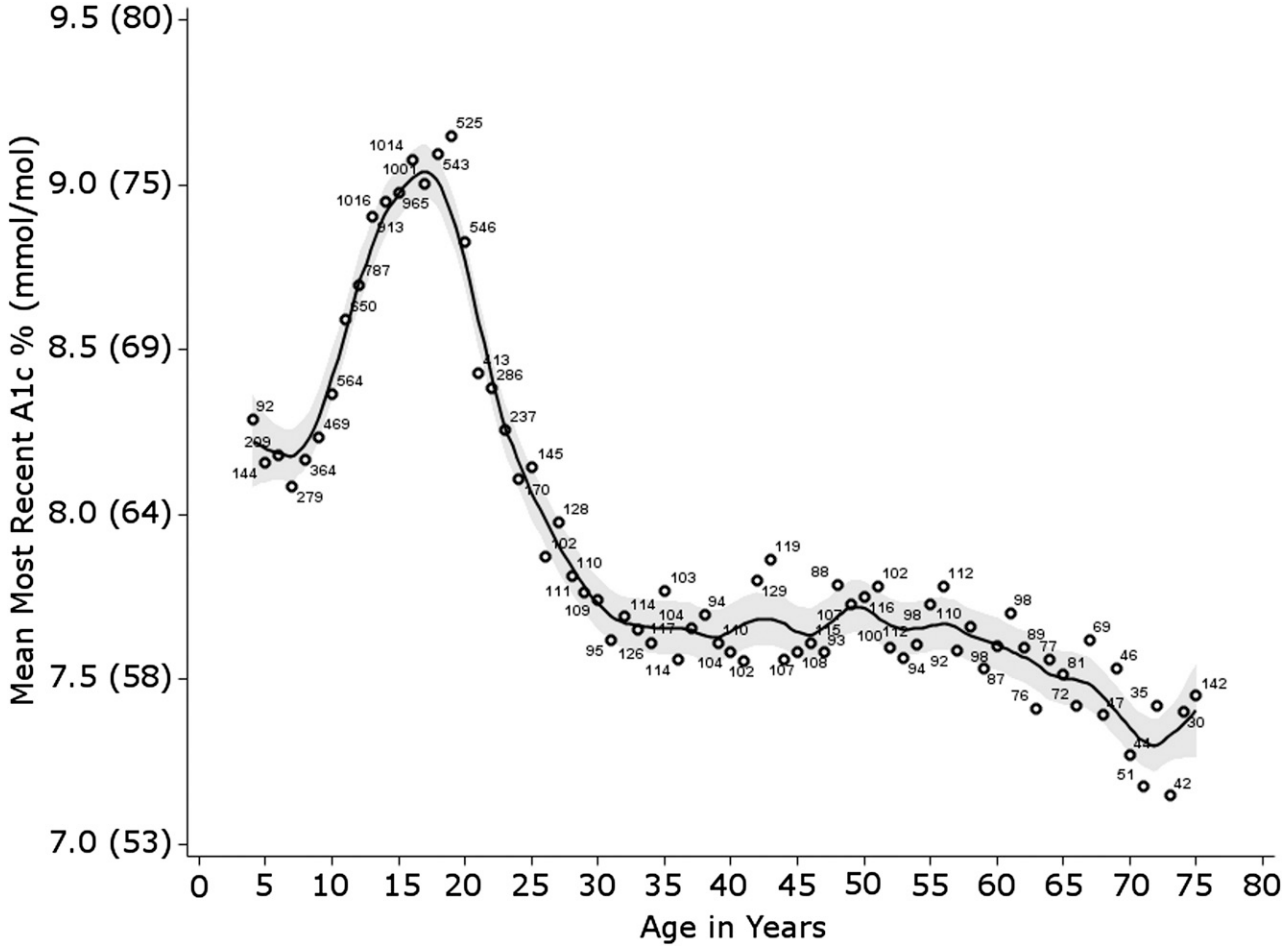

Figure 1—Mean HbA_{1c} by age. Average HbA_{1c} for each year of age was plotted using the most recent HbA_{1c} value available for each of the 16,057 participants with a recent update. The line was estimated using local regression scatter plot smoothing (LOESS), which is a nonparametric method for estimating the regression equation that fits a smoothing parameter. Circles represent the mean HbA_{1c} for each year of age. Participants <4 years were lumped as age 4 and participants ≥75 years were lumped at age 75. Gray shaded area represents the 95% CI around the smoothed LOESS line. Numbers next to circles are the *n* for each year of age.

achieved lower HbA_{1c} levels did so without increased frequency of SH (Table 4).

At least one DKA event in the prior 3 months was reported by 3% of the 2,561 participants, with the highest occurrence being young adults (5%). With the exception of the 2–5-year-old age-group where the sample size was small, the frequency of DKA tended to be higher among participants with higher HbA_{1c} levels and slightly lower among participants using an insulin pump.

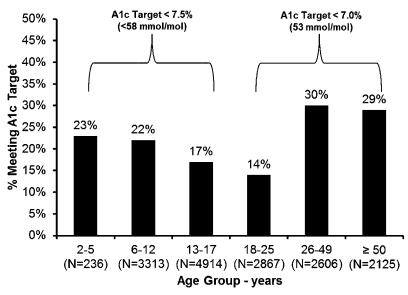

Figure 2—Percent of patients achieving HbA_{1c} ADA targets by age-group. HbA_{1c} target for those aged <18 years is <7.5% (<58 mmol/mol). HbA_{1c} target for those aged ≥18 years is <7.0% (<53 mmol/mol).

CONCLUSIONS

The HbA_{1c} data collected by the T1D Exchange clinic registry at a large, geographically diverse number of pediatric and adult diabetes treatment centers provide an up-to-date picture of metabolic control of type 1 diabetes across the life span. A positive aspect of these data is that the mean HbA_{1c} levels in patients ≥30 years of age are lower than the ~8.0% (~64 mmol/mol) that has been observed in DCCT/EDIC patients during the past 20 years (1). The most troubling aspect of the data is that the mean HbA_{1c} level of 9.0% (75 mmol/mol) in 13–17-year-olds in the registry is only slightly lower than the 9.5% (80 mmol/mol) seen in 13–17-year-olds at the start of the DCCT in the 1980s (15). Clearly, advances in diabetes management over the past two decades have been less successful in overcoming the special challenges in managing teenagers than adults with type 1 diabetes. Our data also indicate that the majority of "emerging adults" in their 20s do not fully emerge with regard to glycemic control until they reach 30 years of age. Given DCCT/EDIC data on the persistent benefit of intensive versus conventional glucose control (7.3 vs. 9.1% [56 vs. 76 mmol/mol] during the DCCT) on vascular outcomes 20 years later (16), the contemporary elevated HbA_{1c} seen in the adolescents and young adults in the T1D Exchange suggests a similarly elevated risk for future complications until they reach 30 years of age.

In a cross-sectional comparison, the average HbA_{1c} at the most recent update was higher than at enrollment (8.4 vs.

Table 3—HbA_{1c} according to demographic and clinical characteristics

	2–5 years old		6–12 years old		13–17 years old		18–25 years old		26–49 years old		≥50 years old	
	n	Mean ± SD (mmol/mol)	*n*	Mean ± SD (mmol/mol)	*n*	Mean ± SD (mmol/mol)	*n*	Mean ± SD (mmol/mol)	*n*	Mean ± SD (mmol/mol)	*n*	Mean ± SD (mmol/mol)
Overall	236	8.2 ± 1.0 (66 ± 10.9)	3,313	8.4 ± 1.3 (68 ± 14.2)	4,914	9.0 ± 1.8 (75 ± 19.7)	2,867	8.7 ± 1.9 (72 ± 20.8)	2,606	7.7 ± 1.3 (61 ± 14.2)	2,125	7.6 ± 1.1 (60 ± 12.0)
Race/ethnicity												
White non-Hispanic	179	8.2 ± 0.9 (66 ± 9.8)	2,610	8.3 ± 1.2 (67 ± 13.1)	3,823	8.8 ± 1.6 (73 ± 17.5)	2,357	8.6 ± 1.8 (71 ± 19.7)	2,327	7.7 ± 1.3 (61 ± 14.2)	2,014	7.5 ± 1.1 (58 ± 12.0)
Black non-Hispanic	16	—	164	9.6 ± 1.7 (81 ± 18.6)	292	10.2 ± 2.1 (88 ± 23.0)	124	10.2 ± 2.4 (88 ± 26.2)	89	8.5 ± 1.5 (69 ± 16.4)		8.4 ± 1.3 (68 ± 14.2)
Hispanic or Latino	25	8.3 ± 0.9 (67 ± 9.8)	336	8.6 ± 1.3 (71 ± 14.2)	540	9.2 ± 1.9 (77 ± 20.8)	263	9.1 ± 2.0 (76 ± 21.9)	106	7.9 ± 1.3 (63 ± 14.2)	24	7.6 ± 1.1 (60 ± 12.0)
Other	16	—	194	8.7 ± 1.6 (72 ± 17.5)	255	9.3 ± 2.0 (78 ± 21.9)	121	9.3 ± 2.0 (78 ± 21.9)	81	7.6 ± 1.7 (60 ± 18.6)	32	7.8 ± 1.7 (62 ± 18.6)
Annual household income*												
<$50,000	76	8.4 ± 1.1 (68 ± 12.0)	823	8.9 ± 1.5 (74 ± 16.4)	1,045	9.5 ± 2.0 (80 ± 21.9)	514	9.1 ± 2.0 (76 ± 21.9)	652	8.0 ± 1.5 (64 ± 16.4)	430	7.7 ± 1.2 (61 ± 13.1)
$50,000 to <$100,000	77	8.0 ± 0.8 (64 ± 8.7)	934	8.3 ± 1.1 (67 ± 12.0)	1,246	9.0 ± 1.7 (75 ± 18.6)	639	8.7 ± 1.9 (72 ± 20.8)	814	7.7 ± 1.2 (61 ± 13.1)	589	7.6 ± 1.1 (60 ± 12.0)
≥$100,000	45	8.0 ± 1.0 (64 ± 10.9)	845	8.0 ± 1.1 (64 ± 12.0)	1,324	8.5 ± 1.4 (69 ± 15.3)	653	8.2 ± 1.6 (66 ± 17.5)	693	7.3 ± 1.0 (56 ± 10.9)	556	7.4 ± 1.0 (57 ± 10.9)
Insulin delivery method												
Pump	146	8.0 ± 0.9 (64 ± 9.8)	2,131	8.2 ± 1.2 (66 ± 13.1)	2,810	8.7 ± 1.5 (72 ± 16.4)	1,555	8.4 ± 1.6 (68 ± 17.5)	1,625	7.6 ± 1.2 (60 ± 13.1)	1,263	7.5 ± 1.0 (58 ± 10.9)
Injections	87	8.5 ± 1.1 (69 ± 12.0)	1,136	8.8 ± 1.4 (73 ± 15.3)	2,008	9.4 ± 2.0 (79 ± 21.9)	1,277	9.1 ± 2.1 (76 ± 23.0)	940	7.8 ± 1.5 (62 ± 16.4)	833	7.7 ± 1.2 (61 ± 13.1)
CGM												
Yes	20	7.4 ± 0.6 (57 ± 6.6)	164	7.9 ± 0.9 (63 ± 9.8)	153	8.2 ± 1.4 (66 ± 15.3)	130	8.1 ± 1.3 (65 ± 14.2)	399	7.3 ± 1.1 (56 ± 12.0)	238	7.4 ± 1.0 (57 ± 10.9)
No	216	8.3 ± 1.0 (67 ± 10.9)	3,149	8.4 ± 1.3 (68 ± 14.2)	4,761	9.0 ± 1.8 (75 ± 19.7)	2,737	8.7 ± 1.9 (72 ± 20.8)	2,207	7.8 ± 1.4 (62 ± 15.3)	1,887	7.6 ± 1.1 (60 ± 12.0)
SMBG#												
0–3 times per day	3	—	253	9.5 ± 1.9 (80 ± 20.8)	1,316	9.7 ± 1.9 (83 ± 20.8)	994	9.2 ± 1.9 (77 ± 20.8)	689	8.0 ± 1.3 (64 ± 14.2)	375	7.9 ± 1.2 (63 ± 13.1)
4–6 times per day	63	8.4 ± 1.0 (68 ± 10.9)	1,174	8.5 ± 1.2 (69 ± 13.1)	1,575	8.6 ± 1.4 (71 ± 15.3)	625	8.0 ± 1.3 (64 ± 14.2)	712	7.4 ± 1.0 (57 ± 10.9)	632	7.5 ± 1.0 (58 ± 10.9)
6–9 times per day	75	8.1 ± 0.9 (65 ± 9.8)	627	8.1 ± 1.0 (65 ± 10.9)	360	8.0 ± 1.1 (64 ± 12.0)	124	7.5 ± 1.0 (58 ± 10.9)	193	7.1 ± 0.9 (54 ± 9.8)	187	7.1 ± 0.8 (54 ± 8.7)
≥10 times per day	28	7.5 ± 0.7 (58 ± 7.7)	286	7.7 ± 0.9 (61 ± 9.8)	87	7.9 ± 1.1 (63 ± 12.0)	48	7.2 ± 1.1 (55 ± 12.0)	73	7.0 ± 1.1 (53 ± 12.0)	56	7.0 ± 0.8 (53 ± 8.7)

Dash (—) indicates $n < 20$. *Income is from participant report at enrollment. #SMBG from meter download was available for 10,555 participants.

Table 4—Number (%) of patients reporting one or more severe hypoglycemic and one or more DKA events

	2–5 years old		6–12 years old		13–17 years old		18–25 years old		26–49 years old		≥50 years old	
	n	≥1 event (%)	*n*	≥1 event (%)	*n*	≥1 event (%)	*n*	≥1 event (%)	*n*	≥1 event (%)	*n*	≥1 event (%)
Frequency of ≥1 SH event in prior 3 months												
Overall	47	3 (6)	534	12 (2)	455	24 (5)	451	26 (6)	661	50 (8)	413	35 (8)
Insulin delivery method												
Pump	31	1 (3)	388	9 (2)	304	14 (5)	272	14 (5)	433	28 (6)	255	19 (7)
Injections	16	2 (13)	128	3 (2)	124	8 (6)	158	12 (8)	204	18 (9)	129	13 (10)
Most recent HbA_{1c}*												
<7.0% (<53 mmol/mol)	5	—	50	3 (6)	29	1 (3)	72	2 (3)	215	13 (6)	120	7 (6)
7.0 to <7.5% (53 to <58 mmol/mol)	6	—	66	2 (3)	44	4 (9)	45	2 (4)	104	6 (6)	80	7 (9)
7.5 to <8.0% (58 to <64 mmol/mol)	9	—	105	1 (1)	76	2 (3)	75	2 (3)	100	12 (12)	80	5 (6)
8.0 to <9.0% (64 to <75 mmol/mol)	15	—	181	4 (2)	145	8 (6)	90	8 (9)	102	9 (9)	64	5 (8)
≥9.0% (≥75 mmol/mol)	9	—	102	2 (2)	133	6 (5)	97	8 (8)	52	7 (13)	20	2 (10)
Frequency of ≥1 DKA event in prior 3 months												
Overall	47	2 (4)	534	17 (3)	455	20 (4)	451	22 (5)	661	12 (2)	413	5 (1)
Insulin delivery method												
Pump	31	2 (6)	388	13 (3)	304	8 (3)	272	9 (3)	433	4 (1)	255	2 (1)
Injections	16	—	128	4 (3)	124	11 (9)	158	10 (6)	204	7 (3)	129	1 (1)
Most recent HbA_{1c}*												
<7.0% (<53 mmol/mol)	5	—	50	2 (4)	29	1 (3)	72	1 (1)	215	0	120	1 (1)
7.0 to <7.5% (53 to <58 mmol/mol)	6	—	66	0	44	0	45	3 (7)	104	1 (1)	80	1 (1)
7.5 to <8.0% (58 to <64 mmol/mol)	9	—	105	3 (3)	76	0	75	0	100	2 (2)	80	1 (1)
8.0 to <9.0% (64 to <75 mmol/mol)	15	—	181	5 (3)	145	3 (2)	90	2 (2)	102	5 (5)	64	2 (3)
≥9.0% (≥75 mmol/mol)	9	—	102	5 (5)	133	13 (10)	97	12 (12)	52	2 (4)	20	0

Dash (—) indicates n <20. *Most recent HbA_{1c} 6 months prior to when participant questionnaire was completed (270 participants were missing HbA_{1c} within 6 months of questionnaire).

8.2% [68 vs. 66 mmol/mol]), suggesting a worsening in glycemic control over time. The greatest increase in HbA_{1c} was observed in the 13–17 (9.0 vs. 8.7% [75 vs. 72 mmol/mol]) and 18–26-year-old (8.7 vs. 8.3% [72 vs. 67 mmol/mol]) groups. Although this could reflect differences in age and type 1 diabetes duration, the results nevertheless indicate that there certainly is no indication of improving glycemic control in these age-groups. Additional studies are needed to understand and overcome the special challenges in treating teenagers with type 1 diabetes, as well as the racial/ethnic factors that contribute to elevated HbA_{1c} levels in African American children and adolescents (17). Since only 30% of adults aged >30 years had achieved target HbA_{1c} levels, there remains considerable room for improving metabolic control and long-term clinical outcomes in patients with type 1 diabetes across all age-groups.

The observation that many patients in the registry were able to achieve target HbA_{1c} levels without the exponential increase in the frequency of SH seen in the DCCT is a very positive finding (6,7). Similar decreases in HbA_{1c} levels without concomitant increases in SH have been observed in clinical trials of new insulin analogs (18), with use of new insulin pumps (19), and in CGM trials (20). Our data also indicate that DKA remains a problem in a substantial percentage of patients (11,12). Since the risk of DKA was increased in participants with HbA_{1c} levels >9.0% (75 mmol/mol), poor compliance with their diabetes treatment regimens undoubtedly contributes to the increased risk of DKA. Conversely, greater compliance with the daily tasks of managing diabetes may help explain the lower frequency of DKA that we observed in pump versus injection patients. The data provide no indication of a higher DKA rate in pump users, a theoretical concern due to the potential for infusion set failure.

Despite elevations in HbA_{1c} levels in every age-group of participants with type 1 diabetes, only ~5% were being treated with an adjunctive glucose-lowering agent, mostly metformin. Treatment with metformin has been associated with only a modest lowering of HbA_{1c} in adults with type 1 diabetes (21), whereas no change in metabolic control was seen in a recent large-scale clinical trial in overweight adolescents (22). These observations underscore the continuing need for the testing of new classes of glucose-lowering agents that have been approved for treatment of type 2 diabetes in patients with type 1 diabetes. Since adolescents with type 1 diabetes are at greatest need for new treatment options, pivotal trials for approval of these drugs in type 1 diabetes in adolescents should not be delayed until completion of adult studies.

A limitation in interpreting these results is that all subjects in the T1D Exchange clinic registry are treated at centers that focus on the care of type 1 diabetes. Thus, uninsured individuals likely are underrepresented in the cohort and pump use may

be higher than it is in the overall population of type 1 diabetes in the U.S. Even higher HbA_{1c} values might be expected in a national, population-based sample of type 1 diabetes, especially in adults who are more likely to be treated in primary care settings rather than in diabetes specialty practices than are children with type 1 diabetes. The T1D Exchange pediatric participant characteristics generally are similar to those of participants in the SEARCH for Diabetes in Youth Study (SEARCH), a study of individuals <20 years of age with diabetes in six areas of the U.S. that began in 2001 (23). We do not know of a population-based cohort in adults with type 1 diabetes for comparison with our T1D Exchange adult cohort.

Even if certain biases are present, it is highly unlikely that the T1D Exchange data demonstrating that only a minority of children and adults with type 1 diabetes achieve HbA_{1c} targets is an underestimate. The high proportions of individuals not achieving glycemic targets with current therapies highlighted in our analyses make development and dissemination of an artificial pancreas or safe and effective islet replacement imperative.

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