Diabetes Epidemiology and Management 12 (2023) 100153

Contents lists available at ScienceDirect

Diabetes Epidemiology and Management

journal homepage: www.elsevier.com

Original article

Characteristics of people with optimally-managed type 1 diabetes

Gijsbert Stoet[a,*], Richard IG Holt[b,c]

[a] Department of Psychology, Faculty of Science and Health, University of Essex, UK
[b] Human Development and Health, Faculty of Medicine, University of Southampton, UK
[c] Southampton National Institute for Health Research Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, UK

ARTICLE INFO

Article History:
Received 19 May 2023
Accepted 1 June 2023
Available online 3 June 2023

Keywords:
Adult
Self-management
CGM
Hybrid closed loop
Age
Inequality

ABSTRACT

Objective: The aim is to describe the characteristics of people with type 1 diabetes who are meeting all seven glycemic targets set by international consensus.
Research Design & Methods: We analyzed continuous glucose monitoring (CGM) data from 497 participants (aged 18-70 yrs). Time-in-range, time above and below range, co-efficient of variability, and glucose management indicator (GMI) were combined with demographic data, insulin delivery, and exercise.
Results: While 68% of participants achieved a GMI below 7% (53 mmol/mol), 39% met all seven glycemic targets. Older people and those of White ethnicity were more likely to meet these targets. Men and women were equally likely to meet all targets, although men were more likely to experience hypoglycemia while women were more likely to experience hyperglycemia. Hybrid-closed loop (HCL) system users were more likely to meet all targets than people using a standard pump or multiple daily injections.
Conclusions: Only 56% of those with a GMI below 7% (53 mmol/mol) met all seven targets, illustrating how glycemic management involves more than GMI/HbA_{1c} lowering alone, which has implications for estimates of optimally managed participants in the wider population of people with type 1 diabetes. Demographic inequalities were prevalent. Using a HCL system clearly facilitated the achievement of glycemic targets.

The importance of glycemic management of type 1 diabetes has been shown beyond doubt by the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) follow-up study [1,2]. The results have informed international recommendations that an HbA_{1c} goal of < 7.0% (53 mmol/mol) is appropriate for most adults with type 1 diabetes as long as this can be achieved without significant hypoglycemia. However, current recommendations go beyond HbA_{1c}. The American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) consensus report on the management of type 1 diabetes recommended seven glycemic targets [3] (Table 1).

Previous reports on glycemic management have focused on HbA_{1c} [4,5]. The current study characterizes how often people with diabetes meet all recommended glycemic targets combined. We define optimal management as meeting these seven targets. This type of characterization has become practically attainable due to the wide availability of continuous glucose monitoring (CGM). The use of CGMs is now considered the standard of care for most adults with type 1 diabetes. These devices measure interstitial glucose to estimate plasma glucose. Metrics including average glucose, time in range (TIR), as well as time above and below range and glucose variability can be derived from the interstitial glucose data. The GMI is calculated from the average sensor glucose over the preceding 14 days and provides an approximation of a laboratory-measured HbA_{1c} [5] although it may be higher or lower than the actual HbA_{1c} for some individuals [6].

Achieving even some of these targets is difficult for many people with type 1 diabetes under normal daily living conditions. Recent research showed that only 21% of adults with type 1 diabetes had an HbA_{1c} below the recommended 7% (53 mmol/mol) [7] with similar numbers found internationally [5]. These numbers are likely to improve with the introduction of improved diabetes technology and novel insulin types. Therefore, it is important to know what percentage of people with diabetes are currently able to achieve the recommended ADA/EASD glycemic targets under daily life conditions and what sets them apart from those who do not. It is also of interest to know what percentage of people with diabetes are optimally managed rather than only achieving the HbA_{1c} target.

In the current study, we use data collected in the T1DEXI program, which was conducted in the US by the Jaeb Center for Health Research. Participants with type 1 diabetes recorded CGM data as well as insulin dosages, food, and exercise data for up to four weeks. We focus on those participants who met all seven ADA/EASD glycemic targets [3],

Abbreviations: CGM, Continuous Glucose Monitoring; eAG, estimated Average Glucose; GMI, Glucose Management Indicator; HCL, Hybrid Closed Loop; MDI, Multiple Daily Injections; TIR, Time in range

* Corresponding author.
E-mail address: g.stoet@essex.ac.uk (G. Stoet).

https://doi.org/10.1016/j.deman.2023.100153

Table 1
Seven glycemic targets for most adults with type 1 diabetes as defined in the ADA/EASD Consensus report for the management of type 1 diabetes in adults (3).

1	GMI < 7% (53 mmol/mol)
2	>70% of data were between 70-180 mg/dL,
3	less than 4% of data were < 70 mg/dL,
4	less than 1% of data were < 54 mg/dL,
5	less than 25% of data were > 180 mg/dL,
6	less than 5% of data were > 250 mg/dL, and
7	glucose variability (expressed as coefficient of variance) was ≤36%.

that is, participants who were optimally managed. Our main research questions were what percentage of the participants were optimally managed and the demographic characteristics and insulin delivery method of those with optimal diabetes management.

Research design and methods

Design: The T1DEXI program is an experimental cross-sectional study of people with type 1 diabetes living in the US. We analyzed data which were collected between December 2018 and July 2021. Data were provided by the Helmsley Trust and Jaeb foundation via the Vivli center for global clinical research data. Participants were randomly assigned to one of three different exercise programs, namely aerobic, high-intensity interval, or resistance training. There were no major differences in the effect of these three types of training [8]. In this study, we included the average daily time spent on any time of recorded exercise as a control variable in some of our analyses.

Participants

The T1DEXI program included 502 participants aged 18-70 years of whom 497 had up to 28 days of CGM data. The clinical characteristics are shown in Table 2. Participants used a variety of basal insulin (brand names Tresiba, Lantus, Toujeo, Levemir, or Basaglar) and fast acting insulin (brand names Humalog, Fiasp, Novorapid, Apidra, Lyumjev, or Admelog).

Procedure: The T1Dexi program followed adult participants for up to 28 days. Among other things, CGM data, exercise data, and insulin doses were electronically recorded. All participants used a Dexcom G6 CGM device, which records interstitial glucose every five minutes and sends data via BlueTooth to a receiver (Dexcom G6 receiver or mobile phone), which in turn sends data to the Dexcom Clarity web site for storage. Participants recorded start and stop time of exercise on their dedicated T1DEXI cellphone app. Insulin delivery was recorded either in the app or electronically via a smart pen or insulin pump.

Table 2
Clinical characteristics of participants. Data are mean ± standard deviation or percentage.

Total number of participants	497
Age (years)	37 ± 14
Sex	
Men	134 (27%)
Women	383 (73%)
Race	
White	454 (91%)
Black/African American	10 (2%)
Asian	10 (2%)
American Indian or Alaska Native	2 (<1%)
Multiple	8 (2%)
Not reported or unknown	13 (3%)
Body mass index (kg/m^2)	25.4 ± 4.1
Duration of diabetes	18 ± 13 years
HbA_{1c}	7%±1% (49±8mmol/mol)
Insulin delivery	
Multiple Daily Injection	18%
Insulin pumps without HCL system	38%
HCL system	45%

Measurements: In our study, we used demographic data (age, sex, race, education, and income), body mass index, CGM data, insulin dosages, insulin delivery and exercise data.

Data analysis: CGM data were available for 497 participants. On average, participants had 7,852 CGM data points (roughly corresponding to one interstitial glucose measure estimate of blood glucose every 5 minutes). We defined optimal glycaemic management if all of the following seven of the ADA/EASD criteria [3] were met as described in Table 1. Because manually recorded insulin doses were not always reliably entered by participants, we only report total insulin for those using a standard pump or HCL which recorded insulin dosages electronically (Table 3).

We used the statistical software R [9] for all data analyses. For analysis of variance (ANOVA), we used the R package eZ. We used $\chi 2$ tests for comparing percentages of participants meeting glycemic criteria. For each participant, we calculated the mean daily duration in minutes spent on any type of exercise (including experimentally assigned exercise and voluntarily chosen exercise).

Results

Glycemic profiles

The average estimated average glucose (eAG) (±SD) of the 497 participants during the sampling period was 147±26 mg/dL (ranging from 94 to 258 mg/dL); this corresponds to a mean GMI of 6.8 ± 0.9% (51 ± 9 mmol/mol).

Table 3
Clinical characteristics of those who met or did not meet all 7 targets. P values refer to statistical comparisons between those who met all 7 targets and those who did not. Data are mean ± standard deviation, except for age.

	Met all 7 targets	Did not meet 7 targets	P value
Number	196 (39%)	301 (61%)	*P*<0.01
Age (years)	37 (IQR=23.2)	31 (IQR=18)	*P*<0.01
Sex			
Men	43%	57%	*P*=0.02
Women	38%	62%	*P*<0.01
Estimated average glucose	134±11	155±29	*P*<0.01
Glucose Management Indicator	6.3±0.38%	7.0±1.0%	*P*<0.01
Ethnicity			
White	42%	52%	*P*<0.01
Black/African American	0%	100%	*P*<0.01
Asian	30%	70%	*P*=0.18
American Indian or Alaska Native	0%	100%	*P*=0.32
Multiple	13%	87%	*P*=0.01
Body mass index (kg/m^2)	25.1±4.1	25.6±4.1	*P*=0.268
Duration of diabetes	19	18	*P*=0.432
HbA_{1c}	6.4% (46±6) mmol/mol)	6.8% (51±9 mmol/mol)	*P*<0.01
Insulin delivery			
Multiple Daily Injection	28%	72%	*P*<0.01
Standard insulin pump	25%	75%	*P*<0.01
Hybrid closed loop system	56%	44%	*P*=0.01
Average total daily insulin dose (units per kg)	0.53±0.18	0.62 ± 0.21	*P*<0.01
Proportion of basal Insulin	51 ± 11%	51 ± 13%	*P*=0.82

Table 4
Percentages of participants meeting individual glycemic targets from consensus report (3). Percentages of men and women were compared with χ^2 tests.

	Total	Men	Women	Difference
All 7 glycemic targets met	39%	43%	38%	χ2=0.57, *P*=0.45
1) Glucose Management Indicator < 7%	70%	84%	65%	χ^2=15.2, *P*<0.01
2) Time in range (70-180 mg/dL)	68%	80%	64%	χ^2=10.7, *P*<0.01
3) Hypo 1,2 measures (<70 mg/dL)	74%	63%	78%	χ^2=9.57, *P*<0.01
4) Hypo 2 measures (<54 mg/dL)	82%	80%	83%	χ^2=0.66, *P*=0.42
5) Hyper 1,2 measures (>180 mg/dL)	63%	76%	58%	χ^2=12.46, *P*<0.01
6) Hyper 2 measures (>250 mg/dL)	65%	77%	61%	χ^2=10.67, *P*<0.01
7) Coefficient of variance ≤ 36%	70%	75%	68%	χ^2=1.68, *P*=0.17

39% of participants met all seven glycemic targets (Table 2). The individual targets are, by definition, strongly related to one another. The TIR, for example, is highly correlated with GMI (r = -0.93, P<0.01). Even so, participants were far less likely to achieve all seven targets than the most commonly used targets of glycemic (HbA_{1c} /GMI and TIR). Of the people who met the GMI target alone, 56% met all seven targets.

Participants identifying as White were more likely than those not identifying as White to achieve all seven targets (42% vs 13%, χ^2=8.4, P<0.01). Using a binomial regression model, we found that the effect of race on being optimally managed is still found after adjustment for levels of income, education, time spent on exercise, body mass index, and access to a hybrid closed loop system (P=0.03).

Although there was no difference between the percentages of men and women meeting all seven targets, there were differences in their time in range indicators and average blood glucose (Table 4). These findings correspond to the observation that the eAG of women (150±26 mg/dL) was 12 mg/dL higher than that of men (P<0.01). While women experienced more hyperglycemia, men experienced more hypoglycemia; these two indicators canceled each other out in regard to meeting all seven targets.

We analyzed whether the menstrual cycle could explain the sex difference in time in range, but a 2 × 2 ANOVA with the factors age (below 40 or above 60 years old) and sex revealed no interaction between age and sex (F<0.01, P=0.99).

Conclusions

We found that nearly 4 in 10 of all participants met all seven targets (i.e., optimally managed type 1 diabetes), even though the majority achieved the time-in-range or GMI targets. White participants were more likely to achieve all targets than people of other ethnicity. Further, we found that the majority of those using a HCL system were achieving all seven targets. While there were no differences between the percentages of men and women achieving all targets, women spent more time above range and men more time below range. This latter effect could not be explained by women's age.

One of the implications of our study is that meeting all targets (i.e., optimal management) is considerably more difficult than meeting an HbA_{1c}/GMI<7% or a time-in-range over 70% alone. Our data suggest that optimal management as recommended in the ADA/EASD consensus report [3] will be nearly half as low as estimates based on HbA_{1c} alone. This has implications for interpreting another large and potentially more representative data set of people with type 1, namely the T1D exchange data [7]. If we apply our finding in regard to the relation between achieving the GMI target alone and achieving all seven targets, only around one in ten of people with type 1 diabetes in that sample would be optimally managed.

Our findings reflect ethnic health inequalities seen in other studies [7,10,11]. Our findings expand these previous observations by showing that the gap between White and non-White participants could not be explained by controlling for the use of a HCL, income, education, body mass index, or time spent on exercise. Our study suggests that because a range of socioeconomic, health, and treatment factors cannot fully explain the differences, a closer look at biological and psycho-social variables is necessary.

The success of HCL has been clearly shown elsewhere [7,12], including in randomly controlled studies [13]. However, the uptake of HCL among adult people with type 1 diabetes is limited due to funding challenges, despite being cost effective compared to other forms of insulin delivery [14–16].

The differences between men and women in meeting targets could not be explained by age (i.e., menstrual cycle common in women under 40), and further research is needed to understand why glucose levels tend to be lower in men.

Clinical implications

The advantages of closed loop systems over standard insulin pumps or multiple daily injections are considerable. This matches earlier insights into the benefits of diabetes technology [17]. Although HCL systems come at a cost for health care systems, they not only have the benefit of increasing user well-being, they might also reduce the costs associated with the complications of sub-optimally managed diabetes [18,19].

Demographic differences in treatment outcomes are considerable and cannot simply be explained by socioeconomic differences or hormonal differences. The lack of simple explanations makes more attention for other possibly manageble factors (e.g., healthy eating habits) important.

Limitations

Participation in this study was self-selective, which might have excluded highly disengaged people with diabetes or those demotivated to exercise. We know such people are less likely to have optimal glycemic management [20] and this might explain the relatively large percentage being within the recommended glycemic targets compared to other studies. For example, in the 2016-2018 data of the T1D Exchange registry [7], 21% of adults managed the HbA_{1c}<7% target (compared to 70% meeting the GMI<7% target in the T1DEXI adult cohort analyzed here). If we assume that 56% of those who meet the GMI<7% target meet all seven targets, the target of achieving optimal management in the wider population of people with type 1 diabetes might be around 10%.

In summary, meeting all ADA/EASD CGM targets is nearly twice as difficult as achieving a GMI below 7% (53 mmol/mol) alone. Given the relatively high proportion of people with type 1 diabetes meeting a GMI below 7% target alone, it is likely that in the wider population of adults with type 1 diabetes just over 10% are optimally managed. Whether a person will achieve optimal glycaemic management is strongly related to both age and ethnicity. Greater access to HCL systems should increase the number of people obtaining optimal glycaemic management.

Author contributions and guarantor statement

GS and RH researched data and contributed to the discussion. GS wrote the first draft of the manuscript and RH reviewed and edited the manuscript. All authors approved the final version of the manuscript. GS is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Funding and assistance. This study was supported by the University of Essex (UK) and University of Southampton (UK). This manuscript is based on research using data from the Type 1 Diabetes EXercise Initiative (T1DEXI) Study that has been made available through Vivli, Inc. Vivli has not contributed to or approved, and is not in any way responsible for, the contents of this publication.

References

[1] Diabetes Control and Complications Trial. DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Study Research Group. Intensive Diabetes Treatment and Cardiovascular Outcomes in Type 1 Diabetes: The DCCT/EDIC Study 30-Year Follow-up. Diabetes Care 2016 May;39(5):686–93.

[2] Diabetes Control and 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. N Engl J Med 1993 Sep 30;329(14):977–86.

[3] 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). Diabetes Care 2021 Oct 18;44(11):2589–625.

[4] Mannucci E, Monami M, Dicembrini I, Piselli A, Porta M. Achieving HbA1c targets in clinical trials and in the real world: a systematic review and meta-analysis. J Endocrinol Invest 2014 May 1;37(5):477–95.

[5] 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 Sep 17;41(11):2275–80.

[6] Beck RW, Bergenstal RM, Riddlesworth TD, Kollman C, Li Z, Brown AS, et al. Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials. Diabetes Care 2019 Mar;42(3):400–5.

[7] 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 Feb;21(2):66–72.

[8] Riddell MC, Li Z, Gal RL, Calhoun P, Jacobs PG, Clements MA, et al. Examining the Acute Glycemic Effects of Different Types of Structured Exercise Sessions in Type 1 Diabetes in a Real-World Setting: The Type 1 Diabetes and Exercise Initiative (T1DEXI). Diabetes Care 2023 Feb 7 dc221721.

[9] R Core Team. R: A language and environment for statistical computing. [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2023. Available from: http://www.r-project.org/

[10] Coulon SJ, Velasco-Gonzalez C, Scribner R, Park CL, Gomez R, Vargas A, et al. Racial differences in neighborhood disadvantage, inflammation and metabolic control in black and white pediatric type 1 diabetes patients. Pediatr Diabetes 2017;18(2):120–7.

[11] Danielson KK, Drum ML, Estrada CL, Lipton RB. Racial and Ethnic Differences in an Estimated Measure of Insulin Resistance Among Individuals With Type 1 Diabetes. Diabetes Care 2009 Dec 10;33(3):614–9.

[12] Boughton CK, Hovorka R. Is an artificial pancreas (closed-loop system) for Type 1 diabetes effective? Diabet Med 2019;36(3):279–86.

[13] Choudhary P, Kolassa R, Keuthage W, Kroeger J, Thivolet C, Evans M, et al. Advanced hybrid closed loop therapy versus conventional treatment in adults with type 1 diabetes (ADAPT): a randomised controlled study. Lancet Diabetes Endocrinol 2022 Oct 1;10(10):720–31.

[14] Lambadiari V, Ozdemir Saltik AZ, de Portu S, Buompensiere MI, Kountouri A, Korakas E, et al. Cost-Effectiveness Analysis of an Advanced Hybrid Closed-Loop Insulin Delivery System in People with Type 1 Diabetes in Greece. Diabetes Technol Ther 2022 May;24(5):316–23.

[15] Serné EH, Roze S, Buompensiere MI, Valentine WJ, De Portu S, de Valk HW. Cost-Effectiveness of Hybrid Closed Loop Insulin Pumps Versus Multiple Daily Injections Plus Intermittently Scanned Glucose Monitoring in People With Type 1 Diabetes in The Netherlands. Adv Ther 2022 Apr;39(4):1844–56.

[16] Jendle J, Buompensiere MI, Holm AL, de Portu S, Malkin SJP, Cohen O. The Cost-Effectiveness of an Advanced Hybrid Closed-Loop System in People with Type 1 Diabetes: a Health Economic Analysis in Sweden. Diabetes Ther 2021 Nov;12(11):2977–91.

[17] Murphy HR, Holt RIG. Technology: an increasingly important component in the management of diabetes. Diabet Med 2018;35(4):407–8.

[18] Wagner EH, Sandhu N, Newton KM, McCulloch DK, Ramsey SD, Grothaus LC. Effect of Improved Glycemic Control on Health Care Costs and Utilization. JAMA 2001 Jan 10;285(2):182–9.

[19] Association American Diabetes. Economic Costs of Diabetes in the U.S. in 2012. Diabetes Care 2013 Mar 14;36(4):1033–46.

[20] Nicolucci A, Kovacs Burns K, Holt RIG, Comaschi M, Hermanns N, Ishii H, et al. Diabetes Attitudes, Wishes and Needs second study (DAWN2™): Cross-national benchmarking of diabetes-related psychosocial outcomes for people with diabetes. Diabet Med 2013;30(7):767–77.