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Source / Izvornik: **Diabetes/Metabolism Research and Reviews, 2021, 37**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.1002/dmrr.3430

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:481279

Received: 7 April 2020 | Revised: 20 October 2020 | Accepted: 10 December 2020

DOI: 10.1002/dmrr.3430

RESEARCH ARTICLE

WILEY

The SAGE study: Global observational analysis of glycaemic control, hypoglycaemia and diabetes management in T1DM

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Funding information
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Abstract

Aims: To describe glycaemic control and diabetes management in adults with type 1 diabetes (T1DM), in a real-life global setting.

Materials and Methods: Study of Adults' GlycEmia (SAGE) was a multinational, multicentre, single visit, noninterventional, cross-sectional study in adult patients with T1DM. Data were collected at a single visit, analysed according to predefined age groups (26–44, 45–64 and ≥65 years) and reported across different regions. The primary endpoint was the proportion of participants achieving HbA_{1c} less than 7.0 % in each age group. Secondary endpoints included incidence of

Data from this manuscript has been published in abstract form (Renard E et al. Abstract 13. *Diabetologia* [2019] 62[Suppl 1]: 1. https://doi.org/10.1007/s00125-019-4946-6; Seufert J et al. Abstract 14. *Diabetologia* [2019] 62[Suppl 1]: 1. https://doi.org/10.1007/s00125-019-4946-6; Wilmot EG et al. P015. *Pediatric Diabetes.* 2019;20 [Suppl. 28]:41–231; Seufert J et al. P101 *Pediatric Diabetes.* 2019;20 [Suppl. 28]:41–231; Renard E et al. P179. *Pediatric Diabetes.* 2019;20 [Suppl. 28]:41–231) and presented as oral presentations at the European Association for the Study of Diabetes (EASD) 2019 congress, and as posters at the International Society for Pediatric and Adolescent Diabetes (ISPAD) 2019 congress.

hypoglycaemia, severe hypoglycaemia and severe hyperglycaemia leading to diabetic ketoacidosis (DKA) and therapeutic management of T1DM.

Results: Of 3903 included participants, 3858 (98.8%) were eligible for the study. Overall, 24.3% (95% confidence interval [CI]: 22.9–25.6) of participants achieved the glycaemic target of HbA_{1c} less than 7.0 %, with more participants achieving this target in the 26–44 years group (27.6% [95% CI: 25.5–29.8]). Target achievement was highest in Eastern and Western Europe, and lowest in the Middle East. The incidence of hypoglycaemia and of severe hyperglycaemia leading to DKA tended to decrease with age, and varied across regions. Age and regional differences were observed in therapeutic management, including types of device/insulin usage, frequency of insulin dose adjustment and technology usage.

Conclusions: Glycaemic control remains poor in adults with T1DM globally. Several areas of treatment may be optimised to improve outcomes, including supporting patient self-management of insulin therapy, increasing use of technologies such as CGM, and greater provision of healthcare support.

KEYWORDS
adults, clinical practice, global, glycaemic control, hypoglycaemia, type 1 diabetes

1 | INTRODUCTION

Glycaemic control is a modifiable risk factor for diabetes-related complications, but many people with type 1 diabetes (T1DM) do not meet appropriate glycaemic targets. The T1D Exchange registry found that only 21% of adults with T1DM achieved the American Diabetes Association (ADA)-recommended HbA_{1c} target of less than 7.0 %, while 37% achieved HbA_{1c} less than 7.5 %.[1] Additionally, average HbA_{1c} levels had not improved over a 5-year period despite increased use of insulin pumps and continuous glucose monitoring (CGM).[1] By comparison, a National Diabetes Audit in the UK reported 30% of patients with T1DM achieving HbA_{1c} less than 7.5 %; an increase of 10% over a 6-year period.[2]

In T1DM, poor glycaemic control is associated with long-term complications and increased mortality.[3–5] The Diabetes Control and Complications Trial found intensive treatment was associated with lower HbA_{1c} levels than conventional treatment (approximately 7 % vs. 9 %), with lower long-term mortality and incidence of cardiovascular disease according to the Epidemiology of Diabetes Interventions and Complications extension.[6] Although intensive treatment was associated with a threefold increased risk of severe hypoglycaemia,[7] more recent data have not confirmed an association between severe hypoglycaemia and HbA_{1c} levels.[8] Nevertheless, fear of hypoglycaemia represents a major physician- and patient-related barrier to glycaemic control.[9,10] Moreover, hypoglycaemia directly and indirectly impacts the cost of diabetes management, through increased need for hospitalisation, clinic visits and absence from work.[11]

While global real-life data have been previously reported for people aged 8–25 years, limited data are available examining regional differences in diabetes management in adults with T1DM, although the International Diabetes Management Practice Study documented treatment practices in developing countries (in Africa, Asia, Eastern Europe, Latin America and the Middle East) and identified factors including self-monitoring and patient education that impacted glycaemic target achievement.[12]

Study of Adults' GlycEmia in T1DM (SAGE) examined socio-demographics, glycaemic control, therapy and comorbidities, in addition to psychosocial aspects related to the disease in adults with T1DM of different ages across 17 non-US countries in five regions.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

SAGE was a multinational, multicentre, single visit, cross-sectional, observational study to describe glycaemic control and quality of life (QoL) in adults with T1DM. QoL outcomes will not be presented in this report.

Selected sites were expected to see ≥100 people with T1DM per year with ≥1 visit per year for each individual. Endocrinologists, general practitioners and other physicians familiar with the management of people with T1DM participated in the study. In each country, physicians were selected independently and randomly from the pre-established country specific lists of potential sites.

Included participants were aged ≥26 years with T1DM for ≥1 year, treated with insulin and with an HbA_{1c} value available within 30 days preceding the study visit or planned to be obtained in routine practice within 7 days after the study visit. Exclusion criteria included non-T1DM, switch from insulin pump to multiple insulin injections regimen, or vice versa, within 3 months preceding the study, treatment with thiazolidinedione, sulfonylurea or dipeptidyl peptidase-4

inhibitors at any time since T1DM diagnosis and treatment with any investigational drug within the last 3 months. Participants provided written informed consent.

2.2 | Data collection

At a single study visit, investigators collected data from the participant's file and interview into an electronic case report form. HbA_{1c} assessments were performed locally in routine practice, using the standard methodology at the laboratory of each site. No investigations for the purpose of the study were performed. The study was performed according to local regulatory requirements including Institutional Review Board and Independent Ethical Committee approvals where required, and conducted in accordance with the Declaration of Helsinki and guidelines for Good Epidemiology Practice.[13] Data were collected between January 2018 and December 2018.

2.3 | Endpoints

The primary endpoint was the proportion of participants who achieve the HbA_{1c} target of less than 7 % in predefined age groups (26–44 years; 45–64 years; ≥65 years).

Secondary clinical endpoints were HbA_{1c}, fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) levels, achievement of physician-established individualised HbA_{1c} targets, hypoglycaemia frequency (documented symptomatic hypoglycaemic episodes during the last 3 months and severe hypoglycaemia during the last 6 months), severe hyperglycaemia leading to DKA during the last 6 months, concomitant diseases and therapeutic management of T1DM (Supporting Information Materials). FPG and PPG were defined as the last available laboratory or self-monitored glucose value.

2.4 | Data analysis and statistics

Assuming that the HbA_{1c} target would be achieved in 20%–27% of participants, and that a lack of sufficient information on HbA_{1c} (nonevaluability criterion) would apply to approximately 5% of the population, the inclusion of 500–1000 participants per country/region (e.g., group of countries) would allow the calculation of a two-sided 95% confidence interval (CI) with a precision of between 2.5% and 3.9% (all age groups considered). With a recruitment ratio of 40%, 40% and 20% in the different predefined age groups of 26–44, 45–64 and ≥65 years, respectively, the precision would be between 4.0% and 6.3% in the first two age classes and between 5.7% and 9.2% in the last age group of ≥65 years. All analyses were conducted in the eligible population, defined as participants meeting the inclusion criteria. The time window for HbA_{1c} evaluation was extended to within 45 days preceding the study visit or within 15 days following the study visit to define the eligible population. All data were reported and analysed using descriptive statistics.

3 | RESULTS

3.1 | Participant disposition

Of 3903 included participants, 3858 (98.8%) were eligible for the study. Reasons for noneligibility were: no HbA_{1c} available in the time windows (n = 39), age less than 26 years or missing (n = 17) and no clinical diagnosis of presumed autoimmune T1DM (n = 3). It should be noted that an individual participant could have several reasons for noneligibility. Of the eligible population, 1724 (44.7%), 1512 (39.2%) and 622 (16.1%) comprised the 26–44, 45–64 and ≥65 years age groups, respectively. Participants were recruited from 17 different countries, assessed according to the following regions: Asia (India, Japan, Thailand; n = 780), Eastern Europe (Bulgaria, Croatia, Serbia, Ukraine; n = 996), Latin America (Argentina, Brazil, Chile, Colombia; n = 488), Middle East (Iran, Saudi Arabia; n = 444) and Western Europe (France, Germany, Italy, UK; n = 1150; Table S1).

3.2 | Participating centres

Two hundred and thirty centres participated in SAGE with regional differences in the types of participating centres and physician specialities. Overall, participating centres were mostly public hospitals, but also included private clinics/offices, private hospitals and "other" classifications, with some centres categorised as more than one "type". Most participating physicians were Endocrinologists/Diabetologists (Table 1).

3.3 | Participant characteristics

Participants had a mean (standard deviation [*SD*]) age of 47.44 (14.00) years and a mean body mass index (BMI) of 25.15 (4.48) kg/m^2, which was similar across all age groups (Table 2). Mean (*SD*) duration of diabetes was 20.73 (12.63) years overall, ranging from 15.92 (9.05) years in the youngest age group to 28.79 (15.10) years in the oldest age group. Overall, 20.6% had a family history of T1DM, and this was similar across all age groups.

Mean BMI was lowest in Asia (23.3 kg/m^2) and highest in the Middle East (26. 3 kg/m^2). Mean BMI in Eastern Europe, Western Europe and Latin America was 25.4, 25.6 and 25.5 kg/m^2, respectively. Duration of diabetes was lowest in Asia and highest in Western Europe, while the proportion of participants with a family history of T1DM was highest in Latin America, Western Europe and Middle East (Table 3).

3.4 | Education level, employment status, health insurance coverage and lifestyle

Globally, most participants were educated to secondary or university/higher education level and were in employment (Table 2). The

TABLE 1 Participating centres and physicians by region

Parameter	Asia	Eastern Europe	Western Europe	Latin America	Middle East	Global
Number of sites	44	44	67	27	48	230
Type of centre (multiple answers possible), *n* (%)						
Public hospital	9 (20.5)	34 (77.3)	53 (79.1)	3 (11.1)	25 (52.1)	124 (53.9)
Private clinic or office	18 (40.9)	7 (15.9)	8 (11.9)	24 (88.9)	31 (64.6)	88 (38.3)
Private hospital	17 (38.6)	1 (2.3)	2 (3.0)	1 (3.7)	11 (22.9)	32 (13.9)
Other centre	1 (2.3)	4 (9.1)	4 (6.0)	1 (3.7)	6 (12.5)	16 (7.0)
Physician speciality, *n* (%)						
Endocrinology/diabetology	42 (95.5)	44 (100.0)	59 (88.1)	23 (85.2)	30 (62.5)	198 (86.1)
Internal medicine	2 (4.5)	0	4 (6.0)	3 (11.1)	12 (25.0)	21 (9.1)
Primary care physician	0	0	1 (1.5)	0	2 (4.2)	3 (1.3)
Other	0	0	3 (4.5)	1 (3.7)	4 (8.3)	8 (3.5)

majority had health insurance with comparable coverage across age groups with public, private and both public and private insurance. Health insurance coverage was lowest in Eastern Europe (57.1%, with most of the participants lacking health insurance coming from Ukraine; Table 3). Most participants had public health insurance in all regions except Latin America.

Regardless of age group, most participants lived in urban areas (82.7%) and lived with another adult (88.4%). Professional drivers (a job category for which relevant data were available and for whom poorly controlled diabetes may have particularly dangerous consequences) constituted 13.5% of participants globally, ranging between 8.4% and 15.3% of the population across age groups, while in Asia, the proportion of participants who were professional drivers was particularly high (36.5%).

Overall, most participants (71.4%) adhered to dietary advice (recommendation for carbohydrate intake, a balanced healthy diet with appropriate caloric, fat and fibre intake and/or other special dietary advice), with comparable results across all age groups. Only 34.3% of participants reported recommended activity levels (4 or more days/week with at least 30 min of physical activity), which was similar across age groups. Adherence to dietary recommendations was lowest in the Middle East (59.2%) and Asia (45.1%), while recommended activity levels were highest in Eastern Europe (48.4%) and lowest in Latin America (24.4%).

3.5 | Primary endpoint

Overall, the proportion (95% CI) of participants who achieved the glycaemic target of HbA_{1c} less than 7.0 % was 24.3% (22.9–25.6). A higher proportion of participants achieved HbA_{1c} less than 7.0 % in the 26–44 years age group (27.6% [25.5–29.8]), compared with the 45–64 years (21.0% [19.0–23.2]) and ≥65 years (22.8% [19.6–26.3]) age groups (Table 4). Achievement of HbA_{1c} less than 7.0 % was highest in Western Europe (27.0% [24.4–29.6]) and Eastern Europe (26.2% [23.5–29.1]) and was lowest in the Middle East (18.9% [15.4–22.9]; Table 5).

4 | SECONDARY CLINICAL ENDPOINTS

4.1 | Mean HbA_{1c}

Mean (*SD*) HbA_{1c} was 7.95 (1.42) % and was similar across age groups (Table 4). Mean (*SD*) HbA_{1c} was lowest in Western Europe (7.70 [1.21] %) and highest in the Middle East (8.21 [1.55] %; Table 5).

4.2 | Individualised HbA_{1c} targets

Overall, 20.9% of participants (95% CI: 19.6–22.2) reached their physician-defined individualised HbA_{1c} target, while 26.2% reached these targets in the oldest subgroup (22.8–29.8). Notably, individualised targets were between 7.0 and 7.5 % for most participants (56% overall), but were generally higher in the older subgroup (Table 4). Individualised target achievement was greatest in Western Europe (23.9% [21.5–26.5]) and lowest in the Middle East (14.4% [11.3–18.0]; Table 5).

4.3 | FPG and PPG

Mean (*SD*) FPG and PPG were 144.8 (62.92) mg/dl and 171.3 (67.00) mg/dl and did not appear to differ between age groups, although FPG and PPG data were missing for approximately 20% and 30% of participants, respectively. Mean (*SD*) FPG and PPG were lowest in Eastern Europe 137.2 (49.89) and 159.5 (50.92) mg/dl, respectively, and were highest in the Middle East 153.0 (73.18) and 190.1 (78.78) mg/dl, respectively.

TABLE 2 Participant characteristics by age group

Parameter[a]	Age groups, years ≥26 to <45 N = 1724	≥45 to <65 N = 1512	≥65 N = 622	All ages N = 3858
Proportion of total population, %	44.7	39.2	16.1	100.0
Mean (*SD*) age, years	34.63 (5.44)	52.74 (5.58)	70.04 (4.88)	47.44 (14.00)
Gender, % female/male	58.1/41.9	51.1/48.9	53.9/46.1	54.6/45.4
Mean (*SD*) body mass index, kg/m^2	24.49 (4.31)	25.62 (4.49)	25.84 (4.64)	25.15 (4.48)
Body mass index, *n* (%)				
<25 kg/m^2	1055 (61.3)	747 (49.5)	288 (46.3)	2090 (54.3)
25–30 kg/m^2	496 (28.8)	529 (35.1)	227 (36.5)	1252 (32.5)
≥30 kg/m^2	169 (9.8)	233 (15.4)	107 (17.2)	509 (13.2)
<27 kg/m^2	1330 (77.3)	1002 (66.4)	399 (64.1)	2731 (70.9)
≥27 kg/m^2	390 (22.7)	507 (33.6)	223 (35.9)	1120 (29.1)
Mean (*SD*) duration of diabetes, years	15.92 (9.05)	22.91 (12.73)	28.79 (15.10)	20.73 (12.63)
<10 Years, *n* (%)	514 (29.8)	262 (17.3)	79 (12.7)	855 (22.2)
≥10 Years, *n* (%)	1210 (70.2)	1250 (82.7)	542 (87.3)	3002 (77.8)
Family history of T1DM, % Yes/No	20.1/79.9	21.7/78.3	19.2/80.8	20.6/79.4
Education level, *n* (%)				
Primary	69 (4.0)	145 (9.6)	97 (15.6)	311 (8.1)
Secondary	688 (39.9)	719 (47.6)	295 (47.4)	1702 (44.1)
University/higher education	907 (52.6)	598 (39.6)	198 (31.8)	1703 (44.1)
Employment status				
Student	40 (2.3)	1 (0.1)	0	41 (1.1)
Employed[b]	1332 (77.3)	1000 (66.1)	89 (14.3)	2421 (62.8)
Unemployed	257 (14.9)	212 (14.0)	61 (9.8)	530 (13.7)
Retired	19 (1.1)	187 (12.4)	421 (67.7)	627 (16.3)
Incapacity	17 (1.0)	39 (2.6)	7 (1.1)	63 (1.6)
Other/unknown	59 (3.4)	73 (4.8)	44 (7.0)	176 (4.6)
Health insurance, *n* (%)				
Yes	1319 (76.5)	1158 (76.6)	481 (77.5)	2958 (76.7)
Public	952 (55.2)	861 (57.0)	369 (59.4)	2182 (56.6)
Private	229 (13.3)	145 (9.6)	47 (7.6)	421 (10.9)
Public and private	138 (8.0)	152 (10.1)	65 (10.5)	355 (9.2)
No	405 (23.5)	353 (23.4)	140 (22.5)	898 (23.3)

Abbreviations: *SD*, standard deviation; T1DM, type 1 diabetes.

[a]Data are not complete for all participants. Presented results are for participants with data available for each given parameter.

[b]Employee status is "employee" or "independent".

4.4 | Hypoglycaemia

Symptomatic hypoglycaemia (≤3.9 and <3.0 mmol/L) incidence within the last 3 months was similar across all age groups. The proportion of participants who experienced ≥1 severe hypoglycaemic event in the previous 6 months increased modestly with age (Table 4). Of these participants, the incidence of at least one hospitalisation or emergency room visit linked to severe hypoglycaemia was higher in the ≥65-year age group. The incidence of symptomatic hypoglycaemia (≤3.9 and <3.0 mmol/L) was lowest in the Middle East and Asia compared with the other regions (Table 5). The proportion who experienced ≥1 severe hypoglycaemic event was highest in the

TABLE 3 Participant characteristics by region

Parameter[a]	Asia (*n* = 780)	Eastern Europe (*n* = 996)	Western Europe (*n* = 1150)	Latin America (*n* = 488)	Middle East (*n* = 444)
Mean (*SD*) age, years	49.03 (14.04)	48.58 (13.91)	46.72 (14.09)	45.59 (13.85)	45.95 (13.59)
Gender, % female/male	59.2/40.8	52.3/47.7	50.9/49.1	61.5/38.5	54.1/45.9
Mean (*SD*) body mass index, kg/m^2	23.28 (4.01)	25.37 (4.30)	25.64 (4.55)	25.51 (4.23)	26.27 (4.81)
Body mass index, *n* (%)					
<25 kg/m^2	566 (72.7)	510 (51.2)	578 (50.5)	238 (48.8)	198 (44.6)
25–30 kg/m^2	177 (22.7)	344 (34.5)	399 (34.9)	180 (36.9)	152 (34.2)
≥30 kg/m^2	36 (4.6)	142 (14.3)	167 (14.6)	70 (14.3)	94 (21.2)
<27 kg/m^2	666 (85.5)	691 (69.4)	774 (67.7)	330 (67.6)	270 (60.8)
≥27 kg/m^2	113 (14.5)	305 (30.6)	370 (32.3)	158 (32.4)	174 (39.2)
Mean (*SD*) duration of diabetes, years	16.84 (11.57)	19.80 (12.14)	22.95 (13.26)	22.49 (12.40)	21.98 (12.25)
<10 Years, *n* (%)	254 (32.6)	231 (23.2)	209 (18.2)	83 (17.0)	78 (17.6)
≥10 Years, *n* (%)	525 (67.4)	765 (76.8)	941 (81.8)	405 (83.0)	366 (82.4)
Family history of T1DM, % Yes/No	12.0/88.0	16.8/83.2	25.0/75.0	24.3/75.7	28.1/71.9
Education level, *n* (%)					
Primary	21 (2.7)	38 (3.8)	107 (9.3)	50 (10.2)	95 (21.4)
Secondary	366 (46.9)	496 (49.8)	544 (47.3)	153 (31.4)	143 (32.2)
University/higher education	381 (48.8)	457 (45.9)	387 (33.7)	277 (56.8)	201 (45.3)
Employment status, *n* (%)					
Student	2 (0.3)	3 (0.3)	16 (1.4)	11 (2.3)	9 (2.0)
Employed[b]	531 (68.1)	595 (59.7)	744 (64.7)	326 (66.8)	225 (50.7)
Unemployed	83 (10.6)	138 (13.9)	109 (9.5)	64 (13.1)	136 (30.6)
Retired	94 (12.1)	228 (22.9)	186 (16.2)	70 (14.3)	49 (11.0)
Incapacity	3 (0.4)	28 (2.8)	24 (2.1)	4 (0.8)	4 (0.9)
Other/unknown	67 (8.6)	4 (0.4)	71 (6.1)	13 (2.6)	21 (4.8)
Health insurance, *n* (%)					
Yes	663 (85.0)	569 (57.1)	926 (80.7)	433 (88.7)	367 (82.7)
Public	561 (71.9)	553 (55.5)	651 (56.7)	105 (21.5)	312 (70.3)
Private	84 (10.8)	8 (0.8)	26 (2.3)	293 (60.0)	10 (2.3)
Public and private	18 (2.3)	8 (0.8)	249 (21.7)	35 (7.2)	45 (10.1)
No	117 (15.0)	427 (42.9)	222 (19.3)	55 (11.3)	77 (17.3)

Abbreviations: *SD*, standard deviation; T1DM, type 1 diabetes.

[a]Data are not complete for all participants. Presented results are for participants with data available for each given parameter.

[b]Employee status is "employee" or "independent".

Middle East and Latin America and lowest in Asia; rates of hospitalisation or emergency visits varied considerably (Table 5).

4.5 | Hyperglycaemia

The incidence of severe hyperglycaemia leading to DKA within the last 6 months was 4.2% overall and was lower in the ≥65-year age group compared with the other age groups (Table 4). In participants who experienced DKA, predisposing factors present in more than 20% of participants overall were infection (21.6%) and missing insulin dose (23.5%), with similar proportions across all age groups. Pump malfunction was the predisposing factor in 13.6% of participants with DKA and decreased with age. Of those participants who had experienced severe hyperglycaemia leading to DKA within the last 6 months, 46.9% had an associated hospitalisation.

TABLE 4 Endpoints by age group

Parameter[a]	Age groups, years			
HbA_{1c}	**≥26 to <45 *N* = 1724**	**≥45 to <65 *N* = 1512**	**≥65 *N* = 622**	**All ages *N* = 3858**
HbA_{1c} <7 %, *n* (%) [95% CI]	476 (27.6)[25.5–29.8]	318 (21.0) [19.0–23.2]	142 (22.8) [19.6– 26.3]	936 (24.3) [22.9–25.6]
$HbA_{1c,}$ *n* (%)				
7.0%–7.5 % (53.0–58.5 mmol/mol)	278 (16.1)	249 (16.5)	101 (16.2)	628 (16.3)
7.5%–8 % (58.5–63.9 mmol/mol)	258 (15.0)	254 (16.8)	109 (17.5)	621 (16.1)
8.0%–9 % (63.9–74.9 mmol/mol)	367 (21.3)	370 (24.5)	162 (26.0)	899 (23.3)
9.0%–10 % (74.9-85.8 mmol/mol)	182 (10.6)	194 (12.8)	67 (10.8)	443 (11.5)
10.0%–11.0 % (85.8-96.7 mmol/mol)	76 (4.4)	84 (5.6)	29 (4.7)	189 (4.9)
≥11.0 % (≥96.7 mmol/mol)	87 (5.0)	43 (2.8)	12 (1.9)	142 (3.7)
Mean (*SD*) HbA_{1c}				
%	7.91 (1.52)	8.02 (1.37)	7.91 (1.24)	7.95 (1.42)
mmol/mol	62.98 (16.66)	64.17 (14.97)	62.96 (13.60)	63.44 (15.56)
Individualised HbA_{1c} target value, *n* (%)				
<6.5 % (<47.5 mmol/mol)	97 (5.6)	59 (3.9)	17 (2.7)	173 (4.5)
6.5%–7.0 % (47.5–53.0 mmol/mol)	522 (30.3)	288 (19.0)	78 (12.5)	888 (23.0)
7.0%–7.5 % (53.0–58.5 mmol/mol)	959 (55.6)	909 (60.1)	289 (46.5)	2157 (55.9)
7.5%–8 % (58.5–63.9 mmol/mol)	115 (6.7)	203 (13.4)	169 (27.2)	487 (12.6)
8.0%–9 % (63.9–74.9 mmol/mol)	27 (1.6)	50 (3.3)	65 (10.5)	142 (3.7)
≥9 % (≥74.9 mmol/mol)	4 (0.2)	3 (0.2)	4 (0.6)	11 (0.3)
Achieved individualised HbA_{1c} target, *n* (%) [95% CI]	373 (21.6) [19.7–23.7]	269 (17.8) [15.9–19.8]	163 (26.2) [22.8–29.8]	805 (20.9) [19.6–22.2]
Hypoglycemia and hyperglycemia				
≥1 Symptomatic hypoglycaemia with BG ≤ 3.9 mmol/L (≤70 mg/dl) in the previous 3 months, *n* (%)	1183 (69.6)	991 (66.3)	402 (65.7)	2576 (67.7)
Events/participant, median (min, max)	4 (0, 180)	3 (0, 180)	3 (0, 180)	3 (0, 180)
≥1 Symptomatic hypoglycaemia with BG < 3.0 mmol/L (<54 mg/dl) in the previous 3 months, *n* (%)	882 (51.8)	728 (48.6)	293 (47.9)	1903 (49.9)
Events/participant, median (min, max)	1 (0, 90)	0 (0, 90)	0 (0, 90)	0 (0, 90)
≥1 Severe hypoglycaemia in the previous 6 months, *n* (%)	197 (11.5)	185 (12.2)	78 (12.6)	460 (11.9)
Mean (*SD*) number of events/participant	0.46 (2.24)	0.45 (2.91)	0.41 (1.62)	0.45 (2.45)
Median (min, max)	0 (0, 36)	0 (0, 90)	0 (0, 20)	0 (0, 90)
≥1 Hospitalisation/emergency visit linked to severe hypoglycaemia in the previous 6 months, *n* (%)[b]	49 (24.9)	47 (25.4)	25 (32.1)	121 (26.3)
≥1 Severe hyperglycaemia leading to DKA in the previous 6 months, *n* (%)	83 (4.8)	61 (4.0)	18 (2.9)	162 (4.2)
Events/participant, median (min, max)	0 (0, 23)	0 (0, 10)	0 (0, 3)	0 (0, 23)
Insulin treatment				
Device, *n* (%)				
Pump	413 (24.0)	290 (19.2)	66 (10.6)	769 (19.9)

(Continues)

TABLE 4 (Continued)

Parameter[a] HbA$_{1c}$	Age groups, years ≥26 to <45 N = 1724	≥45 to <65 N = 1512	≥65 N = 622	All ages N = 3858
Injection/pens	1310 (76.0)	1218 (80.6)	553 (88.9)	3081 (79.9)
Pump and injection/pens	0 (0.0)	4 (0.3)	3 (0.5)	7 (0.2)
Sometimes pump and sometimes injection/pen	1 (0.1)	0 (0.0)	0 (0.0)	1 (<0.1)
Mean (*SD*) total insulin daily dose				
U/kg/day	0.74 (0.31)	0.70 (0.30)	0.65 (0.28)	0.71 (0.30)
U/day	51.0 (23.1)	50.4 (25.2)	46.4 (23.7)	50.0 (24.1)
Recommended insulin dose adjustment approach *n* (%)				
Physician-driven	703 (41.4)	648 (43.3)	291 (47.0)	1642 (43.0)
Patient-driven	996 (58.6)	850 (56.7)	328 (53.0)	2174 (57.0)
Insulin type				
Pump only	413 (24.0)	290 (19.2)	66 (10.6)	769 (19.9)
Basal[c]	1213 (70.4)	1108 (73.3)	497 (79.9)	2818 (73.0)
Intermediate acting NPH	155 (9.0)	159 (10.5)	69 (11.1)	383 (9.9)
Long acting analogues	1058 (61.4)	949 (62.8)	428 (68.8)	2435 (63.1)
First generation	669 (38.8)	554 (36.6)	243 (39.1)	1466 (38.0)
Second generation	389 (22.6)	395 (26.1)	185 (29.7)	969 (25.1)
Premix[c]	78 (4.5)	85 (5.6)	52 (8.4)	215 (5.6)
Short acting insulin[c]	1196 (69.4)	1100 (72.8)	480 (77.2)	2776 (72.0)
Basal insulin dose adjustment frequency, *n* (%)[d]				
More than weekly	255 (22.1)	229 (21.9)	112 (24.1)	596 (22.4)
Weekly	263 (22.8)	255 (24.4)	114 (24.6)	632 (23.7)
Less than weekly but more than every 2 weeks	73 (6.3)	69 (6.6)	31 (6.7)	173 (6.5)
Less than every 2 weeks but more than monthly	214 (18.5)	214 (20.5)	103 (22.2)	531 (19.9)
Less than monthly	351 (30.4)	277 (26.5)	104 (22.4)	732 (27.5)
Short-acting insulin dose adjustment frequency, *n* (%)				
More than weekly	906 (57.4)	731 (53.6)	263 (49.3)	1900 (54.7)
Weekly	195 (12.4)	179 (13.1)	77 (14.4)	451 (13.0)
Less than weekly but more than every 2 weeks	50 (3.2)	46 (3.4)	22 (4.1)	118 (3.4)
Less than every 2 weeks but more than monthly	171 (10.8)	181 (13.3)	88 (16.5)	440 (12.7)
Less than monthly	256 (16.2)	227 (16.6)	83 (15.6)	566 (16.3)

Abbreviations: BG, blood glucose; CI, confidence interval; DKA, diabetic ketoacidosis; NPH, neutral protamine Hagedorn; *SD*, standard deviation.

[a]Data are not complete for all participants. Presented results are for participants with data available for each given parameter.

[b]Percentage calculated among those patients with ≥1 severe hypoglycaemia.

[c]Alone or in combinations, including participants using only injections/pens, or those using pump and injections/pens or those sometimes using pump and sometimes using injections/pens.

[d]Calculated as percentages of those participants on basal insulin.

TABLE 5 Endpoints by region

Parameter[a] HbA$_{1c}$	Asia (n = 780)	Eastern Europe (n = 996)	Western Europe (n = 1150)	Latin America (n = 488)	Middle East (n = 444)
Mean (*SD*) HbA$_{1c}$					
%	7.98 (1.37)	8.02 (1.48)	7.70 (1.21)	8.15 (1.64)	8.21 (1.55)
mmol/mol	63.68 (14.99)	64.11 (16.16)	60.68 (13.22)	65.62 (17.88)	66.28 (16.90)
HbA$_{1c}$ <7 %, *n* (%) [95% CI]	165 (21.2) [18.3–24.2]	261 (26.2) [23.5–29.1]	310 (27.0) [24.4– 29.6]	116 (23.8) [20.1–27.8]	84 (18.9) [15.4–22.9]
HbA$_{1c,}$ *n* (%)					
7.0%–7.5 % (53.0–58.5 mmol/mol)	127 (16.3)	136 (13.7)	228 (19.8)	71 (14.5)	66 (14.9)
7.5%–8 % (58.5–63.9 mmol/mol)	135 (17.3)	137 (13.8)	220 (19.1)	72 (14.8)	57 (12.8)
8.0%–9 % (63.9–74.9 mmol/mol)	212 (27.2)	229 (23.0)	234 (20.3)	100 (20.5)	124 (27.9)
9.0%–10 % (74.9–85.8 mmol/mol)	84 (10.8)	139 (14.0)	98 (8.5)	67 (13.7)	55 (12.4)
10.0%–11.0 % (85.8–96.7 mmol/mol)	32 (4.1)	49 (4.9)	41 (3.6)	33 (6.8)	34 (7.7)
≥11.0 % (≥96.7 mmol/mol)	25 (3.2)	45 (4.5)	19 (1.7)	29 (5.9)	24 (5.4)
Individualised HbA$_{1c}$ target value, *n* (%)					
<6.5 % (<47.5 mmol/mol)	20 (2.6)	40 (4.0)	77 (6.7)	16 (3.3)	20 (4.5)
6.5%–7.0 % (47.5–53.0 mmol/mol)	64 (8.2)	281 (28.2)	374 (32.5)	79 (16.2)	90 (20.3)
7.0%–7.5 % (53.0–58.5 mmol/mol)	574 (73.6)	428 (43.0)	543 (47.2)	350 (71.7)	262 (59.0)
7.5%–8 % (58.5–63.9 mmol/mol)	64 (8.2)	211 (21.2)	127 (11.0)	34 (7.0)	51 (11.5)
8.0%–9 % (63.9–74.9 mmol/mol)	53 (6.8)	36 (3.6)	23 (2.0)	9 (1.8)	21 (4.7)
≥9 % (≥74.9 mmol/mol)	5 (0.6)	–	6 (0.5)	–	–
Achieved individualised HbA$_{1c}$ target, *n* (%) [95% CI]	169 (21.7) [18.8–24.7]	201 (20.2) [17.7–22.8]	275 (23.9) [21.5–26.5]	96 (19.7) [16.2–23.5]	64 (14.4) [11.3–18.0]
Hypoglycaemia and hyperglycaemia					
≥1 Symptomatic hypoglycaemia BG ≤ 3.9 mmol/L (≤70 mg/dl) in the previous 3 months, *n* (%)	458 (59.2)	746 (74.9)	851 (76.7)	356 (73.4)	165 (37.2)
Events/participant, median (min, max)	2 (0, 180)	3 (0, 100)	8 (0, 180)	5 (0, 180)	0 (0, 90)
≥1 Symptomatic hypoglycaemia BG < 3.0 mmol/L (<54 mg/dl) in the previous 3 months, *n* (%)	319 (41.3)	536 (53.8)	663 (59.6)	278 (57.2)	107 (24.1)
Events/participant, median (min, max)	0 (0, 80)	1 (0, 90)	2 (0, 90)	1 (0, 54)	0 (0, 50)
≥1 Severe hypoglycaemia in the previous 6 months, *n* (%)	72 (9.2)	116 (11.6)	142 (12.4)	68 (14.0)	62 (14.0)
Mean (*SD*) number of events/participant	0.29 (1.23)	0.38 (1.63)	0.59 (2.79)	0.48 (4.23)	0.50 (1.90)
Median (min, max)	0 (0, 12)	0 (0, 20)	0 (0, 36)	0 (0, 90)	0 (0, 20)
≥1 Hospitalisation/emergency visit linked to severe hypoglycaemia in the previous 6 months, *n* (%)[b]	30 (41.7)	24 (20.7)	13 (9.2)	26 (38.2)	28 (45.2)
≥1 Severe hyperglycaemia leading to DKA in the previous 6 months, *n* (%)	18 (2.3)	30 (3.0)	77 (6.7)	22 (4.5)	15 (3.4)
Events/participant, median (min, max)	0 (0, 5)	0 (0, 5)	0 (0, 23)	0 (0, 10)	0 (0, 3)
Insulin treatment					
Device, *n* (%)					
Pump	138 (17.7)	45 (4.5)	498 (43.3)	74 (15.2)	14 (3.2)
Injection/pens	638 (81.8)	950 (95.4)	650 (56.5)	413 (84.6)	430 (96.8)
Pump and injection/pens	4 (0.5)	0	2 (0.2)	1 (0.2)	0

(Continues)

TABLE 5 (Continued)

Parameter[a] HbA_{1c}	Asia (n = 780)	Eastern Europe (n = 996)	Western Europe (n = 1150)	Latin America (n = 488)	Middle East (n = 444)
Sometimes pump and sometimes injection/pens	0	1 (0.1)	0	0	0
Mean (*SD*) total insulin daily dose					
U/kg/day	0.7 (0.3)	0.8 (0.3)	0.6 (0.3)	0.7 (0.3)	0.8 (0.4)
U/day	41.4 (21.1)	57.4 (21.5)	45.9 (22.9)	49.5 (25.5)	59.3 (28.1)
Recommended insulin dose adjustment approach					
Physician-driven	436 (56.3)	286 (28.7)	355 (31.0)	242 (53.1)	323 (72.7)
Patient-driven	338 (43.7)	710 (71.3)	791 (69.0)	214 (46.9)	121 (27.3)
Insulin type					
Pump only	138 (17.7)	45 (4.5)	498 (43.3)	74 (15.2)	14 (3.2)
Basal[c]	545 (69.9)	899 (90.3)	621 (54.0)	397 (81.4)	356 (80.2)
Intermediate acting NPH	29 (3.7)	217 (21.8)	15 (1.3)	75 (15.4)	47 (10.6)
Long acting analogues	516 (66.2)	682 (68.5)	606 (52.7)	322 (66.0)	309 (69.6)
First generation	181 (23.2)	431 (43.3)	323 (28.1)	223 (45.7)	308 (69.4)
Second generation	335 (42.9)	251 (25.2)	283 (24.6)	99 (20.3)	1 (0.2)
Premix[c]	77 (9.9)	50 (5.0)	11 (1.0)	3 (0.6)	74 (16.7)
Short acting insulin[c]	570 (73.1)	898 (90.2)	623 (54.2)	351 (71.9)	334 (75.2)
Basal insulin dose adjustment frequency, *n* (%)[d]					
More than weekly	58 (11.4)	247 (28.7)	165 (29.0)	75 (20.3)	51 (14.3)
Weekly	70 (13.8)	287 (33.3)	140 (24.6)	54 (14.6)	81 (22.8)
Less than weekly but more than every 2 weeks	12 (2.4)	82 (9.5)	24 (4.2)	9 (2.4)	46 (12.9)
Less than every 2 weeks but more than monthly	210 (41.3)	154 (17.9)	72 (12.7)	37 (10.0)	58 (16.3)
Less than monthly	158 (31.1)	91 (10.6)	168 (29.5)	195 (52.7)	120 (33.7)
Short-acting insulin dose adjustment frequency, *n* (%)					
More than weekly	233 (33.1)	677 (71.9)	730 (67.5)	179 (44.9)	81 (23.3)
Weekly	100 (14.2)	116 (12.3)	121 (11.2)	51 (12.8)	63 (18.1)
Less than weekly but more than every 2 weeks	14 (2.0)	30 (3.2)	33 (3.0)	7 (1.8)	34 (9.8)
Less than every 2 weeks but more than monthly	208 (29.5)	75 (8.0)	70 (6.5)	31 (7.8)	56 (16.1)
Less than monthly	149 (21.2)	44 (4.7)	128 (11.8)	131 (32.8)	114 (32.8)

Abbreviations: BG, blood glucose; CI, confidence interval; DKA, diabetic ketoacidosis; NPH, Neutral Protamine Hagedorn; *SD*, standard deviation.

[a]Data are not complete for all participants. Presented results are for participants with data available for each given parameter.

[b]Percentage calculated among those patients with ≥1 severe hypoglycaemia.

[c]Alone or in combinations, including participants using only injections/pens, or those using pump and injections/pens or those sometimes using pump and sometimes using injections/pens.

[d]Calculated as percentages of those participants on basal insulin.

Rates of severe hyperglycaemia leading to DKA ranged from 2.3% in Asia to 6.7% in Western Europe (Table 4). The rate of being hospitalised at least once in relation to severe hyperglycaemia leading to DKA ranged from 18.2% in Western Europe to 83.3% in Eastern Europe.

4.6 | Complications and comorbidities

Overall, 46.7% of participants reported at least one microvascular diabetes complication. The incidence of diabetic neuropathy, diabetic retinopathy and diabetes-related renal function impairment was

32.5%, 33.2% and 15.9% of participants overall, respectively and increased with age (Table S2). The incidence of each of these comorbidities was particularly high in Eastern Europe compared with other regions (Table S3).

Rates of macrovascular complications (such as coronary heart disease and peripheral vascular disease), other complications and hypertension were highest in the ≥65-year age group and in Eastern Europe compared with the other regions (Tables S2 and S3).

5 | THERAPEUTIC MANAGEMENT

5.1 | Insulin device and formulation use

Injections/pens, pumps or a combination of the two were used by 79.9%, 19.9% and 0.2% of participants, respectively (Table 4). Insulin pump use decreased as age increased, while injection/pen use increased with increasing age. Neutral Protamine Hagedorn (NPH) use tended to increase with age. Long-acting basal insulin (BI) analogues (first-generation [insulin glargine 100 U/ml; insulin detemir] or second-generation [insulin glargine 300 U/ml; insulin degludec]) were used by 63.1% of participants and increased with age. Second-generation long-acting BI analogues were used by more participants in the older age groups (Table 4).

Insulin pump use ranged from 43.3% in Western Europe to 3.2% in the Middle East (Table 5). NPH was used most frequently in Eastern Europe and Latin America. Long acting BI analogue use was highest in the Middle East (mostly first-generation analogues), while most participants from Asia used second-generation long-acting BI analogues (Table 5).

5.2 | Insulin dose and dose adjustment

Mean (*SD*) total insulin doses were 50.0 (24.1) U/day or 0.71 (0.30) U/kg/day (Table 4). The mean daily dose decreased from 51.0 U/day or 0.74 U/kg/day in the youngest subgroup to 46.4 U/day or 0.65 U/kg in the oldest subgroup. Overall, 2660 (68.9%) participants were receiving a basal-bolus regimen, the majority (78.8%) were injecting one daily basal dose, administered in the evening in most cases (70.1%).

Most participants followed a patient-driven protocol for insulin dose adjustments (insulin titration; 57.0%), but as age progressed more participants followed physician-driven insulin adjustments (Table 4). Physician-driven insulin dose adjustment was most common in Asia, Latin America and the Middle East (Table 5).

Overall, 27.5% of participants adjusted their BI dose less than every month, and this was more common in the younger age groups (Table 4). Approximately 20% of participants adjusted their BI dose more than every month but less than every 2 weeks (Table 4). By comparison, most participants adjusted short-acting insulin doses more than once a week (54.7% overall; Table 4). Over 50% of participants in Latin America adjusted their BI dose less than once a month, while BI dose adjustment more than every month but less than every 2 weeks, was most common in Asia. Frequency of short-acting insulin dose adjustment also varied by region, with particularly high proportions of participants in Eastern (71.9%) and Western Europe (67.5%) adjusting doses more than once a week (Table 5).

5.3 | Concomitant glucose-lowering therapies

Globally, 11.1% of participants used ≥1 glucose-lowering drug in addition to insulin, most commonly metformin (9.3%). Metformin use increased with age (6.9% in the 26–44 years group; 11.7% in the ≥65 years group) and was most common in Latin America and the Middle East (13.7% and 19.4%) and lowest in Eastern Europe (3.6%). Use of sodium-glucose linked transporter-2, alpha-glucosidases inhibitors and glucagon-like peptide-1 was low; 1.2%, 1.1% and 0.3%, respectively. It should be noted that thiazolidinedione, sulfonylurea or dipeptidyl peptidase-4 inhibitor use at any time since T1DM diagnosis was an exclusion criterion.

5.4 | Structure of medical care

Globally, the healthcare team of most people with T1DM included a diabetes specialist (54.6%) and/or an endocrinologist (52.1%), which was consistent across age groups. For each participant, multiple healthcare professionals could be involved. Healthcare teams also included an ophthalmologist for 29.7%, a diabetes-specialist nurse for 22.0% and a dietician/nutrition specialist for 17.8% of the global population. Only 3.0% of participants had access to a psychologist.

5.5 | Technology use

Based on responses to the technology use questionnaire, finger-stick blood glucose meters were used by most participants worldwide (92.0%) and did not vary by age group, with use being lowest in Western Europe (83.1%) and Asia (90.8%) and highest in Eastern Europe (98.4%).

The proportion who used CGM (23.2% globally) tended to decrease with age: 24.4% and 20.1% in the 26–44 and ≥ 65 years age group, respectively. The proportion who used CGM also varied from 46.4% in Western Europe to 2.5% in the Middle East. Insulin pump use (19.5% overall) decreased with age (23.4% in the youngest and 10.9% in the oldest age groups) and ranged from 42.3% in Western Europe to 2.7% in the Middle East. Blood ketone meters were used by only 11.1% of participants globally. The use of apps to monitor diet/provide carbohydrate counting (11.3%), to remind users to take their diabetes medication (4.2%), to assist with insulin dose adjustment (4.6%), to manage weight (4.7%) or to store personal health information (5.4%) was low and was mostly used when recommended by the HCP. In general, younger participants were more likely to use

apps than older participants (e.g., 14.3% of the youngest and 5.5% of the oldest subgroups used a diet/carbohydrate counting app).

6 | DISCUSSION

SAGE adds further evidence that glycaemic control remains poor in adults with T1DM in real-life. Approximately a quarter of participants achieved HbA_{1c} less than 7.0 % across age groups, while target achievement declined with increasing age. Despite being low, this proportion is higher than 18% of the young adult cohort (aged 19–25 years) reported in the Global Teens Registry and 21% of adults in the T1D Exchange registry.[1,14] Suboptimal glycaemic control was identified across every region analysed, notably in the Middle East and Asia where only approximately one-fifth of participants achieved HbA_{1c} less than 7.0 %.

While guidelines provide generalised HbA_{1c} targets, they also recommend individualised targets according to factors such as age, diabetes duration, pregnancy, lifestyle, hypoglycaemia risk, life expectancy, diabetes complications, comorbidities and occupation.[15–17] Few participants (20.9%) achieved individualised HbA_{1c} targets overall but rates of achievement were highest in the ≥65 years age group, potentially reflecting more relaxed HbA_{1c} targets of <7.5 to ≤8.5 % (depending on coexisting illnesses, cognitive function and functional status) in this age group.[18]

Previous studies have shown that technology usage by patients with T1DM has increased in recent years; during 2016–2018 in T1D Exchange study in the US, pumps and CGM were used by 63% and 30% of participants, respectively. By comparison, overall rates of pump and CGM use were lower in SAGE (approximately 20% and 23% globally). However, usage varied considerably across the regions analysed, with the highest use of pumps (42%) and CGM (46%) observed in Western Europe. Therefore, technology usage potentially reflects differences in insurance coverage or physician training for CGM.

Interestingly, HbA_{1c} target achievement rates seem to be higher in regions where patient-led insulin dose adjustment was more common (Eastern and Western Europe), with BI dose adjustment at least once a week also more frequent in these regions.

Of note, rates of microvascular and macrovascular complications were highest in Eastern Europe, while there were no major differences in factors such as current glycaemic control, age, BMI or duration of diabetes between Eastern Europe and the other regions. However, complications result from long-term diabetes control,[19] on which no data were available in this study and the current HbA_{1c} levels captured may not represent historical glycaemic control. Such a discrepancy between historic and current glycaemic control may be a particularly relevant consideration for Eastern Europe (comprising Bulgaria, Croatia, Serbia and Ukraine in SAGE) because of evolving healthcare systems associated with the dramatic political, economic and social changes in this region since the early 1990s[20] Additionally, it is important to highlight that health insurance coverage was lowest in Eastern Europe, with most of the participants who lacked insurance coming from Ukraine. Differences in access to healthcare must be considered as many patients in some countries included in SAGE (e.g., India) face considerable challenges accessing treatment (including insulin), screening for complications and support.[21] Ethnical, cultural and healthcare system-related factors and type of centres that recruited the participants may also impact outcomes. Further analyses on the SAGE data, including patient-reported outcomes, may help elucidate the association between these factors and glycaemic control.

Regions in which a higher percentage of participants achieved their HbA_{1c} target, also recorded a higher incidence of ≥1 symptomatic hypoglycaemia event. The poor glycaemic control observed overall, may be due to suboptimal insulin management. Use of structured education programmes can support reduction in HbA_{1c} levels and variability[22] and may help enforce the benefits of self-management tools.

As may be expected given the HbA_{1c} data, rates of DKA reported in SAGE were similar to those reported in the literature.[23–25] For example, in a UK retrospective study approximately 1%–2% of participants experienced DKA episodes leading to hospital visits over a 6-month period,[25] while in SAGE the incidence of hospitalisation/emergency visits linked to severe hyperglycaemia leading to DKA was approximately 2%. In SAGE, this rate of hospitalisation/emergency visits corresponded to approximately half of the participants who experienced severe hyperglycaemia leading to DKA, which appears lower than expected given the clinical consequences of DKA. Of note, as DKA and hospitalisations were reported by physicians who may not have had direct contact with patients in the emergency room, it is possible the incidence of hospitalisation/emergency visits linked to severe hyperglycaemia leading to DKA may have been under reported.

It is of interest that approximately 21% of participants had a family history of T1DM. This is somewhat higher than previous reports that suggest that approximately 15% of people with T1DM have a family history of T1DM.[26] However, our data are comparable to a Finnish study, which reported approximately 24% of children with T1DM has a first- or second-degree relative with the disease.[27]

The strengths of this study include the insights provided by the assessment of a large population of adults with T1DM across five geographic regions and comprehensive collection of data on various aspects of diabetes management. These data are of interest as there are limited data describing real-life outcomes in this population. The status of T1DM management in the United States was recently reported in the T1D Exchange study, and SAGE expands on this evidence to non-US regions. However, limitations of the SAGE study include the lack of North American and African participants. While participants were representative of each region (although selection bias cannot be completely ruled out), not all countries from each region were included. Furthermore, country-specific analyses were not performed, so conclusions about the impact of factors such as health care systems on T1DM outcomes cannot be made, since healthcare systems may differ between countries within a region.

Data were collected retrospectively, and in accordance with local clinical practice, so it is possible that there were some variations between sites in areas such as how T1DM was diagnosed and how endpoints such as DKA were defined. Additionally, while a longer study period may present a challenge in terms of maintaining data collection from patients, 6 months represent a relatively short period over which to collect severe hypoglycaemia and DKA data, so this may have influenced results.

In conclusion, results from this global study confirm that glycaemic control is suboptimal in adults with T1DM. SAGE identified several areas where treatment can be optimised in order to improve outcomes, including better supporting patients to self-manage their insulin therapy, increasing the use of technologies such as CGM and the provision of greater healthcare support. The results of this study will be of importance when taking into account the current incremental incidence in T1DM over the globe.[28]

ACKNOWLEDGEMENTS

The authors would like to thank the study participants, trial staff and investigators for their participation. This work was supported by Sanofi, Paris, France. Editorial assistance was provided by Fishawack Communications Ltd., and funded by Sanofi. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.

CONFLICT OF INTERESTS

Eric Renard is a consultant/advisor for Abbott, Air Liquide, Cellnovo, Eli Lilly, Insulet, Johnson & Johnson (Animas, LifeScan), Medtronic, Novo Nordisk, Roche Diagnostics and Sanofi-Aventis and research grant/material support from Abbott, Dexcom, Insulet, Roche Diagnostics and Tandem Diabetes Care. Hiroshi Ikegami receives honoraria for lectures: Astellas, MSD, Terumo, Eli Lilly Japan, Novartis, Novo Nordisk, Research Support: Sumitomo Dainippon Pharma, Otsuka Pharmaceutical, Takeda, Mitsubishi Tanabe Pharma, Novo Nordisk, Abott, Johnson & Johnson, Astellas, Ono Pharmaceutical, Kyowa Kirin, Daiichi Sankyo, Boehringer Ingelhaim Japan and Bayer. André Gustavo Daher Vianna is on advisory board and received speaker fees from Sanofi, Abbott Diabetes Care, Medtronic, Novo Nordisk, Lilly, Servier and Astra-Zeneca and research grant support from Sanofi, Lilly, Astra-Zeneca and Novo Nordisk. Paolo Pozzilli is a consultant for Astra Zeneca, Sanofi, Lilly and Abbott. Sandrine Brette is an Aixial employee, mandated by Sanofi. Zsolt Bosnyak, Felipe Lauand and Valerie Pilorget are Sanofi employees and shareholders. Anne Peters received advisory board fees from Abbott diabetes Care, Bigfoot, BI, Eli Lilly, Livongo, MannKind, Novo, Sanofi, Whole Biome and research support: Dexcom, vTvTherapeutics. Stock Options: Mellitus Health, Omada Health, Stability Health, Pendulum Therapeutics. Dubravka Jurišić-Eržen received consultancy fees from Astra Zeneca, Boehringer Ingelheim, Eli Lily, Novo Nordisk, Sanofi Aventis and Takeda. Jothydev Kesavadev received advisory board and speaker fees from Sanofi, Novo Nordisk, MSD, AstraZeneca, Biocon, Abbott Diabetes Care, Medtronic, Boehringer Ingelheim and Johnson & Johnson. Jochen Seufert is an advisory board member of Abbott, AstraZeneca, Boehringer Ingelheim, GI Dynamics, Janssen, LifeScan Mundipharma Novartis, Novo Nordisk, Sanofi Speaker Abbott, AstraZeneca, Bayer, Berlin Chemie Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Eli Lilly, Merck Sharp Dohme (MSD) MedScape Novartis, Novo Nordisk, Omniamed Sanofi; research support from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, GI Dynamics, Intarcia Ipsen, Janssen, Novartis, Novo Nordisk, Sanofi, Ypsomed. Emma G. Wilmot received personal fees from Abbott Diabetes Care, Dexcom, Eli Lilly, Medtronic, Novo Nordisk and Sanofi Aventis.

AUTHOR CONTRIBUTIONS

Eric Renard, André Gustavo Daher Vianna, Paolo Pozzilli, Dubravka Jurišić-Eržen, Jothydev Kesavadev and Emma G. Wilmot participated as an investigator, provided comments and input to all drafts of the manuscript and interpretation of the results. Hiroshi Ikegami, Felipe Lauand Anne Peters and Jochen Seufert provided comments and input to all drafts of the manuscript and interpretation of the results. Sandrine Brette contributed to acquisition of data and analysis, provided comments and input to all drafts of the manuscript and interpretation of the results. Zsolt Bosnyak contributed to original design of the trial, provided comments and input to all drafts of the manuscript and interpretation of the results. Valerie Pilorget contributed to original design, acquisition of data and analysis, provided comments and input to all drafts of the manuscript and interpretation of the results.

DATA AVAILABILITY STATEMENT

Qualified researchers may request access to patient level data and related study documents including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan and dataset specifications. Patient level data will be anonymised, and study documents will be redacted to protect the privacy of trial participants. Further details on Sanofi's data sharing criteria, eligible studies and process for requesting access can be found at: https://www.clinicalstudydatarequest.com.

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SUPPORTING INFORMATION

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

How to cite this article: Renard E, Ikegami H, Daher Vianna AG, et al. The SAGE study: global observational analysis of glycaemic control, hypoglycaemia and diabetes management in T1DM. *Diabetes Metab Res Rev*. 2021;37(7):e3430. doi:10.1002/dmrr.3430