Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Real-world flash glucose monitoring patterns and associations between self-monitoring frequency and glycaemic measures: A European analysis of over 60 million glucose tests

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ARTICLE INFO

Article history:
Received 12 July 2017
Received in revised form
8 November 2017
Accepted 18 December 2017
Available online 24 December 2017

Keywords:
Flash glucose monitoring
Blood glucose monitoring frequency
Real-world data
Glycaemic measures

ABSTRACT

Aims: Randomised controlled trials demonstrate that using flash glucose monitoring improves glycaemic control but it is unclear whether this applies outside trial conditions. We investigated glucose testing patterns in users worldwide under real life settings to establish testing frequency and association with glycaemic parameters.

Methods: Glucose results were de-identified and uploaded onto a dedicated database once readers were connected to an internet-ready computer. Data between September 2014 and May 2016, comprising 50,831 readers and 279,446 sensors worldwide, were analysed. Scan rate per reader was determined and each reader was sorted into twenty equally-sized rank-ordered groups, categorised by scan frequency. Glucose parameters were calculated for each group, including estimated HbA_{1c}, time above, below and within range identified as 3.9–10.0 mmol/L.

Results: Users performed a mean of 16.3 scans/day [median (IQR): 14 (10–20)] with 86.4 million hours of readings and 63.8 million scans. Estimated HbA_{1c} gradually reduced from 8.0% to 6.7% (64 to 50 mmol/mol) as scan rate increased from lowest to highest scan groups (4.4 and 48.1 scans/day, respectively; $p < .001$). Simultaneously, time below 3.9, 3.1 and 2.5 mmol/L decreased by 15%, 40% and 49%, respectively (all $p < .001$). Time above 10.0 mmol/L decreased from 10.4 to 5.7 h/day (44%, $p < .001$) while time in range increased from 12.0 to 16.8 h/day (40%, $p < .001$). These patterns were consistent across different countries.

Conclusions: In real-world conditions, flash glucose monitoring allows frequent glucose checks with higher rates of scanning linked to improved glycaemic markers, including increased time in range and reduced time in hyper and hypoglycaemia.

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https://doi.org/10.1016/j.diabres.2017.12.015
0168-8227/

1. Introduction

Diabetes is reaching epidemic proportions and managing glycaemia is key to prevent microvascular complications as well as long-term macrovascular disease [1–5]. HbA_{1c} remains the gold standard for monitoring glycaemic control and given the detrimental effects of hyperglycaemia, guidelines recommend tight HbA_{1c} targets [6]. However, treatment of hyperglycaemia can precipitate hypoglycaemia, particularly in insulin-treated patients, which is associated with adverse clinical outcome [7–11].

Self-monitoring of blood glucose (SMBG) in diabetes is essential for safe and effective adjustment of glycaemic therapy in insulin treated patients [12–14]. Although a higher rate of glucose testing (in excess of 8 times/day) is associated with improved glycaemic control [15,16], repeated daily glucose checks are painful, inconvenient and can be difficult to maintain long-term. A recent UK-based analysis of pharmacy records reported 2.1 tests per day for those using insulin [17], whereas in those using modern blood glucose meters and sophisticated cloud-based analysis software, rates of testing range between 2.5 and 5.5 per day across Europe and North America [18].

Continuous glucose monitoring (CGM) is an alternative to SMBG, but the use of conventional CGM has been limited due to the need for repeated calibration using capillary glucose testing, relatively short sensor life and high costs. However, the emergence of FreeStyle Libre™ (Abbott Diabetes Care, Witney, UK) flash glucose monitor, a new generation of glucose testing devices, has made glucose checks easier with the ability to scan a sensor for glucose reading at any time. The flash glucose monitoring system does not require calibration, has a long sensor lifetime of 14 days and is relatively affordable, explaining the proliferation in device use.

Randomised controlled trials in patients with diabetes have shown increased glucose testing frequency with flash glucose monitoring, which was associated with improved glycaemic markers; a reduction in hypoglycaemia was observed in both type 1 and type 2 diabetes mellitus patients. The reduction in hypoglycaemia was evident whilst maintaining good HbA_{1c} in type 1 diabetes mellitus patients, whereas in younger type 2 diabetes mellitus patients with inadequate glycaemic control it was associated with the added benefit of decreasing HbA_{1c} [19,20]. The improvement in hypoglycaemia was observed early with flash glucose monitoring use [19,20]. Furthermore, these studies indicated high patient acceptability and satisfaction with the system [19,20].

Whilst data from these trials are encouraging, it remains unclear whether these findings apply outside trial conditions. Therefore, our overall aim was to investigate the use of flash glucose monitoring in real life clinical practice worldwide over a period of 20 months to establish: (i) number of glucose checks and their pattern across the day, (ii) associations between glucose testing frequency and glycaemic markers, (iii) potential geographical differences in glycaemic parameters and (iv) evolution of glycaemic markers during first sensor use.

2. Materials and methods

2.1. Sensors and readers

The FreeStyle Libre system is a sensor-based glucose monitor, with an on-body patch and a sensor filament in the subcutaneous tissue that measures interstitial fluid glucose levels and remains *in situ* for up to two weeks. A dedicated reader is placed over the on-body patch to wirelessly collect the current glucose and glucose trend, along with up to 8 h of glucose readings which are automatically stored every 15 min. When connected to the PC-based software with an active internet connection, the reader's 90-day memory is de-identified and uploaded to a database, the contents of which were analysed for this study. The commercial availability (from a webshop for approximately 70 euro for the single reader and 70 euro per 14-day sensor) of the system began in September 2014 in seven European countries (Germany, United Kingdom, France, Italy, Spain, Sweden and Netherlands), and subsequently expanded to other countries. The report software was also available for free download, which included an agreement that de-identified data would be collected by a database at each internet-connected use of the software. From September 2014 to May 2016, this database collected data from 55,343 readers with 64,288,918 sensor scans and 392,187,678 automatically-stored glucose readings.

2.2. Scanning details

Scanning frequency for each sensor was calculated by counting the number of scans divided by duration of sensor use according to recorded start and end times. Scanning frequency per reader was assessed by calculating mean scans of all its sensors followed by determining cumulative frequency distribution and summary metrics (mean, median and IQR). To understand the daily patterns of scanning, frequency of scans by hour of the day was evaluated.

2.3. Glycaemic measures analysed

The analysis required each sensor have at least 120 h of automatically-stored readings (480 readings) to ensure reliable glucose control measures. Data from all sensors belonging to the same reader were combined and calculated as the mean of all sensor measures. The readers were rank-ordered by scan frequency and allocated to twenty equally-sized groups of 2542 readers each. Glucose measures assessed included time in euglycaemic range (defined as glucose between 3.9 and 10 mmol/L), time in hyperglycaemia (>10 mmol/L) and time in hypoglycaemia (<3.9 mmol/L). Hypoglycaemia was further divided into subcategories of time spent below 3.1 mmol/L or below 2.5 mmol/L, cut offs in accordance with recent guidelines and publications in the field [19–23]. Finally, mean glucose was converted into estimated HbA_{1c} by the method accepted by international professional diabetes societies [24] and was also analysed. The glucose control measures were inspected as a function of the twenty

scan-frequency groups of readers, and comparisons between scan frequency groups were evaluated.

2.4. Assessment of regional differences

The glucose check frequency and relationship to glycaemic markers was evaluated across six different regions: five included countries having the highest use of flash glucose monitoring (Germany, Spain, France, UK and Italy), whereas the last "region" grouped all remaining countries together. Each reader was allocated to a country of origin determined by the country-code element of the initial internet protocol address of the software instance connected to the database, and was utilised to examine regional differences in the relationships of glycaemic measures and scan frequency.

2.5. Change in glycaemic measures

Glucose metrics were evaluated by day of sensor use for all days available for the first sensor. A subset of readers (n = 14,617) were selected that had sufficient measurements for their first, second, and third sensors (at least 240 h for all three) and were used consecutively (within 24 h). The daily glycaemic metrics of the first sensor were adjusted by day to correct for any systematic artifacts by sensor day.

2.6. Statistical analysis

The cumulative frequency of scan rates were calculated for each five percent of available readers, and descriptive statistics were calculated. The frequency distribution of scans by hour of the day was inspected for scanning patterns across the day.

Given the large number of readers, twenty equally-sized groups, divided along scan rate, were analysed by descriptive measures (mean and standard error) of glycaemic metrics. Statistical comparisons across the groups were performed by one-way analysis of variance (ANOVA), and the span of glycaemic measures and relative changes were reported from the lowest to highest scan rate groups.

For the analysis by region, ten scan rate groups were analysed due to the smaller numbers of available readers in the regional subgroups, but were otherwise evaluated similarly. ANOVA was done for mean rates of scanning and hypoglycaemia across the geographic regions and used for statistical comparisons by day of glycaemic measures across the first 14 days of sensor use.

The database was analysed by structured query language routines, and further summarized by KNIME (www.knime.org) and R statistical package (www.r-project.org). In view of the large sample size and multiple comparisons, only $P < .01$ was considered statistically significant. Confidence intervals were calculated for each group least square mean of each measure for each scan rate group, and comparisons were made across the scan groupings.

3. Results

3.1. User base

The analysis set had 50,831 readers with 279,446 sensors spanning 86.4 million monitoring hours (345.6 million automatically-stored readings) and 63.8 million sensor scans. The initial seven launch countries detailed above provided 93% of the readers in the analysis set. Germany was the most frequent (46%), followed by Spain (11%), France (10%), United Kingdom (8.8%), Italy (8.2%), Sweden (5.2%) and Netherlands (3.8%). Austria (2.5%) and Belgium (0.9%) were the only other countries with more than 0.5% of the readers, with the remaining 4% collected from 37 different countries around the world.

3.2. Frequency and pattern of glucose testing

Users of the readers performed an average of 16.3 and median (IQR) of 14 (10–20) daily glucose scans (Fig. 1a). The mean number of days of monitoring across the scan groups in the analysis set averaged 70.8 days (range 38.5–82.0, Table 1). The scanning occurred approximately five times more often during typical awake hours (6 AM to midnight) compared with typical sleeping periods (midnight to 6 AM). The most frequent hour of the day for scanning was 8 PM, with the least frequent at 3 AM. Despite lower scan rates at night, there was still an average of 1.6 scans between midnight and 6 AM. The pattern of daily scanning is shown in Fig. 1b.

3.3. Relationship between frequency of glucose testing and glycaemic markers

The following glycaemic markers were analysed: estimated HbA_{1c}, time spent in euglycaemia (3.9–10.0 mmol/L), hyperglycaemia (>10.0 mmol/L) and hypoglycaemia (<3.9, <3.1, and <2.5 mmol/L).

3.3.1. Estimated HbA_{1c}

Estimated HbA_{1c} reduced in groups with increasing number of scans (Fig. 2a). At each end of the scale, those scanning on average 4.4 times/day had an estimated HbA_{1c} of 8.0% (95% CI: 7.91–8.04%, 64 mmol/mol, 95% CI: 63–64 mmol/mol) decreasing to 6.7% (95% CI: 6.66–6.75%, 50 mmol/mol, 95% CI: 50–51 mmol/mol) in those performing an average of 48.1 scans/day ($p < .001$; Fig. 2a).

3.3.2. Time spent in hyperglycaemia

From the lowest to highest scan rate groups, time above 10.0 mmol/L decreased from 10.5 to 5.9 h/day, representing 44% reduction ($p < .001$; Fig. 2b).

3.3.3. Time spent in euglycaemia

Time in range, defined as glucose levels between 3.9 and 10.0 mmol/L, increased from 12.0 to 16.8 h/day comparing lowest

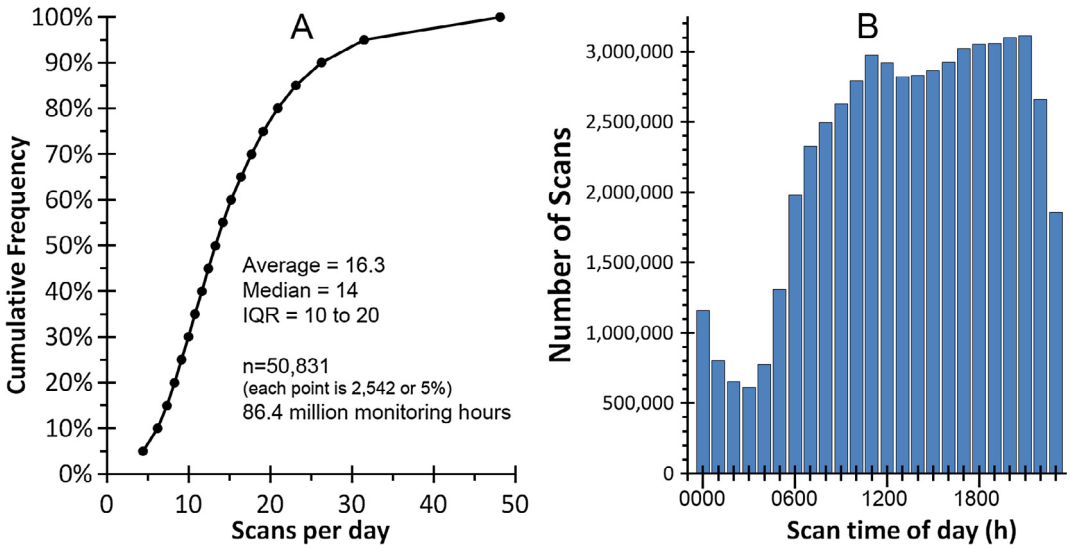

Fig. 1 – Cumulative distribution of glucose check frequencies (A) and total number of scans by hour of day (B).

with highest scan rate users, representing a 40% increase in time spent in euglycaemia ($p < .001$; Fig. 2c).

3.3.4. *Time spent in hypoglycaemia*

Time in hypoglycaemia was evaluated at three levels, in accordance with recent guidance and reporting of randomised controlled trials [19–23]. When low glucose levels were defined as readings below 3.9 mmol/L, time in hypoglycaemia decreased from 93.4 to 79.3 min per day comparing the lowest with highest scan rate groups, representing a 15% reduction in exposure to hypoglycaemia ($p < .001$; Fig. 2d). At a more extreme level of hypoglycaemia (<3.1 mmol/L), there was a 40% reduction comparing the lowest to highest scan rate groups, with reduction from 43.4 to 26.2 min per day ($p < .001$, Fig. 2e). The most extreme hypoglycaemic exposure (<2.5 mmol/L) had the largest relative reduction of 49% across the scale of scan rate frequency, from 23.4 to 11.9 min per day ($p < .001$, Fig. 2f).

3.4. *Regional differences in scanning frequency and relationship with glycaemic markers*

We analysed whether the patterns described above remain consistent in the different geographical regions.

3.4.1. *Glucose scanning frequency*

The scan frequency was found to vary significantly across the regions ($p < .001$), with the UK having the highest daily scans at 18.4. The scan rates across the regions all averaged over 16 per day, except France which had a scan frequency of 13.6 per day (Fig. 3).

3.4.2. *Relationship between scanning frequency and glycaemic parameters*

All countries showed a clear correlation between frequency of glucose scans and reduction in both hyperglycaemia and hypoglycaemia (Fig. 4). Moreover, increased scan frequency was associated with longer time spent in range and lower estimated HbA_{1c} (Fig. 5).

Although results were generally similar comparing the various countries, some differences were observed. For example, time spent in hypoglycaemia was most pronounced in patients from France, followed by Spain, particularly in those with less frequent scanning, whereas patients from Italy displayed the least hypoglycaemic exposure ($p < .001$).

The change in glucose levels, comparing low with high frequency scanning groups, was most prominent in patients from the UK, with time spent above 10.0 mmol/L decreasing from 11 to 5 h/day, representing a 46% reduction in time spent in hyperglycaemia. This was a more pronounced reduction compared with Germany (40%), France (34%), Spain (32%) and Italy (27%), respectively ($p < .001$). The decreased time spent in hyperglycaemia for frequent users was associated with decreased time spent in hypoglycaemia, emphasizing both the efficacy and safety of frequent glucose scanning at optimizing glycaemic control. When low glucose levels were defined as those below 3.1 mmol/L, the ranking of the reductions across the regions were Spain (46%), Italy (45%), "Other" (40%), France (32%), UK (30%) and Germany (26%).

3.5. *Glycaemic markers during the initial 14 days of system use*

Within the first 14 days of sensor use, time in hyperglycaemia and time in range were all found to be stable (Fig. 6a–c). However, reduction in hypoglycaemia was observed in the initial days of use, with the most dramatic change being from the first to second day. When low glucose levels were defined as readings below 3.9 mmol/L, time in hypoglycaemia decreased from 94.6 to 82.0 min per day from the first to fourteenth day of use ($p < .001$), representing a 13% reduction in exposure to hypoglycaemia (Fig. 6d). At a more extreme level of hypoglycaemia (<3.1 mmol/L), there was a 23% reduction across the two week period, with reduction from 36.3 to 27.9 min per day ($p < .001$, Fig. 6e). The most extreme hypoglycaemic exposure (<2.5 mmol/L) had the largest relative reduction of 32% across fourteen day period, from 17.1 to 11.6 min per day ($p < .001$, Fig. 6f). Furthermore, 74% of the reduction in time

Table 1 – Glucose control measures by scan rate group.

Scan rate per day	Readers (n)	Days of monitoring	Estimated HbA_{1c} (%)	Estimated HbA_{1c} (mmol/mol)	Minutes per day below			Hours per day	Hours per day
					2.5 mmol/L	3.1 mmol/L	3.9 mmol/L	3.9–10.0 mmol/L	Above 10.0 mmol/L
4.4 (0.017)	2542	71.4 (1.6)	7.98 (0.033)	64 (0.3)	23.4 (0.80)	43.4 (1.20)	93.4 (1.99)	12.0 (0.10)	10.5 (0.10)
6.2 (0.007)	2542	78.4 (1.6)	7.74 (0.028)	61 (0.3)	23.0 (0.72)	43.7 (1.12)	96.7 (1.84)	12.5 (0.09)	9.9 (0.09)
7.4 (0.006)	2542	75.6 (1.6)	7.56 (0.026)	59 (0.3)	22.8 (0.70)	44.3 (1.09)	101.1 (1.86)	12.9 (0.08)	9.4 (0.09)
8.3 (0.005)	2542	79.3 (1.7)	7.56 (0.025)	59 (0.3)	20.8 (0.62)	41.3 (0.96)	97.3 (1.64)	13.0 (0.08)	9.4 (0.09)
9.2 (0.005)	2542	82.0 (1.7)	7.44 (0.025)	58 (0.3)	22.0 (0.67)	43.4 (1.05)	100.6 (1.81)	13.4 (0.08)	9.0 (0.09)
10 (0.005)	2542	80.7 (1.7)	7.38 (0.024)	57 (0.2)	19.5 (0.59)	39.8 (0.98)	97.8 (1.80)	13.6 (0.08)	8.7 (0.09)
10.8 (0.005)	2542	81.0 (1.6)	7.37 (0.023)	57 (0.2)	18.8 (0.57)	38.4 (0.93)	94.4 (1.66)	13.7 (0.08)	8.7 (0.08)
11.6 (0.005)	2542	80.8 (1.7)	7.28 (0.022)	56 (0.2)	18.6 (0.59)	38.1 (0.93)	95.7 (1.66)	14.1 (0.08)	8.4 (0.08)
12.4 (0.005)	2542	79.0 (1.7)	7.23 (0.022)	55 (0.2)	18.6 (0.58)	38.3 (0.96)	96.3 (1.74)	14.2 (0.08)	8.2 (0.08)
13.3 (0.005)	2542	78.3 (1.6)	7.22 (0.022)	55 (0.2)	17.4 (0.58)	36.5 (0.93)	94.2 (1.68)	14.3 (0.08)	8.1 (0.08)
14.2 (0.005)	2542	76.8 (1.7)	7.20 (0.022)	55 (0.2)	17.5 (0.56)	36.9 (0.92)	95.2 (1.68)	14.3 (0.08)	8.1 (0.08)
15.2 (0.006)	2542	73.5 (1.6)	7.15 (0.022)	55 (0.2)	17.5 (0.60)	36.6 (0.95)	94.9 (1.72)	14.6 (0.08)	7.8 (0.08)
16.4 (0.007)	2542	74.3 (1.6)	7.16 (0.022)	55 (0.2)	16.4 (0.52)	34.7 (0.87)	91.9 (1.65)	14.6 (0.08)	7.9 (0.08)
17.7 (0.008)	2542	68.3 (1.5)	7.08 (0.021)	54 (0.2)	17.1 (0.56)	36.3 (0.96)	94.4 (1.74)	14.8 (0.08)	7.6 (0.08)
19.1 (0.009)	2542	68.6 (1.5)	7.09 (0.022)	54 (0.2)	15.4 (0.53)	33.2 (0.88)	90.4 (1.65)	14.9 (0.08)	7.6 (0.08)
20.9 (0.011)	2542	62.3 (1.4)	7.01 (0.021)	53 (0.2)	15.4 (0.53)	32.7 (0.88)	89.5 (1.66)	15.2 (0.08)	7.3 (0.08)
23.1 (0.015)	2542	62.2 (1.4)	6.96 (0.021)	53 (0.2)	15.3 (0.58)	32.5 (0.95)	89.4 (1.78)	15.4 (0.08)	7.1 (0.08)
26.3 (0.021)	2542	55.1 (1.2)	6.91 (0.022)	52 (0.2)	14.2 (0.51)	30.9 (0.88)	87.4 (1.75)	15.7 (0.08)	6.8 (0.08)
31.5 (0.041)	2542	50.5 (1.2)	6.84 (0.023)	51 (0.2)	14.5 (0.56)	31.4 (0.98)	89.0 (1.94)	16.0 (0.08)	6.6 (0.09)
48.1 (0.300)	2533	38.5 (1.0)	6.70 (0.023)	50 (0.2)	11.9 (0.55)	26.2 (0.94)	79.3 (1.92)	16.8 (0.08)	5.9 (0.09)

Values are mean (standard error) unless otherwise specified.

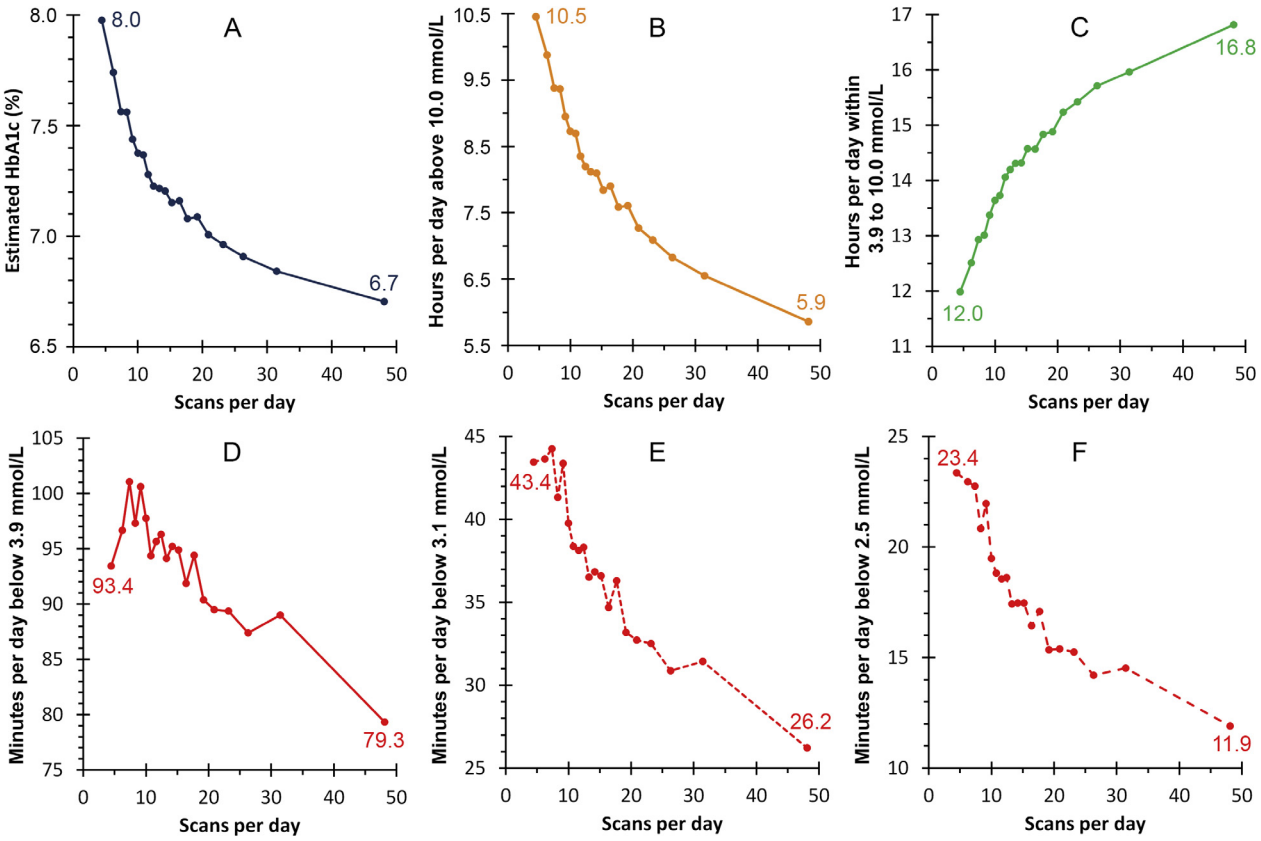

Fig. 2 – Glucose control measures by glucose check frequency.

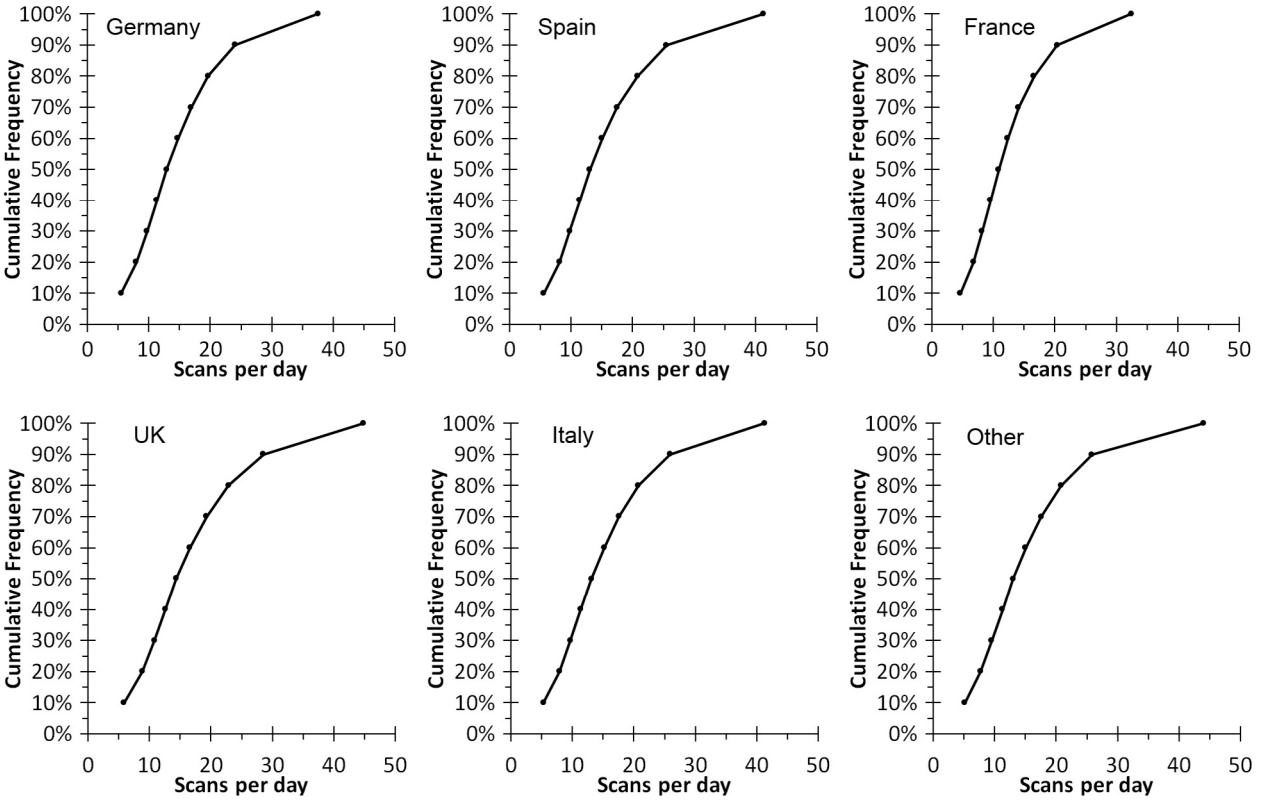

Fig. 3 – Cumulative distribution of glucose check frequencies for different geographic regions.

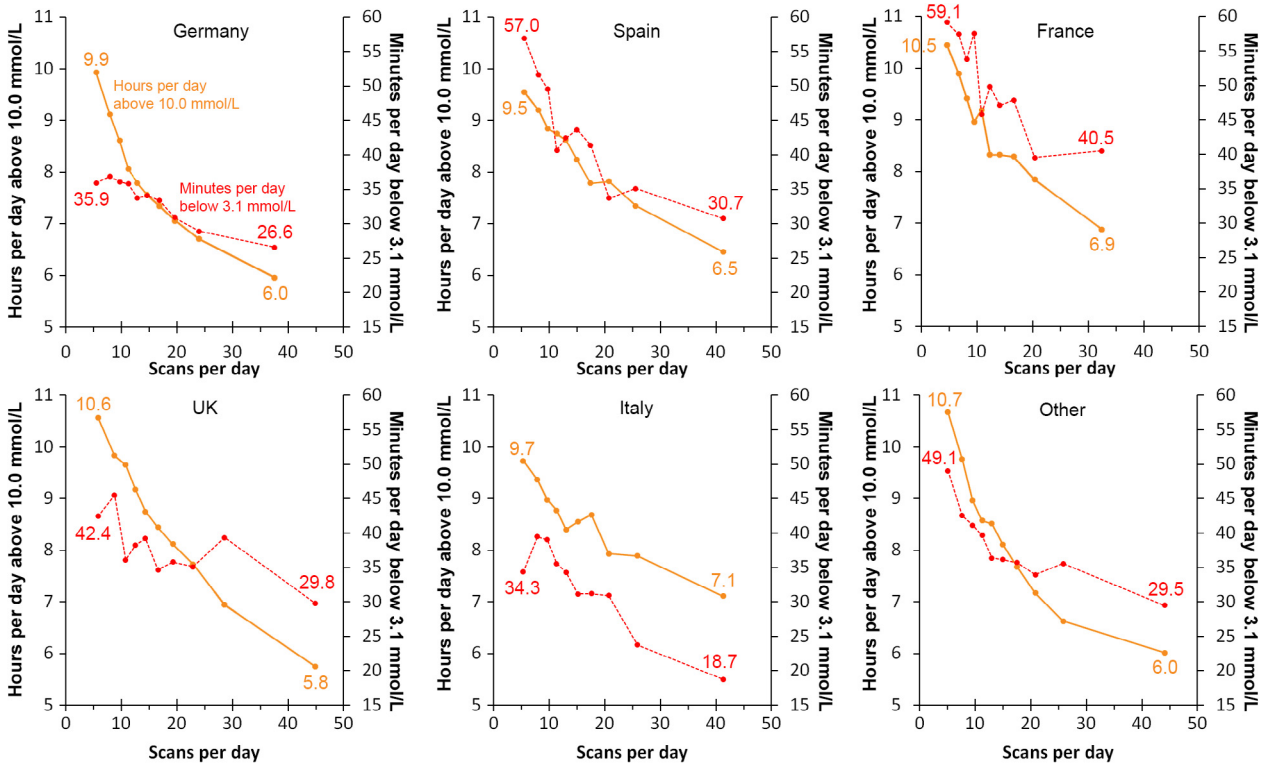

Fig. 4 – Glucose control measures for hyperglycaemia and hypoglycaemia by glucose check frequency for different geographic regions.

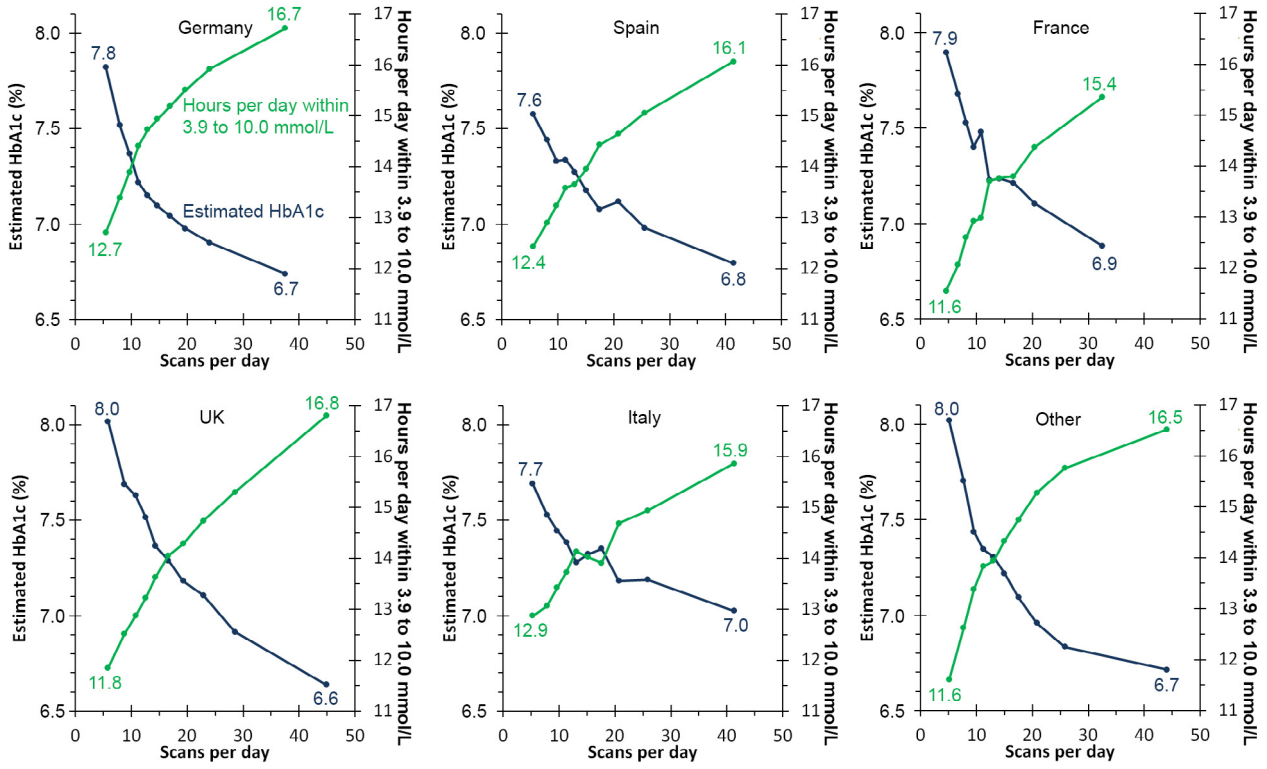

Fig. 5 – Glucose control measures for estimated HbA1c and time in range by glucose check frequency for different geographic regions.

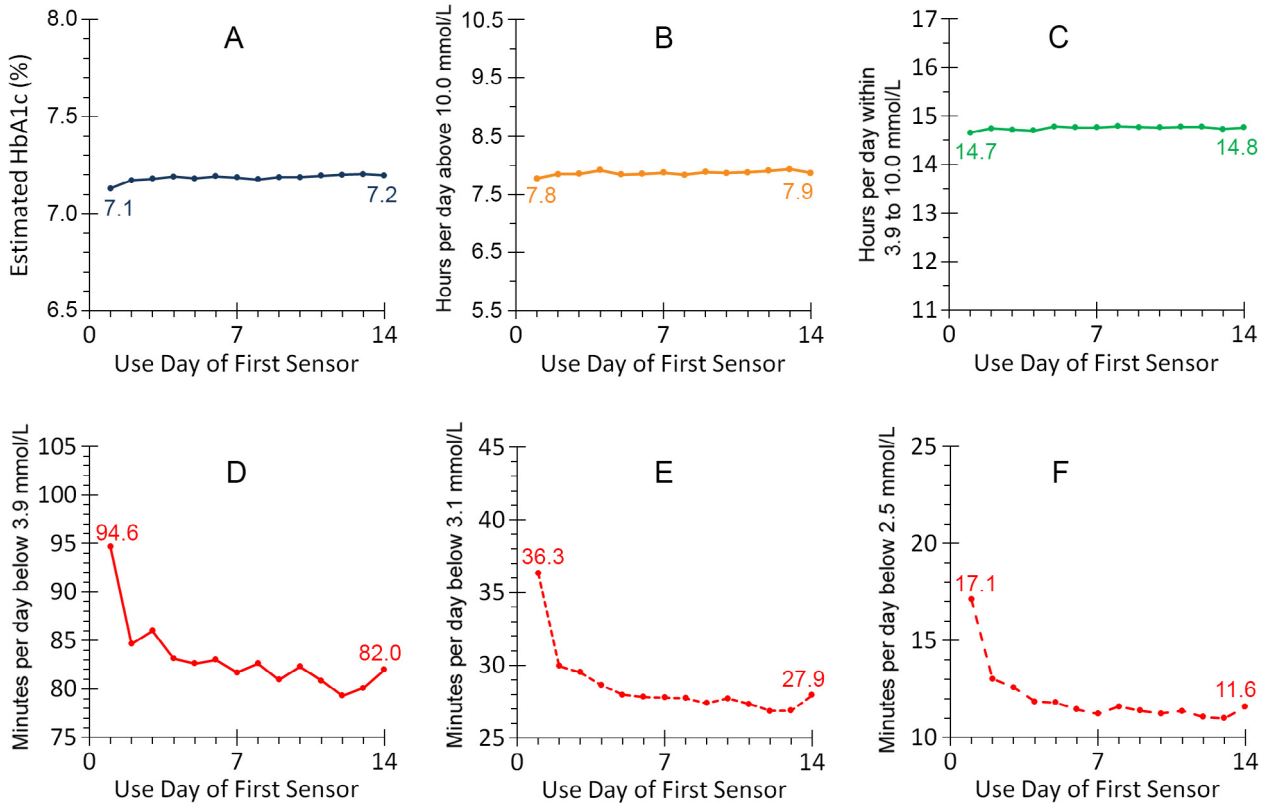

Fig. 6 – Glucose control measures by day for only the first sensor of each reader.

in hypoglycaemia (<2.5 mmol/L) occurred in the first two days with a further 26% reduction taking place over approximately 9 days, consistent with a rapid improvement.

4. Discussion

This is the first study to analyse the effects of flash glucose monitoring, in over 50,000 users worldwide, on glycaemic markers using a real world observational study design. Our work provides a number of novel observations, including: (i) a high frequency of glucose scanning compared to traditional SMBG, (ii) a diurnal variation in scanning frequency is observed with the majority undertaken between 6AM and midnight, but relatively high rate of testing is still performed overnight, (iii) higher scanning frequency is associated with better glycaemic measures including lower estimated HbA_{1c}, decrease in time in hyper and hypoglycaemia and increased time in euglycaemia with reduction in hypoglycaemic exposure occurring early during sensor use, and (iv) the associations between frequency of glucose scans and improvement in glycaemic parameters is consistent across different countries, although some subtle differences were evident related to baseline and level change.

The observed high rate of glucose checks is explained by the ease of testing and is consistent with data from two recent randomised controlled trials. In a study in type 1 diabetes mellitus patients [19], mean scanning frequency was 15 times/day whereas in a study in type 2 diabetes mellitus patients [20] it was lower at an average of 8 times/day. The current study is also in agreement in finding the majority of tests conducted during the day, although a significant proportion of tests were also performed overnight. No data on the type of diabetes were available and therefore it is not possible to ascertain whether a difference in scanning frequency is evident in type 1 and type 2 diabetes mellitus patients in real life clinical practice. A strong association between scanning frequency and improved glycaemic parameters was observed, which agrees with previous reports of increased frequency of capillary glucose testing is associated with lower HbA_{1c} [15,16]. However, glucose scanning frequency with flash glucose monitoring was significantly higher than SMBG checks reported previously by almost four fold.

In addition to reduced hyperglycaemia, this work shows that frequent scanning is simultaneously correlated with decreased time spent in hypoglycaemia. The relationship between hypoglycaemia and frequency of capillary glucose testing is currently unclear, although CGM studies suggest that a more thorough glucose profile helps to reduce hypoglycaemic events [25,26]. Taken together, this indicates that the frequent glucose data provided by flash glucose monitoring is key to reducing hypoglycaemic events. The effects of this glucose monitoring strategy on hypoglycaemia were found to occur primarily early, within the first 48 h of sensor use, followed by a further reduction in hypoglycaemia in the ensuing week, which is consistent with the data reported by Bolinder and colleagues [19]. Lowering glucose levels in diabetes is associated with increased risk of hypoglycaemic events, but as our work shows, those frequently testing glucose reduced both hyper and hypoglycaemia. This clearly has important clinical implications and suggests that flash monitor use

has the ability to optimise glycaemic control both effectively and safely.

It was reassuring that the relationship between glucose testing frequency and improvement in glycaemic markers was consistent across various countries. However, some differences were evident when analyzing the five countries with the largest numbers of users. For example, the largest reduction in glucose levels, comparing low with high frequency glucose scanners, was observed in patients from the UK, whereas the least reduction between groups was found in Italy. Time spent in hypoglycaemia was most pronounced in patients from Spain and France with the least exposure in Italy. However, increased scanning had the largest effect on reducing hypoglycaemia in groups of patients from Spain and the least reduction observed in groups of patients from Germany. The clinical significance of these findings is not entirely clear and these findings are best described as hypothesis-generating. Future research is warranted to investigate potential regional glycaemic heterogeneity in detail.

The strengths of the current study include real life settings, large sample size, broad geography and unrestricted inclusion criteria. However, there are a number of limitations that should be acknowledged. First, the basic characteristics of patients including gender, age, type of diabetes, duration of disease, and clinical parameters (including laboratory-based HbA1c values) are unknown. Further characteristics regarding employment profile, education, and socio-economic status are not available. Diabetes management self-efficacy markers and the methods and access to diabetes counselling and behavior support are lacking. Therefore, deeper clinical or scientific observations within these relevant subgroups are not possible. Second, there may be selection bias by unknown factors like age, job profile or disease status including towards those more motivated to improve glycaemia and those from higher socio-economic status, as the flash monitoring device was likely self-funded by most of the users. Third, the variability of scanning frequency from first to subsequent sensor use is currently unknown and the long-term effect of this monitoring strategy remains to be investigated. Our study did not examine any long-term complications that may be associated with use of the device, and does not include any health economic impact assessment, as these were beyond the scope of the analysis. Work is currently ongoing to collect longer-term longitudinal data on patients using flash monitoring. Finally, the device has other features that may have also contributed to our findings. The arrow trend and 8-hour glucose history (32 glucose readings) displayed by the reader, which are features not provided by conventional SMBG devices, may have played a role in improving glycaemic outcome. Moreover, the data transfer indicates that users were likely to have reviewed daily traces and summary reports of glucose patterns, including the Ambulatory Glucose Profile [27], further helping to adjust their therapies. These system features need further evaluation with regard to successful integration into diabetes self-care practices and therapy adjustments guided by clinicians. Despite these short-comings, the work provides an expansive view of the typical use of flash monitoring, and the substantial clinical benefits observed in those who attend more frequently to their glucose levels. Future work is still required to understand the role of flash glucose monitoring in modulating patient behavior, such as adjusting diet and exercise, and adherence to therapy as well as the ability to make self-management decisions with insulin treatment.

This worldwide multinational database of over 50,000 users, 64.3 million glucose scans and 86.4 million hours of automatic glucose monitoring provides an unprecedented view into the usage of a new glucose monitoring technology. The data demonstrate high frequency of scanning, emphasizing the ease by which glucose levels are checked. Moreover, the work shows a strong correlation between the number of glucose scans and improvement in glycaemic markers including reduction in time spent in hypo and hyperglycaemia and increased time in euglycaemia. This indicates that the system, under real life settings, represents a powerful glucose monitoring strategy to improve glycaemia in patients with diabetes.

Acknowledgements

Parts of these data were presented at the 10th International Conference on Advanced Technologies & Treatments for Diabetes, Paris, France, 15–18 February, 2017.

Funding

This work was funded by Abbott Diabetes Care.

Duality of interest

TD, YX, and GH are employees of Abbott Diabetes Care. RA received Honoraria and research support from Abbott Diabetes Care but none in relation to this work.

Contribution statement

All authors were involved in the design of the research, analysis and interpretation of the data. All authors worked collaboratively to review and prepare the final manuscript. TD is the guarantor and takes full responsibility for the work as a whole.

REFERENCES

[1] The Diabetes Control and Complications Trial Research Group. 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;329:977–86.
[2] Nathan DM, Cleary PA, Backlund JY, Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med 2005;353:2643–53.
[3] Nathan DM. Long-term complications of diabetes mellitus. N Engl J Med 1993;328(23):1676–85.
[4] Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321(7258):405–12.

[5] Patel A, MacMahon S, Chalmers J, ADVANCE Collaborative Group, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008;358(24):2560–72.
[6] American Diabetes Association. Glycemic Targets. Diabetes Care 2017;40 (Suppl. 1):S48–S56.
[7] Frier BM, Schernthaner G, Heller SR. Hypoglycemia and cardiovascular risks. Diabetes Care 2011;34(Suppl. 2):S132.
[8] Johnston SS, Conner C, Aagren M, Smith DM, Bouchard J, Brett J. Evidence linking hypoglycemic events to an increased risk of acute cardiovascular events in patients with type 2 diabetes. Diabetes Care 2011;34(5):1164–70.
[9] Hsu PF, Sung SH, Cheng HM, et al. Association of clinical symptomatic hypoglycemia with cardiovascular events and total mortality in type 2 diabetes: a nationwide population-based study. Diabetes Care 2013;36(4):894–900.
[10] Elwen FR, Huskinson A, Clapham L, et al. An observational study of patient characteristics and mortality following hypoglycemia in the community. BMJ Open Diabetes Res Care 2015;3(1):e000094.
[11] Khunti K, Davies M, Majeed A, Thorsted BL, Wolden ML, Paul SK. Hypoglycemia and risk of cardiovascular disease and all-cause mortality in insulin-treated people with type 1 and type 2 diabetes: a cohort study. Diabetes Care 2015;38 (2):316–22.
[12] Benjamin EM. Self-monitoring of blood glucose: the basics. Clin Diabetes 2002;20(1):45–7.
[13] Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia 2012;55(6):1577–96.
[14] Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach. Diabetes Care 2015;38:140–9.
[15] Miller KM, Beck RW, Bergenstal RM, et al. Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D Exchange clinic registry participants. Diabetes Care 2013;36(7):2009–14.
[16] Schütt M, Kern W, Krause U, et al. Is the frequency of self-monitoring of blood glucose related to long-term metabolic control? Multicenter analysis including 24,500 patients from 191 centers in Germany and Austria. Exp Clin Endocrinol Diabetes 2006;114(7):384–8.
[17] Lee WC, Smith E, Chubb B, Wolden ML. Frequency of blood glucose testing among insulin-treated diabetes mellitus patients in the United Kingdom. J Med Econ 2014;17 (3):167–75.
[18] Glooko+Diasend. Annual Diabetes Report 2016 Available fromAvailable from: http://www.glooko.com, 2016 [accessed February 22, 2017].
[19] Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kröger J, Weitgasser R. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. Lancet 2016;388:2254–63.
[20] Haak T, Hanaire H, Ajjan RA, Hermanns N, Riveline JP, Rayman G. Flash glucose-sensing technology as a replacement for blood glucose monitoring for the management of insulin-treated type 2 diabetes: a multicenter, open-label randomized controlled trial. Diabetes Ther 2017;8(1):55–73.
[21] The International Hypoglycaemia Study Group. Glucose glycaemia concentrations of less than 3.0 mmol/l (54 mg/dl) should be reported in clinical trials: a joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia 2017;60:3–6.
[22] The International Hypoglycaemia Study Group. Glucose concentrations of less than 3.0 mmol/L (54 mg/dL) should be reported in clinical trials: a joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2017;40:155–7.
[23] Maahs DM, Buckingham BA, Castle JR, et al. Outcome measures for artificial pancreas clinical trials: a consensus report. Diabetes Care 2016;39:1175–9.
[24] Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008;31(8):1473–8.
[25] Vigersky RA. The benefits, limitations, and cost-effectiveness of advanced technologies in the management of patients with diabetes mellitus. J Diabetes Sci Technol 2015;9 (2):320–30.
[26] Rodbard D. Continuous glucose monitoring: a review of successes, challenges, and opportunities. Diabetes Technol Ther 2016;18(Suppl. 2):S3–S13.
[27] Bergenstal RM, Ahmann AJ, Bailey T, et al. Recommendations for standardizing glucose reporting and analysis to optimize clinical decision making in diabetes: the Ambulatory Glucose Profile (AGP). Diabetes Technol Ther 2013;15(3):198–211.