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Real-World Flash Glucose Monitoring Patterns in Portugal: The Association between Self-Monitoring Frequency and Measures of Glycemic Control

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Blood Glucose Self-Monitoring;
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A B S T R A C T

Introduction: Using a multinational database of de-identified FreeStyle Libre sensor readings, we analysed the subgroup of data for Portugal with the aim of understanding the daily scanning behaviour for FreeStyle Libre users in Portugal and the association with performance against internationally agreed measures of glycaemic control.
Methods: De-identified data from FreeStyle Libre readers was collected between September 2014 and December 2020. Data for Portugal was extracted and analysed to determine the relationship between glucose scanning frequency and accepted measures of glycaemic control, including: estimated HbA1c, time in range 70-180 mg/dL, time with glucose <70 mg/dL, time with glucose <54 mg/dL, and time with glucose >180 mg/dL.
Results: The Portugal dataset included 13 323 readers representing 171 million individual glucose readings. Users were rank-ordered by daily scan rate and separated into 10 equal-sized bins groups, ranging from the lowest (mean scan rate of 3.70 scans/day) to highest (mean scan rate of 35.77 scans/day). Users in Portugal performed an average of 13.2 daily glucose scans (median 10.7, IQR 6.6–16.4). Estimated HbA1c decreased from 8.59% to 7.26% as scan rates increased from lowest to highest ($p < 0.05$). Time in range 70-180 mg/dL improved from 44.51% to 61.31% with increasing scan rates ($p < 0.05$) and time with glucose >180 mg/dL fell from 50.18% to 33.80% ($p < 0.05$). Time with glucose <54 mg/dL fell from a median of 1.28% to 0.52% as mean daily scans increased from 8.14 to 35.77 ($p < 0.05$).
Conclusion: Our study shows that, under real-life conditions, flash glucose monitoring enables users in Portugal to regularly monitor their glucose, and higher frequencies of monitoring are associated with improvements in accepted measures of glucose control, including lower estimated HbA1c and increased time in range, as well as less time in hyperglycaemia and clinically significant hypoglycaemia. These results are aligned with those observed world-wide.

Palavras-chave:
Automonitorização da Glicemia;
Diabetes Mellitus Tipo 1;
Glicemia;
Hipoglicemia;
Hiperglicemia;
Sistemas de Infusão de Insulina;
Portugal;
Técnicas Biossensoriais.

Padrões de Monitorização Flash da Glicose na Vida Real em Portugal: Associação entre a Frequência de Auto-Monitorização e o Controlo Glicémico

R E S U M O

Introdução: Utilizando uma base de dados multinacional de leituras anonimizadas de sensores FreeStyle Libre, analisámos o subgrupo de dados de Portugal com o objetivo de compreender o comportamento diário de leitura dos utilizadores FreeStyle Libre em Portugal e a sua associação com as medidas de controlo glicémico aceites internacionalmente.
Métodos: Foram recolhidos dados anonimizados de leitores FreeStyle Libre entre Setembro de 2014

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e dezembro de 2020. Os dados relativos a Portugal foram extraídos e analisados para determinar a relação entre a frequência de leitura de glicose e as medidas aceites para avaliação do controlo glicémico, incluindo: HbA1c estimada, tempo no alvo 70-180 mg/dL, tempo com glicose <70 mg/dL, tempo com glicose <54 mg/dL, e tempo com glicose >180 mg/dL.

Resultados: O conjunto de dados de Portugal incluiu 13 323 leitores que representam 171 milhões de leituras individuais de glicose. Os utilizadores foram ordenados por frequência diária de leitura e separados em 10 grupos de igual tamanho, que vão desde o mais baixo (frequência média de leitura de 3,70 leituras/dia) até o mais alto (frequência média de leitura de 35,77 leituras/dia). Os utilizadores em Portugal realizaram uma média de 13,2 leituras de glicose por dia (mediana 10,7, IQR 6,6-16,4). A HbA1c estimada diminuiu de 8,59% para 7,26% à medida que a frequência de leitura aumentou da menor à maior ($p < 0,05$). O tempo no alvo 70-180 mg/dL melhorou de 44,51% para 61,31% com o aumento da frequência de leitura ($p < 0,05$) e o tempo com glicose >180 mg/dL diminuiu de 50,18% para 33,80% ($p < 0,05$). O tempo com glicose <54 mg/dL diminuiu de uma mediana de 1,28% para 0,52% à medida que a média de leituras diárias aumentou de 8,14 para 35,77 ($p < 0,05$).

Conclusão: O nosso estudo demonstrou que, em condições de vida real, a monitorização flash da glicose permite aos utilizadores em Portugal monitorizarem regularmente a sua glicose, e frequências mais elevadas de monitorização estão associadas a uma melhoria nas medidas aceites para controlo da glicose, incluindo uma menor HbA1c estimada e um maior do tempo no alvo, assim como, menos tempo em hiperglicemia e hipoglicemia.

Introduction

Patient self-monitoring of blood glucose (SMBG) facilitates diabetes self-management and medication adjustment, especially in insulin-treated patients, and is an integral part of effective therapy in people with diabetes.[1] A higher rate of SMBG testing (>8 times/day) has been shown to be associated with superior glycaemic control[2,3]; however, repeated daily SMBG fingerprick testing has limitations, including poor compliance due to pain and discomfort, and inaccurate readings as a result of improper user technique. All of these can result in ineffective identification of adverse hyperglycaemic or hypoglycaemic episodes.[4,5]

Continuous glucose monitoring (CGM), which measures glucose in the interstitial fluid, has emerged as a more effective method for monitoring glucose levels.[6] However, many of the currently available traditional CGM systems are limited in their use both by their high cost and by the requirement for daily calibration using SMBG fingerprick tests. Flash continuous glucose monitoring (flash), using the FreeStyle LibreTM system (Abbott Diabetes Care, Witney, UK) allows users to view their current glucose readings by simply scanning the FreeStyle Libre sensor using a reader or smartphone app. Unlike traditional systems, the flash glucose monitoring system is factory calibrated and does not require SMBG fingerprick calibration. Flash glucose monitoring is also lower in cost.[7]

As use of traditional and flash CGM becomes an accepted standard of care in diabetes, a number of measures of glycaemic control have been established to assess glycaemic performance using the wealth of data that is made available by these systems. Amongst these, the time spent within defined glucose ranges is considered to be of high value in routine clinical care. To this end, the 2019 International Consensus on Time in Range has established a series of target glucose ranges and recommendations for time spent within these ranges that is consistent with good glycaemic control for people with diabetes.[8] For adults with type 1 diabetes or type 2 diabetes, these are: time in range (TIR) with glucose between 70-180 mg/dL; time in hypoglycemia with glucose <70 mg/dL; time in hypoglycemia with glucose <54 mg/dL; time in hyperglycemia with glucose >180 mg/dL; time in hyperglycemia with glucose >250 mg/dL. These are detailed in Table 1. The 2019 International Consensus on Time in Range also recommended a percentage of glucose readings that would constitute good glycaemic performance (Table 1).

A multinational database of de-identified FreeStyle Libre sensor readings has been established that has been valuable in correlating the rate of scanning using the FreeStyle Libre system with glycaemic performance against these international consensus recommendations.[5] This database has allowed an assessment of the impact of real-world flash glucose monitoring patterns across Europe as revealed by an analysis of over 60 million FreeStyle Libre sensor readings. This showed that higher rates of scanning of FreeStyle Libre sensors were linked to improved glycaemic performance for time spent within the target glucose range 70-180 mg/dL, as well as showing improvements for time in hypoglycemia <70 mg/dL or with glucose of <54 mg/dL, as well as for time in hyperglycaemia above 180 mg/dL. In this present study, we provide an analysis of the subgroup of data for Portugal, taken from the same multinational database, with the aim of understanding the daily scanning behaviour for FreeStyle Libre users in Portugal and its association with time in range 70-180 mg/dL, time with glucose <70 mg/dL or <54 mg/dL, and time above 180 mg/dL. This association is also examined within the wider European landscape through comparison with the real-world patterns previously published.[5]

Table 1. Consensus recommendations for TIR, TBR and TAR for adults, children and young people with T1D or T2D, and people at high risk of hypoglycaemia.[8]

	Time in Range (TIR)		Time Below Range (TBR)		Time Above Range (TAR)	
Diabetes group	**Target range**	**% of readings: time per day**	**Below target level**	**% of readings: time per day**	**Above target level**	**% of readings: time per day**
Type 1 / Type 2	70-180 mg/dL	>70%: >16 h, 48 min	70 mg/dL	<4%: < 1 h	>180 mg/dL	<25%: <6 hrs
			54 mg/dL	<1%: < 15 min	>250 mg/dL	<5%: <1 hr, 12 mins
Older/high-risk Type 1 or Type 2*	70-180 mg/dL	>50%: >12 h	70 mg/dL	<1%: < 15 min	>250 mg/dL	<10%: <2 hrs, 24 mins

* People with T1D or T2D at high-risk of hypoglycaemia because of age, duration of diabetes, duration of insulin therapy or impaired awareness of hypoglycaemia (IAH); T1D, Type 1 diabetes; T2D, Type 2 diabetes..

Material and Methods

1. Sensors and readers

The FreeStyle Libre system measures interstitial fluid glucose levels using a glucose sensor that is monitored with a dedicated reader or a smartphone app. By scanning the sensor, the reader or app wirelessly collects the current glucose reading and up to eight hours of the most-recent glucose readings. The system calculates a new glucose reading every one minute. This study uses only data from dedicated readers since the FreeStyle LibreLink app was not available in Portugal at the time of data collection.

When connected to a user-interface with an active internet connection, the data from the reader's 90-day memory is de-identified and uploaded to a database that is queried for analysis. All of the de-identified data is covered by an agreement that users are able to review at the point of downloading the FreeStyle Libre reporting software for their own use. The current study presents the outcomes from de-identified data collected between September 2014 and December 2020 and focuses on results from Portugal as well as those from the overall global dataset.

2. Scanning details

Scanning frequency for each reader was calculated by dividing its total number of scans by its total duration of sensor use according to recorded start and end times.

3. Glycaemic measures analysed

The analysis required each sensor to have at least 120 hours of automatically stored readings (480 readings) to ensure reliable interpretation of glycaemic measures. For each reader, data from all associated sensors were combined to calculate the reader's overall glucose metrics.

Glucose measures assessed included: percent time in range 70-180 mg/dL; percent time below range in hypoglycaemia <70 mg/dL, percent time below range in clinically significant hypoglycaemia <54 mg/dL; percent time above range in hyperglycaemia >180 mg/dL. Readers were rank ordered by mean scan frequency and grouped into 10 deciles based on this ranking. The cumulative frequency of daily scans was determined from these deciles, and the above glucose control measures were also analysed in relation to these 10 scan frequency groupings (Table 2).

4 Assessment of Portugal data compared to all countries

Each FreeStyle Libre reader's country of origin is determined by the internet protocol address of the reader's first data upload via desktop software. Multinational data and data specific to Portugal were extracted and analysed according to the method previously described.

5. Statistical analyses

Descriptive statistics were calculated for the glycaemic metrics defined above using the Python programming language and the

Table 2. Glycaemic control measures by daily scan groupings.

Readers (n)	Cumulative frequency*	Mean Daily Scans	Estimated HbA1c (%)	% Time in Range 70-180 mg/dL	% Time <54 mg/dL	% Time <70 mg/dL	% Time >180 mg/dL
All readers							
102103	10%	3.57	7.95 (6.76-8.88)	53.31 (36.1-71.2)	0.50 (0.04-2.01)	2.42 (0.58-6.18)	42.26 (23.8-59.4)
102103	20%	5.12	7.85 (6.78-8.72)	53.59 (37.9-69.7)	0.76 (0.13-2.54)	3.17 (0.97-7.15)	41.39 (24.8-57.2)
102103	30%	6.51	7.75 (6.76-8.58)	54.46 (39.6-69.2)	0.87 (0.17-2.66)	3.53 (1.18-7.48)	40.28 (24.7-55.4)
102103	40%	7.98	7.65 (6.72-8.44)	55.45 (41.4-69.3)	0.95 (0.21-2.71)	3.80 (1.35-7.68)	39.09 (24.2-53.5)
102103	50%	9.61	7.56 (6.66-8.31)	56.61 (43.2-69.7)	0.99 (0.23-2.69)	3.93 (1.48-7.78)	37.85 (23.4-51.7)
102103	60%	11.41	7.46 (6.61-8.18)	57.77 (45.0-70.1)	0.99 (0.25-2.63)	4.01 (1.58-7.75)	36.63 (22.6-50.0)
102103	70%	13.51	7.36 (6.54-8.06)	59.22 (46.9-71.4)	0.95 (0.26-2.51)	3.98 (1.63-7.67)	35.19 (21.2-48.3)
102103	80%	16.30	7.24 (6.42-7.93)	61.11 (48.8-73.6)	0.89 (0.23-2.41)	3.91 (1.57-7.69)	33.29 (18.8-46.3)
102103	90%	20.88	7.10 (6.26-7.79)	63.55 (51.4-76.7)	0.77 (0.19-2.41)	3.68 (1.43-7.54)	30.91 (15.6-44.0)
102105	100%	37.12	6.85 (5.95-7.55)	67.89 (55.8-82.8)	0.54 (0.09-1.78)	3.25 (1.11-7.23)	26.67 (9.5-39.6)
Portugal							
1332	10%	3.70	8.59 (7.29-9.76)	44.51 (27.8-59.4)	0.90 (0.13-3.07)	3.24 (1.01-7.69)	50.18 (34.3-67.8)
1332	20%	5.29	8.35 (7.28-9.26)	46.01 (32.5-57.3)	1.09 (0.28-3.05)	3.91 (1.40-7.41)	48.56 (35.7-63.1)
1332	30%	6.65	8.10 (7.11-8.93)	48.41 (35.6-60.5)	1.26 (0.34-3.40)	4.42 (1.74-8.40)	45.78 (33.2-59.2)
1332	40%	8.14	8.01 (7.01-8.85)	49.41 (36.6-60.5)	1.28 (0.37-3.01)	4.37 (1.86-7.91)	44.75 (31.4-59.0)
1332	50%	9.82	7.89 (6.99-8.69)	51.57 (38.6-62.0)	1.11 (0.36-2.49)	4.06 (1.80-7.06)	43.21 (30.2-57.0)
1332	60%	11.65	7.76 (6.91-8.55)	52.54 (40.4-63.2)	1.06 (0.34-2.70)	4.10 (1.85-7.45)	42.02 (29.3-55.6)
1332	70%	13.71	7.62 (6.77-8.36)	54.70 (43.0-65.6)	1.08 (0.33-2.46)	4.05 (1.86-7.38)	39.72 (26.6-52.6)
1332	80%	16.48	7.59 (6.72-8.36)	55.32 (42.8-67.2)	0.97 (0.30-2.55)	3.90 (1.66-7.40)	39.32 (24.8-53.4)
1332	90%	20.90	7.43 (6.61-8.10)	57.58 (46.5-68.5)	0.83 (0.23-2.54)	3.73 (1.61-7.69)	36.89 (23.0-49.6)
1335	100%	35.77	7.26 (6.36-7.98)	61.31 (49.2-75.0)	0.52 (0.13-1.60)	2.94 (1.21-6.34)	33.80 (17.9-47.4)

* Data from all sensors belonging to the same reader were combined to determine measurements for that reader. Readers were rank-ordered by mean scan frequency and divided into 10 equal-sized groups based on ranking. Data shown are means (interquartile range), except time <54 mg/dL and time <70 mg/dL which are medians (interquartile range).

KNIME analytics platform. Comparison of group means were conducted via independent samples t-tests, and comparison of group medians were performed by calculating their 95% bootstrapped confidence intervals of the median. The span of glycaemic measures were reported from the lowest to highest scan rate groups.

Results

1. Reader data and frequency of glucose scanning

The analysis set for all countries included 1 021 032 readers, with 11 850 548 sensors spanning 3.5 billion monitoring hours and 1.9 billion glucose scans, which yielded 13.8 billion automatically stored individual glucose readings. For the dataset specific to Portugal, there were 13 323 readers, with 171 013 sensors, 28.3 million glucose scans, and 201.4 million individual glucose readings. Users of the readers across all countries and in Portugal performed an average of 13.2 daily glucose scans (median 10.5 in 'all countries' and 10.7 in Portugal) (Fig. 1). Across the data for all countries, the mean scan rate in the lowest decile of scan frequency was 3.57 scans/day, rising to a mean of 37.12 scans/day in the highest scan frequency decile (Table 2, Fig. 1). For Portugal, the mean daily scans in the lowest decile of scan frequency was 3.70 scans/day, rising to a mean of 35.77 scans/day in its highest decile of scan frequency (Table 2, Fig. 1).

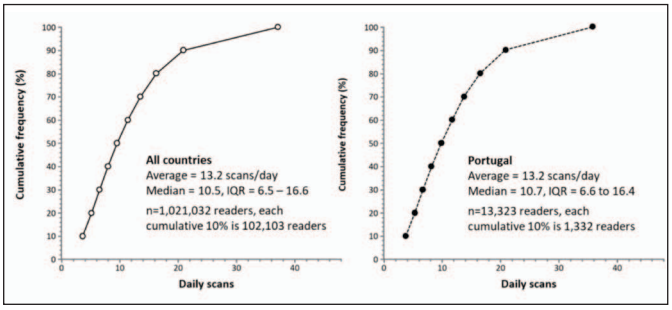

Figure 1. Cumulative distribution of glucose sensor scanning frequencies for all countries and for Portugal.

IQR, Interquartile range

2. Relationship between frequency of glucose scanning and estimated HbA1c

Estimated HbA1c decreased with increasing number of scans, both for the global dataset and for Portugal (Table 2, Fig. 2). For the global dataset, patients with the lowest scan rates (mean 3.57 scans/day) had an estimated HbA1c of 7.95%, which fell to 6.85% ($p <$ 0.05) in those with the highest scan rates (mean 37.12 scans/day). A similar pattern was observed for Portugal: estimated HbA1c was 8.59% for the scan frequency group with mean daily scans 3.70 scans/day, falling to 7.26% ($p < 0.05$) in the group with mean daily scans 35.77 scans/day (Fig. 2). For both users world-wide and users in Portugal, the differences in estimated HbA1c between the highest and lowest scan frequency deciles were comparable, showing a 13.9% relative reduction for all readers in the global dataset and a 15.5% relative reduction for the Portuguese readers.

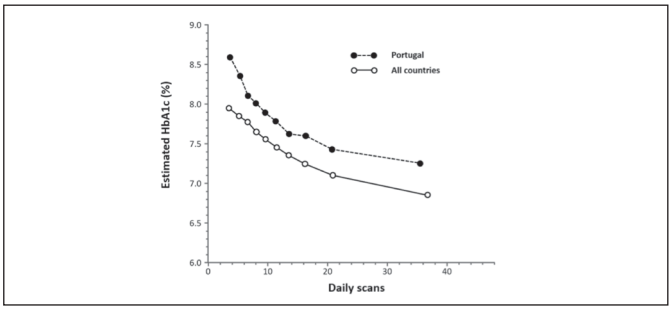

Figure 2. Estimated HbA1c by sensor scanning frequency.

Data are mean eA1c observed for each of the 10 ranked scan-frequency groups of readers, from lowest to highest mean scans/day. Each point on the graph represents 10% of all readers.

All-countries refers to the full analysis set for all countries in the multinational dataset.

3. Time in range 70-180 mg/dL

For the global dataset, the percent time in range with glucose readings between 70-180 mg/dL was 53.31% in the lowest scan frequency group (3.57 scans/day), rising to 67.89% ($p < 0.05$) in the highest scan frequency group (37.12 scans/day; Fig 3). For Portugal, percent time in range in the lowest scan frequency decile was 44.51%, rising to 61.31% ($p < 0.05$) in the highest scan frequency decile (Fig. 3).

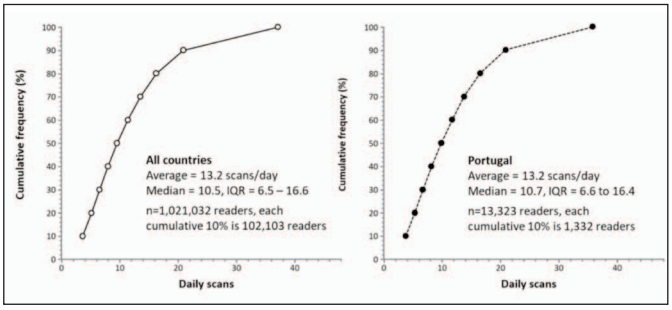

Figure 3. Percent time in range 70-180 mg/dL and above range with glucose >180 mg/dL by sensor scanning frequency.

Data are mean % time in range 70-180 mg/dL and > 180 mg/dL observed for each of the 10 ranked scan-frequency groups of readers, from lowest to highest mean scans/day. Each point on the graph represents 10% of all readers.

All-countries refers to the full analysis set for all countries in the multinational dataset.

4. Time below range in hypoglycaemia <54 mg/dL or hypoglycaemia <70 mg/dL

The most notable change with increasing scanning rates was seen for readings in the range of hypoglycaemia, both for percentage time <54 mg/dL and <70 mg/dL (Fig. 4). The data from Portugal show an initial rise in time with glucose <54 mg/dL, from

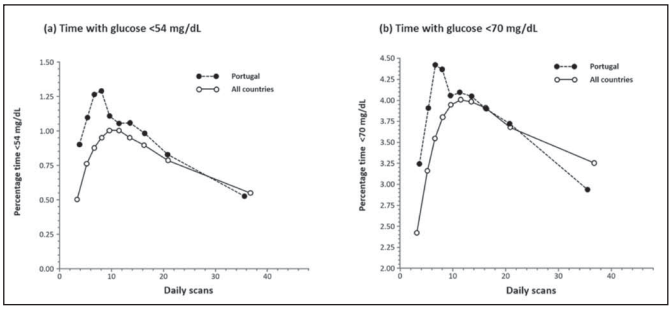

Figure 4. Percent time below range with glucose <54 mg/dL or <70 mg/dL by sensor scanning frequency.

Data are median (a) % time <54 mg/dL or (b) % time <70 mg/dL, observed for each of the 10 ranked scan-frequency groups of readers, from lowest to highest mean scans/day. Each point on the graph represents 10% of all readers.

All-countries refers to the full analysis set for all countries in the multinational dataset.

a median of 0.90% (95% CI of the median: 0.79% – 1.01%) to 1.28% (95% CI of the median: 1.14 – 1.39%) ($p < 0.05$) as the scan rate increased from 3.70-8.14 scans/day, but thereafter falling at higher scan rates to a median of 0.52% (95% CI of the median: 0.46% – 0.58%) ($p < 0.05$) at 35.77 scans/day (Fig. 4a). The combined data from the global readers also showed an initial rise in median time <54 mg/dL as scan rates increased, from 0.50% (95% CI of the median: 0.49 – 0.51%) at 3.57 scans/day to 0.99% (95% CI of the median: 0.98% – 1.00%) ($p < 0.05$) at 11.41 scans/day before declining to a median of 0.54% (95% CI of the median: 0.53% – 0.55%) ($p < 0.05$) at 37.12 scans/day (Fig. 4). The same pattern is revealed in the association between scan rates and median time with glucose <70 mg/dL (Fig. 4b). For Portugal, there is an initial rise from a median of 3.24% (95% CI of the median: 2.94 – 3.56%) to 4.42% (95% CI of the median: 4.21 – 4.70%) ($p < 0.05$) as scan rates increase from 3.70- 6.65 scans/day, thereafter falling to a median of 2.94% (95% CI of the median: 2.77% – 3.14%) ($p < 0.05$) at 35.77 scans/day. For the global dataset, median percentage time <70 mg/dL increases from 2.42% (95% CI of the median: 2.39% – 2.45%) to 4.01% (95% CI of the median: 3.98% – 4.05%) ($p < 0.05$) as scan rates rise from 3.57-11.41 scans/day, and thereafter decreasing only to a median percentage time <70 mg/dL of 3.25% (95% CI of the median: 3.22% – 3.28%) ($p < 0.05$) at 37.12 scans/day, which is above the median 2.42% at the lowest scan rates.

Although time in hypoglycaemia increases with scan rates initially both for Portugal and for the global dataset, it is notable that for the Portuguese users, percentage time <54 mg/dL is significantly lower at the highest scan rates than it is at the lowest scan rates ($p < 0.05$) (Fig. 4).

5. Time above range with glucose >180 mg/dL

Time in hyperglycemia with glucose >180 mg/dL decreased as scanning rates increased, both for the global dataset and also for the Portuguese set of readers (Fig. 5). The percent time >180 mg/dL recorded in the global reader dataset decreased from 42.26% to 26.67% as scanning rates rose from 3.57 scans/day to 37.12 scans/day ($p < 0.05$). The Portugal dataset showed a reduction in time >180 mg/dL from 50.18% (3.70 scans/day) to 33.80% (35.77 scans/day) ($p < 0.05$). The Portuguese data and the global data showed a similar decrease in the time spent in hyperglycaemia with increased frequency of glucose testing (32.6% and 36.9% reductions, respectively).

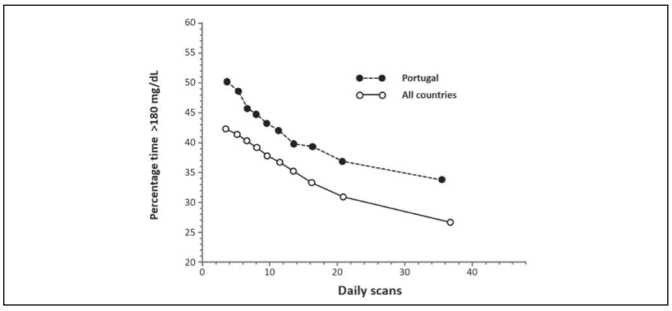

Figure 5. Percent time above range with glucose >180 mg/dL by scanning frequency.

Data are mean % time >180 mg/dL observed for each of the 10 ranked scan-frequency groups of readers, from lowest to highest mean scans/day. Each point on the graph represents 10% of all readers.

All-countries refers to the full analysis set for all countries in the multinational dataset.

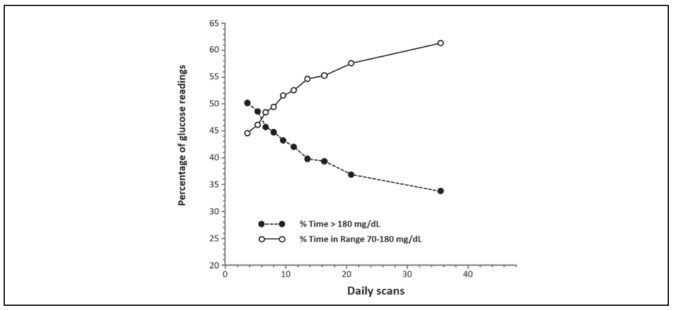

Figure 6. Percent time in range 70-180 mg/dL compared to percent time >180 mg/dL for Portugal.

Data are mean % time in range 70-180 mg/dL and % time >180 mg/dL for the Portugal dataset, observed for each of the 10 ranked scan-frequency groups of readers, from lowest to highest mean scans/day. Each point on the graph represents 10% of all readers..

Discussion

This study is one of a series that describes the relationship between daily scanning rates of the FreeStyle Libre flash glucose monitoring system and glycaemic markers using a real-world observational study design.[5,9] The current study is unique since it focuses on results from Portugal and provides an analysis of data collected from September 2014 to December 2020, in comparison to the global landscape of FreeStyle Libre use. Overall, our observations on glucose readings from the FreeStyle Libre system specific to its use in Portugal support previous findings that higher sensor scanning frequencies are associated with improved measures of glycaemic control, including lower estimated HbA1c, increased time in range 70-180 mg/dL, lower time in hyperglycaemia >180 mg/dL, and reduced time with hypoglycaemia, both below 54 mg/dL and below 70 mg/dL. A recent study in Portugal has also reported on 140 people with T1DM on continuous subcutaneous insulin infusion (CSII) pumps who used the FreeStyle Libre system.[10] Users performed a mean of 8.6 scans per day, and higher rates of scanning were associated with increased TIR, as well as reduced GMI and glycemic variability. These findings are aligned with our own observations, although the mean scan rates in our study were higher than those reported in the study on flash glucose monitoring and CSI. However, our user population was considerably larger and was not differentiated by treatment regimens.

The International Consensus on Time in Range[8] has recommended that people with type 1 diabetes or type 2 diabetes should aim to spend greater than 70% of time in range with glucose 70-180 mg/dL. Our analysis shows that, in both the global and the Portugal datasets, users of the FreeStyle Libre system had higher time in range associated with increased scanning, clearly showing that increased engagement, measured via scan frequency, is associated with improved glucose control. While most of the users' behaviors that might drive glucose control are unobserved, it is plausible that increased glucose monitoring enables more frequent or more precise interventions surrounding high and low glucose events.

Improvements in time in range with increased scanning rates were accompanied by reductions in the time spent in hyperglycaemia with glucose readings >180 mg/dL (Fig. 6). Each consecutive 10% of reader scanning group was associated with a trend towards increased time in range 70-180 mg/dL and a decrease in time above range >180 mg/dL.

In contrast with the scan frequency associations observed for time in range and time in hyperglycaemia, median percent time <54 mg/dL in Portugal rises from mean daily scans 3.70 to 8.14, and median percent time <70 mg/dL in Portugal rises from mean

daily scans 3.70 to 6.65. For these groups, time in hyperglycaemia is quite high, indicating a hyperglycaemia problem. One might speculate that these users were not at a level of engagement that can sufficiently minimize both hyperglycaemia and hypoglycaemia, and were most concerned with controlling hyperglycaemia. For example, they may be inappropriately bolusing after meals to correct peak hyperglycemia without considering active insulin. Between mean daily scans 8.14 and 35.77, the decrease in median percent time <54 mg/dL is consistent with the increase in time in range and the decrease in time in hyperglycaemia as scan frequency increases, suggesting that higher levels of engagement can increasingly control both time in hyperglycaemia and time in hypoglycaemia effectively. Median percent time <70 mg/dL in Portugal between 6.65 and 35.77 mean daily scans is similarly consistent. Fig. 4 shows that this same result exists for the global data. Our results provide evidence of the utility of the FreeStyle Libre system in reducing clinically relevant hypoglycemia, clearly showing that increased engagement, as measured by increased scanning, is associated with improved glucose control. The data presented in this study do not allow us to draw conclusions regarding symptomatic hypoglycemic events or hypoglycemia awareness. However, Deshmukh *et al* have observed a significant improvement in hypoglycemia awareness[11], as measured by reduced mean Gold scores, amongst 2801 people with diabetes 6 months after starting to use the FreeStyle Libre system.

While similar results were observed between the global and Portuguese data, the study population in Portugal may have specific characteristics that reflect the local market and reimbursement policy. Reimbursement and clinical guidelines for flash CGM were initially provided only to people with type 1 diabetes on insulin therapy with either MDI or CSII. Also, from a clinical point of view, patients with previous very poor glucose control also had a very poor compliance with SMBG use, despite all previous patient education. Therefore, these non-compliant patients were strong candidates to initiate the flash CGM system that has provided an opportunity to improve their glucose monitoring and control.

As with other real-world studies that use aggregated and de-identified data from FreeStyle Libre systems, our analysis has strengths and limitations. Strengths include the real-life setting, the large sample size and the unrestricted inclusion criteria. Limitations include the de-identified data structure which lacks characteristics such as gender, age, type of diabetes, duration of disease, clinical parameters (including laboratory-tested HbA1c values) or socioeconomic status indicators. Equally, regional differences in implementing flash glucose monitoring cannot be factored into our analysis, including reimbursement and access, additional diabetes education and lifestyle management advice that may accompany the initiation process in different national health systems.

Conclusion

This is the first and largest real-world study that investigates the utility of the FreeStyle Libre flash glucose monitoring system in a broad population of people with diabetes in Portugal, under different treatment regimens. The data clearly show that, under real-life conditions, flash glucose monitoring enables users in Portugal to regularly check their glucose levels. Importantly, higher rates of monitoring are associated with increased time in range and reduced time in hyperglycaemia and hypoglycaemia. These findings for Portugal are aligned with the outcomes for the wider global community of people with diabetes who use the FreeStyle Libre system to monitor their immediate and longer-term needs for glucose control.

Contributorship statement / Declaração de contribuição:

DC: First author and assumes full responsibility for the work as a whole.
All authors were involved in the design of the investigation, analysis and interpretation of the data; worked on the review and preparation of the final manuscript.

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.
Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.
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Ethical Disclosures

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.
Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).
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