The long-term impact of glucose monitoring with the FreeStyle Libre on glycaemic control and hypoglycaemia awareness in people with insulin-dependent diabetes mellitus: Insights from the Association of British Clinical Diabetologists national audit

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Aims

To investigate the change in glycated haemoglobin (HbA1c), hypoglycaemia awareness and diabetes-related distress in people with type 1 diabetes (T1D) using FreeStyle Libre (FSL) over a 2-year follow-up period.

Methods

FSL user data from U.K wide hospitals collected during routine clinical care were analysed. People living with T1D were categorised into four groups based on the duration of follow-up. Group I (< 1 year, n=6940), group II (1 to 1.5 years, n=662), group III (1.5 to 2 years, n=385), and group IV (> 2 years, n=642). The t-test was used to compare the baseline and follow-up HbA1c, GOLD score (a measure of hypoglycaemia awareness) and diabetes-related distress scale (DDS score) (quality of life measure).

Results

The study consisted of 16,834 people, with follow-up data available for 8,629 participants. The change in HbA1c, GOLD and DDS score from baseline within the follow-up sub-groups (group I vs group II vs group III vs group IV) was **HbA1c** (-6 vs -6 vs -4 vs -4 mmol/mol; P<0.001) (-0.55 vs -0.55 vs -0.37 vs -0.37 %), **GOLD score** (-0.31 vs –0.45 vs –0.26 vs –0.42; P<0.0001 group I, II, IV and P 0.07 group III), and **DDS score** (-0.59 vs –0.58 vs –0.63 vs –0.50; P<0.001), respectively.

Conclusion

In people with T1D, FSL use resulted in a sustained improvement in HbA1c, hypoglycaemia awareness and diabetes-related distress for over two years.

People with type 1 diabetes (T1D) continuously pursue optimal glycaemic control to prevent devastating clinical (micro- and macrovascular) and psychological consequences. Blood glucose monitoring is an integral part of achieving optimal glycaemic control, which has been revolutionised in the last decade with the introduction of glucose–sensing technologies which can measure the glucose concentration in the interstitial fluid. The FreeStyle Libre (FSL) glucose monitoring system is one such technology. To obtain a glucose reading, the libre reader is held near the sensor, and the device then displays glucose information over the preceding 8 hours, which includes current glucose and forecasts changes in glucose levels, thus allowing the operator to make necessary adjustments to diet and/or insulin dosing[1,2]. In clinical practice, the FSL monitoring system was first introduced in 2014. It became available in the National Health Service (NHS), U.K, in November 2017 for people with T1D, and, since then, has been widely used for glucose monitoring in this cohort[2]. Previously, using data from the Association of British Clinical Diabetologists (ABCD) nationwide audit on FSL use in people with T1D, our research group has shown that FSL users demonstrated a -5 mmol/mol (0.5%) change in HbA1c, reducing from 67 ± 21mmol/mol (8.3 ± 1.9%) at baseline to 62 ± 19 mmol/mol (7.9 ± 1.7%) after 7.5 (interquartile range 3.4–7.8) months of follow-up ($P < 0.0001$). The baseline GOLD score (to assess hypoglycaemia awareness) was 2.7 (±1.8), which improved to 2.4 (±1.7) ($P < 0.0001$) at follow-up. Furthermore, we showed that FSL users reported a reduction in diabetes-related distress (using the 2-point Diabetes Distress Screening scale questionnaire – DDS score), hospital admissions[3], and that the improvement in glycaemic control and hypoglycaemia awareness was independent of structured education attendance[2]. In this study we explore the impact of long-term FSL use on glycaemic control, hypoglycaemia awareness and diabetes-related distress in people living with T1D. This observational study analysed data collated from November 2017 to August 2022 as part of the nationwide ABCD audit on FSL[4]. The methodology of the nationwide audit has been described in an article[5] reporting previous results of the audit. We categorised people with T1D (≥ 95%) into four groups based on the duration of follow-up. Group I (< 1 year), group II (1 to 1.5 years), group III (1.5 to 2 years) and group IV (> 2 years). The t-test was used for comparing the baseline and follow-up HbA1c, GOLD and DDS score in the study population within the follow-up groups. Rolling HbA1c values were used in our analysis i.e., if someone had a follow-up, we used the HbA1c value available immediately before their follow-up as their baseline. For the calculation of the DDS score, we took the mean of the 2-point DDS2

questionnaire. Statistical analyses were done in R 4.1 programme. The baseline data were available for 16,834 participants of the study out of which 8,629 participants had at least one follow-up. There was a statistically significant improvement in HbA1c, GOLD, and DDS score across the studied population with follow-up **(Table 1).** In group I, the HbA1c improved from 69 ± 17mmol/mol (8.5 ± 1.6%) to 63 ± 17mmol/mol (7.9 ± 1.6%) (P<0.001), in group II from 68 ± 17mmol/mol (8.4 ± 1.6%) to 62 ± 14mmol/mol (7.9 ± 1.3%) (P<0.001), in group III from 65 ± 15mmol/mol (8.1 ± 1.3%) to 61 ± 11mmol/mol (7.7 ± 1.0%) (P<0.001) and in group IV from 63 ± 14mmol/mol (7.9 ± 1.3%) to 59 ± 11mmol/mol (7.5 ± 1.0%) (P<0.001). Similarly, statistically significant improvement in GOLD and DDS score was noted across all groups (apart from group III for GOLD score). **Figure 1** is a graphical representation of the GOLD and DDS score showing improvement from baseline to > 2 years of follow-up. Using data from this large, nationwide, real-world observational study examining FSL monitoring, we show that after commencing FSL monitoring, there is a sustained and statistically significant fall in HbA1c levels in all follow-up strata (Group I-IV). In addition to this, our analysis also suggests that there are sustained improvements in hypoglycaemia awareness (GOLD score) and diabetes-related distress (DDS score) during the follow-up period with FSL use. In terms of limitations, as this is an observational study with a lack of a comparator arm, causality cannot be established. We did not have the exact dates of hospital admissions in the database; therefore, we had to refrain from calculating sequential reduction/change in frequency of hospitalisations with ketoacidosis/severe hypoglycaemia in FSL users. Nevertheless, we believe this to be the first study describing the change in HbA1c, GOLD and DDS score with FSL monitoring over a substantial follow-up period (> 2 years) to date. Centres across Europe have published their results on long-term effectiveness of FSL monitoring[6-8]; however, their results describe a change in HbA1c and/or hypoglycaemia awareness/quality of life but do not examine all three variables as reported in our analysis. These data support the recent NICE guidance[9], which recommends that all individuals with Type 1 diabetes should have access to continuous glucose monitoring.

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NOVELTY STATEMENT

- Use of the FreeStyle Libre (FSL) glucose monitoring system by people with type 1 diabetes has previously been demonstrated to improve glycaemic control, hypoglycaemia awareness and reduce diabetes-related distress.

- This study demonstrates that significant improvements in these parameters in those using FSL glucose monitoring are sustained for over two years.

- The benefits demonstrated in people with type 1 diabetes using FSL glucose monitoring suggest that its role should be considered for people with type 2 diabetes, especially those requiring multiple daily insulin injections.

AUTHORSHIP

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AUTHOR CONTRIBUTION

NS is the first author of this article, assisted in the statistical analysis of the data, interpreted findings, wrote the first draft and all subsequent revisions. **HD** did the statistical analysis on the data and takes overall responsibility of the findings. **JP, PC and DJB** reviewed the article and made suggestions to improve its quality. **EGW, CW, REJR and TS** conceived and provided overall supervision for the project, making numerous suggestions to improve its quality. All authors have reviewed and approved the final version of this article.

CONFLICT OF INTEREST STATEMENT

EGW serves on the advisory panel for Abbott Diabetes Care, Dexcom and Eli Lilly and Company; has received research support from Diabetes U.K; and is on the speakers' bureau for Abbott Diabetes Care, Dexcom, Eli Lilly and Company, Insulet Corporation, Novo Nordisk and Sanofi. **CW** has a spouse/partner serving on the advisory panel for Celgene and on the speakers' bureau for LEO Pharma and Novartis. **REJR** serves on the advisory panel for Novo Nordisk A/S and is on the speakers' bureau for BioQuest. **TS** serves on the speakers' bureau for Novo Nordisk Foundation and reports a relationship with Bristol-Myers Squibb, Eli Lilly and Company, and Sanofi. The other authors have no conflicts of interest in relation to this article.

ETHICAL APPROVAL

The ABCD nationwide audit programme has Caldicott Guardian approval. The NHS encourages audit of clinical practice, and there are guidelines which were followed. Anonymisation of the collected data was ensured at the point of uploading to the central database, and the contributing centres were required to collect data from routine clinical practice only.

DATA AVAILABILITY STATEMENT

Data will be made available on reasonable request with the approval of the ABCD nationwide FSL audit committee.

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