Effect of flash glucose monitoring on glycemic control, hypoglycemia, diabetes-related distress, and resource utilization in the Association of British Clinical Diabetologists (ABCD) nationwide audit

Deshmukh, Harshal; Wilmot, Emma G; Gregory, Robert; Barnes, Dennis; Narendran, Parth; Saunders, Simon; Furlong, Niall; Kamaruddin, Shafie; Banatwalla, Rumaisa; Herring, Roselle; Kilvert, Anne; Patmore, Jane; Walton, Chris; Ryder, Robert E J; Sathyapalan, Thozhukat

DOI:
10.2337/dc20-0738

Effect of Flash Glucose Monitoring on glycaemic control, hypoglycaemia, diabetes-related distress and resource utilization in the Association of British Clinical Diabetologists (ABCD) nationwide audit

Harshal Deshmukh[1]*, Emma G. Wilmot[2]*, Robert Gregory[3], Dennis Barnes[4], Parth Narendran[5], Simon Saunders[6], Niall Furlong[7], Shafie Kamaruddin[8], Rumaisa Banatwalla[9], Roselle Herring[10], Anne Kilvert[11], Jane Patmore[1], Chris Walton[1], Robert E J Ryder[12¥], Thozhukat Sathyapalan[1¥]

Affiliations

1. Hull University Teaching Hospitals NHS Trust and University of Hull, Hull UK
2. Royal Derby Hospital, Derby UK
3. Leicester General Hospital, Leicester UK
4. The Tunbridge Wells Hospital, Tunbridge Wells UK
5. Queen Elizabeth Hospital Birmingham and The University of Birmingham, UK
6. Warrington and Halton teaching Hospitals Warrington UK
7. St. Helens and Knowsley Hospital St Helen UK
8. Darlington Memorial Hospital, Darlington UK
9. St Peter's Hospital, Chertsey, UK
10. Royal Surrey County Hospital, Guildford UK
11. Northampton General Hospital NHS Trust,Northampton, UK
12. City Hospital, Birmingham, UK

***joint first authors**

¥ Joint senior authors

Address for Correspondence

Prof. T. Sathyapalan
Honorary Consultant Endocrinologist
Academic Endocrinology, Diabetes and Metabolism
University of Hull/Hull University Teaching Hospitals NHS Trust

Tel. 01482 675312
Fax. 01482 675370

Abstract

Aims

The FreeStyle Libre (FSL) flash glucose monitoring device was made available on the UK National Health Services (NHS) drug tariff in 2017. This study aims to explore the UK real-world experience of FSL and the impact on glycaemic control, hypoglycaemia, diabetes-related distress and hospital admissions.

Methods

Clinicians from 102 National Health Service hospitals in the United Kingdom submitted FSL user data, collected during routine clinical care, to a secure web-based tool held within the NHS N3 network. T-tests and Mann-Whitney-U tests were used to compare the baseline and follow-up HbA1c and other baseline demographic characteristics. Linear regression analysis was used to identify predictors of change in HbA1c following the use of FSL. Within-person variations of HbA1c calculated adj-HbA1c-SD=SD/sq. Root [n/ (n−1)].

Results

Data were available for 10,370 (97% with Type 1 diabetes) FSL users; age 38.0 (±18.8) years, 51% female, diabetes duration 16.0 (±49.9) years, and BMI of 25.2 (±16.5) kg/m^2. FSL users demonstrated a -5.5mmol/mol change in HbA1c, reducing from 67.5 (±20.9) (8.3%) at baseline to 62.3 (±18.5) (7.8%) mmol/mol after 7.5 (IQR=3.4-7.8) months of follow up (n=3182) ($P<0.0001$)). HbA1c reduction was greater in those with initial HbA1c ≥69.5 (>8.5%) mmol/mol, reducing from 85.5mmol/mol (±16.1) (10%) to 73.1 mmol/mol (±15.8) (8.8%)) ($P<0.0001$). The baseline Gold score (score for hypoglycaemic unawareness) was 2.7 (±1.8) and reduced to 2.4 (±1.7) ($P<0.0001$) at follow-up. 53% of those with a Gold score of ≥4 at baseline had a score <4 at follow-up. FSL use was also associated with a reduction in diabetes distress ($P<0.0001$). FSL use was associated with a significant

reduction in paramedic callouts and hospital admissions due to hypoglycaemia and to hyperglycaemia/Diabetic Ketoacidosis (DKA).

Conclusions

We show that the use of FSL was associated with significantly improved glycaemic control and hypoglycaemia awareness, and a reduction in hospital admissions.

Introduction

Continuous glucose monitoring (CGM) is an established method of monitoring interstitial glucose levels to improve metabolic control in diabetes. The benefits include improvements in glycaemic control and hypoglycaemia[1-4]. Another form of interstitial glucose monitoring known as "flash" glucose monitoring (FreeStyle Libre; Abbott Diabetes Care) became available on the UK National Health Services (NHS) drug tariff in 2017. In contrast to CGM devices, the FSL does not have alarms to alert the user to hypo/hyperglycaemia. However, the advantages of FSL include lower costs and factory calibration, removing the need for frequent painful fingerstick calibrations during the 14-day wear period [5]. FSL is also known as intermittent continuous glucose monitoring (iCGM) as data from FSL sensor are only transmitted when the sensor is scanned with a reading device (reader or mobile phone app).

Randomized controlled trials have demonstrated that FSL use is associated with a significant reduction in the incidence of hypoglycaemia in people with Type 1 and Type 2 diabetes, but to date, a reduction in HbA1c has not been reported [6-8]. However, several observational studies have reported improvements in glycaemic control[9-14]. There are no comprehensive, real-world, large population-based data sets looking at the impact of FSL on multiple aspects of diabetes care. In this study, we utilize data from the nationwide audit for FSL conducted by the Association of British Clinical Diabetologists (ABCD) to assess the patterns of use of FSL and to study its effect on glycaemic control, hypoglycaemia, diabetes-related distress and hospital admissions due to hypoglycaemia and hyperglycaemia/diabetic ketoacidosis (DKA).

Methods

Patient recruitment and data collection

Data for this study were obtained from the nationwide audit of FSL conducted by ABCD (http://www.diabetologists-abcd.org.uk/n3/FreeStyle_Libre_Audit.htm). This nationwide audit was launched in November 2017. A secure online tool was launched in August 2018 on the National Health Services N3 network. NHS N3 network provides maximum security and allows analysis of anonymized national audit data The tool has the facility to detect data from the same patient entered in two sites (e.g. hospital and primary care) and to merge the data when exported (centres and sites below). Data were collected at baseline and follow-up during routine clinical care (Appendix 1). Baseline pre-FSL data included demographics, source of FSL funding, previous structured education completion, HbA1c values from the previous 12 months, Gold score[15] (to assess hypoglycaemia awareness), severe hypoglycaemia, paramedics callouts and hospital admissions due to hyperglycaemia and DKA and hypoglycaemia over the previous 12 months. The Gold score is a 7-point questionnaire validated for identifying impaired awareness of hypoglycaemia (IAH); Gold score ≥4 determines IAH.

We also collected diabetes-related distress scores at baseline and follow-up using the 2-item diabetes distress-screening instrument (DDS2) [16]. The DDS2 asks respondents to rate on a 6-point scale the degree to which the following items caused distress: (1) “feeling overwhelmed by the demands of living with diabetes”, and (2) “feeling that I am often failing with my diabetes regimen”. At follow-up, we collected data on all the above along with FSL specific measures, such as the number of scans/day and time in range. At follow-up, we also collected data on adverse effects and reasons for discontinuation due to FSL.

Ethical approval

The ABCD nationwide audit programme has Caldicott Guardian approval. The programme is an audit, not research. The NHS encourages audit of clinical practice, and there are guidelines, which were followed, in particular, that we only to collect data from routine clinical practice and analysis is of data, which is anonymized.

Statistical Methods

For reporting all the study outcomes, including HbA1c, GOLD score, and paramedic outcalls and hospital admissions, we restricted the statistical analysis to those with at least one follow-up. The chi-squared test of association was used to compare categorical variables, and the Mann–Whitney-*U* test or t-tests were used to compare continuous variables before and after the use of FSL. An analysis stratified by various strata of age, baseline body mass index (BMI), duration of diabetes, baseline HbA1c and gender looking at pre and post-FSL HbA1c and Gold score[15] and diabetes-related distress screening score (DDS)[16] were performed to understand the usefulness of FSL across these subgroups.

To identify independent predictors of HbA1c reduction in response to use, change in the post-FSL HbA1c was modelled as an independent variable with an average of the pre-FSL HbA1c, age, gender, BMI, duration of diabetes, baseline BMI and number of FSL scans and structured diabetes education as independent predictors. The follow-up period was defined as the difference between the time of FSL initiation and the date of the most recent HbA1c measurement. The comparison of hospital admissions and paramedic callouts were also restricted only to patients with at least one follow-up. To investigate the effects of intra-individual variations of HbA1c with FSL use, we calculated the intra-individual mean (HbA1c-MEAN) and standard deviation (HbA1c-SD), respectively. HbA1c values obtained prior to FSL initiation of FSL and follow-up values post FSL were used. The inter-individual difference in the number of HbA1c assessments was adjusted according to the formula: adj-HbA1c-SD=SD/$\sqrt{[n/(n-1)]}$ as previously described [16]. All the statistical analysis were done in R 3.6.3 (http://www.R-project.org/).

Results

Demographic characteristics of the study population

The available data from the study participants started on FSL are shown in **Figure 1**. Baseline demographics, indications for starting FSL, structured education completion, and funding for FSL were available for 10,370 study participants from 102 National Health Services hospitals across the United Kingdom. Baseline HbA1c, Gold score and Diabetes Distress score were recorded for 9,968, 8737 and 8320 patients, respectively, while follow-up data were available for 3182, 2801 and 2532 patients, respectively. **Table 1** shows the baseline characteristics of the whole study population in comparison to those with at least one follow-up. The mean age of the study participants was 38.0 (±18.0) years with 51% females with a mean duration of diabetes 16.0 (±49.9) years and a mean baseline HbA1c of 69.8 (±18.2) (8.5%) mmol/mol and baseline BMI of 25.2 (±16.5) kg/m^2. The majority of those in the study 10,058 (97%) had Type 1 diabetes, while the remaining had Type 2 diabetes or other forms of diabetes. Structured education had been completed by 6764 (65%) of study participants; the majority of FSL users were NHS funded 7602 (73%). The baseline demographic characteristics in those with at least one follow-up were similar to the entire study cohort.

Indications for starting FSL

There were multiple indications for FSL initiation in the study population (Figure 2). The most common indication for starting FSL was the replacement of self-monitoring of blood glucose (38.5%) followed by high baseline HbA1c (34.5%), frequent hypoglycaemia (21.7%) and fear of hypoglycaemia (20.2%).

Effect on Glycaemic Control and HbA1c variability

Across the entire study population, the mean HbA1c reduced from 67.5 (±20.9) to 62.3(±18.5), and in those with baseline HbA1c >69.5, reduced from 85.5 (±16.1) to 73.2

(±15.8). (**Figure 3A and 3B**). **Table 2** shows baseline and follow-up HbA1c in various strata of age, duration of diabetes, baseline BMI and baseline HbA1c. The greatest reduction in HbA1c was seen in those with baseline HbA1c >69.5 (-12.4 mmol/mol) followed by females (-10 mmol/mol), the age range of 19-60 (-8.6 mmol/mol) and duration of diabetes <5years (-8.4 mmol/mol).

Predictors of HbA1c reduction (Table 3) were higher baseline HbA1c (beta 0.37 (±0.1) P<0.0001), and greater number of FSL scans/day (beta 0.10 (±0.1) P<0.0001). Age, gender, BMI, structured diabetes education completion and duration of diabetes did not predict a change in HbA1c following FSL initiation. This model explained 29% variability (adjusted R-squared=0.29) in the change in HbA1c following FSL initiation.

We did a subset analysis in patients with Type 1 diabetes on with insulin pump (n=862) with both baseline and follow-up HbA1c data. In this subgroup of patients, the mean HbA1c reduced from 65.3(±13) (8.1%) to 60.2(±25) (7.7%) mmol/mol. When the analysis was restricted to those with an insulin pump and a baseline HbA1c of >=69.5 mmol of HbA1c, the baseline HbA1c reduced from 80.8(±11) (9.5%) to 70.1 (±13) (8.6%).

To understand the effect of the number of FSL scans on the change in glycaemic control we stratified the patients into two groups, Group 1, those with ≥10 scans per day and Group 2, those with less than ten scans per day. The baseline HbA1c reduced from 71.8 (±17) (8.7%) to 66.5 (±15) (8.2%) in group 1 while it reduced from 63.5 (±14) (8%) to 57.9 (±21) (7.4%) in group 2. The absolute drop in HbA1c was more significant in those with higher baseline HbA1c of >=69.5 with a reduction in HbA1c from 82.1 (±11) (9.7%) to 66.9 (±12) (8.3%) in Group 1 and reduction in HbA1c from 85.2 (±16) (9.9%) to 75.8 (±15) (9.1) in Group 2.

The median number of HbA1c readings in the year pre- FSL were 2 (IQR=2-4), and post-FSL HbA1c were 1 (IQR=1-3). The HbA1c variability, calculated as the adjusted standard deviation for HbA1c, reduced significantly from pre-FSL use to 24 (±14) to post-FSL 23 (±12) (P =0.01).

Effect on self-reported Hypoglycaemia awareness

In the entire study population, the baseline Gold score was 2.7 (±1.8), which reduced to 2.4 (±1.7) (P<0.0001) at follow-up. **Table 2** shows baseline and follow-up Gold score in various strata of age, duration of diabetes, baseline BMI and baseline HbA1c. The greatest improvement in Gold score following FSL was seen in those with age >60 years, a longer duration of diabetes, lower BMI and lower HbA1c. In those with paired baseline and follow-up data, 53% of those with baseline Gold score of ≥4 reported a score of <4 at follow-up (regaining hypoglycaemia awareness), while 5% of those with baseline Gold score of <4 reported a follow-up score of ≥4 (IAH). We did an analysis in patients with Type1 diabetes on with insulin pump (n=862) with both baseline and follow-up GOLD score (n=1145). In this subgroup of patients, the GOLD score reduced from 2.75 (±1.6) 2.49 (±1.6).

Diabetes Distress Score

The mean DDS1 (feeling overwhelmed with demands of living with diabetes) significantly improved from 2.9 at baseline to 2.2 at follow-up (P<0.0001) and the mean DDS2 (feeling that I am often failing with my diabetes routine) improved significantly from 3.0 to 2.2 at follow-up (P<0.0001) (**Figure 4**)

FSL use, Time in Range (TIR), user-experience and side effects

At follow up 89% reported FSL use >70% of the time with a mean of12.9(±14.1) scans per day and mean captured sensor data of 87(±16) %.

Of those with both follow-up HbA1c and TIR data (n=2191), in only 343 (15%) of cases did clinicians report on the internationally accepted TIR (3.9-10mmol/l; 70 to 180mg/dl), with a median TIR of 43% (27%-56%).

With the use of FSL, 68% of patients said that they detected a greater proportion of time in hypoglycaemia, while 80% said that they were able to reduce the proportion of time in hypoglycaemia. With regards to the rate of hypoglycaemia 85% of the patients were able to reduce to rate of hypoglycaemia (56% said "a little less", and 29% said "a lot less") and 75% were able to reduce the rate of nocturnal hypoglycaemia (45% said "a little less", and 30% said "a lot less"). Of the 3,182 patients with follow-up 358 patients (11%) reported problems with FSL; of these, 224 (7%) had technical problems concerning the sensor or the device. 101 patients (3%) reported itching, redness, rash or allergic reaction while 33 patients (1%) reported bleeding at the site of the device.

Severe hypoglycaemia, paramedic callouts and hospital admissions

These analyses were restricted to those who had both baseline and follow-up events recorded on the audit form. Comparing the 12-month pre-FSL with 7.5 (IQR=3.4-7.8) months (range 0.3-to 64 months) of follow up in this cohort, the total number of paramedic call outs (n=1940) decreased from 275 to 38 while the total number of hospital admissions due to hyperglycaemia/DKA (n=1978) decreased from 269 vs 86 following FSL and the number of admissions due to hypoglycaemia (n=1952) decreased from 120 vs 45 following FSL initiation. In the adult cohort, the total number of episodes of severe hypoglycaemia (n=1944) defined as those requiring third party assistance reduced from 1032 to 237; the total number of people with at least one episode of severe hypoglycaemia at baseline was 357 which reduced 104 at follow-up. (**Figure 5**).

In a prorated analysis by month, with the use of FSL, the number of hyperglycaemia & DKA reduced from 22/month to 11/month; the number of hypoglycaemia related admissions reduced from 10/month to 6/month; paramedic callouts reduced from 22/month to 5/month and episodes of severe hypoglycaemia reduced from 86/month to 31/month

In a sensitivity analysis restricted to those with 12 months follow-up (n=409); the number of paramedics callouts for hypoglycaemia decreased from 83 to 4 following FSL, the number of hospital admissions due to hyperglycaemia/DKA decreased from 38 to 30, and the number of hospital admissions due to hypoglycaemia decreased by 27 to 2 following FSL initiation.

Discussion

We present the analysis of the largest real-world dataset from the nationwide study of flash glucose monitoring (FSL) in people with Type1 diabetes in United Kingdom (UK). We show that FSL use is associated with improved glycaemic control, hypoglycaemia awareness, reduced diabetes-related distress and reduced hospital admissions. In this large observational study, FSL use was associated with significant improvements in glycaemic control, especially in those with a higher baseline HbA1c and in those with a greater number of scans/day. While several randomized controlled trials (RCT) for CGM have shown improved glycaemic control in those with Type 1 diabetes, to date, there are no RCT data which demonstrate a reduction in HbA1c through FSL use. The SELFY study, a single-arm paediatric study, showed enhanced glucose time in range (TIR) and a 4.4 mmol/mol reduction in HbA1c compared to SMBG after an eight-week follow-up period. The IMPACT trial[8], primarily designed to assess the effect of FSL use on hypoglycaemia in those with well-controlled Type 1 Diabetes, demonstrated a significant reduction in hypoglycaemia but no significant change in HbA1c, a likely reflection of the low baseline HbA1c (50 mmol/mol). The findings of our study are in keeping with the IMPACT study in terms of reported reductions in hypoglycaemia. We also found a less substantial change in HbA1c in those with a lower baseline HbA1c and is in agreement with previous studies which have reported a more beneficial effect of FSL in those with higher baseline HbA1c[12, 14].

The findings of our study are also in agreement with a recent meta-analysis[9] of 1,723 participants with type 1 or type 2 diabetes which showed similar reductions in HbA1c following FSL use. This meta-analysis also demonstrated that the change in HbA1c with FSL use is highly correlated with baseline HbA1c. A real-world study of 900 FSL users from Edinburgh by Victoria Tyndall et al.[12], demonstrated a -4mmol/mol reduction in HbA1c overall and similar to our findings they observed a more substantial reduction in HbA1c in those with a higher baseline HbA1c and also those with a higher number of scans per day at follow up. Overall, these results confirm the findings from clinical trials showing that the degree of engagement with the FSL device is an independent predictor HbA1c response in people with diabetes.

In this study, FSL use was associated with a significant reduction in HbA1c-variability during the follow-up period of 7.5 months, as seen in randomized controlled trials with CGM. Since HbA1c variability is associated with both micro[17, 18] and macro-vascular complications, at least in people with type 2 diabetes[19], if this pattern is sustained it is possible that FSL may be associated with reduced complication rates in due course, beyond the benefits from the described reduction in HbA1c.

The FSL has been shown to reduce the amount of time spent in hypoglycaemia in people with Type 1 diabetes and Type 2 diabetes in RCT and observational data. In this study, we used the Gold score to assess hypoglycaemia awareness. Following the use of the FSL, the Gold score reduced significantly; almost half who had a Gold score of ≥4 at baseline had restoration of hypoglycaemia awareness at follow-up, which may be a reflection of the significant reductions in self-reported hypoglycaemia. However, our findings are in contrast with a previous observational study[12], which showed no improvement in Gold score or the proportion with impaired awareness of hypoglycaemia as assessed by the Gold score. This may reflect the higher proportion of individuals with impaired awareness of hypoglycaemia (25% vs 13%) and higher baseline Gold score (2.7 vs 2) in our cohort. We observed significant improvements in both components of the Diabetes Distress score (2-item diabetes distress-screening instrument) in those who started on FSL. A recent study[12] described improvements in diabetes-related distress but a paradoxical increase in the anxiety and depression on the Hospital Anxiety and Depression Scale (HADS) in those using FSL. This could potentially reflect the demands which access to continuous glucose data places on an individual; although not assessed in our study this is an area which would benefit from future qualitative research.

We report significant reductions in paramedic call out, and hospital admissions with the use of FSL in the 7.6 months follow-up period. The most significant reductions were seen in paramedic callouts followed by admissions due to hyperglycaemia/DKA, and those due to hypoglycaemia. These findings are consistent with the data reported from the Edinburgh cohort[12] and Belgian cohort[14]; however, a long-term follow-up and cost-effectiveness analysis are needed to evaluate the long-term clinical and economic benefits.

Our study has several limitations. The data for this study were obtained from a national-wide audit of FSL of routine clinical care and as such, lacked a comparator arm and the methodically controlled data collection in RCTs. Nonetheless, these data represent the largest nationwide, real-world experience with FSL in all aspects of diabetes care. Most of our study participants consisted of people with Type 1 diabetes who fulfilled the criterion set by NHS England, funded by the National Health Service (NHS) the UK. The majority received NHS funding for their FSL device. The access criteria have resulted in ~1/3 of people living with diabetes being reimbursed for the FSL, which gives an indication of our representative selection criterion. The mean HbA1c at baseline was 69.8 mmol/mol (8.5%) in comparison to our national audit data which shows a mean Hba1c of 64mmol/l (8%) for pump users and 71mmol/l (8.6%) for those on MDI. The study participants were, therefore, as the wider group of people with Type 1 diabetes in the United Kingdom. The average baseline HbA1c in our real-world study was higher as compared to the IMPACT trial[8] and the FUTURE study[14]. However, this reflects the real-world nature of the study, which report HbA1c values like our national HbA1c data.

Our study may also be affected by regression to mean in HbA1c measures [20], a tendency for HbA1c to fall on repeat testing. However, we have minimized this effect by taking an average of available HbA1c measures one year prior to FSL use and including all HbA1c measures available during the follow-up period. We compared the paramedic callouts and hospital admissions, one year before starting FSL with the paramedic call out and hospital admissions in seven and half month's follow-up period. However, we have also done a sensitivity analysis in a subset of patients with a twelve-month follow-up period and show that the beneficial effects of FSL persist for key outcomes. Given the significant reduction in the episodes of severe hypoglycaemia and paramedic callouts, these findings will have implications for morbidity and mortality related to diabetes and further studies are needed to confirm these.

In summary, we report an analysis of the largest real-world dataset observing FSL use in Type 1 Diabetes and show that its use is associated with significant improvements in glycaemic control, hypoglycaemia awareness, severe hypoglycaemia and a reduction in hospital admissions. Long term follow-up and cost-effectiveness analysis are needed to assess if these benefits from FSL are sustained and affordable to health care systems.

Disclosure Statement

Disclosure **E.G. Wilmot**: Advisory Panel; Self; Dexcom, Inc. Research Support; Self; Diabetes UK. Speaker's Bureau; Self; Abbott, Eli Lilly and Company, Novo Nordisk Inc., Sanofi**. R.E. Ryder**: Advisory Panel; Self; Novo Nordisk A/S. Speaker's Bureau; Self; Bioquest. **C. Walton**: Advisory Panel; Spouse/Partner; Celgene Corporation. Speaker's Bureau; Spouse/Partner; Leo Pharma, Novartis Pharmaceuticals Corporation. **T. Sathyapalan**: Speaker's Bureau; Self; Novo Nordisk Foundation. Other Relationship; Self; Bristol-Myers Squibb Company, Eli Lilly and Company, Sanofi-Aventis. None of the other authors had any competing interests.

Author Contribution statement

TS , EW , REJR, and CW, conceived of the presented idea. HD, TS, EW, REJR, CW contributed to the data analysis. HD wrote the first draft of the manuscript. All the authors contributed to the writing of the manuscript and made extensive comments, criticism and changes in the final draft of the paper. All the authors saw the final version of the manuscript.

Guarantor : Dr Harshal Deshmukh

Table 1: Baseline demographic characteristics of study participants with and without follow-up

	Baseline data in all study participants (n=10,370)	Baseline data in patients with follow-up (n=3,182)
Age (years)	38.0 (±18.8)	39.5(±19.6)
Gender (% Females)	5322 (51%)	1688 (53%)
Baseline BMI	25.2 (±6.4)	25.1 (±6.2)
Duration of Diabetes	16.0 (±49.9)	17 .1(±15.5)
Type 1 Diabetes (%)	10058 (97%)	3126 (98%)
Insulin Pump	2428 (23%)	862 (27%)
British citizens(%)	8524 (82%)	2713 (88%)
NHS funded	7602 (73%)	2354 (74%)
Number of tests strips used per day	7.7 (±9.8)	8.1(±10.1)
Mean Pre-FSL HbA1c	69.8 (±18.2)	67.5 (±20.9)
Baseline Gold score	2.7(±1.8)	2.7(±1.9)
Completion of Structured Education	6764 (65%)	2002 (65%)

Table 2: Baseline and post-FSL HbA1c and GOLD score in various strata of age, duration of diabetes, baseline BMI and baseline HbA1c

	Pre FSL HbA1c	**Post- FSL HbA1c**	**P-value**	**Pre FSL-GOLD score**	**Post- FSL GOLD score**	**P-value**
All	69.8(±18.2)	62.3(±18.5)	<0.0001	2.7(±1.8)	2.4(±1.7)	<0.0001
Age						
<=18	63.3(±19.02)	58(±14.9)	<0.0001	NA	NA	NA
19-60	71.3(±17.5)	62.7(±31)	<0.0001	2.5(±1.7)	2.2(±1.5)	<0.0001
>60	65.3(±13.5)	60.4(±11.4)	<0.0001	3.1(±1.9)	2.6(±1.8)	<0.0001
Gender						
Male	69.1(±18.5)	61.9(±22.4)	<0.0001	2.70(±1.7)	2.3(±1.6)	<0.0001
Female	70.4(±17.8)	60.0(±14.7)	<0.0001	2.7(±1.7)	2.4(±1.6)	<0.0001
Baseline BMI						
<=25	69.7(±19.9)	62.6(±23.5)	<0.0001	2.8(±1.6)	2.4(±1.7)	<0.0001
25-30	69.3(±13.8)	61.8(±16.9)	<0.0001	2.6(±1.7)	2.3(±1.6)	<0.0001
>30	70.6(15.3)	63.4(±13.7)	<0.0001	2.6(±1.7)	2.4(±1.7)	<0.0001
Duration of Diabetes						
<-5	68.8(±19.7)	60.4(15.0)	<0.0001	2.69(±1.7)	2.55(±1.6)	0.10
5-15 years	73.1(±19.3)	66.9(±28.4)	<0.0001	2.44(±1.6)	2.15(±1.4)	<0.0001
>15 years	68.4(±16.6)	61.2(±12.7)	<0.0001	2.89(±1.8)	2.4(±1.7)	<0.0001
Baseline HbA1c						
<=69.5	57.7(±7.7)	56.2(±17.4)	<0.0001	2.8(±1.7)	2.4(±1.6)	<0.0001
>69.5	85.5(±16.0)	73.1(±15.8)	<0.0001	2.5(±1.7)	2.3(±1.6)	0.0005
Diabetes Education						
Yes	68.3(±16.2)	61.7(±19.2)	<0.0001	2.7(±1.7)	2.4(±1.6)	<0.0001
No	72.6(±21.2)	63.8(±16.3)	<0.0001	2.8(±1.7)	2.5(±1.6)	0.0007

Table 3: Linear regression model showing predictors of decline in HbA1c following the use of FSL

	Beta	SE	P-value
Pre FSL HbA1c	0.37	0.01	<0.0001
Number of FSL scans	0.10	0.01	<0.0001
Completion of Structured Education	0.82	0.48	0.090
Age	-0.02	0.01	0.153
Baseline BMI	0.04	0.04	0.237
Gender	-0.30	0.42	0.483
Duration of Diabetes	-0.02	0.02	0.382

Figure 1 Title: Study schematic showing data for HbA1c, Gold score and Diabetes Distress Screening score in the ABCD nationwide audit of FSL

Figure 1 legend: Study Schematic showing the number of patients recruited in the study and sample size those with follow-up for HbA1c, Gold score and Diabetes distress score

Figure 2 Title: Indications for starting FSL in the ABCD nationwide audit of FSL

Figure 2 legend: Figure 2 shows multiple indications for FSL initiation in the study population

Figure 3a and 3b Title: Distribution of HbA1c change pre and post FSL use in the ABCD nationwide audit of FSL

Figure 3a and 3b legend: Figure 3a and 3b shows the change in the HbA1c in the study population following FSL initation and in those with a baseline HbA1c of ≥ 69.5

Figure 4: Diabetes Distress Screening score before and after use of FSL in the ABCD nationwide audit of FSL

Figure 4 legend: Figure 4 shows the change in the two components of the Diabetes Distress Screening score before and after FSL initiation. The DDS2 asks respondents to rate on a 6-point scale the degree to which the following items caused distress: (1) "feeling overwhelmed by the demands of living with diabetes", and (2) "feeling that I am often failing with my diabetes regimen".

Figure 5: Total number of Paramedic call outs, severe hypoglycaemia and hospital admissions during the 12months before and the 7.5 months of follow up using FSL in the ABCD nationwide audit

Figure 5 legend: Figure 5 shows the change in Type 1 diabetes related resource utilization following FSL initiation.

References

1. Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T, Bosi E, Buckingham BA, Cefalu WT, Close KL *et al*: **Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range**. *Diabetes Care* 2019, **42**(8):1593-1603.
2. Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Bergenstal R, Haller S, Kollman C, Kruger D, McGill JB, Polonsky W *et al*: **Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections: The DIAMOND Randomized Clinical Trial**. *JAMA* 2017, **317**(4):371-378.
3. Heinemann L, Deiss D, Hermanns N, Graham C, Kaltheuner M, Liebl A, Price D: **HypoDE: Research Design and Methods of a Randomized Controlled Study Evaluating the Impact of Real-Time CGM Usage on the Frequency of CGM Glucose Values <55 mg/dl in Patients With Type 1 Diabetes and Problematic Hypoglycemia Treated With Multiple Daily Injections**. *J Diabetes Sci Technol* 2015, **9**(3):651-662.
4. Heinemann L, Freckmann G, Ehrmann D, Faber-Heinemann G, Guerra S, Waldenmaier D, Hermanns N: **Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial**. *Lancet* 2018, **391**(10128):1367-1377.
5. Bilir SP, Hellmund R, Wehler B, Li H, Munakata J, Lamotte M: **Cost-effectiveness Analysis of a Flash Glucose Monitoring System for Patients with Type 1 Diabetes Receiving Intensive Insulin Treatment in Sweden**. *Eur Endocrinol* 2018, **14**(2):73-79.
6. Campbell FM, Murphy NP, Stewart C, Biester T, Kordonouri O: **Outcomes of using flash glucose monitoring technology by children and young people with type 1 diabetes in a single arm study**. *Pediatr Diabetes* 2018, **19**(7):1294-1301.
7. Haak T, Hanaire H, Ajjan R, 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.
8. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kroger J, Weitgasser R: **Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial**. *Lancet* 2016, **388**(10057):2254-2263.
9. Evans M, Welsh Z, Ells S, Seibold A: **The Impact of Flash Glucose Monitoring on Glycaemic Control as Measured by HbA1c: A Meta-analysis of Clinical Trials and Real-World Observational Studies**. *Diabetes Ther* 2020, **11**(1):83-95.
10. Fokkert MJ, Damman A, van Dijk PR, Edens MA, Abbes S, Braakman J, Slingerland RJ, Dikkeschei LD, Dille J, Bilo HJG: **Use of FreeStyle Libre Flash Monitor Register in the Netherlands (FLARE-NL1): Patient Experiences, Satisfaction, and Cost Analysis**. *Int J Endocrinol* 2019, **2019**:4649303.
11. Alawadi F, Rashid F, Bashier A, Abdelgadir E, Al Saeed M, Abuelkheir S, Khalifa A, Al Sayyah F, Bachet F, Elsayed M *et al*: **The use of Free Style Libre Continues Glucose Monitoring (FSL-CGM) to monitor the impact of Ramadan fasting on glycemic changes and kidney function in high-risk patients with diabetes and chronic kidney disease stage 3 under optimal diabetes care**. *Diabetes Res Clin Pract* 2019, **151**:305-312.

12. Tyndall V, Stimson RH, Zammitt NN, Ritchie SA, McKnight JA, Dover AR, Gibb FW: **Marked improvement in HbA1c following commencement of flash glucose monitoring in people with type 1 diabetes**. *Diabetologia* 2019, **62**(8):1349-1356.
13. Moreno-Fernandez J, Pazos-Couselo M, Gonzalez-Rodriguez M, Rozas P, Delgado M, Aguirre M, Garcia-Lopez JM: **Clinical value of Flash glucose monitoring in patients with type 1 diabetes treated with continuous subcutaneous insulin infusion**. *Endocrinol Diabetes Nutr* 2018, **65**(10):556-563.
14. Charleer S, De Block C, Van Huffel L, Broos B, Fieuws S, Nobels F, Mathieu C, Gillard P: **Quality of Life and Glucose Control After 1 Year of Nationwide Reimbursement of Intermittently Scanned Continuous Glucose Monitoring in Adults Living With Type 1 Diabetes (FUTURE): A Prospective Observational Real-World Cohort Study**. *Diabetes Care* 2020, **43**(2):389-397.
15. Gold AE, MacLeod KM, Frier BM: **Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia**. *Diabetes Care* 1994, **17**(7):697-703.
16. Fisher L, Glasgow RE, Mullan JT, Skaff MM, Polonsky WH: **Development of a brief diabetes distress screening instrument**. *Ann Fam Med* 2008, **6**(3):246-252.
17. Virk SA, Donaghue KC, Cho YH, Benitez-Aguirre P, Hing S, Pryke A, Chan A, Craig ME: **Association Between HbA1c Variability and Risk of Microvascular Complications in Adolescents With Type 1 Diabetes**. *J Clin Endocrinol Metab* 2016, **101**(9):3257-3263.
18. Penno G, Solini A, Zoppini G, Orsi E, Fondelli C, Zerbini G, Morano S, Cavalot F, Lamacchia O, Trevisan R *et al*: **Hemoglobin A1c variability as an independent correlate of cardiovascular disease in patients with type 2 diabetes: a cross-sectional analysis of the renal insufficiency and cardiovascular events (RIACE) Italian multicenter study**. *Cardiovasc Diabetol* 2013, **12**:98.
19. Parry HM, Deshmukh H, Levin D, Van Zuydam N, Elder DH, Morris AD, Struthers AD, Palmer CN, Doney AS, Lang CC: **Both high and low HbA1c predict incident heart failure in type 2 diabetes mellitus**. *Circ Heart Fail* 2015, **8**(2):236-242.
20. McDonald TJ, Warren R: **Diagnostic confusion? Repeat HbA1c for the diagnosis of diabetes**. *Diabetes Care* 2014, **37**(6):e135-136.