Assessing Glycaemic Impact of FreeStyle Libre Monitoring in Patients with Insulin-Treated Type 2 Diabetes: A Retrospective Real-World Analysis

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Abstract

Objectives:

FreeStyle Libre (FSL) monitoring is available for all patients in Wales with insulin-treated diabetes. English guidance permits FSL in patients with type 1 diabetes mellitus (T1D) and type 2 diabetes mellitus (T2D) requiring multiple daily insulin doses (MDI) [1] [2]. The literature suggests benefits from using FSL, specifically improved glycaemic control and reduced hypoglycaemia.

Methods:

Patients aged >18 years with insulin-treated T2D using FSL for ≥3 months were identified from Libreview. Those with pre- and post-FSL HbA1c were included. Days 1-14 of FSL data were taken as baseline. Patients were categorised by insulin regime (OD basal, premixed, basal bolus).

Results:

236 patients were identified and 189 patients included. The median follow-up duration was 14.6 [10.3-15.0] months. There were significant reductions in median HbA1c [8 mmol/mol, $p<0.001$], time below range [<4.0 mmol/L](1.2±3.4 vs 0.6±1.5%,$p=0.01$), and low glucose average duration [52.1±77.3 vs 35.6±58.7 minutes,$p=0.01$]. HbA1c improvements were greatest in OD basal [12 mmol/mol,$p<0.001$] and pre-mixed [12.5 mmol/mol,$p<0.001$] insulin regimes. Those taking premixed insulin had an increased time in target [7%,$p<0.05$], reduced time above target [5.5%,$p<0.05$] and reduced average glucose [0.3 mmol/L,$p<0.05$] and GMI [2 mmol/mol,$p<0.01$]. Patients on basal bolus insulin had significantly reduced time below range [0.5% $p<0.05$].

Conclusions:

Improvements in HbA1c were greatest in those taking OD basal or premixed insulins. Reductions in hypoglycaemia are likely to positively impact quality of life. Further studies will elucidate whether these improvements are directly related to improved quality of glycaemic data facilitating closer treatment titration, or behaviour changes related to FSL use.

Wordcount : 249

Keywords: type 2 diabetes mellitus, FreeStyle libre, flash glucose monitoring, hypoglycaemia

Introduction

Epidemiology

Diabetes effects approximately 4.3 million people in the UK, and 90% of new diagnoses are of type 2 diabetes mellitus (T2D) (https://www.diabetes.org.uk/about-us/news-and-views/number-people-living-diabetes-uk-tops-5-million-first-time). It is well-established that suboptimal glycaemic control leads to significant co-morbidity and mortality [3]. Furthermore, there is a wealth of evidence highlighting that many patients with T2D are unable to meet glycemic targets [4]. Patients treated for T2D with insulin are at risk of hypoglycaemia [5]. Recurrent hypoglycaemia can cause loss of hypoglycaemia awareness, increased mortality and morbidity, and a negative impact on lifestyle such as the suspension of driving licening [6] [5].

Continuous Glucose Monitoring Technology in the management of diabetes

The last decade has seen exponential progress in the development and uptake of glucose-sensing technology: Real-time continuous glucose monitoring (rtCGM) and intermittently viewed CGM (iCGM), also known as flash glucose monitoring (FGM). There is an abundance of real-world evidence for the benefit of glucose-sensing technology in patient with type 1 diabetes (T1D) [7] and hence the use of glucose-sensing technology is embedded in the management of T1D [1] [8]. However, real-world evidence of its use in patients with type 2 diabetes (T2D) is limited. There is emerging evidence on the benefit of glucose-sensing technology in patients with T2D who are treated with insulin. [9] [10].

The ongoing use of minimally invasive glucose sensors reduces the need for the traditional invasive finger-prick testing which can be inconvenient and painful. Diabetes burnout is well-recognised [11] [12] and it is likely that invasive fingerpick monitoring is a significant contributor to this leading to psychological distress and disengagement. The rtCGM or iCGM not only eliminates, or at least significantly reduces the need for finger prick testing, but also generates a wealth of data to guide treatment titration. This is particularly the case for nocturnal hypoglycaemia and post-prandial glucose excursions which are far more challenging to capture by fingerpick testing alone. In addition to the superior quality of data generated, both rtCGM and ICGM represent a far more convenient and less socially intrusive method of glucose monitoring for those living with diabetes.

Welsh policy

The devolved nature of NHS Wales has resulted in some variation in heath policy and commissioning arrangements between Wales and the rest of the UK. One such variation is detailed in a 2021 Health Technology Wales (HTW) Guidance 004-2 [13], which allows for the use of FSL monitoring in any patient with any type of diabetes who uses insulin. Consequently, there is a large and relatively unique population of patients in Wales who have been using FSL monitoring to assist in the management of T2D.

FSL

FreeStyle Libre is manufactured by Abbott. Initially introduced to market in 2014, at its inception and until July 2023 FSL was an example of FGM, i.e. glucose data was only recorded when the patient actively scanned their FSL device. This is in contrast to continuous glucose monitoring (CGM) which continuously senses and records glucose data at specific and usually short time intervals. However, the introduction of FSL2 and a subsequent software upgrade in July 2023 marked a move from FGM to CGM. CGM technology continues to be used in FSL2 and FSL3.

In this study, we aimed to determine whether the routine use of FSL for glucose monitoring in people with insulin-treated T2D was associated with improvements in glycaemic control, or hypoglycaemia frequency or duration.

Methods

This is a retrospective observational study of patients from one hospital site who were treated with insulin for T2D and who were using FSL identified from the LibreView database. Patients who had <60% sensor usage time, those who had been using FSL for <3 months, and those without a post-FSL HbA1c were excluded from further analysis. Those who met the inclusion criteria were analysed according to type of insulin (OD basal insulin, premixed insulin, and basal bolus insulin). Demographic data was recorded as pre- and post-FSL HbA1c. The initial two weeks' of FSL data constituted pre-FSL data as it was assumed that minimal insulin adjustment would have been undertaken during this period. In addition to pre- and post FSL HbA1c, glycemic data was collected including Time in Range, Time Below Range, and Time Above Range, and Average Glucose, Glucose Management Indicator,

and Coefficient of Variance. Hypoglycaemia was assessed via Sensor Low Glucose Average Duration and number of patients with recorded hypoglycaemia.

Statistical analysis

Data analysis was undertaken using SPSS (Version 29.0). Categorical data are presented as the number (%), and statistical significance of differences in categorical data were determined using a Chi-squared test. Continuous data were checked for normality using the Kolmogorov-Smirnov test and were visualised using Q-Q plots. Data following a normal distribution are presented by the mean ± standard deviation, and data not following a normal distribution are presented by the median [interquartile range]. The statistical significance of changes in non-parametric data over patient follow-up were determined by the Wilcoxon signed ranks test. The statistical significance of differences in data following a normal distribution between three or more groups was determined by one-way ANOVA, and in data not following a normal distribution by the Kruskal-Wallis test. Statistical significance was usually considered at $p < 0.05$.

Results

Baseline characteristics

236 patients with insulin-treated T2D using the FSL were identified and 189 were included. At the time of commencing FSL, these patients had a mean age 61.1±10.1 years, median HbA1c 73 [61.0-85.5] mmol/mol and 85 (45%) patients were female. In total, 30 (15.9%) patients were treated with once daily basal insulin, 70 (37.0%) patients were treated with twice-daily premixed insulin, and 89 (47.1%) patients were treated with a basal-bolus regime. These baseline characteristics and the glucose metrics derived from the FSL over the first 14 days of FSL use are presented in Table 1.

Changes over follow-up: overall cohort

In the overall cohort, the median duration of follow-up was 14.6 [10.3-15.0] months (1.2 years). Over this period, there was a significant reduction in the median HbA1c [8 mmol/mol, $p<0.001$]. There was also a significant reduction in the time below range [<4.0 mmol/L] (1.2±3.4 vs 0.6±1.5%, $p=0.01$). Amongst those experiencing hypoglycaemia there was a significant reduction in the sensor low glucose average duration [52.1±77.3 vs 35.6±58.7 minutes, $p=0.01$], and a trend to a reduced number of patients experiencing hypoglycaemia.

There were no other significant changes in the available glycaemic metrics in the overall group. These data are presented in Table 1.

Changes over follow-up: insulin type at baseline

Next, we sought to confirm whether the observed glycaemic changes over follow-up were related to sub-groups treated with different insulin regimes. The data comparing changes over follow-up in those treated with basal only, premixed, or basal-bolus insulin regimes are presented in Table 2. There was no significant difference in the mean age of the individuals between the three groups. However, there was a significant difference in the duration of follow-up between groups, with those in the premixed treatment group having shorter median follow-up (12.2 [9.1-15.0] months) than those in the basal only (14.7 [11.0-15.0] months) or basal-bolus (14.7 [12.1-15.1] months) groups (p=0.003).

In patients prescribed a basal-only insulin regime, there were significant reductions in the median HbA1c [11.5 mmol/mol, p<0.001], and a trending reduction in time below range and sensor low glucose average duration. In those prescribed a premixed insulin, there was a significant reduction in the median HbA1c [7 mmol/mol, p<0.001], increase in time in target [5.5%, p<0.05], reduction in time above target [5%, p<0.05] and reduction in both average glucose [0.6 mmol/L, p<0.05] and GMI [4 mmol/mol, p<0.01]. In those prescribed a basal-bolus insulin regime, there was a trending reduction in the HbA1c [1mmol/mol, p=0.05], and a significant reduction in time below range [0.5%, p<0.05].

Changes over follow-up: Age and HbA1c at baseline

Patients aged 65 years or greater (n=69) had a significant reduction in median HbA1c [6.0 mmol/mol, p<0.01], and patients aged less than 65 years (n=120) had a reduction in mean time below range [1.4±2.8 vs 0.6±1.3%, p<0.01], mean low glucose average duration [58.7±83.1 vs 37.6±60.3 minutes, p<0.05], and median HbA1c [5.5 mmol/mol, p<0.001]. Patients with a HbA1c 75 mmol/mol [9.0%] or greater (n=89) had a significantly greater median time in range [5%, p<0.05], reduced time above range [5%, p<0.05], reduced average glucose [0.8 mmol/L, p<0.05], and reduced HbA1c [16 mmol/mol, p<0.001]. Patients with a HbA1c less than 75mmol/mol [9.0%] (n=100) had a significantly reduced time below range [1.6±2.9 vs 0.9±1.8, p<0.01], and low glucose average duration [71.5±82.0 vs 44.3±63.3 minutes, p<0.01].

Changes over follow-up: patients switched insulin regime

Importantly, eighteen patients underwent insulin regime alterations during the study period. Of these, two were initially on basal bolus insulin and were converted to a more simple regime which resulted in a higher HbA1c in both cases. Eleven patients were converted from premixed insulin to basal bolus insulin, and nine of these subsequently had an improved HbA1c. Of the five patients who were initially using OD basal insulin and underwent insulin regime changes, three were converted to a basal bolus insulin regime, two of whom had an improved HbA1c at follow up, and two were converted to premixed insulin who both had an improved HbA1c at follow up (see Table 3).

Discussion

Statement of major findings

This retrospective observational analysis of 189 patients adds to the growing body of evidence supporting the use of FSL in patients with insulin-treated T2D. This analysis demonstrated a significant overall reduction of 8 mmol/mol ($p<0.001$) in HbA1c for patients on all insulin regimes following ≥3 months of FSL use. The reduction in HbA1c was most marked and was significant in those taking basal (11.5 mmol/mol, $p<0.001$) and premixed insulins (7 mmol/mol, p=<0.001). There was also a significant reduction hypoglycaemia, specifically in time below range (<4.0 mmol/L, 1.2±3.4 vs 0.6±1.5%, $p=0.01$), and the average duration of hypoglycaemic episodes amongst those who experienced them was also reduced (52.1±77.3 vs 35.6±58.7 minutes, $p=0.01$) in the whole cohort. Those with higher baseline HbA1c demonstrated a greater reduction in HbA1c ($p<0.001$).

When the cohort was analysed by insulin regime, those taking OD basal insulin had a significant reduction in the median HbA1c [11.5 mmol/mol, $p<0.001$], and a trend of reduction in time below range and sensor low glucose average duration. In those taking premixed insulin, again the median HbA1c was improved [7 mmol/mol, $p<0.001$], time in target range was increased [5.5%, $p<0.05$], and time above target range, average glucose, and GMI were all reduced. A trending reduction in HbA1c [1 mmol/mol, $p=0.05$], and a significant reduction in time below range [0.5%, $p<0.05$] was observed in those taking basal bolus insulin.

Comparison with relevant literature

One of the earliest studies examining the use of FSL in patients with T2D was the 2017 REPLACE trial [14]. In this study, 224 participants from 26 centres were randomised to control (self-monitoring of blood glucose [SMBG]) or intervention (glucose-sensing technology) arms. At 6 months' follow up there was no difference in change in HbA1c between the two groups. However, time in the hypoglycaemic range <3.9 mmol/L was reduced by 0.47 ± 0.13 h/day [mean ±SE (p = 0.0006)], and in the range of <3.1 mmol/L was reduced by 0.22 ±0.07 h/day (p = 0.0014) in the intervention group. Subsequent studies in this area have also shown reductions in time spent in the hypoglycaemic range whilst HbA1c remained unchanged [15]. The REPLACE trial also found that patients in the intervention group reported superior treatment satisfaction than those in the control group (DTSQ 13.1 ±0.50 (mean ±SE) and 9.0 ±0.72, respectively; p 0.0001).

The association illustrated in this analysis highlights the benefit of FSL in insulin-treated T2D following at least three months' use, but with a median duration of follow-up for the overall cohort of over 12 months (14.6 [10.3-15.0] months). A recent large meta analysis of 2415 patients with type 2 diabetes (on insulin and non-insulin treatments) from 13 trials also supports the notion that the glycemic improvements following FSL initiation are sustained and pertain at up to 12 months [16], with an absence of data beyond this point. Indeed, this large meta-analysis confirmed -0.45% (95% CI -0.57 to -0.33) reduction in HbA1c at 3-4 months' follow up, and at 4.5-7.5 months' this improvement stood at a further improved -0.59% (95% CI -0.80 to -0.39), which was actually superior to the improvement seen in patients with type 1 diabetes mellitus (T1D) (-0.42%, 95% CI -0.58 to -0.27). Overall, larger improvements were observed in those with a higher starting HbA1c and patterns of improvement were sustained at 12 months in patients with T2DM [16]. For each percentage increase in initial HbA1c from 6.6% (48 mmo/mol), HbA1c at 3-4 months had improved by an average of -0.33% (95% CI -0.92 to 0.25) for patients with T2D [16].

Data from the US examining the use of FSL in 2463 patients with insulin-treated T2D has suggested an association between FSL use and a reduction in acute diabetes-related events (decreased from 0.180 to 0.072 events/patient-year (hazard ratio [HR]: 0.39 [0.30, 0.51]; P < 0.001)); and in all-cause inpatient hospitalisations (decreased from 0.420 to 0.283 events/patient year (HR: 0.68 [0.59 0.78]; P < 0.001) [17]. Improvements in acute diabetes complications requiring hospitalisations were also mirrored in data from France [18] [19]. The RELIEF study from 2021 [20] analysed rates of hospitalisation for acute diabetes

complications (specifically diabetic ketoacidosis [DKA], severe hypoglycaemia, diabetes-related coma, and hyperglycaemia) in 74,011 patients with both type 1 and type 2 diabetes within 12 months of FSL initiation. Overall rates of hospitalisation for patients with T2D fell by -39.4% following FSL initiation, with reductions for DKA, diabetes related coma, hypoglycaemia, and hyperglycaemia of 52.1%, -31.9%, -10.8%, and -26.5% respectively. It has been suggested that this reduction in acute diabetes events is especially significant in patients aged 65 years or older [19].

Some evidence exists that those with T2DM on non-insulin therapies may also benefit, and to a greater degree, from FSL monitoring in comparison to patients with T2D on insulin therapy with a matched starting HbA1c [21].

Implications

The results of this analysis add to the growing body of evidence demonstrating the utility of FSL for patients living with T2D. The wide inclusion criteria for the use of FSL for patients in Wales has highlighted its use both for improvements in HbA1c, particularly amongst patients on basal only, or premixed insulins, and reduction in hypoglycaemia which was more marked in those using either premixed or basal bolus regimes.

Whilst there is a clear link between FSL use and improvement in glycaemic metrics, it is harder to elucidate whether the initiation of FSL represented part of an overall re-engagement with diabetes management for some patients. It is likely that the vastly improved quantity and quality of glycemic data generated by FSL facilitates and encourages more intensive management towards target. It is possible that FSL enables identification of areas of dysglycaemia. Postprandial hyperglycaemic excursions are easier to identify with FSL compared to standard finger prick testing and can be tackled with a combination of insulin titration, correct timing of prandial insulin, and identification of particularly potent short-acting carbohydrates. Furthermore, nocturnal hyperglycaemia (and hypoglycaemia) can be more readily identified, and insulin doses titrated accordingly. The alarm option available with FSL can also be useful in promptly identifying such issues. Average glycaemic metrics such as Time in Range and Glucose Management Indicator are generated and updated in real-time, allowing for accurate and contemporaneous surrogate markers instead of HbA1c which can be used to encourage engagement, reassure, or identify areas for attention more quickly.

The cost of FSL to the NHS currently is approximately £900/patient/year. This is in the context of estimates that sub-optimally controlled diabetes leads to complications which cost the NHS approximately £ 7.7 billion annually. The HTW guidance indicated that FSL is a cost effective intervention compared to usual care with an incremental cost effectiveness ratio (ICER) of £13,137 per QALY for T2D [13]. Studies from Brazil [22] and Spain [23] echoed similar findings confirming cost effectiveness of FSL use compared to conventional self-monitoring of blood glucose in both T1D and T2D. Further studies would be useful to elucidate the health economic benefits of FSL in T2D as well as to identify groups within the T2D population who should be prioritised for its use.

Limitations

Limitations of the present study include an absence of information regarding duration of diabetes and duration of insulin treatment, and use of other oral hypoglycaemic agents. It may also be useful to collect BMI data as a surrogate indicator for insulin resistance. Qualitative data around pre- and post-FSL compliance with medications, and information around whether either patients or healthcare professionals analysed glycemic data and titrated treatments may also be relevant. Subgroup analysis around Total Daily Dose (TDD) of insulin would also have been relevant. Previous studies highlighted that frequency of scanning was associated with better outcomes; however this is likely to now become less relevant with the advent of FSL as continuous rather than flash glucose monitoring. The frequency of daytime versus nocturnal hypoglycaemia and data concerning the use of alarms in these circumstances may also have been useful.

This retrospective observational analysis also lacked a control group which may have helped mitigate for variables such as dietetic, specialist nurse, and medical input which may have coincided with FSL initiation, and which may have also influenced outcomes. It is likely that FSL initiation was part of a range of measures to improve glycemic control. Furthermore, the ease of access to FSL data for patients who link to the link database would facilitate easier virtual healthcare professional (HCP) review following patient-initiated follow up as occurs in many diabetes departments. It may also be relevant to record if treatment titrations were done by patients or by HCPs as FSL also allows greater patient ownership of diabetes management and treatment and may have had a significant influence on patients' behaviour.

In terms of tolerability of the device, it would have been pertinent to report how many patients discontinued FSL monitoring before 3 months and whether this was due to device issues (e.g. adhesiveness, skin irritation etc), or psychological problems related to the burden of additional information or the invasive nature of the device. Experiential evidence is that the device is generally well-tolerated. It is possible that for some patients, additional glycaemic data is burdensome and could contribute to diabetes burnout. Ultimately, it is hoped that improved glycemic control reduces the incidence of both chronic and acute complications of diabetes. Data illustrating rates of hospitalisation for acute complications of diabetes such as hypoglycaemia and hyperglycaemic hyperosmolar state (or ketoacidosis) may also be useful to collect.

Conclusion

This real-world study of patients with insulin-treated T2D demonstrates sustained improvements in HbA1c and reduced time below range following FSL use of at least 3 months' of use and on average following over a year's use. The improvements in HbA1c were most marked in patients on basal once daily and premixed insulin who had a higher median starting HbA1c. Improvements in HbA1c are likely to lead to a reduction in micro- and macro-vascular complication whilst improvement in frequency and duration of hypoglycaemia are likely to improvements in quality of life and reductions in mortality and morbidity. Cost-effectiveness analyses will be essential in identifying the health economic benefits of FSL use in T2D, and in illustrating pre-FSL patient characteristics which can be use to prioritise those who are likely to have the greatest benefit. Further qualitative studies taking into account patient satisfaction and will also be crucial.

Wordcount : 3 235

Table 1

Variable	Baseline (n=189)	Follow-up (n=189)	Significance
Age at initiation (years)	61.1±10.1	-	-
Sex	Female 85 (45.0%) Male 104 (55.0%)	-	-
HbA1c (mmol/mol)	73.0 [61.0-85.5]	65.0 [56.0-76.0]	<0.001
Time below target [%] (<4.0 mmol/L)	1.2±3.4	0.6±1.5	=0.01
Time in target [%] (4.0-10.0 mmol/L)	49.0 [26.0-71.0]	52.0 [31.5-70.0]	=0.22
Time above target [%] (>10.0 mmol/L)	49.0 [26.5-74.0]	48.0 [29.0-68.0]	=0.34
Average glucose (mmol/L)	10.4 [8.7-12.8]	10.3 [8.8-12.0]	=0.31
GMI (mmol/mol)	62.0 [54.0-73.0]	60.5 [54.0-68.0]	=0.35
Coefficient of variance (%)	28.8 [24.7-32.7]	28.6 [24.8-32.5]	=0.95
Sensor low glucose average duration (minutes)	52.1±77.3	35.6±58.7	=0.01
Number of patients with any number of minutes of hypoglycaemia	86	68	=0.06

Table 1: Baseline characteristics and changes in glucose metrics over follow-up in people with insulin treated T2D using FSL2. Abbreviations used *GMI* Glucose Management Indicator; HbA1c glycated haemoglobin

Table 2

Variable	Baseline Basal only (n=30)	Follow-up Basal only (n=30)	Baseline Premix only (n=70)	Follow-up Premix only (n=70)	Baseline BBI only (n=89)	Follow-up BBI only (n=89)
Age at initiation (years)	61.0±9.6	-	62.5±8.2	-	60.1±11.5	-
Duration of follow-up (days)	439.5 [331.3-449.0]	-	365.0 [273.5-449.0]	-	442.0 [364.0-452.0]	-
HbA1c (mmol/mol)	74.0 [62.0-91.0]	62.0 [54.8-73.0]***	77.5 [64.0-90.3]	65.0 [56.0-75.3]***	68.0 [58.0-81.0]	66.0 [56.0-79.0]
Time below target [%] (<4.0 mmol/L)	0.7±1.8	0.2±0.6	1.4±4.6	0.7±1.7	1.3±2.7	0.8±1.5*
Time in target [%] (4.0-10.0 mmol/L)	53.5 [35.0-74.5]	58.0 [36.0-71.0]	45.5 [25.0-70.3]	52.5 [30.0-76.5]*	50.0 [22.0-71.0]	49.0 [31.5-67.0]
Time above target [%] (>10.0 mmol/L)	46.0 [23.8-65.0]	42.0 [29.0-64.0]	53.0 [28.3-75.0]	47.5 [21.5-70.0]*	47.0 [27.5-76.5]	50.0 [32.5-68.0]
Average glucose (mmol/L)	10.1 [8.6-12.0]	10.0 [8.7-11.8]	10.6 [8.8-13.0]	10.3 [8.3-11.9]*	10.1 [8.7-13.0]	10.5 [9.1-12.3]
GMI (mmol/mol)	60.5 [52.8-65.0]	59.0 [54.0-65.0]	62.0 [54.0-72.5]	60.0 [51.0-65.0]**	60.0 [53.3-73.8]	62.0 [56.0-69.8]

Coefficient of variance (%)	25.7 [23.3-30.0]	27.6 [24.6-32.5]	28.9 [24.5-31.8]	26.5 [23.5-30.1]	29.6 [26.2-34.2]	29.7 [25.5-33.6]
Sensor low glucose average duration (minutes)	35.4±70.3	15.2±39.5	51.4±72.9	37.5±60.0	58.2±82.6	40.9±62.2
Number of patients with recorded hypos						

Table 2:

Table 2 presents changes in glucose metrics over follow-up in people with insulin treated T2D using FSL2, by the type of insulin therapy prescribed. Abbreviations used BBI basal bolus insulin; *GMI* Glucose Management Indicator; HbA1c glycated haemoglobin. Statistical significance of difference over follow-up in the same group is indicated by *p<0.05, **p<0.01, ***p<0.001

Table 3: Changes in HbA1c amongst patients who changed insulin regime

Sex	Age (years)	Insulin regime at initiation	Insulin regime at follow up	Pre-FSL HbA1c (mmol/mol)	Most recent HbA1c (mmol/mol)	Change in HbA1c (mmol/mol)
More intensive insulin regimes:						
M	66.9	OD basal	Premixed	72	59	-13
M	68.5	OD basal	Premixed	99	81	-18
F	67.9	OD basal	Basal-bolus	56	72	16
F	52.9	OD basal	Basal-bolus	87	61	-26
M	63.6	OD basal	Basal-bolus	52	50	-2
F	57.5	Premixed	Basal-bolus	51	77	-26
M	74.8	Premixed	Basal-bolus	67	60	-7
M	81.9	Premixed	Basal-bolus	71	74	3
F	46.0	Premixed	Basal-bolus	75	64	-11
F	58.3	Premixed	Basal-bolus	83	66	-17
F	70.3	Premixed	Basal-bolus	89	97	8
M	61.4	Premixed	Basal-bolus	98	76	-22
F	66.5	Premixed	Basal-bolus	110	62	-48
F	59.4	Premixed	Basal-bolus	113	65	-48
M	59.1	Premixed	Basal-bolus	113	69	-44
F	54.6	Premixed	Basal-bolus	149	56	-93
Simplified insulin regimes:						
M	63.3	Basal-bolus	OD basal	63	74	11
M	53.8	Basal-bolus	OD basal	76	89	13

Table 3 presents changes in HbA1c associated with changes in insulin regime

Declarations :

Ethical approval
Not required

Funding
The authors did not receive any financial support from any organisation for the submitted work.

Availabilty of data and materials
Data supporting this study are not publicly available. Please contact the corresponding author : michael.atkinson@wales.nhs.uk

Conflict of interests
The authors have no relevant financial or non-financial interests to disclose.

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