

The FreeStyle Libre flash glucose monitoring system: how it has improved glycaemic control for people with type 1 diabetes in Eastern Cheshire, UK

Ghasem Yadegarfar^{a,b}, Simon G. Anderson^c, Zohaib Khawaja^d, Gabriela Cortes^e, Kathryn Leivesley^f, Ann Metters^f, Linda Horne^f, Tom Steele^f and Adrian H. Heald^{a,d}

Introduction Many people with type 1 diabetes continue to run high HbA1c levels with associated elevated risk of cardiovascular events and increased mortality. We describe here how use of the FreeStyle Libre flash monitor has improved the glycaemic control of many people with type 1 diabetes where the new technology has been intensively deployed.

Methods We report the outcomes of 92 consecutive adults (18 years of age or more) with type 1 diabetes who have begun using the FreeStyle Libre flash glucose monitor in East Cheshire, UK. Initiation was with education and support from one of the diabetes specialist nurses. An HbA1c of 60 mmol/mol (7.6%) was taken as the threshold for suboptimal glycaemic control.

Results The mean cohort age was 43 years for men and 39 years for women (overall range 17–83 years). In 92 consecutive users, HbA1c decreased by an average of 10.7 mmol/mol (0.98%) after 3 months, and by 16.1 mmol/mol (1.47%) after 6 months. There was also a narrowing of the distribution of HbA1c, with many fewer people running high HbA1c ≥ 80 mmol/mol (9.5%). After the 6-month follow-up, two 2/92 users did not wish to continue with the monitoring.

Introduction

The achievement of better glycaemic control remains a challenge for people with type 1 diabetes and their healthcare professionals. Continuous glucose monitoring (CGM) devices display an estimate of blood glucose levels, along with trends in direction, in real-time, and in the eyes of many, they are proving to be a step-change in diabetes management. Use of CGM is associated with a reduction in HbA_{1c} [1].

Flash glucose monitoring, allows users retrospectively to review the preceding 8 hours of continuous glucose data [2], along with a contemporary estimated blood glucose value and trend line. The glucose data are made available when the user chooses to swipe the reader over the sensor which, in the case of the FreeStyle Libre monitor, remains in place for up to 14 days.

Despite major advances in the pharmacological management of type 1 diabetes in recent years [3] and increasing access to

Conclusion Flash glucose monitoring has great potential for the management of type 1 diabetes in the adult population and improving metabolic control/quality of life for people across the world. The technology provides significantly more data than the intermittent results obtained by traditional subcutaneous blood glucose monitoring, which may not capture intervals of extreme variability or nocturnal events. *Cardiovasc Endocrinol Metab* 9: 171–176 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

Cardiovascular Endocrinology & Metabolism 2020; 9:171–176

Keywords: cardiovascular, flash blood glucose monitoring, glycaemic control, HbA1c, type 1 diabetes

^aThe School of Medicine and Manchester Academic Health Sciences Centre, University of Manchester, UK, ^bHeart Failure Research Center, Cardiovascular Research Institute, & School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran, ^cUniversity of the West Indies, Cave Hill Campus Barbados, Barbados, ^dDepartment of Diabetes and Endocrinology, Salford Royal Hospital, Salford, UK, ^eHigh Speciality Regional Hospital of Ixtapaluca, Mexico City, Mexico; ^fVernova Healthcare, Watersgreen Medical Centre, Macclesfield, UK

Correspondence to Adrian H. Heald DM, Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford, UK
E-mail: adrian.heald@manchester.ac.uk

Received 19 April 2020 Accepted 18 May 2020

expert patient programmes, many people with type 1 diabetes have continued to run high HbA1c levels [4,5]. Poor glycaemic control is associated with increased likelihood of cardiovascular disease and associated events [6–9].

In the area of Eastern Cheshire, UK, the diabetes specialist nurse (DSN) team has been an early adopter of flash blood glucose monitoring. We describe here how use of the FreeStyle Libre flash monitor has improved the glycaemic control of many people with type 1 diabetes where the new technology has been intensively deployed.

The DSN team in Eastern Cheshire, UK work across a mixed urban and rural catchment area south of the conurbation of Greater Manchester. They provide an outreach service to general practitioner practices across the area, as well as clinics at a central location. There are at least 1000 people known to have type 1 diabetes in Eastern Cheshire, of whom the majority are managed in primary

care. The specialist service sees people with type 1 diabetes in an episodic care model so once glycaemia has been stabilised, the person with diabetes is again looked after in primary care.

Since Spring 2018, the DSN team has been offering the FreeStyle Libre flash glucose monitor for type 1 diabetes management. The FreeStyle Libre is offered according to the National Institute for Health and Care Excellence (NICE) guidance [10]. Three individuals declined to use the device when it was offered to them. We report here the outcome of deploying this technology.

Study methods

We report the outcomes of 92 consecutive adults (18 years of age or more) with type 1 diabetes who have begun using the FreeStyle Libre flash glucose monitor. Initiation was with education and support from one of the DSNs. An HbA1c of 60 mmol/mol (7.6%) was taken as the threshold for suboptimal glycaemic control. Baseline characteristics are given in Table 1. There was no difference by gender in baseline HbA1c.

HbA1c was measured using the Menarini autoanalyser (Menarini Diagnostics UK, Wokingham, Berkshire, UK). HbA1c was recorded at baseline, 3 months after the start of monitoring in all users, and after 6 months in the majority of users. BMI was recorded at the time of initiation of monitoring.

Most changes made were in the dose rather than the type of insulin. None of the participants attended an expert patient programme during the follow-up period nor had attended such a programme in the previous 12 months.

This was a quality improvement project. Ethics approval was not obtained for this study, as the intervention was part of standard care according to the NICE guidance (NICE 2016) [8]. All individual patient data were anonymised prior to statistical analysis.

Statistical analysis

Multiple linear regression was employed to explore the predictors of HbA1c. Kernel Density Estimation is a non-parametric way to estimate the probability density function of a random variable. Kernel density estimation is a fundamental data smoothing problem where inferences about the population are made, based on a finite data sample.

Table 1 Baseline characteristics by sex

	Men (n = 43)	Women (n = 39)
Age (years) (SD)	45.6 (16.2)	46.2 (14.2)
BMI (kg/m ²) (SD)	26.7 (5.6)	25.6 (5.7)
Duration of T1DM (years) (SD)	18.3 (13.5)	22 (13.1)
Baseline HbA1C (mmol/mol) (SD)	83.7 (18.2)	82.5 (21.4)

T1DM, type 1 diabetes.

Results

The mean cohort age was 43 (SD 16.2) years for men and 39 (SD 14.2) years for women (overall range 17–83 years); 42 (45.7%) of the participants were female. Baseline demographics are detailed in Table 1.

One of the 92 individuals was on a mixed insulin regimen (NovoMix 30) and three were on an insulin pump. One person was giving themselves bovine insulin. The rest were on a basal-bolus regime with either Insulin detemir, glargine or degludec as the long-acting insulin and either insulin aspart, glulisine or lispro as the short-acting insulin.

The mean preintervention HbA1c was 83.0 mmol/mol [95% confidence interval (CI) 79.2–86.7 mmol/mol]. At 3 months after the intervention, mean HbA1c fell significantly to 72.3 mmol/mol (95% CI 68.6–76.1 mmol/mol), a reduction of 10.7 mmol/mol (95% CI 5.7–15.7 mmol/mol; $P < 0.0001$).

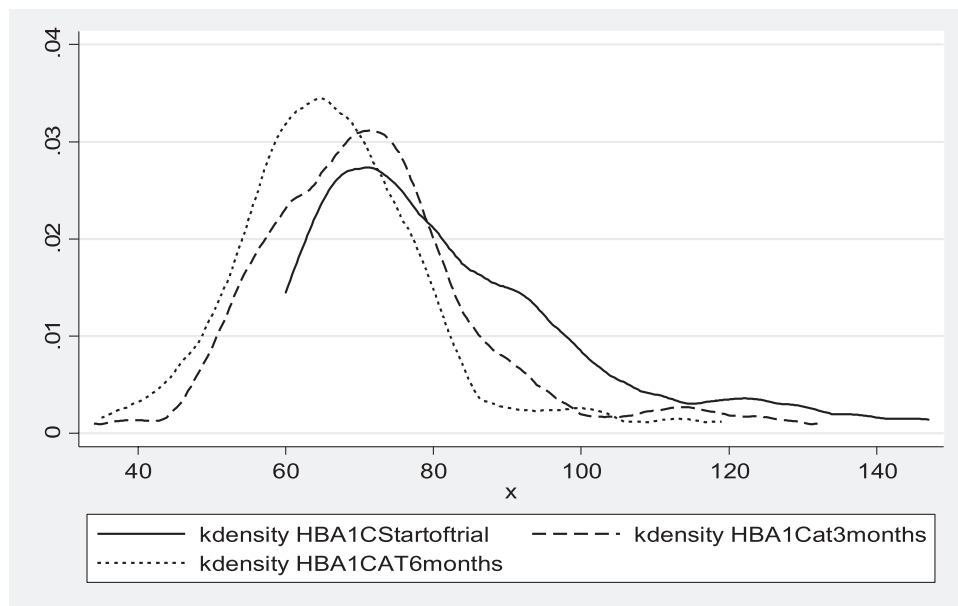
At 6 months, mean HbA1c had fallen further by a sum total 16.1 mmol/mol (2.5%) compared with baseline ($P < 0.0001$) to 66.9 mmol/mol (95% CI 63.4–70.4) (8.3%). The greatest HbA1c reduction at the 6-month follow-up was by 87 mmol/mol (10.1%).

Over the follow-up period, there was not only a fall in mean HbA1c but also a narrowing of the distribution of HbA1c (Fig. 1), with a lower proportion of high outliers: there were significantly fewer people with HbA1c levels of ≥ 80 mmol/mol (9.5%) (seven people at 6 months compared with 24 at baseline). The baseline data starts at 60 mmol/mol (7.6%) as no one in this study had an HbA1c below this as the threshold for suboptimal glycaemic control. Kernel density estimation is a fundamental data smoothing model where inferences about the population are made, based on a finite data sample.

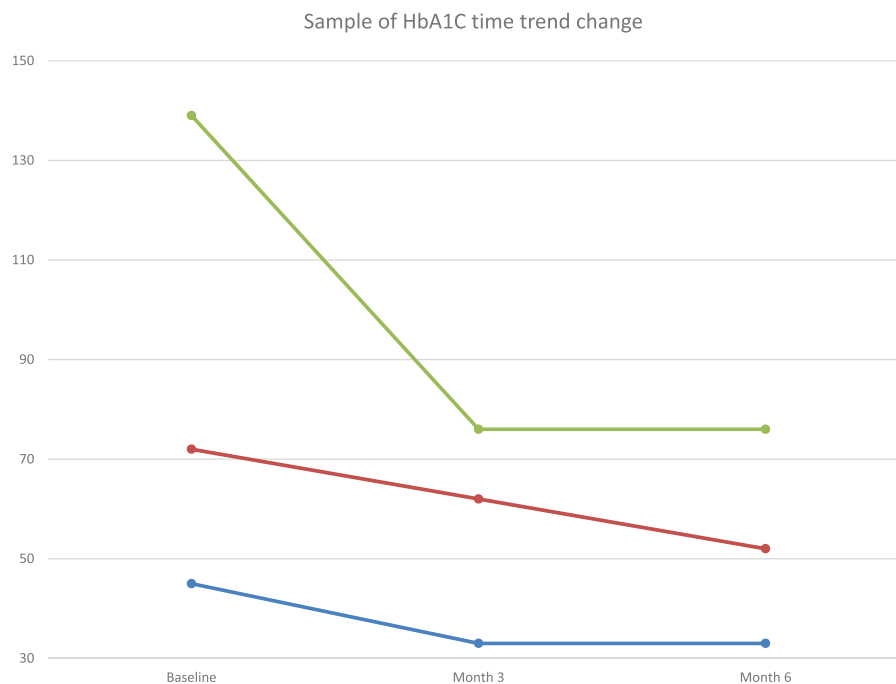
We have also shown changes in HbA1c over time for (baseline, 3 and 6 months) for representative individuals at the mid point (orange) of starting HbA1c and at the upper (grey) and lower (blue) extremes of pre-Libre HbA1c (Fig. 2). The overall fall in HbA1c at various levels of starting HbA1c is clear.

Box plots were created for the HbA1c distributions at baseline, 3 and 6 months with the actual data points overlying each plot also added. These demonstrate as does the Kernel Density plot, the significant reduction in HbA1c (Fig. 3) with a mean 16.1 mmol/mol (2.5%) reduction at 6 months from first use of the FreeStyle Libre device.

The tri-monthly average Libre blood glucose measurements were as follows. The mean blood glucose test results for baseline were 7.5 mmol/L decreasing to 6.8 mmol/L at 3 months and 6.4 mmol/L at 6 months. These are plotted vs HbA1c at the same time points in Fig. 4. The overall Pearson correlation r was 0.68, $P = 0.002$.

Fig. 1

Kernel density plot of HbA1c in FreeStyle Libre users with type 1 diabetes (n = 92) at baseline and after 3 and 6 months follow-up.

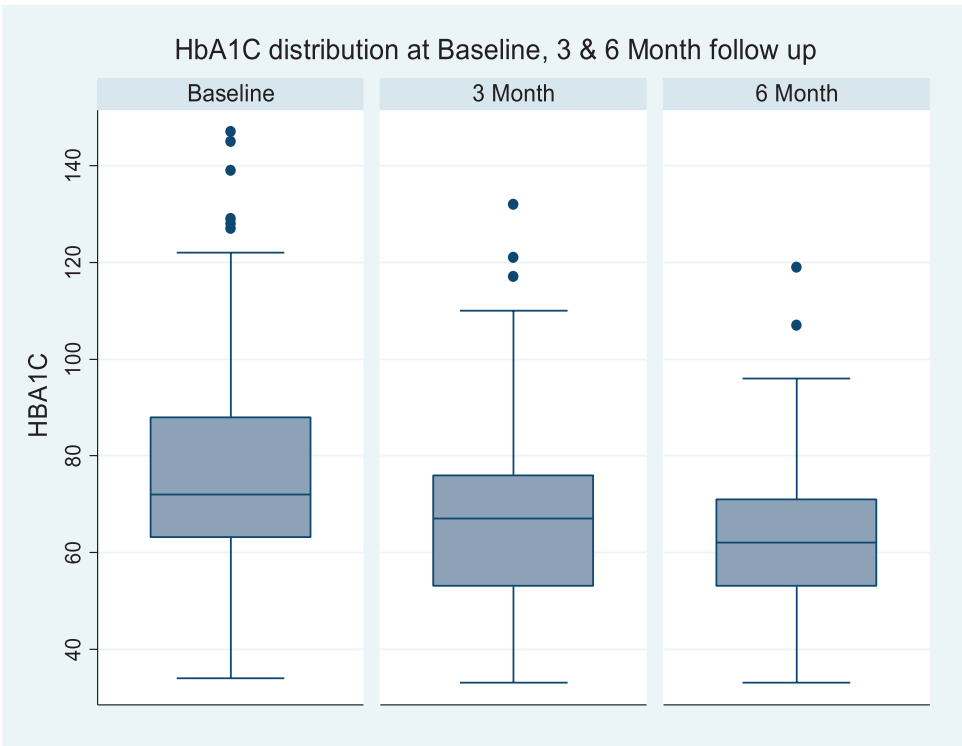
Fig. 2

Changes in HbA1c over time for (baseline, 3 months and 6 months) for individuals at the mid point (orange) of starting HbA1c and at the upper (grey) and lower (blue) extremes of pre-Libre HbA1c.

Sex had no significant effect on the changes in HbA1c nor did duration of diabetes. In multiple regression modelling, increasing age was associated with a lesser fall in

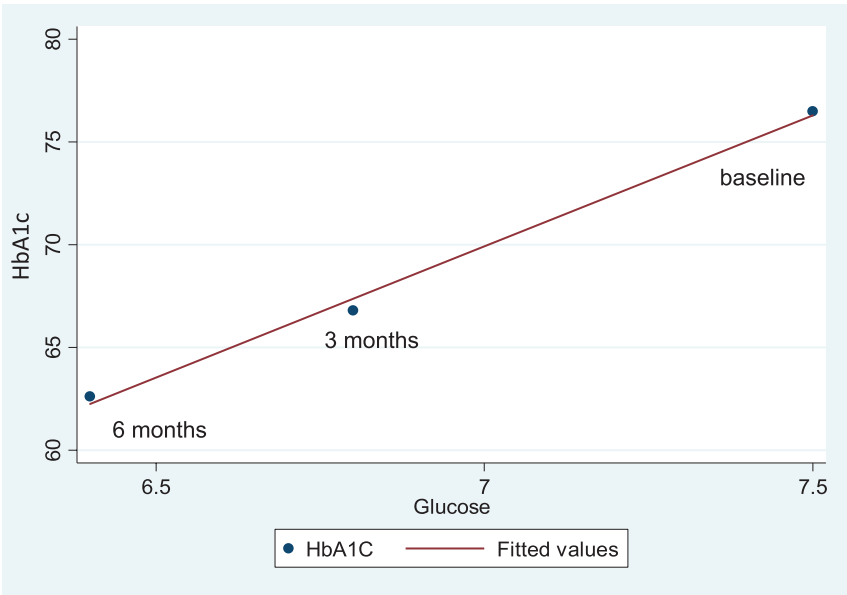
HbA1c at 6 months ($\beta = -0.289$; $P = 0.04$) independent of BMI and sex. However, this association disappeared when HbA1c at baseline was included in the model (for

Fig. 3



Box plots for the HbA1c distributions at baseline, 3 months and 6 months with the actual data points also added.

Fig. 4



Average Libre blood glucose measurements for baseline, 3 months and 6 months. Plotted vs. HbA1c at the same time points.

Table 2 Regression analysis of HbA1c vs. the individual factors measured at baseline

Results of mixed model (two-level linear regression model)			
Predictors	Regression coefficient	95% CI	P-value
Age	−0.29	−0.53 to −0.05	0.019
Sex	−4.04	−11.14 to 3.05	0.264
Female			
BMI	−0.73	−1.40 to −0.06	0.032

CI, confidence interval.

relation of change HbA1c vs baseline HbA1c, $\beta = 0.587$; $P < 0.001$).

We have shown in Table 2 the individual factors at baseline and interactions with HbA1c along with the coefficient and the corresponding P values from this analysis. HbA1c was related to lower BMI and lower age at baseline.

None of the users discontinued the Libre over the 6-month follow-up period. Four users reported some mild skin irritation at the site of the monitor but this was not sufficient to result in discontinuation. After the 6-month follow-up, two users did not wish to continue with the monitoring as they were happy to return to their previous blood glucose monitor.

Discussion

We have here provided persuasive evidence for the effectiveness of flash blood glucose monitoring in improving glycaemia in type 1 diabetes individuals who have a history of high blood glucose levels, in some cases over a number of years. The mean reduction in HbA1c was 16.1 mmol/mol (2.5%) (in these individuals. This technology has the potential to help people across the world manage their diabetes more effectively and although local in its nature, is global in its implications.

The reduction in HbA1c that we found may well be associated with better cardiovascular outcomes as time goes forward for these individuals [6–10]. There was no influence of age, sex or duration of diabetes as covariates known to be associated with glycaemic outcomes, on the outcome when adjustment was made for starting HbA1c.

Flash glucose monitoring is an effective tool with great potential for the management of type 1 diabetes in the adult population that can help people to improve metabolic control and quality of life. The technology provides significantly more data than the intermittent results obtained by traditional subcutaneous blood glucose monitoring, which may not capture intervals of extreme variability or nocturnal events and does not permit visualisation of trends.

For those individuals who drive conventional capillary blood glucose monitoring continued as per United Kingdom Driver and Vehicle Licensing Agency (DVLA) guidance [11].

With the help of a record of insulin dosing, meal intake, physical activity and stress factors, people with type 1 diabetes can achieve the full benefits of flash glucose monitoring and work together with healthcare professionals to act upon the information provided by the sensor. The graphs and trends available with flash glucose monitoring allow an understanding of how different factors (e.g. physical activity and diet) impact glycaemic control, consequently motivating people with type 1 diabetes to take charge of their health [12]. This approach to blood glucose monitoring has the advantage of preventing hypo- and hyperglycaemic events through the blood glucose trend system [2]. However, flash monitoring is different from CGM in that it only provides data on demand and, as such, is unable to provide alerts; it has no alarm feature and so is it not suitable for individuals who have a lack of hypoglycaemia awareness.

In addition to a fall in mean HbA1c, the proportion of outliers with high HbA1c fell. This is likely to have positive consequences over time owing to reduced complication rates, as demonstrated in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study [13].

None of the users in this study attended a structured expert patient programme during the 6-month follow-up or in the previous 12 months. Therefore, the changes in glycaemia are likely to be a result of modifications in insulin dose and lifestyle made as a consequence of the information provided by the flash glucose monitor

Side effects of itchiness and skin irritation were minimal, as reported elsewhere [12]. Although we have not reported it formally here, the feedback from users of flash monitoring was very positive, with little desire to move back to finger-prick monitoring as a way of measuring blood glucose through the day. Only two out of 92 people wished to discontinue the Libre after 6 months. For those individuals who drove, use of conventional capillary blood glucose monitoring continued when driving, as per DVLA guidance at the time [11].

In terms of strengths, we have used national-level data for the UK. In terms of limitations, we accept that participant numbers relatively low but we feel that we have enough participants to justify our conclusions.

Conclusion

We have shown that flash glucose monitoring is an effective tool in improving glycaemic control in people with not well-controlled type 1 diabetes. This has significant health-economic implications which remain the topic of intense discussion.

If sustained, the improvements seen here in glycaemic control should associate with reduced cardiovascular risk as time goes forward.

Acknowledgements

We would like to acknowledge Vernova Healthcare CIC for supporting the evaluation of the intervention.

Any requests for data extracts will be considered by Dr. Adrian Heald as the corresponding author.

Conflicts of interest

There are no conflicts of interest.

References

- Pickup JC, Freeman SC, Sutton AJ. Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data. *BMJ* 2011; **343**:d3805.
- Kalra S, Gupta Y. Ambulatory glucose profile: flash glucose monitoring. *J Pak Med Assoc* 2015; **65**:1360–1362.
- Iqbal A, Novodvorsky P, Heller SR. Recent updates on type 1 diabetes mellitus management for clinicians. *Diabetes Metab J* 2018; **42**:3–18.
- Anderson SG, Narayanan RP, Amlesh J, Qureshi MZ, Heald AH. Type 1 diabetes in Cheshire: cardiometabolic risk factor trends (2004-2009). *Prim Care Diabetes* 2012; **6**:123–126.
- Heald AH, Livingston M, Fryer A, Moreno GYC, Malipatil N, Gadsby R, et al. Route to improving type 1 diabetes mellitus glycaemic outcomes: real-world evidence taken from the national diabetes audit. *Diabet Med* 2018; **35**:63–71.
- Morrish NJ, Wang SL, Stevens LK, Fuller JH, Keen H. Mortality and causes of death in the WHO multinational study of vascular disease in diabetes. *Diabetologia* 2001; **44** (Suppl 2):S14–S21.
- Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, et al.; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med* 2005; **353**:2643–2653.
- Lind M, Svensson AM, Kosiborod M, Gudbjörnsdóttir S, Pivodic A, Wedel H, et al. Glycemic control and excess mortality in type 1 diabetes. *N Engl J Med* 2014; **371**:1972–1982.
- de Ferranti SD, de Boer IH, Fonseca V, Fox CS, Golden SH, Lavie CJ, et al. Type 1 diabetes mellitus and cardiovascular disease: a scientific statement from the American Heart Association and American Diabetes Association. *Diabetes Care* 2014; **37**:2843–2863.
- National Institute for Health Care and Excellence. Type 1 diabetes in adults: diagnosis and management. <https://www.nice.org.uk/guidance/NG17>: last updated July 2016. [Accessed 22 March 2020]
- Diabetes mellitus: assessing fitness to drive - GOV.UK. [Accessed 10 April 2019]
- Mancini G, Beroli MG, Santi E, Rogari F, Toni G, Tascini G, et al. Flash glucose monitoring: a review of the literature with a special focus on type 1 diabetes. *Nutrients* 2018; **10**:E992
- de Boer IH, Rue TC, Cleary PA, Lachin JM, Molitch ME, Steffes MW, et al.; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group. Long-term renal outcomes of patients with type 1 diabetes mellitus and microalbuminuria: an analysis of the diabetes control and complications trial/epidemiology of diabetes interventions and complications cohort. *Arch Intern Med* 2011; **171**:412–420.