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Meta-analysis of average change in laboratory-measured HbA1c among people with type 1 diabetes mellitus using the 14 day Flash Glucose Monitoring System

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ABSTRACT

Aim: FreeStyle Libre™ Flash Glucose Monitoring System (Flash GM), a novel, sensor-based, factory-calibrated system has been compared with self-monitoring of blood glucose in a well-controlled adult type 1 diabetes mellitus (T1D) population (HbA1c $\leq$ 7.5%, 58 mmol/mol), in a randomized controlled trial (RCT). The need for RCTs to recruit homogenous patients and for a well-controlled environment may not necessarily reflect use of a new technology in real clinical practice.

Methods: A random effects meta-analysis of all identified studies in T1D was performed to investigate changes in laboratory-measured HbA1c following introduction of Flash GM.

Results: Flash GM introduction showed a mean change from baseline to longest follow-up timepoint of −0.41% ([95% CI −0.51%, −0.31%]; P < 0.001; −4.5 [95% CI −5.6, −3.3] mmol/mol) in HbA1c in the random effects meta-analysis (34 studies comprising 5,466 participants). When the Flash GM arms of the two RCTs were excluded, there was a similar change in HbA1c of −0.41% ([95% CI −0.50%, −0.32%], P < 0.001; −4.5 [95% CI −5.4, −3.5] mmol/mol) in the 32 uncontrolled studies. Considerable heterogeneity was shown in all meta-analyses (I^2 values > 85%), likely due to the inclusion of diverse populations and variations in study protocols, meaning random effects meta-analyses should be strongly preferred.

Conclusions: In people with T1D, use of Flash GM for 2 to 24 months was associated with an estimated HbA1c reduction from baseline of 0.4%. A similar reduction occurred in uncontrolled studies where baseline HbA1c was generally higher compared with Flash GM arms of well-controlled studies.

Abbreviations: BG, blood glucose; DKA, diabetic ketoacidosis; Flash GM, Flash glucose monitoring system; CI, confidence interval; HbA1c, glycated hemoglobin; MC, multicenter; NR, not reported; PC, prospectively-assessed cohort; RC, retrospectively-assessed cohort; RCT, randomized controlled trial; SD, standard deviation; SE, standard error; SMBG, self-monitoring of blood glucose; T1D, type 1 diabetes mellitus; T2D, type 2 diabetes mellitus

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1. Introduction

FreeStyle Libre™ 14 day Flash Glucose Monitoring System (Flash GM) (Abbott Diabetes Care, Alameda, California) is a novel, sensor-based, factory-calibrated flash glucose monitoring system that continuously measures glucose levels in the interstitial fluid.

The efficacy and safety of Flash GM at improving glycemic control has been compared with self-monitoring of blood glucose (SMBG) using finger prick tests in a parallel group, randomized, controlled, multicenter trial of 6 months' duration. Only Type 1 diabetes mellitus (T1D) adults with good glycemic control were eligible for inclusion (glycated hemoglobin (HbA1c) $\leq$ 7.5% (58 mmol/mol) at entry with a reported mean HbA1c at screening of 6.8% (51 mmol/mol) [standard deviation (SD) 0.52% (5.7 mmol/mol)]) and 6.8% (51 mmol/mol) (0.64% (7.0 mmol/mol) for the Flash GM and SMBG arms, respectively. Subjects with these restrictive eligibility criteria may not have characteristics representative of the general population of people with T1D, such as HbA1c values above well-controlled levels. Although International Diabetes Guidelines generally recommend a target HbA1c level of < 7% (53 mmol/mol) in adults and < 7.5% (58 mmol/mol) in children [2,3], this desired level of control is achieved by a minority of children and adults with T1D in high income countries [4,5]. In the United States, target HbA1c control levels were achieved by <23% of children 2–17 years, 14% of young adults 18–25 years and 29–30% of adults $\geq$ 26 years in a large registry study of 16,061 people with T1D [6]. In Australia, only 27% of pediatric patients (up to and including 18 years) achieve target HbA1c levels [7], and the mean HbA1c for adults with T1D was 8.5% (69 mmol/mol) (standard deviation (SD) 1.8% (19.7 mmol/mol)) [8].

Evidence from a range of studies suggests that higher baseline HbA1c levels have been associated with greater intervention-related reductions in HbA1c [9–11], and therefore, study population baseline HbA1c may be an important covariate when assessing the impact of treatment interventions on HbA1c improvement.

Given the lack of Flash GM RCTs that included patients with elevated HbA1c, non-randomised studies, with their acknowledged limitations, were seen as an alternate source of exploring whether Flash GM may be related to HbA1c. Therefore, meta-analyses of these studies reporting changes in laboratory-measured HbA1c following the introduction of Flash GM in varying T1D populations with varying levels of glycemic control might be useful. Meta-analysis of Flash GM in pediatric/adolescent studies would also be informative since RCT data are not fully available.

2. Methods

Guidelines for Preparing a Submission to the Australian Pharmaceutical Benefits Advisory Committee (PBAC Version 5.0) [12], a key reimbursement decision maker, were followed, which include literature search methods, recommendations on risk of bias assessment for non-randomized studies (based on the ROBINS-1 tool [13]), and identification of relevant studies.

2.1. *Data sources and searches*

In February 2020 comprehensive reviews of PubMed, MEDLINE, EMBASE, ClinicalTrials.gov, Cochrane Database of Systematic Reviews and the Cochrane Register of Controlled Trials were carried out to identify all relevant published clinical studies conducted in humans. Textword searches, adapted for each database, were conducted for ("Flash GM" OR "Flash Glucose Monitori*" OR "FGM") AND ("type 1 diabetes" OR "insulin dependent diabet*" OR "diabetes mellitus [MESH]") AND ("HbA1c" OR "uncontrolled HbA1c" OR "uncontrolled glycated haemoglobin"), restricted to human studies. A manual search for additional studies using references from retrieved articles was also performed.

2.2. *Study selection*

All publications with study designs reporting use of Flash GM for a minimum of 8 weeks to a maximum of 2 years by 5 or more people with T1D that included the outcome 'change from baseline in HbA1c' (or presented sufficient data to allow its calculation) were included in the meta-analysis. Baseline HbA1c measurement was required at –3 to 0 months prior to Flash GM initiation. The minimum requirement for an 8-week duration of Flash GM use was to allow sufficient time for the intervention to produce meaningful results, and the requirement for at least 5 participants was to exclude case reports or small case series.

2.3. *Data extraction and quality assessment*

The identification of relevant abstracts, the inclusion of studies based on the selection criteria and the subsequent data extraction were independently performed by two of the authors (CR and KMK) with conflicts resolved by discussion. Quality of study assessment was not used as a criterion for including studies in the analysis.

2.4. *Data synthesis and analysis*

Laboratory-measured HbA1c data were reported using means or medians, with HbA1c reported in mmol/mol converted to % based on the standard conversion formula. Throughout, it was assumed (when not explicitly stated) that a paired *t*-test on the change from baseline was used for inference. Confidence intervals (CI) and standard deviations (SD) were obtained if reported. Where studies provided the mean change with P-value, the sample size and the P-value were used to determine the t-ratio, and this was used, with the mean change, to determine the standard error (SE). Where medians were reported rather than means, CI for the median was used as an approximation for the CI for the mean, and the SE was derived from it; for normally distributed data, the median estimates, the mean, and a CI for the median will, on average, be wider than a CI for the mean, so this strategy is conservative. Meta-analyses were performed by longest reported timepoint. A fixed-effect and random-effects meta-analysis using the DerSimonian and Laird approach are presented. Heterogeneity was quantified using the I^2 statistic and tested using Cochran's Q test. All analyses were performed using Excel and Minitab statistical software, version 18.

3. Results

The PRISMA diagram, depicting the trial searches and selection flow diagram is reported in Fig. 1. From the 690 citations retrieved, 34 unique studies fulfilling the inclusion criteria were identified comprising a total of 5,466 participants. A number of the identified studies were available as published abstracts and/or conference posters.

Characteristics of the included studies and their populations are reported in Table 1.

All studies recruited people with T1D via treatment clinics, with 24 of the studies including only adults and 10 enrolling adolescents and children. Mean ages reported in the adult studies ranged from 25 to 51 years and from 10 to 14 years in studies with children and adolescents, with some studies reporting median values. Adult studies included subjects with an extensive history of T1D (mean duration 11 to 26 years); and shorter T1D histories in studies that recruited children and adolescents (mean duration of 4.4 to 5.4 years).

Baseline HbA1c ranged from a reported mean of 6.8% (51 mmol/mol) to 10.3% (89 mmol/mol) in the adult studies, with baseline HbA1c $< 7.5\%$ (58 mmol/mol) in the both single arms of the 2 RCTs [1,16]. In the pediatric and adolescent studies, mean baseline HbA1c varied from 7.7% (61 mmol/mol) to 9.6% (81 mmol/mol). One study, even though reporting that HbA1c reduced significantly after Flash GM introduction, did not clearly report when the HbA1c baseline and final timepoints were measured [17]. Therefore, this study identified and listed in Table 1, was excluded from the meta-analysis.

3.1. *Mean HbA1c changes from baseline to longest follow-up timepoint*

The analysis of all studies found a mean change from baseline to longest follow-up timepoint of −0.41% (95% CI −0.51%, −0.31%; −4.5 [95% CI −5.6, −3.3] mmol/mol) in the random-effects meta-analysis with a statistically significant improvement noted ($P < 0.001$) (Fig. 2). All except 4 of the 34 studies showed either a statistically significant or an average improvement in this outcome, with 1 study showing no difference. Considerable heterogeneity was shown in the random-effects analysis ($I^2 = 84.8\%$), likely due to the inclusion of studies with diverse population characteristics that included a range of HbA1c levels at baseline.

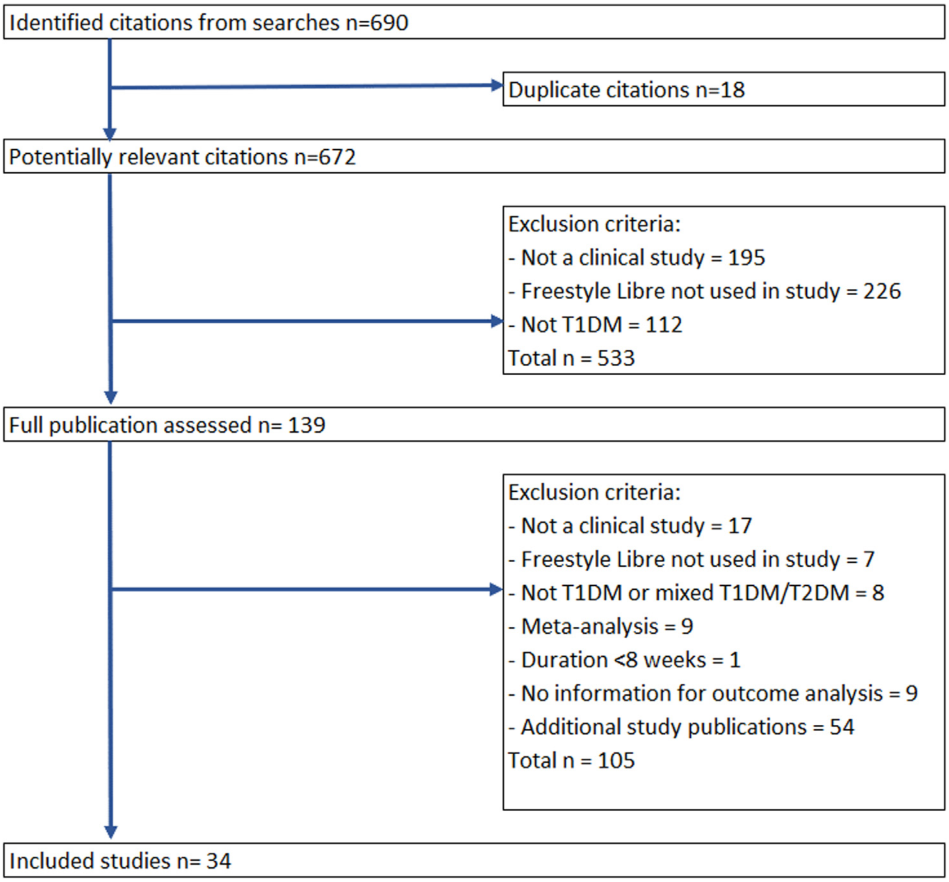


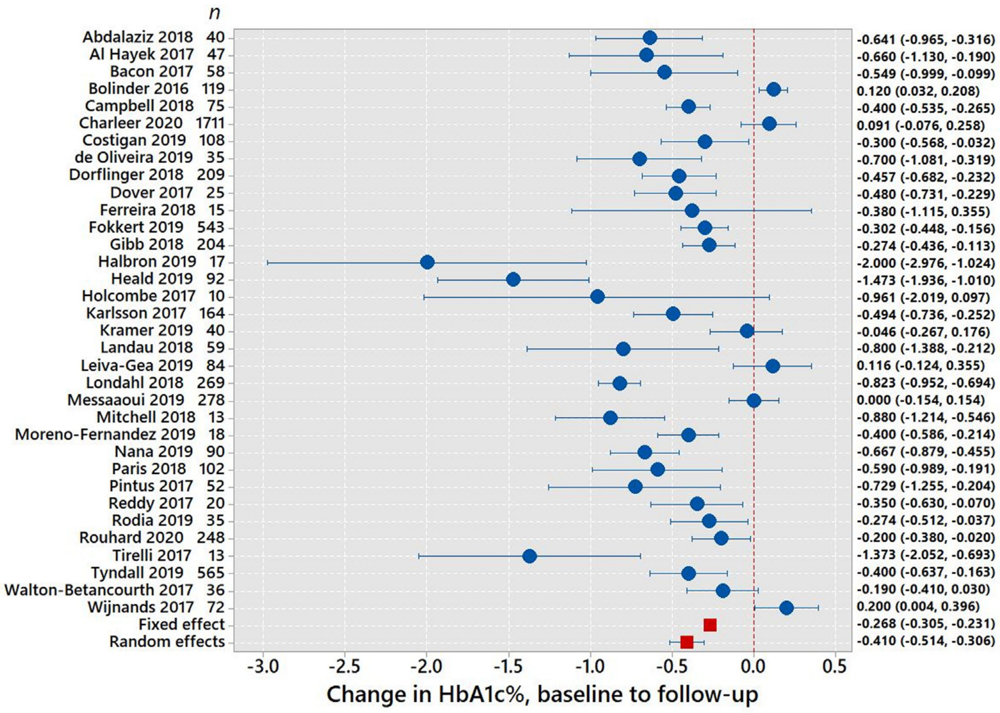
Fig. 1 – Flow chart of literature search and article selection.

Table 1 – Characteristics of Included Studies and their Populations.

Author, year	Adults/ children	Number of subjects	Age[a]	T1D duration[a]	Baseline HbA1c[b]	Final outcome timepoint[c]
Abdalaziz, 2018 [23]	Adults	40	39 (16)	NR	8.5 (1.4)	12 months
Al Hayek, 2017 [30]	Children	47	13–19	NR[k]	8.5 (1.07)	3 months
Bacon, 2017 [24]	Adults	58	46 (16)	NR	8.1 (NR)	3 months
Bolinder, 2016 [1]	Adults	119	42 (13.1)	21 (10)	6.8 (0.52)	6 months
Campbell, 2018 [38]	Children	76[d]	10.3 (4.0)	5.4 (3.7)	7.9 (1.0)	2 months
Charleer, 2020 [39]	Adults	1711	45.8 (15.3)	22.8 (13.7)	7.8 (1.2)	12 months
Costigan, 2019 [40]	Children	108	11.6 (3.9)	5.1 (3.7)	8.0 (1.1)	6 months
De Oliveira, 2019 [41]	Adults	35	31.7 (10.3)	NR	8.6 (1.2)	3 months
Dorflinger, 2018 [42]	Adults	209	NR	NR	8.1 (IQR 7.4, 8.9)	3 months[e]
Dover, 2017 [25]	Adults	25	39.8 (2.0)	19 (2)	8.0 (0.14[f])	4 months
Ferreira, 2018 [43]	Adults	15	30.3 (14.1)	10.5 (5.9)	8.4 (0.9)	3 months
Fokkert, 2019 [44]	Adults	543	NR	NR	7.8 (IQR 7.1, 8.6)	12 months
Gibb, 2018 [45]	Adults	204	NR	NR	NR	10 months
Halbron, 2019 [46]	Adults	17	25 (IQR 20, 32)	13 (IQR 9, 17)	10.8 (IQR 10.3, 12.3)	6 months
Heald, 2019 [47]	Adults	92	45.9 (15.3)	20 (13.3)	9.7 (95% CI 9.4, 10.1)	6 months
Holcombe, 2017 [26,27]	Adults	15 [g]	NR	NR	9.0 (NR)[h]	8 weeks
Karlsson, 2017 [14]	Adults	164	42 (16.6)	NR	8.5 (1.6)	12 months
Kramer, 2019 [48]	Adults	40	50.9	21.9	7.4 (NR)	1 year
Landau, 2018 [49]	Children	59	13.5 (5.2)	3.1 (IQR 1, 7.4)	8.2 (IQR 7.5, 9.4)	12 months
Leiva-Gea, 2019 [50]	Children	145[i]	11.4(3.1)	5.2 (3.2)	NR[j]	6 months
Londahl, 2018 [51]	Adults	269	NR	NR	8.7 (1.5)	2 years
Messaaoui, 2019 [52]	Children	278	13.6 (IQR 10.9, 16.3)	5.5 (IQR 3.4, 7.8)	7.5 (IQR 6.9, 8.1)	12.7 months[k]
Mitchell, 2018 [29]	Adults	16 [l]	34 (14.7)	17 (10.7)	10.3 (NR)	3 months
Moreno-Fernandez, 2018 [53]	Adults	18	37.8 (22–55)	21.2 (8.6)	7.8 (1.0)	6 months
Nana 2019 [54]	Adults	90	45.3 (18–75)	26.0 (15.2)	8.7 (1.4)	6 months
Paris, 2018 [55]	Adults	117[m]	40.1 (13.8)	16.8 (10.8)	8.5 (1.5)	12 months
Pintus, 2017 [31,32]	Children	52	11.7 (5.5–18)	4.4 (0.2–16.7)	8.2 (NR)	3 months
Reddy, 2017 [16]	Adults	20	48.5 (IQR 34–63)	28 (IQR 16.5–36.5)	7.2 (IQR 6.5–8.1)	8 weeks
Rodia, 2019 [56]	Adults	35[n]	NR	NR	8.5 (0.1)	18 months
Rouhard, 2020 [57]	Adults	248	45 (16)	20 (1.3)	8.1 (1.3)	18 months
Tirelli, 2017 [34]	Children	13	14 (4.1)	4.8 (2.2)	9.6 (2.6)	3 months
Tyndall, 2019 [58]	Adults	565	42 (30–55)	19 (10–30)	7.7 (7.0–8.6)	8.2 months[o]
Walton-Betancourth, 2017 [35]	Children	52[p]	12.2 (3.5–18.6)	NR	7.9 (1.0)	12 months
Wijnands, 2017 [36]	Children	78[q]	4.7–17.6	At least 6 months	7.7 (1.1)	8 months
Xatzipsalti 2017 [17,37]	Children	51	10.7 (5.5)	3.4 (0.18–20.3)	NR	1 year

Notes: a. Data are expressed as a range, mean (SD), ,mean (95% CI if stated), median (range) or median (IQR if stated), in years; b. Data are expressed as mean % (SD) or median % (IQR); c. Longest reported timepoint for outcome data (HbA1c); d. HbA1c outcome data reported for 75 subjects; e. 3 month change used as outcomes reported for all 209 subjects with baseline data, with later timepoints only including some subjects; f. Assumed to be a standard error (SE) based on the magnitude of the value as it is not clear from the study publication whether SE or SD was reported; g. HbA1c outcomes data reported for 10 subjects; h. Baseline HbA1c reported for 13 subjects; i. Hb1Ac outcome data were reported for 84 subjects at 6 months; j. Reported for subgroups with baseline HbA1c < 7.5% and ≥ 7.5%); k. median follow-up; l. HbA1c outcome data reported for 13 subjects; m. HbA1c outcome data reported for 102 subjects; n. HbA1c outcome data reported for 35 subjects at 18 months of the 397 subjects initially recruited to the study; o. median follow-up reported in days; p. HbA1c outcomes data reported for 36 subjects at 12 months; q. HbA1c outcomes data reported for 72 subjects.

IQR, interquartile range; NR, not reported; SD, standard deviation; SE, standard error.



Estimates and 95% confidence intervals.

Fig. 2 – Forest plot of mean HbA1c (%) change from baseline to longest follow-up timepoint in all studies (adult and pediatric/adolescent).

3.2. *Mean HbA1c changes in adult and pediatric/adolescent studies*

A similar change from baseline in HbA1c to longest follow-up timepoint was seen in the adult and combined pediatric and adolescent studies. In adults with T1D, mean HbA1c change from baseline to longest timepoint was –0.46% ([95% CI –0.59%, –0.33%] P < 0.001; −5.0 [95% CI −6.5, −3.6] mmol/mol) (Fig. 3). Studies that included only children and adolescents also showed a significant mean change from baseline in HbA1c at endpoint (–0.29% [95% CI –0.47%, –0.10%], P = 0.002; −3.1 [95% CI −5.1, −1.1] mmol/mol) (Fig. 4). Considerable heterogeneity was apparent in both analyses (I^2 = 86.9% in the adult studies and 79.9% in the pediatric and adolescent studies).

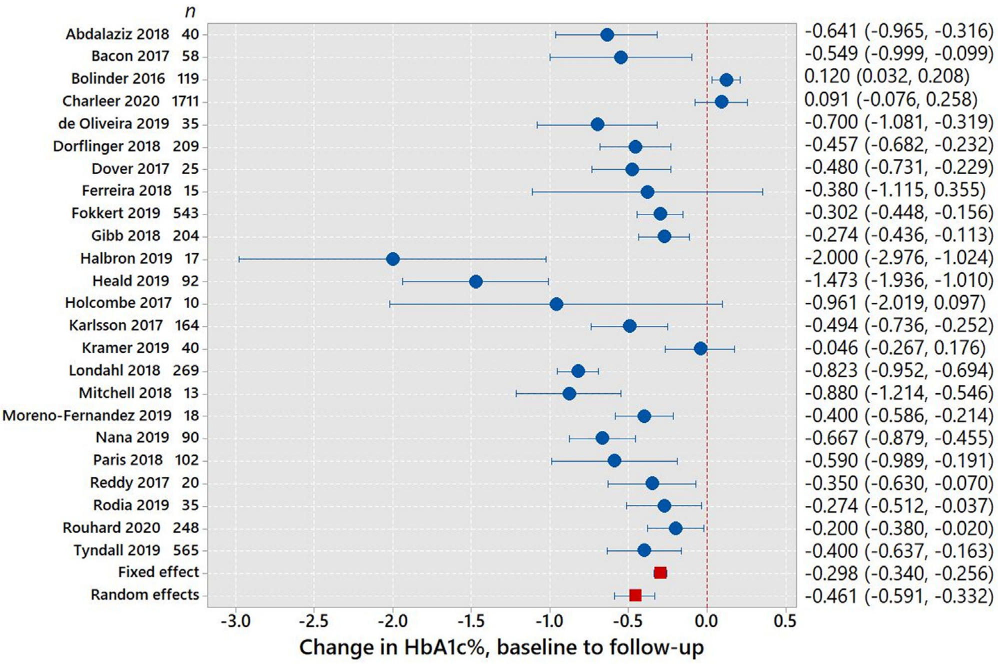
3.3. *Mean HbA1c changes in controlled and uncontrolled studies*

Two of the included adult studies were single arms of RCTs [1,16]. In these studies patients already had well-controlled T1D at study entry. When the Flash GM arm results from these studies were random-effects meta-analysed, there was no mean significant HbA1c change from baseline to longest follow-up timepoint −0.10% ([95% CI −0.55%, 0.36%], P = 0.684; −1.0 [95% CI −6.1, 4.0] mmol/mol) (Fig. 5). Considerable heterogeneity was apparent in the analysis (I^2 = 89.9%).

When the 32 uncontrolled cohort studies were analysed separately, a greater HbA1c improvement was noted at study endpoint, compared with the non-significant results seen in the 2 controlled studies, although the difference between the estimates is consistent with no true difference (P = 0.185). The mean HbA1c change from baseline to endpoint in the 32 uncontrolled studies was −0.41% ([95% CI −0.50%, −0.32%], P < 0.001; −4.5 [95% CI −5.4, −3.5] mmol/mol) (Fig. 6) The greater magnitude of improvement seen in the uncontrolled studies compared with the controlled studies may be explained by differences in baseline HbA1c levels seen between these 2 groups, with a greater change in the uncontrolled studies where baseline HbA1c levels were more elevated (Fig. 6) [10,11]. Regression to the mean may also be a factor.

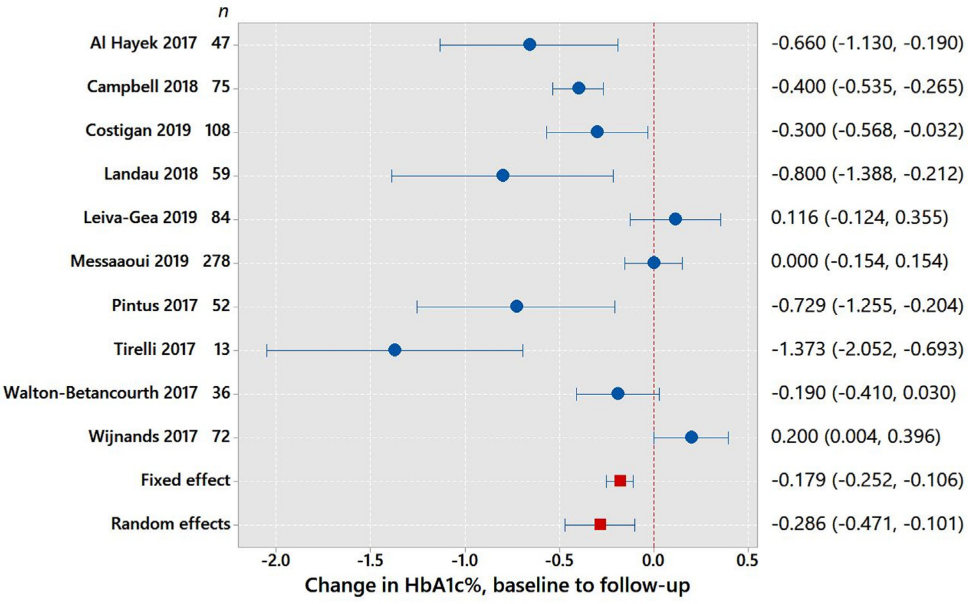
4. Discussion

The effectiveness and safety of Flash GM compared with SMBG via 'fingerprick' testing has been established in a randomized, controlled trial in 241 adults with T1D [1]. The primary study outcome, 'mean time in hypoglycemia' (defined as < 70 mg/dL for the 14 days preceding the end of the 6-month study period), decreased from 3.38 h/day at baseline to 2.03 h/day at 6 months (baseline adjusted mean change − 1.39 h/day) in the Flash GM group, and from 3.44 h/day to 3.27 h/day in the SMBG control group (−0.14); with the between-group difference of − 1.24 (SE 0.239; P < 0.0001), equating to a 38% reduction in time in hypoglycemia in the Flash GM group [1]. At 6 months, HbA1c concentrations were essentially unchanged in the Flash GM group compared with the control SMBG group [1], likely due to the well-controlled study population with subjects required to have a HbA1c ≤ 7.5% (58 mmol/mol) at entry and reporting a mean screening baseline HbA1c of 6.8% (SD 0.52%)



Estimates and 95% confidence intervals.

Fig. 3 – Forest plot of mean HbA1c (%) change from baseline to longest follow-up timepoint in adult studies.

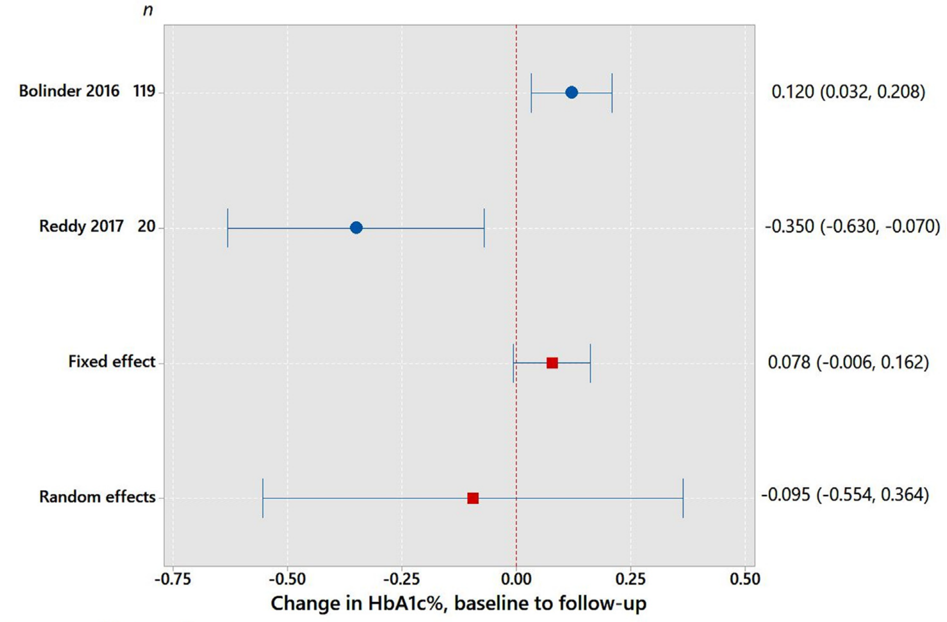


Estimates and 95% confidence intervals.

Fig. 4 – Forest plot of mean HbA1c (%) change from baseline to longest follow-up timepoint in pediatric/adolescent studies.

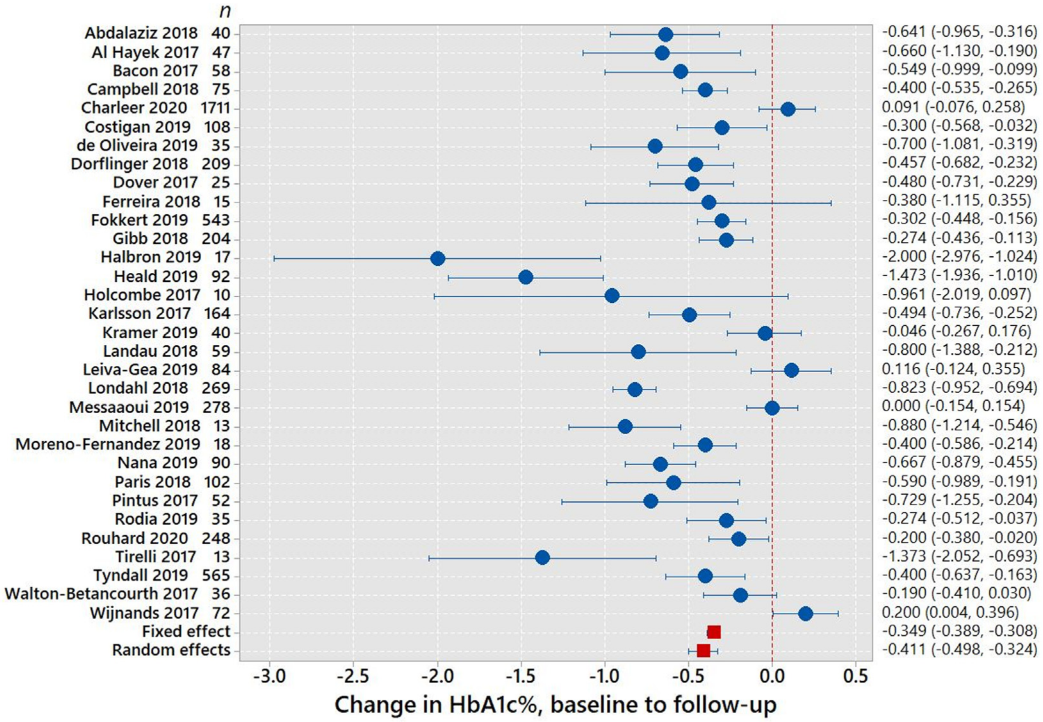
(51 mmol/mol (SD 5.7)) and 6.8% (SD 0.64%) (51 mmol/mol (SD 7.0)) for the Flash GM and SMBG arms, respectively [1]. In contrast, in many high-income countries such as those in Europe, the United States and Australia, only a minority of the T1D population meet generally recommended HbA1c targets of $\leq$ 7% (53 mmol/mol) in adults and $\leq$ 7.5% (58 mmol/mol) in children [2–7].

Random-effects meta-analyses of all 34 T1D studies, as well as adult and children/adolescent subgroups all showed an average lowering of laboratory-measured HbA1c from baseline to longest study endpoint. High levels of heterogeneity were apparent, ranging from 73.2% to 89.9%, likely due to differences in study and patient baseline characteristics resulting from inclusion of a range of study designs with diverse eligibility criteria. Despite the high levels of heterogeneity shown, the generally consistent, statistically significant magnitude of the clinically meaningful HbA1c improvement supports the use of Flash GM; evidence from



Estimates and 95% confidence intervals.

Fig. 5 – Forest plot of mean HbA1c (%) change from baseline to longest follow-up timepoint in the Flash GM treatment arm of RCTs.



Estimates and 95% confidence intervals.

Fig. 6 – Forest plot of mean HbA1c (%) change from baseline to longest follow-up timepoint in the Flash GM treatment arm of uncontrolled studies.

randomised controlled trials in such patient populations would give clearer evidence. The European Medicines Agency, in discussing pre-defined non-inferiority margins for therapeutic confirmatory trials in diabetes, highlight that even apparently small reductions in HbA1c have been shown to be clinically relevant in terms of risk reduction of diabetes complications, with a minimum improvement of 0.3% generally considered acceptable [18], supporting the 0.4% change seen with Flash GM across 5,466 participants in 34 studies as clinically important. A greater level of HbA1c lowering occurred in studies that recruited participants with uncontrolled HbA1c levels at baseline ('uncontrolled studies') compared with the Flash GM arms of RCTs that recruited participants with controlled HbA1c levels at baseline ('controlled studies').

The baseline HbA1c level is an important study characteristic shown to be predictive of subsequent HbA1c improvement with clinical interventions, including insulin use in Type 2 diabetes mellitus (T2D). In a systematic review and meta-analysis of 98 studies with 24,163 subjects following treatment with dipeptidyl peptidase-4 inhibitors in T2D, the strongest predictive factor of HbA1c response was baseline HbA1c level [10]. The DIAMOND study which included both T1D and T2D subjects treated with multiple daily injections and monitored with continuous glucose monitoring, found that the highest changes in HbA1c were seen in those with the highest baseline HbA1c [9].

Although RCTs provide the best evidence [20], there are currently no published RCTs comparing Flash GM with SMBG or other blood glucose measurement methods in T1D populations recruited with poor glycemic control. Published systematic reviews are increasingly including non-randomized studies [19], which can be particularly useful when RCT evidence directly relevant to the context of usage is not available [20]. A recent random effects meta-analysis of clinical and observational studies of the impact of Flash GM monitoring in adults and children included 21 studies [22]. This meta-analysis reported a mean HbA1c change from baseline of −0.56% (95% CI −0.70%, −0.39%; 6.1 mmol/mol (95% CI −7.7, −4.3 mmol/mol)) over a more limited follow-up of 2 – 4 months, similar to the −0.41% (4.5 mmol/mol) reported in this analysis that included HbA1c changes up to a maximum of 2 years, indicating the long-term impact on the reduction in HbA1c. Sustainability of the improvement in HbA1c over 12 months was also demonstrated [22].

There are a number of weaknesses associated with using non-randomized cohort studies utilising 'before and after' treatment outcome measurements. Differences in subject baseline characteristics both between and within study populations are likely to be a key contributor to the considerable levels of heterogeneity seen in all analyses, in addition to other unknown confounding factors. Entry criteria were not standardised across the studies, with few eligibility criteria specified, likely leading to variable study subject characteristics.

Other potential sources of the heterogeneity seen include differences in the quality of trial methods and laboratory measurements, as well as geographical and health system differences across the trial settings. All studies were undertaken recently (published in 2016–2020) with patients enrolled via diabetes clinics, likely reducing heterogeneity that can arise with the use of studies conducted over different eras and in differing healthcare settings. The RCTs for Flash GM were of a short 2 – 6 months' duration [1,16]. The meta-analysed studies had a differing duration of follow-up across the studies (2 months to 2 years). allowing a better understanding of the long-term effect Flash GM has on real-world glycaemic control.

Potential biases include attrition bias leading to loss to follow-up of some participants and consequent exclusion from the analysis and selective publication bias. While an extensive literature search was conducted, it is possible that relevant studies were not identified or that studies have been conducted and not published. Some studies were published only as abstracts resulting in reduced information available on the study design and patient populations, as well as patient follow-up; studies were not excluded based on quality assessments or incomplete trial descriptions unless impacting on interpretation of study results [17]. A further limitation is that the reported meta-analysis was not prospectively registered in the PROSPERO website, having initially been conducted for a reimbursement application in Australia (and since then updated).

Despite limitations with the use of non-randomized trials in meta-analyses, the baseline glycemic control levels in the included study populations are broadly consistent with real-world T1D populations, providing information on the likely changes in HbA1c in users of Flash GM in a population for whom improved disease control is desirable. The studies included are observational, without a comparison group, placebo or otherwise. They are therefore subject to the well-known issues of a "before-and-after" design. In particular, to the extent that individuals were selected, explicitly or implicitly, when their HbA1c was high, there is the potential for a contribution to the observed reduction from regression to the mean.

5. Conclusions

In people with T1D, use of Flash GM for 2 months to 2 years across 5,466 participants in 34 studies resulted in an average reduction in laboratory-measured HbA1c of 0.4% from baseline levels, with a similar reduction seen in subgroup analyses of adults and children/adolescents. The results indicate sustainability of the reduction in HbA1c. Greater reduction occurred in uncontrolled studies where average baseline HbA1c levels were higher compared to the Flash GM arms of controlled studies, where patients were well controlled already at baseline. Participants from uncontrolled studies may be more representative of real-world T1D populations who may exhibit poorer glycemic control.

Declaration of Competing Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. FreeStyle, FreeStyle Libre and related brands are trademarks of the Abbott Group of Companies (together "Abbott") in various jurisdictions.

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Declaration of conflicting interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2020.108158.

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