Pilot and Feasibility Studies

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Flash glucose monitoring for Indigenous Australians with type 2 diabetes: a randomised pilot and feasibility study

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Abstract

Background Flash glucose monitoring (FGM) can improve diabetes management, but no randomised controlled trials (RCTs) of FGM have been undertaken in Indigenous Australian populations. This study aimed to assess the feasibility of performing a RCT of FGM in Indigenous Australians with type 2 diabetes.

Methods In this open-labelled pilot RCT, Indigenous adults with type 2 diabetes were randomised to FGM or standard care for 6 months. Eligible participants were being treated with injectable diabetes medications and had a glycosylated haemoglobin (HbA1c) ≥ 7.0%. The feasibility outcome was the proportion of participants completing the trial, and the primary outcome for the future trial was change in HbA1c from baseline to 6 months. Secondary outcomes included change in time spent in target blood glucose (4.0–10.0 mmol/L), safety (hypoglycaemic episodes), and quality of life (EuroQol 5-dimension 3-level (EQ-5D-3L) score).

Results Of 126 screened individuals, 74 were eligible, 40 (54%) were randomised, and 39 (97.5%) completed the study. Participants' baseline characteristics were similar between the FGM and usual care groups, except for sex and body mass index. No between-group differences were observed for the following: change in HbA1c; percentage of time spent in target blood glucose (4.0–10.0 mmol/L), low glucose (< 3.9 mmol/L), and high glucose (> 15.0 mmol/L); or EQ-5D-3L scores. No severe hypoglycaemic episodes occurred.

Conclusions This is the first pilot RCT of FGM in Indigenous Australians with type 2 diabetes. The results support a larger RCT.

Trial registration Australian New Zealand Clinical Trials Registry (ANZCTR12621000021875), retrospectively registered on 14 January 2021.

Keywords Indigenous, Type 2 diabetes, Randomised controlled study, Pilot study, Flash glucose monitoring

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Key messages regarding feasibility

What uncertainties existed regarding the feasibility?

- It was not known whether conducting a randomised controlled trial using diabetes technology in an Indigenous Australian population with diabetes would be feasible.

What are the key feasibility findings?

- It was feasible to conduct this trial in Indigenous Australians. However, it is important to acknowledge that this trial was successful because it was led by Indigenous Australian researchers after extensive community consultation and was performed in accordance with a Culturally Adaptive Governance Framework.

What are the implications of the feasibility findings for the design of the main study?

- It is feasible to conduct clinical trials in Indigenous populations. However, to do so successfully, the research needs to be led by and conducted by Indigenous researchers and after community consultation.

Background

Diabetes mellitus contributes substantially to poor health outcomes [1] and disproportionately affects Indigenous Australians, in whom the prevalence is 3–4 times higher [2]. Indigenous Australians also experience diabetes complications more frequently and at an earlier age than non-Indigenous Australians [3]. Diabetes management in Indigenous populations has historically been suboptimal due to the interplay of social determinants of health including access to healthcare and medications, food insecurity, cultural losses, dispossession, and racial discrimination [4]. It is therefore imperative to find sustainable strategies that build on the many strengths of Indigenous Australian communities to improve their diabetes care. This study explored the potential of a specific strategy — of introducing a new diabetes technology that could improve the management of blood glucose levels.

Optimising blood glucose levels is essential to reducing diabetes complications [5–7]. Large, multicentre clinical trials have demonstrated that effective glucose-lowering therapies reduce the risk of micro- and macrovascular complications [5–9]. Despite the availability of these therapies, a disproportionate number of Indigenous people with diabetes continue to experience significant hyperglycaemia and remain at risk of diabetes-related complications. Conversely, many individuals require insulin and/or sulphonylureas [3] which can cause hypoglycaemia that if severe can precipitate macrovascular complications and/or death [10]. Safe and effective implementation of these therapies requires individuals to check their blood glucose readings frequently.

Structured intensive self-monitoring of blood glucose (SMBG) can improve glycaemic levels [11]. However, there are barriers to successful implementation [12], especially in people receiving multiple insulin injections or pump therapy [13–16] who may experience diabetes distress from painful fingerprick glucose measurements [17]. SMBG readings also need to be initiated by the person with diabetes and only provide information at the time of measurement. Consequently, there is insufficient data to identify patterns of blood glucose levels at particular times of the day (e.g. overnight) and over a longer period of time [18]. Since the development of continuous glucose monitoring (CGM) [19] and flash glucose monitoring (FGM), clear and comprehensive data can now be obtained with minimal user inconvenience [19, 20].

Real-time CGM/FGM in individuals with type 2 diabetes has been shown to reduce HbA1c without the intensification of treatment or an increased risk of hypoglycaemia [21]. This suggests that the availability of real-time glucose data results in behavioural and lifestyle changes [22, 23]. Yet CGM/FGM remain largely inaccessible due to cost (AUD $102/fortnight in 2023 [24]). In Australia, these technologies are subsidised for people with type 1 diabetes but not for people with type 2 diabetes on injectable therapies, including Indigenous Australians. Assisting Indigenous Australians with diabetes to use CGM or FGM technologies is a strategy that could not only improve diabetes care but also facilitate greater independence for individuals managing this chronic disease.

International bodies have called for randomised controlled trials (RCTs) in people from diverse health literacy and sociodemographic backgrounds, to confirm the benefits of CGM/FGM in type 2 diabetes [18, 20, 25, 26]. The current study meets this call for action, as there are no studies of FGM in Indigenous Australians. Furthermore, this research directly addresses the Australian government's *National Diabetes Strategy*, which aims to reduce the impact of diabetes among Indigenous Australians.

This study was initiated after extensive consultation with the Rumbalara community (an Indigenous Australian community in regional Victoria), in response to the identified need to improve diabetes care and access to diabetes technology. This pilot study aimed to evaluate whether a RCT of FGM could be successfully undertaken in an Indigenous Australian population with type 2 diabetes. The findings will guide the planning for a larger multicentre trial comparing FGM to

SMBG in Indigenous Australians with type 2 diabetes on injectable therapies.

Methods

Design

Indigenous Australians with type 2 diabetes were recruited to a prospective, open-labelled, individually randomised controlled pilot study that compared FGM to standard care (SMBG) over 6 months. A wait-list design was utilised, whereby participants randomised to the standard care arm (SMBG) were offered FGM for 6 months after the conclusion of the study.

Setting and participants

Participants were recruited from three outpatient sites: the Rumbalara Aboriginal Co-operative (RAC), Goulburn Valley Health (GVH), and Austin Health. RAC is a Victorian Aboriginal Community Controlled Health Organisation in regional Victoria, which has one of the largest Indigenous Australian populations outside metropolitan Melbourne. Participants were initially recruited from RAC and GVH only, commencing March 2018. Recruitment was later extended to Austin Health in metropolitan Melbourne (October 2020). Potential participants were identified through clinical databases at RAC and GVH and then contacted by study investigators.

Community engagement and consultation sessions were undertaken between 2016 and 2018 and involved community elders, RAC staff, Indigenous Australian health workers, and study investigators. Indigenous Australian researchers and health workers were integral to the study team. Several study investigators were in direct contact with participants and were familiar to and/or community members, which facilitated recruitment.

Eligible participants identified as Aboriginal and/or Torres Strait Islander, were aged ≥ 18 years with type 2 diabetes, had suboptimal diabetes management (defined as glycosylated haemoglobin [HbA1c] $\geq 7.0\%$), and were on diabetes treatment including insulin and/or glucagon-like peptide-1 (GLP-1) receptor agonists.

The exclusion criteria were as follows: active illicit drug use or heavy alcohol use (>4 standard drinks/day), active malignancy requiring chemotherapy, planning pregnancy/pregnant, known allergy to medical-grade adhesives, taking varying doses of corticosteroid therapy, using amphetamines and anabolic or weight-reducing therapies, significant renal impairment (defined as $eGFR < 15$ ml/min/1.73 m^2 or end-stage kidney disease), using erythropoiesis stimulating agents, or a known haemoglobinopathy.

Trial intervention (blinded CGM)

Participants were randomised to the intervention (FGM) or standard care (SMBG) for 6 months. Blinded CGM devices were also worn for 7–14 days by all participants at two time points — baseline (before randomisation) and 6 months. These blinded CGM systems were used to measure time spent in target glucose, low glucose and high glucose. Two systems (Medtronic iPro2 and Abbott FreeStyle Libre Pro) were used, because the FreeStyle Libre Pro — preferred because it was similar to the intervention device — only became available in August 2020. The first 19 participants used the iPro2, and the remaining 21 participants used the FreeStyle Libre Pro.

Intervention device (flash glucose monitor — FGM)

The FreeStyle® Libre™ [27] is a single-use, factory-calibrated FGM sensor, which is worn for up to 14 days [20]. Real-time glucose data is obtained by scanning the sensor with the reader, which stores information from the preceding 8-h period. Historical data in the reader can be uploaded to a computer to generate summary glucose reports for review by users or clinicians [20].

Standard care (SMBG)

This involved measuring blood glucose levels through capillary glucose testing with a glucometer and test strips. Participants were instructed to follow their usual diabetes care procedure as advised by their treating clinician. This included measuring blood glucose levels up to four times per day and when experiencing symptoms of hypoglycaemia/hyperglycaemia.

Data collection

Demographic and clinical characteristics and blood and urine tests were collected at baseline, 3 months, and 6 months. These included measurements of the following: HbA1c, fasting or random glucose, lipid profile, urine albumin-to-creatinine ratio, full blood examination, electrolytes, and liver function tests. Qualitative data were collected, the results of which are published elsewhere [28]. No data was collected as part of the wait-list component of the study.

Outcomes

The feasibility outcomes were whether participants could be recruited and retained (primary) in this RCT. The primary outcome for the future trial was change in HbA1c from baseline to 6 months. HbA1c was measured on venous blood tested at National Association of Testing Authorities (NATA) accredited laboratories [29]. Secondary potential effectiveness outcomes were

change in percentage of time spent in target blood glucose (4.0–10.0 mmol/L), low glucose (< 3.9 mmol/L), and high glucose (> 15.0 mmol/L). These data were collected from the blinded CGM systems.

Exploratory outcomes were change in percentage of time spent in CGM metrics as per the international consensus on time in range [30]: time above range (TAR) level 1 (glucose > 13.9 mmol/L), TAR level 2 (glucose = 10.1–13.9 mmol/L), time in range (glucose = 3.9–10.0 mmol/L), time below range (TBR) level 1 (glucose = 3.0–3.8 mmol/L), and TBR level 2 (glucose < 3.0 mmol/L). Further outcomes included changes in diabetes medications from baseline to 6 months for (a) the number of glucose-lowering medications and (b) insulin usage and total daily dose.

The quality-of-life outcome was assessed by the change in EuroQol 5-dimension 3-Llevel (EQ-5D-3L) score from baseline to 6 months. EQ-5D-3L index values were computed using the Australian value set developed by Viney et. al [31]. The safety outcome was the number and percentage of participants who experienced at least one severe hypoglycaemic event (defined as requiring third-party assistance). Adverse event occurrence was assessed at each study visit.

Data management

Study data (except data from the CGM and FGM devices) were collected and managed using REDCap electronic data capture tools hosted at The University of Melbourne [32, 33]. Device data from the blinded CGM devices were downloaded in an Excel (version 16.16.27) csv file.

Randomisation, allocation, and blinding

Following baseline measurements, participants were randomised to the FGM (intervention) or SMBG (standard care) in a 1:1 ratio, using a computer-generated randomisation list of randomly permuted blocks by an independent statistician. Individual study participant treatment codes were prepared in sequentially numbered opaque envelopes by independent support staff. Eligible participants learned their group allocation when opening these envelopes at randomisation. Participants, investigators, and study staff were not masked to group allocation because of the nature of the intervention. Study statisticians were blinded to the allocation until the database was cleaned and ready for analysis.

Sample size

The planned sample size was 40 participants, with 20 participants per arm. This was initially informed by the rule of thumb of 24 evaluable participants for the total sample size of a parallel-group two-arm pilot trial [34] and later increased to 40 participants determined by the available resources. With 40 participants recruited, if 90% (36/40) completed the trial, then the 95% confidence interval (CI) of the true underlying retention rate is 81 to 99% using the Clopper-Pearson method.

Statistical methods

Statistical analyses followed a prespecified statistical analysis plan (Supplementary file). Study participants were analysed according to their randomised treatment group ("as-randomised") for the intention-to-treat population and actual treatment group ("as-treated") for the safety population. The feasibility outcomes were analysed by reporting the number and proportion of participants. A two-sided 95% CI for the proportion was calculated using the Clopper-Pearson method. The primary outcome for the future trial HbA1c was analysed using a likelihood-based longitudinal data analysis model, with response consisting of all values (baseline, 3, and 6 months) and the model including factors representing treatment group, time-point, and treatment group by time interaction. Due to the small sample size, restricted maximum likelihood estimation with a Kenward-Roger correction was applied. Secondary potential effectiveness outcomes were summarised by treatment group, and within each treatment group by blinded CGM device (iPro2 or FreeStyle Libre Pro) using mean and standard deviation (SD) for symmetrical variables, or median and quartiles (25th and 75th percentile) for nonsymmetrical variables. No statistical tests were performed for secondary potential effectiveness and exploratory outcomes. The EQ-5D-3L score was summarised by treatment group. The number and percentage of participants with at least one adverse event (including hypoglycaemic events) were reported by treatment group. Analyses were performed using Stata/SE software, version 17.0 (StataCorp).

Ethics

This study was approved by the GVH Human Research Ethics Committee (HREC), GVH 6–20(38–27), and Austin Health HREC/54334/Austin-2019. This trial was registered with the Australian and New Zealand Clinical Trials Registry (ANZCTRN12621000021875). All participants provided written informed consent using the National Health and Medical Research Council (NHMRC) Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research. This trial was completed in accordance with the Culturally Adaptive Governance Framework for Indigenous Health Research [35].

COVID-19

The COVID-19 pandemic occurred whilst the trial was underway which delayed recruitment and data collection

(the latter extended until June 2022). The state of Victoria had extensive lockdowns during the COVID-19 pandemic and had cities with the highest number of days under lockdown. Furthermore, there were strict restrictions on research activity. Therefore, the COVID-19 pandemic had a major impact on the trial. Study visit attendance also shifted from in person to virtual (following a protocol amendment), which allowed participants to minimise interaction and adhere to public health measures. This change did not impact the recruitment target, which was achieved.

Results

Trial participants

A total of 126 participants were assessed for eligibility between November 2017 and December 2021. Fifty-two individuals were ineligible after screening; 5 had type 1 or gestational diabetes, and 47 were not managed with injectable diabetes medications. Of the 74 eligible people, 42 participants were recruited, and 2 withdrew before randomisation (see Fig. 1). Subsequently, 40 (54%) participants were randomised, with 20 allocated to FGM and 20 to standard care (SMBG). Two participants (1 from the FGM arm and 1 from the SMBG arm) did not receive the allocated intervention. Twenty-nine participants (72.5%) were recruited from the Rumbalara Aboriginal Health Service. Baseline demographic and clinical characteristics were similar between groups except sex, body mass index, and systolic blood pressure (see Table 1).

Feasibility outcome

The primary outcome of the pilot study was feasibility. The primary feasibility outcome was the proportion of participants completing the trial. Thirty-nine (97.5%, 95% *CI* 87 to 100%) participants completed the study. One participant did not complete their final study visit due to hospitalisation for a diabetes complication unrelated to this trial. The proportion of eligible people who provided informed consent and underwent randomisation into the trial was 54% (95% *CI* 42 to 66%).

Potential effectiveness outcomes

The current trial was not powered to assess effectiveness. Nevertheless, we examined potential effectiveness as a secondary outcome. The mean (SD) HbA1c decreased from 8.9% (1.1%) to 8.4% (1.8%) in the intervention group and from 9.3% (1.3%) to 8.4% (1.4%) in the control arm. No apparent difference was observed in the change in HbA1c values (mean between-group difference in change in HbA1c between FGM and SMBG at 6 months from baseline was −0.19%; 95% *CI* −1.20 to 0.81%) (see Table 2).

There were no clear trends for changes in time in high glucose (>15.0 mmol/L), target glucose (4.0–10.0 mmol/L), or low glucose (<3.9 mmol/L) in either treatment arm (Fig. 2). Similarly, no clear trends emerged for changes in CGM metrics as per the international consensus on time in range [30] in either treatment arm (Appendix Fig. 1).

There was no change in the proportion of participants using insulin from baseline to 6 months in either group. The median total daily insulin dose increased from baseline to 6 months (Appendix Table 1). The number of participants in the control arm requiring three non-insulin glucose-lowering medications increased from baseline ($n=5$, 25%) to 6 months ($n=6$, 33%) but stayed unchanged in the intervention group ($n=5$, 25%). There was no difference in EQ-5D-3L scores between groups at baseline and 6 months (see Table 2).

Safety outcomes

Eight participants (20%) experienced a serious adverse event (AE), 3 (15%) from the FGM arm and 5 (25%) from the SMBG arm. There was no difference in the safety outcome of the current trial. All serious AEs involved hospital admission. No participant experienced a severe hypoglycaemic event. Six participants (30%) in the FGM arm had device-related AEs (pain, tenderness, or skin irritation). A total of 29 AEs (including serious AEs but excluding device-related AEs) were reported across both arms combined (see Table 3).

Discussion

This is the first pilot RCT comparing FGM to SMBG in Indigenous Australians with type 2 diabetes. The primary feasibility outcome, defined as the proportion of participants completing the trial, was very high, with 39 out of 40 (97.5%, 95% *CI* 87% to 100%) participants completing the trial. The trial was successfully undertaken as demonstrated by the high completion and retention rates, despite a difficult COVID-19 period. This is a testament to Indigenous Australians and their communities, Aboriginal Health Services where the trial was conducted, and the depth of engagement between Indigenous Australian people with diabetes, diabetes researchers, and the dedication of the clinical trial staff. This is one of the very few RCTs involving Indigenous people with type 2 diabetes in Australia. This is significant because RCTs in Indigenous populations are uncommon, and it has been suggested that recruitment of Indigenous people into RCTs may be difficult [36].

There were several reasons for why this RCT was so successfully completed in an Indigenous Australian population. Firstly, this trial was initiated in response to a community-identified need to improve diabetes

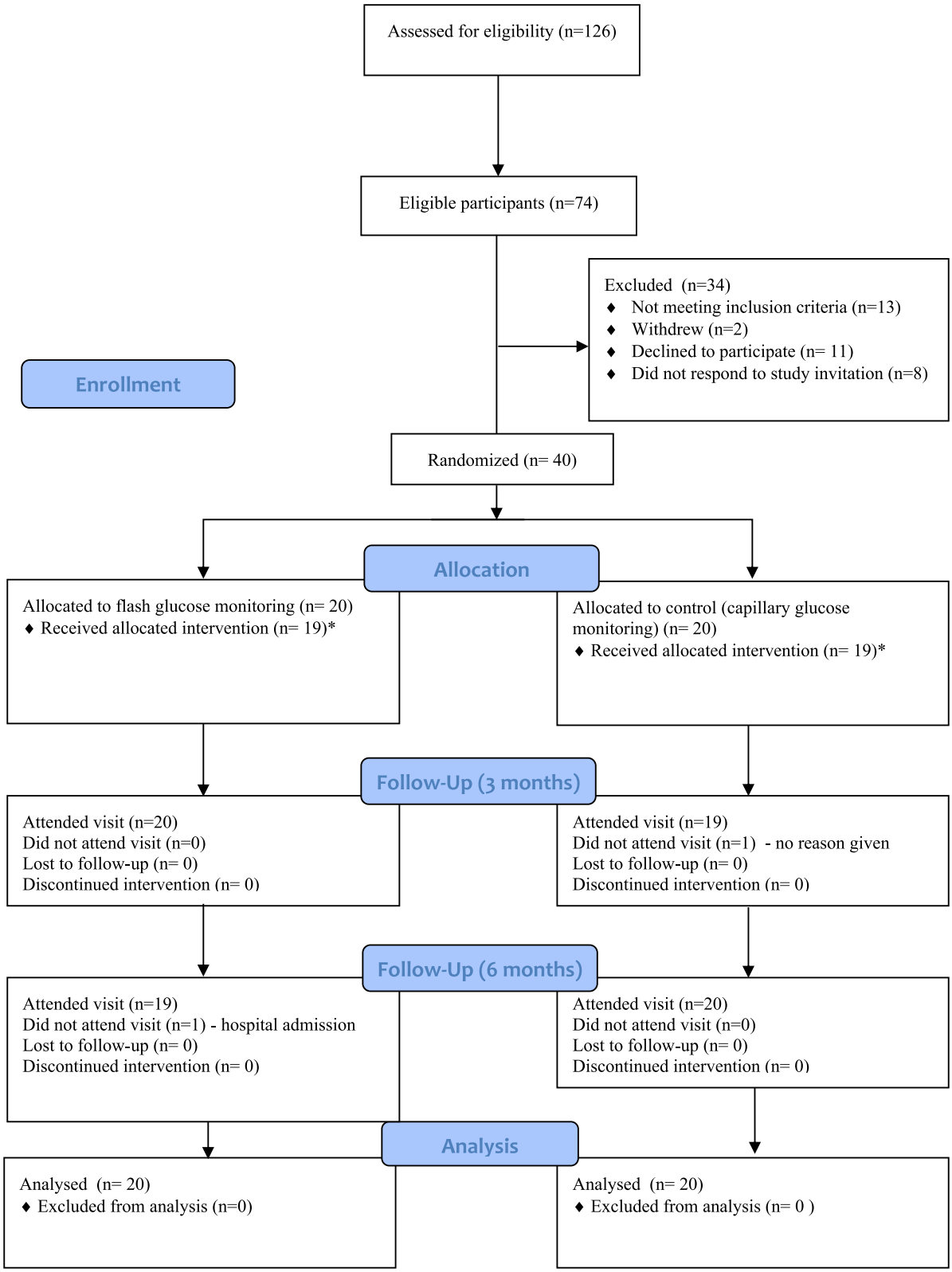

Fig. 1 Consort diagram. FGM, flash glucose monitoring; SMBG, self-monitored blood glucose. *Thirty-eight participants received the allocated intervention. One participant in the intervention arm received SMBG instead of FGM, and one participant in the control arm received FGM instead of SMBG

Table 1 Baseline demographic and clinical characteristics of participants and their medications by treatment group (intention-to-treat population)

	Flash glucose monitoring ***N*** **= 20**	**Self-monitored blood glucose** ***N*** **= 20**
Demographic characteristics		
Age (years), mean (SD)	57.3 (13.9)	60.7 (11.1)
Male sex, *n* (%)	7 (35%)	12 (60%)
HbA1c (%)*, mean (SD)	8.9 (1.1)	9.3 (1.3)
Body mass index, mean (SD)	38.8 (8.3)	32.5 (7.8)
Systolic blood pressure (mmHg), mean (SD)	138.6 (17.7)	127.0 (11.4)
Diastolic blood pressure (mmHg), mean (SD)	77.1 (12.7)	73.8 (9.1)
Diabetes duration (years), median (IQR)	13.0 (6.0–20.0)	15.0 (10.0–23.0)
Clinical characteristics		
Significant medical history, *n* (%)		
Stroke or transient ischaemic attack	1 (5%)	2 (11%)
Heart failure	3 (15%)	4 (20%)
Peripheral vascular disease	2 (10%)	1 (5%)
Retinopathy	4 (20%)	3 (15%)
Chronic kidney disease	5 (26%)	7 (35%)
Peripheral neuropathy	4 (20%)	5 (25%)
Total cholesterol (mmol/L), mean (SD)	4.0 (0.9)	4.1 (1.3)
Triglycerides (mmol/L), median (IQR)	2.1 (1.4–3.0)	2.6 (1.8–3.0)
LDL-C (mmol/L), mean (SD)	1.7 (0.6)	2.0 (1.1)
Creatinine (μmol/L), median (IQR)	73.0 (59.0–89.0)	86.5 (71.0–119.5)
Estimated glomerular filtration rate (mL/min/1.73 m^2), *n* (%)		
≥ 60	16 (80%)	11 (55%)
45–59	1 (5%)	4 (20%)
25–44	2 (10%)	4 (20%)
< 25	1 (5%)	1 (5%)
Urine albumin-to-creatinine ratio (mg/mmol), *n* (%)		
< 30	13 (81%)	16 (89%)
30–299	2 (13%)	2 (11%)
≥ 300	1 (6%)	0 (0%)
Medications		
Cardiovascular medications, *n* (%)		
Antiplatelet	12 (60%)	11 (55%)
Renin-angiotensin system inhibitor	12 (60%)	12 (60%)
HMG-CoA reductase inhibitor	16 (80%)	16 (80%)
Glucose-lowering therapy, *n* (%)		
Insulin	15 (75%)	13 (65%)
Metformin	19 (95%)	17 (85%)
Sulphonylurea	2 (10%)	4 (20%)
SGLT2 inhibitor	5 (25%)	7 (35%)
GLP-1 receptor agonist	10 (50%)	11 (55%)
DPP4 inhibitor	4 (20%)	2 (10%)
Thiazolidinediones	0 (0%)	0 (0%)
Alpha-glucosidase inhibitors	0 (0%)	0 (0%)

Abbreviations: *SD* standard deviation, *IQR* 25th to 75th percentile, *LDL-C* low-density lipoprotein cholesterol, *HMG-CoA* 3-hydroxy-3-methyl-glutaryl-coenzyme A; *SGLT2*, sodium–glucose co-transporter 2; *GLP-1*, glucagon-like peptide 1; *DPP4*, dipeptidyl peptidase 4; *FGM*, flash glucose monitoring; *SMBG*, self-monitored blood glucose

* Among those randomised with a HbA1c assessment within 2 months before randomisation. Two HbA1c values at baseline were excluded as a result

One participant in the intervention arm received SMBG instead of FGM, and one participant in the control arm received FGM instead of SMBG. These participants were included in the group "as-randomised"

Table 2 Primary outcome for future trial and quality-of-life outcomes by treatment group (intention-to-treat population)

	Flash glucose monitoring	Self-monitored blood glucose	Treatment effect
	N = 20	*N* = 20	Mean difference (95% CI)
Primary effectiveness outcome, mean (SD)*			
HbA1c (%)			
Baseline	8.9 (1.1)	9.3 (1.3)	
3 months	8.0 (0.9)	8.7 (1.1)	−0.44 (−1.31, 0.42)
6 months	8.4 (1.8)	8.4 (1.4)	−0.19 (−1.20, 0.81)
Quality-of-life outcome, median (IQR)			
EQ-5D-3L score			
Baseline	0.7 (0.5–0.8)	0.7 (0.6–0.8)	
6 months	0.7 (0.5–0.8)	0.7 (0.7–0.8)	-

Abbreviations: *SD* standard deviation, *IQR* 25th to 75th percentile, *CI* confidence interval, *EQ-5D-3L* EuroQol 5-dimension 3-level, *FGM* flash glucose monitoring, *SMBG* self-monitored blood glucose

* HbA1c and EQ-5D-3L values measured outside of the scheduled visit windows were excluded from the analysis. As a result, 2 HbA1c values at baseline, 4 at 3 months, and 5 at 6-month follow-up were excluded. Similarly, 5 EQ-5D-3L values at baseline and 5 at 6-month follow-up were excluded

One participant in the intervention arm received SMBG instead of FGM, and one participant in the control arm received FGM instead of SMBG. These participants were included in the group "as-randomised"

management and was conducted after extensive community consultation with the Rumbalara community. Secondly, the conduct of this trial and recruitment of participants was led by Indigenous Australian researchers and performed in accordance with a Culturally Adaptive Governance Framework which we developed [35]. The success of this approach is reflected by the study results, which showed that 29 of the 40 (72.5%) participants were patients of the RAC medical clinic. Both recruitment and follow-up of these participants occurred at the Aboriginal Health Service (AHS), which allowed participants to feel safe and comfortable as AHS are more culturally sensitive than non-Indigenous health services. Furthermore, the conduct of the study was led by Indigenous Australian researchers and health workers at local Aboriginal health services, and one of the trial nurses was also employed by RAC as a nurse in a clinical capacity, and this trust and familiarity may have facilitated recruitment. Moreover, extensive community consultation, with recruitment and conduct of the study led by Indigenous Australian researchers and health workers at local Aboriginal health services, was crucial for the successful completion of this study.

This trial had a prolonged recruitment time to reach the target sample size, for several reasons. Firstly, this study was initially investigator-funded until a small grant was secured in 2019. From November 2017 until February 2019, first author A. E. performed all recruitment and follow-up at RAC whilst also undertaking full-time clinical work. When more funding became available, this enabled the sample size to be increased from 24 to 40 participants, as well as the employment of a trial nurse. A dedicated trial nurse commenced in the middle of 2019, improving the logistics of participant recruitment and follow-up. Secondly, diabetes management in the RAC clinic was better than anticipated [37], and there were insufficient eligible participants available for recruitment. Recruitment was then extended to include Austin Health to increase the availability of eligible participants. Thirdly, the COVID-19 pandemic occurred in 2020, and research activities were for paused for several months until amendments were made to allow virtual follow-up visits so participants could feel safe and adhere to public health measures. In 2021, there was a large COVID outbreak in Shepparton, near RAC, which affected staffing levels for basic services such as supermarkets, health services, and hospitals. This impacted study visits and pathology collection. Despite all these challenges, the trial was successfully completed.

Participant completion of this trial was 97.5%. This suggests that the convenience of painlessly monitoring blood glucose levels was highly acceptable in this population, and most people had a positive experience of using this technology [28]. The acceptability and convenience of FGM are similar to findings from an observational study of pregnant Indigenous Australian women [38]. These positive experiences occurred despite 30% of participants in the intervention group experiencing device-related adverse effects. The occurrence of AEs in both groups were similar. This not only reflects the multiple comorbidities of this population but also suggests that the intervention did not increase the risk of AEs. FGM and CGM are relatively expensive for people with type 2 diabetes, as its use is only subsidised for people with type 1 diabetes in Australia. Participation in this trial gave participants the opportunity to use this technology.

The pilot study had several limitations. The use of two different blinded CGM systems affected data quantity, as the iPro2 and FreeStyle Libre Pro provided up to 7 and 14 days of data, respectively. Additionally, the iPro2 required calibration every 12 h; otherwise, the amount of interpretable data was reduced. The FreeStyle Libre Pro was factory-calibrated, so data quantity was not limited by calibration. Consequently, participants using the iPro2 blinded CGM had less data available for analysis. CGM metrics were therefore analysed and reported by both treatment arm and blinded CGM device, to ensure consistency [39]. Whilst the option of using only the iPro2 blinded CGM would have improved data consistency, it

A) Percentage time in glucose >15.0 mmol/L by Treatment Group and Device

Figure A: Individual participant profiles

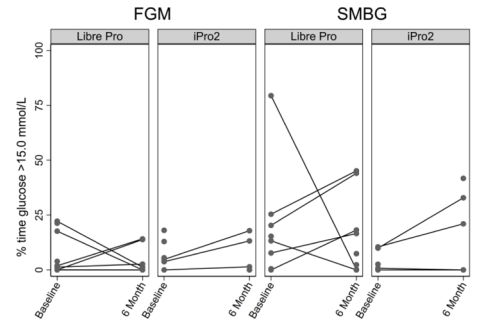

Table A: Median (25th and 75th percentile)

	Flash glucose monitoring (FGM)		Self-monitored blood glucose (SMBG)	
	Libre Pro N=11	**iPro2** N=9	**Libre Pro** N=10	**iPro2** N=10
Baseline	1.6 (0.0-17.7)	5.2 (3.7-12.9)	14.3 (4.1-22.8)	0.8 (0.0-9.9)
6-month	1.3 (0.0-13.8)	7.3 (0.7-15.5)	12.0 (1.2-31.1)	10.5 (0.0-32.9)

B) Percentage time in glucose 4.0 – 10.0 mmol/L by Treatment Group and Device

Figure B: Individual participant profiles

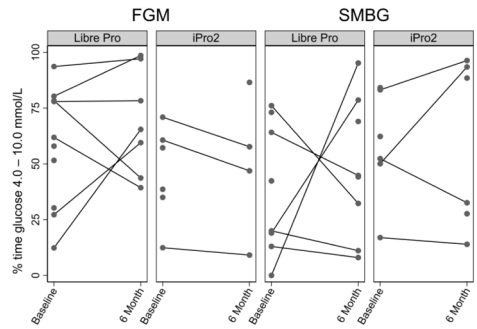

Table B: Median (25th and 75th percentile)

	Flash glucose monitoring (FGM)		Self-monitored blood glucose (SMBG)	
	Libre Pro N=11	**iPro2** N=9	**Libre Pro** N=10	**iPro2** N=10
Baseline	59.9 (30.3-78.3)	47.9 (35.0-60.7)	31.2 (16.0-68.6)	62.3 (50.1-83.9)
6-month	65.5 (43.7-97.1)	52.3 28.0-72.1)	44.5 (21.7-73.8)	60.5 (27.6-93.5)

C) Percentage time in glucose <3.9 mmol/L by Treatment Group and Device

Figure C: Individual participant profiles

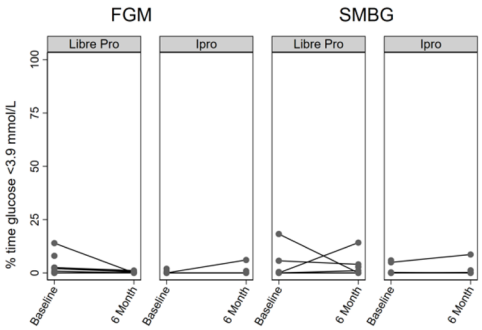

Table C: Median (25th and 75th percentile)

	Flash glucose monitoring (FGM)		Self-monitored blood glucose (SMBG)	
	Libre Pro N=11	**iPro2** N=9	**Libre Pro** N=10	**iPro2** N=10
Baseline	1.4 (0.0-2.5)	0.0 (0.0-0.7)	0.0 (0.0-3.1)	0.0 (0.0-5.0)
6-month	0.3 (0.0-0.7)	0.5 (0.0-3.5)	1.9 (0.0-3.4)	0.1 (0.0-1.2)

Fig. 2 Secondary potential effectiveness outcomes by treatment group and device (intention-to-treat population). FGM, flash glucose monitoring; SMBG, self-monitored blood glucose. Data are presented as median (25th to 75th percentile). One participant in the intervention arm received SMBG instead of FGM, and one participant in the control arm received FGM instead of SMBG. These participants were included in the group "as randomised". Data measured outside of the scheduled visit windows were excluded from the analysis. As a result, one participant data at baseline and 3 at 6 months follow-up were excluded

was important to trial the preferred blinded CGM system in view of planning for a larger trial.

Furthermore, this was a pilot trial with the primary outcome being feasibility. Whilst we did not pre-define a target precision or set a criterion for defining success a priori, 54% of the eligible people were enrolled of whom the majority (97.5%) completed the trial. These findings may indicate feasibility of a future larger randomised trial comparing FGM to SMBG in Indigenous Australians with type 2 diabetes. The main limitation of not having defined progression criteria is that our evaluation may have been optimistic [40]. Additionally, whilst the trial was not powered to demonstrate effectiveness, we examined potential effectiveness as a secondary objective. The mean HbA1c decreased in both groups, but the study was not powered to show a difference in HbA1c. There

Table 3 Number (%) of participants with at least one adverse event by treatment group (safety population)

	Flash glucose monitoring *N* = 20	Self-monitored blood glucose *N* = 20
Adverse events	10 (50%)	13 (65%)
Serious adverse events	3 (15%)	5 (25%)
Hospitalisation	3 (15%)	5 (25%)
Death	0 (0%)	0 (0%)
Device-related adverse events	6 (30%)	-

Adverse events exclude device-related adverse events. Serious adverse events include hospitalisation and death. Device-related adverse events included pain/irritation from sensor site and FGM sensor falling off prematurely

FGM flash glucose monitoring, *SMBG* self-monitored blood glucose

One participant in the intervention arm received SMBG instead of FGM, and one participant in the control arm received FGM instead of SMBG. These participants were included in the group "as-treated"

were no clear patterns in changes in time spent in target glucose (4.0–10.0 mmol/L), low glucose (< 3.9 mmol/L) or high glucose (> 5.0 mmol/L), or quality-of-life outcomes, but this was limited by sample size.

Research into the use of CGM/FGM in diabetes is a rapidly evolving field. Many studies have shown CGM/FGM use improves HbA1c in type 1 diabetes [13, 14, 41–44], but few RCTs have shown improved HbA1c in type 2 diabetes [15, 16, 20, 45–50]. The continuous monitoring in type 2 diabetes basal insulin users study [46] and multiple daily injections and continuous glucose monitoring in diabetes [45] trial demonstrated improvements in HbA1c in people with insulin-treated type 2 diabetes [49, 51], and one RCT has shown FGM can improve HbA1c in non-insulin-treated type 2 diabetes [49]. There are increasing numbers of RCTs demonstrating that FGM/CGM use leads to improvements in diabetes management in type 2 diabetes without reducing HbA1c [15, 16, 20, 45–51]. However, until now, no RCT has evaluated FGM or CGM in Indigenous people with diabetes.

The success of this study was facilitated by extensive community consultation and performance in accordance with a Culturally Adaptive Governance Framework [35]. Notably, this study was not designed to demonstrate change in HbA1c but to determine if a RCT using this technology could be successfully undertaken in an Indigenous Australian population. Larger studies are needed to evaluate the potential benefit of FGM and CGM in Indigenous people with diabetes. Following on from this pilot study, a larger multicentre RCT has been funded (ACTRN12621000753853) [52], and aims to recruit 350 participants. Progression criteria were not applied, but the success of this pilot study enabled a large grant to be secured to support a larger RCT.

Conclusion

This is the first randomised pilot study of FGM in Indigenous Australians with type 2 diabetes and one of few RCTs in Indigenous Australians with diabetes. It confirms that a RCT of FGM can be successfully undertaken in an Indigenous Australian population, with a 97.5% retention rate. Extensive community consultation, with recruitment and conduct of the study led by Indigenous Australian researchers and health workers at local Aboriginal health services, was crucial for the successful completion of this study. A larger multicentre RCT in this population is currently in progress. It is hoped that findings from this and future studies will improve diabetes care and reduce the health gap in this population.

Abbreviations

FGM	Flash glucose monitoring
RCT	Randomised controlled trial
HbA1c	Glycosylated haemoglobin
EQ-5D-3L	EuroQol 5-dimension 3-level
SMBG	Self-monitoring of blood glucose
CGM	Continuous glucose monitoring
RAC	Rumbalara Aboriginal Co-operative
GVH	Goulburn Valley Health
GLP-1	Glucagon-like peptide-1
eGFR	Estimated glomerular filtration rate
TAR	Time above range
TBR	Time below range
HREC	Human Research Ethics Committee
NHMRC	National Health and Medical Research Council
CI	Confidence interval
SD	Standard deviation
AHS	Aboriginal Health Service
AE	Adverse effect
COVID-19	Coronavirus disease 2019

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40814-025-01607-7.

Additional file 1. Appendix: Figure 1. Exploratory effectiveness outcomes by treatment group and device (Intention-To-Treat population). Table 1 – Number (%) of participants with insulin and other glucose lowering medications use by treatment group (Safety population)

Additional file 2. Supplementary file 1: Statistical Analysis Plan (SAP): FLASH_pilot_SAP_Version_2.0

Acknowledgements

Audrey S. Eer is supported by the Australian Government Research Training Program Scholarship, Sheppard M. Lowe Scholarship, Melbourne Medical Postgraduate Committee Gordan-Taylor Scholarship, and the Janice and Colin Smith Scholarship in Diabetes Research. We acknowledge all the study participants, the site staff, and the Rumbalara community.

Authors' contributions

EIE was the principal investigator; she conceived the study and led the proposal and protocol development. AE wrote the protocol, was responsible for the day-to-day management and oversight of the trial, and was involved with data analysis and the statistical analysis plan. DNK contributed the development of the statistical analysis plan and statistical analysis. SB contributed to the study design and statistical analysis. All authors read and approved the final manuscript.

Funding
This trial was funded from grants from the Indigenous Research Initiative (University of Melbourne Hallmark Research Initiative) Seed Funding Scheme (2017) and a Melbourne Academic Centre for Health (MACH) Medical Research Future Fund (MRFF) Rapid Applied Research Translation grant (2019).

Data availability
Researchers who wish to access our data should submit a proposal with a valuable research question. Proposals will be assessed by a committee formed from the trial management group, including Indigenous researchers. Data will be shared after assessment by the trial management group.

Declarations

Ethics approval and consent to participate
This study was approved by the GVH Human Research Ethics Committee (HREC), GVH 6–20 (38–27), and Austin Health HREC/54334/Austin-2019. All participants provided written consent to participate in this study. This trial was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12621000021875).

Consent for publication
All participants provided written consent to participate in this study.

Competing interests
E. I. E.'s institution has received funding which is unrelated to this study for clinical research from Novo Nordisk, Eli Lilly, and Boehringer. The other authors declare that they have no competing interests.

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Received: 21 February 2024 Accepted: 14 February 2025
Published online: 24 May 2025

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