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Title:
Cost-effectiveness of professional-mode flash glucose monitoring in general practice among adults with type 2 diabetes: Evidence from the GP-OSMOTIC trial

Date:
2022-03-01

Citation:
Hua, X., Catchpool, M., Clarke, P., Blackberry, I., Chiang, J., Holmes-Truscott, E., Jenkins, A., Khunti, K., O'Neal, D., Speight, J., Furler, J., Manski-Nankervis, J. A., Dalziel, K., Best, J., Liew, D., Kennedy, M., Audehm, R., Thuraisingam, S., De La Rue, K. ,... Januszewski, A. (2022). Cost-effectiveness of professional-mode flash glucose monitoring in general practice among adults with type 2 diabetes: Evidence from the GP-OSMOTIC trial. Diabetic Medicine, 39 (3), https://doi.org/10.1111/dme.14747.

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Article type : Research Article

Title: Cost-effectiveness of professional-mode flash glucose monitoring in general practice among adults with type 2 diabetes: evidence from the GP-OSMOTIC trial

Running title: Cost-effectiveness of professional-mode flash glucose monitoring

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Manuscript word count: 3058
Abstract word count: 245

Conflict of interest:

JS has served on advisory boards for Medtronic, Roche Diabetes Care, and Sanofi Diabetes; her research group (Australian Centre for Behavioural Research in Diabetes [ACBRD]) has received honoraria for this advisory board participation and has also received unrestricted educational grants and in-kind support from Abbott Diabetes Care, AstraZeneca, Medtronic, Roche Diabetes Care, and Sanofi Diabetes. JS has also received sponsorship to attend educational meetings from Medtronic, Roche Diabetes Care, and Sanofi Diabetes, and consultancy income or speaker fees from Abbott Diabetes Care, AstraZeneca, Medtronic, Novo Nordisk, Roche Diabetes Care, and Sanofi Diabetes.

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JF has received unrestricted educational grants for research support from Roche, Sanofi and Medtronic.

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What's new (maximum 100 words)

What is already known? Three monthly use of professional-mode flash glucose monitoring among people with type 2 diabetes in general practice can improve short-term clinical measures such as glycaemic outcomes.

What this study has found? Professional-mode flash glucose monitoring for the management of type 2 diabetes in general practice is not cost-effective if monitoring occurs every three months. It can be cost-effective with a lower monitoring frequency and sensor price.

What are the clinical implications of the study? This research provides evidence for routine provision of professional-mode flash glucose monitoring in general practice settings.

Acknowledgments

Katie de la Rue, Louise Ginnivan, Kylie Crisp, Rebecca Hannam and Emily Knights assisted with running the clinical study and data collection. Katie de la Rue facilitated the process for linkage of the trial to health services data. Rita McMorrow assisted with analysis of Medicare data.

Abstract

Aim: To assess the cost-effectiveness of professional-mode flash glucose monitoring in adults with type 2 diabetes in general practice compared with usual clinical care.

Methods: An economic evaluation was conducted as a component of the GP-OSMOTIC trial, a pragmatic multicentre 12-month randomised controlled trial enrolling 299 adults with type 2 diabetes in Victoria, Australia. The economic evaluation was conducted from an Australian healthcare sector perspective with a lifetime horizon. Health-related quality of life (EQ-5D) and total healthcare costs were compared between the intervention and the usual care group within the trial period. The 'UKPDS Outcomes Model 2' was used to simulate post-trial lifetime costs, life expectancy and quality adjusted life years (QALYs).

Results: No significant difference in health-related quality of life and costs was found between the two groups within the trial period. Professional-mode flash glucose monitoring yielded greater QALYs (0.03 (95% CI: 0.02, 0.04)) and a higher cost (A$3,807 (95% CI: 3,604, 4,007)) compared with usual clinical care using a lifetime horizon under the trial-based monitoring frequency, considered not cost-effective (incremental cost-effectiveness ratio =A$120,228). The intervention becomes cost-effective if sensor price is reduced to lower than 50%, or monitoring frequency is decreased to once per year while maintaining the same treatment effect on HbA1c.

Conclusions: Including professional-mode flash glucose monitoring every three months as part of a management plan for people with type 2 diabetes in general practice is not cost-effective, but could be if the sensor price or monitoring frequency can be reduced.

Keywords: Type 2 diabetes, flash glucose monitoring, cost-effective analysis, economic evaluation

Background

Improving glycaemia reduces healthcare costs in people with type 2 diabetes, which are quadrupled by the presence of diabetes-related complications [1, 2]. However, most people with type 2 diabetes do not achieve recommended glycaemic targets [3], with detrimental long-term consequences. Given the high prevalence [4], burden and healthcare costs, there is a need for interventions that are both clinically and cost-effective to improve glycaemia for people with type 2 diabetes.

In Australia, the majority of medical care for people with type 2 diabetes is provided in general practice and includes clinical guidance about lifestyle modifications and stepwise introduction of diabetes medications. Day-to-day and within-day glucose profiles can provide useful information for guiding personalised decisions about optimising glycaemia[5, 6]. Flash glucose monitoring is a type of ambulatory glucose monitoring system with factory-calibrated sensor technology, which can continuously record a person's glucose profile without the need for fingerprick blood glucose monitoring. It can be used in real time or retrospectively (also known as personal or professional modes respectively). Professional-mode flash glucose monitoring involves the person with diabetes wearing a sensor for up to two weeks with the glucose data downloaded by a health care professional and reviewed retrospectively with the patient.

The professional-mode flash glucose monitoring can be a useful tool for optimising glycaemia in people with type 2 diabetes, whose glucose profiles tend to be reproducible on a day-to-day basis [7]. Currently, there is little evidence about the cost-effectiveness of flash glucose monitoring in type 2 diabetes. One Swedish study reported that real-time flash glucose monitoring was cost-effective compared with traditional self-monitoring of blood glucose in a sample of adults with insulin-treated type 2 diabetes [8]. To our knowledge, no previous study has evaluated the cost-effectiveness of professional-mode flash glucose monitoring in a broader type 2 diabetes population.

In this study, we conducted an economic evaluation as part of the GP-OSMOTIC trial [9], which is to date the largest randomised controlled trial of professional-mode flash glucose monitoring in adults with type 2 diabetes in general practice. We modelled the lifetime healthcare cost and quality-adjusted life years (QALYs) of professional-mode flash glucose monitoring and assessed its cost-effectiveness compared to usual clinical care to inform clinical practice and funding decisions regarding government subsidy or payer provision of the monitoring devices.

Methods

Trial design

The economic evaluation was conducted from a healthcare perspective alongside the GP-OSMOTIC trial, which was a two-arm, open label, 12-month, individually randomised controlled trial in 25 general practices in Victoria, Australia. The detailed design and primary results of the GP-OSMOTIC trial have been published previously [9, 10]. Briefly, eligible participants were aged 18–80 years, with type 2 diabetes diagnosed ≥1-year and HbA1c ≥5.5

mmol/mol (0.5%) above their individualised target in the past month despite being prescribed at least two non-insulin glucose-lowering drugs, insulin, or both (with therapy stable for ≥4-months). All participants had a baseline HbA1c of ≥58mmol/mol (7.5%); 299 eligible participants were randomly assigned (1:1) to either use of a professional-mode flash glucose monitoring system or usual clinical care. Intervention participants were asked to wear the professional-mode sensor (applied at the general practice) for two-week period at baseline, three, six, and nine months. Following each two-week monitoring period, they were invited to attend a consultation with their GP and discuss the sensor reports. Participants randomised to the usual clinical care group wore the sensor at baseline and twelve months for data analysis purposes only, and had usual care visits every three months, consistent with clinical practice guidelines.

Within-trial outcomes

We described and compared the health-related quality of life and total healthcare cost in the two groups for the within-trial period. Health-related quality of life was measured at baseline and 12 months using the EuroQol 5 Dimension (EQ-5D) 3-level instrument [11]. We calculated utility values using Australian preference weights [12].

Healthcare costs were collected through data linkage to the Medicare Benefits Schedule (MBS) and the Pharmaceutical Benefits Scheme (PBS) – which covers health services and prescription medications subsidised by the Australian Government, the Victorian Admitted Hospital Episodes Dataset (VAED), and the Victorian Emergency Department Hospital Minimum Dataset (VEMD). More details on Australian health system and costing methods are in Supplementary material 1.

The baseline utility value and pre-intervention (one year pre-trial) healthcare cost was lower in the professional-mode flash glucose monitoring group compared to the usual clinical care group. These differences were not statistically significant, however they were important enough to potentially modify results for the economic evaluation and, as such, were adjusted. For example, the 12-month utility difference between the two groups is a key parameter for the modelling, which has direct impact on the predicted QALYs. This difference may come from the utility difference already present at baseline between the two groups rather than the treatment effect during the intervention period. Regression-based adjustments for 12-month utility values and healthcare costs were applied to correct for pre-intervention differences between groups, taking the randomisation group and baseline measures as the independent variable [13] .

Cost-effectiveness analysis

The cost-effectiveness analysis was pre-specified in protocol and statistical analysis plans [9, 10]. The UKPDS Outcomes Model 2 (UKPDS-OM2) [14], a patient-level simulation tool for predicting lifetime health outcomes of people with type 2 diabetes, was used to simulate post-trial costs, life expectancy and QALYs in both trial arms. The incremental cost-effectiveness ratio (ICER) was calculated as the difference in costs divided by the differences in QALYs, and compared with a willingness-to-pay threshold at A$50,000 [15-18]. A bootstrap method with 1,000 replications was used to generate the 95% CI of the ICER and a cost-effectiveness plane. 100,000 internal loops were conducted to reduce Monte-Carlo Error.

The model was run with an annual cycle over a lifetime horizon (70 years), which means that extrapolations can be extended to the full life expectancy of all patients in the model, with all future costs and clinical benefits discounted at an annual rate of 5% consistent with Australian national guidelines [19]. In the base case analysis, we used the monitoring frequency observed in the GP-OSMOTIC trial (on average 3.5 times per year) for the model. We also conducted a real-life case scenario of annual monitoring. We tested the modelled results (ICER) with other assumptions on monitoring frequency in sensitivity analysis.

Clinical inputs for the model

The GP-OSMOTIC trial found that participants in the professional-mode flash glucose monitoring had a lower HbA1c level compared to the control group in the trial period, with the difference being significant at six months but not at twelve months [9]. In the modelling, an average annual HbA1c level for each group is required in the extrapolated years. To account for the variation of HbA1c and to capture the whole treatment benefit across a year's time, we calculated the area under curve (average HbA1c between six and twelve month) in each group and used its difference as the treatment effect in post-trial years. We tested the results with the 12-month HbA1c difference as the treatment effect in the sensitivity analysis. Treatment effect was presumed to correspond with the period of time that flash glucose monitoring is continuing, under the assumption of a constant persistent rate.

Individual-level data for the 149 participants in the flash glucose monitoring group were used as the treatment cohort in the economic modelling to obtain the HbA1c effect and to provide patient characteristics. The mean observed difference in HbA1c was applied to this group. For risk factors that were required by the UKPDS-OM2 model, but not collected in the GP-OSMOTIC trial, mean population values in Australia were used. All risk factors were kept constant throughout the simulation. Full details on model clinical inputs can be found in supplementary material 2.1.

Cost inputs for the model

Two types of costs were analysed: cost of therapy and the cost of subsequent complications. The following therapy costs were calculated for the intervention group: device cost (the Abbott FreeStyle Libre Pro Flash Glucose Monitoring System), standard GP visits (every three months), practice nurse visit to apply the sensor, and GP training cost. For the control group, the cost of the standard three-monthly GP visits was included in the analysis as therapy cost [20].

The costs for diabetes complications were collected from a published study, where multiple regression analysis was used to estimate inpatient and primary care costs for complications that matched those reported by the UKPDS Outcomes Model in Australia [21].

Full details on model cost inputs can be found in supplementary material 2.2.

Utility values for the model

The 12-month utility values measured in the GP-OSMOTIC trial were used in the post-trial modelling. Utility decreases for diabetes complications were taken from the UKPDS study [22], supplemented in a few cases (renal failure and active ulcer) by values from other studies [23].
Full details on model utility inputs can be found in supplementary material 2.3.

Sensitivity analysis

Sensitivity analyses were performed to investigate the impact of the following assumptions:

1) Frequency of flash glucose monitoring in the intervention group (one/two/three times per year);
2) Price of the sensor (75%/50%/25% of current price);
3) Discounting rate (0%/3%);
4) Complication costs to be 25% less or more compared to those used in the base case;
5) Complication utilities to be 25% less or more compared to those used in the base case; and
6) The treatment effect on HbA1c, with the lower and upper 95% CI of the average six-to-twelve-month difference or the twelve-month difference as treatment effect.

The economic modelling conducted adhered to the Mount Hood Transparency Diabetes Modelling Input Transparency Checklist [24], using the UKPDS-OM2 software (version 2.1). Economic evaluation reporting was in accordance with the CHEERS reporting guidelines[25]. Other analyses were performed with the Stata statistical software package (version 14.0;

StataCorp LLC, College Station, Texas). All costs were inflated to 2019 prices using the total health price index constructed by the Australian Institute of Health and Welfare [26] .

Results

Participant characteristics at baseline were similar between study groups (Table 1), as previously shown [9]. The between-group difference in six to twelve months average HbA1c was -4 mmol/mol (95%CI: -7mmol/mol, -0.5mmol/mol) (-0.35% (95% CI: -0.65%, -0.05%)). The adjusted 12-month utility values in the two groups were similar (Table 2). Overall, 288 (96.3%) of the participants consented to have their healthcare datasets (Medicare, VAED, VEMD) linked with the trial data and were therefore included in the within-trial cost analysis. The adjusted healthcare costs were lower in the intervention group (Mean A$10,081, SD A$13,650) compared to the usual clinical care group (Mean A$12,293, SD A$25,218) across the 12-month trial; the difference was not statistically significant (-A$2,212 (95%CI: -A$6,925, A$2,500)).

In the trial-based base case analysis, where the monitoring was used on average 3.5 times per year, professional-mode flash glucose monitoring had a net gain of 0.03 (95% CI: 0.02, 0.04) QALYs over lifetime at an additional cost of A$3,807 (95% CI: 3,604, 4,007) per person with diabetes compared with usual care. This yielded an ICER of A$120,228 per QALY gained with professional-mode flash glucose monitoring (Table 3), which was considered not cost-effective at an often-used threshold of A$50,000 (£28,256, € 32,137) per QALY (Figure 1). As shown in Figure 2, professional-mode flash glucose monitoring was unlikely to be cost-effective with the willingness-to-pay threshold under A$100,000 in this trial-based case scenario. In the real-life case scenario where the monitoring was presumed to be conducted annually with the same HbA1c outcome, the additional cost for professional-mode flash glucose monitoring reduced to A$776 (95% CI: 559, 948) with a ICER of A$24,493 per QALY which was under the willingness-to-pay threshold and therefore becomes cost-effective (Table 3 & Figure 1).

Table 4 presents the ICERs with various assumptions in terms of monitoring frequency and sensor price. In the trial-based analysis with monitoring 3.5 times per year, the sensor price would need to be reduced to less than half price to make professional-mode flash glucose monitoring cost-effective compared to usual clinical care at a willingness-to-pay threshold of A$50,000 per QALY. Table 5 shows that the results were stable (with various discounting rates and variations in complication costs and utilities) but sensitive to treatment effect on HbA1c.

Discussion

In this study, we conducted economic evaluation to investigate the cost-effectiveness of professional-mode flash glucose monitoring compared with usual care in adults with type 2 diabetes in general practice. No significant difference in health-related quality of life or costs between groups was found in the 12-month trial. Using a lifetime horizon, professional-mode flash glucose monitoring yielded greater QALYs with a higher cost compared with usual care (on the basis of the improved HbA1c modelled result) and was estimated to be not cost-effective in the trial-based base case analysis, with average monitoring of 3.5 times per year.

Professional-mode flash glucose monitoring was found to be not cost-effective in the base case analysis and would require a reduction in price in the order of 50% to come under the threshold. We also recognise the possibility that in everyday clinical practice less monitoring will occur, and one or two monitoring episodes per year may achieve the same effect on HbA1c. In such an analysis it is assumed that annual sensor wear for health professional evaluation and treatment guidance occurs without erosion of outcomes, though this has yet to be formally tested. This assumption regarding the frequency of monitoring in "real-life" practice was made based on recent evidence that 51% of adults with any type of diabetes had at least one HbA1c out of target range during the 12 months between 2018–19 [27]. Further research is required to test the impact of less frequent professional-mode flash glucose monitoring in primary care.

This study highlights the impact of sensor price on the cost-effectiveness of professional-mode flash glucose monitoring compare with usual care. These results may be used to inform future funding and pricing decisions on professional-mode flash glucose monitoring in adults with type 2 diabetes. Globally, payers for monitoring vary by country. For example, in countries with universal healthcare (like Australia and the UK), the payer would be the government, whereas in other countries (like the US), it would often be insurance companies. Irrespective of who pays, these findings provide valuable information on how price and monitoring frequency can be considered when making listing and subsidy decisions. Device companies may also consider adjusting sensor prices to provide cost-effective technology for primary care. With an increasing number of commercially available devices and increasing efficiencies in production, the relative cost of professional-mode flash glucose monitoring devices is falling and the cost-effectiveness of these devices will require periodic reassessment.

Under different assumptions of monitoring frequency and sensor price, the cost-effectiveness results are sensitive to the willingness-to-pay threshold. We used A$50,000 (£28,256, € 32,137) here in based on Harris *et al's* study which found that the ICER of most interventions funded by Australian Pharmaceutical Benefits Advisory Committee in 1994-2004 was A$40 - A$70k [15]. This threshold is also similar to that found in recent empirical studies on the Australian public's willingness-to-pay for a QALY[16-18]. If A$70,000 were applied as the willingness-to-pay threshold, the monitoring would become cost-effective at current price with monitoring 2 times per year.

Another study investigated the cost-effectiveness of personal (real-time) flash glucose monitoring in people with type 2 diabetes using intensive insulin therapy [8]. The study used a range of sources to populate the model, with the effectiveness data derived from the REPLACE trial, where benefits were seen at six months for both hypoglycaemia and health-related quality of life (measured by Diabetes Quality of Life questionnaire) but not for HbA1c [28]. Our study was able to follow-up participants for longer (12 months) and for the first time, to our knowledge, evaluated cost-effectiveness of professional-mode flash glucose monitoring used in primary care among a broader population of adults with type 2 diabetes (not just those using insulin). This retrospective mode monitoring, which can be applied intermittently, is particularly appropriate for people with type 2 diabetes, which is characterised by recurring patterns of glycaemia that do not require intensive daily glucose monitoring [7].

A major strength of this economic evaluation is that the analysis occurred in the context of a robust RCT with rigorous within-trial efficacy data, which represents the largest RCT of professional-mode flash glucose monitoring in adults with type 2 diabetes in general practice. This study also collected health-related quality of life and accurate cost data on the same participants to match the efficacy results, with data linkage near complete (96%). The economic model applied in this study has been well-validated and extensively researched and calibrated.

A limitation of the study is that in the GP-OSMOTIC trial, compliance with training and the provision of clinical consultation to review the monitoring data was not high, e.g., 27% of participating GPs did not complete any form of educational training; 32/117 (27%) participants who wore the sensor at nine months did not have a discussion about the trace with their GP [10]. With greater practitioner adherence to the study protocol, we might have identified a larger effect of the intervention and better cost-effectiveness results. However,

the current results may reflect a real-world roll out as the GP-OSMOTIC is a pragmatic trial. Another potential limitation is that due to the lack of a specific Australian diabetes model, this study applied the UKPDS model and associated utility values. The UKPDS participants were recruited in the UK between 1977 and 1991 and were followed until the trial concluded in 1997, so it is possible that the model and utility values are not applicable to contemporary Australians living with type 2 diabetes. However, the model has been widely applied in many countries around the world, including Australia.

Further research is needed to investigate the long-term application of professional-mode flash glucose monitoring in adults with type 2 diabetes regarding treatment effect and monitoring frequency. In particular, more information is needed regarding barriers for GPs to provide these reviews, as well as the acceptability and responsiveness of this method of monitoring in both GPs and people with type 2 diabetes, and whether and how that would impact the treatment effect of the intervention.

Conclusion

This study describes economic value of professional-mode flash glucose monitoring compared with usual clinical care in type 2 diabetes in general practice. Including professional-mode flash glucose monitoring in general practice is not cost-effective unless the sensor price or monitoring frequency is substantially reduced. Our finding could help guide practice and funding of professional-mode flash glucose monitoring in general practice.

Funding sources

The GP-OSMOTIC trial was supported by a National Health and Medical Research Council of Australia Project Grant (ID APP1104241). Additional funding was provided by Sanofi Australia. In-kind support (Flash Libre Pro reader devices, sensors and software) was provided by Abbott Diabetes Care.

KK is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM) and the NIHR Leicester Biomedical Research Centre (BRC).

JS and EHT are supported by the core funding to the Australian Centre for Behavioural Research in Diabetes, provided by the collaboration between Diabetes Victoria and Deakin University.

Author contributions

The GP-OSMOTIC study team includes: John Furler, James Best, David O'Neal, Jane Speight, Irene Blackberry, Kamlesh Khunti, Kim Dalziel, Danny Liew, Mark Kennedy, Philip Clarke, Ralph Audehm, Elizabeth Holmes-Truscott, Jo-Anne Manski-Nankervis, Sharmala Thuraisingam, Katie De La Rue, Louise Ginnivan, Rebecca Hannam, Max Catchpool, Xinyang Hua, Jason Chiang, Malcolm Clarke, Alicia Jenkins, Amelia Lake, Andrzej Januszewski.

JF, DO'N, JS, IB, JM-N, KK, KD developed the GP-OSMOTIC study concept and aims, initiated the project and developed the study protocol, with assistance from EH-T, JC, MC, AJ and PC. XH, MC, PC and KD developed the plan for the current study. XH conducted the statistical analyses and prepared the first draft, with input from MC and KD. All other authors reviewed the draft and provided critical input. All authors approve the final version.

Ethical approval

This trial is registered at the Australian and New Zealand Clinical Trials Registry, ACTRN12616001372471. The study protocol was approved by the University of Melbourne's Health Sciences Human Research Ethics Subcommittee (Ethics ID: 1647151). All participants gave informed consent prior to enrolment.

Conflicts of interest

JS has served on advisory boards for Medtronic, Roche Diabetes Care, and Sanofi Diabetes; her research group (Australian Centre for Behavioural Research in Diabetes [ACBRD]) has received honoraria for this advisory board participation and has also received unrestricted educational grants and in-kind support from Abbott Diabetes Care, AstraZeneca, Medtronic, Roche Diabetes Care, and Sanofi Diabetes. JS has also received sponsorship to attend educational meetings from Medtronic, Roche Diabetes Care, and Sanofi Diabetes, and consultancy income or speaker fees from Abbott Diabetes Care, AstraZeneca, Medtronic, Novo Nordisk, Roche Diabetes Care, and Sanofi Diabetes.

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Table 1 Participant Characteristics

	Professional-mode flash glucose monitoring N=149	Usual clinical care N=150
Age, years	60.4 (9.8)	59.8 (10.3)
Sex		
Men	87 (58.4%)	89 (59.3%)
Women	62 (41.6%)	61 (40.7%)
Country of birth		
Australia	104 (73.8%)	100 (70.9%)
Other	37 (26.2%)	41 (29.1%)
Highest level of education		
Primary or less	11 (7.8%)	11 (7.8%)
Secondary or trade	100 (70.9%)	91 (64.5%)
Tertiary	30 (21.3%)	39 (27.7%)
Employed	59 (41.8%)	65 (46.1%)
IRSD (decile)	5 (2-7)	6 (2-7)
Diabetes duration (years)	13.5 (9.0-20.0)	11.0 (8.0-20.0)
History of severe hypoglycaemia	2 (1.6%)	2 (1.5%)
HbA1c, mmol/mol	74 (14)	74 (13)
HbA1c, %	8.9 (1.3)	8.9 (1.2)
Diabetes distress (PAID)	11 (4-20)	13 (5-22)
Severe diabetes distress (PAID ≥40)	11 (7.4)	10 (6.7)
Body weight, kg	97.3 (23.9)	96.7 (22.1)
Blood pressure, mm Hg		
Systolic	132.2 (17.8)	133.0 (14.1)
Diastolic	76.3 (11.2)	77.7 (11.4)
Medications		
Insulin	75 (50.3%)	81 (54.0%)
Metformin	131 (87.9%)	134 (89.3%)
Sulfonylureas	59 (39.6%)	67 (44.7%)
DPP-4 inhibitors	41 (27.5%)	41 (27.3%)
GLP-1 receptor agonists	30 (20.1%)	19 (12.7%)
SGLT2 inhibitors	50 (33.6%)	54 (36.0%)
Acarbose	2 (1.3%)	1 (0.7%)
Thiazolidinediones	2 (1.3%)	2 (1.3%)

Data are presented as mean (SD) or median (IQR) for continuous measures, and n (%) for categorical measures. IRSD=Index of relative socioeconomic disadvantage (tenth decile for IRSD represents least disadvantaged individuals). PAID=Problem Areas In Diabetes questionnaire. DPP-4=dipeptidyl peptidase-4. GLP-1=glucagon-like peptide-1. SGLT2=sodium glucose co-transporter-2.

Table 2. Utility values and costs in within trial period

	Professional-mode flash glucose monitoring		Usual clinical care		Diff (95% CI)	P-value
	n	Mean (SD)	n	Mean (SD)		
Utility*						
Baseline	149	0.75 (0.24)	150	0.78 (0.23)	-0.03 (-0.08, 0.02)	0.24
12-month	129	0.72 (0.28)	132	0.75 (0.23)	-0.03 (-0.09, 0.03)	0.32
Adjusted 12-month	129	0.73 (0.20)	132	0.74 (0.18)	-0.01 (-0.06, 0.03)	0.61
Cost, A$						
Baseline (one-year before trial start)	143		145			
Out of hospital health services		2,088 (1,608)		2,101 (1,717)	-13 (-398, 373)	0.95
Pharmaceutical		1,738 (1,680)		1,822 (2,188)	-84 (-538, 369)	0.72
Emergency department		193 (670)		225 (570)	-32 (-176, 112)	0.66
Hospital inpatient stays		3,575 (11,263)		4,496 (10,956)	-921 (-3,498, 1,656)	0.48
Total healthcare cost		7,594 (13,232)		8,632 (12,793)	-1,037 (-4,056, 1,981)	0.50
12-month	143		145			
Out of hospital health services		2,747 (1,929)		2,503 (1,719)	244 (-179, 668)	0.26
Pharmaceutical		2,594 (3,871)		2,170 (3,030)	423 (-388, 1,234)	0.31
Emergency department		245 (717)		246 (486)	-1 (-143, 141)	0.99
Hospital inpatient stays		4,274 (13,591)		7,637 (22,821)	-3,363 (-7,727, 1,001)	0.13
Total healthcare cost		9,859 (16,673)		12,511 (25,161)	-2,652 (-7,610, 2,306)	0.29
Adjusted total healthcare cost		10,081 (13,650)		12,293 (25,218)	-2,212 (-6,925, 2,500)	0.36

SD=standard deviation

*Utility values were measured with the EuroQol 5 Dimension (EQ-5D) 3-level instrument

Table 3. Cost-effectiveness components and ratios

	Professional-mode flash glucose monitoring	Usual care	Difference (95% CI)
Trial-based (base case)			
Life expectancy	11.66	11.63	0.03 (0.02, 0.04)
QALY	8.41	8.37	0.03 (0.02, 0.04)*
Cost, A$	45,423	41,615	3,807

Incremental adjusted cost-effectiveness ratio (ICER), A$	120,228		
Real-life case scenario			
Life expectancy	11.66	11.63	0.03 (0.02, 0.04)
QALY	8.41	8.37	0.03 (0.02, 0.04)*
Cost	42,391	41,615	776 (559, 948)
Incremental adjusted cost-effectiveness ratio (ICER), A$	24,493		

QALY=Quality adjusted life year

*The difference for QALY is stated as 0.03 but not 8.41-8.37=0.04 due to rounding (8.406-8.374=0.032)

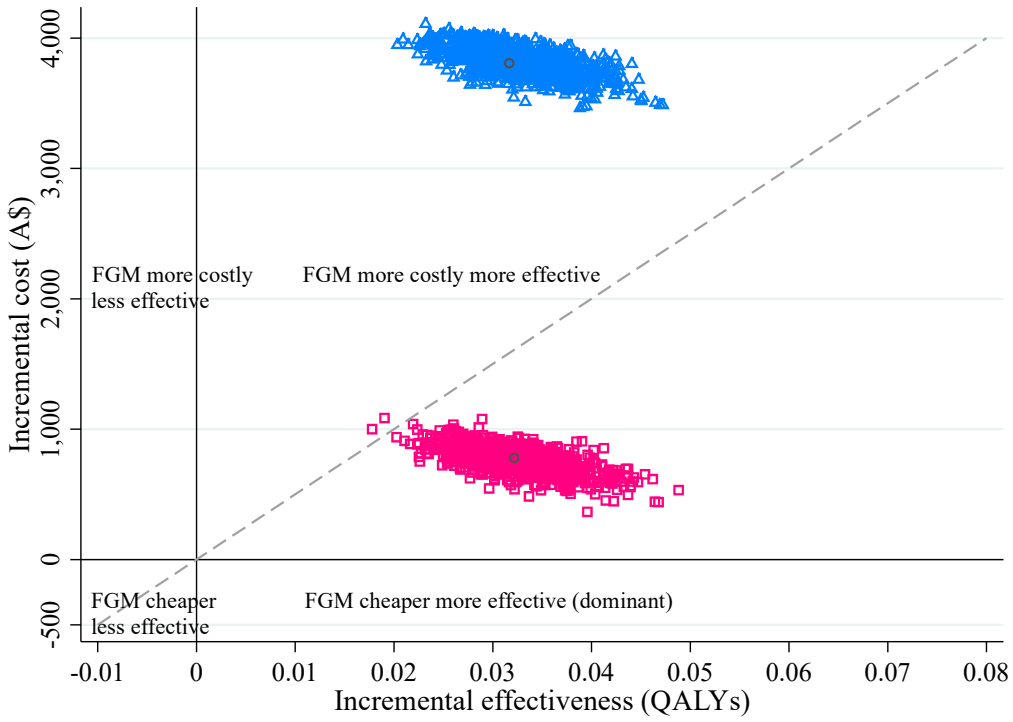

Figure 1. Cost effectiveness plane comparing professional-mode flash glucose monitoring (FGM) vs usual clinical care with bootstrapping. Triangle: trial-based base case (in blue); Square: real-life case scenario (in pink)

QALYs=Quality adjusted life years

WTP=willingness-to-pay

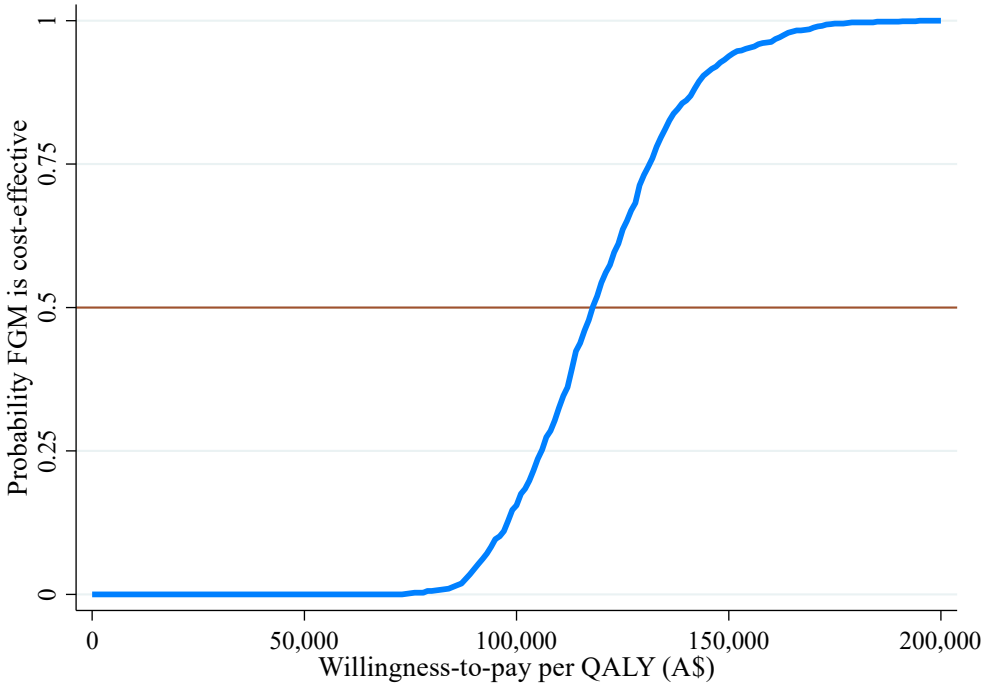

Figure 2. Cost-effectiveness acceptability curve comparing professional-mode flash glucose monitoring (FGM) vs usual clinical care in the trial-based base case.
QALY=Quality adjusted life year

Table 4. Sensitivity analysis: Incremental adjusted cost-effectiveness ratio (ICER) with different assumptions on monitoring frequency and sensor price, A$

Monitoring frequency	Sensor price			
	100% (base case)	75%	50%	25%
Once per year (real-life case scenario)	24,493	16,024	7,555	FGM dominates*
2 times per year	63,155	46,218	29,280	11,974
3 times per year	101,818	76,411	50,636	25,229
3.5 times per year (trial-based)	120,228	90,115	60,385	30,655

*FGM is cheaper and more effective compare to usual clinical care.
FGM=Flash glucose monitoring
Red colour: ICER>A$50,000; green colour: ICER<A$50,000

Table 5. Sensitivity analysis: results with different assumptions on discounting rate, complication cost and treatment effect on HbA1c

		Diff. in QALYs	Diff. in cost, A$	ICER, $A
Trial-based (base case)				
Discounting rate				
	0%	0.08	6,469	83,253
	3%	0.04	4,576	104,550
Complication cost				
	- 25%	0.03	3,950	124,730
	+ 25%	0.03	3,665	115,727
Complication utility				
	-25%	0.030	3,807	126,760
	+25%	0.033	3,807	114,337
Treatment effect on HbA1c				
	Lower 95% CI of the average difference	0.06	3,269	54,638
	Upper 95% CI of the average difference	0.004	4,295	1,056,096
	12-month difference	0.02	4,006	196,546
Real-life case scenario				
Discounting rate				
	0%	0.08	1,270	16,349
	3%	0.04	918	20,981
Complication cost				
	- 25%	0.03	918	28,995
	+ 25%	0.03	633	19,991
Complication utility				
	-25%	0.030	776	25,824
	+25%	0.033	776	23,293
Treatment effect on HbA1c				
	Lower 95% CI of the average difference	0.06	237	3,960
	Upper 95% CI of the average difference	0.004	1,263	310,583
	12-month difference	0.02	974	47,787

ICER= Incremental adjusted cost-effectiveness ratio

Red colour: ICER>A$50,000; green colour: ICER<A$50,000