Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1785 – Dexcom ONE+ continuous glucose monitoring system for people with insulin-dependent type 2 diabetes

Applicant: **Australasian Medical & Scientific Limited**

Date of MSAC consideration: **31 July 2025**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

An application requesting National Diabetes Services Scheme (NDSS) funding of the Dexcom ONE+ continuous glucose monitoring (CGM) system for people with insulin-dependent type 2 diabetes (T2D) was received from Australasian Medical & Scientific Limited by the Department of Health, Disability and Ageing.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC deferred its advice on NDSS subsidisation of the Dexcom ONE+ continuous glucose monitoring (CGM) system for people with insulin dependent type 2 diabetes (T2D). MSAC considered the clinical claim that CGM leads to an overall improvement in glycaemic control measured using glycated haemoglobin (HbA1c) was not fully supported. The trials were relatively small, short term, and did not report end-organ outcomes. The reduction in HbA1c was lower than the level considered a meaningful improvement by the Pharmaceutical Benefits Advisory Committee and regulatory agencies. However, MSAC considered that CGM had other benefits for patients and T2D management. This includes empowering patients to manage their T2D and manage blood sugar levels during times of acute illness. MSAC considered CGM could improve quality of life and this was reflected in strong consumer support for public funding. MSAC considered that the proposed population was large, with variable clinical needs and anticipated benefits from CGM. MSAC considered the economic evaluation presented was not transparent and could not be used to reliably establish cost-effectiveness because it modelled treatment effects that appeared implausibly large and sustained. MSAC considered that the proposed population was heterogeneous and considered that CGM may be more clinically effective and cost-effective for some of the subpopulations, including patients who use both long acting and short acting insulin, people using insulin with higher levels of glycated haemoglobin (e.g. > 8%) as well as Aboriginal and Torres Strait Islander people. MSAC also noted that CGM may be used intermittently to establish better glycaemic control rather than continuously. MSAC considered that there was substantial uncertainty around estimated utilisation. MSAC considered the budget impact of subsidising CGM for the proposed population would be very large.

MSAC advised that a resubmission should present a revised economic evaluation focussed on the populations with a higher clinical need, two different patterns of usage, and any more recent clinical evidence of effectiveness, as well as addressing the issues in the model. MSAC also

considered revised estimates of utilisation would be required to more accurately estimate the size of the subpopulations. MSAC considered there was limited evidence available to suggest a significant difference in clinical outcomes between different brands of CGM devices with comparable functionality, but that further consideration should be given as to whether devices that have specific features should be considered equivalent.

Consumer summary

This is an application from Australasian Medical & Scientific Limited requesting public funding under the National Diabetes Services Scheme (NDSS) for the Dexcom ONE+ continuous glucose monitoring (CGM) system for people with insulin-dependent type 2 diabetes (T2D).

Diabetes is a condition that can cause high blood sugar, which is when sugar (glucose) builds up in the bloodstream. The most common types of diabetes are called type 1 and type 2. There are also other types of diabetes (such as type 3c), which are less common. High blood sugar (hyperglycaemia) caused by diabetes can cause a range of issues including heart disease, nerve damage, and kidney damage, and can even be life-threatening. The amount of sugar in a person's bloodstream is usually controlled by a hormone called insulin. Insulin is like a key, which unlocks cells and allows sugar to move from the bloodstream into the cells. People with diabetes either do not produce enough insulin (type 1) or cannot properly use the insulin they produce (type 2). Many people with diabetes use insulin injections to help keep their blood sugar levels under control, but too much insulin can cause low blood sugar (hypoglycaemia), which can also cause health problems.

People with diabetes need to regularly check their blood sugar levels, particularly around mealtimes, to help them know if they might need to use insulin, and their blood sugar level will help them work out how much insulin they need. If their blood sugar levels are too low, they might need to eat more food to raise their blood sugar level and not use insulin. Most people check their blood sugar level by pricking their finger and placing the drop of blood onto a test strip that can measure blood glucose levels. This is called self-monitoring of blood glucose (SMBG). Some people need to do several finger prick tests over the day, which can be painful and inconvenient. Another way to test blood sugar is by using a continuous glucose monitor (CGM). This is a small device that sits on the skin (usually worn on the back of the upper arm), with a sensor that is inserted just under the skin and continuously measures the glucose level in the fluid under the skin. The CGM device sends the results via Bluetooth to the person's smartphone or other type of receiver, so they can monitor their blood sugar levels in real time. This information lets people with diabetes see their blood sugar at any point in time, and also lets them see trends in their blood sugar levels. This could be for example over the past 24 hours, or longer time periods (e.g. over past 90 days), which helps people understand the effects of their behaviour (for example, what they eat, or how much they exercise) on their blood sugar levels. CGM can also reduce the burden on carers, provide information to doctors about treatment, and enable remote monitoring, which may improve access to care.

One such CGM device is called Dexcom ONE+. The Dexcom G series of CGM devices are funded under Australia's NDSS for people with type 1 diabetes. This application is requesting funding for Dexcom ONE+ for people with type 2 diabetes who have trouble controlling their blood sugar levels. A similar application was also considered by MSAC for another CGM device (Application 1786).

MSAC acknowledged the large amount of public consultation input received for this application and appreciated the effort that people had gone to in sharing their experiences. MSAC noted that a major theme in the feedback was the importance of supporting self-management through patient education and empowerment.

MSAC considered that CGM systems with similar features and functionality were likely similarly safe and effective, regardless of the brand of device. MSAC considered using CGM systems to be as safe as finger pricking for SMBG. MSAC noted the application claimed CGM was more

Consumer summary
effective than SMBG for monitoring blood glucose levels, and that this claim was based on monitoring using CGM resulting in more of a reduction in long-term average blood glucose levels using a measure called glycated haemoglobin, also known as HbA1c than SMBG. On average, CGM resulted in a reduction in HbA1c that was around 0.3% more than SMBG, which the application stated was clinically meaningful. However, MSAC noted that a difference in reduction in HbA1c of 0.5% has previously been accepted as the smallest difference needed to show better clinical outcomes by international committees that evaluate medicines and medical services and by diabetes organisations. The follow-up time in the studies was also relatively short (1 year or less), so MSAC considered that the long-term benefits of CGM were not shown in these studies. MSAC noted that there is a large group of people with type 2 diabetes, with a wide range of different backgrounds and clinical needs, and therefore that it was not likely the effects of CGM would be the same for everyone with type 2 diabetes. MSAC also noted that sometimes CGM is used intermittently rather than continuously, to achieve better glucose control, and then check that control has been obtained. MSAC also noted that the estimated financial impact to the NDSS of funding CGM for everyone with type 2 diabetes was very large, which MSAC considered may not be reasonable for a technology that has not been demonstrated to have significant clinical benefit. MSAC also identified some problems with the economic modelling used to assess the costs and benefits to the health system of funding this technology, which meant that its cost effectiveness was uncertain. However, MSAC considered that CGM could be particularly beneficial for some groups of people with type 2 diabetes and at certain times. Such groups could include First Nations people, who may particularly benefit from this intervention and for whom finger prick testing may not be culturally appropriate; people who have a disability that increases the burden of finger prick testing on carers or on themselves; and people with baseline HbA1c levels over 8%. MSAC also considered that it may be most beneficial and cost-effective to fund CGM for shorter periods rather than continuously. More evidence is needed to determine whether CGM is especially useful in these circumstances; however, MSAC advised that, if CGM is funded for people with type 2 diabetes in the future, the funding arrangements should match those in place for type 1 diabetes, to ensure that public funding of CGM is equitable. **MSAC's advice to the Commonwealth Minister for Health, Disability and Ageing** MSAC deferred its decision on public funding for this application, with a mind to support a resubmission if the applicant addresses the issues raised by MSAC. MSAC requested that more work is done to clearly identify the subgroups of people with type 2 diabetes who would gain the most benefit from CGM, and to fix problems with the economic model to ensure the results are reliable

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this application from Australasian Medical & Scientific Limited requested National Diabetes Services Scheme (NDSS) funding for the Dexcom ONE+ continuous glucose monitoring (CGM) system for people with insulin-dependent type 2 diabetes mellitus (T2D). This funding avenue does not require a Medicare Benefits Schedule (MBS) listing.

MSAC noted the recommendations from the Royal Australian College of General Practitioners (RACGP) regarding when blood glucose levels (BGLs) should be actively checked. BGL checking is usually conducted using self-monitoring of blood glucose (SMBG) via finger prick testing. MSAC

noted that the number of times per day a patient needs to check their BGL varies widely and depends on the context. MSAC noted that people on long-acting once daily insulin generally need to check their blood glucose only once a day (in the morning), except for during times of illness, dosage adjustment or if they are on other medications that cause hypoglycaemia (such as sulfonylureas which is now rarely used). People who are on both short- and long-acting insulin may need to check their blood glucose more often.

CGM systems are designed to replace SMBG. MSAC noted that the Dexcom ONE+ CGM system uses a sensor to measure glucose concentrations in interstitial fluid, then reports the measurements in real time via a Bluetooth-enabled display device. The system issues alerts if the readings are indicative of hypo- and hyperglycaemia to aid timely blood glucose management. Patients using Dexcom ONE+ only require finger prick testing if the system fails to give a reading or if a reading is inconsistent with their symptoms.

MSAC noted the history of funding under the NDSS for people with type 1 diabetes mellitus (T1D) in Australia. Funding was initially made available to people with T1D aged under 21 in April 2017, with access further expanded in 2019 and in 2022. For some groups, there is a co-payment (equivalent to around $35.90 per month). MSAC noted that NDSS funding is not currently available for CGM for people with T2D.

MSAC noted that the NDSS currently funds CGM products from 3 manufacturers, 2 of which have submitted applications for consideration at the July 2025 meeting. MSAC Application 1786 seeks funding for the FreeStyle Libre 2 (FSL2) CGM system.

MSAC noted the similarities and differences between this application and Application 1786. Both applications requested funding for CGM systems in patients with T2D who use insulin and specific subpopulations of these patients. The subpopulations in this application are people using intensive insulin therapy (IIT; defined as treatment with basal insulin and rapid-acting insulin) users and people using non-IIT (basal insulin only). In application 1786, the subpopulations of the T2D group are also IIT and non-IIT users, although the definition of IIT differs (multiple daily insulin injections or continuous subcutaneous insulin infusion) . Application 1786 also included 2 additional populations: pregnant women with gestational diabetes and people aged ≥21 years with other types of diabetes similar to T1D requiring insulin, such as type 3c diabetes. The primary outcome in both applications was change in glycated haemoglobin (HbA1c).

MSAC recalled its previous review of CGM products provided via the NDSS for people with T1D in 2021 (MSAC Review 1663). MSAC recalled it considered further work was required to define the patient populations that would benefit most from CGM, noting that available guidelines recommend CGM for all people with T1D treated with multiple daily insulin injections. MSAC recalled the review concluded that based on the available evidence, CGM is likely no different to SMBG in terms of HbA1c change and safety for most patients. MSAC recalled the review's conclusion that the economic model failed to provide a reliable basis for estimating the cost-effectiveness of CGM compared to SMBG and failed to adequately capture the range of clinical and quality of life (QoL) benefits that CGM devices could potentially offer. The review recommended that the primary outcomes modelled should also include avoidance of hypoglycaemic events, time in optimal glycaemic range and QoL measures. In the review, MSAC further noted the lack of evidence available to suggest a significant difference in clinical outcomes between CGM devices and considered the revised economic model should be device agnostic.

The applicant was granted a hearing at the MSAC meeting. Representatives of the applicant highlighted that there is currently inequity in Australia in accessing CGM as it is only funded by the NDSS for T1D, which means people with T2D can only access the technology if they can

afford the associated costs. Applicant representatives also stated that better control of diabetes offered by CGM may lead to fewer complications of T2D such as cardiovascular events and microvascular complications and the associated long-term cost savings to the health system. The applicant considered there may be a reduction in dialysis costs arising from diabetes-related kidney disease in Australia, which would benefit the healthcare system. Representatives reaffirmed the decision to use 0.3% reduction in Hba1c as the minimal clinically important difference (MCID) rather than the internationally accepted MCID of 0.5%, stating that any reduction has patient benefits, especially in the long term. MSAC noted that while living guidelines for people with T1D covering use of CGM had been developed,[1] there were currently only living guidelines for people with T2D covering use of medications. Representatives clarified that living guidelines for people with T2D covering CGM are yet to be developed due to funding constraints.

MSAC noted the large amount of consumer feedback on this application, which focused on the reduced risk of hypoglycaemic events, the importance of supporting self-management through patient education and empowerment, and the potential to improve access to care through remote monitoring in underserved populations. MSAC acknowledged the effort that people had gone to in sharing their experiences.

MSAC noted the clinical management algorithm, in which CGM is used in conjunction with insulin and/or other glucose-lowering therapies. MSAC noted that finger prick testing is only required if a patient's symptoms are not aligned with the BGL reported by the CGM system, or in the case of CGM system failures.

MSAC noted that funding of Dexcom ONE+ was requested for people with T2D and suboptimal glycaemic control. 'Suboptimal glycaemic control' was defined as laboratory-measured HbA1c levels of >7.0% for adults, and >6.5% for children and adolescents. This application included 2 subpopulations: IIT users and non-IIT users. MSAC considered that the HbA1c targets proposed were a low threshold that would capture the vast majority of, if not all, patients with diabetes on insulin.

MSAC considered that, although the ideal target for Hba1c is generally less than 7.0%, this target should be individualised to account for factors such as the patient's context, age, risks, life goals and co-morbidities, and therefore it may not be accurate to conclude that all patients with a HbA1c over 7.0% have 'suboptimal glycaemic control'. MSAC considered that alternative thresholds for baseline HbA1c to determine eligibility for CGM should be considered, to more appropriately capture the group of people for whom CGM would provide the most benefit.

MSAC noted that the comparator was SMBG, which it considered appropriate.

MSAC noted the evidence base presented in the applicant-developed assessment report (ADAR), which consisted of 4 unblinded randomised controlled trials (RCTs). MSAC noted the evidence presented was from an older version of the Dexcom device, not Dexcom ONE+, which MSAC did not consider to be of concern, noting that version updates would be unlikely to impact overall functionality and clinical benefit. MSAC noted that the studies were relatively small, with 116 patients in the intervention arm of the largest trial, and that only one of the studies included an IIT population. None of the studies had participants under the age of 16 or included Aboriginal and/or Torres Strait Islander peoples; there were no Australian studies; and all patients in the studies had an entry Hba1c level of above 7.5%, however mean baseline Hba1c levels that were much higher (8.2% to 10%). MSAC noted the observations made by the assessment group and ESC regarding inconsistent follow-up time points and short overall timeframe (12 months or less),

[1] https://www.diabetessociety.com.au/living-evidence-guidelines-in-diabetes/

and agreed with their concerns regarding validity of the meta-analysis given these issues. MSAC further noted that the trials did not report end organ outcomes. MSAC noted that these studies used an older version of the device but considered this acceptable as the newer version was likely to be comparable.

MSAC noted that the clinical claim was non-inferior safety and superior effectiveness compared with SMBG. MSAC noted that the safety outcomes measured were adverse events (episodes of severe hyper- and hypoglycaemia) and local adverse events associated with SMBG or placement of the CGM sensor. MSAC considered that most safety issues were minor. MSAC also noted potential delays in the detection of hypoglycaemic events with CGM due to the time lag between bloodstream and interstitial fluid glucose levels. Overall, MSAC considered that despite the lack of a strong evidence base regarding safety, the claim of non-inferior safety was appropriate.

MSAC noted that comparative effectiveness was measured through changes in HbA1c and time in range (TIR) at follow-up. Measures of T2D-related complications, mortality, quality of life (QoL), psychological health, subjective treatment satisfaction, and hypo- and hyperglycaemic events resulting in emergency department or hospital visits were also included. MSAC noted that the change in HbA1c showed an adjusted difference between SMBG and CGM of approximately 0.4%. In the ADAR, the MCID for change in HbA1c is specified as 0.3%, and on this basis the result is argued to demonstrate clinical superiority. MSAC agreed with ESC's observation that this threshold is lower than the MCID of 0.5% for superiority that has previously been used by the Pharmaceutical Benefits Advisory Committee (PBAC). The International Diabetes Federation[2], England's National Institute for Health and Care Excellence[3,4], the Australian Diabetes Society[5] and the Royal Australian College of General Practitioners[6] have also nominated 0.5% as the MCID for HbA1c. The European Medicines Agency[7] guidance supports the use of a 0.3% HbA1c to establish non-inferiority. MSAC noted the applicant's argument in the hearing that any reduction in HbA1c is beneficial to a person with diabetes because of reduced complications, including renal complications, ophthalmic complications, ulceration and amputations, in the long term. However, MSAC agreed with ESC that the evidence base presented was not sufficient to accept a MCID of 0.3%. MSAC noted ESC advice that Appendix 12 of the MSAC Guidelines outlines an approach to establishing an alternative MCID (p 296) using a meta-regression of randomised trials (in this case of any intervention in T2D) comparing the observed treatment effect on the proposed surrogate measure (in this case HbA1c within the first 12 months) with the observed treatment effect on the target patient-relevant clinical outcome (in this case any one or more of the modelled diabetes complications over subsequent years).

MSAC also agreed with ESC that if a claim of superior effectiveness cannot be established based on HbA1c, then it would need to be supported by additional data, such as QoL measures. MSAC considered that CGM has other benefits for patients and T2D management. This includes empowering patient to manage their T2D and manage blood sugar levels during times of acute

[2] International Diabetes Federation. Recommendations for managing type 2 diabetes in primary care, 2017. www.idf.org/managing-type2-diabetes

[3] National Institute for Health and Care Excellence (NICE). Type 2 diabetes in adults: management (NICE guideline). [NG28]. London: NICE; 2015.

[4] National Institute for Health and Care Excellence (NICE) Surveillance of diabetes (type 1 and type 2) in children and young people: diagnosis and management [NG18]. London: NICE; 2022.

[5] https://treatment.diabetessociety.com.au/plan/

[6] The Royal Australian College of General Practitioners. Management of type 2 diabetes: a handbook for general practice. East Melbourne, Vic: RACGP, 2020.

[7] European Medicines Agency (2023). Guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus. CPMP/EWP/1080/00 Rev.2. https://www.ema.europa.eu/en/clinical-investigation-medicinal-products-treatment-or-prevention-diabetes-mellitus-scientific-guideline

illness as well as avoid hypoglycaemia, particularly nocturnal. MSAC considered CGM could improve quality of life and this was reflected in strong consumer support for public funding.

Regarding the economic analysis, MSAC noted ESC's concerns regarding the transparency of the IQVIA Core Diabetes Model (CDM) and considered that they had only been partially addressed in the pre-MSAC response. MSAC accepted, as per the pre-MSAC response, that the model did not include a Markov trace (the proportion of patients in each health state at each point in time) because it was an individual microsimulation model and noted the outputs provided, which show the cumulative incidence of each individual complication in the model over 50 years. MSAC noted that, as clarified in the pre-MSAC response, QoL was measured through averted complications of T2D over the 50 year period which was driven by persistent changes in HbA1c.

However, the pre-MSAC response did not address the key concern relating to transparency, namely whether the model remained valid given the use of Western Australia-based risk equations and changes to the model structure from the original model (such as the merging of 17 health states in the original model into 10 health states). MSAC considered that although the Australian risk equations had been validated for an Australian population, their specific application in the current model was not validated.

MSAC considered that the applicant's pre-MSAC response partially addressed ESC's concern regarding the realisation of projected cost savings after the average life expectancy in the model insofar as it clarified that approximately 50% of patients in the model would live beyond the average life expectancy and would continue to accrue the cost savings estimated. However, MSAC noted that the treatment effect in the model was calculated based on between 3 and 12 months of data and then extrapolated to continue accruing at a constant rate over the patient's lifetime. MSAC considered this effect implausible, and therefore judged the projected cost savings as unlikely to be realised. MSAC noted that the pre-MSAC response did not address this issue. MSAC considered it would be more appropriate to assume that the incremental benefits of CGM would decline over time as the key benefit of CGM systems is that it provides additional information to patients and clinicians that may lead to improved clinical management. Therefore, MSAC considered CGM may have an initial effect that would decrease over time.

MSAC noted that the ADAR presented a base case showing that CGM is cheaper and more effective than SMBG across both subpopulations. CGM was also dominant across most of the sensitivity analysis. Where it was not dominant, incremental cost-effectiveness ratios (ICERs) were under $45,000 to $55,000 per quality-adjusted life year (QALY). MSAC highlighted that Australia is the only jurisdiction where economic modelling had CGM as dominant (more effective and less costly). However MSAC considered that the modelled outputs and resulting ICERs were not reliable for the reasons previously discussed.

MSAC noted that to account for the consideration that HbA1c benefits had not been sufficiently established by the evidence due to the MCID threshold of 0.5%, additional analyses were provided in the pre-MSAC response, which assume no HbA1C benefit. In a scenario without the HbA1c benefit, the ICER for IIT users was $15,000 to $25,000/QALY and $55,000 to < $75,000/QALY for non-IIT users.

The pre-MSAC response also produced a weighted model in which the HbA1c benefit was only applied to the proportion of the patient population that met the MCID of 0.5% – 26% of the IIT population and 10% of the non-IIT population – the ICER benefit for IIT users was $5,000 to < $15,000 and $45,000 to < $55,000 for the non-IIT population leading to an overall population weighted ICER of $15,000 to < $25,000. MSAC noted that further evaluation would be useful on whether this alternative interpretation of the same evidence base would constitute sufficient evidence for superior effectiveness. MSAC considered it clinically plausible that the IIT group may be most likely to benefit from CGM, as indicated by the results of these additional analyses.

MSAC questioned the disutility figure of 0.03 for finger prick testing for several reasons: the applicability of the population in the study (209 members of the UK general public) from which this estimate was derived to the proposed population (Australians living with diabetes); it might overlap with the fear of hypoglycaemia utility estimate; and the disutility in practice would vary according to the patient's ability to undertake their own finger prick testing . Additionally, MSAC noted the EuroQol-5 Dimension QoL measure scores used for baseline utility appear not to have been mapped using Australian values.

Regarding the financial analyses, MSAC noted that the number of people estimated to be eligible for CGM in the IIT population was 162,889, around 70% of the population of insulin-dependent T2D patients with inadequate HbA1c control. MSAC noted the differences in eligible population estimates between this application and Application 1786 which need to be resolved (although noting the differences were partly based on different definitions of the IIT population). MSAC noted that, notwithstanding these uncertainties, the financial impact of funding CGM was still expected to be high due to the broadly defined criteria for eligibility. MSAC also considered that if uptake is faster than predicted, this would lead to a significantly increased financial cost to the health system.

MSAC noted that the net financial impact on the NDSS of funding the Dexcom ONE+ CGM system for the non-IIT population was estimated in the ADAR at $40 million to < $50 million in year 1, increasing to $90 million to < $100 million in year 6. The net financial impact to the NDSS for the IIT population was estimated at $90 million to < $100 million in year 1, rising to $200 million to < $300 million in year 6.

MSAC also noted a revised estimate of the eligible population was provided by the department, based on a proportional reduction in numbers relying on previous Pharmaceutical Benefits Scheme (PBS) figures for the number of people who were insulin dependent with T2D. Using the revised estimate reduced the net costs for IIT users to $60 million to < $70 million (year 1), rising to $100 million to < $200 million (year 6) and for non-IIT users to $20 million to < $30 million (year 1), rising to $60 million to < $70 million (year 6).

MSAC considered that all of these estimates would constitute a significant budgetary impact, even if the eligible population estimate were revised down significantly as detailed above. MSAC also considered that if uptake were greater and earlier than estimated, net costs would increase significantly. Given the high cost to the health system of funding all people with insulin-dependent T2D across the entire lifespan, and the uncertain evidence regarding superior clinical benefit, MSAC considered that the financial impact could be reduced by targeting specific populations that are more likely to benefit from CGM and/or limiting the frequency of CGM use.

MSAC considered intermittent use (e.g. CGM provided for a set number of months per year) may be sufficient to obtain the desired clinical benefit for some populations with T2D who may benefit from CGM.

MSAC noted the applicant's argument in the pre-MSAC response that the Dexcom ONE+ should be assessed individually. However, MSAC considered the evidence presented in this application, and that of application 1786, and considered that there was likely no difference between the FSL and Dexcom devices in terms of clinical effectiveness. On balance, MSAC agreed with ESC that there is likely to be some degree of class effect with this technology when CGM systems have similar features and functionality, but that further consideration should be given as to whether devices with specific features should be considered equivalent.

Given that the outcomes for the Dexcom ONE+ and FSL CGM systems were judged to be comparable, MSAC considered that price is the main difference between the 2 applications.

MSAC agreed with ESC that either a price premium for the more expensive device (paid for by the patient) or price competition approach would be appropriate.

MSAC also considered that fully funding CGM for T2D would raise equity issues due to the current co-payment model for T1D, where, for people with T1D aged 21 years and over who do not have concessional status, there is an equivalent monthly co-payment of around $35.90 for CGM. MSAC therefore considered that any funding of CGM for T2D should match the approach taken for T1D.

MSAC noted that most patients with T2D are managed in a general practitioner (GP) setting, but GPs are not currently included in the set of health professionals who can certify eligibility for CGM products through the NDSS. MSAC considered that the insufficient numbers of endocrinologists and diabetes educators (who are currently able to certify eligibility for CGM products) would create inappropriate barriers to access if CGM devices are funded for people with T2D. MSAC considered that allowing GPs to approve CGM for both T1D and T2D (if funded), with guidance, would be appropriate. MSAC noted that consumer feedback also supports an extended role for GPs. MSAC noted that the RACGP does not support mandating GPs to complete additional education before they are able to sign CGM application forms. MSAC considered that changes to the NDSS IT system may also be needed to ensure access to CGM products is limited to those who are in cohorts that have newly received access.

Overall, MSAC considered that the population proposed in this application is very broad and heterogeneous and that the evidence presented is not sufficient to support a claim of superior clinical effectiveness. The reduction in HbA1c reported from the evidence base was lower than the level considered to be a meaningful improvement by the PBAC and regulatory agencies. The economic evaluation presented was not transparent and could not be used to reliably establish cost-effectiveness because it modelled treatment effects that appeared implausibly large and sustained and the budget impact of subsidising CGM for the proposed population would be very large. MSAC considered that CGM may be more clinically effective and cost-effective for some of the subpopulations and this should be further considered. MSAC therefore deferred its advice on public funding of the Dexcom ONE+ CGM system until these issues are adequately addressed. MSAC noted that one possible approach to resubmission could involve redefining the key glycaemic outcome measures in terms of the percentage of patients achieving a ≥0.5% HbA1c reduction (as per the reinterpretation of evidence supplied in the pre-MSAC response as discussed above) though the resubmission would still need to re-evaluate the clinical data in light of this new interpretation of the outcome measure, address the economic and financial issues already discussed and revise the economics and financials based on this new outcome measure.

MSAC considered that certain subpopulations are likely to have greater clinical need, derive more clinical benefit and/or show greater QoL improvements if they use a CGM device, although further evidence that is more up-to-date and specific to these groups is required.

MSAC therefore considered that a resubmission may wish to consider the clinical evidence for these and other subpopulations with T2D to evaluate whether CGM would be better targeted to these subpopulations. This included:

- people using insulin with higher baseline levels of glycated haemoglobin (e.g. >8% and >9%)
- First Nations people (e.g. with baseline HbA1c >7%)
- people who use both long acting and short acting insulin
- people with disability (including mental health issues and neurodivergence) for which checking BGLs creates a high burden on the individual and/or carer

For example, MSAC noted that finger prick testing does not constitute culturally respectful care in many First Nations communities due to the shame and stigma surrounding this testing method.

Additionally, First Nations people typically have worse diabetes outcomes, and therefore may derive more benefit from CGM. MSAC noted that CGM systems may be especially useful for First Nations community members, and considered that funding access to the technology will be beneficial in closing the gap. MSAC also noted that based on consultation input, CGM may also have increased utility in the case of people living with conditions such as depression, attention-deficit/hyperactivity disorder (ADHD) and neuropathy, and that these people may not have been captured in the clinical trials. MSAC also considered that CGM systems may be useful on a temporary basis for people on long-acting insulin in periods of illness or when hypoglycaemic events are suspected.

MSAC considered the following groups may benefit from short-term or intermittent CGM, although as for the more targeted subpopulations, MSAC noted that evidence of intermittent vs continuous use should be presented in a resubmission:

- people with intercurrent illness that affects blood glucose management and requires additional short-term monitoring of blood glucose levels
- people who are pregnant and have type 2 diabetes or gestational diabetes, as high glucose levels during pregnancy can lead to abnormal development and later health problems for the child
- people who are starting insulin therapy and require frequent BGL measurements
- situations in which nocturnal hypoglycaemic events are suspected.

MSAC advised that, if the applicant maintains a claim of clinical superiority, a resubmission would need to demonstrate superior effectiveness based on the MCID threshold of 0.5% unless an alternative threshold could be justified as per the section of the MSAC Guidelines previously cited).

MSAC further considered that, as discussed previously, the educational benefits of CGM in inducing behavioural changes may taper off over time. MSAC therefore queried whether evidence is available regarding the effectiveness of using a CGM for a limited period (e.g. 2 months in a calendar year), which may be considered as a potential option in a resubmission.

MSAC advised that a resubmission should present a revised economic evaluation focussed on the populations with a higher clinical need and addresses the issues in the model especially validation of the structural changes in the model and adjustment of the treatment effect. MSAC also considered revised estimates of utilisation would be required to more accurately estimate the size of the subpopulations. MSAC advised that the resubmission would need to be considered by ESC in addition to MSAC.

MSAC advised that if CGM for any of the identified populations is supported in future, co-payment arrangements for these populations should align with existing co-payments for people with type 1 diabetes, to ensure equity of access. MSAC considered that, based on the evidence presented, different CGM systems with similar features were likely to be equivalent and did not yield differences in magnitude or type of benefit. MSAC therefore considered it appropriate to fund different brands of CGM systems with comparable functionality in a device agnostic manner, but noted that further consideration should be given as to whether devices with specific features should be considered equivalent.

4. Background

The Medical Services Advisory Committee (MSAC) has not previously considered CGM systems for people with T2D requiring insulin. In addition to the application discussed in this public summary document, an MSAC application for the FreeStyle Libre 2 CGM system for people with

T2D requiring insulin, gestational diabetes, and other types of diabetes (including type 3c) is currently under consideration (MSAC Application 1786).

In 2021, MSAC conducted a review of CGM products for people with type 1 diabetes (T1D) that are provided through the CGM Initiative by the NDSS (MSAC Review 1663). After considering the available evidence, MSAC deferred providing advice on the clinical effectiveness and cost-effectiveness of subsidised CGM products, and concluded that further work was required to better establish the patient population, clinical effectiveness and cost-effectiveness of CGM devices in T1D.

5. Prerequisites to implementation of any funding advice

Dexcom ONE+ is listed as a medical device on the Australian Register of Therapeutic Goods (ARTG). Table 1 provides details of the Therapeutic Goods Administration status from the ARTG for Dexcom ONE+. The ADAR did not state that there were any prerequisites for Dexcom ONE+.

Table 1: Dexcom ONE+ listed on the ARTG

Product name (sponsor)	ARTG summary	Intended purpose
Subcutaneous glucose sensor (AA-Med Pty Ltd)	**ARTG ID:** 462866 **Start date:** 25/09/2024 **Category:** Medical Device Included Class IIb **GMDN:** 59016 Subcutaneous glucose sensor	The subcutaneous glucose sensor is intended to be used as part of the CGM System. The CGM is a glucose monitoring system indicated for persons with diabetes mellitus aged 2 years and older where SMBG is indicated. The device is designed to replace finger prick BG testing for treatment decisions. Interpretation of the device results should be based on the glucose trends and several sequential readings over time. The device also aids in the detection of episodes of hyperglycaemia and hypoglycaemia, facilitating both acute and long-term therapy adjustments. It is intended for use by patients at home and in healthcare facilities.

Abbreviations
AID = automated insulin dosing, **ARTG** = Australian Register of Therapeutic Goods, **BG** = blood glucose, **CGM** = continuous glucose monitoring, **GMDN** = Global Medical Device Nomenclature, **SMBG** = self-monitoring of blood glucose.
Source
ARTG Public Summary Documents. Verified by assessment group on 25 February 2025.

6. Proposal for public funding

The applicant-developed assessment report (ADAR) for Dexcom ONE+ proposed that public funding should be provided for 2 T2D subpopulations requiring insulin with suboptimal glycaemic control: intensive insulin therapy (IIT) users and non-IIT users. These 2 subpopulations account for all people with T2D requiring insulin.

The applicant proposed that the technology is publicly funded through the NDSS (i.e. no Medicare Benefits Schedule listing is required). The proposed population for NDSS funding of Dexcom ONE+ is narrower than the indication in the ARTG listing, which is for 'persons with diabetes mellitus aged 2 years and older where SMBG is indicated'. Currently, subsidised CGM products are only available through the NDSS for people with T1D and some people <21 years with rare conditions similar to T1D. Other Dexcom real-time CGM (RT-CGM) systems (Dexcom G6 and G7) with advanced features (e.g. connectivity to pumps) are currently available through the NDSS for T1D. Dexcom ONE+ does not have these advanced features.

Expanding subsidised access to RT-CGM technology aligns with recent recommendations from the Parliamentary Inquiry into Diabetes in Australia, which advocates equitable access to advanced diabetes technologies for all individuals who require insulin: *'The Committee recommends that subsidised access to Continuous Glucose Monitors (CGMs) be further expanded. In the first instance, all access limitations in relation to patients with Type 1 diabetes should be removed. Furthermore, individuals with insulin-dependent Type 3c diabetes and patients with gestational diabetes should be made eligible for subsidised CGMs and for those with Type 2 diabetes requiring regular insulin. The Committee recommends prioritising the removal of age limitations on access to subsidised access for Type 1 diabetes patients'* (Recommendation 15, Diabetes Inquiry).

Dexcom ONE+ is a new CGM technology for diabetes that continuously measures and reports glucose concentrations in the interstitial fluid. The sensor can be applied to the skin on either the abdomen or back of arms (also on the buttocks in children aged 2 to 6 years) using the inbuilt sensor applicator. It is designed to replace SMBG for treatment decisions and adjunctive use of finger prick SMBG testing because the Dexcom ONE+ system is factory calibrated, negating the need for ongoing calibration of the device. Finger prick testing is only required in the event that glucose alerts and readings from the Dexcom ONE+ do not match symptoms or expectations, or if the Dexcom ONE+ system fails to display a blood glucose level and trend arrow. The Dexcom ONE+ system consists of 2 main components:

- A Dexcom ONE+ all-in-one transmitter and sensor (including sensor wire).
- A Bluetooth-enabled display device, either a mobile phone with application and/or optional receiver.

The glucose readings are automatically transmitted from the transmitter to the receiver/compatible smart device every 5 minutes if they are within a range of 10 metres, and no scanning is required. The main consumables associated with Dexcom ONE+ are the all-in-one transmitter and sensor. The all-in-one transmitter and sensor are replaced every 10 days. Therefore, it is anticipated that people with T2D using the Dexcom ONE+ system will require 36 sensors per year, conservatively assuming 100% adherence/compliance. The ADAR stated that replacement/failure of sensors was rare and, therefore, are accounted for in the conservative adherence/compliance estimate. In the absence of specific data on adherence/compliance, this approach is appropriate. The Dexcom ONE+ system is not compatible with continuous subcutaneous insulin infusion pumps. As the patient self-inserts the sensor and attaches the transmitter, the ADAR did not describe any geographical barriers to implementing the Dexcom ONE+ system. The device is also intended for use by people with T2D at home and in healthcare facilities.

Components of the Dexcom ONE+ system should not be worn during magnetic resonance imaging, computed tomography or high-frequency electrical heat (diathermy) treatment. Also, the system should not be exposed to scanners in an airport setting, such as an advanced imaging technology body scanner (also called a millimetre wave scanner) or scanned through a baggage X-ray machine.

It is expected that patients with T2D accessing Dexcom ONE+ will be registered on the NDSS and see an authorised health professional to determine whether they meet the eligibility criteria for the device. Authorised health professionals may include endocrinologists, certified diabetes educators and other health professionals specialising in diabetes (physicians, paediatricians or nurse practitioners).

The ADAR noted that patients in the existing and proposed treatment pathways will be managed in very similar ways. For example, Dexcom ONE+ will similarly be used in conjunction with oral and injectable medications and/or basal rapid-acting insulin, suggesting that this will displace

the need for routine SMBG. People using Dexcom ONE+ will also still need to be assessed by a GP or diabetes educator at least every 3 months.

While not reported in the ADAR, the size of the proposed subpopulations is reported within the ratified PICO document. The Australian National Diabetes Audit (ANDA) in 2022 reported that just over half (53.2%) of people with T2D included in the audit were being treated with insulin.[8] According to data from the NDSS, 304,527 (25%) Australians living with T2D required insulin therapy as of 30 June 2023.[9] In 2022, ANDA reported on the use of different insulin regimens among insulin users. Other data from ANDA (2022) suggested that 70.1% of people with T2D using insulin require IIT (basal and rapid-acting insulin therapy regimens including pre-mixed or co-formulated insulin) and 27.2% require non-IIT (basal insulin therapy only). Additionally, ANDA in 2022 estimated that 71% of all people with T2D (including both insulin-requiring and non-insulin-requiring populations) had suboptimal glycaemic control despite treatment (lifestyle intervention or drug treatment).

The Dexcom ONE+ sensor is disposable and can be worn for a maximum period of 10 days. The cost of CGM is the same for both proposed subpopulations (i.e. regardless of intensity of insulin use). Therefore, each eligible person would require 36 sensors per year. The proposed annualised fee for the Dexcom ONE+ system is $REDACTED. For the IIT population, the cost of SMBG is based on the mean number of finger prick testing of 3.8 times per day, as observed in the DIAMOND T2D trial. For the non-IIT subpopulation, this was assumed to be 2 times per day, based on the MOBILE study. The true purchase price for blood glucose monitoring strips is not in the public domain. However, they are subsidised through the NDSS at a cost of $15 per 100 strips. In the economic evaluation, a cost of $0.15 per strip was assumed. When annualised, the total cost of testing is $208.05 and $109.5 per patient per year for the IIT and non-IIT subpopulations, respectively. The subsidised products available to perform SMBG (e.g. Accu-Chek, CareSens) also vary in costs. According to Diabetes SA, Accu-Chek brands have a recommended retail price (RRP) of $65 per 100 strips (or $48.75 for Diabetes SA members) while CareSens brands have a RRP of $30 per 100 strips (or $22.50 for Diabetes SA members). The analysis included in the ADAR did not consider any other resource use in relation to SMBG.

7. Population

While there are 2 populations of interest for the Dexcom ONE+ technology, one defined population, intervention, comparator and outcome (PICO) set was presented in the ADAR (Table 2). The 2 populations were reflected in the PICO as subpopulations. Dexcom ONE+ would be an alternative to SMBG in people with T2D who use insulin and have suboptimal glycaemic control, with the 2 subpopulations differing in terms of the intensity of their insulin treatment regimen. The clinical management algorithm incorporating Dexcom ONE+ was based on the 2024 *Management of T2D: a handbook for general practice* guidelines developed by the Royal Australian College of General Practitioners (RACGP).

The clinical management algorithms for Dexcom ONE+ or SMBG are relatively similar. Following assessment by an authorised health professional to determine whether someone meets the eligibility criteria, people will start treatment with insulin and/or other glucose-lowering therapies, using either SMBG or Dexcom ONE+ to monitor blood glucose levels. Following this, all patients using SMBG or Dexcom ONE+ should have at least 3-monthly appointments with a general

[8] Australian National Diabetes Audit. *Australian National Diabetes Audit Annual Report 2022*. Monash University, School of Public Health and Preventive Medicine.

[9] National Diabetes Services Scheme. Insulin Therapy. https://www.ndss.com.au/wp-content/uploads/Insulin-Therapy-1.pdf

practitioner (GP) or diabetes educator to monitor HbA1c levels and optimise therapies. There is one additional step in the clinical management algorithm for Dexcom ONE+ compared with SMBG: if the individual's symptoms are not aligned with the Dexcom ONE+ results, SMBG should be used to confirm blood glucose levels. The ADAR did not state how often this may be required.

The ADAR also suggested that there will be a decreased consumption of resources following Dexcom ONE+ implementation because of overall improved blood sugar control, thereby leading to the avoidance of short-term (i.e. hypoglycaemia and hyperglycaemia) and long-term (e.g. cardiovascular disease) complications of T2D.

The ADAR addressed most of the requirements of the ratified PICO. Outcomes included in the ratified PICO but not reported in the eligible evidence base were not presented in the ADAR. The population in the ratified PICO also focused on individuals ≥2 years. The ADAR described that there is an increasing incidence of T2D in children and adolescents in tandem with childhood obesity, with adolescents facing more frequent complications and a higher mortality rate than people diagnosed as adults. However, no evidence related to children or adolescents was presented in the ADAR, and inputs for a paediatric population were not considered in the model. During the commentary process, the assessment group identified one study that reported the use of Dexcom G6 in adolescents.[10]

The suggested threshold of suboptimal glycaemic control in children and adolescents of HbA1c levels >6.5% seems reasonable based on recommendations in the literature, including Peña et al. (2020) and the 2024 RACGP guidelines.

Table 2: PICO criteria for assessing Dexcom ONE+ in patients with T2D that have suboptimal glycaemic control on insulin therapy

Component	Description
Population	People aged ≥2 years with T2D who have suboptimal glycaemic control confirmed by laboratory measured glycated haemoglobin (HbA1c) levels of >7.0% for adults and >6.5% for children and adolescents: **Subpopulation 1:** Require treatment with basal insulin and rapid-acting insulin. **Subpopulation 2:** Require treatment with basal insulin only.
Prior tests	Diagnostic tests for T2D if: a) asymptomatic and at high-risk (Australian type 2 diabetes risk assessment tool [AUSDRISK] score ≥12 or in specific high-risk categories): • HbA1c ≥6.5% (48 mmol/mol) on 2 separate occasions, or • FBG ≥7.0 mmol/L, or • random blood glucose ≥11.1 mmol/L confirmed by a second abnormal FBG on a separate day, or • OGTT consisting of blood glucose measurement taken before (fasting) and 2 hours after an oral 75 g glucose load is taken. Diabetes is diagnosed if FBG ≥7.0 mmol/L or 2-hour post-challenge blood glucose ≥11.1 mmol/L, or b) if symptoms of hyperglycaemia present and • patient presenting with hyperglycaemic crisis, or • single elevated FBG ≥7.0 mmol/L, or • single HbA1c ≥6.5% (48 mmol/mol), or • random blood glucose ≥11.1 mmol/L
Intervention	Dexcom ONE+ CGM System
Comparator	SMBG using a finger prick blood sample

[10] Manfredo, J, et al. (2023). Short-term use of CGM in youth onset type 2 diabetes is associated with behavioral modifications. *Front Endocrinol* 14:1182260. doi: 10.3389/fendo.2023.1182260.

Component	Description
Reference standard	Laboratory-conducted plasma venous blood glucose test
Outcomes	**Patient-relevant outcomes** *Direct evidence for safety and effectiveness:* **Safety:** • Local AEs associated with glucose testing **Effectiveness:** ~~• T2D complications (e.g. cardiovascular and microvascular complications including kidney disease, neuropathy/nerve damage, retinopathy/eye disease, amputations/foot ulcers)~~ • Mortality • QoL ~~• Psychological health~~ ~~• Hypoglycaemic or hyperglycaemic events resulting in emergency room visit/hospitalisation~~ **Intermediate/surrogate outcomes:** • Glycaemic control • Glycated haemoglobin (HbA1c) • TIR, TBR and TAR • Number of hypoglycaemic/hyperglycaemic excursions • Glycaemic variability • Change in body weight/BMI *Additional outcomes using linked evidence approach:* **Analytical validity:** • Accuracy, concordance ~~• Monitoring (CGM or SMBG) failure rate~~ **Change in management:** • Adherence to CGM or SMBG • Adherence to treatments ~~• Uptake or alteration of lifestyle interventions (e.g. diet and exercise) and treatment (e.g. glucose-lowering therapy)~~ **Other relevant considerations** ~~• Acceptability, wearability and usability of CGM versus SMBG~~ ~~• Ability to share blood glucose data with physician, relative or carer~~ • Patient/carer satisfaction ~~• Self-efficacy (person's belief in their ability to effectively manage their T2D and achieve their clinical goals)~~ ~~• Work/school absenteeism and daily functioning~~ **Healthcare system outcomes** • Cost, cost-effectiveness • Financial implications (financial impact, overall healthcare costs, etc.)
Systematic review questions: What is the safety, effectiveness and cost-effectiveness of the Dexcom ONE+ CGM system versus SMBG in people aged ≥2 years with T2D and suboptimal glycaemic control who require insulin therapy?	

Abbreviations

AEs = adverse events, **AUSDRISK** = Australian Type 2 Diabetes Risk Assessment Tool, **BMI** = body mass index, **CGM** = continuous glucose monitoring, **FBG** = fasting blood glucose, **HbA1c** = glycated haemoglobin, **OGTT** = oral glucose tolerance testing, **PICO** = population, intervention, comparator, outcome, **QoL** = quality of life, **SMBG** = self-monitoring of blood glucose, **TAR** = time above range, **TBR** = time below range, **T2D** = type 2 diabetes, **TIR** = time in range.

Notes

Not all outcomes in the PICO confirmation were supported by evidence in the literature. Where outcomes were not available, these have a ~~strikethrough~~ line. Where the outcomes are found in modelling or have been added for the ADAR, they are coloured green.

8. Comparator

The nominated comparator is SMBG, which is appropriate for people with T2D who use insulin and is the current standard of care for blood glucose testing for the proposed population in Australia. The frequency of SMBG is individualised, but international guidelines suggest that SMBG is needed 6 to 10 times per day for people with IIT regimens. People with T2D requiring IIT are usually required to test their blood glucose more frequently than those receiving non-IIT. The ADAR quoted evidence that suggests an increased frequency of SMBG is correlated with improved HbA1c in T1D and T2D.

The NDSS provides subsidised blood glucose monitoring strips for SMBG for a 6-month period after initial diagnosis of T2D. Ongoing access, in 6-monthly increments, is available when assessed as clinically necessary and authorised by a general practitioner or diabetes educator. The subsidised SMBG products also all vary substantially in costs.

The number of subsidised glucose test strips that a person with T2D can purchase from the NDSS in a 180-day period is 900 strips; this would only be sufficient to carry out SMBG 5 times per day, which may not meet the needs of people with T2D using IIT. Typically, additional strips purchased during that period would not be subsidised. However, registrants can access more product if their limit has been reached and unique circumstances are present. This restriction on glucose testing strips may encourage people with T2D to deviate from the recommended frequency of SMBG, potentially increasing the risk that glycaemic targets would not be achieved.

Access to some NDSS-subsidised glucose test strips would still be required if a person with T2D is using CGM to account for those periods and circumstances when SMBG is recommended during CGM use. For example, if a person's diabetes symptoms do not match their CGM glucose readings, if their CGM malfunctions, or if their sensor becomes lost or detached.

Currently, there are no subsidised CGM systems available for T2D through the NDSS in Australia. The ADAR noted that some people with T2D may be able to obtain CGM systems privately or through their private healthcare insurance plan.

9. Summary of public consultation input

Consultation input was welcomed from:

1785 – Dexcom ONE continuous glucose monitoring system for people with insulin dependent type 2 diabetes (Australasian Medical & Scientific Limited)	No. of Inputs Received
Organisations (12)	
I am providing input on behalf of a consumer group or organisation. Consumer organisations are not-for-profit organisations representing the interests of healthcare consumers, their families, and carers.	4
I am providing input on behalf of a medical, health, or other (non-consumer) organisation. For example, input on behalf of a group of clinicians, research organisation, professional college, or from an organisation that produces a similar service or technology.	8
Health Professionals (35)	
I am a health professional or health academic working in the area.	35
Consumers (289)	
I have the health condition that this health service or technology is for.	82
I have the health condition that this health service or technology is for and have experience with the proposed health service or technology.	169
I am a parent, partner or another person caring for someone from the above two groups.	33
I am an interested individual who does not fall into any of the above categories.	5
Grand Total	**336**

The organisations that submitted input were:

- The Royal Australian College of General Practitioners (RACGP)
- Pharmaceutical Society of Australia (PSA)
- Primary Care Diabetes Society of Australia (PCDSA)
- Diabetes WA
- Diabetes Alliance
- Diabetes Victoria
- MITO FOUNDATION
- Australian Diabetes Society (2)
- Medtronic Australasia (2)
- Roche Diagnostics Australia (RDA)

Level of support for public funding

There was strong support for public funding of Dexcom ONE continuous glucose monitoring (CGM) system for people with insulin dependent type 2 diabetes. In response to the question 'Do you support public funding for the health service or technology, as it is proposed to be delivered':

- >96% of those with the health condition, their family or carers and other interested individuals answered 'support'. Of those that did not support public funding, the main reason given was that type 2 diabetes was a 'lifestyle' condition.
- All bar two respondents who self-identified as health practitioners or health academics answered 'support'. The two remaining respondents did not answer the question.

Organisational input was supportive of public funding but there were a range of comments in respect of the PICO and implementation (see below).

Comments on PICO

- While respondents were generally supportive of the proposed population, a number saw benefits in broadening the criteria, noting that it should be based on clinical need rather than diabetes type. Specific groups who respondents indicated would benefit from access to CGM included:
    - People with cognitive or physical disability who are unable to manage the logistics of doing and/or understanding blood glucose levels.
    - First nations people at high risk of negative outcomes from their diabetes.
    - Refugee families
    - GDM and T2DM in pregnancy in last trimester
    - T3cDM, those with pancreatic cancer, or had pancreatic surgery, or have pancreatic scarring requiring insulin
    - T2DM on > 1 injection/day, even basal bolus insulin regimes as a minimum.
    - Under 18 year olds with T2D.
- The Primary Care Diabetes Society of Australia proposed an expansion of the eligibility criteria to all people living with diabetes who are on insulin, regardless of HbA1c. They argued that HbA1c is an average, and there are a significant portion of individuals who experience hypoglycaemic events that are missed, as many also have higher glycaemic levels at other times leaving an average that is within target range.
- The Primary Care Diabetes Society of Australia also argued that those with non-insulin dependent diabetes, including newly diagnosed individuals, would benefit from interim access to CGM as a learning tool to help them understand the impact of food and exercise etc on their blood glucose levels. Others proposed subsidising CGM for these individuals but at a lower rate.
- The MITO foundation noted that the eligible populations for CGM should be aligned across MSAC applications 1785 and 1786 and include people with mito-related diabetes.
- Medtronic Australasia considered that the intervention should be amended to include all CGMs approved for diabetes in Australia and that it should reference the requirement for insulin and form or insulin delivery. They asserted that if MSAC establishes the precedent of evaluation by device type for CGM, this will result in multiple brand-specific assessments for the same therapy, increasing MSAC costs and workload. Roche Diagnostics Australia also urged MSAC to clarify as part of its advice to the Minister whether MSAC assessment of other CGMs will be required to enable inclusion on the NDSS and if so, under what circumstances.

Perceived Advantages

- Respondents with experience of CGM outlined a range of benefits including:
    - Enhanced blood glucose monitoring and blood glucose control. Respondents reported they were able to observe how different factors (food, exercise, stress etc) impacted their blood glucose, leading to more informed decisions regarding their health.
    - Improved quality of life by reducing the need for painful finger pricks and providing peace of mind/reduced anxiety. Users of CGM felt empowered to engage in daily activities, such as exercise, driving and sleeping, knowing their glucose levels were being continuously monitored and that they would be alerted if there was an issue.
    - Reduced risk of severe hypoglycaemic episodes and hospitalisation.
    - Real time monitoring, which assisted users to make informed decisions about their food intake and insulin administration.

- Ability to share data with health professionals or loved ones, providing an additional layer of safety and support.

- Clinicians noted that they see improved HbA1c levels in patients utilising CGM and that CGM aids in insulin and medication titration. It also engages people in their own health journey and provides insights that encourage better decision making. These respondents also noted flow on impacts to the health system, with reduced complications and hospitalisations.

Perceived Disadvantages

- While noting the perceived benefits of CGM, many respondents highlighted issues with affordability and accessibility. Respondents noted that the high cost creates a barrier to access, particularly for those on fixed incomes. This creates equity issues. “Only certain groups—typically those in urban areas, with private health cover, or higher incomes—can fully benefit from this technology. First Nations people, those living in rural or remote areas, and individuals from culturally diverse or lower socioeconomic backgrounds may be at a disadvantage, either due to poor access to healthcare services, digital literacy barriers, or simply because they are not aware of the technology or cannot afford it."

- Some additional disadvantages or barriers to use of CGM were also cited:

  - Device reliability, with a small number of respondents noting the potential for sensor inaccuracies, occasional device failures or signal loss
  - Reactions to the adhesive
  - Potential psychological impact, with alerts and 24/7 monitoring feeling overwhelming for some users.
  - Children, teens, or people with sensory sensitivities may find it difficult to wear a sensor continuously.
  - Older adults or those with disabilities may find the need to manage apps, Bluetooth connections, or calibration requirements a barrier.

Support for Implementation and Issues

- Respondents noted the importance of access to dieticians and diabetes educators to ensure that people understand how to use a CGM, interpret the data, and respond in appropriate ways. Several health practitioners and organisations (e.g., the Diabetes Alliance, Diabetes WA) noted the need to increase the number of visits to diabetes educators that attract a rebate per year. Access to endocrinologists was also seen as important.

- The Australian Diabetes Society argued that in implementing this measure there needs to be:

  - appropriate education for general practitioners and practice nurses. It noted that the Society has developed an educational module on CGM and T2D, specifically targeting primary care.

  - financial support for endocrinologists, credentialed diabetes educators, nurse practitioners and general practitioners via a specific MBS item number.

- Several respondents noted the current limited number of professional groups who can certify subsidised CGM access for Type 1 diabetics. The Primary Care Diabetes Society of Australia considered this a barrier to access for many and recommended that certification be broadened to include GPs, practice nurses, Aboriginal health workers, dietitians, and pharmacists. The RACGP argued that GPs are a central part of the care team for diabetes, and often the most accessible, and that, as such, GPs should be allowed to provide access

to CGM without endocrinologist approval. Removing patients from the GP setting they argue, could impact healthcare economics, patient satisfaction and accessibility, particularly in regional and rural areas with more limited access to endocrinologists and CDEs.

- The Australian Diabetes Society was also supportive of GPs and practice nurses being able to sign the CGM access form, as:
    - people with type 2 diabetes are generally managed by general practice and
    - this would address the equity of access issue for people living in regional/remote Australia and for Aboriginal and Torres Strait Islander people.
- It was noted that expanding the list of professionals who can 'certify' access may necessitate some online training for GPs and practice nurses as well as changes to the NDSS form/system.

10. Characteristics of the evidence base

Data from 4 randomised controlled trials formed the main evidence for this application on the direct effects of Dexcom CGM systems on glycaemic outcomes (Table 3). No evidence on change in management was supplied, which was in line with PASC's consideration in the ratified PICO, namely that, if adequate direct from test to intermediate health outcome evidence was available to support the assessment (where the intermediate health outcome was HbA1c levels), a full linked evidence approach may not be necessary. However, PASC further advised that this would require sufficient evidence linking HbA1c levels (i.e. glycaemic outcomes) to more direct and long-term health outcomes. Although evidence linking glycaemic outcomes to more direct health outcomes is not discussed in the clinical section of the ADAR, the economics section of the ADAR contains a brief discussion of the Fremantle Risk equations on complications of T2D (used in the economic model to correlate HbA1C levels to risk of T2D complications) based on the Fremantle Diabetes Study, including some discussion of why the applicant considered it appropriate to apply this to the Australian population.

Table 3: Key features of the included evidence

Study details Funding source Conflicts of interest	Study design/ NHMRC level of evidence Quality appraisal	Study population	Key inclusion criteria	Intervention Comparator	Outcomes	Risk of bias (commentary)	Used in modelled evaluation
DIAMOND (NCT02282397) Conflict: Dexcom funded the trial, but Dexcom had no approval authority for the manuscript before submission. Data management, monitoring and analyses were independent of the sponsor. Conflicts of interest were noted in the publication.	**Study design** RCT, MC, OL 2014–2016 25 centres in the US and Canada 6-month follow-up Level II **Risk of bias** LOW	Aged ≥25 years with T2D treated for ≥1 year with MDIs of insulin, HbA1c level of 7.5–10.0% and SMBG averaging ≥2 times per day	Aged ≥25 years Diagnosis: T2D for ≥1 year Treatment: MDIs of insulin for ≥1 year HbA1c: 7.5–10.0% SMBG frequency: Averaging ≥2 times/day eGFR: ≥45 mL/min/1.73 m2	**Intervention** Dexcom G4 (n=105) **Comparator** SMBG (n=53)	**Primary** HbA1c level Change from baseline in HbA1c **Secondary** HbA1c metrics % time per day in TIR (day and nighttime)/TAR/TBR QoL/PRO measures Metabolic measures Treatment adherence Patient satisfaction **Safety** AEs	Moderate	Yes
2GO-CGM (ACTRN 12621000889853) Conflict: Dexcom funded the trial, but was not involved in the data collection, data analysis or writing of the manuscript. Two authors received honoraria from Dexcom and 2 authors are current members of the	**Study design** RCT, MC, OL 2021–2023 Multiple centres in NZ 3-month follow-up Level II **Risk of bias** LOW	Aged ≥16 years with T2D and HbA1c >8.0% despite taking ≥0.2 units insulin/kg/day for ≥3 months	Aged ≥16 years Diagnosis: T2D Treatment: Taking ≥0.2 units of insulin/kg/day for ≥3 months HbA1c: ≥8.0% SMBG frequency: NS eGFR: NS	**Intervention** Dexcom G6 (n=33) **Comparator** SMBG (n=34)	**Primary** Between-group difference in % change of TIR **Secondary** Change in HbA1c from baseline % time per day in TAR/TBR QoL measure Metabolic measures **Safety** AEs	Moderate	No

Study details Funding source Conflicts of interest	Study design/ NHMRC level of evidence Quality appraisal	Study population	Key inclusion criteria	Intervention Comparator	Outcomes	Risk of bias (commentary)	Used in modelled evaluation
NZ Advisory Board for Dexcom.							
Steno2tech (NCT04331444) Conflict: Devices were supported/funded by Dexcom. One author had received research funding from Dexcom.	**Study design** RCT, SC, OL 2020–2023 Single centre in Denmark 12-month follow-up Level II **Risk of bias** LOW	Aged ≥18 years with insulin-treated T2D with HbA1c ≥7.5%	Aged ≥18 years Diagnosis: T2D for >1 year Treatment: Treatment with ≥1 insulin injections daily for >1 year HbA1c: ≥7.5% SMBG frequency: NS EGFR: ≥45 mL/min/1.73 m2	**Intervention** Dexcom G6 (n=40) **Comparator** SMBG (n=36)	**Primary** Between-group difference in % change of TIR **Secondary** Change in HbA1c from baseline % time per day in TAR/TBR QoL/PRO measures Metabolic measures Patient satisfaction **Safety** AEs	Moderate	Yes
MOBILE (NCT03566693) Conflict: All authors received funding from Dexcom. The study/study devices were funded by Dexcom, but were not involved in the data collection, management, analysis or writing of the manuscript.	**Study design** RCT, MC, OL 2018–2019 15 centres in the US 8-month follow-up Level II **Risk of bias** LOW	Aged ≥30 years with T2D treated with 1-2 daily injections of insulin with HbA1c of 7.8-11.5% and SMBG averaging ≥3 times per week	Aged ≥30 years Diagnosis: T2D Treatment: Treated with 1 or 2 daily injections of long- or intermediate-acting basal insulin for ≥ 6 months HbA1c: 7.8–11.5% SMBG frequency: Averaging ≥ 3 times/week EGFR: NS	**Intervention** Dexcom G6 (n=116) **Comparator** SMBG (n=59)	**Primary** HbA1c level Change from baseline in HbA1c **Secondary** HbA1c metrics % time per day in TIR/TAR/TBR Metabolic measures Patient satisfaction **Safety** AEs	Moderate	Yes

Abbreviations

AEs = adverse events, **DB** = double blind, **HbA1c** = glycated haemoglobin, **MC** = multicentre, **MDIs** = multiple daily injections, **NHMRC** = National Health and Medical Research Council, **OL** = open label, **OS** = overall survival, **PFS** = progression-free survival, **PRO** = patient-reported outcome, **QoL** = quality of life, **RCT** = randomised controlled trial, **SMBG** = self-monitoring of blood glucose, **TAR** = time above range, **TBR** = time below range, **T2D** = type 2 diabetes, **TIR** = time in range.

Methodological considerations

Study selection and data extraction

The listed study selection criteria were uniformly and correctly applied. However, no details were provided regarding how study selection was undertaken (e.g. by one reviewer only, by one reviewer with checking by a second reviewer, or by 2 reviewers independently) or how disagreements were adjudicated in the case that 2 reviewers were involved in the process. It was also unclear how data extraction was undertaken and by whom. Best practice for systematic reviews requires that data extraction forms and procedures be established a priori, regardless of the reviewers' expectations of what the final evidence base will include.

Risk of bias

There were several issues with the risk-of-bias assessment undertaken in the ADAR. The National Heart, Lung and Blood Institute (NHLBI) Study Quality Assessment tool was used to undertake the risk-of-bias assessment (an acceptable tool as per the MSAC technical manual). However, issues were noted with both the assessment and interpretation of the likelihood that biases impact the direction of effect. All studies had baseline imbalances, no study attempted to blind outcome assessors, 2 studies were underpowered to detect differences in their primary outcomes, and intention-to-treat (ITT) analysis was cited as having been conducted when it was not. The assessment group reviewed and informally reassessed the risk of bias during the commentary process. The included trials were considered to be moderate quality instead of good quality, as they were rated in the ADAR.

GRADE

The Grading of Recommendations Assessment, Development and Evaluations (GRADE) approach was applied incorrectly in the ADAR. The intention of the GRADE approach is to create summary tables by outcome. The ADAR included GRADE tables for each individual trial and, therefore, did not provide a coherent summary of the quality of evidence across the included studies

Evidence synthesis

The applicant conducted a meta-analysis for the overall population using data from all 4 studies and for the non-IIT population using data from the MOBILE and Steno2tech trials.

The change in HbA1c was reported at 3 months in the 2GO-CGM trial, 6 months in the DIAMOND trial, 8 months in the MOBILE trial, and 12 months in the Steno2tech trial. Results from different timepoints should not be combined in a standard meta-analysis without clear justification. An example of clear justification might be if there was evidence that the effect of using CGM plateaued at 3 months; this was not discussed in the ADAR and seems unlikely given that the effect size of the Steno2tech trial (with the longest follow-up—12 months) was much larger than all other trials. The results of these meta-analysis should be considered within the context of these limitations and may overestimate the treatment effect.

Minimum clinically important difference

The ratified PICO stated that *'the minimum clinically important difference (MCID) for change in HbA1c levels is reported as a reduction of 0.5% (Kaiafa et al. 2020). PASC noted that the minimum clinically important difference (MCID) for HbA1c in T2D reported in the published literature ranges from 0.3% to 0.5% and that supporting evidence for selection of the MCID for HbA1c would be included in the assessment report'.* In the ADAR, a threshold of 0.3% was used for the HbA1c MCID, referencing 3 articles to support this decision. However, these references are all by the same author, and one article reported data for T1D. This is not adequate

justification to change the long-standing 0.5% threshold for meaningful change, particularly when the harms of doing so have not been explored. The ADAR reported that Dexcom products are associated with 0.4% reduction in HbA1c.

The ADAR also claimed that there is no clear consensus on the magnitude of reduction in HbA1c that is considered clinically meaningful. However, the available evidence suggested otherwise. According to the International Diabetes Federation,[11] NICE guideline in adults[12] and in children and young people,[13] the Australian Diabetes Society,[14] and the Royal Australasian College of General Practitioners,[15] the consensus for the MCID in HbA1c is a change of 0.5%. One of the dangers of therapy changes based on small changes in HbA1c is undue adjustments in treatment.[16] Aggressive attempts to lower HbA1c can sometimes lead to greater variability in blood sugar levels, with frequent swings between high and low. The Pharmaceutical Benefits Advisory Committee (PBAC) has previously not accepted less than 0.5% reduction in HbA1c for a claim of superiority.

The ADAR also claimed that the MCID threshold for meaningful change for time in glycaemic range (TIR) should be 5%—a suggestion that is based on a single study. The assessment group noted that a more thorough search for appropriate publications to establish an MCID for TIR would have been beneficial. There are open access, published systematic reviews reporting correlations between TIR and complications in T2D.[17] Eleven studies in 13,987 patients showed that a 10% increase in TIR was associated with a reduction in albuminuria, severity of diabetic retinopathy, and prevalence of diabetic peripheral neuropathy and cardiac autonomic neuropathy.

These thresholds have implications for the clinical claim; if the lower threshold is not accepted, the clinical claim is not justified. Conversely, if lower, unjustified thresholds are accepted, then Dexcom products are being assessed at a lower threshold than other available products, and may be less effective.

11. Comparative safety

The MOBILE trial reported 2 episodes of severe hypoglycaemia—one in the CGM group and one in the control group. There were no other episodes of severe hypoglycaemia in either group. Similarly, the MOBILE trial reported one patient in the RT-CGM group with diabetic ketoacidosis. There were no other episodes of severe hyperglycaemia in the CGM group or the control group.

[11] International Diabetes Federation. Recommendations for managing type 2 diabetes in primary care, 2017. www.idf.org/managing-type2-diabetes

[12] National Institute for Health and Care Excellence (NICE). Type 2 diabetes in adults: management (NICE guideline). [NG28]. London: NICE; 2015.

[13] National Institute for Health and Care Excellence (NICE) Surveillance of diabetes (type 1 and type 2) in children and young people: diagnosis and management [NG18]. London: NICE; 2022.

[14] https://treatment.diabetessociety.com.au/plan/

[15] The Royal Australian College of General Practitioners. Management of type 2 diabetes: a handbook for general practice. East Melbourne, Vic: RACGP, 2020.

[16] Lenters-Westra, E et al. (2014). Differences in interpretation of haemoglobin A1c values among diabetes care professionals. *Neth J Med* 72(9):462-6.

[17] Raj, R et al. (2022). Time in range, as measured by continuous glucose monitor, as a predictor of microvascular complications in type 2 diabetes: a systematic review. *BMJ Open Diabetes Res Care* 10(1):e002573. doi: 10.1136/bmjdrc-2021-002573.

There were no serious or severe adverse events that were considered to be device related. A very small number of patients experienced minor issues such as skin rashes related to the placement of the CGM sensor. RT-CGM likely has non-inferior safety; no significant safety events related to the device were identified in any trial.

12. Comparative effectiveness

Comparative effectiveness was measured by the difference in mean change in HbA1c from baseline and time in range, which are appropriate outcomes given the alternative assessment framework. It should be noted that no evidence was documented that was specific to the populations identified by the ratified PICO as being populations with high unmet needs for CGM, e.g. Indigenous people, pregnant women, children, people with low social support, and individuals with multiple comorbidities.

HbA1c

The DIAMOND, Steno2tech and MOBILE trials reported a statistically significantly greater reduction in HbA1c (%) for patients monitored with Dexcom RT-CGM versus SMBG (adjusted differences [95% CI]: 0.3% [0.0, 0.5], p=0.022; 0.9% [0.3, 1.4], p=0.002; and 0.4% [0.1, 0.8], p=0.02, respectively). 2GO-CGM did not provide a comparative analysis for this outcome. Two trials reported the proportion of patients achieving a reduction of ≥0.5%. One trial reported a greater proportion of patients with ≥0.5% reduction in HbA1c in the CGM group at 8 months (MOBILE: mean difference 9.9% (0.1%, 21.1%); p=0.05). The other reported a significantly greater proportion of patients with ≥0.5% reduction in HbA1c in the CGM group at 24 weeks (DIAMOND; adjusted mean difference[18] 26% (0, 50); p=0.007).

The applicant conducted a meta-analysis. However, the change in HbA1c was reported at 3-month timepoints in the 2GO-CGM trial, 6-month timepoints in the DIAMOND trial, 8-month timepoints in the MOBILE trial, and 12-month timepoints in the Steno2tech trial. The results of the meta-analysis should be considered within the context of the limitations outlined in Section 10 and may overestimate the treatment effect.

The ADAR claimed that the results of all 4 studies showed that Dexcom RT-CGM is superior to SMBG at a threshold of 0.3% reduction in HbA1c. However, the conventionally accepted threshold for MCID in HbA1c is 0.5%. If MSAC were to reject the 0.3% threshold proposed in this ADAR, 3 of the 4 Dexcom trials would not meet the 0.5% threshold for superiority. The final trial demonstrated a 0.9% difference in HbA1c at 12 months and would be considered an outlier.

Subpopulations

For the IIT subpopulation, the only relevant trial (DIAMOND) reported a statistically significant improvement in HbA1c at 6 months using the applicant's chosen 0.3% threshold. However, this effect was not considered clinically meaningful at the conventional 0.5% threshold for MCID.

For the non-IIT subpopulation, 2 trials reported data relevant to this outcome. One trial reported a statistically significant and clinically meaningful reduction in HbA1c (Steno2tech: 0.9% [0.3, 1.4], p=0.002). However, the trial was underpowered to detect differences in HbA1c; HbA1c was a secondary outcome in this trial and the risk of bias was considered to be moderate. HbA1c was reported at 12 months and the mean difference was between 2 times and 4 times greater than it was for the other included trials. A second trial reported a statistically significant improvement in

[18] For binary outcomes, a mixed-effects logistic regression model was fitted, adjusting for baseline HbA1c level and a random site effect.

HbA1c (MOBILE: 0.4% [0.1, 0.8], p=0.02) using the applicant's chosen 0.3% threshold. However, this effect was not considered clinically meaningful at the conventional 0.5% threshold for MCID.

Table 4: HbA1c (%) and mean (95% CI) difference in change across the RCTs

Study ID (analysis set)	Timepoint	RT-CGM	SMBG	Mean (95% CI) adjusted difference; p value
DIAMOND (ITT) [a]	Baseline	8.5 (0.6)	8.5 (0.7)	-
	12 weeks	−1.0 (−1.2, −0.8)	−0.6 (−0.8, −0.4)	−0.3 (−0.6, −0.1); p=0.005
	24 weeks	−0.8 (−1.0, −0.7)	−0.5 (−0.7, −0.3)	−0.3 (−0.5, 0.0); p=0.022
2GO-CGM (ITT) [a]	Baseline	10.0 (1.7)	9.6 (1.1)	-
	12 weeks	−1.8 (−2.3, −1.3)	−1.6 (−2.1, −1.1)	−0.2 (−0.9, 0.4); p=NR
2GO-CGM (PP) [a]	Baseline	9.8 (1.7)	9.6 (1.1)	-
	12 weeks	NR	NR	−0.4 (−1.0, 0.1); p=0.124
Steno2tech (ITT) [a]	Baseline	8.2 (7.8, 9.1)	8.4 (7.8, 9.1)	-
	6 months	NR	NR	−0.8 (−1.3, −0.2); p=0.005
	12 months	NR	NR	−0.9 (−1.4, −0.3); p=0.002
MOBILE (ITT) [b]	Baseline	9.1 (1.0)	9.0 (0.9)	-
	8 months	−1.1 (1.5)	−0.6 (1.2)	−0.4 (−0.8, −0.1); p=0.02
MOBILE (PP) [b]	Baseline	9.0 (0.9)	9.0 (0.9)	-
	3 months	−1.3 (1.0)	−0.7 (0.9)	NR
	8 months	−1.4 (1.2)	−0.7 (1.2)	−0.6 (−0.9, −0.3); p<0.001

Abbreviations
CI = confidence interval, **DIAMOND (ITT)** = Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes (Intention-To-Treat), **ITT** = intention-to-treat, **MOBILE (ITT/PP)** = MOBILE Application-Based CGM Study (Intention-To-Treat/Per-Protocol), **NR** = not reported, **PP** = per-protocol, **RT-CGM** = real-time continuous glucose monitoring, **SMBG** = self-monitoring of blood glucose, **Steno2tech (ITT)** = Steno 2 Technology Study (Intention-To-Treat), **2GO-CGM (ITT/PP)** = 2nd Generation Continuous Glucose Monitoring Study (Intention-To-Treat/Per-Protocol).
Notes
[a] Data expressed as mean (SD) for HbA1c (%) and mean (95% CI) for change from baseline/for differences in change.
[b] Data expressed as mean (SD) for HbA1c (%) / change from baseline and mean (95% CI) for differences in change.
DIAMOND: A mixed-effects linear model adjusting for baseline HbA1c level as a fixed effect and clinical site as a random effect was used to analyse continuous outcomes. Baseline variables imbalanced between treatment groups were included as covariates.
2GO-CGM: A constrained longitudinal data analysis (cLDA) was used to analyse continuous outcomes. Linear mixed-effects models were fitted with treatment by time (SMBG during run-in, SMBG during RCT or rt-CGM during RCT), stratification variables entered as fixed effects and participants as random effects with unstructured covariance. Models were adjusted for potential differences in medication usage (metformin, basal and bolus insulin, GLP-1 receptor agonists and/or SGLT-2 inhibitors) at weeks 10 to 12.
Steno2tech: A constrained linear mixed model (cLMM) including follow-up time (6 and 12 months) as a fixed effect was used to analyse the repeated measurements with continuous data over time between groups.
MOBILE: A mixed-effects linear regression model adjusting for baseline HbA1c level and a random site effect was used to analyse continuous outcomes.

Time in range

There was a statistically significant increase in TIR (% of time between 3.9–10.0 mmol/L) among patients randomised to RT-CGM in the MOBILE trial at 8 months (15% [95%CI: 8, 23; p<0.001]) and in the Steno2tech trial at 12 months (15.2% [95%CI: 4.6, 25.9; p=0.006]), compared to the control group. There was no statistically significant difference in TIR between RT-CGM and SMBG in either the 2GO-CGM trial or the DIAMOND trial. All trials also reported similar results for time above range (TAR) and time below range (TBR); that is, statistically significant differences for TAR and TBR in MOBILE and Go-CGM trials, and no significant differences in the DIAMOND or Steno2tech trials.

Subpopulations

In the IIT subpopulation, the only relevant trial (DIAMOND) reported no differences between groups for TIR.

In the non-IIT subpopulation, 2 trials were relevant to this outcome. One trial reported a statistically significant and clinically meaningful difference in TIR (Steno2tech: 15.2% [95%CI: 4.6, 25.9; p=0.006]). However, it should be noted that the trial was underpowered to detect differences in the primary outcome (TIR), and the risk of bias was considered to be moderate. A second trial reported a statistically significant improvement and clinically meaningful change in TIR (MOBILE: 15% [95%CI: 8, 23; p<0.001]).

The median time spent in TIR across all RCTs (regardless of subpopulation) is presented in Table 5.

Table 5: Mean (SD)/Median (IQR) % of time (per day) spent in TIR (3.9–10.0 mmol/L) across the RCTs

Study ID (analysis set)	Timepoint	RT-CGM	SMBG	Mean (95% CI) adjusted difference; p value
DIAMOND (ITT) [a]	Baseline (daytime)	55 (43, 67)	55 (43, 70)	-
	Baseline (nighttime)	55 (42, 71)	59 (36, 75)	-
	12 weeks (daytime)	61 (47, 76)	57 (41, 74)	NR
	12 weeks (nighttime)	66 (45, 78)	55 (35, 72)	NR
	24 weeks (daytime)	64 (46, 74)	56 (39, 66)	NR
	24 weeks (nighttime)	63 (39, 78)	57 (38, 73)	NR
2GO-CGM (ITT) [b]	Baseline	37.0 (23.9)	45.2 (21.4)	-
	12 weeks	53.3 (24.2)	44.8 (24.7)	10.4 (−0.9, 21.7); p=0.070
2GO-CGM (PP) [b,c]	Baseline	38.3 (24.3)	45.2 (21.4)	-
	12 weeks	54.6 (23.6)	45.0 (24.9)	12.0 (0.6, 23.4); p=0.039
Steno2Tech (ITT)[b]	Baseline	47.1 (41.6, 52.6)	47.1 (41.6, 52.6)	-
	6 months	61.4 (54.2, 68.5)	48.9 (40.7, 57.2)	12.4 (1.9, 22.9); p=0.021
	12 months	61.7 (54.3, 69.2)	46.5 (38.1, 54.9)	15.2 (4.6, 25.9); p=0.006
MOBILE (ITT)[b]	Baseline	40 (26)	40 (25)	-
	8 months	59 (25)	43 (26)	15 (8, 23); p<0.001

Abbreviations
CGM = continuous glucose monitoring, **CI** = confidence interval, **HbA1c** = haemoglobin A1c, **IQR** = interquartile range, **ITT** = intention-to-treat, **K** = number of studies (in meta-analysis), **NR** = not reported, **PP** = per-protocol, **PSQI** = Pittsburgh Sleep Quality Index, **RCT** = randomised controlled trial, **RT-CGM** = real-time continuous glucose monitoring, **SD** = standard deviation, **SMBG** = self-monitoring of blood glucose, **TBR** = time below range (glucose <3.9 mmol/L), **TIR** = time in range (glucose 3.9–10.0 mmol/L).
Notes
[a] Data expressed as median (IQR) for point estimates. Daytime defined as 6:00 am to <10:00 pm.
[b] Data expressed as mean (SD) for point estimates and mean (95% CI) for difference in change.
[c] PP population excludes 5 participants' data in the RT-CGM group due to ≤70% sensor wear after week 10 of the RCT phase as per international CGM reporting consensus guidelines. Two of the 5 participants stopped using the sensor prior to week 10, and the mean sensor wear for the remaining 3 participants was 49%.

Quality of life measures

Quality of life (QoL) and/or patient-reported outcome (PRO) measures showed no differences between RT-CGM and SMBG (DIAMOND; Steno2tech; 2GO-CGM).

Subjective treatment satisfaction scores reported for RT-CGM groups appeared high (DIAMOND; Steno2tech; MOBILE). This was also reflected in the high adherence rates.

Interpretation and limitations of the clinical effectiveness data

The main limitations of the clinical effectiveness data in presented in the ADAR include:

- The ADAR did not report any details about study selection or data extraction.
- The risk-of-bias assessments for RCTs were conducted incorrectly. The ADAR reported that studies had a low risk of bias despite clear issues within the studies.
- The GRADE assessment was incorrectly applied, resulting in no accurate summary of the quality of evidence across the included studies.
- No justification was provided for conducting a meta-analysis across studies with different timepoints.
- The ADAR used a lower MCID in HbA1c levels (0.3%) than is internationally accepted (0.5%), and the ADAR did not provide sufficient justification for this decision. PBAC has not previously accepted a claim on superiority with a MCID lower than 0.5%.
- Two of the 4 included trials were underpowered to detect differences (i.e. the studies enrolled fewer patients than power calculations suggested would be needed).
- Several outcomes were incorrectly reported to be derived from ITT data.

Clinical claim

The clinical claim made by the applicant is that RT-CGM has superior efficacy and non-inferior safety compared with SMBG. While the evidence provided supports the claim of non-inferior safety, the claim for superior effectiveness is less clear.

The superiority claim depends on the acceptance of the proposed MCID. For the semaglutide submission to PBAC in 2019, the following was reported: '*PBAC has suggested 0.5% to be a clinically meaningful improvement in HbA1c for a superiority claim, with an improvement of 0.3% to 0.4% also considered meaningful for a non-inferiority claim (Semaglutide Public Summary Document November 2019)'*[19]. If MSAC accepts an MCID of 0.3% for change in HbA1c for a superiority claim, as proposed by the applicant, then there is moderate-quality evidence of superiority. If MSAC does not accept the 0.3% threshold, then the claim of superiority is unjustified.

For the IIT subpopulation, there is no evidence that RT-CGM improves HbA1c, reduces time in range, or improves QoL or PROs. For the non-IIT subpopulation, there is conflicting evidence for HbA1c; one trial reported statistically and clinically meaningful change, while the second trial reported statistical differences only. There is stronger evidence for this subpopulation in terms of time in range. However, one of the trials was underpowered to detect differences in TIR, which was the primary outcome (Steno2tech). There were no differences in QoL or PROs.

No evidence was provided for the use of RT-CGM in children, even though the population in the PICO included people aged ≥2 years.

[19] 5.10 Semaglutide Public Summary Document – November 2019 PBAC Meeting. https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2019-11/files/semaglutide-psd-november-2019.pdf

13. Economic evaluation

The cost-effectiveness analysis (CEA) modified the IQVIA CORE Diabetes Model (CDM) (version 10) to capture and evaluate the direct healthcare system costs and health outcomes associated with the RT-CGM over a lifetime time horizon, assumed to be 50 years. An Australian healthcare system perspective was taken.

The IQVIA CDM is a generic web-based microsimulation model designed to estimate the cost-effectiveness of diabetes care interventions with adaptability to national and regional care-specific settings. The IQVIA CDM has been extensively evaluated and validated, and its reliability in informing reimbursement decisions has been internationally tested and accepted. Therefore, use of the IQVIA CDM is appropriate. Baseline clinical characteristics and Monte Carlo simulation methods are used to simulate 2 populations (IIT and non-IIT), each containing 1,000 unique adults with uncontrolled diabetes. The 2 populations were modelled separately, and an overall population (containing IIT and non-IIT) was not evaluated.

The properties of a microsimulation model allow for each individual to experience a unique 'journey' through the model. This means that the heterogeneity of T2D was appropriately captured and quantified.

Upon model entry, an individual was assigned to either the RT-CGM arm or the SMBG arm. Those receiving RT-CGM experienced a treatment effect in the form of a reduction of HBA1c. The individual's HBA1c, along with other clinical characteristics and disease histories, were 'fed' into a set of risk equations to estimate the 1-year probability of a diabetes-related complication. The Monte Carlo methods were employed to determine whether the event occurred.

If an event occurred in that cycle, the individual would be at higher risk of mortality. Focus events, event histories and clinical characteristics of the individual, were 'fed' into the mortality risk equations to estimate the probability of mortality in that year. Monte Carlo methods were employed to determine whether mortality occurred.

The ADAR used the most recent (at time of lodgement) version of the IQVIA CDM: version 10. This model using the UKPDS-82 equations has been extensively validated against clinical and epidemiological data and was used to compare RT-CGM with SMBG in T1D. Therefore, it was appropriate for the analysis. However, the ADAR used an Australian adaptation of the UKPDS-82 equations to model cardiovascular (CV) complications; namely, the Fremantle Diabetes Study (Davis et al. 2010) and an Australian adaptation of UKPDS mortality equations by Hayes et al. (2013). It is unclear what risk equations were used for the other types of diabetes complications, nor whether the model has been similarly validated when using these Australian adaptations.

The model structure is presented in Figure 1 (McEwan et al. [2014], as presented in the ADAR) and Figure 2 (adapted by the assessment group from the information provided in the ADAR and McEwan et al. [2014]). Figure 2 clarifies what data sources (in particular which risk equations) were used for which event rate, and where the methods used are undefined.

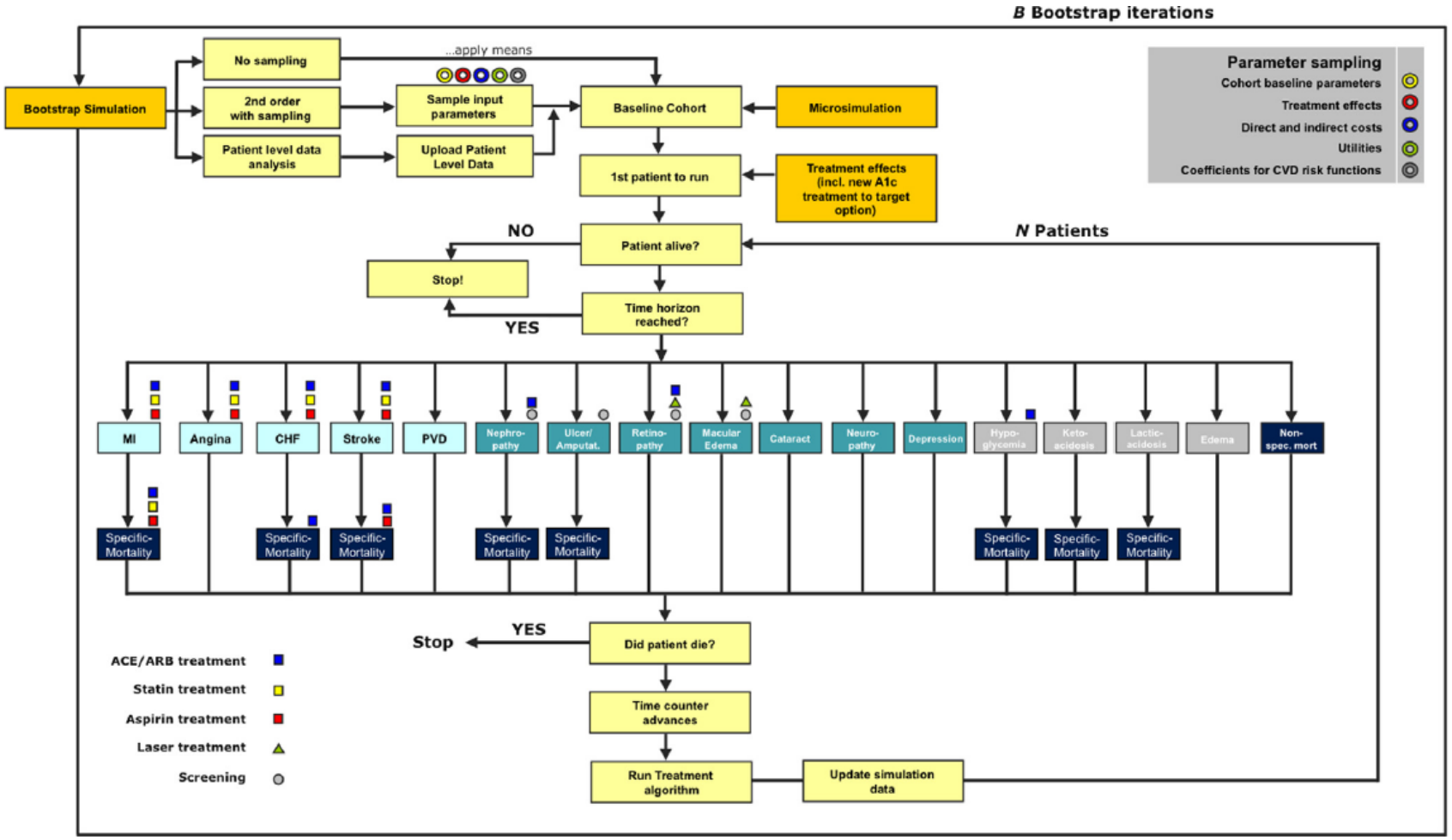
The base-case analyses of the IIT and non-IIT populations were performed independently. Each analysis was a second-order probabilistic analysis, with 1,000 simulated individuals over 1,000 lifetimes. Model parameters were sourced mainly from literature. Table 6 provides a summary of the economic evaluation and an overview of the model parameters.

Table 6: **Summary of the economic evaluation**

Component	Description
Perspective	Australian health care system. No indirect/societal costs are captured.
Population	Two populations of individuals with T2D who are treated with basal insulin and suboptimal glycaemic control confirmed by laboratory measured HbA1c levels of >7.0% for adults and >6.5% for children and adolescents. 1. IIT: who are treated with basal insulin and rapid-acting insulin. 2. Non-IIT: who are treated with basal insulin with no regular use of rapid-acting insulin.
Prior testing	Not relevant to the economic model
Comparator	SMBG = current standard of care
Type of analysis	Cost-utility analysis
Outcomes	Life years gained, quality-adjusted life years
Time horizon	Lifetime
Computational method	Microsimulation
Generation of the base case	A modelled approach using the IQVIA CDM
Health states	As specified in CDM; 17 interdependent submodels inform the modelling of complication incidences (myocardial infarction, congestive heart failure, stroke, neuropathy, ulcer/amputation/hypoglycaemia, ketoacidosis, lactic acidosis, angina, peripheral vascular disease, retinopathy, macular oedema, cataract, neuropathy, depression, oedema and non-specific mortality).
Cycle length	Annual
Transition probabilities	HbA1c reductions offered by RT-CGM vs SMBG result in less complication risks as modelled by CDM.
Discount rate	5% per annum as per MSAC preference
Software	IQVIA CDM (CDM, v10)

Abbreviations
CDM = CORE Diabetes Model, **HbA1c** = glycated haemoglobin, **IIT** = intensive insulin therapy, **MSAC** = Medical Services Advisory Committee, non-**IIT** = non-intensive insulin therapy, **SMBG** = self-monitoring of blood glucose, **RT-CGM** = real-time continuous glucose monitoring.

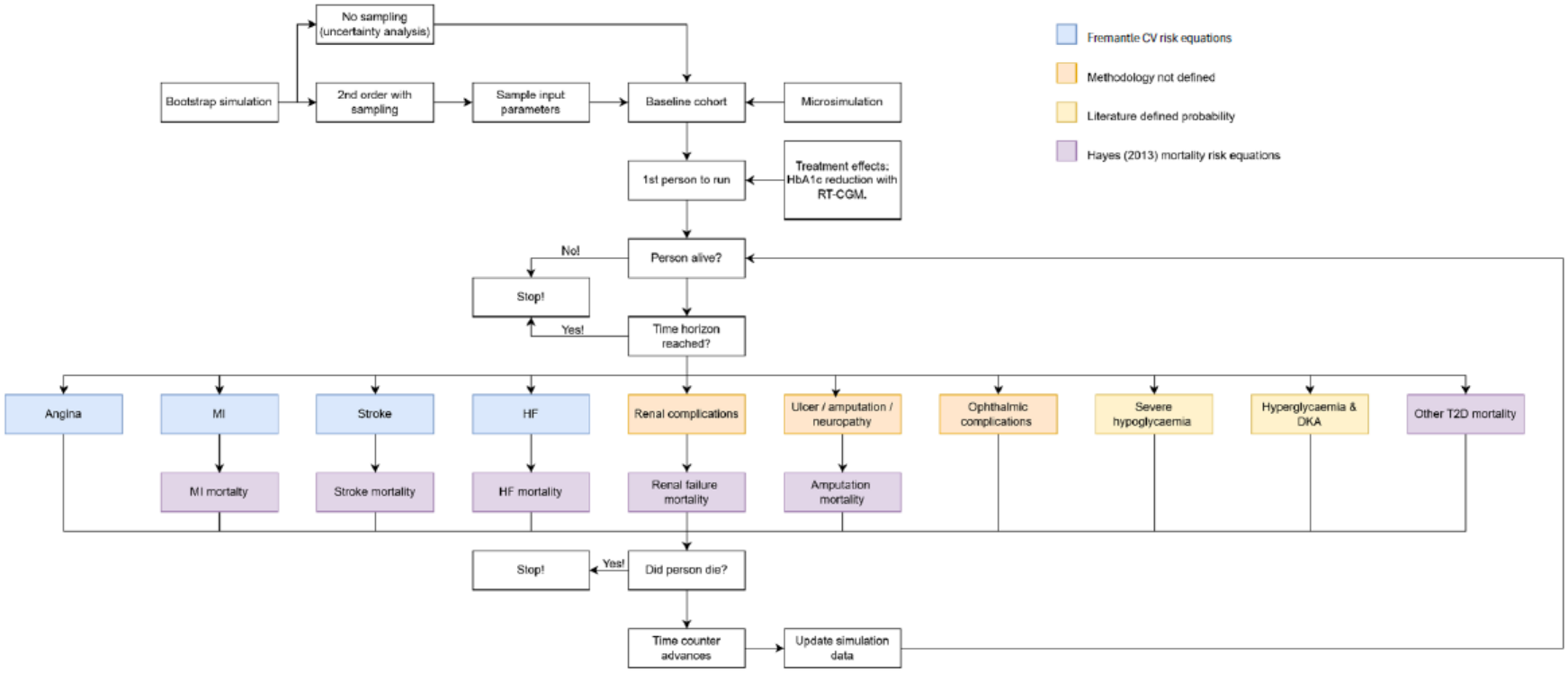
Figure 1 Structure of the IQVIA CDM (from the ADAR, originally taken from McEwan 2014)



Abbreviations

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; CHF = congestive heart failure; CVD = cardiovascular disease; MI = myocardial infarction; PVD = peripheral vascular disease

Figure 2 Assessment group model structure (adapted from ADAR and McEwan (2014))



CV; cardiovascular, DKA; diabetic ketoacidosis, HbA1c; glycated haemoglobin, HF; heart failure, MI; myocardial infarction, RT-CGM; real time glucose monitor
Adapted from McEwan (2014)

Population

The PICO outlined the population as those aged ≥2 years. It is unlikely that these individuals were captured in the model because the mean age (SD) in the model is 64.5 (SD:12.2). The ADAR did not present any clinical or economic evidence for children or adolescents.

The ADAR presented economic results for the IIT and non-IIT populations separately. The outcomes for all people with uncontrolled T2D (IIT and non-IIT combined) were not presented.

Baseline characteristics

Baseline characteristics were informed by published literature. Demographic and clinical parameters were primarily sourced from 2 US-based studies: a retrospective cohort study of a US claims database (Karter 2021) and a 17-year-old US- and Canada-based study with data from 2001 to 2005 (Gerstein et al. 2008). However, Gerstein et al. (2008) was not described in the ADAR. The ADAR justified use of US data by stating that there was no single Australian study to inform all risk-factor variables, and it was preferential to use one source. The ADAR stated that Australian data were similar. However, no comparison was presented, nor was a scenario conducted with Australian data.

Cultural diversity data were informed by Australian Bureau of Statistics from 2021, and data on screening for eye disease and renal disease were informed by Isitt et al. (2022), which was an economic evaluation of RT-CGM in T1D. No subgroups by age were considered.

Baseline characteristics extracted from Karter 2021 were predominantly for an IIT population. It was assumed that baseline characteristics were equivalent for both the IIT and non-IIT populations. The ADAR did not state whether this assumption was validated by clinical experts. This was justified by stating that the Steno2tech and MOBILE trials (which were comprised predominantly of non-IIT participants) had similar HbA1c level, age and duration of diabetes compared with Karter (2021) (Table 7). The baseline characteristics from Karter (2021) informed the mean HbA1c, age (years, SD), and diabetes duration in the base case. Table 7 provides a summary of the baseline characteristics of these trials. No subgroups by age were considered. Figure 3 presents a crude comparison of the means and 95% confidence intervals, derived using the standard deviations and the sample sizes.

<u>HbA1c</u>

There appears to be overlap between the 95% confidence interval for HbA1c in Karter (2021) and the Steno2tech interquartile range. However, given the difference in the types of averages, no firm conclusion can be drawn on statistical significance. There was no overlap between the HbA1c 95% confidence intervals for MOBILE and Karter (2021), suggesting a significant difference between the baseline HbA1c estimates.

<u>Mean age</u>

The age in Karter (2021) appears to be significantly higher compared with MOBILE and Steno2tech.

<u>Mean diabetes duration</u>

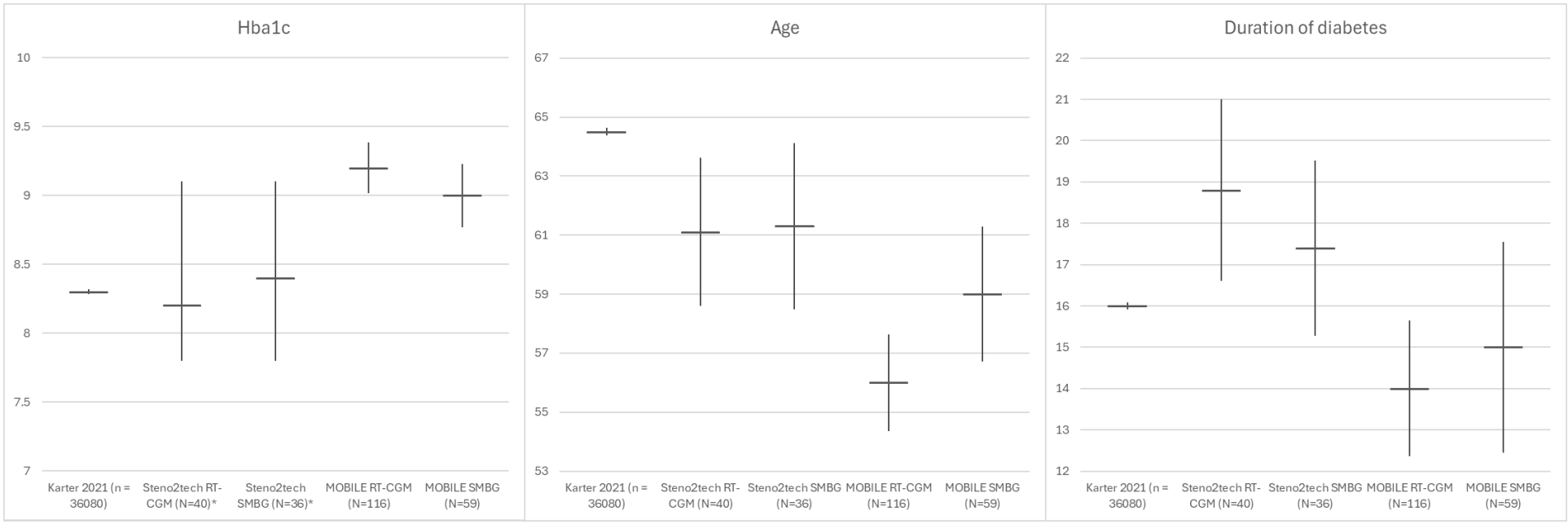
The duration of diabetes for Karter (2021) overlaps with the tails of the 95% confidence intervals for MOBILE and Steno2tech SMBG arm of the analysis.

Table 7: **Summary of the trial baseline characteristics**

	Karter 2021 (n=36,080)	Steno2tech		MOBILE	
		RT-CGM (n=40)	SMBG (n=36)	RT-CGM (n=116)	SMBG (n=59)
HbA1c (%, SD/IQR)	8.3 (1.6)	8.2 (7.8, 9.1)	8.4 (7.8, 9.1)	9.2 (1.0)	9.0 (0.9)
Mean age (years, SD)	64.5 (12.2)	61.1 (8.1)	61.3 (8.6)	56 (9)	59 (9)
Mean diabetes duration (years, SD)	16 (8.8)	18.8 (7.1)	17.4 (6.5)	14 (9)	15 (10)

Abbreviations
HbA1c = glycated haemoglobin, **IQR** = interquartile range, **SD** = standard deviation, **SMBG** = self-monitoring of blood glucose, **RT-CGM** = real-time continuous glucose monitoring.

Figure 3: Comparison of mean and 95% confidence intervals (*median and interquartile range) of HbA1c, age and duration of diabetes



Treatment effect

The model used the reduction in HbA1c as the treatment effect, based upon clinical evidence demonstrating a statistically significant HbA1c benefit with RT-CGM. In particular, the treatment effect of RT-CGM was assumed to reduce HbA1c levels compared with SMBG. As a result, patients on RT-CGM had a lower probability of a CV event relative to those using SMBG, given that HbA1c was a covariable in the CV risk equations. Occurrence of specific events increased mortality risk in the cycle in which the event occurred and for future events. These interactions are appropriate. Patients on RT-CGM also had a lower probability of other diabetic complication events, presumably based on other risk equations using HbA1c as a covariable.

The ADAR assumed a treatment effect of 3 years, holding the HbA1c reduction in the RT-CGM arm constant for 3 years whilst the HbA1c increased by 0.15% per year in the comparator arm. After this time, it was assumed HbA1c would increase by 0.15% per year in both arms. The ADAR stated that longitudinal studies show improvements in glycaemic outcomes for up to 10 years. The commentary noted that the ADAR did not explore the length of the treatment effect in the uncertainty analysis. Lengthening the treatment effect would not change the conclusion with the current model; that is, Dexcom ONE+ would remain the dominant treatment option. Shortening the treatment effect would shift the results in favour of SMBG. The commentary noted that the ADAR also did not explore the rate of HbA1c increase in an uncertainty analysis, nor did it explore a scenario in which the HbA1c of the intervention arm become equivalent to the comparator arm. This would shift the results in favour of SMBG; however, the magnitude of this shift is uncertain. Reporting on this scenario would reduce the uncertainty regarding the long-term effect of Dexcom ONE+.

In response to the above queries, the pre-ESC response reported on the results of additional sensitivity analyses where the convergence of HbA1c between the two treatment arms was considered as well as providing other analyses requested by the assessment group. These are summarised in Table 13 below.

Version 10 of the CDM allows for TIR to be used to inform treatment effect. However, the ADAR did not explore scenarios around this, despite the claim of superiority in TIR.

<u>IIT population</u>

The clinical section of the ADAR stated that DIAMOND reported a 0.3% reduction in HbA1c for the IIT population. Instead of using this value as the treatment effect for the IIT population, the ADAR used real-world evidence from Karter et al. (2021), which reported a 0.56% reduction in HbA1c (almost a twofold larger treatment effect). The population of Karter et al. (2021) consisted of people who made RT-CGM-related durable medical equipment insurance claims in the US between 2015 and 2018. A 0.3% reduction in HbA1c was investigated in a scenario analysis. The overall conclusion (i.e. that Dexcom ONE+ was dominant) did not change.

Using real-world evidence (from a community setting) to inform the treatment effect would more accurately show how people with T2D interacted with the technology. However, at the time of study publication, there were several brands of CGM available in the US. The study did not report brand-specific HbA1c reductions, nor discuss the market share of Dexcom ONE+. Furthermore, US data were used. The Commentary noted that there are differences in the US and Australian healthcare systems, which was highlighted by Blumenthal et al. (2024)[20]: Australia was ranked in the top 3 healthcare system (of 10 countries) while the US ranked last, with barriers preventing

[20] Blumenthal et al., Mirror, Mirror 2024: A Portrait of the Failing U.S. Health System — Comparing Performance in 10 Nations (Commonwealth Fund, Sept. 2024). https://doi.org/10.26099/ta0g-zp66

access to healthcare. Therefore, the commentary considered that there is uncertainty as to whether the US claims data can be extrapolated to or is reflective of an Australian setting.

Non-IIT population

In the non-IIT population, the clinical section reported outcomes of a meta-analysis in MOBILE and Steno2tech, which showed a significant reduction in HbA1c with RT-CGM (0.6% [95% CI: 0.12, 1.08]). The product assessed in this ADAR (Dexcom ONE+) is relatively new, and appropriate clinical data were not available. Therefore, the ADAR used data from Dexcom G-series products and claimed that this will underestimate the treatment effect. However, the commentary noted that no data to substantiate this claim were presented.

Risk of severe hypoglycaemia and hyperglycaemia events

Severe hypoglycaemic events (SHE) were informed by the difference in the proportions of emergency room visits or hospitalisations reported in US claims data of fully insured patients extracted from the Kaiser Permanente Health Maintenance Organisation by Karter et al. (2021). The hyperglycaemic events were informed by the difference in the proportions of diabetic ketoacidosis (DKA) hospitalisation events reported in the same non-randomised retrospective cohort study by Karter et al. (2021). Given the differences in the Australian and US health states, use of this source was not considered appropriate by the Commentary. *However, ESC concluded otherwise (refer to ESC discussion).*

Karter et al. (2021) showed people on RT-CGM experienced a change in the probabilities of SHE and DKA events of −4.0% (95% CI: −7.8% to −0.2%, p=0.04) and −2.5% (95% CI: −5.1% to 0.2%, p=0.07), respectively, compared with SMBG. Therefore, in the IIT population, the ADAR assumed a rate of 4.0% and 2.5% in the SMBG arm and 0% in the RT-CGM arm. The commentary considered that this approach appropriately captured the difference in outcomes associated with these events; however, the commentary considered that it was inappropriate to assume individuals using Dexcom ONE+ would never experience SHE or DKA during their lifetimes. Furthermore, the difference between DKA events in the RT-CGM and SMBG arms was not statistically significant. The ADAR did not discuss this.

For the non-IIT population, the ADAR halved the probability of SHE and DKA events in the SMBG arm to 2.0% and 1.25%, respectively. The ADAR noted that there was limited evidence regarding frequency and impact of hypoglycaemic episodes in a non-IIT population, but stated that the assumption was based on a review of hypoglycaemic outcomes in patients with T2D (Rosenstock et al. [2024]) and noted this was further supported by US survey data (Harris 2023).

These assumptions had a large impact on the cost savings. While not directly explored in sensitivity analyses, removal of the probabilities of these events in the comparator arm resulted in halving the cost savings in both populations.

Cardiovascular risk equations

The ADAR cited Davis et al. (2009), which highlighted that the UKPDS equations had poor applicability to the Australian T2D patient population. Therefore, the ADAR used the Australian-specific Fremantle CV risk equation to predict cardiovascular disease (CVD) complications.

This risk equation was developed based on the Fremantle Diabetes Study cohort, considering the Australian context and cultural background. The cohort contained 1,240 people with T2D between 1993 and 1996 (follow-up of 5,570 patient-years). The final model contained 8 covariables. It was shown to be a valid and accurate engine with good calibration and discrimination for predicting CVD (both stroke and coronary heart disease) in a validation dataset of 180 people from Australia with T2D.

Age, sex, history of CVD (prior to or post model entry), urinary albumin, creatinine ratio, HbA1c (%), high-density lipoprotein (HDL) cholesterol and race are covariables in the Fremantle CV risk equation. These were informed by baseline or updated clinical characteristics of each individual in each cycle. These data were 'fed' into the risk equation and output a 5-year probability of a CV event. Changes to the covariables (i.e. increased age / HbA1c) will increase the probability of a CV event.

The 5-year probability was subsequently converted into a 1-year probability of a CV event. A weighting algorithm was used to tease out specific CV events (myocardial infarction [MI], angina, congestive heart failure and stroke) from the 1-year CV event probability. The applicant did not provide the algorithm used to determine probabilities of these events. Therefore, there is uncertainty around whether these were appropriately derived.

In the uncertainty analysis, the ADAR explored the UKPDS 82 CV risk equation (no changes to other inputs) and found no change in the conclusion.

A key positive of this approach was that the Fremantle Diabetes Study allowed for more applicability to the Australian population. The risk equations include an explicit covariate to adjust for an individual being Aboriginal. This captures the social disparities (e.g. level of remoteness and socioeconomic disadvantage) that drive racial differences in T2D. Davis (2009) validated these risk equations with a validation data set.

However, in the base case and scenario analyses, the ADAR did not provide detail on how other microvascular and macrovascular complications were modelled (including ophthalmic and renal disorders).

Mortality risk equations

Occurrence of specific events (MI, stroke, heart failure, renal failure and amputation) in a particular cycle increased a person's probability of death beyond that of an individual who had not experienced an event.

Mortality risk equations were employed to determine a per-cycle (1 year) probability of death. The ADAR used combined Western Australian mortality risk equations, for people with T1D and T2D, published by Hayes et al. (2013). This allowed for outcomes to be extrapolated to an Australian population. These risk equations were built using historic data (1990 to 1999) from 13,844 people with either T1D (13%) or T2D (87%).

Covariables in the risk equations were sex, age, the focus event (e.g. if an MI occurred in that cycle, the MI would be the focus event). History of chronic events (stroke, heart failure and amputation) are other covariables (i.e. the event occurred in a previous cycle or prior to model entry).

The study showed that the Western Australian population had longer life expectancy and quality-adjusted life years (QALYs) predicted after an MI but shorter life expectancy and QALYs for other complications.

Use of UKPDS mortality in combination with the UKPDS 82 CV risk equation was investigated in a scenario analysis. It was not investigated independently. Use of the UKPDS CV and mortality risk equations caused the conclusion to change (i.e. RT-CGM was cost-effective but not dominant).

HRQoL inputs

The ADAR used published literature to inform health-related quality of life (HRQoL). The baseline utility and utility decrements were from a systematic literature review and meta-analysis

(Beaudet 2014). The ADAR assumed an equivalent baseline utility value in both IIT and non-IIT populations.

The utility decrements for all events were applied the year the event occurred. Long-term impact on HRQoL as a result of a chronic complications (e.g. MI, stroke, blindness, amputation) was not included, even though long-term event-specific costs were included in the model. Beaudet (2014) used the EuroQol 5-dimension 3-level questionnaire to gather utility and decrements. Most studies in the meta-analysis used a UK tariff. The utility decrement for DKA was informed by a Chinese study in people with T1D (Zhao et al. 2021).

The ADAR did not state whether utilities were applied additively or multiplicatively. The ADAR also did not state whether any adjustments were made to align the utility decrements with the Australian population.

The ADAR applied additional utility decrement for frequent finger pricks of 0.03, based upon a UK-based study by Matza (2017). Matza (2017) reported higher baseline rates for diabetes than used generate the model (0.851 vs 0.785). No age, sex or country adjustments were made. The 0.03 value is the difference between the derived utilities for sensor-based glucose monitoring and conventional glucose monitoring. Therefore, it was not explicitly rated by individuals and was not limited to the impact of finger pricking. The ADAR claimed that this was a conservative estimate because finger pricking is likely to occur more frequently in the IIT population. However, this decrement implies that regular finger pricks are modelled as roughly half as impactful as either having a heart attack (−0.03 vs −0.055) or being blind (−0.03 vs −0.074). It is also comparable with macular oedema or diabetic retinopathy (−0.03 vs −0.04). For the non-IIT population, the ADAR assumed that the magnitude of HRQoL benefit was half of that assumed for the IIT analysis (0.015).

These decrements solely impacted the QALYs generated in the comparator arm and had no impact at all on the treatment arm. The impact on model outputs of omitting this decrement was not presented in the ADAR.

Cost inputs

RT-CGM

The sensor must be replaced after 10 days of use. Each pack contains 3 sensors at a requested price of $**REDACTED**, and each person on average required 12.17 packs per annum, resulting in a calculated total annual cost of $**REDACTED**. The ADAR acknowledged early replacement of sensors was a rare occurrence. However, these occurrences were offset by the assumption of 100% adherence/compliance to the sensor replacement schedule, which the ADAR stated was unrealistic. The commentary considered that this was appropriate.

SMBG

The ADAR highlighted the price difference between brands of blood glucose monitoring strips and that the true purchase price was not available in the public domain. It conservatively selected a low-costing brand, whereby a pack of 100 strips cost $30. The ADAR identified that the general patient co-payment was $15, but noted that it was unclear what the full cost of 100 strips was. Given the limited information available, the ADAR assumed that $15 covered the true economic cost of 100 strips, but acknowledged that this assumption may be biased against RT-CGM.

The DIAMOND trial and the MOBILE study informed the mean number of finger prick tests per day for the IIT population (3.8 per day) and the non-IIT population (2 per day), respectively. The total annual cost was derived to be $208.05 and $109.50 for IIT and non-IIT populations, respectively.

It is anticipated that the number of SMBG strips under controlled conditions in clinical trials will differ from those observed in the real-world setting (when people are not being observed).

The number of SMBG strips in the real world setting may be lower than 3.8 per day, which may result in inadequate management of T2D.

The retrospective cohort study (Karter et al. [2021]), which showed a larger treatment effect of RT-CGM than the DIAMOND RCT, was used to inform the modelling for the IIT population. However, Karter et al. (2021) did not report the number of finger pricks per day. The ADAR quoted evidence that suggests an increased frequency of SMBG is correlated with improved HbA1c in T1D and T2D. Use of the number of SMBG strips in DIAMOND and the treatment effect in Karter et al. (2021) in the IIT population was not appropriate as the cost of SMBG may have been over estimated, skewing the results in favour of RT-CGM.

The modelled number of SMBG strips used falls below the lower bound of recommendations cited in the ADAR, which was between 6 and 10 for the IIT population. The uncertainty analysis investigated the number of SMBG strips per day and found no change in the overall conclusion. The ADAR quoted evidence that suggests an increased frequency of SMBG is correlated with improved HbA1c in T1D and T2D. However, in the aforementioned scenarios, the ADAR did not investigate the correlation between increased SMBG tests and efficacy (i.e. whether those adhering to the recommendations of 6 to 10 SMBG strips per day were more likely to have more adequately controlled diabetes than those on 3.8 or fewer strips per day). Increasing the number of strips and accounting for the decreased the change in HbA1c would likely have marginally increased the cost of SMBG and the overall incremental costs, and QALYs would decrease because RT-CGM would be less effective compared with SMBG.

Complication costs

The cost estimates were sourced from Australian publications on the modelled cost-effectiveness of RT-CGM (Isitt 2022; Pease 2022), supplemented by Zhang (2023) for peripheral arterial disease of lower extremities (i.e. ulcer and amputation). The ADAR inflated all cost inputs to 2024 values. However, it did not trace the cost back to the source, preferring to inflate a cost that had previously been inflated. The ADAR acknowledged that many of the cost estimates did not specifically relate to diabetic patient population. Costs of medication use (aspirin, statin and angiotensin-converting enzyme inhibitor) were updated to reflect the current subsidies on the Pharmaceutical Benefits Scheme. For chronic complications, costs were accrued in the year of event and each subsequent year.

Results

The base-case analysis was a second-order probabilistic analysis, with 1,000 simulated individuals over 1,000 lifetimes. The ADAR did not present confidence intervals, a scatter plot of probabilistic iterations, or the percentage of iterations that are cost effective (information relating to the number of iterations before the results converge).

The ADAR highlighted that RT-CGM was dominant (cost saving and QALY incurring) for both populations. Despite being more costly, RT-CGM costs were offset by reductions in microvascular and macrovascular complications costs over a lifetime horizon. This interpretation was consistent in both populations. The results for the IIT and non-IIT populations are presented in Table 8 and Table 9, respectively.

The ADAR stated that ‘use of RT-CGM result in reduced micro- and macrovascular complications, as well as severe acute events of diabetes for the overall population of interest, regardless of their racial characteristics’. However, the key drivers of the model were not discussed in detail. During the ADAR process, the assessment group analysed key drivers of the model (Table 10).

There are some uncertainties associated with the QALY benefits, the number of SMBG strips per day and the treatment effect, including the model duration. The ADAR stated that a stepped sensitivity analysis was conducted, which varied the model duration between 1 and 30 years.

The results of key univariate sensitivity analyses are summarised in Table 11 and Table 12.

As noted previously, additional sensitivity analyses presented in the pre-ESC response are summarised in Table 13 below. Additional sensitivity analyses provided by the applicant in its pre-MSAC response to illustrate the impacts on ICERs with and without HbA1C treatment effects are summarised in Table 14.

Table 8: Results of the economic evaluation (IIT)

Base-case costs and outcomes	RT-CGM	SMBG	Difference
Glucose monitoring costs, AUD	**Redacted**	**Redacted**	**Redacted**
Management (preventative screening, medication) costs, AUD	3,026	2,984	42
CV complications, AUD	140,862	146,701	−5,839
Renal complications, AUD	48,242	62,860	−14,617
Ulcer/amputation/neuropathy complications, AUD	12,704	13,859	−1,155
Ophthalmic complications, AUD	32,189	37,316	−5,127
Severe hypoglycaemia (req. medical assistance), AUD	0.00	3,861	−3,861
Hyperglycaemia and DKA, AUD	0.00	3,224r	−3,224
Total direct (medical) cost, AUD	**Redacted**	**Redacted**	**Redacted**
Life years	10.481	10.393	0.088
QALYs	7.761	7.200	0.561
ICER per QALY gain	**DOMINANT**		

Abbreviations
AUD = Australian dollars, **CV** = cardiovascular, **DKA** = diabetic ketoacidosis, **ICER** = incremental cost-effectiveness ratio, **IIT**= intensive insulin therapy, **QALY** = quality-adjusted life year, **RT-CGM** = real-time continuous glucose monitoring, **SMBG** = self-monitoring of blood glucose.

Table 9: Results of the economic evaluation (non-IIT)

Base-case costs and outcomes	RT-CGM	SMBG	Difference
Glucose monitoring costs, AUD	**Redacted**	**Redacted**	**Redacted**
Management (preventative screening, medication) costs, AUD	3,043	2,984	58
CV complications, AUD	141,626	146,941	−5,315
Renal complications, AUD	48,327	62,717	−14,390
Ulcer/amputation/neuropathy complications, AUD	12,666	13,893	−1,228r
Ophthalmic complications, AUD	32,280	37,209	−4,929
Severe hypoglycaemia (req. medical assistance), AUD	0.00	1,931	−1,931
Hyperglycaemia and DKA, AUD	0.00	2,159	−2,159
Total direct (medical) cost, AUD	**Redacted**	**Redacted**	**Redacted**
Life years	10.481	10.392	0.089
QALYs	7.529	7.211	0.318
ICER per QALY gain	**DOMINANT**		

Abbreviations
AUD = Australian dollars, **CV** = cardiovascular, **DKA** = diabetic ketoacidosis, **ICER** = incremental cost-effectiveness ratio, **IIT** = intensive insulin therapy, **QALY** = quality-adjusted life year, **RT-CGM** = real-time continuous glucose monitoring, **SMBG** = self-monitoring of blood glucose.

Table 10: Key drivers of the model

Description	Method/value	Impact: Base-case ICER: Dominant Incremental costs: −$Redacted Incremental QALYs: 0.561
Renal complications	This was not varied in the uncertainty analysis. However, relative risk of end-stage renal disease 30% lower for the intervention versus the comparator. The cost difference between arms that was associated with renal complications was $14,617 rand $14,360 for IIT and non-IIT, respectively. These costs were instrumental in offsetting the higher costs of RT-CGM.	The ADAR did not vary renal complications nor describe how they were implemented in the model.
Risk equations (complications)	The base-case model used the Australian adaptation of the cardiovascular UKPDS-82 to allow for generalisability to the Australian population. The ADAR conducted a scenario using the UKPDS-82 complication risk equations with the Australian mortality risk equations.	The ICER in this scenario remained dominant for both populations. Incremental costs reduced by 1/3.
Risk equations (mortality)	The base-case model used the Australian adaptation of the mortality UKPDS risk equations, to allow for generalisability to the Australian population.	It is important to note that the ADAR did not conduct a scenario with the UKPDS mortality risk equations and the Australian adaptation of the cardiovascular UKPDS-82.
Risk equations (complications and mortality)	A scenario was conducted using the UKPDS-82 complication risk equations with the UKPDS mortality risk equations.	The ICERs in this scenario remained cost effective but became cost incurring: IIT ICER: $**Redacted**[1] per QALY gained Non-IIT ICER: $**Redacted**[2] per QALY gained QALYs decreased by 1.5 for each arm, which does not make sense given the conclusions from Hayes et al. (2013) that life expectancy in the UK post-complication was higher than Australia. The ADAR did not discuss this further.
HbA1c treatment effect (IIT)	The base-case reduction in HbA1c (0.56%) was informed by a study of US claims data by Karter et al. (2021): • Aligned reduction in HbA1c with DIAMOND clinical trials (0.3%) • Percentage change in HbA1c ±30%	The ICER in this scenario remained dominant. • Decreasing the mean HbA1c effect to 0.3% reduced the cost difference from −$**Redacted** to −$**Redacted** (cost saving decreased). • Decreasing HbA1c to 0.3% decreased QALY difference from 0.561 to 0.540 (fewer QALYs were gained). • Increasing or decreasing the change in HbA1c by 30% showed an almost proportional effect on the incremental cost. Decreasing HbA1c by 30% reduced the incremental cost by 32% and increasing HbA1c by 30% increased the incremental cost by 22%.
HbA1c treatment effect (non-IIT)	Note that the base case was informed by a meta-analysis of MOBILE and Steno2tech outcomes (reduction in HbA1c of 0.6%). These scenarios change in HbA1c with the aforementioned clinical trials. • Reduction in HbA1c: 0.4% (MOBILE trial) • Reduction in HbA1c: -0.9% (Steno2tech study)	The ICER in this scenario remained dominant. There was a large change in incremental costs. The HbA1c is, therefore, very influential on the costs. This is likely because of the impact of HbA1c on clinical complications, and the long-term costs associated with clinical complications. Given that no long-term utility decrements are applied to chronic complications, there was only a small change in QALYs.

Description	Method/value	Impact: Base-case ICER: Dominant Incremental costs: −$Redacted Incremental QALYs: 0.561
		• Decreasing HbA1c reduction to 0.4% decreased cost difference to −$**Redacted** (half that of the base case). • Increasing HbA1c reduction to 0.9% increased cost difference to −$**Redacted** (almost half).
Age and duration of diabetes	The baseline population were average age 64.5 with a diabetes duration of 16 years. The following 3 populations were assessed: • Mean age 35 years – 1 year duration • Mean age 45 years – 5 years duration • Mean age 55 years – 5 years duration The ADAR did not state whether these populations were clinically plausible, nor did it state the reason for these choices.	The ICER in this scenario remained dominant for both populations. Incremental costs and QALYs increased for both populations if RT-CGM was initiated at an earlier age.
Model time horizon	The cumulative QALY and cost benefits are not fully captured when the model duration is short. Different time horizons were included in the uncertainty analysis. The ADAR included 1, 5, 10, 20 and 30 years for both IIT and non-IIT.	Time horizon needed to be at least 20 years for RT-CGM to be cost saving (dominant) vs SMBG. People enter the model at a mean age of 64.5 years, and the model assumes a 3-year treatment effect (HbA1c decrease) followed by a linear increase in HbA1c (0.15% per year). Therefore, the assumption that that those with RT-CGM have a lower HbA1c than SMBG over at least 20 years, to be cost saving, is required. There are no long-term data to support this assumption. Therefore, the estimated long-term benefits are highly uncertain. Additional scenarios around treatment effect would explore this uncertainty further.

Abbreviations
HbA1c = glycated haemoglobin, **ICER** = incremental cost-effectiveness ratio, **IIT** = intensive insulin therapy, **non-IIT** = non-intensive insulin therapy, **SMBG** = self-monitoring of blood glucose, **RT-CGM** = real-time continuous glucose monitoring, **QALY** = quality-adjusted life year.
The redacted values correspond to the following ranges:
[1] $0 to < $15,000
[2] $15,000 to < $25,000

Table 11: Sensitivity analyses for the IIT population

Analyses	Incremental cost	Incremental QALY	ICER
Base case	$**Redacted**	0.561	DOMINANT
Discount rate			
3.50%	$**Redacted**	0.645	DOMINANT
0.00%	$**Redacted**	0.969	DOMINANT
Mean age of RT-CGM initiation and duration of diabetes			
Mean age 35 years – 1 year duration	$**Redacted**	0.848	DOMINANT
Mean age 45 years – 5 years duration	$**Redacted**	0.776	DOMINANT
Mean age 55 years – 5 years duration	$**Redacted**	0.666	DOMINANT
HbA1c treatment effect			
HbA1c treatment effect 0.3 (DIAMOND T2D RCT; -0.3)	$**Redacted**	0.540	DOMINANT
HbA1c treatment effect −0.392 (-30%)	$**Redacted**	0.545	DOMINANT

Analyses	Incremental cost	Incremental QALY	ICER
HbA1c treatment effect −0.728 (+30%)	$**Redacted**	0.584	DOMINANT
FoH utility			
DIAMOND FoH utility (0.025)	$**Redacted**	0.660	DOMINANT
No FoH utility	$**Redacted**	0.405	DOMINANT
DKA and SHE incidence and FoH			
−50% DKA and SHE in SMBG arm and −50% FoH utility in RT-CGM arm	$**Redacted**	0.472	DOMINANT
No DKA or SHE in SMBG arm and no FoH utility for RT-CGM	$**Redacted**	0.386	DOMINANT
Number of SMBG strips/day			
1 strip	$**Redacted**	0.561	DOMINANT
2 strips	$**Redacted**	0.561	DOMINANT
5 strips	$**Redacted**	0.561	DOMINANT
8 strips	$**Redacted**	0.561	DOMINANT
10 strips	$**Redacted**	0.561	DOMINANT
Time horizon			
1 year	$**Redacted**	0.045	$**Redacted**[1]
5 years	$**Redacted**	0.200	$**Redacted**[2]
10 years	$**Redacted**	0.338	$**Redacted**[3]
20 years	$**Redacted**	0.491	DOMINANT
30 years	$**Redacted**	0.553	DOMINANT
Racial distribution			
100% White	$**Redacted**	0.566	DOMINANT
100% Southern European	$**Redacted**	0.601	DOMINANT
100% Indigenous	$**Redacted**	0.516	DOMINANT
Cardiovascular risk			
UKPDS 82 Cardiovascular Risk Prediction Equation/ Combined Australian mortality equation	$**Redacted**	0.572	DOMINANT
UKPDS 82 Cardiovascular Risk Prediction Equation/ UKPDS mortality equation	$**Redacted**	0.522	$**Redacted**[3]

Abbreviations
HbA1c = glycated haemoglobin, **DKA** = diabetes ketoacidosis, **FoH** = fear of hypoglycaemia, **ICER** = incremental cost-effectiveness ratio, **IIT** = intensive insulin therapy, **non-IIT** = non-intensive insulin therapy, **SHE** = severe hypoglycaemic events, **SMBG** = self-monitoring of blood glucose, **RT-CGM** = real-time continuous glucose monitoring, **QALY** = quality-adjusted life year.

The redacted values correspond to the following ranges:
[1] $15,000 to < $25,000
[2] $5,000 to < $15,000
[3] $0 to < $5,000

Table 12: Sensitivity analyses for the non-IIT population

Analyses	Incremental cost	Incremental QALY	ICER
Base case	$**Redacted**	0.318	DOMINANT
Discount rate			
3.50%	$**Redacted**	0.369	DOMINANT
0.00%	$**Redacted**	0.569	DOMINANT
Mean age of RT-CGM initiation and duration of diabetes			
Mean age 35 years – 1 year duration	$**Redacted**	0.485	DOMINANT
Mean age 45 years – 5 years duration	$**Redacted**	0.439	DOMINANT
Mean age 55 years – 5 years duration	$**Redacted**	0.387	DOMINANT
HbA1c effect			
HbA1c treatment effect −0.4% (MOBILE trial)	$**Redacted**	0.308	DOMINANT
HbA1c treatment effect −0.9% (Steno2tech study)	$**Redacted**	0.352	DOMINANT
FoH utility			
COACH study FoH utility (0.015)	$**Redacted**	0.391	DOMINANT
No FoH utility	$**Redacted**	0.240	DOMINANT
FoH And AFS utility			
COACH study FoH (0.015) + Matza AFS (0.03); 0.0455 utility	$**Redacted**	0.546	DOMINANT
DKA and SHE incidence			
Karter SHE and DKA incidence + COACH study FoH (0.015)	$**Redacted**	0.402	DOMINANT
−50% DKA and SHE in SMBG arm and −50% FoH utility in RT-CGM arm	$**Redacted**	0.268	DOMINANT
No DKA or SHE in SMBG arm and no FoH utility for RT-CGM	$**Redacted**	0.232	DOMINANT
Number Of SMBG strips/day	$**Redacted**		
0 strips	$**Redacted**	0.318	DOMINANT
1 strip	$**Redacted**	0.318	DOMINANT
3 strips	$**Redacted**	0.318	DOMINANT
5 strips	$**Redacted**	0.318	DOMINANT
Time horizon	$**Redacted**		
1 year	$**Redacted**	0.023	$**Redacted**[1]
5 years	$**Redacted**	0.105	$**Redacted**[2]
r10 years	$**Redacted**	0.188	$**Redacted**[3]
20 years	$**Redacted**	0.279	DOMINANT
30 years	$**Redacted**	0.306	DOMINANT
Racial distribution			
100% White	$**Redacted**	0.315	DOMINANT
100% Southern European	$**Redacted**	0.330	DOMINANT
100% Indigenous	$**Redacted**	0.303	DOMINANT

Analyses	Incremental cost	Incremental QALY	ICER
Cardiovascular risk			
UKPDS 82 Cardiovascular Risk Prediction Equation/ Combined Australian mortality equation	$**Redacted**	0.321	DOMINANT
UKPDS 82 Cardiovascular Risk Prediction Equation/ UKPDS mortality equation	$**Redacted**	0.343r	$**Redacted**[3]

Abbreviations
HbA1c = glycated haemoglobin, **AFS** = Avoidance of Finger Stick testing **DKA** = diabetes ketoacidosis, **FoH** = fear of hypoglycaemia, **ICER** = incremental cost-effectiveness ratio, **IIT** = intensive insulin therapy, **non-IIT** = non-intensive insulin therapy, **SHE** = severe hypoglycaemic events, **SMBG** = self-monitoring of blood glucose, **RT-CGM** = real-time continuous glucose monitoring, **QALY** = quality-adjusted life year.
The redacted values correspond to the following ranges:
[1] $45,000 to < $55,000
[2] $35,000 to < $45,000
[3] $15,000 to < $25,000.

Table 13 Additional scenario analyses requested by the evaluators

Analysis	Total costs, AUD			Quality-adjusted life expectancy, QALYs			ICUR, AUD per QALY gained
	RT-CGM	SMBG	Difference	RT-CGM	SMBG	Difference	
IIT analysis							
Base case	**Redacted**	**Redacted**	**Redacted**	7.761r	7.200	0.561	DOMINANT
Improvement of 10% in TIR in the RT-CGM arm as treatment effect (-0.56% HbA1c in the base case)							
+10% TIR	**Redacted**	**Redacted**	**Redacted**	7.747	7.200	0.547	DOMINANT
Length of HbA1c Treatment effect (3 years in the base case)							
1 year	**Redacted**	**Redacted**	**Redacted**	7.739	7.200	0.539	DOMINANT
5 years	**Redacted**	**Redacted**	**Redacted**	7.811	7.200	0.611r	DOMINANT
10 years	**Redacted**	**Redacted**	**Redacted**	7.865	7.200	0.665	DOMINANT
UKPDS 68 HbA1c progression	**Redacted**	**Redacted**	**Redacted**	7.744	7.243	0.501	**Redacted**[1]
No HbA1c progression in either arm (flat trajectory)	**Redacted**	**Redacted**	**Redacted**	7.846	7.309	0.538	DOMINANT
Avoidance of finger stick disutility (0.03 in the base case)							
AFS = 0.02	**Redacted**	**Redacted**	**Redacted**	7.660	7.200	0.461	DOMINANT
Non-IIT analysis							
Base case	**Redacted**	**Redacted**	**Redacted**	7.529	7.211	0.318	DOMINANT
Improvement of 10% in TIR in the RT-CGM arm as treatment effect (-0.60% HbA1c in the base case)							
+10% TIR	**Redacted**	**Redacted**	**Redacted**	7.519	7.211	0.308	DOMINANT
Length of HbA1c Treatment effect (3 years in the base case)							
1 year	**Redacted**	**Redacted**	**Redacted**	7.520	7.211	0.309	DOMINANT
5 years	**Redacted**	**Redacted**	**Redacted**	7.579	7.211	0.368	DOMINANT
10 years	**Redacted**	**Redacted**	**Redacted**	7.636	7.211	0.425	DOMINANT
UKPDS 68 HbA1c progression	**Redacted**	**Redacted**	**Redacted**	7.511	7.260	0.251	**Redacted**[2]
No HbA1c progression in either arm (flat trajectory)	**Redacted**	**Redacted**	**Redacted**	7.612	7.318	0.295	**Redacted**[1]
Avoidance of finger stick disutility (0.03 in the base case)							

Analysis	Total costs, AUD			Quality-adjusted life expectancy, QALYs			ICUR, AUD per QALY gained
	RT-CGM	SMBG	Difference	RT-CGM	SMBG	Difference	
Reduced to 0.01	**Redacted**	**Redacted**	**Redacted**	7.479	7.211	0.268	DOMINANT

The redacted values correspond to the following ranges:
[1] $15,000 to < $25,000
[2] $45,000 to < $55,000.

Table 14 Results of the cost-effectiveness analysis with and without the application of Hba1c

Row	Scenario	Population	Incremental costs	Incremental QALYs	ICER	Reference
A	Base case (with HbA1c benefit)	IIT	-$**Redacted**	0.561	Dominant	Model results
B		non-IIT	-$**Redacted**	0.318	Dominant	Model results
C	Scenario (without HbA1c benefit)	IIT	$**Redacted**	0.471	$**Redacted**[1]	Model result calculated by setting HbA1c in RT-CGM arm to the same as in the SMBG arm
D		non-IIT	$**Redacted**	0.234	$**Redacted**[2]	
E	Weighted[a] (HbA1c benefit only applied to proportion meeting MCID; 26% and 9.9% of the IIT and non-IIT populations respectively)	IIT	$**Redacted**	0.494	$**Redacted**[3]	A*26%+C*74%
F		non-IIT	$**Redacted**	0.242	$**Redacted**[4]	B*9.9%+D*90.1%
G		All	$**Redacted**	0.419	$**Redacted**[1]	E*70.1% + F*29.9%

a Note the ICER itself is not weighted, it is calculated from the weighted incremental costs and QALYs
The redacted values correspond to the following ranges:
[1] $15,000 to < $25,000
[2] $55,000 to < $75,000
[3] $5,000 to < $15,000
[4] $45,000 to < $55,000.

14. Financial/budgetary impacts

The ADAR presented financial analysis results for the IIT and non-IIT populations separately. The results for all people with T2D requiring insulin (IIT and non-IIT combined) were not presented in the ADAR.

The financial impact analysis took an epidemiological approach. This approach was chosen because no reliable usage statistics for SMBG (relevant to the population groups of interest) were available, prohibiting a market share approach. The ADAR used NDSS T2D statistics from 2017 to 2024 to derive a linear equation to estimate the future prevalence of T2D requiring insulin. The number of eligible patients was derived from these estimates and data from the Australian National Diabetes Audit.

The ADAR assumed that RT-CGM uptake would be REDACTED% in year 1 increasing to REDACTED% in year 6, in both IIT and non-IIT populations for RT-CGM. This assumption was based on the claim that uptake of RT-CGM is expected to be gradual because familiarity and acceptance of new technology tends to be gradual. The ADAR did not state whether clinical experts were consulted to inform the uptake, nor did it leverage data from the uptake of RT-CGM in people with T1D.

The ADAR calculated that each person with Dexcom ONE+ would require 12 packs of sensors per year (each sensor lasts 10 days and each pack contains 3 sensors). Additional sensors may be required in a rare event (e.g. sensor detachment). The total annual cost of Dexcom ONE+ was stated to be $REDACTED, assuming full adherence. Blood glucose monitoring strips are currently subsidised through NDSS, with the T2D patient paying either $1.20 (concessional) or $15 (general) towards the total cost. The ADAR assumed the cost to the healthcare payer would be $15.00 for 100 strips. The total annual cost was derived to be $208.05 and $109.50 for IIT and non-IIT users.

Additional costs included in the financial analysis were the cost per 1% change in HbA1c, which was obtained from Fitch et al. (2013). This paper estimated the cost per patient per month (PPPM) associated with an annual decrease of 1% in HbA1c over a 3-year time horizon. Fitch et al. (2013) used a cohort 466 people with T2D, with access to commercial insurance, from the National Health and Nutrition Examination Survey (2005–2006 and 2007–2008). The UKPDS risk equations were used to estimate the complications over 3 years and associated costs. Other costs that were considered were inpatient visits, outpatient visits and drug costs. The cost saving over 3 years associated with a 1% HbA1c reduction was calculated to be USD 99 PPPM. This cost saving was converted into AUD$ and inflated to a 2024 cost using the Australian CPI. The ADAR did not describe the study or methods in the report.

The analysis also costs per severe hypoglycaemia and/or hyperglycaemia hospitalisation. The ADAR did not discuss whether these would be accounted for in the US cost. There may be double counting if severe hypoglycaemia and/or hyperglycaemia hospitalisation is already accounted for in assumed cost savings from each 1% reduction in HbA1C. Costs were consistent with those in the CEA. The ADAR used the difference between RT-CGM and SMBG to calculate the net impact to the cost for each of the costs discussed above.

The financial implications to the NDSS resulting from the proposed listing of Dexcom ONE+ are summarised in Table 15 and Table 16. Overall, the ADAR estimated Dexcom ONE+ would cost the NDSS $90 million to < $100 million in year 1, which was expected to increase to $200 million to < $300 million in year 6 in the IIT population. In the non-IIT population, the ADAR estimated Dexcom ONE+ would cost the NDSS $40 million to < $50 million in year 1, which was expected to increase to $90 million to < $100 million in year 6.

Other healthcare cost savings, because of a reduction in HbA1c and complication avoidance, are presented in Table 17. Overall, the ADAR estimated Dexcom ONE+ would be cost saving in the IIT population and cost incurring in the non-IIT population. It should be noted that the ADAR assumed that individuals using RT-CGM do not experience severe hypoglycaemia and hyperglycaemia. This assumption was based on 1-year follow-up data and had a large impact on the financial analysis, resulting in cost savings of approximately $90 million to < $100 million by year 6 (across both IIT and non-IIT populations). Note that the finding of cost savings for the IIT population appears to contradict the finding of the economic evaluation of a net cost in this population over 5 years.

Table 15: Net financial implications of RT-CGM use to NDSS in the IIT population

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated use and cost of the proposed health technology in IIT population						
Number of people eligible for RT-CGM	162,889	166,828	170,767	174,706	178,645	182,584
Number of people who receive RT-CGM	**Redacted**[1]	**Redacted**[2]	**Redacted**[3]	**Redacted**[4]	**Redacted**[4]	**Redacted**[4]
Number of Dexcom ONE+ sensor packs	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**
Cost to the NDSS	$**Redacted**[5]	$**Redacted**[5]	$**Redacted**[5]	$**Redacted**[5]	$**Redacted**[6]	$**Redacted**[6]
Change in use and cost of other health technologies						
Glucose strips replaced (100-strip packs)	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**
Total cost offsets	$**Redacted**[7]	$**Redacted**[7]	$**Redacted**[7]	$**Redacted**[8]	$**Redacted**[8]	$**Redacted**[8]
Net financial impact to the NDSS	$**Redacted**[9]	$**Redacted**[5]	$**Redacted**[5]	$**Redacted**[5]	$**Redacted**[5]	$**Redacted**[6]

Abbreviations
IIT = intensive insulin therapy, **NDSS** = National Diabetes Subsidiary Scheme, **RT-CGM** = real-time continuous glucose monitoring.
NotesAll currencies are representative of AUD.
The redacted values correspond to the following ranges:
[1] 50,000 to < 60,000
[2] 70,000 to < 80,000
[3] 90,000 to < 100,000
[4] 100,000 to < 200,000
[5]$100 million to < $200 million
[6] $200 million to < $300 million
[7] $10 million to < $20 million
[8] $20 million to < $30 million
[9] $90 million to < $100 million

Table 16: Net financial implications of RT-CGM use to NDSS in the non-IIT population

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated use and cost of the proposed health technology in the non-IIT population						
Number of people eligible for RT-CGM	68,781	70,444	72,107	73,770	75,434	77,097
Number of people who receive RT-CGM	**Redacted**[1]	**Redacted**[2]	**Redacted**[2]	**Redacted**[3]	**Redacted**[3]	**Redacted**[4]
Number of Dexcom ONE+ sensor packs	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**
Cost to the NDSS	$**Redacted**[5]	$**Redacted**[6]	$**Redacted**[7]	$**Redacted**[8]	$**Redacted**[9]	$**Redacted**[10]
Change in use and cost of other health technologies						
Glucose strips replaced (100-strip packs)	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**	**Redacted**
Total cost offsets	$**Redacted**[11]	$**Redacted**[11]	$**Redacted**[11]	$**Redacted**[11]	$**Redacted**[11]	$**Redacted**[11]
Net financial impact to the NDSS	**$Redacted**[5]	**$Redacted**[12]	**$Redacted**[7]	**$Redacted**[7]	**$Redacted**[8]	**$Redacted**[9]

Abbreviations
NDSS = National Diabetes Subsidiary Scheme, **non-IIT** = non-intensive insulin therapy, **RT-CGM** = real-time continuous glucose monitoring.
Notes
All currencies are representative of AUD
The redacted values correspond to the following ranges:
[1] 20,000 to < 30,000
[2] 30,000 to < 40,000
[3] 40,000 to < 50,000
[4] 50,000 to < 60,000
[5] $40 million to < $50 million
[6] $60 million to < $70 million
[7] $70 million to < $80 million
[8] $80 million to < $90 million
[9] $90 million to < $100 million
[10] $100 million to < $200 million
[11] $0 to < $10 million
[12] $50 million to < $60 million

Table 17: Estimated extent of other healthcare cost savings in Year 1 to Year 6

Year	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
For the IIT population:						
Total costs of Dexcom ONE+	$**Redacted**[1]	$**Redacted**[1]	$**Redacted**[1]	$**Redacted**[1]	$**Redacted**[2]	$**Redacted**[2]
Substitution-related cost offsets	−$**Redacted**[3]	−$**Redacted**[3]	−$**Redacted**[3]	−$**Redacted**[4]	−$**Redacted**[4]	−$**Redacted**[4]
Net costs to NDSS	$**Redacted**[5]	$**Redacted**[1]	$**Redacted**[1]	$**Redacted**[1]	$**Redacted**[1]	$**Redacted**[2]
Other savings	−$**Redacted**[5]	−$**Redacted**[1]	−$**Redacted**[1]	−$**Redacted**[1]	−$**Redacted**[1]	−$**Redacted**[2]
Net impact to healthcare system	−**$Redacted**[6]	−**$Redacted**[6]	−**$Redacted**[6]	−**$Redacted**[6]	−**$Redacted**[6]	−**$Redacted**[6]
For the non-IIT population:						
Total costs of Dexcom ONE+	$**Redacted**[7]	$**Redacted**[8]	$**Redacted**[9]	$**Redacted**[10]	$**Redacted**[5]	$**Redacted**[1]
Substitution-related cost offsets	−$**Redacted**[6]	−$**Redacted**[6]	−$**Redacted**[6]	−$**Redacted**[6]	−$**Redacted**[6]	−$**Redacted**[6]
Net costs to NDSS	$**Redacted**[7]	$**Redacted**[11]	$**Redacted**[9]	$**Redacted**[9]	$**Redacted**[10]	$**Redacted**[5]
Other savings	−$**Redacted**[12]	−$**Redacted**[7]	−$**Redacted**[11]	−$**Redacted**[8]	−$**Redacted**[9]	−$**Redacted**[10]
Net impact to healthcare system	**$Redacted**[6]	**$Redacted**[6]	**$Redacted**[3]	**$Redacted**[3]	**$Redacted**[3]	**$Redacted**[3]

Abbreviations
IIT = intensive insulin treatment, **NDSS** = National Diabetes Services Scheme, **non-IIT** = non-intensive insulin treatment, **RT-CGM** = real-time continuous glucose monitoring, **T2D** = type 2 diabetes.
Notes
All currencies are representative of AUD
Calendar year totals are presented; pro rata adjustments may be necessary.
The redacted values correspond to the following ranges:
[1] $100 million to < $200 million
[2] $200 million to < $300 million
[3] $10 million to < $20 million
[4] $20 million to < $30 million
[5] $90 million to < $100 million
[6] $0 to < $10 million
[7] $40 million to < $50 million
[8] $60 million to < $70 million
[9] $70 million to < $80 million;
[10] $80 million to < $90 million
[11] $50 million to < $60 million
[12] $30 million to < $40 million.

15. Other relevant information

Post-ESC analysis - economics

Post-ESC the assessment group was requested to provide its opinion summarising its views on the transparency of the economic model used in this ADAR with reference to TG 18.3 of the MSAC Guidelines. The assessment group's views are provided below.

The Applicant used a generic web-based simulation model, namely, the IQVIA core diabetes model (CDM). The Applicant justified their use of the IQVIA CDM by highlighting that it had been "extensively evaluated and validated and its reliability in informing reimbursement decisions internationally has been tested and accepted". The IQVIA CDM uses proprietary code and the Evaluator did not have access to the model. For transparency, the Applicant provided a

workbook template for the IQVIA CDM which outlined model settings and inputs. The information provided was sufficient for the Evaluation process.

The Applicant did not explicitly justify the use of a microsimulation model. However, the Applicant did justify use of the IQVIA CDM by citing research showing it was "a reliable predictive tool for diabetes natural history and translation of treatment effects into patient relevant outcomes". Furthermore, the use of the built-in risk equations to appropriately predict the progression of risk factors and complications in type 2 diabetes could not be modelled transparently in a cohort model. The microsimulation approach is appropriate. The Applicant adapted the model to align with an Australian setting using published, peer-reviewed Australian-specific risk equations.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- The ADAR proposed a minimal clinically important difference (MCID) for change in glycated haemoglobin (HbA1c) at 0.3%. This is lower than the threshold of 0.5% previously used by the PBAC (for example, semaglutide Public Summary Document [PSD], March 2021 PBAC meeting). An MCID of 0.5% is also accepted by NICE (England). The ADAR did not establish that a HbA1c reduction of 0.3% is clinically significant. If 0.5% remains accepted as the MCID for HbA1c in type 2 diabetes mellitus (T2D), the claim of superior clinical effectiveness based on the change in HbA1c cannot be accepted. If a claim of superior clinical effectiveness based on HbA1c change cannot be established, an alternative may be for the applicant to establish a claim of non-inferior effectiveness. The applicant may also wish to consider establishing a claim of superior effectiveness if there is substantial evidence of improvement in other patient-relevant outcomes, such as quality of life (QoL). While QoL improvements for patients using continuous glucose monitoring (CGM) would be expected because of the reduced need for finger prick testing, this was not supported by QoL outcomes reported in the studies presented in the application.
- The applicant has requested funding for the device in 2 subpopulations: intensive insulin therapy (IIT) users and non-IIT users. However, it may be sufficient for the eligible population to be defined as patients with T2D who require insulin.
- REDACTED. Therefore, device-agnostic funding for these products would likely be appropriate as these devices likely have a class effect.

Economic issues:

- There are several issues with the transparency, structure and performance of the economic model in the ADAR. An editable version was not provided, as required by the MSAC Guidelines. The applicant is requested to provide model traces for patients transitioning through health states in the model to support the clinical plausibility of the model outcomes (e.g. all patients deceased at the end of the model lifetime) and additional information to support the contention that the economic model has been sufficiently validated following modifications to its structure and inputs.
- The model only shows net cost savings after 20 years, yet the average life expectancy in the model was 17.4 years. Given that the vast majority of T2D patients using insulin are aged over 50 years, ESC considered that the projected net cost savings are unlikely to be realised.

Financial issues:

- Estimates of the number of Australians with T2D requiring treatment with insulin are varied and figures based on NDSS data (as used in the ADAR) may be overestimated. ESC advised

that the T2D patient numbers (at least for those using insulin) should be confirmed ahead of MSAC's consideration.

- The estimates of hospitalisation-based cost offsets are unlikely to be fully realised as financial savings to state and territory health budgets.
- There was a difference in device cost per year presented between the Dexcom ONE+ ($**REDACTED**) and the FSL ($**REDACTED**) for likely similar clinical outcomes. ESC advised that, if a device-agnostic listing is approved, MSAC could consider a cost-minimisation approach for CGM products accessed via the NDSS, accounting for the different durations of sensor performance, such as direct price competition or the introduction of a price premium for more expensive options.

Other relevant information:

- MSAC may wish to consider equity issues in relation to co-payments across different diabetes types and subpopulations, noting that currently a co-payment is applicable for CGM funding for non-Aboriginal and Torres Strait Islander and non-concessional beneficiaries aged 21 years or over with T1D. Applying a full subsidy of CGM for T2D patients would therefore create an inequity in subsidy access compared to the existing NDSS subsidy co-payment arrangements for similar patients with T1D (and for blood glucose strips).
- Most patients with T2D are managed in a general practitioner (GP) setting, but GPs are currently not included in the set of health professionals who can certify eligibility for the populations eligible for CGM products through the NDSS. Allowing GPs to approve the device would eliminate authorisation bottlenecks and improve equity of access. Consumer feedback also supports an extended role for GPs.

ESC discussion

ESC noted that this application from Australasian Medical & Scientific Limited requested National Diabetes Services Scheme (NDSS) funding for the Dexcom ONE+ continuous glucose monitoring (CGM) system for people with insulin-dependent type 2 diabetes mellitus (T2D). The proposal for funding through the NDSS would not require a Medicare Benefits Schedule (MBS) listing.

The application requests funding for this CGM system in two T2D populations requiring insulin for management of T2D: intensive insulin therapy (IIT) users and non-IIT users. The standard of care in both populations is currently self-monitoring of blood glucose (SMBG) through finger prick testing. IIT users typically conduct SMBG tests more frequently throughout the day than non-IIT users.

CGM systems are designed to replace finger prick testing for the purpose of treatment decisions. The Dexcom ONE+ CGM system uses a sensor to measure glucose concentrations in interstitial fluid and reports these measurements in real time via a Bluetooth-enabled display device (smartphone or dedicated receiver). The system issues alerts for hypo- and hyperglycaemia to assist in timely blood glucose management. Patients using Dexcom ONE+ only require finger prick testing if the CGM system fails to give a reading or if an alert or reading is not consistent with their symptoms.

Dexcom ONE+ is already listed as a medical device on the Australian Register of Therapeutic Goods (ARTG). The ARTG listing states that the device is intended for use with 'persons with diabetes mellitus aged 2 years and older where SMBG is indicated'.

ESC noted the history of subsidised CGM monitoring in Australia. CGM technology has received public funding in Australia since 2017, when the NDSS provided full subsidies for type 1 diabetes mellitus (T1D) patients under the age of 21 years. In March 2019, access was expanded to include:

- T1D patients aged 21 years and over with concession status and a specified set of clinical needs
- T1D patients who are pregnant, actively planning pregnancy or immediately post-pregnancy
- patients aged under 21 years who have conditions similar to T1D and require insulin.

In 2022, the NDSS expanded funding of CGM technology to all patients with T1D (with an equivalent monthly co-payment of around $35.90 for people aged 21 years and over who do not have concessional status).

MSAC conducted a review of CGM products provided via the NDSS for people with T1D in 2021 (see MSAC Review 1663). After considering the available evidence, the review concluded that there is most likely no difference between CGM and SMBG in terms of safety and effectiveness. However, the review noted that clinically relevant outcomes and clinical needs vary according to patient factors and recommended that the clinical and quality of life (QoL) benefits of CGM be further explored.

ESC noted that there are currently 3 manufacturers of CGM products on the NDSS, 2 of which have submitted applications to be considered at this meeting. The application for the FreeStyle Libre 2 (FSL) CGM system (MSAC Application 1786) seeks funding for people with insulin-dependent T2D, as well as specific subpopulations with gestational diabetes and other conditions similar to T1D requiring insulin.

The application requests public funding for Dexcom ONE+ through the NDSS for 2 subpopulations of patients with T2D. Both subpopulations consist of people aged ≥2 years who have been diagnosed with T2D, require insulin to manage the condition, and have suboptimal glycaemic control (defined as laboratory-measured glycated haemoglobin [HbA1c] levels of >7.0% for adults and >6.5% for children and adolescents).

The 2 subpopulations are distinguished as follows:

- Intensive insulin therapy (IIT): patients who are currently being treated with basal insulin and rapid-acting insulin.
- Non-IIT: patients who are currently being treated with a basal insulin regimen and do not regularly use rapid-acting insulin.

ESC suggested that MSAC could consider combining the two proposed subpopulations for NDSS funding, e.g. ‘patients with T2D requiring insulin’.

ESC noted that GPs are not authorised to certify eligibility to access CGM products through the NDSS. Endocrinologists, certified diabetes educators and other health professionals specialising in diabetes can determine whether patients meet the eligibility criteria for CGM on the NDSS. However, ESC considered it appropriate that general practitioners (GPs) be authorised to certify eligibility to access CGM products through the NDSS. ESC noted that most patients with T2D are diagnosed and managed by a GP who regularly monitors their HbA1c. ESC considered that there was no capacity for all patients to see an endocrinologist or diabetes educator (currently authorised to certify eligibility) and that this was a significant issue for equity, especially in rural areas where patients may have less access to non-GP health professionals. ESC also considered the ability for GPs to certify eligibility would be especially important for GDM patients. ESC discussed whether a pharmacist could authorise eligibility; however, ESC considered that it was unclear how they could do this without requesting data from a GP or how they would manage CGM use and outcomes going forward.

ESC considered the public consultation feedback received for this application alongside the feedback received for MSAC Application 1786. ESC noted that a large number of submissions had been received in this feedback and that the feedback came from a variety of sources,

including professional organisations, peak bodies, medical device companies, individual healthcare providers and Aboriginal health and community service providers.

The feedback focused on the potential benefits of CGM products, highlighting the capacity for real-time monitoring to reduce hypoglycaemic events, especially at night. This capability reduces the fear of hypoglycaemic events and provides peace of mind to patients and their carers, especially when a patient is older, has cognitive disability or is living alone. The feedback also noted that the real-time feedback afforded by CGM helps people understand the impact of their lifestyle on blood glucose levels (BGLs) in real time, which in turn builds confidence and self-efficacy, facilitates more informed and timely decision-making, and helps people feel more engaged in their own treatment.

Additional potential benefits highlighted through public consultation included the potential for reduced comorbidities and complications; reduced anxiety about insulin dosing and fluctuations in BGLs, especially for people with needle aversion; reduced need for painful finger prick testing. CGM allows more discreet monitoring which reduces stigma, fear and shame, especially for Aboriginal and Torres Strait Islander patients. The feedback also mentioned the capacity for remote monitoring by carers (which may be especially useful for patients in aged or supported care), higher confidence for carers, reduced emotional and logistical load on carers, enhanced opportunities for patient education, and (where relevant) improved support for the involvement of families in informed and collaborative care decisions. Some of the feedback highlighted the potential for CGM to improve equity and access to care, especially for people with physical disability or those in rural and remote areas. ESC considered that formal evidence was needed for some of the potential benefits proposed by the public consultation feedback.

Several submissions in the feedback flagged a need for workforce skill-building opportunities to ensure the technology is used effectively. Support was expressed for the inclusion of general practitioners (GPs) in the list of health professionals authorised to certify eligibility to access CGM products through the NDSS. There were also suggestions that subsidised access to CGM products could be expanded to include their short-term use in newly diagnosed T2D patients for the purpose of education and prevention of progression.

ESC noted the clinical management algorithms, in which SMBG is only required in the proposed clinical management algorithm if a patient's symptoms are not aligned with the CGM results.

ESC considered that the populations, comparator and outcome measures were appropriate. However, it noted that a target HbA1c of 7.0% may be unrealistic for many older patients.

ESC noted that the primary evidence base provided by the applicant to support its clinical claims consists of 4 unblinded randomised controlled trials (RCTs): DIAMOND (population aged ≥25 years; 6-month follow-up), 2GO-CGM (population aged ≥16 years; 3 month follow-up), Steno2tech (population aged ≥18 years; 12-month follow-up) and MOBILE (population aged ≥30 years; 8-month follow-up).

ESC noted that no Australian studies were included and that there has been no review of the intervention for Aboriginal and Torres Strait Islander populations. ESC also noted that no participants under the age of 16 were included and that only one of the studies had been conducted in a population requiring intensive insulin therapy.

ESC noted that the 4 RCTs used the Dexcom G series, rather than the Dexcom ONE+ device for which funding is being requested. ESC noted the applicant's pre-ESC response, which confirmed that Dexcom ONE+ uses the same technology as the G series. ESC noted that the Dexcom ONE+ is able to issue hypoglycaemia alerts but not predictive hypoglycaemia alerts, unlike the G series which does have the capability to provide predictive hypoglycaemia alerts.

ESC noted that the clinical claim was for non-inferior safety compared with SMBG. ESC noted that the outcomes for comparative safety were adverse events (episodes of severe hyper- and hypoglycaemia) and local adverse events associated with SMBG or placement of the CGM sensor.

ESC noted that in the MOBILE RCT, one episode of severe hypoglycaemia was reported in each of the CGM and control groups and one episode of ketoacidosis was reported in the CGM group. Neither of the severe adverse events were considered to be device-related. A small number of patients experienced minor issues, such as skin rashes, related to the placement of the CGM sensor.

ESC suggested that MSAC consider whether CGM use alone would have an impact on hyperglycaemia events. While CGM may alert patients to increasing BGL in a more timely manner than SMBG alone, many hyperglycaemia events in T2D are related to intercurrent illness. ESC noted that this consideration is relevant in modelling the benefits of CGM. ESC therefore raised a possible difference in hospitalisations for hyper- vs. hypoglycaemia in people using CGM. Given that potential hypoglycaemia events are more likely to be related to insulin use, they may be more preventable if CGM is being used due to the ease of monitoring pre-insulin BGL. This means that the rate of hypoglycaemia hospitalisations would be expected to be lower under CGM than SMBG. This distinction is relevant to the economic modelling, which relied on a non-randomised study to estimate reductions in both types of hospitalisation events. ESC noted that the Dexcom ONE+ system issues hypoglycaemia alerts but not predictive hypoglycaemia alerts like the Dexcom G series used in the non-randomised study. ESC also noted that the system estimates BGLs differently compared to finger prick testing. ESC noted that CGM indirectly measures BGL by measuring glucose levels within the interstitial fluid. Therefore, with a 3-5 minute lag between blood glucose and interstitial glucose changes, if blood glucose levels are changing rapidly, detection of these changes by the CGM device will lag behind. ESC further noted that the sensor becomes less reliable towards the end of its performance life (approximately 10 days).

ESC concluded that the clinical claim of non-inferior safety was not well supported directly by the evidence but, on balance, was appropriate.

ESC noted that the clinical claim is for superior effectiveness compared with SMBG. Comparative effectiveness was measured through changes in HbA1c and time in range (TIR) at follow-up. Measures of T2D-related complications, mortality, quality of life (QoL) and subjective treatment satisfaction were also included.

ESC noted that the Dexcom ONE+ does not have the capability to attach to an insulin pump, but the G series does. One study states that the use of an insulin pump was an exclusion criterion; no information is provided regarding insulin pump use for the other studies. ESC considered that outcomes may differ if the device is linked to an insulin pump, and therefore clarity is needed regarding whether the impact of insulin pump use was captured in the other studies.

ESC noted the results for TIR. Statistically significant increases of around 15% were found in the MOBILE and Steno2tech trials; no statistically significant improvement was found in the other 2 studies. ESC also noted that the chosen MCID for TIR in the ADAR was 5%, which is inconsistent with the internationally accepted threshold of 10%.

ESC noted the results of patient-related measures, including quality of life (QoL) and subjective treatment satisfaction. No QoL differences between the CGM and SMBG groups were reported. ESC noted anecdotal evidence suggesting that many patients prefer CGM. Subjective treatment satisfaction scores reported for CGM appeared high in 3 trials, and this was reflected in high adherence rates. However, ESC noted that the run-in phase of the trials had selected patients for their perseverance, which may be linked to satisfaction.

ESC noted the results for the change in HbA1c, which showed an adjusted difference of approximately 0.3%–0.4% for 3 of the studies and 0.9% in one study. ESC considered that the 0.9% result could be an outlier, also noting that HbA1c was a secondary outcome in this study and therefore carried less weight. ESC noted that the ADAR reported that a meta-analysis using data from the intention to treat (ITT) population from all 4 studies resulted in a mean difference in HbA1c of −0.40% (95% CI: −0.63, −0.18). ESC considered that aspects of the meta-analysis may have questionable validity due to the use of different time points in each study for the reporting of changes in HbA1c (ranging from 3 to 12 months).

ESC noted that the applicant had proposed a minimal clinically important difference (MCID) of 0.3% as the threshold for clinical effectiveness. This threshold is lower than the MCID of 0.5% that has previously been accepted by the Pharmaceutical Benefits Advisory Committee (PBAC), including to assess clinical effectiveness in HbA1c changes in T2D (refer to the PBAC PSD for semaglutide). The International Diabetes Federation, England's National Institute for Health and Care Excellence, the Australian Diabetes Society and the Royal Australian College of General Practitioners have also nominated 0.5% as the MCID for HbA1c. The European Medicines Agency[21] guidance supports the use of a 0.3% HbA1c to establish non-inferiority.

ESC considered that the PBAC has set a long standing precedent for 0.5% as the MCID for HbA1c and the ADAR did not provide a basis to accept a smaller MCID. ESC considered that use of the 0.5% MCID would lead to a conclusion of non-superiority of Dexcom ONE+ compared to SMBG in clinical effectiveness based on the primary outcome of change in HbA1C. ESC acknowledged that there was some evidence of a linear epidemiological relationship between HbA1C and various diabetes-related complications from the UK Prospective Diabetes Study (UKPDS) but this study was conducted more than 25 years ago.

ESC advised that substantive evidence should be provided in support of any change to the 0.5% MCID that was accepted by the PBAC. ESC noted that HbA1c is a surrogate outcome for diabetes-related health outcomes. ESC referred to Appendix 12 of the MSAC Guidelines, which describes (p 296) an approach to establishing a surrogate threshold effect using a meta-regression of randomised trials (in this case of any intervention in T2D) comparing the observed treatment effect on the proposed surrogate measure (in this case HbA1c within the first 12 months) with the observed treatment effect on the target patient-relevant clinical outcome (in this case any one or more of the modelled diabetes complications over subsequent years).

ESC considered that if a claim of superior clinical effectiveness cannot be established based on mean change in HbA1c, an alternative, consistent with MSAC suggestions in MSAC Review 1663, may be to establish a claim of superior effectiveness accompanied by substantial evidence of improvement on other patient-relevant outcomes, such as quality of life (QoL). However, ESC noted that the ADAR did not provide such evidence. ESC acknowledged that gathering such evidence is difficult, given that it is not possible to conduct blinded studies comparing SMBG and CGM. ESC suggested that alternative measures of effectiveness, such as the percentage of patients achieving a target HbA1c level of less than 7%, could also be considered.

REDACTED. ESC considered that a device-agnostic NDSS listing may be appropriate.

ESC noted that the economic evaluation was a cost-utility analysis and includes two subpopulations of individuals with T2D requiring insulin and with suboptimal glycaemic control (as confirmed by laboratory-measured HbA1c levels of >7.0% for adults and >6.5% for children and adolescents). Subpopulation 1 (IIT) is treated with basal insulin and rapid-acting insulin; subpopulation 2 (non-IIT) is treated with basal insulin and no regular use of rapid-acting insulin.

[21] European Medicines Agency (2023). Guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus. CPMP/EWP/1080/00 Rev.2. https://www.ema.europa.eu/en/clinical-investigation-medicinal-products-treatment-or-prevention-diabetes-mellitus-scientific-guideline

ESC noted that the economic model was based on the IQVIA CORE Diabetes Model (CDM), a micro-simulation model designed to translate surrogate endpoints to long term health economic outcomes.

The economic model as originally designed comprises 17 interdependent sub-models that inform the modelling of diabetes complications (or health states).

ESC noted that Dexcom ONE+ sensors must be replaced after 10 days of use. Each pack contains 3 sensors at a requested price of $REDACTED, and each person on average required 12.17 packs per annum, resulting in a calculated total annual cost of $REDACTED. The applicant-developed assessment report (ADAR) noted that early replacement of sensors was a rare occurrence that is offset by the unrealistic assumption of 100% adherence to the sensor replacement schedule. ESC considered 90% adherence to be more appropriate.

ESC noted that the reported results of the base case showed that CGM was more effective and cheaper than SMBG for both subpopulations. ESC further noted that all of the sensitivity analyses provided either remained dominant or generated an incremental cost-effectiveness ratio per quality-adjusted life year (ICER/QALY) of below $45,000 to < $55,000.

However, ESC identified several key issues with the model's transparency, structure and performance. In terms of transparency, ESC noted that a fully editable model had not been provided, as required by the MSAC Guidelines for assessment preparation (TG 18.3 and 18.5), and queried whether this model in any form has previously been accepted by the PBAC. In terms of structure, ESC noted that the 17 original health states appeared to have been merged or removed without explanation and reduced to 10 health states and it is unclear which of these health states then contribute to mortality. In terms of model performance, ESC noted that, compared with the CDM, the submitted model has substituted a different method of projecting hospitalisations for severe hypoglycaemia and diabetic ketoacidosis. Similarly, the submitted model replaces data from the UKPDS 82 simulation model, which has been validated, with Western Australian-sourced predictive risk equations for diabetes-related cardiovascular events and diabetes-related overall mortality, which may not have been validated in the context of the rest of the "interdependent" CDM. Regarding the assumed utility gain of 0.03 for finger prick avoidance in the model, ESC considered that the methodology used to generate this result led to an overestimate because the study was vignette-based and based on a survey of the general population rather than T2D patients who have adapted to finger prick testing.

ESC agreed with other important issues with the model raised in the commentary. The size of the effect on HbA1c is questionable, given that the more favourable base case of the IIT model relies on a retrospective cohort study rather than an RCT (though an RCT-based estimate is assessed in the sensitivity analysis). ESC noted that the base case of the non-IIT model relies on the treatment effect found in the meta-analysis, which is greater than the result used for the IIT model. ESC considered it implausible that CGM would have a lesser effect on HbA1c in the IIT subpopulation than in the non-IIT subpopulation.

ESC also observed that it was unclear how HbA1c change varied over time in the two arms of the model and identified a need to verify the base case increments. The assessment group reconstructed the general approach used to model the treatment effect as assuming the change in HbA1c in both arms would increase by 0.15% per year except for a treatment effect in the first 3 years in the CGM arm. This projected rate of HbA1c increase did not change over time, meaning that the modelled change in HbA1c would reach 10.85% at life expectancy and 23.15% at the model's end.

ESC noted that many of the modelled benefits were generated by people living beyond average life expectancy. ESC also noted that the model only showed cost savings after 20 years, yet the average life expectancy in the model was 17.4 years. Given that the vast majority of T2D patients are aged over 50 years, ESC considered that the projected cost savings are unlikely to be

realised. ESC also noted that the model assumed lifelong use of the product, in contrast with public consultation feedback that suggested CGM devices could be used temporarily during an initial transition phase.

ESC noted that the following assumptions in the model led to minor uncertainties. However, ESC noted that these assumptions had conservative implications (i.e. were biased against CGM), and therefore considered that the associated uncertainties were ultimately not of concern:

- A 1-year disutility duration for chronic diabetic complications was assumed.
- The unit cost of blood glucose monitoring strips was based on the patient copayment to the NDSS only. This leads to a less than full cost offset (thus biasing the result against CGM).
- A lower than recommended number of blood glucose monitoring strips used per day was assumed in the model, which again leads to a less than maximum cost offset.

ESC also noted the following minor issues associated with the model raised in the Commentary, which can either be considered resolved or can be put aside because of their insignificant impacts on model results:

- The Commentary confirmed that the model's projected overall survival matches Australian expected survival of 83 years for patients with T2D. However the model only generated 0.2 incremental life-years gained over 17.4 overall years or a 1% difference, so QALY increments in the model were not driven by increments in overall survival.
- Although there was poor exchangeability between the model and trial populations, only the differences in baseline HbA1c levels were likely to change the conclusions of the model in terms of treatment effects i.e. lead to a lack of transitivity.
- While the use of the US retrospective cohort study by Karter et al as a source of model inputs could be considered inappropriate due to the poor healthcare system in USA, the cohorts were fully insured patients extracted from the Kaiser Permanente Health Maintenance Organisation and therefore the level of healthcare they would receive is likely more comparable to healthcare access under the Australian system than the rest of the USA healthcare system.
- Zero hospitalisations for severe hypoglycaemia or diabetic ketoacidosis in CGM arm were assumed but the modelled increments in these events reflected observed differences, so an increase in the CGM arm would require an equal increase in the SMBG arm.
- The model assumes that health states and their disutilities are independent, and thus would be additive for the same individual's lifetime. Although this overestimates the modelled incremental QALYs (because such disutilities are not additive), this is likely to only have a miniscule impact on the ICER because the extent of such additions is small.

ESC noted that the modelled budget impact took an epidemiological approach, which it considered reasonable because a market share approach was not possible.

ESC identified several issues with the financial estimates, but considered that a significant budgetary impact would be expected.

ESC noted several varying estimates for insulin use by T2D patients. ESC noted the department's advice that, because NDSS data (which was used as the basis for the ADAR's projections) covers all people that have T2D that may have used insulin at some point, it will overestimate the number of T2D patients using insulin.

ESC considered that the estimated uptake rates of CGM in older populations were questionable and were not supported by any evidence from similar markets. Assumptions of full compliance and longevity with CGM are both unclear.

The assumed unit cost of SMBG equipment was the amount of the patient's co-payment rather than the cost to the NDSS, and the estimated SMBG cost offsets were therefore not appropriately calculated. ESC considered that the NDSS would be able to correct this error.

ESC considered that the hospital-related financial modelling overestimated the magnitude of cost offsets due to treatment effects reducing diabetic complications:

- The price per patient per month for every 1% change in HbA1c was derived from 2013 US data on commercially insured patients and therefore may not be applicable to the Australian healthcare system. The larger and less relevant weighted incremental cost for commercially insured US patients (applying to patients ≤65 years of age) was selected for the cost modelling rather than Medicare insured USA patients (applying to patients >65 years of age).
- Each unit cost was divided by 36 to get a monthly cost, meaning that these costs were brought forward in time before being inflated by 5% per annum to 2024 costs.
- UKPDS-based projections which may be a poor fit for the Australian population were used to model the absolute reduction in each type of event over time assuming a 1% reduction in HbA1c.
- No timeframe for UKPDS-based projections of these events was provided, so lifelong accrued events over time were assumed, maximising any increments associated with a reduction in complications due to the treatment effect.
- The weighted incremental cost was calculated by applying the monthly unit costs for each type of event to the numbers of events reduced, bringing the avoided costs further forward in time.

In addition, ESC considered it inappropriate to include most of these cost offsets, given that in practice freed resources are likely to be redeployed within hospitals rather than being realised as reductions in the state and territory health budgets.

For these reasons, ESC considered that none of the financial estimates were reliable.

In relation to the differences between the 2 CGM systems to be considered by MSAC, ESC noted that the device cost per annum of Dexcom ONE+ is REDACTED than the device cost per annum of FSL (Application 1786) for the assumed same outcome: a Dexcom ONE+ monitor lasts 10 days while the FSL lasts 14 or 15 days, yielding a total cost per year of $REDACTED for FSL and $REDACTED for Dexcom ONE+.

ESC noted equity of access issues related to CGM. In particular, ESC noted that while CGM is fully funded for concessional status patients with T1D an equivalent monthly co-payment of $35.90 currently applies for people aged 21 years and over who do not have concessional status. ESC noted that the T2D population is much larger and that funding CGM for this population will have a considerable impact on the NDSS budget. ESC noted that consultation feedback suggested that funding of CGM should extend beyond patients with T2D on insulin. Some additional candidate subgroups suggested (gestational diabetes and type 3c diabetes) are included in the FSL application 1786. However, ESC noted that there are limited clinical data for these subgroups. ESC noted that CGM could also be considered for short-term use in newly diagnosed T2D patients for education and prevention of progression.

ESC suggested that if MSAC supports any aspect of the requested funding, MSAC may also wish to consider advising on 3 broader aspects of government policy regarding NDSS funding:

- MSAC could consider recommending that a co-payment be applicable for CGM funding for non-Aboriginal and Torres Strait Islander and non-concessional beneficiaries aged 21 years or over. This is because ESC considered that applying a full subsidy of CGM for T2D patients would create an inequity in subsidy access compared to the existing NDSS subsidy co-payment arrangements for similar patients with T1D (and for blood glucose strips). ESC considered that while applying the T1D CGM co-payment may marginally

reduce the rate and extent of expected uptake and the associated costs, it would give the subpopulations with greatest need access to the full subsidy.

- MSAC could recommend adoption of a device-agnostic cost-minimisation approach across suitable TGA-approved CGM systems. This approach could potentially also be extended to flash glucose monitors (FGMs). If MSAC is not satisfied that a particular CGM (and/or FGM) would provide superior health outcomes over any other CGM (and/or FGM), at least two cost-minimisation approaches could be considered to improve cost-effectiveness, noting that the upfront costs of changing between these options are relatively small (compared to T1D, in which there are clearer links for some patients using insulin pumps). The approach should also account for the different durations of sensor performance. One possible approach is straight price competition, where options which are more expensive than the cheapest option(s) are not NDSS-subsidised. An alternative approach would be similar to the PBS Therapeutic Group Premium Policy, in which the subsidy is only provided up to the cost of the cheapest option so patients pay the premium associated with the more expensive option, so there is more patient choice for more NDSS-subsidised options.
- MSAC could consider whether the proposed restriction on allowing GPs to authorise requests for the NDSS subsidy should be retained given that similar restrictions on GP authorisation do not apply to blood glucose test strips. Although PASC advised that this is not a matter for MSAC, MSAC may wish to consider whether retaining a tighter group of approved authorisers might inappropriately restrict access for the larger T2D population, reducing the rate and extent of expected uptake and the resulting financial implications. However, the equity issues raised above regarding access to authorised health professionals should be taken into account if this option is considered with expected large impact on rural and remote patients.

ESC requested any further information from IQVIA (via the applicant) and the department ahead of MSAC consideration to clarify whether PBAC has previously considered the IQVIA CORE Diabetes Model and if so, to

- Identify the submission(s) and PBAC meeting date(s) for independent verification.
- In each case, determine whether the model included the two WA-based equations driving the cardiovascular and mortality events.
- In each case, determine whether PBAC accepted or rejected the model.

ESC requested that the applicant provide the following additional information to support its contention that the economic model has been sufficiently validated:

- Provide a basis to accept that the model has been validated to estimate incremental effects on the patient-relevant health states following any HbA1c improvement. This should include a basis for assessing the effect of expected lags in onset of the treatment effect and less than a full epidemiological-based prediction, noting the duration of change of HbA1c levels in any of the RCTs identified in the evidence base used for the validation.
- Provide a basis to accept that any such previously established model validity is still relevant despite changes to model structure, changes to methods of generating some outcomes, and changes to risk equations affecting other outcomes (as outlined in the ADAR). This should include an assessment of the consequence of broken links in a model with 'interdependent Markov sub-models designed to interact' and, given that the model is most sensitive to the changed risk equations, an assessment of the consequences of the mortality equations that have been substituted into the ADAR model being based on the smallest evidence base (Hayes et al. (2013)).

The applicant is also requested to explain precisely what HbA1c effect in each arm was applied to the HbA1c output from the previous cycle in each cycle of the model, and thus the increment in each cycle to assess the effect of expected lag of onset of effect and less than full epidemiological prediction. The applicant should assess more clearly the assumptions made in the model for the onset and any waning of incremental effect.

Finally, given the absence of an editable electronic version of the model, the applicant is requested to provide per year traces over the duration of the model (refer to MSAC Guidelines TG 23.5) for each of the following scenarios of year 1 HbA1c reductions: 0.56% and 0.3%, and for each of the CGM arm, the SMBG arm and the increment:

- HbA1c (tabulated and graphed)
- proportions of patients in each of the health states (graphed), with proportions free of complication and death in a separate graph, and identifying any merged or omitted diabetes complication health states compared to the publicly reported IQVIA CORE Diabetes Model
- modelled aggregate discounted costs and modelled discounted QALYs (graphed, accrued)
- modelled discounted cost/QALY (increment only, graphed, accrued).

The model traces should demonstrate clinical plausibility (e.g. all patients deceased at the end of the model lifetime).

ESC also requested that further information be extracted from the studies identified in the ADAR on (i) the longevity of the treatment effect (on HbA1c levels) related to CGM use and (ii) the impact of CGM in reducing the risk of hypo- and hyperglycaemic episodes in patients who have acute intercurrent illness (e.g. urinary tract infection). ESC also requested clarification on whether studies other than DIAMOND excluded the impacts of insulin pump use.

17. Applicant comments on MSAC's Public Summary Document

We acknowledge MSACs decision to defer at this time. Dexcom remains committed to working collaboratively with MSAC and the Department of Health to achieve a positive outcome in the near future. Our goal is to ensure equitable access to CGM for all individuals with insulin-treated Type 2 diabetes, recognising the significant clinical and quality-of-life benefits this technology provides.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website.