

MSAC Application 1786

FreeStyle Libre 2 continuous glucose monitoring system for people with insulin dependent type 2 diabetes, gestational diabetes and type 3c diabetes

Applicant: Abbott Australasia Pty Ltd

PICO Confirmation

Summary of PPICO criteria to define question(s) to be addressed in an Assessment Report to the Medical Services Advisory Committee (MSAC)

Table 1 PICO for Freestyle Libre 2 continuous glucose monitoring in people with Type 2 diabetes: PICO Set 1

Component	Description
Population	<p>People with type 2 diabetes (T2D) requiring insulin therapy.</p> <p>Subpopulation: those requiring intensive insulin therapy (IIT) (i.e. require multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII) who are recommended to carry out frequent monitoring of their blood glucose).</p>
Prior tests	<p>Diagnostic tests for T2D if</p> <p>a) asymptomatic and at high risk (Australian type 2 diabetes risk assessment tool [AUSDRISK] score ≥ 12 or in specific high-risk categories):</p> <ul style="list-style-type: none"> • glycated haemoglobin (HbA1c) $\geq 6.5\%$ (48 mmol/mol) on two separate occasions, or • fasting blood glucose (FBG) ≥ 7.0 mmol/L, or • random blood glucose ≥ 11.1 mmol/L confirmed by a second abnormal FBG on a separate day, or • oral glucose tolerance testing (OGTT) before (fasting) and two hours after an oral 75 g glucose load is taken. Diabetes is diagnosed as FBG ≥ 7.0 mmol/L or two-hour post-challenge blood glucose ≥ 11.1 mmol/L, or <p>b) if symptoms of hyperglycaemia present and</p> <ul style="list-style-type: none"> • a patient presenting with hyperglycaemic crisis, or • a single elevated FBG ≥ 7.0 mmol/L, or • single HbA1c $\geq 6.5\%$ (48 mmol/mol), or • a random blood glucose ≥ 11.1 mmol/L.
Intervention	FreeStyle Libre 2 Continuous Glucose Monitor (CGM) system
Comparator/s	Self-monitoring of blood glucose (SMBG) test using a finger prick blood sample.
Reference standard	Laboratory conducted plasma venous blood glucose test
Outcomes	<p><u>Patient relevant outcomes</u></p> <p><i>Direct evidence for safety and effectiveness:</i></p> <p>Safety:</p> <ul style="list-style-type: none"> • Local adverse events (AEs) associated with glucose testing <p>Effectiveness:</p> <ul style="list-style-type: none"> • T2D complications (e.g. cardiovascular and microvascular complications including kidney disease, neuropathy/nerve damage, retinopathy/eye disease, amputations/foot ulcers) • Mortality • Quality of life • Psychological health • Hypoglycaemic or hyperglycaemic events resulting in emergency room visit/hospitalisation

Component	Description
	<p>Intermediate/surrogate outcomes:</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ glycated haemoglobin (HbA1c) ○ time in range (TIR), time below range (TBR) and time above range (TAR) ○ number of hypoglycaemic/hyperglycaemic excursions ○ glycaemic variability • Change in body weight/ body mass index (BMI) <p><i>Additional outcomes using linked evidence approach:</i></p> <p>Analytical validity:</p> <ul style="list-style-type: none"> • Accuracy, concordance • Monitoring (CGM or SMBG) failure rate <p>Change in management:</p> <ul style="list-style-type: none"> • Uptake or alteration of lifestyle interventions (e.g. diet and exercise) and treatment (e.g. glucose-lowering therapy) • Adherence to CGM or SMBG • Adherence to treatments <p><u>Other relevant considerations</u></p> <ul style="list-style-type: none"> • 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 <p><u>Healthcare system outcomes</u></p> <ul style="list-style-type: none"> • Cost, cost-effectiveness • Financial implications (financial impact, overall healthcare costs, etc.)
Assessment questions	What is the safety, effectiveness and cost-effectiveness of Freestyle Libre 2 CGM versus SMBG in people with T2D requiring insulin therapy?

Table 2 PICO for Freestyle Libre 2 continuous glucose monitoring in people with gestational diabetes: PICO Set 2

Component	Description
Population	Pregnant women with gestational diabetes mellitus (GDM)
Prior tests	<p>Glycaemic assessment of pregnant mother between 24 – 28 weeks gestation:</p> <p>Royal Australian College of General Practitioners (RACGP) criteria:</p> <ul style="list-style-type: none"> • fasting plasma glucose ≥ 5.5 mmol/L, or • two-hour plasma glucose ≥ 8.0 mmol/L (75 g OGTT). <p>Australian Diabetes in Pregnancy Society (ADIPS) criteria:</p> <ul style="list-style-type: none"> • fasting plasma glucose 5.1–6.9 mmol/L, or • one-hour plasma glucose (75 g OGTT) ≥ 10.0 mmol/L, or • two-hour plasma glucose (75 g OGTT) 8.5–11.0 mmol/L

Component	Description
Intervention	Freestyle Libre 2 Continuous Glucose Monitor (CGM) system
Comparator/s	Self-monitoring of blood glucose (SMBG) using a finger prick capillary blood sample, glucose test strips and a glucose meter.
Reference standard	Laboratory conducted plasma venous blood glucose test
Outcomes	<p><u>Patient relevant outcomes</u></p> <p><i>Direct evidence for safety and effectiveness:</i></p> <p>Safety:</p> <ul style="list-style-type: none"> • Local adverse events (AEs) associated with glucose testing <p>Effectiveness for mother:</p> <ul style="list-style-type: none"> • GDM complications (e.g. cardiovascular complications, hypertension etc) • Mortality • GDM leading to hospitalisations/emergency room visits • Complications during birth • T2D post-partum and related complications • Quality of life • Psychological health <p>Intermediate/surrogate outcomes:</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ glycated haemoglobin (HbA1c) ○ mean fasting glucose concentration during the first 4 weeks of glucose monitoring (CGM or SMBG) ○ post prandial mean glycaemia ○ time in range (TIR), time below range (TBR) and time above range (TAR) ○ number of hypoglycaemic/hyperglycaemic excursions ○ glycaemic variability • Change in body weight/ body mass index (BMI) <p>Effectiveness for child:</p> <ul style="list-style-type: none"> • Neonatal complications (neonatal hypoglycaemia; large for gestational age; gestational age at birth; respiratory complications; high birth weight) • Complications during birth • Admission to neonatal intensive care unit (NICU) • Long-term outcomes for child (e.g. obesity, diagnosis of T2D, heart disease) <p><i>Additional outcomes using linked evidence approach:</i></p> <p>Analytical validity:</p> <ul style="list-style-type: none"> • Accuracy, concordance • Monitoring (CGM or SMBG) failure rate <p>Change in management:</p> <ul style="list-style-type: none"> • Uptake or alteration of lifestyle interventions (e.g. diet and exercise) and treatment (e.g. glucose-lowering therapy)

Component	Description
	<ul style="list-style-type: none"> Adherence to CGM or SMBG Adherence to treatments <p>Other relevant considerations</p> <ul style="list-style-type: none"> 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 GDM and achieve their clinical goals) Work/school absenteeism and daily functioning <p>Healthcare system outcomes</p> <ul style="list-style-type: none"> Cost, cost-effectiveness Financial implications (financial impact, overall healthcare costs, including cost of ongoing surveillance of mother and child post-partum for complications of GDM and development of T2D).
Assessment questions	What is the safety, effectiveness and cost-effectiveness of Freestyle Libre 2 CGM versus SMBG in pregnant women with GDM?

Table 3 PICO for Freestyle Libre 2 continuous glucose monitoring in people with “other types of diabetes”: PICO Set 3

Component	Description
Population	People aged ≥ 21 years with “other types of diabetes” (e.g. Type 3c diabetes) similar to T1D requiring insulin
Prior tests	For type 3c diabetes: Fasting blood glucose (FBG), HbA1c test, imaging of the pancreas, blood tests for pancreas function, blood test to rule out type 1 diabetes. Other rare types of diabetes similar to T1D: Testing as recommended by the American Diabetes Association guidelines (American Diabetes Association 2024a).
Intervention	Freestyle Libre 2 Continuous Glucose Monitor (CGM) system
Comparator/s	Self-monitoring of blood glucose (SMBG) using a finger prick capillary blood sample, glucose test strips and a glucose meter.
Reference standard	Laboratory conducted plasma venous blood glucose test
Outcomes	<p>Patient relevant outcomes</p> <p><i>Direct evidence for safety and effectiveness:</i></p> <p>Safety:</p> <ul style="list-style-type: none"> Local adverse events (AEs) associated with glucose testing <p>Effectiveness:</p> <ul style="list-style-type: none"> Diabetes-related complications (e.g. cardiovascular and microvascular complications including kidney disease, neuropathy/nerve damage, retinopathy/eye disease, amputations/foot ulcers) Mortality Quality of life

Component	Description
	<ul style="list-style-type: none"> • Psychological health • Hypoglycaemic or hyperglycaemic events resulting in emergency room visit/hospitalisation <p>Intermediate/surrogate outcomes:</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ glycated haemoglobin (HbA1c) ○ time in range (TIR), time below range (TBR) and time above range (TAR) ○ number of hypoglycaemic/hyperglycaemic excursions ○ glycaemic variability • Change in body weight/ body mass index (BMI) <p><i>Additional outcomes using linked evidence approach:</i></p> <p>Analytical validity:</p> <ul style="list-style-type: none"> • Accuracy, concordance • Monitoring (CGM or SMBG) failure rate <p>Change in management:</p> <ul style="list-style-type: none"> • Adherence to CGM or SMBG • Adherence to treatments • Uptake or alteration of lifestyle intervention or treatment (e.g. glucose-lowering therapy) <p><u>Other relevant considerations</u></p> <ul style="list-style-type: none"> • 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 diabetes and achieve their clinical goals) • Work/school absenteeism and daily functioning <p><u>Healthcare system outcomes</u></p> <ul style="list-style-type: none"> • Cost, cost-effectiveness • Financial implications (financial impact, overall healthcare costs, etc.)
Assessment questions	What is the safety, effectiveness and cost-effectiveness of Freestyle Libre 2 CGM versus SMBG in people with “other types of diabetes” similar to T1D requiring insulin (e.g. type 3c diabetes)?

Purpose of application

An application requesting National Diabetes Services Scheme (NDSS) funding of the FreeStyle Libre 2 CGM for monitoring of glucose levels in people with type 2 diabetes (T2D) requiring treatment with insulin (PICO Set 1), pregnant women with gestational diabetes (PICO Set 2) and people with Type 3c diabetes requiring insulin (PICO Set 3) was received from Abbott Australasia Pty Ltd by the Department of Health and Aged Care. PICO Set 3 was subsequently expanded (following a meeting including the Department of Health and Aged Care and the applicant) to include all people aged ≥ 21 years with “other types of diabetes” that require insulin to address the current NDSS funding inequity.

The clinical claim relevant to all populations is that FreeStyle Libre 2 (FSL2) provides superior efficacy in terms of glycaemic control and non-inferior safety compared to self-monitoring of blood glucose (SMBG) using a finger prick capillary blood sample, blood glucose test strips and a glucose meter.

The rationale for the claim provided in the MSAC 1786 application is that use of FSL2 results in statistically and clinically significantly greater improvement in glycaemic control as measured by change in glycated haemoglobin (HbA1c) level, other markers of glycaemic control including time in the normal glycaemic range,¹ and the occurrence of hypoglycaemic or hyperglycaemic excursions. Improvement in HbA1c observed in the clinical studies is associated with improvement in long-term diabetes control and reduced development of macrovascular and microvascular complications. Use of FSL2 also results in reduced healthcare resource use (e.g. reduced hospital admissions), and improved patient satisfaction and quality of life (QoL) as reported in clinical studies and during real world use.

The applicant highlighted that improvement in glycaemic control by use of FSL2 CGM is achieved by providing additional information over SMBG. This facilitates better informed decisions (e.g. use of insulin, diet and exercise), changes in clinician management and in patient behaviour which contribute to the clinical improvements observed. Other features of CGM devices, such as the real-time alarms in FSL2, also help CGM users reduce or prevent acute hypoglycaemic and hyperglycaemic events.

PICO Set 1

Population

The population for PICO Set 1 is people with T2D requiring insulin therapy. This includes use of insulin in combination with other glucose-lowering therapies for T2D. The applicant has proposed that all people with T2D requiring insulin therapy should have access to FSL2 because a meta-analysis of FreeStyle Libre (FSL) clinical studies for inclusion in the MSAC assessment report has reported a clinically meaningful HbA1c reduction (i.e. 0.3–0.5% MCID) with use of FSL2 in subpopulations of people with T2D using either IIT or using basal insulin alone.

The proposed population also includes a subpopulation of people with T2D using intensive insulin therapy (IIT) defined in the application as patients requiring multiple daily insulin injections (≥ 3 injections) or, less commonly, continuous subcutaneous insulin infusion (CSII). This subpopulation is recommended to carry

¹ Improved time in range refers to the time per day [% of CGM readings or minutes/hours] within the target glycaemic range of 70–180 mg/dL [3.9–10.0 mmol/L] for T2D as defined by the international consensus report for time in range for CGM (Battelino et al. 2019).

out frequent monitoring of their blood glucose (i.e. multiple times per day and usually with meals) and therefore could be considered to have a higher need for CGM. Importantly, the applicant's preference is that patients who use co-formulated or pre-mixed insulin are not included within this subpopulation of people with T2D who receive IIT. Unlike the MSAC 1785 application for Dexcom ONE+, the applicant has not proposed that NDSS-funded access to FSL2 is limited to only those T2D patients with "suboptimal glycaemic control". These differences in definition of IIT and sources of diabetes data result in a significant difference between MSAC Applications 1785 and 1786 in terms of the number of people with T2D classified as "intensive insulin therapy" users.

PASC noted that the proposed population is all people with T2D who require treatment with insulin. They also noted that the application included a subpopulation of users of intensive insulin therapy (IIT) defined in the application as people with T2D requiring multiple daily insulin injections (basal and bolus insulin) or, less commonly, continuous subcutaneous insulin infusion (CSII).

PASC noted that the definition of an "intensive insulin user" was different in the Dexcom ONE+ CGM and FSL2 CGM applications. In the FSL2 application, the subpopulation defined as "intensive insulin users" were those receiving multiple (three or more) injections daily (basal insulin and prandial bolus insulin) or a CSII; this subpopulation did not include people receiving treatment with co-formulated or pre-mixed insulin. The applicant stated this was because patients on pre-mixed insulin generally only receive insulin injections once to twice daily but acknowledged that there was no fixed definition of an "intensive insulin user". The applicant further noted that the evidence identified for the IIT population was not inclusive of patients on pre-mixed insulin but clarified that these patients should still be considered part of the proposed overarching population of people with T2D who require treatment with insulin (although not intensive insulin users)PASC also noted that suboptimal glycaemic control was not a requirement included in the population definition in the FSL2 application.

The FSL2 system sensors and readers are TGA approved (ARTG 233514). FSL2 is indicated for "measuring interstitial fluid glucose levels in people (age 4 years and older) with diabetes mellitus, including pregnant women. The Reader and Sensor are designed to replace blood glucose testing in the self-management of diabetes, including dosing of insulin. The indication for children (age 4 - 12) is limited to those who are supervised by a caregiver who is at least 18 years of age. The caregiver is responsible for managing or assisting the child to manage the Reader and Sensor and also for interpreting or assisting the child to interpret Sensor glucose readings".

The proposed population in PICO Set 1 (people with T2D requiring insulin therapy) for NDSS funding of FSL2 CGM is narrower than the approved TGA indication.

Currently, all people with type 1 diabetes (T1D) are eligible to apply for access to subsidised CGM products through the NDSS, as well as some people under the age of 21 years who have other rare conditions that are similar to T1D if they have a listed eligible condition.² People with T1D who: hold valid concessional status; or are pregnant, planning pregnancy or immediately post-pregnancy; or are under the age of 21 years are eligible to access fully subsidised CGM products (i.e. no co-payment is required). People with T1D

² NDSS. Conditions very similar to type 1 diabetes, eligible to access the CGM Initiative through the NDSS. <https://www.ndss.com.au/about-the-ndss/cgm-access/other-eligible-conditions-age-under-21-years/>

aged 21 years or older who do not hold valid concessional status can access these products with a co-payment.

Prevalence of T2D

Type 2 diabetes (T2D) is the most common form of diabetes representing around 85–90% of all people with diabetes mellitus in Australia³. In 2021, almost 1 in 20 Australians (1.2 million or 4.6% of the population) were living with T2D based on NDSS registration and Australasian Paediatric Endocrine Group (APEG) state-based registers, although the true prevalence may be higher⁴. Around 45,700 people were newly diagnosed with T2D in Australia in 2021 i.e. around 125 people per day. Published data (as of 30 September 2023) for the number of people with diabetes registered with the NDSS are shown below:

- Type 1 diabetes: 135,423 (9.4%)
- Type 2 diabetes: 1,256,493 (86.7%)
- Gestational diabetes: 44,577 (3.1%)
- Other diabetes: 11,622 (0.8%)

Additionally, it was estimated in 2023 that around 15% of Australian adults aged ≥ 25 years (~2 million people) are either living with prediabetes or are at high risk of developing T2D and approximately 500,000 people had undiagnosed T2D (Diabetes Australia).

Overall, males are 1.3 times more likely to be living with T2D than females and the prevalence of T2D increases with age, from 3.1% in people aged <40 years to 59% in people aged >65 years. The peak of prevalence is in people aged 80 – 84 years (22% and 17% for males and females, respectively) although the incidence and prevalence of T2D among children, adolescents and young adults (early-onset T2D) is increasing. A family history of T2D or having gestational diabetes during pregnancy increases the risk of developing T2D in addition to lifestyle factors such as poor diet, physical inactivity, smoking, and high alcohol consumption.

Aboriginal and Torres Strait Islander Australians have higher rates of T2D compared to the general population (Diabetes Australia). Other racial groups and ethnicities at increased risk of T2D include African American, Hispanic, Pacific Islander, Asian and Middle Eastern populations (Titmuss et al. 2024). The prevalence of T2D is higher in socially disadvantaged populations and those living in more remote areas of Australia. It was estimated in 2018-2019 that around 10.7% (51,900) of Aboriginal and Torres Strait Islander people were living with T2D.³ The age-standardised prevalence of T2D was similar among Indigenous men and women. Onset in these communities often occurs at a younger age with more severe outcomes including premature mortality. T2D is a particular problem for indigenous children, with Western Australian data from 1990-2012 suggesting an incidence of 31.1 per 100,000 compared to 1.4 per 100,000 in non-indigenous children (Haynes et al. 2016).

PASC recognised that there was likely to be a hierarchy of clinical need within the T2D population requiring insulin, with some patients having a greater need for CGM, such as those at increased risk of severe hypoglycaemia or people lacking hypoglycaemia awareness. PASC noted that there were likely other

³ diabetes australia, Type 2 diabetes <https://www.diabetesaustralia.com.au/about-diabetes/type-2-diabetes/>

⁴ Australian Government Australian Institute of Health and Welfare (Accessed November 2024). Diabetes: Australian facts. Type 2 diabetes.

<https://www.aihw.gov.au/reports/diabetes/diabetes/contents/how-common-is-diabetes/type-2-diabetes>

populations with T2D considered to have a high unmet need such as Indigenous Australian populations, children, pregnant women, people who are vulnerable or socially disadvantaged and people living in regional or remote areas.

PASC accepted the independent clinical expert's advice that young people (<18y) are generally perceived to "do well" on completion of learning how to use CGM. The applicant noted that people with onset of T2D earlier in life also present with more severe and debilitating symptoms; this group may have more to gain from CGM as they are experiencing more severe illness and initially present with a higher HbA1c level than people with T2D onset later in life. However, patients with less severe disease may also benefit from CGM, particularly given the small minimum clinically important difference (MCID) in HbA1c level that equates to clinical benefit.

Estimates of the number of people with T2D using insulin vary. According to data from the NDSS, 315,432 (25%) of Australians with T2D required insulin therapy as of 30 June 2024.⁵ These estimates are higher than data included in the application indicating that the prevalence of people with T2D who require insulin in Australia is approximately 201,080, based on the number of people with T2D who had an insulin script dispensed over a 12-month period on the NDSS (Prospection 2022).

PASC noted that the estimates of people with T2D using insulin varied substantially between this application and application 1785 because they relied on different data sources, and an accurate population estimate was uncertain.

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, either as a monotherapy or in combination with other glucose-lowering drugs (Australian National Diabetes Audit).

According to the ANDA in 2022, 70.1% of people with T2D require IIT (basal and rapid acting insulin therapy) and 27.2% require non-intensive insulin therapy (basal insulin therapy only) (Australian National Diabetes Audit). It is unclear whether the distribution of insulin therapy for T2D is comparable across different age groups.

Natural history and disease burden of T2D

T2D is a chronic progressive condition caused by insulin resistance and pancreatic islet cell dysfunction leading to a relative insulin deficiency. The relative insulin deficiency results in chronic hyperglycaemia and affects carbohydrate, protein and fat metabolism. This leads to potentially life-threatening long-term macrovascular and microvascular complications (e.g. cardiovascular disease, renal failure, eye problems), has a significant impact on mental health (e.g. treatment-related distress, anxiety, depression) and significantly impacts on quality of life.

T2D is attributed to a combination of modifiable lifestyle-related risk factors interacting with non-modifiable and genetic risk factors. An umbrella review of meta-analyses identified numerous risk factors for T2D, with obesity, gestational diabetes, metabolic syndrome, and lack of exercise being some of the key risk factors (Bellou et al. 2018). Almost 60 per cent of all cases of T2D can be delayed or prevented with changes to diet and lifestyle (Diabetes Australia). There is an inverse linear relationship between

⁵ National Diabetes Services Scheme. Insulin Therapy. <https://www.ndss.com.au/wp-content/uploads/Insulin-Therapy-1.pdf>

obesity and age of T2D onset (Hillier & Pedula 2001). A review of T2D in young adults in the United Kingdom reported that an increase in obesity and a less physically active lifestyle in the general population over the last 20 years have both contributed to an earlier average age of onset for T2D (Htike et al. 2015). The mean \pm SD body mass index (BMI) of people with T2D included in the ANDA in 2022 was in the obese range (≥ 30 kg/m²) at 33.2 ± 7.9 kg/m² (Australian National Diabetes Audit).

The burden of disease of T2D in Australia is substantive. In 2022 in Australia, T2D was responsible for 125,500 disability-adjusted life years (DALY) which equates to 3.9 DALYs per 1,000 population (AIHW 2023). This resulted in T2D being attributed as the 12th leading contributor to total disease burden in Australia. Diabetes in general places a great burden on Australia's healthcare system, having been allocated approximately \$3.4 billion of Australia's expenditure in 2020-21, of which 2.3 billion was allocated to T2D (Australian Institute of Health and Welfare 2023).

T2D is associated with microvascular (e.g., diabetic retinopathy, nephropathy) and macrovascular (e.g., cardiovascular disease, strokes) complications that significantly influence the morbidity and mortality of patients. Because more people are being diagnosed with T2D at an earlier age, more people are living longer with T2D and are at increased risk of developing severe complications. T2D results in a 2 to 4-fold increase in the mortality rate of adults from heart disease and stroke. Accelerated development of atherosclerosis associated with dyslipidaemia leads to severe peripheral vascular disease, premature coronary artery disease (CAD) and increased risk of cerebrovascular diseases (Battisti, Palmisano & Keane 2003; Beckman, Creager & Libby 2002; Haffner et al. 1998; Nesto 2004). Myocardial infarctions and angioplasties together account for ~7% of T2D complications in Australia (Australian National Diabetes Audit). Other comorbidities included peripheral neuropathy (accounted for 24% of T2D foot complications), kidney disease (45% had Stage 3 to 5 kidney disease) eye disease (e.g. 75% attended optometrist/ophthalmologist) as well as 50% of people reporting depression, anxiety or diabetes distress (Australian National Diabetes Audit).

In Australia, diabetes was among the 10th leading causes of death in 2021, contributing to around 19,300 deaths (11.2% of all deaths). Diabetes death rates were 4.4 times higher among Indigenous Australians than non-Indigenous Australians (Australian Institute of Health and Welfare). Where diabetes was listed as the underlying and/or associated cause of death, 58% were due to T2D compared to 4.2% for T1D and 38% for other or unspecified diabetes types, although this may be an underestimation. Where diabetes was listed as the underlying cause of death in 2021, common associated causes of death include coronary heart disease (41%), kidney failure (41%) and hypertensive diseases (34%) (Australian Institute of Health and Welfare).

Prior tests

There are currently no national screening programs for T2D, pre-diabetes or obesity in Australia (Parliament of Australia).

Adults with T2D are usually diagnosed by their general practitioner (GP) either via a routine blood test that identifies abnormal glycaemia without associated symptoms or after presenting with characteristic symptoms of diabetes (e.g. increased thirst, urination, tiredness, blurred vision).

In Australia, regular screening for T2D is recommended for at-risk populations. Early detection of T2D can reduce a person's risk of developing complications and improve long-term outcomes. The primary

screening measure for T2D in a primary care setting is the Australian Diabetes Risk Assessment (AUSDRISK) tool. AUSDRISK predicts a person's five-year risk of developing T2D. The Royal Australian College of General Practitioners (RACGP) handbook for T2D recommends using the AUSDRISK tool for screening of asymptomatic adults aged ≥ 40 years every three years (The Royal Australian College of General Practitioners 2020). The AUSDRISK tool is not validated for use in children, adolescents, younger adults or Aboriginal and Torres Strait Islanders. Aboriginal and Torres Strait Islander adults are screened annually using fasting blood glucose (FBG) and HbA1c testing because of their increased risk of developing T2D.

Adults who do not have symptoms of hyperglycaemia but are identified as being at increased risk of T2D during screening (AUSDRISK score >12 or with other designated risk factors) are assessed for the following diagnostic outcomes using venous blood tests (The Royal Australian College of General Practitioners 2020):

- HbA1c $\geq 6.5\%$ (48 mmol/mol) tested on two 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
- oral glucose tolerance test (OGTT) before (fasting) and two hours after an oral 75 g glucose load is taken. Diabetes is diagnosed as FBG ≥ 7.0 mmol/L or two-hour post-challenge blood glucose ≥ 11.1 mmol/L.

Prediabetes is a metabolic condition characterised by elevated blood glucose levels that do not meet the diagnostic criteria for T2D. People with prediabetes have an impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and/or elevated HbA1c. If IFG or IGT are identified during testing, then subsequent diabetes screening is carried out annually. If initial tests are within the normal range, screening continues every 3 years or earlier if the individual's BMI increases. Prediabetes affects around 1 in 6 Australian adults over the age of 25 years. Unless lifestyle interventions such as change in diet, weight loss and increase in exercise are adopted, approximately 1 in 3 people with prediabetes will develop T2D within ten years. Additionally, people with prediabetes are already at increased risk of developing cardiovascular disease (Bell et al. 2020).

For adults presenting with symptoms of hyperglycaemia (e.g. tiredness, increased urination and thirst, frequent infections, blurred vision, loss of sensation, poor wound healing, weight loss), one of the following test outcomes is considered confirmatory of a diagnosis of T2D (The Royal Australian College of General Practitioners 2020):

- a patient presenting with hyperglycaemic crisis
- a single elevated FBG ≥ 7.0 mmol/L
- single HbA1c $\geq 6.5\%$ (48 mmol/mol)
- a random blood glucose ≥ 11.1 mmol/L.

Adults with signs of insulin resistance (i.e. acanthosis nigricans, skin tags, central obesity, hirsutism) should also receive FBG or HbA1c tests for T2D.

Paediatric T2D is typically diagnosed in the second decade of life, coinciding with the physiological pubertal increase in insulin resistance (Peña et al. 2020). The Australasian consensus guidelines for screening, assessment and management of children and adolescents with T2D recommends targeted screening every 2 to 3 years in non-indigenous children and adolescents aged >10 years or who have reached puberty,

(whichever occurs earlier) who are overweight or obese and have one or more additional risk factors (e.g. family history of diabetes mellitus, race or ethnicity at increased risk) or signs of insulin resistance using the OGTT or HbA1c test (Peña et al. 2020). A diagnosis of T2D is confirmed using either the FGT, 2-hour OGTT or HbA1c test. Testing for diabetes autoantibodies is also carried out to rule out T1D, which occurs in children at a 10-fold higher rate than T2D. Further testing may also be carried out to exclude other rarer types of diabetes (Peña et al. 2020).

The Australasian consensus guidelines recommends point-of-care HbA1c screening for all Aboriginal and Torres Strait Islander children aged ≥ 10 years with one or more risk factors (overweight/obese, family history of DM, signs of insulin resistance, other comorbid conditions and using psychotropic medications) as these children have an earlier age of T2D onset with T2D being reported in children aged ≤ 5 years (Peña et al. 2020). Screening is repeated at 6 monthly intervals if an individual is identified as being at-risk of diabetes or annually if no diabetes is confirmed during screening.

After a T2D diagnosis is established, a detailed assessment of the person with T2D is carried out including a full medical history, physical assessment, assessment of comorbidities that could impact on glycaemic control and assessment of cardiovascular risk status. Cardiovascular disease (CVD) is the leading cause of death in people with diabetes making assessment, prevention and management of CVD risk a critical element of diabetes care. All people with T2D should be assessed for absolute CVD risk at diagnosis using a validated tool, unless they are already confirmed as being at high risk of CVD (The Royal Australian College of General Practitioners 2020). The absolute CVD risk determines the frequency of CVD reassessment, ranging from every 2 years in those at low absolute risk ($<10\%$) to as clinically indicated in those at high risk ($>15\%$) (The Royal Australian College of General Practitioners 2020).

T2D management

The Australian Diabetes Society Type 2 Diabetes Glycaemic Management Algorithm updated in 2024 is based on the Australian Evidence-Based Clinical Guidelines for Diabetes from the Living Evidence for Diabetes Consortium (Figure 1) (Australian Diabetes Society). The Living Evidence for Diabetes Consortium is a collaboration between the Australian Diabetes Society, Diabetes Australia, the Australian Diabetes Educators Association and the Australasian Paediatric Endocrine Group, with representation from the Royal Australian College of General Practitioners, the Australian Government Department of Health and Cochrane Australia (Australian Diabetes Society).

This Type 2 Diabetes Glycaemic Management Algorithm should be read in conjunction with the Living Evidence Guidelines in Diabetes (please click here).

All patients should receive education regarding lifestyle measures: healthy diet, physical activity and **weight management**.
 Determine the individual's HbA1c target – commonly ≤ 53 mmol/mol (7.0%) but should be appropriately individualised (refer to ADS position statement).

+ Weight loss of $\geq 10\%$ will likely allow a reduction or cessation of glucose lowering medication. Consider intensive weight management options including:

- Low energy or very low energy diets with meal replacements
- Pharmacotherapy
- Bariatric surgery.

Click here for the Australian Obesity Management Algorithm

Review treatment: if **not** at target HbA1c or if presence of cardiovascular/chronic kidney disease –

- Check patient understanding of self-management including drug treatment
- Ensure current therapies are clinically appropriate including comorbidities/therapies impacting glycaemic control
- Review medication adherence
- Assess tolerability, adverse effects and risk of interactions

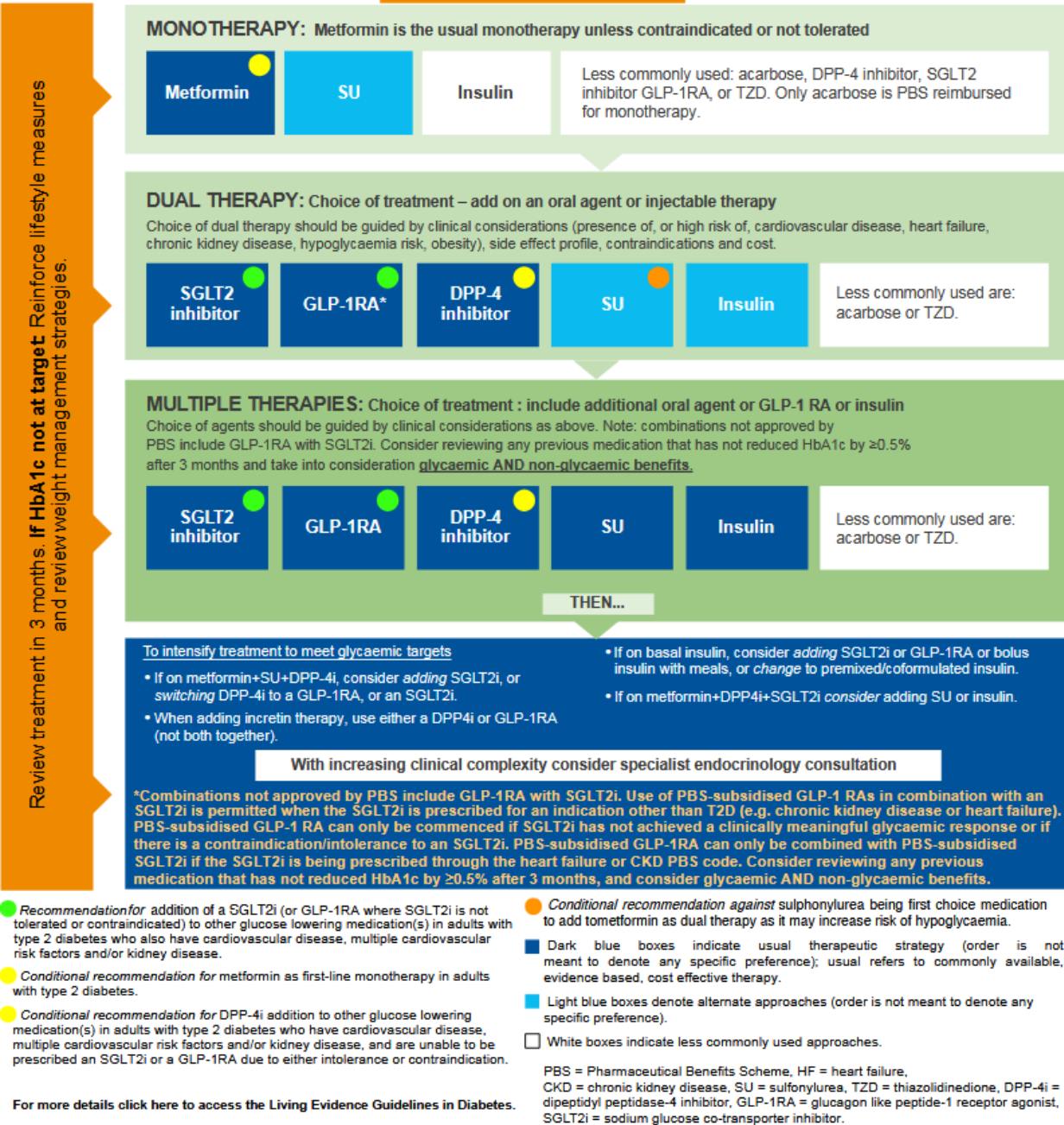


Figure 1 The Australian Diabetes Society T2D glycaemic management algorithm

Source: Reproduced from the Australian Diabetes Society. <https://www.diabetessociety.com.au/guideline/australian-t2d-glycaemic-management-algorithm-june-2024/>

Ratified PICO Confirmation – December 2024 PASC Meeting
 Application 1786 FreeStyle Libre 2 continuous glucose monitoring system for people with insulin dependent type 2 diabetes, gestational diabetes and type 3c diabetes

Because of its heterogeneity and complexity, T2D is managed using a multidisciplinary approach involving paediatric or adult endocrinologists, certified diabetes educators, dietitians, social workers and psychologists. The patient-centred management approach is individualised. Provision of adequate ongoing education and support for people living with T2D or their parents/carers is essential to achieve positive lifestyle changes and appropriate therapeutic management of T2D (Australian Diabetes Society ; Davies et al. 2022; The Royal Australian College of General Practitioners 2020).

According to the Australian T2D Diabetes Glycaemic Management Algorithm (Figure 1), patients diagnosed with T2D or prediabetes should receive education regarding lifestyle including weight loss, healthy diet and physical activity and be investigated for any comorbidities that can impact glycaemic control (The Royal Australian College of General Practitioners 2020). Identification of prediabetes permits earlier introduction of diabetes self-management education and support to promote changes in health and lifestyle behaviours and reduce the risk of progression to T2D. Any comorbidities that could impact on effective glycaemic control are also recorded for subsequent management. Intensive lifestyle changes, including weight loss, may achieve T2D remission, defined as HbA1c levels remaining <6.5% [48 mmol/mol] for at least three months in the absence of glucose-lowering drugs. If T2D remission criteria are met, HbA1c (or, if HbA1c unreliable, fasting plasma glucose or an oral glucose tolerance test) should be performed at least every 6 months to assess persistence of diabetes remission or relapse of diabetes (The Royal Australian College of General Practitioners 2024).

T2D is managed by using appropriate individualised glycaemic targets and subsequently maintaining glycaemic control in line with these targets to achieve an optimal balance between preventing complications associated with hyperglycaemia and reducing the risk of hypoglycaemia. In addition to managing glycaemia, management of cardio-renal risk associated with T2D is also important (The Royal Australian College of General Practitioners 2020).

Glycaemic control targets are individualised considering the benefits and risk of achieving the target HbA1c level, the individual's preferences and available support resources. The common target HbA1c in adults with T2D is $\leq 7\%$ (≤ 53 mmol/mol) and HbA1c levels should be assessed every 3 months (The Royal Australian College of General Practitioners 2020). For children and adolescents, the recommended target HbA1c level is lower at $\leq 6.5\%$ (≤ 48 mmol/mol) due to the likely longer disease duration, the quicker development of T2D-associated complications and the higher mortality rate compared with T2D in adults (Peña et al. 2020). Pregnant women with T2D have an increased risk of poor pregnancy outcomes as observed for gestational diabetes (their babies may be large or small for gestational age, maternal hypertensive complications, preterm birth, caesarean section, birth trauma, neonatal intensive care unit admission, and neonatal hypoglycaemia) (Rudland et al. 2020). The Australian Diabetes in Pregnancy Society (ADIPS) recommends that women with T2D planning a pregnancy require specialist care and should be advised about preparation for pregnancy, achieving and maintaining optimal glycaemic targets, and improving their outcomes; ideally, their HbA1c should be <6.5% prior to conception and during pregnancy (Callaway & Britten 2024; Rudland et al. 2020). The ADIPS guideline recommends glycaemic targets that are appropriate for both the preconception period and pregnancy for use with both SMBG and CGM (Rudland et al. 2020).

Treatment of T2D to establish glycaemic control follows a stepwise approach. If it is not possible to maintain glycaemic control using lifestyle interventions, oral therapies and injectable therapies are available for use, either as mono, dual or multiple therapies, to reduce the risk of microvascular

complications due to uncontrolled hyperglycaemia (Figure 1). Available therapies include biguanide (metformin), sulfonylureas (SU), sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 receptor agonists (GLP-1RA), dipeptidylpeptidase-4 (DPP-4) inhibitors and insulin. Alpha-1-glucosidase inhibitors or thiazolidinediones (TZD) are less frequently used therapies. Monotherapies are used in patients when lifestyle changes are not effective at achieving glycaemic control. First line oral therapy may include metformin or sulphonylurea although metformin is usually recommended unless contraindicated or not tolerated. Reinforcement of the importance of lifestyle measures including healthy diet, physical activity and weight management is also emphasized (Australian Diabetes Society).

If HbA1c levels do not meet agreed targets using monotherapies, dual therapies and, ultimately, multiple therapies may be required for T2D treatment (Australian Diabetes Society 2022). Dual therapy can be considered by addition of a DPP-4 inhibitor or SGLT2 inhibitor or GLP-1RA to the monotherapy (Figure 1). Dose adjustments to and/or addition of glucose-lowering therapies should be carried out so that target HbA1c levels are achieved within 3 to 6 months of treatment initiation. Each class of glucose-lowering therapy has different side effects (e.g. weight gain or increased risk of hypoglycaemia) that can impact on the individual's quality of life. Changes and adjustments to T2D treatment require careful clinical assessment and ongoing consultation with the individual receiving therapy (or their parent/carer) in line with a person-centred approach to diabetes management (The Royal Australian College of General Practitioners 2020). Treatment with multiple therapies for more than two months is recommended to determine their glucose-lowering effectiveness. While it is common for multiple oral therapies to be ineffective, they may still be useful in overcoming a patients' hesitancy about starting insulin therapy.

As the complexity of T2D therapy increases over time, the T2D Diabetes Glycaemic Management Algorithm (Figure 1) recommends that GPs consider referral for a specialist endocrinology consultation which usually occurs before patients are prescribed insulin therapy (Australian Diabetes Society ; The Royal Australian College of General Practitioners 2020).

In contrast to the general T2D population, risk of hypoglycaemia, impaired hypoglycaemia awareness, and complications from insulin are higher in older people with T2D and people who are more vulnerable (e.g. after a recent hospitalisation, poor social support, comorbidity) (Battelino et al. 2019; Bremer et al. 2009). More conservative glycaemic targets and treatments with a lower risk of hypoglycaemia should be selected for these populations. For example, guidance for these populations is to reduce time below 3.9 mmol/L glucose in the hypoglycaemic range to less than 1% of daily time (15 minutes) rather than for less than 4% of daily time (1 hour) as recommended for other people with T2D (unless pregnant) (Battelino et al. 2019; The Royal Australian College of General Practitioners 2020) (The Royal Australian College of General Practitioners 2024).

Insulin for T2D management

Insulin therapy is started in patients who are unable to maintain glycaemic goals using oral glucose-lowering therapies. A range of devices are available to deliver insulin, including insulin pens, syringes and pumps for CSII or hybrid closed loops depending on patient preference, clinical need and ability to self-manage insulin injections. A certified diabetes educator (CDE) or a diabetes nurse practitioner can provide patient support during insulin initiation and a GP or CDE can provide authorisation so that people with T2D requiring insulin are able to access syringes or pen needles through the NDSS.

Insulin is an effective glucose-lowering agent for T2D and can be titrated to suit an individual's requirements. As insulin has a narrow therapeutic window, its use for glycaemic control must be carefully monitored. If glycaemic control by a patient's existing glucose-lowering treatment is sub-optimal, initiating insulin treatment should not be delayed. Reluctance on the part of the individual or their clinician to initiate insulin when glycaemic targets are not achieved is referred to as therapeutic inertia and is often multifactorial. Targeted interventions addressing the reasons for therapeutic inertia have been shown to improve glycaemic management and increase appropriate insulin use (Davies et al. 2022).

Once a decision is made to initiate insulin therapy, patients may start treatment on either basal insulin or on co-formulated/pre-mixed insulin with treatment intensified or reduced if needed according to glycaemic response (The Royal Australian College of General Practitioners 2020). Non-insulin glucose-lowering medicines should generally be continued when insulin is started (Figure 1) (The Royal Australian College of General Practitioners 2020). Basal insulin has a slightly lower risk of hypoglycaemia, especially if the fasting glucose is consistently above target.

If it becomes necessary to intensify insulin treatment further to meet glycaemic targets, the following therapies can be added to or substituted for basal insulin (Australian Diabetes Society):

- Add a sodium-glucose cotransporter-2 (SGLT2) inhibitor, or
- Add a glucagon-like peptide-1 receptor agonist (GLP-1RA), or
- Add bolus rapid-acting insulin with meals, or
- Change to premixed/co-formulated insulin (if not on this already).

Many people with T2D require more intensive insulin therapy, i.e. insulin with meals (prandial insulin) and basal insulin, to achieve their glycaemic target. People with T2D are generally more insulin resistant than those with T1D, require higher daily insulin doses, and have lower rates of hypoglycaemia. Intensification of insulin treatment can be achieved by using multiple daily injections of bolus (prandial) insulin with basal insulin. Alternatively, a co-formulated or premixed insulin may be used. Premixed insulins have various combinations of different concentrations of intermediate-acting basal insulin and rapid-acting insulin and may be more appropriate and simpler for a patient where fasting and postprandial glucose are both consistently elevated. However, dosage adjustment can be more complex with premixed and co-formulated insulins as both insulin components are adjusted simultaneously with an increased risk of hypoglycaemia. Initiation or changes to the type and/or regimen of insulin should ideally be made following consultation with diabetes specialists, a CDE and dietitians.

Rationale

Optimising glycaemic control can improve both immediate and longer-term health outcomes. SMBG is recommended for people with T2D who are using insulin and have been educated in appropriate alterations in insulin dose.

Routine SMBG for people with T2D who are considered low risk and who are using oral glucose-lowering drugs is not recommended, apart from use of sulfonylureas which are associated with an increased risk of hypoglycaemia (The Royal Australian College of General Practitioners 2020). SMBG in people with T2D is also recommended for:

- for people not on insulin who are having difficulty achieving glycaemic control

- when monitoring hypo/hyperglycaemia arising from intercurrent illness
- during pre-pregnancy and pregnancy management for people with established diabetes or gestational diabetes
- when there is a clinical need for monitoring (e.g. during changes in management or lifestyle) or for conditions or medications (e.g. corticosteroids) that require data on glycaemic patterns that measurement of HbA1c cannot provide
- when HbA1c estimations are unreliable (e.g. haemoglobinopathies) (The Royal Australian College of General Practitioners 2020).

Targets for SMBG levels for people with T2D are 4.0–7.0 mmol/L for fasting blood glucose and pre-prandial blood glucose, and 5.0–10.0 mmol/L for postprandial blood glucose, although these targets may be individualised (The Royal Australian College of General Practitioners 2020).

A subpopulation of people with T2D using insulin require IIT, (i.e. require multiple insulin injections per day) may have a higher unmet need for CGM, as they are required to test their blood glucose multiple times per day. The need to frequently ‘finger prick’ to obtain a capillary blood sample and test blood glucose using glucose strips and glucose meter is both painful and time consuming. Depending on the results, they may need to adjust their insulin dose. In the short term, use of FSL2 allows T2D patients on insulin to appropriately manage their insulin dosing regimen. Optimised insulin dosing allows patients to maintain glycaemic control more consistently. Use of CGM with FSL2 to monitor interstitial glucose levels may provide a more easily managed, less painful way of monitoring glycaemic control. The level of information provided by FSL2 is more extensive than provided by SMBG and was considered superior in the application for this subpopulation.

Data for Australia suggests that only 28.7% of people with T2D were able to achieve an HbA1c of <7% having a mean HbA1c of 8.3% indicating that there remains a need for achievement of greater glucose control, although it should be considered that HbA1c levels are individualised with some people having higher or lower HbA1c targets (Australian National Diabetes Audit). A retrospective cohort study used administrative claims data (2012-2015, United States) from adults with T2DM prescribed an oral glucose-lowering therapy, basal insulin, or multiple daily injections of basal-bolus insulin therapy reported that glycaemic control (defined as an HbA1c value of <7% during the last 9 months) was only achieved by 15% of people receiving multiple daily injections of basal-bolus insulin therapy and 22% of patients receiving basal insulin alone. This contrasted with 64% for people using oral glucose-lowering therapy (Brixner et al. 2019).

Poor glycaemic control is associated with long term T2D complications including (The Royal Australian College of General Practitioners 2020):

- cardiovascular complications (stroke, myocardial infarction),
- microvascular ophthalmic complications (retinopathy, refractive errors, cataracts, maculopathy, glaucoma)
- microvascular neuropathy (peripheral and autonomic neuropathy, foot complications)
- microvascular nephropathy (chronic kidney disease)

An alternative option to SMBG is CGM. The recently updated 2024 RACGP guidelines for T2D management state that CGM should be considered for continual or intermittent use in all individuals with T2D on IIT

(multiple daily injections or insulin pumps), subject to individual factors and the availability of resources (The Royal Australian College of General Practitioners 2024). Individuals who might benefit most from CGM include those at increased risk of hypoglycaemia, those with hypoglycaemic unawareness and/or those with high glycaemic variability. The guidelines considered that intermittent use of CGM can be a useful adjunct to use of SMBG. The minimum duration of CGM to obtain enough data to effectively characterise and interpret glycaemia patterns has been reported as at least 7 days (The Royal Australian College of General Practitioners 2024).

Similarly, the recent Parliamentary Inquiry into “The State of Diabetes Mellitus in Australia in 2024” noted that “there is a general consensus among medical professionals and patient groups that all insulin dependent patients, regardless of diabetes type, should have access to subsidised new technologies” (paragraph 5.65, Diabetes Inquiry) (Parliament of Australia).

PASC queried the continued use of CGMs in the event of people with T2D implementing lifestyle changes and achieving glucose control to the extent that they no longer require insulin therapy. The applicant responded that it is rare for people with T2D to achieve the required changes in HbA1c to achieve “remission”, and that cessation of insulin therapy may be temporary. The applicant considered that it would be “counterintuitive” to cease use of the CGM system that facilitated remission because although patients may be symptom-free, they will continue to require ongoing monitoring of glucose levels. PASC acknowledged that any decision to discontinue insulin and hence the requirement for blood glucose monitoring is complex and multifactorial and that the appropriate time to discontinue NDSS subsidised access to CGM would likely need to be based on the clinical judgement of the treating diabetes healthcare professional.

Intervention

The intervention for PICO Set 1 is the FSL2 CGM system. The FSL2 system is a sensor-based, factory-calibrated monitoring system with two key components (Figure 2):⁶

- a disposable 14-day sensor for measuring interstitial glucose levels
- a reader which can either be an app on a compatible smart phone device or a dedicated reader device.

⁶ <https://www.freestylelibre.com.au/>



Figure 2 FreeStyle Libre 2 CGM system: Mobile FreeStyle LibreLink app, FreeStyle Libre 2 reader, and sensor

Source: Figure 5, MSAC 1786 Application

PASC noted the proposed intervention is the FSL2, a sensor-based, factory-calibrated CGM system. FSL2 has two key components: a disposable 14-day sensor for measuring interstitial glucose levels, and a reader which can function either via an app on a compatible smart phone device or a dedicated reader device. PASC noted that in principle it supported a device-agnostic consideration of CGM.

There are also optional alarms for low and high glucose levels, and for signal loss. The alarms are available through the FSL2 reader and app, and low-energy Bluetooth technology is used to enable the alarms.

The disposable single use FSL2 14-day sensor includes the sensor wire and sensor housing. It is inserted using an applicator into the subcutaneous tissue at the back of the upper arm to measure glucose levels every minute in the interstitial fluid. It cannot be used in another area of the body, such as the abdomen or buttocks. These glucose readings are automatically converted via an algorithm to represent blood glucose levels. The level of glucose in interstitial fluid lags behind the level observed in blood by 2.4 minutes in adult and 2.1 minutes in paediatric populations; the lag time varies particularly when blood glucose levels are rapidly rising or falling. While the algorithm corrects for these differences as far as possible, the accuracy of reported blood glucose assessed with CGM is lower in the hypoglycaemic and hyperglycaemic range and during periods when glucose levels are rapidly rising or falling (e.g. following meals, insulin dosing or during exercise). The readings are also less accurate at the beginning and end of the sensor wear period. There is also acknowledged variability in accuracy between individual sensors. Sensor accuracy and variability following manufacture is assessed during quality assurance using a paired comparison between sensors, comparison to SMBG which measures glucose in capillary blood from a finger prick using a glucose test strip and meter or comparison to laboratory assessment of blood glucose in venous blood samples (the reference standard in the PICO).

The FSL2 sensor includes an inbuilt transmitter that sends glucose data to the FreeStyle LibreLink app on a smart phone via Bluetooth. If connection between the sensor and the app is lost, it is possible to manually scan the sensor with the smart phone app to backfill up to 8 hours of glucose data. If the sensor is started with the FreeStyle LibreLink app, a FreeStyle Libre 2 reader will not be able to read data from that sensor and vice versa. The FSL2 system includes two smart phone apps that are only compatible with certain smart phones. The FreeStyle LibreLinkUp app is used to enable up to 20 people such as family, friends or

authorized caregivers to remotely share glucose threshold alarm notifications and glucose data. This can provide the person with T2D some additional reassurance when sleeping which is a time when the risk of hypoglycaemia is higher or if out socialising. The FreeStyle LibreLink app is also able to connect with the NovoPen 6 (NovoNordisk) insulin pen to allow tracking of insulin usage without manually uploading data and enables sharing of insulin use data with a diabetes healthcare professional via LibreView.

FSL2 continuously measures glucose levels every minute and provides glucose trend arrows, predictive messages about glucose levels, optional individualised threshold alarms for hyperglycaemia and hypoglycaemia, information about glucose variability, and glucose patterns across a 24-hour period. Data is automatically sent to the FreeStyle LibreLink app every minute, removing the need to scan the sensor with the smartphone app to obtain glucose data. Therefore, the FSL2 CGM, unlike earlier versions of the FreeStyle Libre, when paired with the FreeStyle LibreLink app is a continuous glucose monitor rather than a Flash glucose monitor as it is not necessary to scan the sensor to obtain glucose readings.

The FSL2 reader does not connect to the internet or require mobile data. It can be used as a dedicated reader device by people who do not have access to a smart phone that is compatible with the FreeStyle LibreLink app. If the FSL2 reader is used (rather than a smart phone and the FreeStyle LibreLink app), glucose readings are not sent automatically to the reader. The FSL2 reader must be held within 4 cm of the sensor to scan it. The sensor wirelessly sends glucose readings to the FSL2 reader using Near Field Communication (NFC) to ensure data security. If sounds are turned on, the FSL2 reader beeps when the sensor has been successfully scanned. Scanning the sensor retrieves the current glucose reading from the sensor and the last 8 hours of glucose data and glucose trend arrow showing whether glucose levels are going up, down or changing slowly. To receive glucose alarms or signal loss alarms, the alarm function must be enabled on the Reader and the Reader should be within 6 metres of the sensor with information transmission taking place via Bluetooth. The FSL2 reader includes a glucose and ketone testing strip port to allow SMBG using glucose or ketone test strips when required; those people using a smart phone and the FreeStyle LibreLink app would require a separate glucose meter for SMBG. Only FreeStyle Optium test strips can be used with the glucose/ketone strip test port on the FSL2 reader. The reader includes a built-in insulin dose calculator but this feature can only be used when a blood glucose reading is available from a glucose test strip.

Glucose readings can be viewed on the reader or FreeStyle LibreLink app for the last 7, 14, 30, or 90 days. The data on the FreeStyle LibreLink app can be uploaded to LibreView (Figure 3) via the LibreLinkUp smart phone app, which enables the person with T2D and their diabetes healthcare professional to see the Ambulatory Glucose Profile (AGP) and other data during consultations, which provides information about the patients glycaemic control over the monitoring period. FSL2 AGP reports are available via the LibreView app for use during telehealth consultations and improve access to support from diabetes healthcare professionals.

The FSL2 system has some limitations regarding use. It is not compatible with automated insulin dosing systems, including closed loop and insulin suspend systems. The sensor must be removed prior to Magnetic Resonance Imaging (MRI), CT scans or with some airport body scanning systems. It is necessary to apply a new sensor and allow it to proceed through the 1-hour warm-up period before CGM readings are available again for use. Taking ascorbic acid (vitamin C) supplements above therapeutic recommended dosages while wearing the FSL2 sensor may falsely raise sensor glucose readings; the volume of Vitamin C which cause such readings is 500mg of ascorbic acid for the FSL2.



Figure 3 LibreView

Source: Figure 7, MSAC 1786 Application

FSL2 is TGA approved for people (aged ≥ 4 years) with diabetes who use insulin. It is intended that FSL2 replaces SMBG. FSL2 does not require adjunctive SMBG calibrations during use as it is calibrated at the point of manufacture. SMBG is not required to manage titration of insulin dose even when glucose levels are low or changing rapidly. While FSL2 is intended to replace SMBG, limited use of SMBG is still recommended under certain circumstances (e.g. CGM readings do not match an individual's symptoms, sensor or reader malfunction, sensor loss or removal, signal loss between sensor and reader/app). SMBG is also required during the 1-hour sensor warmup period when CGM is not active.

FSL2 is recommended for all patients who require insulin treatment in the application, including the subpopulation requiring IIT (i.e., patients on a basal/bolus treatment and those on CSII) who may require more frequent glucose monitoring. Following a recommendation from a designated diabetes healthcare professional, patients would obtain the FSL2 system via the NDSS using similar procedures that patients with T1D currently follow to obtain FSL2 (i.e., the designated healthcare professional fills out a request form which is sent to the NDSS and, once processed, applicants can obtain FSL2 products from an NDSS access point, which is usually a community pharmacy). T2D insulin-using patients have a similar recommendation to T1D patients to routinely monitor their glucose levels due to the risk of hypoglycaemia (RACGP 2020). In the subpopulation who are using insulin multiple times per day or a CSII, it is recommended to monitor blood glucose more frequently each day in order to titrate insulin dosing to meet glycaemic targets (The Royal Australian College of General Practitioners 2020).

PASC noted that CGM systems are considered standard of care in many jurisdictions for managing T2D.

The NDSS currently allows the following authorised health professionals to certify use of FSL2 in T1D: certified diabetes educators, nurse practitioner, physician and paediatrician, but not general practitioners (GPs) or practice nurses. It is proposed in the application that GPs, endocrinologists, and diabetes educators would be most likely to recommend use of FSL2 to help a patient manage their T2D on insulin. The FSL2 system is intended to be used at home or in a residential aged care facility (i.e. it does not need to be used in a clinical setting) by people with T2D requiring insulin with assistance from a carer or parent if required/requested by the user.

Comparator

The proposed comparator is SMBG using finger prick capillary blood samples and glucose test strips and glucose meter. Currently, there are no subsidised CGM systems for T2D available through NDSS, although some patients may be able to obtain them through their private healthcare insurance plan. Therefore, the appropriate comparator for FSL2 is SMBG as it is the current standard of care for T2D in Australia.

SMBG is recommended for patients with T2D who are using insulin and have been educated in and capable of appropriate alterations in insulin dose (The Royal Australian College of General Practitioners 2020). People with T2D requiring IIT are usually required to test their blood glucose more frequently than those receiving less intensive insulin therapy (basal insulin).

PASC noted that the proposed comparator is SMBG using finger prick capillary blood samples, glucose test strips and glucose meter. This is the current standard of care for people with T2D in Australia. PASC noted that SMBG is recommended for patients with T2D who are using insulin and have been educated in and capable of making appropriate alterations in their insulin dose.

In the RACGP guidelines for T2D (The Royal Australian College of General Practitioners 2020), SMBG is recommended for:

- People on insulin and/or sulfonylureas, which can cause hypoglycaemia
- People not on insulin who are having difficulty achieving glycaemic control
- When monitoring hypoglycaemia or hyperglycaemia caused by illness
- During pre-pregnancy and pregnancy management for established or gestational diabetes
- When there is a clinical need for monitoring, such as during changes in management or lifestyle, or for conditions or medications requiring data on glycaemic patterns that HbA1c cannot provide
- When HbA1c estimations are unreliable (e.g. haemoglobinopathies).

The RACGP guidelines state that routine SMBG for people with T2D who are considered low risk and who are using oral glucose-lowering therapies (with the exception of sulfonylureas which increase the risk of hypoglycaemia) is not recommended (The Royal Australian College of General Practitioners 2020). The RACGP guidelines state that the method and frequency of monitoring should reflect individual circumstances and therapeutic aims, with SMBG most effective where the person with diabetes and their healthcare providers have the knowledge, skills and willingness to incorporate SMBG and therapy adjustments into diabetes care plans (The Royal Australian College of General Practitioners 2020).

The ANDA data indicates that 83.7% of people with T2D perform regular SMBG, with 81.3% using finger prick blood samples (Australian National Diabetes Audit). Around a third of patients with T2D reported that they do not perform finger pricking as often as recommended by their HCP and 5% were unsure of their recommended testing frequency (Australian National Diabetes Audit). With current SMBG testing, only 28.7% of Australians with T2D achieve the HbA1c target of 7% (although HbA1c targets may be higher or lower as they are individualised) (Australian National Diabetes Audit).

In Australia, the frequency of SMBG is individualised; however, evidence suggests that an increased frequency of SMBG is correlated with improved HbA1c in both T1D and T2D (The Royal Australian College of General Practitioners 2020). The American Diabetes Association (ADA) guidelines recommend that

SMBG should be encouraged when appropriate for people who are using insulin to check their blood glucose levels. This may include checking when fasting, prior to meals and snacks, after meals, at bedtime, in the middle of the night, prior to, during, and after exercise, when hypoglycaemia is suspected, after treating low blood glucose levels until they are normoglycemic, when hyperglycaemia is suspected, and prior to and while performing critical tasks such as driving (American Diabetes Association 2024c). Insulin has a very narrow therapeutic index and hence requires careful, intensive, ongoing glucose monitoring to ensure appropriate dosage titration and maintenance (The Royal Australian College of General Practitioners 2020).

As highlighted above, repeated SMBG can be time consuming, inconvenient, and painful, leading to poor compliance and impaired QoL (Moström et al. 2017). Unlike CGM, SMBG can provide only a 'snapshot' of a patient's glycaemic status at the time of testing. As such, it may not identify glucose excursions and does not provide patients with enough actionable information to optimise self-management of insulin treatment (Ajjan, Slattery & Wright 2019).

In Australia, subsidised blood glucose test strips for SMBG of T2D can be purchased through the NDSS. 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 five times per day which may not meet the needs of people with T2D requiring IIT. Registrants can access more product if their limit has been reached and unique circumstances are present. A recent survey of Australian diabetes health professionals suggested that Australians with T2D requiring IIT currently carry out SMBG from ≤ 4 times to ≥ 9 times per day. The restriction on numbers of glucose testing strips may encourage people with T2D to deviate from the recommended frequency of SMBG potentially increasing the risk that agreed 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.

Currently, there are no subsidised CGM systems for T2D available through NDSS, although some people may be able to obtain them privately or through their private healthcare insurance plan. Therefore, the appropriate comparator for CGM is SMBG as it is the current standard of care for T2D.

Reference standard

The reference standard is laboratory measured plasma venous blood glucose testing (e.g., using a YSI [Yellow Springs Laboratory Instrument] for glucose testing or equivalent). *PASC confirmed that a laboratory conducted plasma venous blood glucose test is the appropriate reference standard.*

Outcomes

The following are relevant to the safety and effectiveness of FSL2 or SMBG in the proposed population.

Safety

AEs attributable to the blood glucose monitoring may include events caused by obtaining a finger prick capillary blood sample, glucose meter or glucose test strip failure, local events (e.g. skin irritation) due to sensor insertion or wear, sensor malfunction or detachment, and broken sensor wire left in the skin after the sensor is removed or accidentally dislodged.

The psychological impact of obtaining finger prick blood samples compared to continuous monitoring of glucose readings/alerts is another relevant safety consideration, to be considered under the effectiveness of monitoring (psychological health).

Although failure of CGM or SMBG testing may be considered a safety issue, this outcome has been included under “analytical validity” to avoid double counting. The downstream implications of a monitoring failure would be considered under effectiveness.

PASC noted that the outcomes related to the safety of testing included local AEs such as broken sensor wire left in the skin after sensor removal.

Analytical validity

Sensor accuracy is measured relative to reference glucose values from standard laboratory plasma venous blood glucose testing or glucose values from SMBG using finger prick capillary blood. The mean absolute relative difference values should be obtained from direct comparative studies. The mean absolute relative difference (MARD) is currently the most common metric used to assess the performance of CGM systems. MARD is the average of the absolute error between all CGM values and matched reference glucose values. A small percentage indicates that the CGM readings are close to the reference glucose value, whereas a larger MARD percentage indicates larger differences between the CGM and reference glucose values and lower accuracy. Although an exact cut-off for accuracy has not been established, a MARD of 10% is generally considered acceptable.

Difference in accuracy between individual sensors both within and between manufactured lots may be relevant as CGM users will use multiple sensors per year with an expectation that data is comparable between sensors. Differences in accuracy at the beginning, middle and end of the sensor wear period may also be relevant. Accuracy is normally assessed during evaluation of investigative tests for reimbursement (Medical Services Advisory Committee). Accuracy is evaluated by the TGA during regulatory approval but these data are not available to MSAC for their subsequent consideration. The applicant stated that FSL2 met the U.S. Food and Drug Administration (FDA) accuracy performance standards for CGM, a standard that was supported by the Australian TGA.

PASC noted that the diagnostic accuracy of FSL2 had already been assessed by the TGA as part of the regulatory approval process. PASC highlighted that, in accordance with the MSAC guidelines, MSAC usually assesses the comparative diagnostic accuracy of investigative tests as part of the evaluation framework. Following discussion, PASC considered that the provision of diagnostic accuracy data in the assessment report would provide additional information to support MSAC discussions when considering the relative merits of CGM versus SMBG for monitoring glycaemic control in people with T2D.

Information on concordance between CGM and SMBG at different glucose concentrations, when glucose levels are rapidly rising and falling and when blood glucose is within the hypoglycaemic and hyperglycaemic range is required to assess the relative performance of CGM and SMBG in circumstances where information would be expected to inform treatment decision making to avoid excursions outside of the target range.

Data on the proportion of sensors that are active (no sensor attenuation, termination or loss) for the 14-day period of wear and the mean and median time a sensor remains active during wear is relevant as it impacts on effective glycaemic control and availability of CGM data.

Glycaemic control

For populations with suboptimal glycaemic control, achieving glycaemic control by maintaining blood glucose levels within the target range using CGM or SMBG is an intermediate/surrogate clinical outcome associated with improvement in health outcomes such as reduction in microvascular and macrovascular T2D complications.

PASC acknowledged that HbA1c levels are a widely-used intermediate/surrogate measure of glycaemic control and was the main effectiveness outcome included in the economic evaluation of CGM cost effectiveness.

The magnitudes of HbA1c change may have differential impacts in different groups, depending on the severity of T2D. Although the MCID for change in HbA1c levels is regarded as a reduction by 0.5% (Kaiafa et al. 2020), the applicant indicated that MCID values of 0.3% to 0.5% for change in HbA1c levels have been reported. *The applicant noted that the minimum clinically important difference (MCID) for change in HbA1c for T2D reported in the published literature ranges from 0.3% to 0.5%.* A median MCID of 0.4% for improvement in HbA1c was nominated by respondents to a recently published online survey of healthcare professionals investigating the importance of different T2D outcomes and their MCID (Dankers et al. 2021). HbA1c levels reflect average glucose levels over the previous 3 months. Therefore, this measurement does not provide information about current glycaemic control, glycaemic excursions and acute complications of hypoglycaemia and hyperglycaemia. HbA1c also fails to provide information on the magnitude and frequency of glucose variability (Battelino et al. 2019).

A list of ten core metrics based on the expert opinion of an international consensus group was developed for use of CGM in clinical practice (Battelino et al. 2019; Danne et al. 2017). These metrics form the basis of outcomes reported in many clinical studies of CGM for both T1D and T2D and were included in this MSAC application. These metrics have been included in the PICO as surrogate/intermediate effectiveness outcomes to be assessed for the comparison of CGM and SMBG (Table 4) (Battelino et al. 2019).

Table 4 Standardized CGM metrics for clinical care in nonpregnant individuals with T1D or T2D included as outcomes in the PICO for PICO Set 1

Metric	Interpretation	Goals
1. Number of days CGM worn		14-day wear for pattern management
2. Percentage of time CGM is active (recommend 70% of data)		70% of CGM data from 14 days
3. Mean glucose	Simple average of glucose values	*
4. Glucose management indicator	Calculated value approximating HbA1c (not always equivalent)	*
5. Glycaemic variability (%CV) target	Spread of glucose values	≤36% †
6. Time above range (TAR): % of readings and time >250mg/dL (>13.9 mmol/L)	Level 2 hyperglycaemia	<5% (most adults); <10% (older adults)
7. Time above range (TAR): % of readings and time 181–250mg/dL (10.1–13.9 mmol/L)	Level 1 hyperglycaemia	<25% (most adults); <50% (older adults)‡
8. Time in range (TIR): % of readings and time 70–180 mg/dL (3.9–10.0 mmol/L)	In range	>70% (most adults); >50% (older adults)
9. Time below range (TBR): % of readings and time 54–69mg/dL (3.0–3.8 mmol/L)	Level 1 hypoglycaemia	<4% (most adults); <1% (older adults)§
10. Time below range (TBR): % of readings and time <54mg/dL (<3.0 mmol/L)	Level 2 hypoglycaemia	<1%

Source: (American Diabetes Association 2024b; Battelino et al. 2019)

CGM = continuous glucose monitoring; %CV = percentage coefficient of variation; TAR = time above range; TBR = time below range; TIR = time in range.

*Goals for these values are not standardized. †Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycaemia for those receiving insulin or sulfonylureas. ‡Goals are for level 1 and level 2 hyperglycaemia combined. §Goals are for level 1 and level 2 hypoglycaemia combined.

The consensus group identified “time in ranges” (i.e. TIR, TAR and TBR; see Table 4) as a metric of glycaemic control that provides more actionable information than HbA1C alone (Battelino et al. 2019). The consensus group agreed that expressing time in the various ranges can be done as the percentage (%) of CGM readings, average hours and minutes spent in each range per day, or both, depending on the circumstances (Battelino et al. 2019). Time in range (TIR) is an important metric in the evaluation of glycaemic control. The international consensus recommendations on TIR have proposed that a target glucose range of 3.9–10 mmol/l is an appropriate standard against which to assess the percentage of readings or time in range for people with either T1D or T2D, both in clinical practice and in clinical trials (Battelino et al. 2019). Percentage of TIR correlates inversely with HbA1c (Wilmot et al. 2021). There is increasing evidence that lower TIR values are linked to macrovascular and microvascular complications (Beck, Bergenstal, Cheng, et al. 2019; Beck, Bergenstal, Riddlesworth, et al. 2019; Lu et al. 2018; Lu et al. 2021).

Although glucose targets for people with diabetes are individualised and collaborative, the International Consensus on Time in Range has established a series of target glucose ranges (TIR, time below range and time above range) and recommendations for time spent within these glucose ranges for different diabetes populations including for people with T2D and older or high-risk individuals. For pregnant women with T2D or gestational diabetes, target ranges were agreed but there was insufficient evidence to develop target percentages of CGM readings or times within the different glucose ranges for these populations (Battelino

et al. 2019; Danne et al. 2017). These CGM metrics are evaluated together with the AGP report for clinical decision making.

Other relevant outcomes from CGM include TBR, TAR, number of hypoglycaemic or hyperglycaemic excursions and their severity, and glycaemic variability (e.g. coefficient of variation [%CV]). People with T2D generally have less glycaemic variability and hypoglycaemic excursions than people with T1D (Rama Chandran et al. 2018). Therefore, people with T2D can often achieve more TIR compared to people with T1D. Short-term glycaemic variability is associated with the development and progression of microvascular complications, and, to a lesser extent, macrovascular complications (Ceriello, Monnier & Owens 2019). It is recommended that the percentage CV for glycaemic variability should be lower than 36% although a lower %CV (<33%) may protect against hypoglycaemic excursions (Battelino et al. 2019).

Other consensus metrics for consideration are the number of days the CGM sensor is worn and proportion of time that CGM is active. This impacts on continuity of CGM use (% of data recorded) and potentially adherence to recommended T2D treatment. It is recommended that CGM is active (i.e. reporting glucose data) for >70% of the time over a 14-day period as lower activity has been associated with reduction in glycaemic control and ability to achieve target HbA1c levels (Battelino et al. 2019).

Treatment decisions based on information obtained from glucose monitoring (e.g. erroneous insulin titration leading to severe hypoglycaemia requiring medical intervention or hospitalisation; incidence of severe hyperglycaemia and hyperosmolar hyperglycaemic state events) can impact on effectiveness.

Change in management

Patient management is immediately and directly informed by use of FSL2 monitoring data with people with T2D (or their parent/carer) titrating their insulin dosing, as recommended by their diabetes healthcare professional, according to whether their glucose targets were achieved. Effective use of data from SMBG or CGM to optimize clinical outcomes of T2D treatment requires the user (or their parent/carer) to interpret the collected data correctly and act upon them appropriately to optimize their T2D treatment (i.e. guide their insulin titration or other interventions).

Other relevant outcomes include adherence to both monitoring (CGM or SMBG) and treatment, as well as the use of lifestyle interventions (e.g. diet and exercise).

Health outcomes

Reduction in diabetes complications (cardiovascular and microvascular complications), mortality, quality of life, improved psychological health has been associated with improved glycaemic control. HbA1c is the most widely accepted measure of overall, long-term blood glucose control in patients with diabetes. Reduced HbA1c leads to decreased incidence and progression of microvascular (i.e. retinopathy, nephropathy, and neuropathy) and macrovascular (i.e. cardiovascular disease [CVD], peripheral vascular, and ischemic heart disease) complications. This also results in a reduction in long-term diseases associated with these complications, such as diabetic neuropathy which is responsible for a large proportion of non-traumatic lower-extremity amputations as well renal disease, heart disease, stroke, erectile dysfunction, and hyperosmolar hyperglycaemic states (HSS). Other relevant measures of improvements in health outcome are all-cause hospitalizations, acute diabetes-related hospitalisations and acute diabetes-related emergency room visits (Garg et al. 2024).

Those living with the condition continue to report not only suboptimal health metrics, but also high burden related to care practices. Qualitative studies identified barriers to SMBG, including frustration with readings of hyperglycaemia, fear of needles, inconvenience, and feels of a lack of self-efficacy (Ida, Kaneko & Murata 2019; Ong, Chua & Ng 2014). Patients using CGM may experience health benefits from the avoidance of daily finger prick testing and burden of SMBG (Matza et al. 2017). In addition, the availability of CGM and option to share monitoring data may have additional psychological benefits (e.g. reduction in anxiety, hypoglycaemic confidence) for carers of older or at-risk people with T2D and parents of children with T2D.

Other relevant considerations

The following outcomes have been identified:

- Acceptability, wearability and usability of CGM versus SMBG
- Impact on daily life and work attendance
- User or carer satisfaction/perceived qualitative benefits and disadvantages of CGM
- Motivation to initiate use of CGM and factors contributing to or impacting on continued use of CGM
- Continuity of supply (sensors etc)
- Impact of CGM on self-management and the model of T2D care for insulin users (e.g. patient empowerment, education and support, change in care location, frequency of routine follow-up, use of telehealth support, remote monitoring of patient's glycaemic control)

PASC noted that the outcome of 'Adherence to glucose testing' should be amended to 'Adherence to CGM or SMBG'. PASC considered that 'adherence to CGM or SMBG' and 'acceptability, wearability and usability of CGM versus SMBG' were intermediate outcomes for health or change in management with the latter under the subheading of 'other relevant considerations'.

The following outcomes are relevant to the safety and effectiveness of CGM in the proposed populations and are included in the PICO:

Patient relevant outcomes

Direct evidence for safety and effectiveness:

Safety:

- Local adverse events (AEs) associated with glucose testing

Intermediate outcomes:

- Glycaemic control
 - glycated haemoglobin (HbA1c)
 - time in range (TIR), time below range (TBR) and time above range (TAR)
 - number of hypoglycaemic/hyperglycaemic excursions
 - glycaemic variability
- Change in body weight/body mass index (BMI)

Effectiveness:

- T2D complications (e.g. cardiovascular and microvascular complications, kidney disease, neuropathy/nerve damage, retinopathy/eye disease, amputations/foot ulcers)
- Mortality
- Quality of life

- Psychological health
- Hypoglycaemic or hyperglycaemic events resulting in emergency room visit/hospitalisation

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.)

PASC noted that uptake of exercise is a separate measure from body weight/BMI which is not a measure of uptake directly and that the latter needs to be recategorized.

PASC noted that the outcome of QoL is a different concept to the outcome of psychological health. Self-efficacy was considered to fall within the category of “other relevant considerations” rather than a direct health outcome. Severe hypoglycaemia and hyperglycaemia are relevant health outcomes that may be measured to an extent by the rate of hospitalisations and emergency room visits for these conditions.

Assessment framework

The clinical claim is that FSL2 provides superior efficacy in terms of glycaemic control and non-inferior safety compared to SMBG.

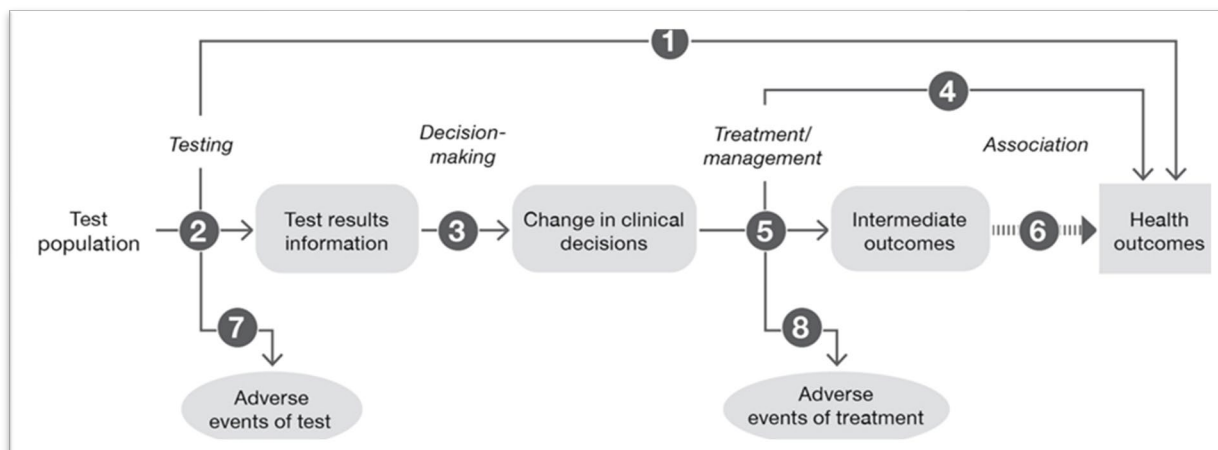
The effectiveness of CGM, as proposed in MSAC 1786 Application, was supported by 19 published studies in people with T2D requiring insulin therapy. Two meta-analyses of observational studies were included that focused on change in HbA1c (Evans et al. 2020; Kröger, Fasching & Hanaire 2020). Three studies (two RCTs and one prospective observation study) compared CGM versus SMBG in people with T2D requiring insulin therapy (Bosi et al. 2022; Haak et al. 2017; Yaron et al. 2019). These studies assessed change in HcA1c (glycaemic control) from baseline, safety and hypoglycaemic events with follow-up of ≤6 months. The remaining studies were retrospective observational and prospective observational studies using earlier versions of the FreeStyle Libre glucose monitoring system and reporting longitudinal change in diabetes-relevant outcomes over time.

PASC noted that applicant has included studies in the application providing direct evidence for change in HbA1c, which PASC considered to be an intermediate/surrogate health outcome. PASC noted that there were no data from comparative studies on direct from test to more direct health and other outcomes such as mortality and quality of life.

It is anticipated that evidence would be required to demonstrate that improving glycaemic control (considered a surrogate/intermediate clinical outcome in the assessment framework) results in clinically significant improvements in health outcomes (e.g. microvascular and macrovascular complications) and other diabetes-relevant qualitative outcomes (e.g. QoL, diabetes distress, patient satisfaction, self-efficacy) for the proposed population. It may be particularly important to demonstrate that glycaemic control (intermediate outcomes) is a valid surrogate for health outcomes in vulnerable populations with T2D (e.g. Aboriginal and Torres Strait Islander adults and children, people with poor social support, and people with multiple comorbidities). These populations are considered to have a high unmet need but the amount of direct evidence for improvement in health outcomes from use of CGM versus SMBG is likely to be very small.

PASC discussed the potential use of a truncated assessment framework, which would require evidence that improvement in glycaemic control results in clinically significant benefits in health and other relevant outcomes. PASC considered that in the event of adequate direct from test to intermediate health outcome evidence being available to support the assessment where the intermediate health outcome was HbA1c levels, a full linked evidence approach may not be necessary as long as there was also sufficient evidence linking HbA1c levels to more direct and long-term health outcomes. However, PASC indicated that it could be useful to report data on analytical validity in the assessment report as this would allow a comparison across CGM systems. The applicants indicated they would use a full linked evidence approach and the standard assessment framework.

The applicant intends to submit an applicant-developed assessment report based on the standard assessment framework (Figure 4). The applicant considered that it may be important to articulate the behavioural changes initiated by FSL2 which leads to the improvement in clinical outcomes (particularly HbA1c and TIR). Treatment satisfaction outcomes (which are linked to self-efficacy and adherence) are reported in some FSL2 studies, providing quantitative data on changes in satisfaction, convenience and flexibility with use of FSL2. There are also qualitative improvements in terms of the patient experience and disease engagement which are critical to long term compliance and therefore maintenance of the clinical outcomes achieved. One example is the reduction in pain from reduced finger pricking, which removes a disincentive for people with T2D to participate in their condition for facilitating the lifestyle changes needed. Therefore, the applicant considers that it would be prudent to adopt an analysis framework which captures these outcomes.



The standard assessment framework used for investigative tests is shown in Figure 4.

Figure 4 Standard assessment framework showing the links from the test population to health outcomes

Figure notes: 1: direct from monitoring to health outcomes evidence; 2: monitoring accuracy; 3: change in management (lifestyle interventions such as diet, exercise; insulin treatment regimen); 4: influence of change in management on health outcomes; 5: influence of the change in management on glycaemic measures; 6: association of intermediate outcomes (e.g. glycaemic control) with health outcomes; 7: adverse events due to monitoring (e.g. psychological impact, serious hypoglycaemic event, hyperosmolar hyperglycaemic states); 8: adverse events due to treatment (e.g. impact on glycaemic control; psychological impact; quality of life; hypoglycaemic or hyperglycaemic events)

Questions to be addressed in the assessment report are:

1. What is the effectiveness of blood glucose monitoring using CGM with FSL2 versus SMBG using finger prick capillary blood (e.g. macrovascular and microvascular complications, mortality, quality of QoL, psychological health)?
2. What is the accuracy of CGM with FSL2 versus SMBG using finger prick capillary blood for monitoring blood glucose? What is the concordance between CGM and SMBG testing? What patient-related, device-related or environmental factors could influence accuracy and concordance of CGM with FSL2 versus SMBG using finger prick capillary blood for monitoring blood glucose?
3. What is the effectiveness of blood glucose monitoring using CGM with FSL2 versus SMBG using finger prick capillary blood in terms of changing clinical decision-making?
4. Are observed changes in clinical management associated with changes in health outcomes (e.g. macrovascular and microvascular complications, mortality, quality of life, psychological health)?
5. Are observed changes in clinical management associated with changes in glycaemic control?
6. Are observed changes in glycaemic control associated with changes in health outcomes (e.g. macrovascular and microvascular complications, mortality, quality of life, psychological health), i.e. is glycaemic control an appropriate surrogate outcome for patient-relevant health outcomes?
7. What is the safety of CGM with FSL2 versus SMBG using finger prick capillary blood for monitoring blood glucose?
8. Is the method of blood glucose monitoring associated with differences in diabetes treatment-related AEs?

Clinical management algorithms

Current management algorithm for blood glucose testing

People with T2D requiring insulin for glycaemic control are recommended to carry out SMBG testing using a finger prick capillary blood sample (The Royal Australian College of General Practitioners 2020). The current clinical management algorithm for SMBG for the proposed population is provided in Figure 5. Comprehensive education regarding blood glucose monitoring, nutrition, and the avoidance and appropriate treatment of hypoglycaemia are considered as critically important for any person using insulin (American Diabetes Association 2024c).

SMBG measures blood glucose levels at a single point in time with testing frequency based on an individual's clinical need as advised by their diabetes healthcare professional. People with T2D receiving IIT (i.e. multiple injections of insulin daily) are at increased risk of a hypoglycaemic event and therefore carry out SMBG more frequently. This could be up to 9 times daily or as recommended by their diabetes healthcare professional. The frequency of SMBG usually reflects the intensity of the insulin treatment regimen such that people with T2D using basal insulin only with less glycaemic variability carry out SMBG at a lower frequency as they may have a lower risk of hypoglycaemia.

However, information provided by the applicant indicates that in clinical practice, finger prick testing is performed less frequently outside of the clinical trial setting. People living with T2D report that they do not perform finger prick testing as often as recommended by their healthcare professional (26.1%) or are unsure of the recommended testing frequency (3.1%) (Australian National Diabetes Audit). With current SMBG testing, around two thirds (67.7%) of Australians with T2D fail to meet a HbA1c target of 7% (Australian National Diabetes Audit). As the frequency of SMBG using finger prick testing varies, the applicant has indicated that this will be explored in the assessment report.

PASC noted the applicant's comments on the pre-PASC PICO that the current treatment algorithm assumes that people with T2D will utilise SMBG using an "agreed frequency" or as "indicated by symptoms" of T2D which was unlikely to represent real world use.

For adults with T2D who SMBG using finger prick capillary blood samples, a structured assessment at least annually should include (The Royal Australian College of General Practitioners 2024):

- the person's self-monitoring skills
- the quality and frequency of testing
- checking that the person knows how to interpret the blood glucose results and what action to take
- the impact on the person's quality of life
- the continued benefit to the individual
- the equipment used.

The target blood glucose range for people with T2D carrying out SMBG is generally 4–7 mmol/L for fasting blood glucose or pre-prandial blood glucose, and 5–10 mmol/L for postprandial blood glucose although these targets may be individualised (The Royal Australian College of General Practitioners 2020).

The blood glucose reading obtained from the meter is displayed in mmol/L blood and is stored in the meter's memory for future reference including the date and time of the blood sample test. This allows the person with T2D or their diabetes healthcare professional to review their readings.

If their blood glucose levels are outside of the target range, their insulin treatment (or other glucose-lowering therapies included in their treatment regimen) may need to be adjusted as insulin has a very narrow therapeutic index. Some people with T2D can self-manage their own insulin treatment by titrating the amount of insulin required to correct their blood glucose levels or other management such as administering rapid acting oral carbohydrate if their blood glucose is in the hypoglycaemic range. Alternatively, they may seek advice from a diabetes healthcare professional about adjusting their insulin regimen based on the monitoring results on their glucose meter. If their blood glucose readings suggest they require an urgent clinical intervention (e.g. their glucose reading indicates they are at risk of severe hypoglycaemia or hyperglycaemia), they may seek emergency care by calling emergency services or going to an emergency department.

Regular follow-up consultations with their diabetes healthcare professional at ~3 to 6 monthly intervals, which includes clinical assessment and HbA1c testing, provides additional information about the effectiveness of a person's T2D treatment regimen over the previous 3 months. This guides on-going treatment and frequency of SMBG if insulin treatment is intensified.

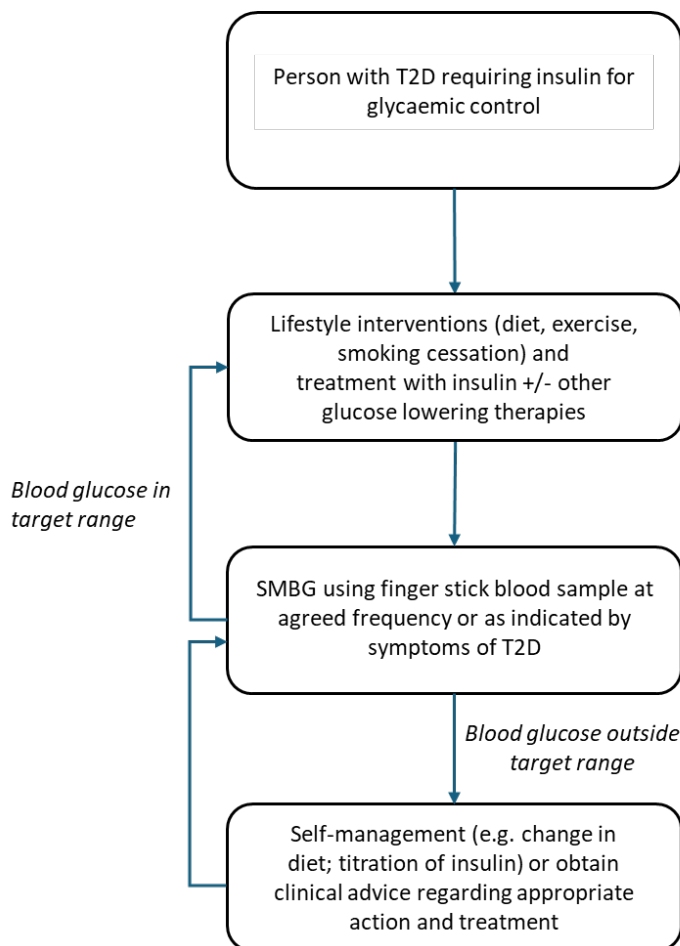


Figure 5 Clinical management algorithm of SMBG for a person with T2D requiring insulin treatment for glycaemic control

Source: Adapted from Figure 8, p.24 of MSAC Application 1786.

SMBG = self-monitoring of blood glucose, T2D = type 2 diabetes

Note: The agreed frequency of SMBG is individualised and is based on a patient's clinical need and advice from their diabetes healthcare professional.

Proposed management algorithm for blood glucose testing

The proposed management algorithm for people with T2D requiring insulin for glycaemic control and using FSL2 CGM rather than SMBG to check their blood glucose levels is shown in Figure 6.

A person aged ≥ 4 years with T2D requiring insulin for glycaemic control, either with or without other glucose lowering therapies, will continue to monitor their blood glucose levels. Instead of carrying out SMBG, they will have the option to use a FSL2 CGM. Even though the FSL2 CGM provides more information than SMBG, not all people with T2D requiring insulin treatment may wish to use a CGM system to check their glucose levels. People with T2D using insulin who choose to continue SMBG will follow the current management algorithm in Figure 5.

CGM using FSL2 provides a continuous AGP of glucose levels and hence information about their glycaemic control over the whole 24-hour period, if the system is being used consistently and correctly. FSL2 provides the user with information (either via the FreeStyle LibreLink app on their smartphone or via their reader device) about how rapidly their blood glucose is rising or falling and alerts when the blood glucose levels exceed or fall below individualised prespecified blood glucose thresholds which helps to detect episodes of

hyperglycaemia and hypoglycaemia facilitating both acute management (e.g. insulin titration or administration of rapid acting oral carbohydrate) and long-term adjustments to therapy. CGM provides glucose level data in real-time to allow the user or their parent/carer to make decisions about insulin titration to prevent their glucose becoming too high (hyperglycaemia) or falling too low (hypoglycaemia). If data from the FSL2 GM indicates that the person's glucose is relatively stable and is within the target range, then no changes to their insulin dose or frequency are likely to be required. If the glucose levels are outside their target range, the person can follow prior clinical advice about the appropriate action to take or seek further advice from their diabetes healthcare professional if they are unsure. If the glucose levels indicate that they require urgent medical assistance, they may call emergency services or attend an emergency department. Because the FSL2 CGM provides an AGP of their glucose levels, more information is available to guide acute and long-term treatment decisions by the user, parent/carer and their diabetes healthcare professional; treatment decisions based on use of the FSL2 CGM may be different than those based on SMBG because more information is available at the point of decision making. As FSL2 CGM data can be shared with a diabetes healthcare professional via LibreView, the diabetes healthcare professional is able to provide appropriate advice based on the continuous AGP. Data from the FSL2 CGM can also be shared via the FreeStyle LibreLinkUp app with a parent or carer which is essential to support use of FSL2 CGM by young children included in the proposed population, people with disabilities who are unable to self-manage their T2D treatment and also frail or elderly people with T2D who may need additional assistance in interpreting their FSL2 CGM data and managing their insulin treatment.

A person using FSL2 CGM would not usually need to carry out SMBG using a glucose meter. However, if the person with T2D experiences acute diabetes-related symptoms that are not aligned with their blood glucose readings from the FSL2 CGM, they would need to check that their FSL2 glucose readings are correct by carrying out SMBG using a finger prick capillary blood sample and a glucose test strip. If the FSL2 glucose readings are incorrect and the person's glucose levels are in the hypoglycaemic or hyperglycaemic range, they can follow prior clinical advice about the appropriate action to take or seek further medical advice regarding the most appropriate course of action including titration of their insulin dose or administration of rapid acting oral carbohydrate. If they require urgent medical attention, they can call the emergency services or attend the emergency department. People with T2D requiring IIT (i.e. multiple insulin injections daily) are at increased risk of hypoglycaemic excursions that may require prompt action such as self-titration of their insulin dose, administration of rapid acting oral carbohydrate or consultation with their diabetes healthcare professional. They may require assistance from a diabetes healthcare professional or emergency services and treatment in an emergency department, depending upon the severity of the hypoglycaemia. The risk of hypoglycaemia is lower in people with T2D requiring less intensive insulin therapy (i.e. basal insulin only). However, they would benefit from access to the same CGM information including the continuous AGP from FSL2 as people with T2D requiring IIT.

Regular follow-up consultations with their diabetes healthcare professional at ~3 to 6 monthly intervals would continue in the proposed management algorithm.

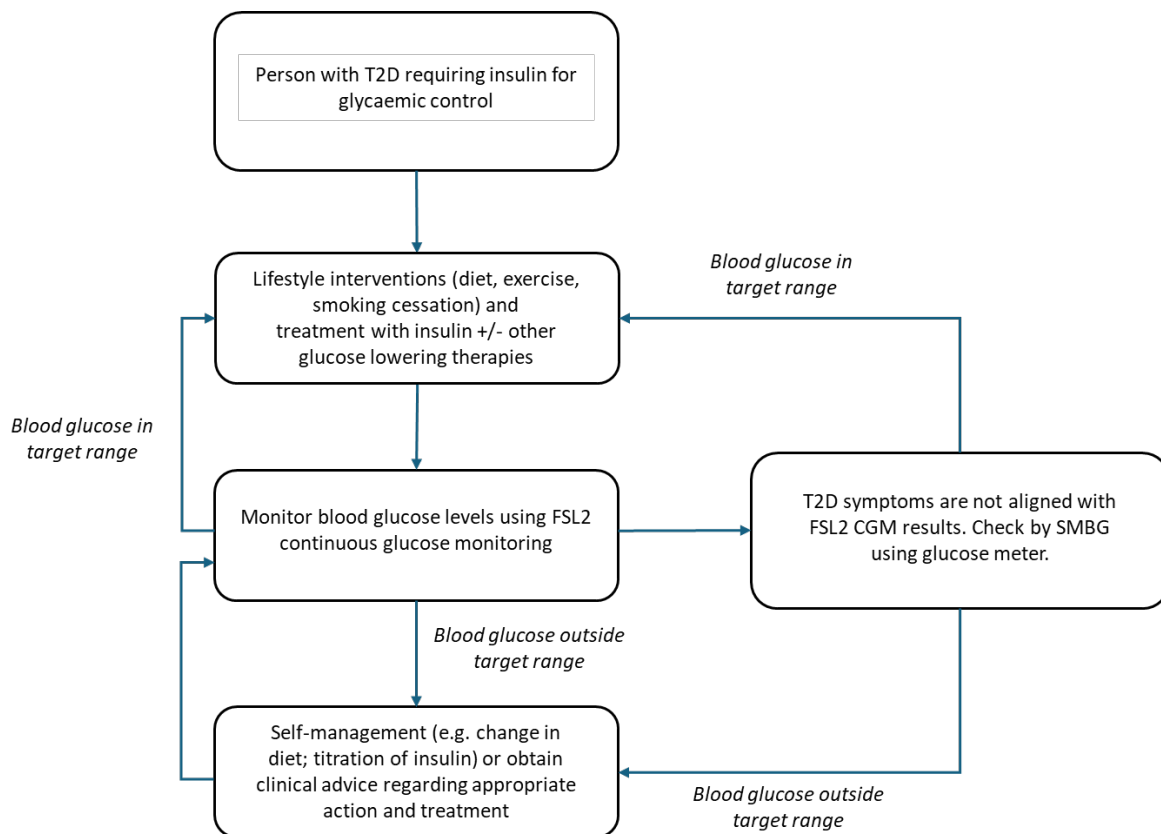


Figure 6 Clinical management algorithm for FSL2 CGM of a person with T2D requiring insulin treatment for glycaemic control

Source: Adapted from Figure 9, p.25 of MSAC Application 1786.

FSL2 = FreeStyle Libre 2, SMBG = self-monitoring of blood glucose, T2D = type 2 diabetes

PASC noted that the current and proposed management algorithms were similar and included management of blood glucose levels (glycaemic control) rather than long term health outcomes. The proposed algorithm for CGM included occasional use of SMBG to confirm blood glucose levels when a person’s symptoms of diabetes did not match their CGM blood glucose readings.

PASC noted that the algorithm does not describe how the use of CGM influences decision-making for patients and health care professionals above that provided by SMBG determination via finger prick testing. However, PASC acknowledged that this was a reasonable omission given the individualised basis of treatments for T2D.

Proposed economic evaluation

The clinical claim is that FSL2 provides superior efficacy in terms of glycaemic control and non-inferior safety compared to SMBG. The appropriate form of economic analysis would therefore be a cost effectiveness analysis or cost-utility analysis (Table 5). The applicant stated there was insufficient evidence to undertake economic evaluations for PICO Sets 2 and 3.

PASC noted that the most appropriate economic evaluation would be a cost-utility analysis for PICO Set 1. The applicant confirmed that a cost-utility analysis would be presented in the applicant-developed assessment report (ADAR).

Table 5 Classification of comparative effectiveness and safety of the proposed intervention, compared with its main comparator, and guide to the suitable type of economic evaluation

Comparative safety	Comparative effectiveness			
	Inferior	Uncertain ^a	Noninferior ^b	Superior
Inferior	Health forgone: need other supportive factors	Health forgone possible: need other supportive factors	Health forgone: need other supportive factors	? Likely CUA
Uncertain ^a	Health forgone possible: need other supportive factors	?	?	? Likely CEA/CUA
Noninferior ^b	Health forgone: need other supportive factors	?	CMA	CEA/CUA
Superior	? Likely CUA	? Likely CEA/CUA	CEA/CUA	CEA/CUA

CEA=cost-effectiveness analysis; CMA=cost-minimisation analysis; CUA=cost-utility analysis

? = reflect uncertainties and any identified health trade-offs in the economic evaluation, as a minimum in a cost-consequences analysis

^a 'Uncertainty' covers concepts such as inadequate minimisation of important sources of bias, lack of statistical significance in an underpowered trial, detecting clinically unimportant therapeutic differences, inconsistent results across trials, and trade-offs within the comparative effectiveness and/or the comparative safety considerations

^b An adequate assessment of 'noninferiority' is the preferred basis for demonstrating equivalence

Proposal for public funding

This MSAC application is requesting NDSS funding for subsidised FSL2 CGM products for people with T2D who require insulin. The proposed T2D insulin-using population includes a subpopulation using intensive insulin therapy (IIT) (i.e. patients requiring multiple daily insulin injections or, less commonly, continuous subcutaneous insulin infusion (CSII) with a pump) who are recommended to undergo frequent SMBG multiple times per day (e.g. with meals).

Currently, all people with T1D are eligible to receive access to subsidised CGM products through the NDSS. As for people with T1D accessing CGM products through the NDSS, it is anticipated that people with T2D applying to access FSL2 CGM products will be required to be registered with the NDSS and see an authorised health professional to determine whether they meet the NDSS eligibility criteria. Authorised health professionals may include endocrinologists, CDE and other health professionals specialising in diabetes (physicians, paediatricians or nurse practitioners). While GPs are currently not considered authorised health professionals by the NDSS, widening access to include GPs who currently prescribe and/or titrate insulin may be beneficial by reducing the treatment burden on secondary care.

PASC confirmed that for people with T2D the proposed source of public funding for CGM was the NDSS, as for T1D (i.e. no MBS listing is being requested).

PASC considered that adequate diabetes support networks for CGM were available to support a staged introduction of CGM for people with T2D, including in regional and remote areas of Australia. These networks were established following the successful introduction and subsequent expansion of NDSS-funded CGM for T1D.

PASC indicated that adding GPs to the list of authorising healthcare professionals for NDSS-funded CGM was not a matter for MSAC consideration.

A FSL2 sensor is disposable and can be worn for a maximum period of 14 days; it costs \$REDACTED. Each eligible person would require a minimum of 26 sensors per year at a total cost per person of AUD \$REDACTED (equivalent to \$REDACTED /month). If a FSL2 reader is required (as well as or instead of using the FSL2 FreeStyle LibreLink app for a smartphone), it costs \$REDACTED. The cost estimates per person assume optimal use of the FSL2 CGM system (i.e. no sensors become detached or malfunction and that the sensors and transmitter remain fully operational for the maximum duration of use). The impact of sensor loss/detachment/removal and system malfunction on the costs of FSL2 CGM should be further explored in the assessment report (ideally based on data from real-world use).

The cost for one year (12 months to 30 June 2024) have been estimated based on an assumption of REDACTED% uptake of FSL2, the current price of a FSL2 sensor and using published data for T2D from the NDSS to provide some context around potential costs of using FSL2 CGM. For 12 months to 30 June 2024, the NDSS reported that 315,432 people with T2D required insulin therapy (National Diabetes Services Scheme). According to the Australian National Diabetes Audit (ANDA) in 2022, 28.5% of people with T2D on insulin therapy required IIT as defined in the application (i.e. comprising basal-bolus treatment used by 26.9% of insulin users, CSII non-automated received by 0.3% of insulin users, and 1.3% of insulin users who are treated with basal bolus + pre-mixed insulin). Based on these estimates, 89,898 people with T2D were receiving IIT as defined in the FSL2 application. However, it is important to note that the ANDA includes a high proportion of tertiary centres who manage patients with more severe disease, compared to the overall population of patients with T2D who require insulin who receive treatment from general practitioners in primary care. Therefore, the ANDA data may overestimate the total number of patients receiving IIT.

If all people with T2D requiring ITT used FSL2 CGM for 12 months to 30 June 2024, the estimated total cost of FSL2 would be \$REDACTED. If all people with T2D requiring insulin used FSL2 CGM over the same period, the current estimated total cost of FSL2 would be \$REDACTED.

The applicant stated that the above costings were highly inaccurate due to the assumed inputs. They confirmed that the budget impact of FSL2 for T2D would be included in the ADAR drawing on information from the current FSL2 reimbursement for T1D (e.g. CGM uptake rates, average sensor use per annum, appropriate cost offsets, population size and proposed CGM pricing).

The application provided data for the projected utilisation of FSL2 if NDSS funded based on confidential information held by the applicant. Therefore, it was not possible to validate the source of the data. According to data supplied in the application, approximately 201,080 Australians with T2D require insulin which includes insulin combined with or without other T2D medicines (Prospection 2022). Whilst >300,000 people with T2D were recorded by the NDSS as insulin users during the 12-month period of June 2021 to May 2022, only 201,080 unique individuals with T2D had an insulin prescription dispensed (Prospection 2022); a >100,000 difference. The data from Prospection (201,080 Australians) has been used to calculate the projected utilisation of FSL2 by the subpopulation of people with T2D requiring IIT, and for the remaining people with T2D not requiring IIT (i.e. those on less intensive insulin regimen) (Prospection 2022). It was estimated that of these 201,080 Australians with T2D require insulin, 32,380 people with T2D required IIT (defined as basal + bolus insulin users and CSII pump users) and 168,700 people with T2D did not require IIT (i.e. on a less intensive insulin regimen).

The projected FSL2 uptake rates by people with T2D over the first 4 years after listing on the NDSS (as provided by the applicant) are provided in Table 6.

Table 6 Projected FSL2 uptake rates by people with T2D over the first 4 years after listing on the NDSS

Year	Estimated average percentage uptake by people with T2D requiring intensive insulin therapy	Estimated average percentage uptake by people with T2D requiring insulin but not intensive insulin therapy
1	REDACTED%	REDACTED%
2	REDACTED%	REDACTED%
3	REDACTED%	REDACTED%
4	REDACTED%	REDACTED%

Source: Table 4 and Table 5 from Part 7 – information about estimated utilisation, MSAC 1786 application.
T2D = type 2 diabetes

PICO Set 2

Population

The proposed population is pregnant women with a confirmed diagnosis of gestational diabetes mellitus (GDM). GDM is defined in the application as any degree of glucose intolerance with onset or first recognition during pregnancy.

The proposed population in PICO Set 2 for NDSS funding is in line with the TGA approved indication for FSL2; the indication for Australia is “measuring interstitial fluid glucose levels in people (age 4 years and older) with diabetes mellitus, including pregnant women.”

Currently, only women with T1D who are actively planning pregnancy, pregnant, or immediately post-pregnancy can access FSL2 GM fully subsidised (i.e. no copayment required). A number of alternative CGM devices are already fully or partially subsidised by the NDSS for use by people with T1D.

PASC sought clarification from the applicant on whether the proposed population was all pregnant women with GDM requiring insulin. The applicant clarified that their preferred position is that all women with GDM (regardless of whether they are on insulin or not) should have access to FSL2 because both mother and their baby were likely to receive clinical benefit irrespective of whether the mother required glucose-lowering therapy. Glycaemic assessment of the pregnant mother generally occurs between 24 – 28 weeks gestation with escalation of glucose-lowering therapy as required from the point of diagnosis. It may be too late in the gestational period to impact on glycaemic levels and/or neonatal outcomes if insulin therapy is a requirement for CGM access. It was noted that evidence of the impact of CGM in pregnant women was limited.

PASC also noted that the 2024 Parliamentary Inquiry into Diabetes favoured broader access by recommending that “patients with gestational diabetes should be made eligible for subsidised CGMs”. The current TGA indication for FSL2 is for “pregnant women, irrespective of whether or not they are on any type of glucose lowering therapy”.

Prevalence of gestational diabetes (GDM)

The global prevalence of GDM is estimated to be 14% by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria (Sweeting, Enticott, et al. 2024). GDM is the fastest growing type of diabetes in Australia, with the age-standardised rate increasing from 6.1% in 2011-12 to 19.3% by 2021-22 (Australian Institute of Health and Welfare). More than 1 in 6 women (17.9%) aged 15–49 who gave birth in Australia in 2021–22 were diagnosed with GDM (53,900 women), based on the National Hospital Morbidity Database (Australian Institute of Health and Welfare). The NDSS report for GDM indicates that 45,290 women with GDM were registered with the NDSS in the last 12 months, as of the 12 months to 30 June 2024 (National Diabetes Services Scheme). Of these, 18,638 women (41%) currently registered with gestational diabetes required insulin to manage their diabetes. The incidence of GDM increases with increasing maternal age, ranging from 8.4% to 31.7% in 2021–22 in women aged 15–19 and 45–49 years, respectively. Compared with women aged 15–19 years, women aged 35–39 years were 2.6 times as likely to be diagnosed with GDM while women aged 40–44 years and 45–49 years were 3.3 and 3.8 times as likely, respectively (Australian Institute of Health and Welfare).

The increase in incidence of GDM over the last ten years is probably due to several factors including increasing maternal age, higher rates of maternal overweight and obesity, and a growing proportion of higher risk ethnic and racial groups in the population (Australian Institute of Health and Welfare). Risk factors for developing GDM include ethnic background (i.e. higher risk in Aboriginal and Torres Strait Islander, Asian, Indian subcontinent, Pacific Islander, Māori, Middle Eastern, non-white African populations), maternal age ≥ 40 years, BMI >30 kg/m², previous hyperglycaemia during pregnancy, family history of diabetes mellitus or GDM in a close relative, previous baby with birth weight >4500 g or >90 th percentile (i.e. macrosomia), polycystic ovary syndrome and using medications such as corticosteroids or antipsychotics (Australian Institute of Health and Welfare).

The incidence of GDM is higher in remote and very remote areas of Australia, in the most socioeconomically disadvantaged group (Group 1, lowest quintile) and in Aboriginal and Torres Strait Islanders (Australian Institute of Health and Welfare). After adjusting for differences in the age structure of the populations, Indigenous women are 1.2 times as likely to be diagnosed with GDM as non-Indigenous women. In 2020–21, there were around 2,400 new cases of GDM among Aboriginal and Torres Strait Islander women, equating to 16% of Indigenous women who gave birth in hospital (Australian Institute of Health and Welfare).

Natural history and disease burden of GDM

The application defines GDM as any degree of glucose intolerance with onset or first recognition during pregnancy. This would also include the Australasian Diabetes in Pregnancy Society (ADIPS) and the World Health Organization (WHO) definition of diabetes mellitus in pregnancy (DMiP) which is defined as pregnant women whose blood glucose levels in pregnancy meet the criteria used for diagnosing diabetes outside pregnancy. Some of these women may have previously undiagnosed diabetes, usually T2D. Most published data that report on GDM include both DMiP and GDM (The Royal Australian College of General Practitioners 2020).

GDM occurs because of either pancreatic β -cell dysfunction or a delayed response of β -cells to glycaemic levels, plus insulin resistance secondary to placental hormone release. Human placental lactogen is the primary hormone associated with increased insulin resistance during pregnancy. In normal pregnancies, human placental lactogen increases insulin secretion and β -cell proliferation to regulate maternal

hyperglycaemia. In patients with GDM, maternal pancreatic β -cell dysfunction or the delayed response of the β cells, resulting in decreased insulin secretion and ultimately leading to maternal hyperglycaemia. Genetic studies have indicated that T2D and GDM may have similar underlying causes (Sweeting et al. 2022).

GDM is usually diagnosed at week 24–28 of gestation. During pregnancy, women with GDM are at increased risk of pre-eclampsia, hypertension, early delivery, induction of labour and caesarean section (Nankervis, Price & Conn 2018). Potential adverse effects in neonates includes macrosomia (high birth weight), fetal death, entrapment of the fetal shoulders after delivery of the head which is an obstetric emergency, nerve palsy, hypoglycaemia and respiratory distress (Nankervis, Price & Conn 2018). Long-term effects of exposure to hyperglycaemia *in utero* are increased likelihood of being overweight or obese, hypertension and metabolic changes that occur in more than 50% of adolescents whose mothers had GDM (Nankervis, Price & Conn 2018). Therefore, careful management of GDM is critical to both mother and baby. In the long-term, women with GDM and their baby have an increased risk of developing T2D, and ongoing surveillance is required (Nankervis, Price & Conn 2018).

Prior testing

Early diagnosis of diabetes in pregnancy enables prompt evaluation and treatment. Australian clinical guidelines for care during pregnancy recommend that women who are at risk of hyperglycaemia, including GDM (as described above), are tested in the first trimester of pregnancy. Women tested in the first trimester of pregnancy with a normal test result are advised to get tested again at week 24–28 of gestation (Australian Living Evidence Collaboration 2024). HbA1c levels of 5.9 – 6.4% early in pregnancy may identify women at increased risk of adverse pregnancy outcomes (Hughes et al. 2014).

The optimal timing and type of testing for women at high risk of GDM is uncertain. There are currently two approaches to diagnostic testing for GDM in Australia, shown below; the RACGP criteria and the Australasian Diabetes in Pregnancy Society (ADIPS) consensus guidelines (Nankervis, Price & Conn 2018; The Royal Australian College of General Practitioners 2020).

RACGP diagnostic criteria:

- fasting plasma glucose ≥ 5.5 mmol/L, or
- two-hour plasma glucose ≥ 8.0 mmol/L (75 g oral glucose tolerance test [OGTT]).

ADIPS diagnostic criteria:

- fasting plasma glucose 5.1–6.9 mmol/L, or
- one-hour plasma glucose (75 g OGTT) ≥ 10.0 mmol/L, or
- two-hour plasma glucose (75 g OGTT) 8.5–11.0 mmol/L

GDM management

All women with GDM who qualify for Medicare access can be registered with the NDSS on the National Gestational Diabetes Register.

Telehealth visits used in combination with in-person visits for pregnant women with GDM can improve outcomes compared with standard in-person care alone (American Diabetes Association 2024d). Lifestyle

interventions and insulin remain the mainstay of treatment for GDM (The Royal Australian College of General Practitioners 2020). In most cases, GDM responds positively to lifestyle management, and women should be referred to an accredited practising dietitian and a CDE. Most (50–70%) women with GDM achieve their GDM management targets using a combination of optimal diet and appropriate exercise. Regular exercise (e.g. walking) is helpful in assisting women to achieve their glycaemic targets (Nankervis, Price & Conn 2018; The Royal Australian College of General Practitioners 2020).

Monitoring of HbA1c is of limited clinical use in GDM as it is affected by haemoglobin turnover during pregnancy (Sweeting, Hannah, et al. 2024).

Regular SMBG is recommended in GDM, including frequent daily checks and is essential for effective GDM management (Nankervis, Price & Conn 2018). Woman can get support with SMBG from a CDE and obtain subsidised glucose testing strips if registered with the NDSS. It is recommended that women initially undertake SMBG four times per day: before breakfast and either one or two hours after the start of each meal (Nankervis, Price & Conn 2018). There is no consensus on blood glucose targets for SMBG, but the ADIPS guidelines suggest:

- Fasting capillary blood glucose: ≤ 5.0 mmol/L
- 1-hour blood glucose: ≤ 7.4 mmol/L
- 2-hour blood glucose: ≤ 6.7 mmol/L

If these values are exceeded, further treatment with glucose-lowering therapies may be recommended (Nankervis, Price & Conn 2018).

Pharmacotherapy is tailored according to disease severity and complications (Sweeting, Hannah, et al. 2024). Insulin is the main treatment for GDM with the insulin regimen individualised to meet glycaemic targets. Of the 18,677 women currently registered on the NDSS, 41% required insulin to manage their GDM (National Diabetes Services Scheme). The insulin dose is usually increased throughout the second half of pregnancy due to increasing insulin resistance caused by placental hormones leading to increases in blood glucose. The insulin dose is adjusted every two to three days to achieve target blood glucose levels (Nankervis, Price & Conn 2018). Basal insulin is used to manage fasting glucose and a short-acting insulin analogue can be used for post prandial hyperglycaemia.

Metformin has been increasingly used and is generally considered safe and effective for GDM, with reduced adverse maternal and neonatal outcomes compared with insulin and a minimal risk of hypoglycaemia (Nankervis, Price & Conn 2018). Other glucose-lowering therapies are rarely used for GDM.

Data from the ANDA in 2022 shows that the average BMI of patients with GDM was in the obese range (mean \pm SD BMI of 33.5 ± 7.3 kg/m²), similar to previous years⁷. Around 60% of patients with GDM managed their GDM with diet alone, and almost 29% of patients were managed with insulin, of which the majority were using a basal regimen, and most of the remainder managed with a basal-bolus regimen (Australian National Diabetes Audit). This is lower than the NDSS estimate of 41% of women registered with the NDSS requiring insulin (National Diabetes Services Scheme).

⁷ Note, a BMI of 25 to 29.9 is defined as overweight during pregnancy, and a BMI of over 30 is defined as obese during pregnancy. <https://www.aihw.gov.au/reports/mothers-babies/australias-mothers-babies/contents/antenatal-period/maternal-body-mass-index>

Most GDM pregnancies, even when insulin treatment is required, are considered at low risk of complications. However, a small number of pregnancies in women with GDM are high risk and additional medical care is required (American Diabetes Association Professional Practice Committee 2023b). Careful clinical monitoring and the use of ultrasonography to assess the wellbeing and size of the fetus are the main focus of management. A growth scan at 28 – 32 weeks is useful to assess fetal growth for early identification of macrosomia (large for gestational age) or fetal growth restriction (Nankervis, Price & Conn 2018). A macrosomic fetus is more likely to have complications during and after delivery and requires more intensive monitoring and careful consideration of the type and timing of delivery. In most women, vaginal delivery at term is usual unless obstetric indications suggest a different approach (Nankervis, Price & Conn 2018).

The primary FSL2 RCT in GDM recruited women diagnosed with GDM between 24-28 weeks of gestation and found no significant difference between FSL2 and SMBG groups in progression to insulin therapy (OR 1.09, 95% CI 0.47–2.57) but did find a significant increase in fetal macrosomia in the SMBG group as compared to FSL2 group (OR 5.63, 95% CI 1.16–27.22) irrespective of glucose-lowering therapy.

Pharmacotherapy for GDM should cease postpartum. The neonate, especially if macrosomic, is prone to hypoglycaemia, and all babies of GDM pregnancies should have their blood glucose tested around 1–2 hours after birth, management instituted if they are hypoglycaemic and regular blood glucose monitoring thereafter if required (Nankervis, Price & Conn 2018). Women with GDM are encouraged to breastfeed or express milk as it may reduce the risk of developing T2D (Nankervis, Price & Conn 2018).

Postpartum follow-up

Women diagnosed with GDM have approximately a 40% risk of a recurrence of GDM in a subsequent pregnancy and a 10-fold increased risk of developing future T2D (American Diabetes Association 2024d; The Royal Australian College of General Practitioners 2020). Breast feeding after birth can reduce this risk of developing T2D for the mother (Nankervis, Price & Conn 2018). Because GDM often represents previously undiagnosed prediabetes, T2D, maturity-onset diabetes of the young, or even developing type 1 diabetes, all women who had GDM should have an OGTT by either their maternity service or GP to confirm their glycaemic status at 6–12 weeks postpartum. There is no clear consensus on long-term follow-up for these women. Measurement of HbA1c and/or fasting blood glucose measurement every 1–3 years, dependent upon risk status, have been recommended and women considering another pregnancy should have an OGTT annually (American Diabetes Association 2024d; The Royal Australian College of General Practitioners 2020). Careful planning and early testing for hyperglycaemia is required for subsequent pregnancies as around 20% of women with GDM during a subsequent pregnancy had a GDM diagnosis during their previous pregnancy (National Diabetes Services Scheme). Ongoing clinical surveillance of both mother and baby is required in the long-term for complications associated with GDM. Education and support for mother and baby to help maintain a healthy lifestyle is also considered beneficial (Nankervis, Price & Conn 2018).

Rationale

GDM is the most common source of hyperglycaemia during pregnancy. In comparison to SMBG, use of FSL2 CGM in women with GDM may have benefits for both the mother and fetus.

The RACGP guidance on management of GDM recommends that pregnant women with gestational diabetes and experiencing severe hypoglycaemia regardless of awareness or if have unstable blood glucose should also be offered continuous glucose monitoring (CGM) (The Royal Australian College of General Practitioners 2024). However, only a small volume of clinical data are currently available on the use of CGM in women with GDM, and there is uncertainty around the most appropriate CGM metrics to use for women with GDM to demonstrate the effectiveness of CGM and benefits in terms of health outcomes (Szmuiłowicz et al. 2024). A consistent benefit of increased glycaemic control during GDM for improving health outcomes in mothers and neonates has not been consistently demonstrated, although it has been proposed that reduction in overall exposure to hyperglycaemia throughout gestation may an important factor in improving neonatal health outcomes (Szmuiłowicz et al. 2024).

PASC queried whether there were differences in monitoring requirements and validity of CGM vs SMBG in PICO Set 2 compared to the other PICO sets but the applicant was of the view that there was no evidence of any such differences.

The international consensus report on clinical targets for CGM recommended blood glucose thresholds for TIR (63–140 mg/dL [3.5–7.8 mmol/L]), TBR (<63 mg/dL [<3.5 mmol/L] and <54 mg/dL [<3.0 mmol/L]), and TAR (>140 mg/dL [>7.8 mmol/L]) for pregnant women with T2D or GDM. These are different to normal recommended thresholds as glucose levels are physiologically lower during pregnancy (Battelino et al. 2019). However, targets for TIR, TBR, and TAR were not specified for pregnant women with T2D or GDM because of the lack of supporting evidence on which to make a recommendation (Battelino et al. 2019).

Intervention

The intervention for PICO Set 2 is the FSL2 (see PICO Set 1 for more details).

Pregnant women are usually diagnosed with GDM in week 24–28 of gestation. It is likely that women with GDM using insulin would only use CGM for the remainder of their pregnancy, as GDM usually resolves postpartum and insulin treatment is discontinued. Those identified as having diabetes at an earlier stage in their pregnancy and requiring insulin may use CGM for a longer period, particularly if their diabetes was pre-existing and not identified prior to pregnancy. If they have T2D identified during pregnancy and require insulin, they may continue to use CGM instead of SMBG after pregnancy to manage their blood glucose levels and inform appropriate insulin titration.

The 2024 RACGP handbook for the management of type 2 diabetes notes that there is a high level of evidence for CGM use for some women with GDM and specifically states that for “pregnant women with other forms of diabetes such as type 2 diabetes or gestational diabetes, and experiencing severe hypoglycaemia regardless of awareness OR if have unstable blood glucose should also be offered continuous glucose monitoring (CGM)” (The Royal Australian College of General Practitioners 2024). The ADA guidelines state that “The decision of whether to use CGM in pregnant individuals with T2D or GDM should be individualized based on treatment regimen, circumstances, preferences, and needs” (American Diabetes Association Professional Practice Committee 2023b). Management of GDM is based on a combination of optimisation of lifestyle, SMBG, intensive patient education and introduction of medication, such as insulin, when required (Nankervis, Price & Conn 2018).

CGM offers people with GDM additional information to better understand their GDM, guide and refine their management of GDM using insulin to maintain their fasting and postprandial blood glucose levels,

and as an educational tool to support ongoing lifestyle interventions that may have an impact post-partum. Other benefits may include improved compliance with monitoring and treatment leading to better glycaemic control, improved mental health through reduction in anxiety or diabetes distress, improved QoL and patient satisfaction, and increased self-efficacy leading to improvements in self-management of their GDM. They would also benefit from not requiring regular finger prick blood samples for SMBG using glucose test strips and a glucose monitor.

PASC noted guideline recommendations for CGM for women with GDM because they are at increased risk of poor glycaemic control. PASC noted that CGM for women who were not receiving insulin therapy would be beneficial because the risk for both mother and infant of developing T2D post-partum is similar, regardless of whether the women are treated with insulin therapy or otherwise.

Comparator(s)

The proposed comparator is SMBG using a finger prick capillary blood sample, blood glucose test strips and a glucose meter (see PICO Set 1 for more details). The RACGP guidelines recommend SMBG for women with GDM (The Royal Australian College of General Practitioners 2020).

PASC noted that the comparator is SMBG using a finger prick capillary blood sample, blood glucose test strips and a glucose meter. SMBG is the current SoC for monitoring of blood glucose in pregnant women with GDM.

Reference standard

The reference standard is laboratory measured plasma venous blood glucose testing (e.g., using a YSI (Yellow Springs Laboratory Instrument) for glucose testing or equivalent). *PASC agreed that laboratory measured plasma venous blood glucose testing is the appropriate reference standard.*

Outcomes

Additional outcomes relevant to GDM for both the mother and child have been added to the PICO, although many of the remaining outcomes are similar to those considered for T2D (see Outcomes for PICO Set 1). Glucose targets for fasting and postprandial glucose used in SMBG are as specified in the ADA and RACGP guidelines (The Royal Australian College of General Practitioners 2020). The glycaemic thresholds used to determine “time in ranges” should be those indicated for pregnant women with T2D or GDM as discussed above under GDM management (Battelino et al. 2019).

PASC noted that the outcomes for PICO Set 2 differ from PICO Set 1 as there are outcomes relevant to the child as well as the mother.

The applicant nominated some additional outcomes for inclusion in PICO Set 2 in their pre-PASC response. The FSL2 clinical studies were of very short duration (2 or 4 weeks) and therefore changes in HbA1c are not a meaningful outcome. The additional outcomes for inclusion in the PICO were:

- mean fasting glucose concentration during the first 4 weeks
- post prandial mean glycaemia
- high birth weight

PASC noted that only a limited number of studies have evaluated the impact of FSL2 in GDM. As study outcomes have typically been measured over either a 14-day or 28-day period, the applicant advised that providing results for some of the long-term outcomes included in PICO Set 2 may not be feasible.

Outcomes included in the PICO are as follows:

Patient relevant outcomes

Direct evidence for safety and effectiveness:

Safety:

- Local adverse events (AEs) associated with glucose testing

Effectiveness for mother:

- GDM complications (e.g. cardiovascular complications, hypertension etc)
- Mortality
- GDM leading to hospitalisations/emergency room visits
- Complications during birth
- T2D post-partum and related complications
- Quality of life
- Psychological health

Intermediate/surrogate outcomes for mother:

- Glycaemic control
 - glycated haemoglobin (HbA1c)
 - mean fasting glucose concentration during the first 4 weeks of glucose monitoring (CGM or SMBG)
 - post prandial mean glycaemia
 - time in range (TIR), time below range (TBR) and time above range (TAR)
 - number of hypoglycaemic/hyperglycaemic excursions
 - glycaemic variability
- Change in body weight/ body mass index (BMI)

Effectiveness for child:

- Neonatal complications (neonatal hypoglycaemia; large for gestational age; gestational age at birth; respiratory complications; high birth weight)
- Complications during birth
- Admission to neonatal intensive care unit (NICU)
- Long-term outcomes for child (e.g. obesity, diagnosis of T2D, heart disease)

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 GDM and achieve their clinical goals)
- Work/school absenteeism and daily functioning

Healthcare system outcomes

- Cost, cost-effectiveness
- Financial implications (financial impact, overall healthcare costs, including cost of ongoing surveillance of mother and child post-partum for complications of GDM and development of T2D).

PASC considered that HbA1c may not be a useful outcome measure in pregnant women because HbA1c can be underestimated due to physiological changes during pregnancy, including haemodilution.

PASC noted that the outcome of 'Adherence to glucose testing' should be amended to 'Adherence to CGM or SMBG'.

PASC considered that 'adherence to CGM or SMBG' and 'acceptability, wearability and usability of CGM versus SMBG' were intermediate outcomes for health or change in management with the latter under the subheading of 'Other relevant considerations'. PASC noted that the outcomes of 'patient/carer satisfaction' and 'work absenteeism and daily functioning' should be added to the subheading of 'Other relevant considerations'.

PASC noted that uptake of exercise is a separate measure from body weight/BMI which is not a measure of uptake directly and that the latter needs to be recategorized.

Assessment framework

The proposed assessment framework is as discussed for T2D in PICO Set 1 above. *PASC noted that the standard assessment framework using a linked evidence approach would be used in the ADAR.*

Clinical management algorithms

Current management algorithm for blood glucose testing

The current management algorithm for people with GDM requiring insulin using SMBG is based on the management algorithm from PICO Set 1 for T2D and is presented in Figure 7.

Following a diagnosis of GDM, the pregnant woman would register on the NDSS National Gestational Diabetes Register provided she is eligible for Medicare.

As GDM responds well to lifestyle management (change in diet, increased exercise, cessation of smoking), the pregnant women with GDM would be referred to an accredited practising dietitian and a certified diabetes educator who would provide educational support and advice of GDM management. Around 70-80% of women are able to achieve their GDM management targets using a combination of optimal diet and appropriate exercise.

Regular SMBG is recommended in GDM, including frequent daily checks, and is essential for effective GDM management. SMBG frequency for GDM is individualised based on clinical need and following discussion with the individual's diabetes healthcare professional. Woman can get support with SMBG from a diabetes educator and obtain subsidised glucose testing strips if registered with the NDSS. SMBG is initially recommended at least four times per day (e.g. before breakfast and either one or two hours after the start of each meal) (Nankervis, Price & Conn 2018).

There is no consensus on blood glucose targets but the ADIPS guidelines suggest:

- Fasting capillary blood glucose: ≤ 5.0 mmol/L
- 1-hour blood glucose: ≤ 7.4 mmol/L
- 2-hour blood glucose: ≤ 6.7 mmol/L

If these blood glucose values are regularly exceeded, treatment with insulin or metformin may be recommended (Nankervis, Price & Conn 2018). Effective SMBG facilitates effective glycaemic management, reduces hyperglycaemia and may improve pregnancy outcomes for the mother and neonate.

Insulin is the main treatment for GDM with the insulin regimen individualised to meet glycaemic targets. Of the 18,677 women currently registered on the NDSS, 41% required insulin to manage their GDM (National Diabetes Services Scheme). If blood glucose is high, early initiation of insulin therapy is recommended and is effective at establishing glycaemic control. The dose of insulin requires regular titration during pregnancy as insulin resistance increases due to the action of pregnancy hormones. In cases of fasting hyperglycaemia, medium-acting or long-acting insulin can be used at bedtime. The starting dose will depend on the degree of hyperglycaemia and the weight of the woman. The dose of insulin is adjusted every 2-3 days to maintain recommended blood glucose levels. A short-acting insulin analogue can be used for postprandial hyperglycaemia.

Treatment with insulin should cease postpartum but lifestyle changes should continue due to the 10-fold increased risk of T2D in women with GDM and children exposed to GDM during gestation (American Diabetes Association 2024d; The Royal Australian College of General Practitioners 2020).

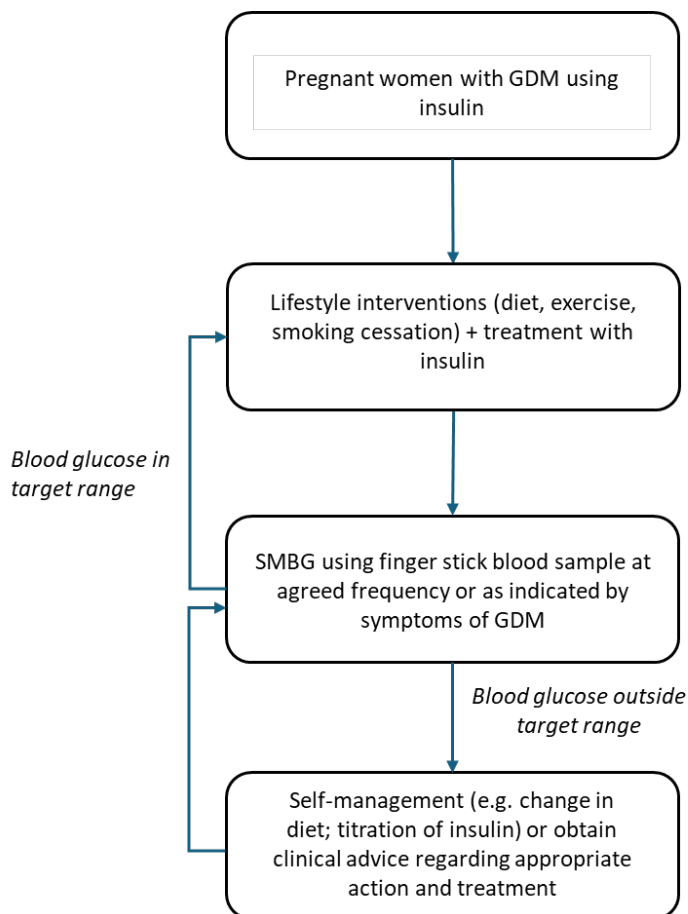


Figure 7 Current clinical management algorithm of SMBG for pregnant women with GDM requiring insulin

Source: Adapted from Figure 8, p.24 of MSAC Application 1786.

GDM = gestational diabetes mellitus, SMBG = self-monitoring of blood glucose.

Note: The agreed frequency of SMBG is individualised and is based on a patient’s clinical need and advice from their diabetes healthcare professional.

Proposed management algorithm for blood glucose testing

The proposed management algorithm for pregnant women with GDM requiring insulin and using CGM is based on the algorithm from PICO Set 1 and is presented in Figure 8.

Effective glucose monitoring is considered essential to GDM management with SMBG recommended at least 4 times per day (e.g. before breakfast and either one or two hours after each meal) (Nankervis, Price & Conn 2018). As SMBG provides only a snapshot of glucose levels, it provides limited information on glycaemic control. However, as noted previously for PICO Set 1, the Applicant considered that this information may be further limited because people with diabetes may not be compliant with their clinician’s recommendations around finger prick testing. Failure to carry out SMBG at a frequency indicated by an individual’s clinical need or as recommended by their diabetes healthcare professional (“agreed frequency”) is likely to have a negative impact on establishing glycaemic control.

The applicant highlighted in the pre-PASC response that if an “agreed frequency” of finger prick testing is assumed in the algorithm, the data obtained may not be representative of real-world use of SMBG. However, the applicant assumed that the “agreed frequency” indicated in the current algorithm for SMBG

is a fixed number. The “agreed frequency” in the algorithm is a variable frequency because SMBG is individualised as clarified in the text above. *PASC noted that issues pertaining to finger prick frequency and lack of compliance with testing protocols may be similar for people with GDM as for populations with T2D; the range of frequency of SMBG by finger-prick testing may be an outcome explored by the assessment.*

CGM provides more information about glycaemic control, glycaemic variability and patterns of hyperglycaemia with at least 14 days use required to provide enough information to characterise a person’s glycaemic patterns and control. As monitoring is carried out continuously over a 24-hour period, more information is available from CGM about fetal exposure to maternal glucose overnight. Nocturnal hyperglycaemia has been associated with women with GDM giving birth to babies who are large for gestational age (Law et al. 2019). The additional information from CGM is used to inform decisions regarding insulin dose and frequency particularly as insulin requirements need to be reassessed every 2 to 3 days during the third trimester of pregnancy. As data provided by the FSL2 CGM is more extensive than from SMBG, clinical decision making for GDM management and self-management by the patient and their diabetes healthcare professional may change.

Use of CGM may provide more reassurance for the pregnant mother regarding her glycaemic control and the impact on her fetus. Increased information from CGM can increase self-efficacy around proactive lifestyle management of GDM through diet and exercise in addition to improving management of insulin titration. This can reduce anxiety and stress leading to improvements in psychological health and QoL.

A woman with GDM using FSL2 CGM would not usually need to carry out SMBG using a glucose meter. However, if they experience GDM-related symptoms that are not aligned with their glucose readings from the FSL2 CGM, they should check that their FSL2 glucose readings are correct by carrying out SMBG from a finger prick blood sample using a glucose test strip. If the FSL2 glucose readings are incorrect and the person’s glucose levels are in the hypoglycaemic or hyperglycaemic range, they can follow prior clinical advice about the appropriate action to take or seek further medical advice regarding the most appropriate course of action including titration of their insulin dose or administration of rapid acting oral carbohydrate therapy. If they require urgent medical attention, they can call the emergency services or attend the emergency department.

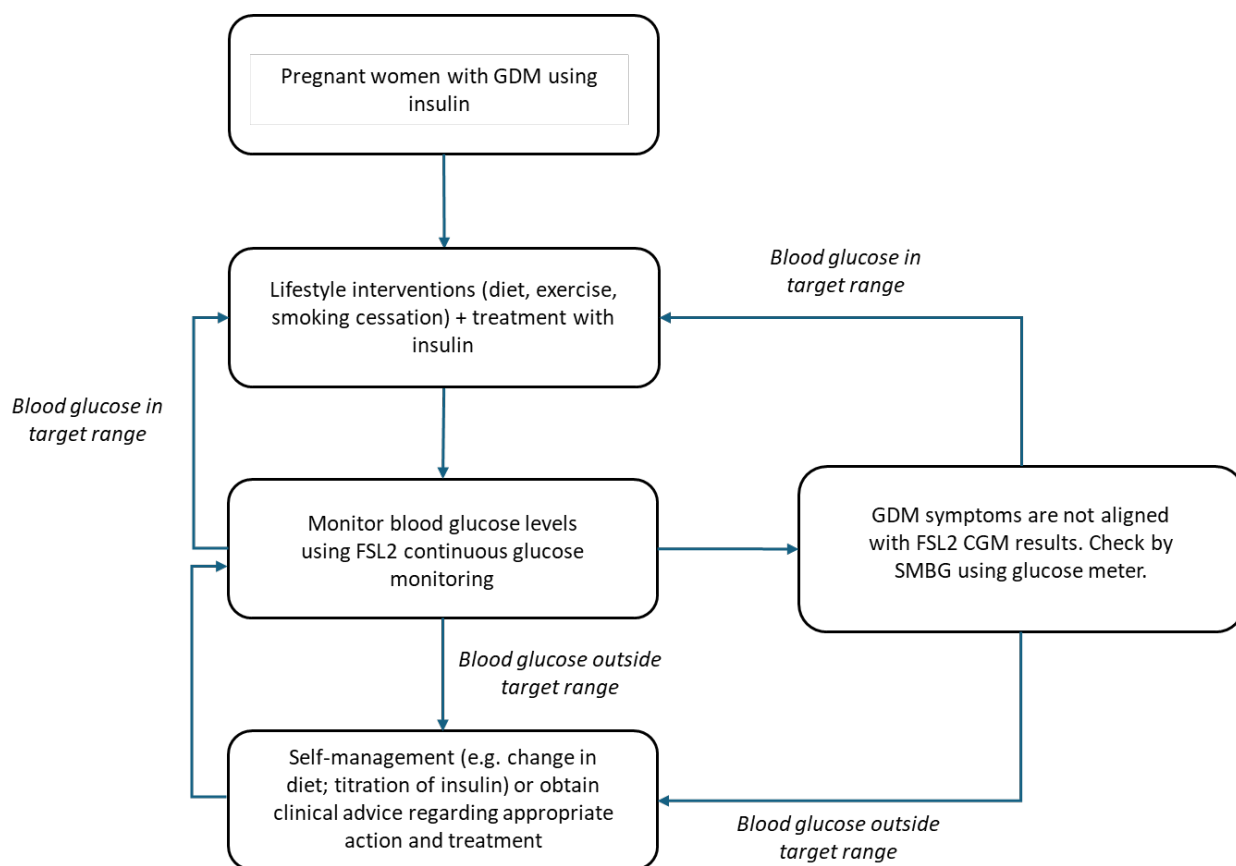


Figure 8 Proposed clinical management algorithm of CGM using FSL2 for pregnant women with GDM requiring insulin

Source: Adapted from Figure 9, p.25 of MSAC Application 1786

CGM = continuous glucose monitoring, FSL2 = FreeStyle Libre 2, GDM = gestational diabetes mellitus, SMBG = self-monitoring of blood glucose.

Proposed economic evaluation

The appropriate form of economic analysis would be a cost-effectiveness analysis or cost-utility analysis if the clinical claim is for superior effectiveness and non-inferior safety of FSL2 CGM versus SMBG for women with GDM using insulin (see Table 5 in PICO Set 1).

PASC noted that the economic evaluation would be a cost-effectiveness analysis or cost-utility analysis as the clinical claim is for superior effectiveness and non-inferior safety of FSL2 CGM versus SMBG for women with GDM. However, PASC noted that while data for short-term outcomes of CGM may be available (e.g. reduction in premature and post-term births, or birth weight), modelling for long term maternal- and child-related diabetes risks may be difficult due to insufficient information.

Proposal for public funding

This MSAC application is requesting NDSS funding for subsidised FSL2 CGM products for women with gestational diabetes.

PASC confirmed that the proposed source of public funding for CGM in women with GDM was the NDSS, as for pregnant women with T1D (i.e. no MBS listing is being requested).

The FSL2 sensor costs \$REDACTED for 14 days, and the overall cost per patient per year would be \$REDACTED. If a FSL2 reader is required (rather than the app), it costs \$REDACTED. The proposal is for FSL2 CGM to be fully subsidised under the NDSS, as is currently the case for pregnant women with T1D.

The application did not provide utilisation data for use of FSL2 by women with GDM; the following information is provided for context only.

The NDSS report for GDM indicates that 45,290 women with GDM were registered with the NDSS as of the 12 months to 30 June 2024 (National Diabetes Services Scheme). A FSL2 sensor is disposable and can be worn for a maximum period of 14 days (2 weeks); it costs \$REDACTED. If all 45,290 women with GDM (regardless of whether they require insulin) used FSL2 CGM, the total cost to the NDSS of FSL2 if GDM was identified at Week 12 of pregnancy or at Week 24 of pregnancy would be \$REDACTED or \$REDACTED, respectively. (This is assuming that FSL2 was fully subsidised by the NDSS, GDM was identified in all women at the same gestational time point, birth occurred at 40 weeks gestation and use of CGM ceased immediately after birth). However, these figures include people with T1D, and CGMs for women with T1D who are pregnant are already fully subsidised through the NDSS, and therefore these costs are likely overestimated. The additional cost of supplying readers for 45,290 pregnant women with GDM would be \$REDACTED. This cost is also likely to be overestimated as many women will have a smartphone device and will not require a reader.

PICO Set 3

Population

The proposed population is people with “other types of diabetes” similar to T1D requiring insulin that are aged ≥ 21 years; the list of eligible conditions is provided in Table 7. Children and young people aged < 21 years with these “other types of diabetes” very similar to T1D who require insulin are currently able to access fully subsidised CGM products via the NDSS.⁸ The purpose of PICO Set 3 is to address inequities in the current funding structure for people with “other types of diabetes” similar to T1D. This inequity of access was recently highlighted by the Parliamentary Inquiry into Diabetes. The list of the NDSS eligible conditions is provided in the Appendix (Table 7). People with these conditions are currently only eligible for NDSS funded CGM if they are aged < 21 years and using insulin.

The MSAC application originally requested that Type 3c diabetes (T3cD) be included in the MSAC 1786 assessment. Type 3c diabetes is caused by disorders that affect exocrine functions of the pancreas and is included in the proposed population. However, it was agreed at the pre-PASC teleconference that the MSAC assessment should be extended to people with rarer “other types of diabetes” requiring insulin for treatment.

More detailed information is provided below for T3cD, which is an “other type of diabetes” caused by disorders that affect exocrine functions of the pancreas, such as cancer or acute infection.

PASC noted that the population in PICO Set 3 are patients aged ≥ 21 years with conditions similar to T1D that require insulin (“other types of diabetes”). Children and young people aged < 21 years with conditions

⁸ NDSS. <https://www.ndss.com.au/wp-content/uploads/resources/registration-eligible-other-diabetes.pdf>

very similar to T1D who require insulin are currently able to access fully subsidised CGM products via the NDSS. The applicant's proposal is for there to be no age limit (i.e. that those aged 21 and over with conditions similar to T1D that require insulin should also be able to access fully subsidised FSL2 CGM via the NDSS). PASC noted that the list of conditions considered to be "similar to T1D that require insulin" for the ≥21 years age group should be the same list as for the <21 years age group, which had been approved by the NDSS. It was noted that estimates of the prevalence of "other types of diabetes" include people younger than 21 years of age, who may already receive subsidised CGMs through the NDSS.

PASC discussed whether any patients would require genetic testing, in order to qualify for subsidised NDSS access to CGM due to having one of the "other types of diabetes" (as the required genetic testing may not be covered under the MBS). However, it was noted that while it was up to the healthcare provider to confirm diagnosis through appropriate testing, the healthcare provider does not need to submit the clinical evidence of diagnosis as part of the application form on behalf of a patient for subsidised access. PASC noted that it would be important for genetic testing to be incorporated into the financial estimates and economic evaluation.

Prevalence of other types of diabetes

According to NDSS registration data, 12,468 (0.8% of people with diabetes) had an "other type of diabetes" (National Diabetes Services Scheme). Of these people with "other types of diabetes", 8,009 (64%) required insulin (National Diabetes Services Scheme).

Type 3c diabetes

Prevalence of T3cD

T3cD falls within the category of "other type of diabetes". It has been estimated that T3cD represents 1 – 9% of all diabetes cases, with a wide range of estimates because T3cD is poorly recognised and so frequently misdiagnosed.⁹ The incidence of T3cD is higher in adults than T1D.⁹

Burden of disease

The symptoms of T3cD are similar to those observed in T2D (e.g. dry mouth, frequent urination, weight loss, blurred vision, fatigue) but also include symptoms associated with exocrine pancreatic insufficiency, including abdominal pain and bloating, constipation, fatty stools, and diarrhoea (American Diabetes Association Professional Practice Committee 2023a).

Following an episode of acute pancreatitis, people should be screened for T3cD within 3–6 months and then annually. Annual screening for T3cD is recommended for people with chronic pancreatitis (American Diabetes Association Professional Practice Committee 2023a; Hart et al. 2016).

Prior testing

T3cD is frequently misdiagnosed as T2D but people with T3cD have a greater likelihood of poor glycaemic control than those with T2D (Woodmansey et al. 2017).

⁹ <https://my.clevelandclinic.org/health/diseases/24953-type-3c-diabetes>

At diagnosis, distinguishing features are concurrent pancreatic exocrine insufficiency, pathological pancreatic imaging on MRI and an absence of T1D-associated autoimmunity (American Diabetes Association Professional Practice Committee 2023a).

Management of T3cD

T3cD can be managed with oral diabetes glucose-lowering drugs and/or insulin, with patients having similar requirements for blood glucose monitoring to T1D and T2D patients^{Error! Bookmark not defined.}. Diabetes following pancreatic disease is associated with earlier initiation of insulin therapy than in people with T2D. Diabetes following chronic pancreatic disease has a higher rate of insulin use than diabetes following acute pancreatitis, and both have a greater requirement for insulin than people with T2D. Early initiation of insulin therapy should be considered if HbA1c goals are not achieved using oral therapies, with many patients requiring intensive insulin therapy. Autologous pancreatic islet cell transplantation may also be considered in people with T3cD to reduce insulin usage (American Diabetes Association 2024a; Hart et al. 2016; Woodmansey et al. 2017).

Rationale for funding of CGM for people with “other types of diabetes” that require insulin

People with “other types of diabetes” aged ≥ 21 years that require insulin to manage their blood glucose levels have the same requirement for glucose monitoring as patients aged < 21 years with “other types of diabetes” (i.e. the same conditions) and as patients with T1D that are currently able to access subsidised CGM via the NDSS. Additionally, as some people with “other types of diabetes” require intensive insulin therapy regimens or are at increased risk of hypoglycaemia, use of CGM provides more information about their glycaemic control over a complete 24-hour period. This has the potential to permit more effective self-management of their diabetes and facilitates more effective advice and support from their diabetes healthcare professional.

Intervention

The intervention for PICO Set 3 is the FSL2 CGM as described in PICO Set 1. The application includes a conference abstract of a study using FSL2 in people with cystic fibrosis-related diabetes (Type3cD), another disease of the exocrine pancreas.

People with T3cD have similar requirements to people with T1D or T2D for monitoring of blood glucose to assess their glycaemic status and to manage their glycaemic control through strategies such as titration of insulin.

PASC noted the proposed intervention is the FSL2 CGM system.

Comparator(s)

The proposed comparator is SMBG using a finger prick capillary blood sample, blood glucose test strips and a glucose meter (see PICO Set 1 for more details).

PASC noted that the proposed comparator is SMBG using finger prick capillary blood samples, glucose test strips and glucose meter. SMBG is the current standard of care for blood glucose monitoring in people aged ≥ 21 years with “other types of diabetes” similar to T1D using insulin who are not currently eligible for NDSS funded CGM in Australia.

Reference standard

The reference standard is laboratory measured plasma venous blood glucose testing (e.g., using a YSI (Yellow Springs Laboratory Instrument) for glucose testing or equivalent). *PASC confirmed that laboratory measured plasma venous blood glucose testing (e.g., using a YSI (Yellow Springs Laboratory Instrument) for glucose testing or equivalent) is the appropriate reference standard.*

Outcomes

The proposed outcomes of interest are as discussed in PICO Set 1 for T2D:

Patient relevant outcomes

Direct evidence for safety and effectiveness:

Safety:

- Local adverse events (AEs) associated with glucose testing

Effectiveness:

- Diabetes-related complications (e.g. cardiovascular and microvascular complications including kidney disease, neuropathy/nerve damage, retinopathy/eye disease, amputations/foot ulcers)
- Mortality
- Quality of life
- Psychological health
- Hypoglycaemic or hyperglycaemic events resulting in emergency room visit/hospitalisation

Intermediate/surrogate outcomes:

- Glycaemic control
 - glycated haemoglobin (HbA1c)
 - time in range (TIR), time below range (TBR) and time above range (TAR)
 - number of hypoglycaemic/hyperglycaemic excursions
 - glycaemic variability
- Change in body weight/ body mass index (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 (e.g. glucose-lowering therapy)
- Uptake or alteration of lifestyle interventions (e.g. diet and exercise) or 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 diabetes 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.)

PASC noted that there is very little relevant clinical evidence specific for people with conditions similar to T1D requiring insulin (other than T2D) and therefore it would be necessary to rely on other data sources to inform an analysis of CGM cost-effectiveness. There is no evidence available for most of the outcomes listed in PICO Set 3 with the exception of some limited data regarding change in HbA1c.

PASC noted that the outcome of ‘Adherence to glucose testing’ should be amended to ‘Adherence to CGM or SMBG’.

PASC considered that ‘adherence to CGM or SMBG and ‘acceptability, wearability and usability of CGM versus SMBG’ were intermediate outcomes for health or change in management with the latter under the subheading of ‘Other relevant considerations’. PASC noted that uptake of exercise is a separate measure from body weight/BMI which is not a measure of uptake directly and that the latter needs to be recategorized.

Assessment framework

The proposed assessment framework is as discussed for T2D in PICO Set 1 above.

The volume of evidence for each of these “other types of diabetes” is likely to be limited. Instead of being able to provide the entire direct from test to health outcomes evidence or linked evidence using studies on “other types of diabetes”, the assessment may require evidence or biological plausibility regarding the similarity of the conditions to T2D (i.e. in the accuracy of the intervention and/or comparators and the way they are managed). (Note, although the conditions may be more similar to T1D than T2D, if comparisons are made against T1D then evidence of the effectiveness of FLS2 for T1D may be required).

PASC acknowledged that as there is very little clinical evidence specific for patients in PICO Set 3, the assessment may require evidence or biological plausibility regarding the similarity of the conditions to T2D, to enable T2D data to be applied to PICO Set 3.

PASC considered that an exemplar approach might be suitable for PICO Set 3, for example, using the population of patients with Type 3c diabetes.

Clinical management algorithms

Current management algorithm for blood glucose testing

The application did not include a management algorithm for glucose monitoring for PICO Set 3. The current management algorithm for people with “other forms of diabetes” requiring insulin is shown in Figure 9 and is based on the current management algorithm for T2D from PICO Set 1.

SMBG is currently used for monitoring blood glucose levels and managing titration of insulin in people with “other forms of diabetes” requiring insulin therapy. The intensity of the insulin regimen varies according to

need and insulin may be administered by injection or by CSII. Patients on insulin should perform SMBG at least four times a day although more frequent monitoring is required for many people and monitoring is individualised according to need.

CGM is currently subsidised via the NDSS for some eligible people aged <21 years with “other types of diabetes” that are similar to T1D and are using insulin to maintain glycaemic control. Some people aged <21 years with “other types of diabetes” requiring intensive insulin therapy may be able to use a hybrid closed loop system, if clinically appropriate, to manage their insulin therapy. However, it should be noted that the FSL2 CGM is not currently compatible with an insulin pump, and therefore is not currently suitable for use in a hybrid closed loop system.

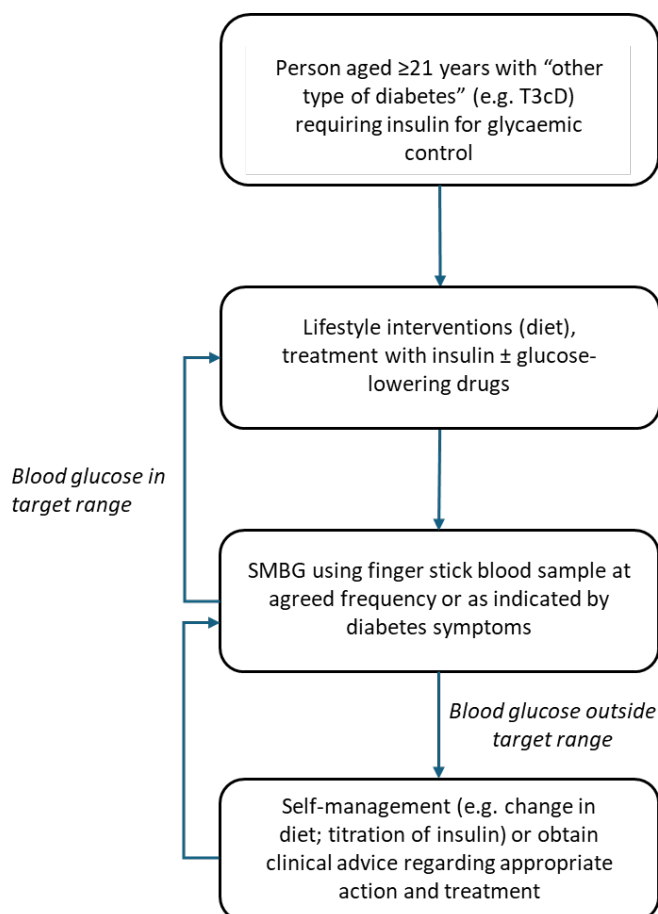


Figure 95 Current clinical management algorithm of SMBG for people aged ≥21 years with “other types of diabetes” similar to T1D requiring insulin

Source: Adapted from Figure 8, p.24 of MSAC Application 1786

SMBG = self-monitoring of blood glucose, T3cD = Type 3c diabetes.

Note: The agreed frequency of SMBG is individualised and is based on a patient’s clinical need and advice from their diabetes healthcare professional.

Proposed management algorithm for blood glucose testing

The proposed management algorithm developed by the assessment group is presented in Figure 60 and is based on the proposed algorithm for T2D in PICO Set 1. Further information about use of FSL2 CGM for glucose level testing is available in PICO Set 1.

If subsidised access to CGM is available via the NDSS to all people with “other types of diabetes” requiring insulin (in line with the TGA indication for FSL2), CGM will be used to measure glucose levels and provide information for management of insulin titration. As FSL2 is currently not compatible with an insulin pump, it cannot be used in a hybrid closed loop system. It can be used with insulin injections or an independent CSII. FSL2 CGM data can be shared via LibreView, so that diabetes healthcare professionals are able to provide appropriate advice based on the continuous AGP. Data from the FSL2 can also be shared via the FreeStyle LibreLinkUp app with a parent or carer who can assist with interpretation of the data or with insulin titration, as required.

A person using FSL2 CGM would not usually need to carry out SMBG using a glucose meter. However, if the person experiences acute diabetes-related symptoms that are not aligned with their blood glucose readings from the FSL2 CGM, they need to check that their FSL2 glucose readings are correct by carrying out SMBG from a finger prick capillary blood sample using a glucose test strip. If the FSL2 glucose readings are incorrect and the person’s glucose levels are in the hypoglycaemic or hyperglycaemic range, they can follow prior clinical advice about the appropriate action to take or seek further medical advice regarding the most appropriate course of action including titration of their insulin dose. If they require urgent medical attention, they can call the emergency services or attend the emergency department.

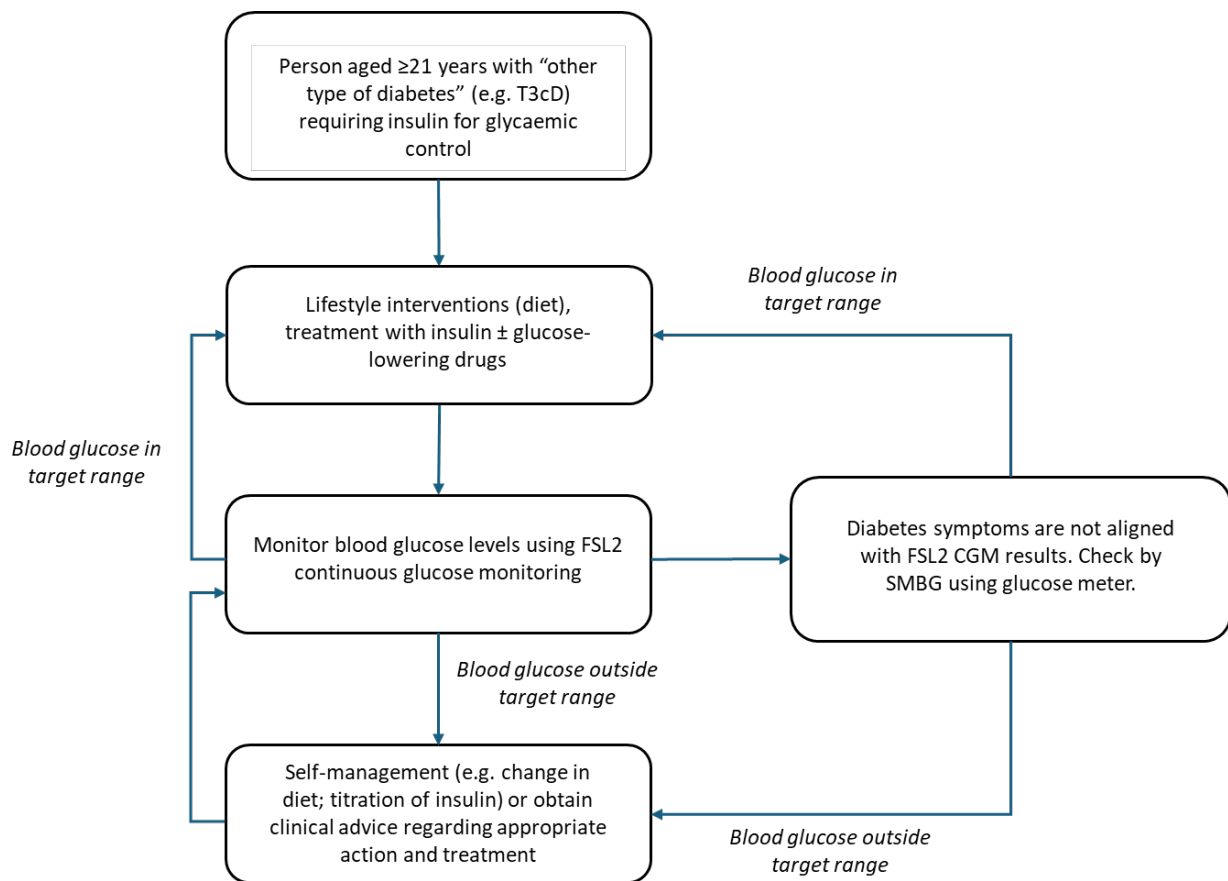


Figure 70 Proposed clinical management algorithm of continuous blood glucose monitoring using CGM with FSL2 for people aged ≥21 years with “other types of diabetes” similar to T1D requiring insulin

Source: Adapted from Figure 9, p.25 of MSAC Application 1786.

CGM = continuous glucose monitoring; FSL2 = FreeStyle Libre 2, SMBG = self-monitoring of blood glucose, T3cD = type 3c diabetes

PASC noted that the current and proposed management algorithms were similar to the clinical algorithms for PICO Set 1.

Proposed economic evaluation

The appropriate form of economic analysis would be a cost-effectiveness analysis or cost-utility analysis as the clinical claim is for superior effectiveness and non-inferior safety of FSL2 CGM versus SMBG for people with “other forms of diabetes” (see Table 5 in PICO Set 1).

PASC noted that the clinical claim is the same as for T2D (PICO Set 1), namely that CGM is superior in terms of efficacy and non-inferior in terms of safety.

PASC confirmed that that the most appropriate economic evaluation would be a cost-effectiveness or cost-utility analysis. However, PASC noted that the applicant considers it is unlikely that there is sufficient information available to model the potential health outcomes specifically for patients in PICO Set 3 and instead inferences from other data sources will need to be made.

Proposal for public funding

A FSL2 sensor is disposable and can be worn for a maximum period of 14 days; it costs \$REDACTED. Each eligible person would require 26 sensors per year at a total cost of AUD \$REDACTED (equivalent to \$REDACTED/month). If a FSL2 reader is required (rather than the FreeStyle LibreLink app for a smartphone), it costs \$REDACTED. The estimates assume optimal use of the FSL2 CGM system (i.e. no sensors become detached or malfunction and that the sensors and transmitter remain fully operational for the maximum duration).

The proposal is for CGM with FSL2 to be subsidised through the NDSS for patients with “other types of diabetes” that require insulin. According to NDSS, there were 8,009 people (all ages included) with “other types of diabetes” using insulin to control their blood glucose level, as of 30 June 2024 (National Diabetes Services Scheme). If all the proposed people were eligible for CGM with FSL2 (and there was REDACTED% uptake), the total cost in the first year would be \$REDACTED. The additional total cost of a FSL2 reader for this population would be \$REDACTED.

It should be noted that people aged <21 years with “other types of diabetes” similar to T1D (on the NDSS eligibility list) and requiring insulin are already eligible for subsidised CGM via the NDSS and therefore the cost of CGM with FSL2 in this subpopulation should be subtracted from the above estimated cost to the NDSS as they would be already using CGM to measure their glucose levels.

PASC noted that patients with “other types of diabetes” or pancreatic dysfunction who require insulin are eligible for NDSS funding of CGM if they are aged <21 years; the proposal for public funding is to address the inequity of the current funding structure whereby patients with T1D of any age have access to CGM funding, whereas patients with “other types of diabetes”, which are accepted by Government as being similar to T1D, only have access until the age of 21 years. The applicant’s proposal is to try to address any inequity of access.

PASC noted that the number of patients diagnosed with “other types of diabetes” includes people age <21 years, and that any financial estimates should exclude the <21 year age group.

Summary of public consultation input

PASC noted and welcomed consultation input from 6 organisations and 1 individual who was a parent, partner or another person caring for a consumer.

The 6 organisations that submitted input were:

- Australian and New Zealand Society for Paediatric Endocrinology and Diabetes (ANZSPED)
- Australian Diabetes Society
- Medtronic Australasia
- Primary Care Diabetes Society of Australia (PCDSA)
- Pharmaceutical Society of Australia (PSA)
- Royal Australian College of General Practitioners (RACGP)

The consultation input received was predominantly supportive of public funding for FreeStyle Libre 2 CGM system for people with insulin dependent type 2, gestational and type 3c diabetes. Medtronic were supportive of public funding for CGM for people with diabetes but not as proposed in the application (see 'Additional Comments' section below for more information). The consultation input raised a number of concerns, primarily in relation to difficulty accessing CGM devices and services via the NDSS.

Consumer Input

Consumer input from a carer for a person with T2D stated that using the sensor to monitor blood glucose levels had dramatically improved the health of the person with T2D, allowing them to see exactly how dietary intake affected blood glucose levels. The carer stated that the sensor is expensive and costs over \$100 per fortnight, meaning it is not affordable in the long term to manage diabetes.

Benefits and Disadvantages

The main benefits of public funding received in the consultation input included dramatically improving glycaemic control, alarms for high or low glucose levels, the ability for people to monitor food choices and increased engagement in diabetes management. PCDSA stated that CGM is beneficial for people with T2D who have cognitive impairment, as carers are able to monitor glycaemic levels and be alerted to approaching hypoglycaemic events, allowing carers to take preventive action. Input also stated that long term use of CGM optimally controlled blood glucose levels and prevented future complications from diabetes including retinopathy, amputations, cardiovascular events, kidney damage and neuropathy. ANZSPED stated that subsidised CGM for young people with T2D would help address inequity in healthcare as youth-onset T2D disproportionately affects Aboriginal and Torres Strait Islander, Māori, and Pasifika communities, and marginalised and socioeconomically vulnerable youth.

The main disadvantages of public funding received in the consultation input included difficulty accessing CGM via the NDSS and the RACGP had concerns about the lack of long-term efficacy data related to the use of CGM. The RACGP queried whether the benefits of CGM would be sustained in practice given the request for permanent ongoing funding (i.e. would real-world data demonstrate the same extent of benefit observed in trials over time?). PCDSA stated that a proportion of the population struggle with technology and may not use a smart phone, and whilst a stand-alone reader is available it is expensive and may pose a barrier to CGM if the reader was not also publicly funded.

Population, Comparator (current management) and Delivery

The consultation input ranged from disagreeing to agreeing with the proposed populations. The RACGP and PSA stated that CGM is most beneficial in people commencing insulin regimes as it allows titration of insulin doses and information on stabilising glycaemia. ANZSPED called for a broadening of the population to include all young people with T2D, not just those on insulin. ANZSPED stated that this population are at risk of the negative impact of hypoglycaemia on the developing brain, high-risk for rapid development of complications and have reduced treatment response.

PASC noted that the consultation feedback included positive stakeholder support for broadening access to CGM including for use in people with DM that do not require insulin and individuals who are newly diagnosed. There was support for intermittent use of CGM for education and in patients during initial titration of insulin while stabilising glycaemia.

The consultation input agreed with the proposed comparator of SMBG.

Other services identified in the consultation input as being needed to be delivered before or after the intervention included patient management and support through a multi-disciplinary team and diabetes education. Most of the input raised the issue of difficulty accessing CGM due to limited professionals who can sign the NDSS forms authorising subsidised CGM. The Australian Diabetes Society support the RACGP position that GPs should be included in the authorised certifier group to provide patients with access to subsidised CGM, as removing patients from the GP setting would increase costs, fragment care and burden patients and carers, particularly in regional and remote areas. *PASC noted that extending CGM authorisation via the NDSS to GPs and involving community pharmacies was considered in stakeholder consultations as a positive move towards increasing patient access to CGM. PASC indicated that adding GPs to the list of authorising healthcare professionals for NDSS-funded CGM was not a matter for MSAC consideration.* Medtronic noted that access and workforce issues are an important policy consideration, especially if there is an increased burden on parts of the workforce without the capacity to support ongoing management of diabetes with the insights from CGM.

Additional Comments

Medtronic stated that CGM alone is investigative not therapeutic, and that it was important to consider the relationship between CGM and insulin use, and whether the CGM is paired with an insulin delivery device. Medtronic considered that the MSAC evaluation should be device agnostic and evaluate CGM as an intervention more broadly, noting that the outcomes are tied to insulin delivery, and that specific devices should be considered through the NDSS. *PASC noted that there was support from manufacturers for a device agnostic approach to the assessment of CGM funding via the NDSS.*

Next steps

The applicant confirmed at the PASC meeting that an ADAR will be submitted for MSAC consideration.

Applicant Comments on Ratified PICO

The applicant had no comment.

Appendix

Table 7: Conditions very similar to type 1 diabetes, eligible to access the CGM Initiative through the NDSS

Category	Condition
A. Genetic defect of beta cell function	Chromosome 20, HNF- 4alpha (MODY 1)
	Chromosome 12, HNF- 1alpha (MODY 3)
	Chromosome 13, IPF-1 (MODY 4)
	Chromosome 17, HNF- 1 beta (MODY 5)
	Chromosome 2, NeuroD1 (MODY 6)
	Chromosome 2, KLF11 (MODY 7)
	Chromosome 9, CEL (MODY 8)
	Chromosome 7, PAX4 (MODY 9)
	Chromosome 11, INS (MODY 10)
	Chromosome 8, BLK (MODY 11)
	Chromosome 11, ABCC8
	Chromosome 11, KCNJ11
	Mitochondrial DNA
	Permanent neonatal diabetes
Transient neonatal diabetes	
B. Genetic defect in insulin action	Type A insulin resistance
	Leprechaunism
	Rabson-Mendenhall syndrome
	Lipoatrophic diabetes
C. Diseases of the exocrine pancreas	Pancreatectomy
	Neoplasia
	Cystic fibrosis
	Insulinoma
D. Endocrinopathies	Glucagonoma
E. Drug or chemical induced	Vacor
	Pentamidine
	Glucocorticoids
	Diazoxide
	Alpha-interferon
	NODAT or Post renal transplant
	Post liver transplant
	Calcineurin inhibitors
	Fluoroquinolones
	Highly active antiretroviral therapy (HAART)
F. Infections	Congenital rubella
	Cytomegalovirus
	Coxsackie

G. Uncommon forms of immune-mediated diabetes	"Stiff-man" syndrome
	Anti-insulin receptor antibodies
H. Other genetic syndromes sometimes associated with diabetes	Down syndrome
	Turner syndrome
	Wolfram syndrome
	Friedreich's ataxia
	Huntington chorea
	Laurence-Moon-Bardet-Biedl syndrome
	Myotonic dystrophy
	Porphyria
	Prader-Willi syndrome
Glycogen storage disease	

Source: NDSS. Conditions very similar to type 1 diabetes, eligible to access the CGM Initiative through the NDSS. <https://www.ndss.com.au/wp-content/uploads/cgm-eligible-conditions-under21.pdf>

MODY = Maturity-Onset Diabetes of the Young; NODAT = New-onset diabetes;

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