

Technology Guidance

Continuous glucose monitoring systems for children and adults with type 1 diabetes mellitus

Technology Guidance from the MOH Medical Technology Advisory Committee

Guidance Recommendations

The Ministry of Health's Medical Technology Advisory Committee has recommended continuous glucose monitoring (CGM) systems for children and adults with type 1 diabetes mellitus (T1DM) in line with the following criteria:

- ✓ CGM systems can be considered for children and adults with T1DM who despite optimal use of insulin therapy (multiple daily injections [MDI] or continuous subcutaneous insulin infusion [CSII]) and conventional blood glucose monitoring to achieve target HbA1c levels:
 - Experience disabling or problematic hypoglycaemia. Disabling hypoglycaemia is defined as frequent or unpredictable hypoglycaemic episodes that lead to constant anxiety about having more episodes. Problematic hypoglycaemia is defined as frequent hypoglycaemia, severe hypoglycaemia, nocturnal hypoglycaemia and/or impaired awareness of hypoglycaemia; or
 - Have unacceptably high HbA1c levels (i.e. at 7.5% or above); or
 - Are unable to recognise or communicate symptoms of hypoglycaemia.
- ✓ CGM must be supported by a multidisciplinary specialist diabetes team and should only be offered where there is a clear expectation of clinical benefit.
- ✓ Individuals and caregivers (if applicable) must be willing to commit to use CGM at least 70% of the time, in addition to other glucose management programmes including attendance of structured education programmes, and regular follow-ups and monitoring.
- ✓ CGM should be discontinued if:
 - It does not result in a sustained improvement in glycaemic control, as evidenced by a reduction in HbA1c levels, an increase in time-in-range blood glucose readings, or improved health-related quality of life.
 - Individuals and caregivers (if applicable) are unable to adhere to regular CGM use at least 70% of the time and glucose management programmes.

Funding status

CGM system is recommended for subsidy in children and adults with T1DM, in line with the abovementioned recommendations. Subsidy applies only to the devices and accessories listed in the Annex.

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Factors considered to inform the recommendations

Technology evaluation

- 1.1. The MOH Medical Technology Advisory Committee (“the Committee”) considered the evidence presented for the technology evaluation of continuous glucose monitoring (CGM) systems for children and adults with type 1 diabetes mellitus (T1DM). The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions and patient experts from local patient and voluntary organisations. Published clinical and economic evidence for CGM systems was considered in line with its registered indications.
- 1.2. The evidence was used to inform the Committee’s deliberations around five core decision-making criteria:
 - Clinical need of patients and nature of the condition;
 - Overall benefit of the technology for the patient and/or the system;
 - Cost-effectiveness (value for money), which considers the incremental benefit and cost of the technology compared to existing alternatives;
 - Estimated annual technology cost and the number of patients likely to benefit from the technology; and
 - Organisational feasibility, which covers the potential impact of adopting the technology, especially barriers for diffusion.
- 1.3. Additional factors, including social and value judgments, may also inform the Committee’s deliberations.

Clinical need

- 2.1. The Committee noted that disabling or problematic hypoglycaemia are common acute complications of insulin therapy among people with T1DM. Disabling hypoglycaemia refers to frequent or unpredictable hypoglycaemic episodes that lead to constant anxiety about having more episodes, while problematic hypoglycaemia is defined as frequent hypoglycaemia, severe hypoglycaemia, nocturnal hypoglycaemia and/or impaired awareness of hypoglycaemia. Physical symptoms of hypoglycaemia can range from headache and dizziness to unconsciousness, or even death in extreme circumstances. Anxiety caused by fear of hypoglycaemia (FoH) has been shown to disrupt everyday activities, impact optimal glycaemic control and impair quality of life (QoL).
- 2.2. The Committee noted that in addition to long-term HbA1c readings every three to six months, frequent self-monitoring blood glucose (SMBG) by finger-pricking is recommended for individuals on insulin treatment, to monitor daily fluctuations. SMBG can only provide glucose levels at the point of testing and is unable to detect

impending hypoglycaemia or hyperglycaemia episodes. The willingness and ability of individuals to perform SMBG is limited by pain from finger pricks, risk of infection, and scarring from multiple daily punctures in the same area. The Committee also noted that the management of T1DM requires structured education and appropriate lifestyle adjustments, in addition to glucose monitoring.

- 2.3. The Committee considered 80 testimonials from local patient experts and their carers about what it is like living with T1DM and their experience with different blood glucose monitors. The Committee heard that more than half of them were using CGM regularly and considered that their devices were accurate, worked well and easy to use. The Committee noted that CGM helped improve diabetes care by allowing the respondents to understand the effect of food and activities on their blood glucose levels so they could adjust their food intake or insulin dose accordingly. Compared to SMBG, the respondents valued the ability to check their blood glucose levels frequently without having to undergo finger pricks.
- 2.4. The Committee noted that half of the patient experts who regularly used CGM, and their carers, reported manageable skin irritation from the sensor. The Committee acknowledged that some respondents felt the readings from CGM devices differed from their blood glucometers, especially when their blood glucose levels were very low or high. Most respondents highlighted that they would like any new CGM device for T1DM to be more affordable, able to automatically and frequently monitor their blood glucose level, and require less frequent calibration with blood glucometers.

Overall benefit of technology

- 3.1. The Committee noted that CGM systems are wearable technologies that monitor glucose levels and trends throughout the day. These systems comprise a sensor (with or without transmitter) and receiver. The sensor is inserted on the skin of the arm or abdomen to measure glucose levels of the interstitial fluid. The readings are then transmitted wirelessly to a receiver, such as a smartphone or reader device, to display glucose readings and trends. The two types of CGM systems are real-time CGM (rtCGM) and intermittently scanned (isCGM). rtCGM automatically and wirelessly sends glucose readings via a transmitter to a receiver or a smartphone application and alerts the user if glucose levels are low or high. isCGM requires users to manually scan the sensor (at least eight-hourly) to obtain the stored glucose data and prevent data loss.
- 3.2. The Committee noted that the main comparator was SMBG. Secondary comparisons between rtCGM and isCGM systems, and between different rtCGM systems were included if the evidence was available.
- 3.3. The Committee agreed that rtCGM and isCGM systems were generally safe compared with SMBG in both children and adults with T1DM, with low rates of sensor-related skin reactions such as redness or irritation at the sensor attachment site.

Limited evidence suggested more frequent skin reactions with isCGM than with rtCGM.

- 3.4. The Committee agreed that in children with T1DM, rtCGM was more effective than SMBG in key clinical outcomes such as reducing HbA1c levels, increasing time in target blood glucose range (TIR), and reducing time above target blood glucose range (TAR). These outcomes were observed at six-months follow-up below the minimal clinically important difference (MCID). At six-month follow up, there was also no difference between rtCGM and SMBG for severe hypoglycaemia or hypoglycaemia episodes, diabetic ketoacidosis (DKA) events, or QoL and treatment satisfaction measures. The results for FoH at six to 12 months follow-up were mixed. In children with T1DM, isCGM was comparable to SMBG for reduction of HbA1c levels, severe hypoglycaemia, or hypoglycaemia episodes, TIR, time below target blood glucose range (TBR) and DKA events, at up to six months follow-up. isCGM was more effective than SMBG in reducing TAR, was associated with greater treatment satisfaction, and showed mixed or no difference for FoH and QoL scores.
- 3.5. The Committee noted two non-randomised studies with short follow-up periods of two weeks to five months suggesting rtCGM gave similar or increased TIR, less TBR, and reduced FoH when compared with isCGM in children with T1DM.
- 3.6. The Committee agreed that in adults with T1DM, both rtCGM and isCGM led to improvements in key clinical outcomes when compared with SMBG. Compared with SMBG, rtCGM significantly reduced HbA1c, severe hypoglycaemia or hypoglycaemia episodes, increased TIR, and reduced TBR and TAR at up to 28 weeks follow-up. The extent of HbA1c reduction by rtCGM also exceeded MCID. rtCGM may improve FoH compared with SMBG, but no significant differences were observed between rtCGM and SMBG for DKA events or QoL score. The Committee noted that isCGM for adults with T1DM improved HbA1c, increased TIR, and reduced TBR and TAR compared with SMBG at up to six months follow-up but showed no difference in severe hypoglycaemia or hypoglycaemia episodes, FoH and QoL scores.
- 3.7. The Committee noted that based on limited comparative evidence at six-month follow-up, reductions in HbA1c, severe hypoglycaemia or hypoglycaemia episodes, TIR, TBR, FoH and treatment satisfaction favoured rtCGM compared with isCGM in adults with T1DM. rtCGM may reduce TAR but there was no difference in reported QoL scores.
- 3.8. The Committee noted that key limitations of the clinical evidence include heterogenous definitions of outcomes used in studies (e.g. hypoglycaemia) and lack of published comparative evidence for certain CGM model(s).

Cost effectiveness

- 4.1. The Committee noted that although there was no local or overseas cost-effectiveness analysis (CEA) comparing rtCGM or isCGM with SMBG in children with T1DM, it was reasonable to extrapolate the available economic evidence from adults with T1DM, assuming similar clinical benefits in both populations.
- 4.2. The Committee agreed that rtCGM and isGCM systems are likely to be cost-effective compared with SMBG for adults with T1DM, based on recently published de novo cost-effectiveness analyses by the National Institute for Health and Care Excellence and Health Technology Wales. The incremental cost-effectiveness ratios ranged from £24,436 per quality-adjusted life year (QALY) gained for rtCGM and £4,706 to £10,157 per QALY gained for isCGM.
- 4.3. There was no published local or overseas CEA comparing rtCGM and isCGM systems in children or adults with T1DM.
- 4.4. CGM is currently reimbursed for children and adults with T1DM in various overseas jurisdictions including Australia, Canada (Ontario), Japan, South Korea and United Kingdom. As part of value-based pricing proposal, one manufacturer offered sufficiently competitive prices deemed acceptable for subsidy listing.

Estimated annual technology cost

- 5.1 The Committee noted that the estimated annual incremental cost of impact to the public healthcare system was between SG\$3 million to <SG\$5 million for adults and children with T1DM, based on the projection of 611 children with T1DM and 1,647 adults with T1DM who would benefit from subsidised CGM each year.

Organisational feasibility

- 6.1. The Committee noted that there are charging mechanisms in place for people with T1DM who meet the subsidy criteria and are prescribed CGM systems. CGM systems can be supplied to people with T1DM via outpatient pharmacies.

Additional considerations

- 7.1. The Committee acknowledged that the development of new CGM systems and updates to their technology is occurring at a rapid pace. New CGM systems are likely to be introduced in Singapore, and some of them may be integrated into automated insulin delivery systems to adjust insulin doses automatically.

Recommendations

- 8.1. Based on the evidence presented, the Committee considered that in children and adults with T1DM, CGM systems were safe and more effective than SMBG for key clinical outcomes such as reducing HbA1c, severe hypoglycaemia and hypoglycaemic episodes and improving TIR, and were comparable in improving QoL. The Committee noted that in children and adults with T1DM, CGM is likely to be cost-effective compared with SMBG. Given the available evidence, the Committee recommended subsidy for CGM in people with T1DM in line with the following criteria:
- ✓ CGM systems can be considered for children and adults with T1DM who despite optimal use of insulin therapy (MDI or CSII) and conventional blood glucose monitoring to achieve target HbA1c levels:
 - Experience disabling or problematic hypoglycaemia. Disabling hypoglycaemia is defined as frequent or unpredictable hypoglycaemic episodes that lead to constant anxiety about having more episodes. Problematic hypoglycaemia is defined as frequent hypoglycaemia, severe hypoglycaemia, nocturnal hypoglycaemia and/or impaired awareness of hypoglycaemia; or
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 - ✓ CGM must be supported by a multidisciplinary specialist diabetes team and should only be offered where there is a clear expectation of clinical benefit.
 - ✓ Individuals and caregivers (if applicable) must be willing to commit to use CGM at least 70% of the time, in addition to other glucose management programmes including attendance of structured education programmes and regular follow-ups and monitoring.
 - ✓ CGM should be discontinued if:
 - It does not result in a sustained improvement in glycaemic control, as evidenced by a reduction in HbA1c levels, an increase in TIR blood glucose readings, or improved health-related QoL.
 - Individuals and caregivers (if applicable) are unable to adhere to regular CGM use at least 70% of the time and glucose management programmes.
- 8.2 Subsidies apply only to models listed in the Annex of this guidance.

 Agency for Care Effectiveness - ACE  Agency for Care Effectiveness (ACE)

About the Agency

The Agency for Care Effectiveness (ACE) was established by the Ministry of Health (Singapore) to drive better decision-making in healthcare through health technology assessment (HTA), clinical guidance, and education.

As the national HTA agency, ACE conducts evaluations to inform government funding decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

This guidance is based on the evidence available to the MOH Medical Technology Advisory Committee as at 21 December 2023. It is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

Find out more about ACE at www.ace-hta.gov.sg/about

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