Continuous Glucose Monitoring for type 1 diabetes (adults and children)

Treatment	Continuous Glucose Monitoring (CGM) for type 1 diabetes (adults and children)
Background	Continuous Glucose Monitoring (CGM) systems are available for use in type 1 diabetes to help patients better manage their blood glucose levels, or as a continuous aid in glycaemic control. They use a glucose sensor placed under the skin that continuously measures glucose levels. The Abbot Freestyle Libre (FSL) system is a flash glucose monitoring system which measures glucose continually but needs to be actively scanned using a digital monitor and does not alert the patient if readings are low. Costs are around £1000 a year. Since NHSE advised that an FSL pathway should be available within the NHS, it has been commissioned by the CCG (from March 2018), with strict criteria and monitoring, but numbers have risen much faster than predicted. More complex (and expensive) CGM devices transmit a continuous reading to a display unit and **alarm** if low or high levels occur. Sensor-augmented devices can communicate directly with an integrated insulin pump to suspend delivery if hypoglycaemia is predicted. Cost is around £3300-6000 a year. Because of the lack of cost-effectiveness data, previous policy has been only to make them available via clinical exceptionality to the IFR panel but requests have been rising. GMC ethical guidance points out the importance of helping to promote the effective use of resources, taking account of any policies that set out agreed criteria for access to particular treatments, as well as be open and honest with patients when resource constraints may affect the treatment options available.[8] NICE issued clinical guidance in 2015 (NG17 and 18[1,2]) but as yet there are no mandatory NICE TAs for CGMs
Commissioning position	NHS Vale of York CCG and NHS Scarborough and Ryedale CCG commissions continuous glucose monitoring with alarms only for those patients who meet the criteria outlined in this document. **Children up to 18 years** CGM is commissioned for children where, despite optimised use of insulin therapy and conventional blood glucose monitoring (by themselves or their parents/guardians), they • fulfil the CCG criteria for flash glucose monitoring (FreeStyle Libre) (FSL)[3] • FSL has been tried for at least 6 months (as per FSL guidance*, with audit), and not demonstrated any improvement in diabetic control and reduction in finger prick testing **OR** • have total hypoglycaemia unawareness (documented with an appropriate scoring system) **OR** • have frequent severe hypoglycaemia **or** • have impaired awareness of hypoglycaemia associated with adverse

consequences (for example, seizures or anxiety) **or**

- have an inability to recognise, or communicate about, symptoms of hypoglycaemia (for example, because of cognitive or neurological disabilities)

Adults
CGM is commissioned for adults where, despite optimised use of insulin therapy and conventional blood glucose monitoring (by themselves or their carers,) they

- fulfil the CCG criteria for flash glucose monitoring (FreeStyle Libre) (FSL)[3],
- FSL has been tried for at least 6 months (as per FSL guidance*, with audit), and not demonstrated any improvement in diabetic control and reduction in finger prick testing

OR

- have total hypoglycaemia unawareness (documented with an appropriate scoring system)

AND

They need to fulfill at least **ONE** of the following criteria:

- Have more than 1 episode a year of documented severe hypoglycaemia with no obviously preventable precipitating cause, requiring assistance of another person (eg family, paramedic)
- Have 2 or more admissions to hospital with DKA or hypoglycaemia
- Have complete loss of awareness of hypoglycaemia (documented with an appropriate scoring system)
- Frequent (more than 2 episodes a week) asymptomatic hypoglycaemia that is causing problems with daily activities

Children and Adults
All patients (and their carers) must fulfil all of the following criteria

- Have, according to their diabetes specialist,
  - A high level of engagement with glucose testing and management
  - A willingness to engage with further education and commit to using it at least 70% of the time, with ability to calibrate it as needed
- The device must be provided by a centre with expertise in its use, as part of strategies to optimise a person's HbA1c levels and reduce the frequency of hypoglycaemic episodes.
- Treatment outcomes must be audited in all patients at, at least 6 and 12 months. Both patient and specialist are responsible for this audit.

The CGM will be provided initially on a 6 month trial basis and it must be possible to demonstrate (where requested by the CCG) at 6 and 12 months, that using the system results in improved diabetic control, including

- Reduction in usage of blood glucose test strips
- Reduction in severe/non-severe hypoglycaemia frequency
- Reduction in hospital admissions

	• Reversal of impaired awareness of hypoglycaemia • Reduction in episodes of DKA • Improved QoL using validated rating scales The requirements of the person or their carer are considerable and not every person or family may be able to fulfil them. Assessment should be carried out by the specialist MDT in secondary care at 6 and 12 months, to ensure the monitor can be used effectively by the person or family concerned, and to provide data to the CCG. **For all other cases, funding will only be considered by the Individual Funding Request Panel (IFR) where exceptional clinical circumstances are demonstrated.**
Summary of evidence	Type 1 diabetes is a common condition. Most are managed with intensive insulin regimes and advised to check their blood glucose at least 6 times daily. Some have access to insulin pumps. NICE issued NG17 and 18 in August 2015 about the diagnosis and management of type 1 diabetes in adults and type 1 and 2 diabetes in children and young people[1,2]. These covered a wide range of issues affecting clinical care, such as diet, exercise and insulin regimes. For adults, NG17 suggested: • Consider real-time continuous glucose monitoring for adults with type 1 diabetes who are willing to commit to using it at least 70% of the time and to calibrate it as needed, and who have any of the following despite optimised use of insulin therapy and conventional blood glucose monitoring: • More than 1 episode a year of severe hypoglycaemia with no obviously preventable precipitating cause. • Complete loss of awareness of hypoglycaemia. • Frequent (more than 2 episodes a week) asymptomatic hypoglycaemia that is causing problems with daily activities. • Extreme fear of hypoglycaemia. • Hyperglycaemia (HbA1c of 75 mmol/mol or higher) that persists despite testing at least 10 times a day. Continue real-time continuous glucose monitoring only if HbA1c can be sustained at or below 53 mmol/mol and/or there has been a fall in HbA1c of 27 mmol/mol or more. For children and young people, NG18 suggested “Offer ongoing real-time continuous glucose monitoring with alarms to children and young people with type 1 diabetes who have: • frequent severe hypoglycaemia or • impaired awareness of hypoglycaemia associated with adverse consequences (for example, seizures or anxiety) or • inability to recognise, or communicate about, symptoms of hypoglycaemia (for example, because of cognitive or neurological disabilities).” Some CCGs have made this more stringent for children eg for episodes requiring hospital admission; complete loss of awareness of hypoglycaemia. Referral to the IFR Panel for prior approval continues for many, including on the grounds of clinical exceptionality.

NICE NG18 also included:

"Consider ongoing real-time continuous glucose monitoring for:

- neonates, infants and pre-school children,
- children and young people who undertake high levels of physical activity
- children and young people who have comorbidities (eg anorexia nervosa) or who are receiving treatments (eg corticosteroids) that can make blood glucose control difficult. "

It is thought that around 30% of people with type 1 diabetes have problematic hypoglycaemia which can affect many aspects of daily life and result in significant anxiety. This can have a substantial impact on quality of life by leading people to restrict their daily activities. It can also cause significant anxiety for carers, particularly parents who may have to wake several times a night to check on their child.

Impaired awareness of hypoglycaemia - Gold score

This scoring system is widely used and based on the response to a single question: '**Do you know when your hypos are commencing?**' Biochemical hypoglycaemia is defined as less than 3 mmol/litre. Results are expressed by a 7-point Likert scale, where 1 = 'always aware' and 7 = 'never aware'. IAH is suggested by a value of more than or equal to 4.

This score is based on results from a prospective case-control study with 60 participants and 12 months follow-up (Gold 1994); 29 participants were noted to have impaired awareness and 31 participants had normal awareness of hypoglycaemia. Participants with IAH had an increased frequency of severe hypoglycaemia episodes (more than or equal to 1 severe hypoglycaemia episodes in 66% with impaired awareness versus 26% with normal awareness; higher incidence of severe hypoglycaemia episodes per patient per year: 2.8 with impaired awareness versus 0.5 with normal awareness).

https://www.ncbi.nlm.nih.gov/books/NBK343319/ IAH 2015 (part of CG17) gives more detail. NICE DG21 refers to a modified Clark and Gold score from King's College Hospital, London but it has not been possible to trace any more information about this[4].

CGM systems

There are many different types of CGM systems, some of which provide alarms, but no clear consensus or NICE guidance about which to use and the NIHR NTA concluded

"…Integrated systems are generally unlikely to be cost-effective given that stand-alone systems are cheaper and, possibly, no less effective. However, evidence in this regard is generally lacking, in particular for children.

In addition "the overall evidence base to support the best use of (these) systems needs to be improved in order to demonstrate that using the system results in a sustained clinical impact on preventing or improving control of disabling hypoglycaemia**."**

CGM systems need to be used under the supervision of a trained MDT who are

experienced in continuous subcutaneous insulin infusion and continuous glucose monitoring for managing type 1 diabetes. The requirements of the person or their carer are also considerable and not every person or family may be able to fulfill them. They must

- agree to use the sensors for at least 70% of the time
- understand how to use it, to calibrate it as needed, and be physically able to use the system
- agree to use the system while having a structured education programme on diet and lifestyle, and counselling.
- only continue to use it if they have a decrease in the number of hypoglycaemic episodes that is sustained. Appropriate targets for such improvements should be set.

Robust evidence is still needed to show the clinical effectiveness of using such alternative technology in practice.

Uncertainties about cost-effectiveness

This depends on many factors, including comparison with standard monitoring with finger prick blood glucose tests, the frequency of which can vary greatly. NICE CG18 points out that "Excessive testing can be more expensive than continuous glucose monitoring, and clinicians can use excessive testing as a rationale for requesting funding for continuous monitoring systems."[2]

The NICE guideline development group also considered the clinical and cost effectiveness of real-time continuous glucose monitoring systems compared to 5 or more capillary blood glucose tests per day in children aged 5 years or younger with type 1 diabetes who use insulin pump therapy. Their recommendation was to "consider" ongoing real-time continuous glucose monitoring systems (CGMS) for neonates, infants and pre-school children with type 1 diabetes. **This weak recommendation reflected a lack of evidence of effectiveness of CGMs in such children (only a few studies having been conducted in this age group) – eg** reduction in adverse neurodevelopmental consequences of type 1 diabetes.

One committee looked at the cost-effectiveness analyses of integrated systems in the severe hypoglycaemia population and concluded that they could not be considered cost effective when compared with capillary blood testing with multiple daily injections or continuous subcutaneous insulin infusion because of the high incremental cost of the technology[4].

A systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes was reviewed by CRD, who concluded that real-time, but not retrospective, continuous glucose monitoring could be more effective than self-monitoring of blood glucose, for children with type 1 diabetes[5].

Abbott FreeStyle Libre
A review by the Regional Drug and Therapeutics Group of the simpler Abbott Freestyle Libre flash glucose monitoring system (which needs to be actively scanned using a digital monitor and does not alert the patient if readings are low) concluded that

	"The device may offer some advantages in terms of patient acceptability and quality of life but good quality clinical trial data to support long-term clinical effectiveness and cost-effectiveness is lacking"[6]. NICE issued MIB110 about the Freestyle Libre flash glucose monitoring system[7]. It updates the evidence base regarding its accuracy and acceptability, but 5 of the 6 trials were based on adults and several were very short. Only one was run over 6 months (a RCT of adults with type 1 DM). The one on 89 children aged 4-17 with type 1 diabetes was a single-arm study which ran for 14 days only. It also states that "A key uncertainty **around** the evidence is that the RCT of people with type 1 diabetes included only adults whose diabetes was well controlled…There are currently no high quality, peer-reviewed studies on the use of FreeStyle Libre by people with very unstable glucose levels. Studies in this patient group would be beneficial to understanding which people with diabetes would benefit most from using FreeStyle Libre." It concluded that "The resource impact is uncertain, and depends upon the extent to which improved glucose control through the adoption of FreeStyle Libre translates into fewer complications, reduced emergency admissions and less use of glucose test strips." Although NHS England has issued details of a price reduction of around 30% in the fortnightly sensors required, and its inclusion within the NHS tariff from 1 November 2017, the actual cost savings (and indeed cost-effectiveness) are uncertain. They depend on compliance and individual use of testing strips – while outcomes such as fewer complications and reduced emergency admissions are undefined. The actual savings with reduced use of testing strips would not be to the CCG budget.
Date effective from	October 2019
Review date	2021
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