GMCA GREATER MANCHESTER COMBINED AUTHORITY

NHS in Greater Manchester

Greater Manchester EUR Policy Statement on:

Real-Time Continuous Glucose Monitoring

GM Ref: GM039

Version: 2.1 (16 June 2020)

Commissioning Statement

Real-Time Continuous Glucose Monitoring	
Policy Exclusions **(Alternative commissioning arrangements apply)**	FreeStyle Libre Flash glucose monitoring systems are excluded from this policy and should be managed in line with the following recommendation from Greater Manchester Medicines Management Group: http://gmmmg.nhs.uk/html/recomm.php Real-time CGM in pregnancy is excluded from this policy – these patients should be managed in line with NICE NG3: Diabetes in pregnancy: management from preconception to the postnatal period. Treatment/procedures undertaken as part of an externally funded trial or as a part of locally agreed contracts / or pathways of care are excluded from this policy, i.e. locally agreed pathways take precedent over this policy (the EUR Team should be informed of any local pathway for this exclusion to take effect).
Policy Inclusion Criteria	All requests for real-time continuous glucose monitoring (CGM) should come from a secondary care diabetic service. The monitor requested should provide real-time monitoring of blood glucose levels and should preferably incorporate a hypoglycaemia alarm. Using CGM to monitor and record glucose levels over time for the sole purpose of improving an individual's diabetes control (by themselves or by the team caring for them) when they do not meet NG17 or 18 is not commissioned and is **NOT** covered by this policy and funding for these should be via a service development/business case. Patients who have self-funded these devices will only be eligible for NHS funding if they meet the criteria. **Adults** Real-time CGM is commissioned for adults with type 1 diabetes in line with NICE NG17 who are willing to commit to using it at least 70% of the time in a 24 hour period 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 (requiring the intervention of another person to manage the episodes) with no obviously preventable precipitating cause **AND** that has resulted in multiple daily testing of blood sugar levels by the individual or their carer. • 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, with supporting evidence of the reason for that fear. • Hyperglycaemia (HbA1c level of 75 mmol/mol [9%] or higher) that persists despite testing at least 10 times a day. Continue real-time CGM only if HbA1c can be sustained at or below 53 mmol/mol (7%) and/or there has been a fall in HbA1c of 27 mmol/mol (2.5%) or more. **Funding Mechanism** Real-time CGM devices with hypoglycemia alarms: Monitored approval for individuals meeting NICE NG17: Referrals may be made in line with the criteria without seeking funding. **NOTE:** May be the subject of contract challenges and/or

audit of cases against commissioned criteria.

For all other cases including devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request.

Children and young people aged under 18

Real-time CGM with alarm is commissioned for children and young people with type 1 diabetes, in line with NICE NG 18, 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).

OR

- Anxiety over the above has resulted in frequent testing of blood sugar in every 24 hour period.

ALSO

Consider ongoing real-time CGM for:

- neonates, infants and pre-school children
- children and young people who undertake high levels of physical activity (for example, sport at a regional, national or international level)
- children and young people who have comorbidities (for example anorexia nervosa) or who are receiving treatments (for example corticosteroids) that can make blood glucose control difficult.

Funding Mechanism

Real-time CGM devices with hypoglycemia alarms: Monitored approval for individuals meeting NICE NG18: Referrals may be made in line with the criteria without seeking funding. **NOTE:** May be the subject of contract challenges and/or audit of cases against commissioned criteria.

For all other funding applications including those for devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request.

Patients using insulin pumps

Real-time CGM is commissioned for patients on insulin pump therapy (provided they meet the criteria in NICE TA151) who are either unable to maintain their HbA1c in the optimum range through testing or who, due to hypoglycaemic anxiety, are intentionally keeping their HbA1c at too high a level.

Funding Mechanism

Real time CGM devices with hypoglycemia alarms: Monitored approval for individuals meeting NICE NG17 or NG18: Referrals may be made in line with the criteria without seeking funding. **NOTE:** May be the subject of contract challenges and/or audit of cases against commissioned criteria.

	For all other cases including devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request. **Patients on real-time CGM who do not meet the above criteria** Patients should meet the above criteria before being given a loan of real-time CGM equipment otherwise the device will not be funded following the end of the loan period. Patients, who are already using real-time CGM provided by the NHS (does not include "on loan" devices) who do not meet the above criteria should be able to continue using the device until they and their NHS clinician consider it appropriate to stop. Replacement devices will require an application clearly stating the case for exceptionality if they do not meet the criteria. **Funding Mechanism** As per loan. If a loan is no longer available: Individual funding request (exceptional case) approval: Requests must be submitted with all relevant supporting evidence as to why this treatment should continue.
Clinical Exceptionality Definition	Clinicians can submit an Individual Funding Request (IFR) outside of this guidance if they feel there is a good case for exceptionality. More information on determining clinical exceptionality can be found in the Greater Manchester (GM) Effective Use of Resources (EUR) Operational Policy. Link to GM EUR Operational Policy
Best Practice Guidelines	All providers are expected to follow best practice guidelines (where available) in the management of these conditions.

Contents

Policy Statement

The GM Effective Use of Resources (EUR) Policy Team, in conjunction with the GM EUR Steering Group, have developed this policy on behalf of Clinical Commissioning Groups (CCGs) within Greater Manchester, who will commission treatments/procedures in accordance with the criteria outlined in this document.

In creating this policy the GM EUR Steering Group has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population of Greater Manchester.

This policy follows the principles set out in the ethical framework that govern the commissioning of NHS healthcare and those policies dealing with the approach to experimental treatments and processes for the management of individual funding requests (IFR).

Equality & Equity Statement

CCGs have a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved, as enshrined in the Health and Social Care Act 2012. CCGs are committed to ensuring equality of access and non-discrimination, irrespective of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, CCGs will have due regard to the different needs of protected characteristic groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which they are responsible, including policy development, review and implementation.

In developing policy the GM EUR Policy Team will ensure that equity is considered as well as equality. Equity means providing greater resource for those groups of the population with greater needs without disadvantage to any vulnerable group.

The Equality Act 2010 states that we must treat disabled people as *more equal* than any other protected characteristic group. This is because their 'starting point' is considered to be further back than any other group. This will be reflected in CCGs evidencing taking 'due regard' for fair access to healthcare information, services and premises.

An Equality Analysis has been carried out on the policy. For more information about the Equality Analysis, please contact gm.policyfeedback@nhs.net.

Governance Arrangements

The Greater Manchester Joint Commissioning Board has given delegated authority to the Greater Manchester Directors of Commissioning and Directors of Finance to approve GM EUR treatment policies for implementation. Further details of the governance arrangements can be found in the GM EUR Operational Policy.

Aims and Objectives

This policy document aims to ensure equity, consistency and clarity in the commissioning of treatments/procedures by CCGs in Greater Manchester by:

- reducing the variation in access to treatments/procedures.

- ensuring that treatments/procedures are commissioned where there is acceptable evidence of clinical benefit and cost-effectiveness.
- reducing unacceptable variation in the commissioning of treatments/procedures across Greater Manchester.
- promoting the cost-effective use of healthcare resources.

Treatment / Procedure

Real-time CGM is not a treatment. It is a system for monitoring the effectiveness of treatment – in this case how well the individual's insulin regimen is controlling their blood sugar levels. The aim is to support avoidance of hypo and hyperglycaemia.

Real-time CGM is usually used in patients with type 1 diabetes where the sensor tests glucose levels continuously throughout the day. Real-time CGM can be carried out using a variety of portable devices. Real-time CGM isn't blood glucose monitoring as the sensors with a real-time CGM machine are placed into the body but not into the bloodstream.

The sensors measure the glucose in the interstitial fluid (the fluid in and around the body's cells).

Real-time CGM can be integrated into an insulin pump or can be standalone devices.

Rationale behind the policy statement

Poorly managed diabetes leads to a number of health issues.

Short-term complications include:

- hypoglycaemia
- diabetic ketoacidosis
- hyperosmolar hyperglycaemic state

Long-term complications include:

- retinopathy with a risk of blindness
- cardiovascular disease
- nephropathy
- neuropathy

Real-time CGM should be targeted to the group of patients in whom it is likely to be effective and in whom better glycaemic control will reduce the risk of the complications of diabetes and the future costs to both patient and the health service.

Epidemiology and Need

Diabetes UK estimates that more than one in 17 people in the UK has diabetes (diagnosed or undiagnosed). Their figures are based on Office for National Statistics (ONS) population data for 2012 (63.7M) with a total diabetes population of 3.85M and from (Quality Outcomes Framework (QoF) and Association of Public Health Observatories (AHPO) modelling.[1]

Diabetes UK estimates that this gives a prevalence of more than one in 17 people in the UK with diabetes (diagnosed).

In 2013, the prevalence of diabetes in the adult population in the UK was 6.0%.[2]

[1] Source: Quality and outcomes framework (QOF) 2012/3 England
[2] Source: Quality and outcomes framework (QOF) 2012/3 England

Type 1 and type 2

For adults and children and young people, we estimate that:

- 10% of people with diabetes have type 1 diabetes
- 90% of people with diabetes have type 2 diabetes

Slightly more men than women have been diagnosed with diabetes. Audits suggest that about 56 per cent of all adults with diabetes in the UK are men and 44% are women.

Table 1: Distribution of diabetes by age group in England and Wales[3]

Age	England and Wales
0 – 9	0.22%
10 – 19	0.99%
20 – 29	1.69%
30 – 39	3.83%
40 – 49	10.69%
50 – 59	18.95%
60 – 69	26.05%
70 – 79	24.14%
80+	13.42%

Children and young people aged under 18

There are about 35,000 children and young people with diabetes, under the age of 19, in the UK. Figures from 2009 suggested that there were about 29,000 children and young people aged under 18under the age of 18 with diabetes.

About 96% have type 1 diabetes; about 2% have type 2 diabetes and 2% have maturity onset diabetes of the young (MODY), other rare forms of diabetes or their diagnosis is not defined.

Slightly more boys seem to have diabetes than girls: 52% boys and 48% girls, though girls are twice as likely to have type 2 diabetes.

Children and young people aged under 18 with type 1 diabetes

The current estimate of prevalence of type 1 diabetes in children and young people under the age of 19 in the UK is one per 430 – 530.

The incidence of type 1 diabetes in children under the age of 14 is 24.5/100,000.

The peak age for diagnosis is between 10 and 14 years of age.

Children and young people aged under 18 with type 2 diabetes

In 2000, the first cases of type 2 diabetes in children were diagnosed in overweight girls aged nine to 16 of Pakistani, Indian or Arabic origin. It was first reported in white adolescents in 2002.

[3]Source: HSCIC: National Diabetes Audit 2011/12: Report 1: Care Processes and Treatment Targets (29,576 registered with GP practices within the NDA survey)

According to the National Paediatric Diabetes Audit, children of Asian origin were 8.7 times more likely to have type 2 diabetes than their white counterparts, and children of black origin were 6.2 times more likely.[4]

There is no epidemiological data specific to those groups likely to need real-time CGM.

Annual inpatient care, to treat short and long term complications of diabetes, is estimated at between £1,800 and £2,500 per patient.[5]

Adherence to NICE Guidance

This policy adheres to the majority of the recommendations made in:

- NICE DG21
- NICE TA151
- NICE NG17
- NICE NG18

Audit Requirements

There is currently no national database. Service providers will be expected to collect and provide audit data on request.

Date of Review

Five years from the date of the last review, unless new evidence or technology is available sooner.

The evidence base for the policy will be reviewed and any recommendations within the policy will be checked against any new evidence. Any operational issues will also be considered at this time. All available additional data on outcomes will be included in the review and the policy updated accordingly. The policy will be continued, amended or withdrawn subject to the outcome of that review.

Glossary

Term	Meaning
Asymptomatic	Producing or showing no symptoms.
Blood sugar	The concentration of glucose in the blood.
Cardiovascular disease	Grouping of all the diseases of the heart and blood vessels.
Cognitive or neurological disabilities	Damage to the brain or nervous system and to the process of acquiring knowledge and understanding through thought, experience, and the senses.
Diabetic ketoacidosis (DKA)	A life-threatening condition that develops when cells in the body are unable to get the sugar (glucose) they need for energy because there is not enough insulin. Because the cells cannot receive sugar for energy, the body begins to

[4] Source: Royal College of Paediatrics and Child Health (2009). Growing up with diabetes: children and young people with diabetes in England / HQIP: National Paediatric Diabetes Audit 2011/12 Report / Ehtisham S, Barrett TG, Shaw NJ (2000). Type 2 diabetes mellitus in UK children: an emerging problem. Diabetic Medicine 17 (12); 867– 871

[5] Source: diabetes.co.uk

	break down fat and muscle for energy. When this happens, ketones, or fatty acids, are produced and enter the bloodstream, causing the chemical imbalance (metabolic acidosis) called diabetic ketoacidosis.
Epidemiological	The incidence, distribution, and other factors relating to health or a specific disease.
Glucose	A simple sugar which is an important energy source in living organisms and is a component of many carbohydrates.
HbA1c level	Hemoglobin A1c (HbA1c) is a minor component of hemoglobin to which glucose is bound. HbA1c also is sometimes referred to as glycated, glycosylated hemoglobin, or glycohemoglobin. It provides a measure of blood sugar.
Hyperglycaemia	Excess of glucose in the bloodstream (high blood sugar).
Hyperosmolar hyperglycaemic state (HHS)	A complication of diabetes mellitus (predominantly type 2) in which high blood sugars cause severe dehydration, increases in osmolarity (relative concentration of solute) and a high risk of complications, coma and death. It is diagnosed with blood tests.
Hypoglycaemia	Deficiency of glucose in the bloodstream (low blood sugar).
Insulin	A hormone produced in the pancreas by the islets of Langerhans, which regulates the amount of glucose in the blood. The lack of insulin causes a form of diabetes.
Insulin pump	Patient controlled pump used to deliver insulin therapy.
Insulin therapy	All type 1 and some type 2 diabetics require insulin replacement to achieve glycaemic control, using mixtures of short-acting, intermediate- and long-acting and/or biphasic insulins, administered as subcuticular injection (or via a patient-controlled pump).
Interstitial fluid	A solution that bathes and surrounds the tissue cells of multicellular animals.
Maturity onset diabetes of the young (MODY)	MODY is a rare form of diabetes which is different from both type 1 and type 2 diabetes, and runs strongly in families. MODY is caused by a mutation (or change) in a single gene.
mmol/mol	A thousandth of a mole / mole = the amount of any chemical substance that equals the number of atoms in 12 grams of carbon-12.
Nephropathy	Disease of the kidneys.
Neuropathy	Disease of the nerves.
NICE DG	NICE Diagnostics Guidance
NICE NG	NICE Guidelines
NICE TA	NICE Technology Appraisal Guidance
ONS population data	Office of National Statistics information on the characteristics of the population of the UK.
QoF and AHPO modelling	Data information and series collected through the NHS to attempt to predict disease patterns.
Real-time CGM	Continuous glucose monitoring giving the current interstitial levels.

Retinopathy	Disease of the retina which results in impairment or loss of vision.
Retrospective CGM	Continuous glucose monitoring giving past interstitial levels for a pre-defined period.
Type 1 diabetes	Once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin.
Type 2 diabetes	Once known as adult-onset or non-insulin dependent diabetes, is a chronic condition that affects the way the body metabolizes sugar (glucose).

References

1. Greater Manchester Effective Use of Resources Operational Policy
2. Royal College of Paediatrics and Child Health (2009). Growing up with diabetes: children and young people with diabetes in England
3. Quality and outcomes framework (QOF) 2012/13
4. HSCIC: National Diabetes Audit 2011/12: Report 1: Care Processes and Treatment Targets (29,576 registered with GP practices within the NDA survey)
5. HQIP: National Paediatric Diabetes Audit 2011/12 Report / Ehtisham S, Barrett TG, Shaw NJ (2000). Type 2 diabetes mellitus in UK children: an emerging problem. Diabetic Medicine 17 (12); 867– 871

Governance Approvals

Name	Date Approved
Greater Manchester Effective Use of Resources Steering Group	18/01/2017 / 17/05/2017 / 15/11/2017
Greater Manchester Directors of Commissioning / Greater Manchester Chief Finance Officers (Delegated authority given to approve policy by Greater Manchester Joint Commissioning Board)	13/11/2018
Bolton Clinical Commissioning Group	25/01/2019
Bury Clinical Commissioning Group	13/11/2018
Heywood, Middleton & Rochdale Clinical Commissioning Group	13/11/2018
Manchester Clinical Commissioning Group	13/11/2018
Oldham Clinical Commissioning Group	13/11/2018
Salford Clinical Commissioning Group	13/11/2018
Stockport Clinical Commissioning Group	13/11/2018
Tameside & Glossop Clinical Commissioning Group	13/11/2018
Trafford Clinical Commissioning Group	13/11/2018
Wigan Borough Clinical Commissioning Group	13/11/2018

Appendix 1 – Evidence Review

Real-Time Continuous Glucose Monitoring
GM039

Search Strategy

The following databases are routinely searched: NICE Clinical Guidance and full website search; NHS Evidence and NICE CKS; SIGN; Cochrane; York; and the relevant Royal College and any other relevant bespoke sites. A Medline / Open Athens search is undertaken where indicated and a general google search for key terms may also be undertaken. The results from these and any other sources are included in the table below. If nothing is found on a particular website it will not appear in the table below:

Database	Result
NICE	NICE DG21: Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system), Published: 12 February 2016 (relevant section cited below)
	NICE TA151: Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus, Published: 23 July 2008 (cited below for background information)
	NICE NG18: Diabetes (type 1 and type 2) in children and young people: diagnosis and management, Published: 26 August 2015 (relevant section cited below)
	NICE NG17: Type 1 diabetes in adults: diagnosis and management, Published: 26 August 2015 (relevant section cited below)
NHS Evidence and NICE CKS	National Institute for Health Research: Integrated sensor-augmented pump therapy systems [the MiniMed® Paradigm™ Veo system and the Vibe™ and G4® PLATINUM CGM (continuous glucose monitoring) system] for managing blood glucose levels in type 1 diabetes: a systematic review and economic evaluation, *Rob Riemsma, Isaac Corro Ramos, Richard Birnie, Nasuh Büyükkaramikli, Nigel Armstrong, Steve Ryder, Steven Duffy, Gill Worthy, Maiwenn Al, Johan Severens and Jos Kleijnen,* Issued: 20 February 2016
SIGN	SIGN 116: Management of Diabetes (not cited here as NICE guidance cited instead)
Cochrane	Continuous glucose monitoring systems for type 1 diabetes mellitus, *Langendam M, Luijf YM, Hooft L, DeVries JH, Mudde AH, Scholten RJPM,* 2012, Issue 1. Art. No.: CD008101
York (CRD)	Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes, *Poolsup N, Suksomboon N, Kyaw AM,* Date abstract record published: 13 Nov 2014
	Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, *Pickup JC, Freeman SC, Sutton,* Date abstract record published: 27 Jul 2011
	Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes: systematic review and meta-analysis, *Wojciechowski P, Rys P, Lipowska A, Gaweska M, Malecki MT,* Date abstract record published: 8 Sep 2012

	Continuous Glucose Monitoring System in children with type 1 diabetes mellitus: a systematic review and meta-analysis, *Golicki DT, Golicka D, Groele L, Pankowska E,* Date abstract record published on CRD: 17 Nov 2010, Earlier publication: Diabetologia. 2008 Feb;51(2):233-40. Epub 2007 Dec 1
	Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials, *Szypowska A, Ramotowska A, Dzygalo K, Golicki D,* Date abstract record published on CRD: 2 Jan 2013, Earlier publication: Eur J Endocrinol. 2012 Apr;166(4):567-74. doi: 10.1530/EJE-11-0642. Epub 2011 Nov 17
General Search (Google)	Continuous Glucose Monitoring: An Endocrine Society Clinical Practice Guideline (US guidelines), *David C. Klonoff, Bruce Buckingham, Jens S. Christiansen, Victor M. Montori, William V. Tamborlane, Robert A. Vigersky, and Howard Wolpert,* First Published Online: 02 July 2013
Medline / Open Athens	Not done due to number of systematic reviews and guidelines found

Summary of the evidence

Evidence on the overall effectiveness of CGM is conflicting however there is consensus that it is effective in selected patient groups.

Real time CGM is more effective than retrospective CGM.

CGM is effective provided there is compliance with the use of the device and it is worn for more than 70% of the time and effectively calibrated.

The evidence is stronger for use in adults than in children.

The evidence

Levels of evidence	
Level 1	Meta-analyses, systematic reviews of randomised controlled trials
Level 2	Randomised controlled trials
Level 3	Case-control or cohort studies
Level 4	Non-analytic studies e.g. case reports, case series
Level 5	Expert opinion

1. LEVEL 1: NICE DIAGNOSTICS GUIDANCE

DG21: Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system), Published: 12 February 2016

1 Recommendations

1.1 The MiniMed Paradigm Veo system is recommended as an option for managing blood glucose levels in people with type 1 diabetes only if:

- they have episodes of disabling hypoglycaemia despite optimal management with continuous subcutaneous insulin infusion and

- the company arranges to collect, analyse and publish data on the use of the MiniMed Paradigm Veo system.

1.2 The MiniMed Paradigm Veo system should be used under the supervision of a trained multidisciplinary team who are experienced in continuous subcutaneous insulin infusion and continuous glucose monitoring for managing type 1 diabetes only if the person or their carer:

- agrees to use the sensors for at least 70% of the time
- understands how to use it and is physically able to use the system and
- agrees to use the system while having a structured education programme on diet and lifestyle, and counselling.

1.3 People who start to use the MiniMed Paradigm Veo system should 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.

1.4 The Vibe and G4 PLATINUM CGM system shows promise but there is currently insufficient evidence to support its routine adoption in the NHS for managing blood glucose levels in people with type 1 diabetes. Robust evidence is needed to show the clinical effectiveness of using the technology in practice.

1.5 People with type 1 diabetes who are currently provided with the MiniMed Paradigm Veo system or the Vibe and G4 PLATINUM CGM system by the NHS for clinical indications that are not recommended in this NICE guidance should be able to continue using them until they and their NHS clinician consider it appropriate to stop.

2. LEVEL 1: NICE TECHNOLOGY APPRAISAL GUIDANCE

TA151: Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus, Published: 23 July 2008

1 Guidance

1.1 Continuous subcutaneous insulin infusion (CSII or 'insulin pump') therapy is recommended as a treatment option for adults and children 12 years and older with type 1 diabetes mellitus provided that:

- attempts to achieve target haemoglobin A1c (HbA1c) levels with multiple daily injections (MDIs) result in the person experiencing disabling hypoglycaemia. For the purpose of this guidance, disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life

  or

- HbA1c levels have remained high (that is, at 8.5% [69 mmol/mol] or above) on MDI therapy (including, if appropriate, the use of long-acting insulin analogues) despite a high level of care.

1.2 CSII therapy is recommended as a treatment option for children younger than 12 years with type 1 diabetes mellitus provided that:

- MDI therapy is considered to be impractical or inappropriate, and
- children on insulin pumps would be expected to undergo a trial of MDI therapy between the ages of 12 and 18 years.

1.3 It is recommended that CSII therapy be initiated only by a trained specialist team, which should normally comprise a physician with a specialist interest in insulin pump therapy, a diabetes specialist nurse and a dietitian. Specialist teams should provide structured education programmes and advice on diet, lifestyle and exercise appropriate for people using CSII.

1.4 Following initiation in adults and children 12 years and older, CSII therapy should only be continued if it results in a sustained improvement in glycaemic control, evidenced by a fall in HbA1c levels, or a sustained decrease in the rate of hypoglycaemic episodes. Appropriate targets for such improvements should be set by the responsible physician, in discussion with the person receiving the treatment or their carer.

1.5 CSII therapy is not recommended for the treatment of people with type 2 diabetes mellitus.

3. LEVEL 1: NATIONAL INSTITUTE FOR HEALTH RESEARCH SYSTEMATIC REVIEW AND EVALUATION

Integrated sensor-augmented pump therapy systems [the MiniMed® Paradigm™ Veo system and the Vibe™ and G4® PLATINUM CGM (continuous glucose monitoring) system] for managing blood glucose levels in type 1 diabetes: a systematic review and economic evaluation, *Rob Riemsma, Isaac Corro Ramos, Richard Birnie, Nasuh Büyükkaramikli, Nigel Armstrong, Steve Ryder, Steven Duffy, Gill Worthy, Maiwenn Al, Johan Severens and Jos Kleijnen,* Issued: 20 February 2016

ABSTRACT

Background: In recent years, meters for continuous monitoring of interstitial fluid glucose have been introduced to help people with type 1 diabetes mellitus (T1DM) to achieve better control of their disease.

Objective: The objective of this project was to summarise the evidence on the clinical effectiveness and cost-effectiveness of the MiniMed® Paradigm™ Veo system (Medtronic Inc., Northridge, CA, USA) and the Vibe™ (Animas® Corporation, West Chester, PA, USA) and G4® PLATINUM CGM (continuous glucose monitoring) system (Dexcom Inc., San Diego, CA, USA) in comparison with multiple daily insulin injections (MDIs) or continuous subcutaneous insulin infusion (CSII), both with either self-monitoring of blood glucose (SMBG) or CGM, for the management of T1DM in adults and children.

Data sources: A systematic review was conducted in accordance with the principles of the Centre for Reviews and Dissemination guidance and the National Institute for Health and Care Excellence Diagnostic Assessment Programme manual. We searched 14 databases, three trial registries and two conference proceedings from study inception up to September 2014. In addition, reference lists of relevant systematic reviews were checked. In the absence of randomised controlled trials directly comparing Veo or an integrated CSII + CGM system, such as Vibe, with comparator interventions, indirect treatment comparisons were performed if possible.

Methods: A commercially available cost-effectiveness model, the IMS Centre for Outcomes Research and Effectiveness diabetes model version 8.5 (IMS Health, Danbury, CT, USA), was used for this assessment. This model is an internet-based, interactive simulation model that predicts the long-term health outcomes and costs associated with the management of T1DM and type 2 diabetes. The model consists of 15 submodels designed to simulate diabetes-related complications, non-specific mortality and costs over time. As the model simulates individual patients over time, it updates risk factors and complications to account for disease progression.

Results: Fifty-four publications resulting from 19 studies were included in the review. Overall, the evidence suggests that the Veo system reduces hypoglycaemic events more than other treatments, without any differences in other outcomes, including glycated haemoglobin (HbA1c) levels. We also found significant results in favour of the integrated CSII + CGM system over MDIs with SMBG with regard to HbA1c levels and quality of life. However, the evidence base was poor. The quality of the included studies was generally low, often with only one study comparing treatments in a specific population at a specific follow-up time. In particular, there was only one study comparing Veo with an integrated CSII + CGM system and only one study comparing Veo with a CSII + SMBG system in a mixed population. Cost-effectiveness analyses indicated that MDI + SMBG is the option most likely to be cost-effective, given the current threshold of £30,000 per quality-adjusted life-year gained, whereas integrated CSII + CGM systems and Veo are dominated and extendedly dominated, respectively, by stand-alone, non-integrated CSII with CGM. Scenario analyses did not alter these conclusions. No cost-effectiveness modelling was conducted for children or pregnant women.

Conclusions: The Veo system does appear to be better than the other systems considered at reducing hypoglycaemic events. However, in adults, it is unlikely to be cost-effective. Integrated systems are also 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. Future trials in specific child, adolescent and adult populations should include longer term follow-up and ratings on the European Quality of Life-5 Dimensions scale at various time points with a view to informing improved cost-effectiveness modelling.

4. LEVEL 1: COCHRANE SYSTEMATIC REVIEW

Continuous glucose monitoring systems for type 1 diabetes mellitus, *Langendam M, Luijf YM, Hooft L, DeVries JH, Mudde AH, Scholten RJPM,* 2012, Issue 1. Art. No.: CD008101

ABSTRACT

Background: Self-monitoring of blood glucose is essential to optimise glycaemic control in type 1 diabetes mellitus. Continuous glucose monitoring (CGM) systems measure interstitial fluid glucose levels to provide semi-continuous information about glucose levels, which identifies fluctuations that would not have been identified with conventional self-monitoring. Two types of CGM systems can be defined: retrospective systems and real-time systems. Real-time systems continuously provide the actual glucose concentration on a display. Currently, the use of CGM is not common practice and its reimbursement status is a point of debate in many countries.

Objectives: To assess the effects of CGM systems compared to conventional self-monitoring of blood glucose (SMBG) in patients with diabetes mellitus type 1.

Search methods: We searched *The Cochrane Library*, MEDLINE, EMBASE and CINAHL for the identification of studies. Last search date was June 8, 2011.

Selection criteria: Randomised controlled trials (RCTs) comparing retrospective or real-time CGM with conventional self-monitoring of blood glucose levels or with another type of CGM system in patients with type 1 diabetes mellitus. Primary outcomes were glycaemic control, e.g. level of glycosylated haemoglobin A1c (HbA1c) and health-related quality of life. Secondary outcomes were adverse events and complications, CGM derived glycaemic control, death and costs.

Data collection and analysis: Two authors independently selected the studies, assessed the risk of bias and performed data-extraction. Although there was clinical and methodological heterogeneity between studies an exploratory meta-analysis was performed on those outcomes the authors felt could be pooled without losing clinical merit.

Main results: The search identified 1366 references. Twenty-two RCTs meeting the inclusion criteria of this review were identified. The results of the meta-analyses (across all age groups) indicate benefit of CGM for patients starting on CGM sensor augmented insulin pump therapy compared to patients using multiple daily injections of insulin (MDI) and standard monitoring blood glucose (SMBG). After six months there was a significant larger decline in HbA1c level for real-time CGM users starting insulin pump therapy compared to patients using MDI and SMBG (mean difference (MD) in change in HbA1c level -0.7%, 95% confidence interval (CI) -0.8% to - 0.5%, 2 RCTs, 562 patients, I2=84%). The risk of hypoglycaemia was increased for CGM users, but CIs were wide and included unity (4/43 versus 1/35; RR 3.26, 95% CI 0.38 to 27.82 and 21/247 versus 17/248; RR 1.24, 95% CI 0.67 to 2.29). One study reported the occurrence of ketoacidosis from baseline to six months; there was however only one event. Both RCTs were in patients with poorly controlled diabetes. For patients starting with CGM only, the average decline in HbA1c level six months after baseline was also statistically significantly larger for CGM users compared to SMBG users, but much smaller than for patients starting using an insulin pump and CGM at the same time (MD change in HbA1c level -0.2%, 95% CI -0.4% to -0.1%, 6 RCTs, 963 patients, I2=55%). On average, there was no significant difference in risk of severe hypoglycaemia or ketoacidosis between CGM and SMBG users. The confidence interval however, was wide and included a decreased as well as an increased risk for CGM users compared to the control group (severe hypoglycaemia: 36/411 versus 33/407; RR 1.02, 95% CI 0.65 to 1.62, 4 RCTs, I2=0% and ketoacidosis: 8/411 versus 8/407; RR 0.94, 95% CI 0.36to 2.40, 4 RCTs, I2=0%). Health-related quality of life was reported in five of the 22 studies. In none of these studies a significant difference between CGM and SMBG was found. Diabetes complications, death and costs were not measured. There were no studies in pregnant women with diabetes type 1 and in patients with hypoglycaemia unawareness.

Authors' conclusions: There is limited evidence for the effectiveness of real-time continuous glucose monitoring (CGM) use in children, adults and patients with poorly controlled diabetes. The largest improvements in glycaemic control were seen for sensor-augmented insulin pump therapy in patients with poorly controlled diabetes who had not used an insulin pump before. The risk of severe hypoglycaemia or ketoacidosis was not significantly increased for CGM users, but as these events occurred infrequent these results have to be interpreted cautiously. There are indications that higher compliance of wearing the CGM device improves glycosylated haemoglobin A1c level (HbA1c) to a larger extent.

5. LEVEL 1: CRD SYSTEMATIC REVIEW

Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes, *Poolsup N, Suksomboon N, Kyaw AM,* Date abstract record published: 13 Nov 2014

CRD summary: This well-conducted review 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. Continuous glucose monitoring improved glycaemic control, compared with self-monitoring, for adults with type 2 diabetes. These conclusions are likely to be reliable.

Authors' objectives: To assess the effects of continuous glucose monitoring on glycaemic control, in children with type 1 diabetes, and adults with type 2 diabetes.

Searching: MEDLINE, CINAHL, Scopus, Web of Science and The Cochrane Library were searched in May 2013; search terms were reported. The reference lists of relevant randomised controlled trials (RCTs) and systematic or narrative reviews were searched for additional relevant studies. No language restrictions were imposed.

Study selection: RCTs, lasting at least eight weeks, comparing the available continuous glucose monitoring devices with self-monitoring of blood glucose, for children (aged 18 years or younger) with type 1 diabetes or adults (aged 18 years or older) with type 2 diabetes, were eligible for inclusion. Trials had to report glycated haemoglobin (HbA1c) as an outcome measure. Trials of pregnant women, critically ill patients, patients after surgery or transplant, or patients in intensive care, were excluded. The included trials were conducted in the UK, Europe, the USA, Australia or Korea, and were published between 2001 and 2012. Trials lasted from three to twelve months. They assessed either real-time or retrospective continuous glucose monitoring. Where stated, the devices were MiniMed, DexCom, FreeStyle Navigator, Guardian REAL-Time or the GlucoDay system. The trials varied in the frequency and duration of continuous monitoring. The average initial glycated haemoglobin level was over 8% in all trials of adults. Most patients received insulin pump therapy, insulin injection therapy, oral hypoglycaemic agents, or a combination of these; two trials included patients who were not treated with insulin. The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality: Two reviewers independently assessed trial quality using the Maastricht Amsterdam Scale, which was based on the Jadad scale and the Delphi list. Disagreements were resolved by a third reviewer. Trials that met six or more of the eleven criteria were considered to be high quality; those meeting fewer than six were considered to be low quality.

Data extraction: The mean difference in final glycated haemoglobin level, between the continuous monitoring group and the self-monitoring group, was extracted from each trial. Two authors independently extracted the data, and disagreements were resolved by a third reviewer.

Methods of synthesis: Trial data were combined using meta-analysis; a random-effects model was used in the presence of significant statistical heterogeneity, and a fixed-effect model was used in the absence of significant heterogeneity. Heterogeneity was assessed using Cochran's Q and I^2. Subgroup analyses were undertaken based on real-time versus retrospective monitoring, initial glycated haemoglobin level (under 8%, 8 to 10%, or over 10%), and trial quality. Sensitivity analyses were undertaken by excluding trials reporting fewer usable continuous monitoring data. Publication bias was assessed using a funnel plot and the Egger regression test.

Results of the review: Fourteen RCTs were included; 10 were of children with type 1 diabetes (817 patients; range 11 to 156), and four were of adults with type 2 diabetes (228 patients; range 25 to 100).

Children: Seven trials were considered to be high quality, and three were low quality. There was no statistically significant difference between continuous glucose monitoring and self-monitoring (MD -0.13%, 95% CI -0.38 to 0.11; 10 RCTs). There was evidence of significant heterogeneity (I^2=71%) and publication bias. The results of subgroup analyses of initial glycated haemoglobin level and trial quality were similar to those for the main analysis. Real-time continuous monitoring was superior to self-monitoring for improving glycaemic control (MD -0.18%, 95% CI -0.35 to -0.02; five RCTs), but retrospective continuous monitoring was not (MD -0.05, 95% CI -0.46 to 0.35; five RCTs).

Heterogeneity was not substantial for real-time monitoring (I^2=48%), but was substantial for retrospective monitoring (I^2=72%).

Adults: Two RCTs were considered to be high quality, and two were low quality. Continuous glucose monitoring was statistically significantly superior to self-monitoring in glycated haemoglobin reduction (MD -0.31%, 95% CI -0.6 to -0.02; four RCTs). There was no evidence of heterogeneity (I^2=0) and publication bias.

CRD commentary: The review question and inclusion criteria were clear. Relevant sources were searched for published trials, in any language. Unpublished data were not sought; publication bias was assessed and found to be present, meaning that some trials with negative results may have been missed. Data extraction and quality assessment were duplicated, reducing the potential for reviewer error and bias, but it was unclear whether the same methods were used for study selection. Trial quality was assessed and the results were used for subgroup analysis. The methods used to pool the data and assess heterogeneity appear to have been appropriate, including the subgroup and sensitivity analyses. The results of trials of adults were consistent, but one trial of real-time monitoring for children found no difference in effectiveness between continuous monitoring and self-monitoring. If additional trials with negative results were missed due to publication bias, this result might no longer be statistically significant. This was a well-conducted systematic review and the conclusions are likely to be reliable, particularly for adult patients.

Implications of the review for practice and research:

Practice: The authors stated that real-time continuous glucose monitoring devices could be effective for children with type 1 diabetes, and continuous glucose monitoring devices could be effective for adults with uncontrolled type 2 diabetes.

Research: The authors stated that trials should aim to determine the appropriate frequency and duration of continuous glucose monitoring, and assess the benefit of the devices in people with nocturnal hypoglycaemia. More adequately powered RCTs were required to assess continuous glucose monitoring for patients with type 2 diabetes.

6. LEVEL 1: CRD SYSTEMATIC REVIEW

Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, *Pickup JC, Freeman SC, Sutton,* Date abstract record published: 27 Jul 2011

CRD summary: This meta-analysis of individual patient data found a significant reduction in final glycated haemoglobin in patients with type 1 diabetes who used continuous glucose monitoring rather than self-monitoring, especially for patients with high baseline glycated haemoglobin and monitor usage. The conclusions are likely to be reliable.

Authors' objectives: To determine the clinical effectiveness of real-time continuous glucose monitoring compared with self-monitoring of blood glucose in patients with type 1 diabetes. A secondary objective was to identify patient-level determinants of glycated haemoglobin (HbA) and hypoglycaemia.

Searching: The Cochrane Library, MEDLINE and EMBASE databases were searched without language restrictions up to June 2010 using specified search terms. Google Scholar was also searched. Hand searching was performed using cited literature in retrieved articles and lists of papers supplied by manufactures of continuous glucose monitors.

Study selection: Randomised controlled trials of two or more months duration in men and non-pregnant women with type 1 diabetes were eligible for inclusion. Trials needed to compare real time glucose monitoring with self-monitoring of blood glucose. Insulin delivery needed to be identical in both groups. Relevant outcomes were HbA percentage and hypoglycaemia. Study duration ranged from 13 to 26 weeks. Insulin delivery was mostly by continuous subcutaneous delivery; multiple daily injections were also used. Two independent reviewers assessed trial eligibility.

Assessment of study quality: Trial quality was assessed using the Jadad scale and an additional item for the method of allocation concealment. Checks for internal consistency, balance between treatment groups by baseline factors, randomisation date, length of follow-up and consistency with publications on trials were not reported. The authors did not state how many reviewers assessed study validity.

Data extraction: Individual patient data (IPD) were obtained from trialists. Information included age, duration of diabetes, treatment allocation, sensor usage, baseline and completion HbA percentage, and

baseline and completion number of episodes of severe hypoglycaemia and hypoglycaemia measured as area under the curve for blood glucose concentrations less than 3.9mmol/L. Area under the curve was obtained from a period of blinded continuous glucose monitoring at the start and completion of the trial (median duration six days). IPD on severe hypoglycaemia were incomplete and supplemented with aggregate data extracted independently by two reviewers. Disagreements were resolved by consensus.

Methods of synthesis: Overall outcomes were assessed using a two-stage random-effects meta-analysis of IPD (with a fixed-effect sensitivity analysis). Heterogeneity was assessed using I2. Funnel plots were used to examine potential differences between large and small studies. Determinants of final HbA and area under the curve of hypoglycaemia were explored using a Bayesian meta-regression with covariates for baseline HbA, sensor use, age, duration of diabetes and interactions between the covariates and baseline HbA. Covariates were considered in a stepwise manner with Deviance Information Criterion used for model choice. Ecological bias was explored by examining within- and between-study effects on individual covariates.

Results of the review: Six trials (953 patients randomised, 908 analysed) were included. All scored 3 out of 6 on the study quality scale as a result of lack of information on allocation concealment and absence of double blinding. The overall mean difference for HbA was -0.30% (95% confidence interval (CI) -0.43% to -0.17%) in favour of continuous monitoring. Overall reduction in area under the curve of hypoglycaemia was -0.28 (95% CI -0.46 to -0.09), which was equivalent to a 23% reduction in median exposure to hypoglycaemia with continuous glucose monitoring. There was evidence of heterogeneity for both outcomes. Heterogeneity in hypoglycaemia response was not strongly related to any independent predictors. Regression coefficients from the best fitting model (of those tested) indicated that reduction in HbA associated with continuous glucose monitoring was greatest in patients with high HbA at baseline (0.744, 95% credibility interval 0.655 to 0.832) who frequently used sensors (-0.15, 95% credibility interval -0.194 to -0.106). There was limited evidence of publication or ecological bias.

Authors' conclusions: Continuous glucose monitoring was associated with a significant reduction in HbA. This was greatest in those with highest HbA at baseline and who had highest weekly sensor use. Exposure to hypoglycaemia was reduced during continuous glucose monitoring.

CRD commentary: This review utilised appropriate methods to minimise bias during identification, selection and acquisition of individual patient data. Quality assessment indicated low potential for risk of bias associated with trials despite lack of reporting of allocation concealment methods. Checks on IPD quality were not reported. Methods of pooling and exploration of the impact of patient level covariates were appropriate and robust to a range of sensitivity analyses. The conclusions of the review were based on the evidence and are likely to be reliable.

Implications of the review for practice and research:

Practice: The authors stated that the most cost effective or appropriate use of continuous glucose monitoring was likely to be when targeted at people with type 1 diabetes who had continued poor control during intensified insulin therapy and who frequently used continuous glucose monitoring. This implication was not derived from the review, which did not examine cost-effectiveness.

Research: The authors stated that further studies of continuous glucose monitoring in those with disabling hypoglycaemia were required.

7. LEVEL 1: CRD SYSTEMATIC REVIEW

Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes: systematic review and meta-analysis, *Wojciechowski P, Rys P, Lipowska A, Gaweska M, Malecki MT,* Date abstract record published 8 Sep 2012

CRD summary: Continuous glucose monitoring, particularly its real-time system, had a favourable effect on glycaemic control in patients with type 1 diabetes, compared with self-monitoring of blood glucose. This was a well conducted systematic review and despite the limited quality of some of the included trials, the authors' conclusions are likely to be reliable.

Authors' objectives: To assess the efficacy and safety of continuous glucose monitoring systems compared with self-monitoring of blood glucose in patients with type 1 diabetes.

Searching: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CRD databases, and Trip Database were searched to June 2011; some search terms were reported. In

addition, clinical trial registers, medical product approval agencies, conference abstracts presented at two international diabetic meetings and the reference lists of retrieved articles were searched for additional relevant studies. Only studies published in full were eligible for inclusion.

Study selection: Randomised controlled trials (RCTs) of at least 12 weeks duration that compared continuous glucose monitoring with self-monitoring of blood glucose were eligible for inclusion. Participants had to be patients with type 1 diabetes on an intensive insulin regimen (with continuous subcutaneous insulin infusion or multiple daily injections). Trials were excluded if patients were pregnant, had new-onset type 1 diabetes, were being treated in an intensive care unit, if insulin was administered intraperitoneally or if only non-invasive systems of glucose monitoring were assessed. Outcomes of interest were HbA1c change from baseline, HbA1c at the end of the study, proportion of patients that achieved target HbA1c, number and duration of hypo- and hyperglycaemic episodes and safety (risk of severe hypoglycaemic events, ketoacidosis, adverse reactions at the sensor implantation site and continuous glucose monitoring system errors). The mean age of participants in the included trials ranged from nine to 52 years; some studies only included children and adolescents, some only included adults and some included both. The mean duration of diabetes ranged from six to 28 years, where reported. Mean baseline HbA1c values ranged from 6.4% to 11.5%. Some studies used continuous glucose monitoring systems in an ongoing manner (device used continuously at least six days per week) and some used continuous glucose monitoring systems in an intermediate manner (device was used less frequently; ranging from one 72-hour reading to a sequence of six readings per month corresponding to up to 18 days of measurement per month). Most studies offered real-time glucose readings, while some provided retrospective readings. Two reviewers independently assessed studies for inclusion; disagreements were resolved by consensus or involvement of a third reviewer.

Assessment of study quality: Study quality was assessed using the Jadad scale. The authors did not state how many reviewers undertook quality assessment procedures.

Data extraction: For dichotomous outcomes, odds ratios (OR) and risk ratios (RR) were calculated with 95% confidence intervals (CI). For continuous outcomes, mean differences (MD) with 95% confidence intervals, were calculated. Data extraction was undertaken independently by two reviewers, disagreements were resolved by consensus or involvement of a third reviewer.

Methods of synthesis: Data were pooled using the inverse variance or Mantel-Haenszel method in the absence of significant statistical heterogeneity and presented as the pooled odds ratio, pooled risk ratios, or weighted mean difference (WMD) with 95% confidence intervals. In the presence of significant heterogeneity the DerSimonian and Laird random-effects model was used. For dichotomous outcomes, if differences between trial groups reached statistical significance, the number-needed-to treat or number-needed-to-harm was also calculated. Subgroup analyses were conducted according to patient age, level of glycaemic control at baseline, type of device and frequency of use. Heterogeneity was assessed using the Cochrane Q-test. Publication bias was assessed using the Egger test.

Results of the review: Fourteen RCTs were included in the review (1,268 participants, range nine to 322). Study duration ranged from three to six months. Seven RCTs scored one or two out of five on the Jadad scale, seven scored three out of five. Patients using continuous glucose monitoring systems had a significantly greater decrease in HbA1c from baseline compared with self monitoring of blood glucose (WMD -0.26, 95% CI -0.34 to -0.19; 14 RCTs). There was no evidence of statistical heterogeneity (I^2=0%). Devices that offered real-time glucose readings for continuous glucose monitoring had a significantly greater decrease in HbA1c from baseline compared with self monitoring of blood glucose (WMD -0.27, 95% CI -0.34 to -0.19; eight RCTs), but the difference was not statistically significant for devices that provided retrospective readings. Results of other subgroup analyses were similar to those of the main analysis. Results were similar for studies of children and adolescents and studies of adults. Similar results were reported for end of trial HbA1c levels, but there was significant heterogeneity associated with these results. A significantly higher proportion of patients using continuous glucose monitoring systems achieved target HbA1c levels compared with patients using self monitoring of blood glucose (OR 2.14, 95% CI 1.41 to 3.26; numbers-needed-to-treat 7.40, 95% CI 4.70 to 17.43; four RCTs). There was a significant reduction in hypoglycaemic events in the continuous glucose monitoring group compared with the self monitoring of blood glucose group (SMD -0.32,95% CI -0.52 to -0.13; four RCTs), but there was no significant difference in the frequency of severe hypoglycaemic episodes. Only a few trials reported adverse events; the most common was mild reactions at the sensor implantation site in the continuous glucose monitoring group. Only a small number of patients reported experiencing

more severe reactions (painful itching, severe pain during sensor implantation, skin abscess formation or cellulitis). The risk of ketoacidosis episodes was rare and not significantly different between groups. Three studies reported technical problems related to the use of continuous glucose monitoring systems. There was no evidence of significant publication bias.

Authors' conclusions: Continuous glucose monitoring, particularly its real-time system, had a favourable effect on glycaemic control and decreased the incidence of hypoglycaemic episodes in both adult and paediatric type 1 diabetic patients, compared with self monitoring of blood glucose.

CRD commentary: The review question and inclusion criteria were clearly reported. A number of relevant sources were searched for eligible trials, but only trials published in full were eligible for inclusion. Publication bias was assessed and there was no evidence of significant publication bias. Study selection and data extraction were undertaken in duplicate, which reduced the potential for reviewer bias and error. The quality of the included trials was assessed using a validated tool. Half of the trials were poor quality (scoring 1 or 2 out of 5 on the Jadad scale), in addition, many trials only included a small number of participants. Study duration was only three to six months. Appropriate methods were used to pool the included studies, heterogeneity was assessed and subgroup analyses were undertaken. Despite the inclusion of some small, limited quality studies, the results of the individual studies consistently favoured continuous glucose monitoring in terms of glycaemic control. However, the results related to the incidence of hypoglycaemic episodes were less consistent. Overall, this was a well conducted systematic review and the authors' conclusions are likely to be reliable.

8. LEVEL 1: CRD SYSTEMATIC REVIEW

Continuous Glucose Monitoring System in children with type 1 diabetes mellitus: a systematic review and meta-analysis, *Golicki DT, Golicka D, Groele L, Pankowska E,* Date abstract record published on CRD: 17 Nov 2010, Earlier publication: Diabetologia. 2008 Feb;51(2):233-40. Epub 2007 Dec 1

CRD summary: This well-conducted review found that the subcutaneous Continuous Glucose Monitoring System was not better than self-monitoring of blood glucose among children with type 1 diabetes, but that this conclusion should be interpreted with caution due to the small sample sizes and methodological limitations of the included trials. The authors' conclusions are supported by the evidence presented.

Authors' objectives: To investigate the effects of the Continuous Glucose Monitoring System (CGMS) compared with self-monitoring of blood glucose on glycaemic control in children with type 1 diabetes.

Searching: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Database of Systematic Reviews were searched from inception to June 2007. Search terms were reported. Reference lists of original articles and reviews were screened. No language restrictions were applied, but studies published only as letters to the editor or abstracts were excluded.

Study selection: Randomised controlled trials (RCTs) that compared the Continuous Glucose Monitoring System (CGMS) plus self-monitoring of blood glucose versus self-monitoring of blood glucose alone in children with type 1 diabetes. The primary outcome measure was improvement in diabetes control according to glycated haemoglobin (HbA1c). Secondary outcome measures were improvement in fructosamine, major and minor hypoglycaemic episodes, mean daily area under the CGMS curve for glucose lower than 3.89 mmol/L, mean daily area over the CGMS curve for glucose above 9.99 mmol/L, adjustments of insulin dose, local adverse effects, and adherence.

Included trials were small single-centre studies conducted in Europe, USA and Australia. Included patients had to wear the subcutaneous CGMS ranging from once every five days to once in three months. The frequency of self-monitoring in the control group ranged from a minimum of twice daily to four to six times daily. The age of included children ranged from two to 19 years; duration of diabetes ranged from less than one year to 11.6 years. The frequency of insulin changes varied from over 11 times in one month (experimental group only) to every two months. Two reviewers independently assessed studies for inclusion. Disagreements were resolved through discussion.

Assessment of study quality: Two reviewers independently assessed trial quality according to the following criteria: allocation concealment, blinding, intention-to-treat analysis and comprehensive follow-up. Disagreements were resolved through discussion. Trials were judged to be at low risk of bias (one or

less inadequate criteria), medium risk of bias (three or less inadequate criteria), and high risk of bias (more than three inadequate criteria). Trials with less than 80% follow-up were excluded.

Data extraction: Two reviewers independently extracted data. For continuous outcomes, the mean and standard deviation (SD) for each treatment group was extracted and used to calculate mean differences, together with 95% confidence intervals (CIs). For dichotomous outcomes, data were extracted to calculate relative risks (RR) together with 95% confidence intervals. Where standard deviations were not reported, these were computed from available data. For cross-over trials, only data from the first period of the trial were included. For parallel-group trials, data from the end of the study were used. Disagreements were resolved through discussion.

Methods of synthesis: Summary relative risks and weighted mean differences (WMD) were calculated together with 95% confidence intervals. Results for both fixed-effect and random-effects were reported. Heterogeneity was assessed using the X2 and I2 statistics. Sensitivity analysis was performed by excluding trials in which standard deviations were imputed.

Results of the review: Five RCTs (n=131 children, range 11 to 36 per trial) were included; three were parallel group RCTs and two were cross-over studies. Only two RCTs reported adequate generation of the allocation sequence. Two trials were double blinded and one single blinded. One trial reported that an intention-to-treat analysis had been conducted. All trials provided an adequate description of drop-outs. Only one trial was judged to be at low risk of bias. Glycated haemoglobin levels (five trials): There was no difference between children whose insulin doses were adjusted on the basis of Continuous Glucose Monitoring System (CGMS) plus self-monitoring data compared with self-monitoring data alone (p=0.87). Sensitivity analysis did not alter the findings.

Secondary outcomes: One RCT found that children using the CGMS had an increased number of insulin dose changes per patient per month compared with those using self-monitoring alone (WMD 6.3 dose changes, 95% CI 2.88 to 9.72). There were no significant differences between treatment groups for any of the other outcomes assessed: improvement in fructosamine (one trial); major hypoglycaemic episodes (no events reported in any group in any trial); minor hypoglycaemic episodes (one trial); mean daily time and daily area under the CGMS curve for glucose below 3.89 mmol/L (one trial); mean daily area over the CGMS curve for glucose above 9.99 mmol/L (one trial); and ketoacidosis (one trial).

Local adverse effects were reported in two RCTs, including redness at the application site (23% children), redness and itching (16% children), and painful redness (one child). One child withdrew after 12 hours of CGMS due to skin irritation at the sensor site.

Authors' conclusions: The Continuous Glucose Monitoring System was not better than self-monitoring of blood glucose with regard to improvement of metabolic control among children with type 1 diabetes. The small number of participants and methodological limitations of the included trials mean these findings should be interpreted with caution.

CRD commentary: The review addressed a focused question and inclusion criteria were clearly defined. The literature search was adequate, but restriction of the review to published full text studies meant that there was a possibility of publication bias. Appropriate steps were taken at all stages of the review process to minimise bias and errors. Trial quality was formally assessed using appropriate criteria and the results were clearly reported. Relevant trial details were summarised in the text and in a table. The methods used to pool data appeared appropriate. The authors' conclusions are supported by the evidence and take into account the small sample sizes and methodological limitations of the included trials. One author disclosed financial links with Medtronic MiniMed (manufacturers of the Continuous Glucose Monitoring System equipment assessed in the review).

9. LEVEL 1: CRD SYSTEMATIC REVIEW

Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials, *Szypowska A, Ramotowska A, Dzygalo K, Golicki D,* Date abstract record published on CRD: 2 Jan 2013, Earlier publication: Eur J Endocrinol. 2012 Apr;166(4):567-74. doi: 10.1530/EJE-11-0642. Epub 2011 Nov 17

CRD summary: This review concluded that the use of real-time continuous glucose monitoring effectively lowered HbA1c in people with type 1 diabetes compared with self-monitoring of blood

glucose. The conclusions of this well-conducted review are limited by the low quality of the evidence and lack of long-term follow-up.

Authors' objectives: To evaluate the use of a real-time continuous glucose monitoring system compared with self monitoring of blood glucose in patients with type 1 diabetes.

Searching: PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1996 to March 2011. Search terms were reported and the reference lists of included papers and reviews were searched for additional studies.

Study selection: Randomised controlled trials with parallel or crossover designs that compared real-time continuous glucose monitoring systems with self-monitoring of blood glucose in the management of type 1 diabetes were eligible. Studies that used commercially available real-time glucose monitors were included. Only studies with the same insulin regimen or with a similar proportion of patients who used continuous subcutaneous insulin infusion or multiple daily injections in both experimental and control groups were included. Study duration had to be at least three months with a follow-up rate of over 80%. Studies performed in pre-sugical, post-surgical or cardiac care units or in pregnant women were excluded. The primary outcome was the change in haemoglobin a1c (HbA1c), secondary outcomes were major and minor hypoglycaemic episodes (as defined by the investigators), mean daily area under the continuous glucose monitoring curve less than 3.89 mmol/l, mean daily area over the continuous glucose monitoring curve less than 9.99 mmol/l, local adverse effects and quality of life. In most studies insulin pump therapy was used in both the experimental and control groups; in the rest the number of patients treated with continuous subcutaneous insulin infusion or multiple daily injections was comparable between groups. One study included a paediatric population only, one included adults only and the rest had mixed populations. Where reported the mean age in the study arms ranged from 8.5 to 44.6 years, one study reported an age range of 25 to 70 years. Two independent reviewers selected the studies.

Assessment of study quality: Study quality was assessed using the following criteria: allocation concealment; blinding of participants, investigators, outcome assessors and data analysts; intention-to-treat analysis; and comprehensive follow-up (greater than 80% of participants included in the final analysis). Study quality was assessed by independent reviewers.

Data extraction: The mean difference between groups was calculated for continuous outcomes and the risk ratio for binary outcomes, both with 95% confidence intervals. Data were extracted by two independent reviewers with disagreements resolved by consensus or referral to a third reviewer

Methods of synthesis: Study results were pooled using a fixed-effect model, a random-effects model was used in cases of substantial heterogeneity. Statistical heterogeneity was assessed with I^2 and substantial heterogeneity was represented by I^2 of 50% or more. Children and adults, and levels of glycaemic control were compared in subgroup analyses.

Results of the review: Seven trials were included (948 patients). Randomisation methods were described and considered adequate in four trials, allocation concealment was adequate in two trials, two trials used intention-to-treat analyses and two trials reported withdrawals and drop-outs. Follow-up ranged from 87 to 98% of participants during a follow-up period ranging from three to 12 months.

HbA1c: Compared with self-monitoring, real-time continuous glucose monitoring systems significantly reduced HbA1c both alone (mean difference (MD) -0.25; 95% CI: -0.34 to -0.17; seven trials) and when combined with an insulin pump (MD -0.26; 95% CI: -0.43 to -0.10; four trials). Heterogeneity was minimal in both analyses (I^2 of 0 and 4%). A statistically significant reduction in HbA1c was seen in subgroups with good and poor glycaemic control but there was no difference between adults and children.

Minor and major hypoglycaemic episodes: Minor hypoglycaemia was reported by five trials, one did not find any difference in hypoglycaemic episodes and the other four found no difference in the time spent in hypoglycaemia between real-time continuous glucose monitoring and self-monitoring. There was also no difference in major hypoglycaemic events (six trials).

Results for other outcomes were reported in the paper: hyperglycaemia, mean amplitude of glycaemic excursions, ketoacidosis and local adverse events, sensor compliance and quality of life.

Authors' conclusions: The use of real-time continuous glucose monitoring effectively lowered HbA1c in people with type 1 diabetes compared with self-monitoring of blood glucose.

CRD commentary: This review had a clear research question and specified inclusion criteria in enough detail to enable independent replication. Three relevant databases were searched but it was not reported

if any language restrictions applied or if there were efforts made to locate unpublished research so the risk of language and publication bias could not be ruled out. Review methods were performed independently to prevent errors or bias. Trial quality was assessed and reported in full. The statistical methods were appropriate and heterogeneity was low for most analyses. The conclusions of this well-conducted review are limited by the low quality of the evidence and lack of long-term follow-up.

10. LEVEL N/A: CLINICAL GUIDELINE

Continuous Glucose Monitoring: An Endocrine Society Clinical Practice Guideline (US guidelines), ***David C. Klonoff, Bruce Buckingham, Jens S. Christiansen, Victor M. Montori, William V. Tamborlane, Robert A. Vigersky, and Howard Wolpert*** **First Published Online: July 02 2013**

ABSTRACT

Objective: The aim was to formulate practice guidelines for determining settings where patients are most likely to benefit from the use of continuous glucose monitoring (CGM).

Participants: The Endocrine Society appointed a Task Force of experts, a methodologist, and a medical writer.

Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe both the strength of recommendations and the quality of evidence.

Consensus Process: One group meeting, several conference calls, and e-mail communications enabled consensus. Committees and members of The Endocrine Society, the Diabetes Technology Society, and the European Society of Endocrinology reviewed and commented on preliminary drafts of these guidelines.

Conclusions: The Task Force evaluated three potential uses of CGM: 1) real-time CGM in adult hospital settings; 2) real-time CGM in children and adolescent outpatients; and 3) real-time CGM in adult outpatients. The Task Force used the best available data to develop evidence-based recommendations about where CGM can be beneficial in maintaining target levels of glycemia and limiting the risk of hypoglycemia. Both strength of recommendations and quality of evidence were accounted for in the guidelines.

Summary of Recommendations

1.0 Real-time continuous glucose monitoring (RT-CGM) in adult hospital settings

1.1 We recommend against the use of RT-CGM alone for glucose management in the intensive care unit (ICU) or operating room until further studies provide sufficient evidence for its accuracy and safety in those settings.

2.0 RT-CGM in children and adolescent outpatients

2.1 We recommend that RT-CGM with currently approved devices be used by children and adolescents with type 1 diabetes mellitus (T1DM) who have achieved glycosylated hemoglobin (HbA1c) levels below 7.0% because it will assist in maintaining target HbA1c levels while limiting the risk of hypoglycemia.

2.2 We recommend RT-CGM devices be used with children and adolescents with T1DM who have HbA1c levels ≥7.0% who are able to use these devices on a nearly daily basis

2.3 We make no recommendations for or against the use of RT-CGM by children with T1DM who are less than 8 yr of age.

2.4 We suggest that treatment guidelines be provided to patients to allow them to safely and effectively take advantage of the information provided to them by RT-CGM.

2.5 We suggest the intermittent use of CGM systems designed for short-term retrospective analysis in pediatric patients with diabetes in whom clinicians worry about nocturnal hypoglycemia, dawn phenomenon, and postprandial hyperglycemia; in patients with hypoglycemic unawareness; and in patients experimenting with important changes to their diabetes regimen [such as instituting new insulin or switching from multiple daily injections (MDI) to pump therapy].

3.0 RT-CGM in adult outpatients

3.1 We recommend that RT-CGM devices be used by adult patients with T1DM who have HbA1c levels of at least 7.0% and who have demonstrated that they can use these devices on a nearly daily basis.

3.2 We recommend that RT-CGM devices be used by adult patients with T1DM who have HbA1c levels less than 7.0% and who have demonstrated that they can use these devices on a nearly daily basis.

3.3 We suggest that intermittent use of CGM systems designed for short-term retrospective analysis may be of benefit in adult patients with diabetes to detect nocturnal hypoglycemia, the dawn phenomenon, and postprandial hyperglycemia, and to assist in the management of hypoglycemic unawareness and when significant changes are made to their diabetes regimen (such as instituting new insulins or switching from MDI to pump therapy).

11. LEVEL 1: NICE GUIDELINE

NG18: Diabetes (type 1 and type 2) in children and young people: diagnosis and management, Published: 26 August 2015

1 RECOMMENDATIONS

1.2 Type 1 diabetes

Blood glucose monitoring

1.2.58 Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. [new 2015]

1.2.62 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). [new 2015]

HbA1c targets and monitoring

1.2.67 Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that an HbA1c target level of 48 mmol/mol (6.5%) or lower is ideal to minimise the risk of long-term complications. [new 2015]

12. LEVEL 1: NICE GUIDELINE

NG17: Type 1 diabetes in adults: diagnosis and management, Published: 26 August 2015

1 RECOMMENDATIONS

1.1 Diagnosis and early care plan

Continuous glucose monitoring

1.6.21 Do not offer real-time continuous glucose monitoring routinely to adults with type 1 diabetes. [new 2015]

1.6.22 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 level of 75 mmol/mol [9%] or higher) that persists despite testing at least 10 times a day (see recommendations 1.6.11 and 1.6.12). Continue real-time continuous glucose monitoring only if HbA1c can be sustained at or below 53 mmol/mol (7%) and/or there has been a fall in HbA1c of 27 mmol/mol (2.5%) or more. [new 2015]

1.6.23 For adults with type 1 diabetes who are having real-time continuous glucose monitoring, use the principles of flexible insulin therapy with either a multiple daily injection insulin regimen or continuous subcutaneous insulin infusion (CSII or insulin pump) therapy. [new 2015]

1.6.24 Real-time continuous glucose monitoring should 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. [new 2015]

Appendix 2 – Diagnostic and Procedure Codes

Real-Time Continuous Glucose Monitoring
GM039

(All codes have been verified by Mersey Internal Audit's Clinical Coding Academy)

GM039 - Real-Time Continuous Glucose Monitoring	
OPCS-4 procedure codes	
Insertion of diagnostic device into subcutaneous tissue	S62.7
With the following ICD-10 diagnosis code(s):	
Type 1 diabetes mellitus - with coma	E10.0
Type 1 diabetes mellitus - with ketoacidosis	E10.1
Type 1 diabetes mellitus - with renal complications	E10.2
Type 1 diabetes mellitus - with ophthalmic complications	E10.3
Type 1 diabetes mellitus - with neurological complications	E10.4
Type 1 diabetes mellitus - with peripheral circulatory complications	E10.5
Type 1 diabetes mellitus - with other specified complications	E10.6
Type 1 diabetes mellitus - with multiple complications	E10.7
Type 1 diabetes mellitus - with unspecified complications	E10.8
Type 1 diabetes mellitus - without complications	E10.9
Hypoglycaemia, unspecified	E16.2
Hyperosmolality and hypernatraemia	E87.0
Exceptions (ICD-10); the following in a primary diagnostic position:	
Pre-existing type 1 diabetes mellitus (assuming this is still related to diabetes patient that are pregnant)	Q24.0
Pre-existing type 2 diabetes mellitus	Q24.1
Pre-existing malnutrition-related diabetes mellitus	Q24.2
Pre-existing diabetes mellitus, unspecified	Q24.3
Diabetes mellitus arising in pregnancy	Q24.4
Diabetes mellitus in pregnancy, unspecified	Q24.9

Appendix 3 – Version History

Real-Time Continuous Glucose Monitoring
GM039

Version	Date	Details
0.1	16/04/2016	Initial draft
0.2	18/05/2016	Amendments made by GM EUR Steering Group on 18/05/2016: <u>Section 4. Criteria for Commissioning</u> • Paragraph added stating 'All requests for CGM should come from a secondary care diabetic service. The monitor requested should provide real time monitoring of blood glucose levels and should ideally incorporate a hypoglycaemia alarm'. • Under 'Adults': o Bullet point 1 amended to include 'requiring the intervention of another person to manage the episodes' and 'that has resulted in multiple daily testing of blood sugar levels by the individual or their carer.' o Bullet point 4 amended to add 'with supporting evidence of the reason for that fear'. • Under 'Children and young people aged under 18': o Note added stating 'Children with complex diabetes being managed by a specialised diabetic unit are covered by NHS England.' o Third bullet point added, preceded by 'AND' to state: 'Anxiety over the above has resulted in frequent testing of blood sugar in every 24 hour period.' • Paragraph under added under 'Patients already on CGM who do not meet the above criteria' regarding loans of CGM equipment and '(not on loan)' added after 'CGM' on second paragraph. • Recommended funding mechanism added for Individual Prior Approval.
0.3	20/07/2016	GM EUR Steering Group agreed the changes made to the policy since the last meeting and the following amendments: • Section 4 - Mandatory Criteria for Adults and Commissioning Recommendation: the wording *'in every 24 hour period'* added to the first sentence after the words *'at least 70% of the time'* in order to add clarification. Subject to the above change being made the GM EUR Steering Group agreed that the policy was ready to go out for a period of clinical engagement.
0.4	16/11/2016	Amendments made by the GM EUR Steering Group on 16/11/2016 following clinical engagement feedback: • New policy format applied. • 'Real-time' added throughout policy before 'CGM' • All instances of 'child' or 'children' changed to 'children and young people under 18' • <u>Policy Inclusion Criteria:</u> o 'Funding Mechanism' box added and text reworded for new policy format. o In first paragraph the word 'preferably' added. o Paragraph added (as 2nd paragraph) to state: 'Historic monitoring for reasons of improved management of an individual's diabetes either by themselves or the team caring for them is NOT covered by this policy and funding for these should be via a service development/business case.'

		o Under 'Adults', the word 'AND' inserted in the first bullet point o Under 'Children and young people aged under 18' the 'AND' before the 3rd bullet point changed to 'OR' and the following added after the same bullet point: *'ALSO* *Consider ongoing real-time CGM for:* • *neonates, infants and pre-school children* • *children and young people who undertake high levels of physical activity (for example, sport at a regional, national or international level)* • *children and young people who have comorbidities (for example anorexia nervosa) or who are receiving treatments (for example corticosteroids) that can make blood glucose control difficult.'* o The word 'already' removed from the heading 'Patients already using insulin pumps' and the word 'intentionally' added to the paragraph under this heading. o The word 'already' removed from the heading 'Patients already on CGM who do not meet the above criteria' and the word 'already' removed from the 2nd paragraph under this heading. • Policy Exclusions: Sentence added to state 'Real-time CGM in pregnancy is excluded from this policy – these patients should be managed in line with NICE NG3.' • Treatment / Procedure: the word 'usually' added to the second paragraph. • Adherence to NICE Guidance: the word 'fully' removed from the first sentence. • Glossary: 'blood sugar' replaced by 'interstitial' for 'Real-time CGM' and 'Retrospective CGM'
0.5	18/01/2017	The GM EUR Steering Group gave final approval of the amendments made at the last meeting (version 0.4) and approved the policy to proceed through the CCG Governance Process.
0.6	17/05/2017	Changes made at GM EUR Steering Group following feedback around funding mechanisms: Commissioning Statement • *'Policy Exclusions'* section moved to the beginning of the *'Commissioning Statement'.* • Under *'Adults'*, *'in line with NICE NG17'* inserted into the first paragraph and *'Funding Mechanism'* amended to state: *'Real-time CGM devices with hypoglycemia alarms: Monitored approval for individuals meeting NICE NG17: Referrals may be made in line with the criteria without seeking funding. NOTE: May be the subject of contract challenges and/or audit of cases against commissioned criteria.* *For all other cases including devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request.'* • Under *' Children and young people aged under 18', 'Funding Mechanism'* added to state: *'Real-time CGM devices with hypoglycemia alarms: Monitored approval for individuals meeting NICE NG18: Referrals may be made in line with the criteria without seeking funding. NOTE: May be the subject of contract challenges and/or audit of cases against commissioned criteria.* *For all other cases including devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with*

		the request.' • Under *'Patients using insulin pumps'*, *'Funding Mechanism' amended to state: 'Real time CGM devices with hypoglycemia alarms: Monitored approval for individuals meeting NICE NG17 or NG18: Referrals may be made in line with the criteria without seeking funding. NOTE: May be the subject of contract challenges and/or audit of cases against commissioned criteria.* *For all other cases including devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request.'* • *'Funding Mechanism'* under *'Patients on real-time CGM who do not meet the above criteria'* clarified to read: *'As per loan.* *If a loan is no longer available: Individual funding request (exceptional case) approval: Requests must be submitted with all relevant supporting evidence as to why this treatment should continue.'*
0.7	15/11/2017	The GM EUR Steering Group agreed following amendment to the policy: • Policy Exclusions: Statement and link to GMMMG recommendation for FreeStyle Libre Flash Glucose Monitoring Systems added
0.8	01/10/2018	Branding changed to reflect change of service from Greater Manchester Shared Services to Greater Manchester Health and Care Commissioning.
1.0	13/11/2018	Approved by Greater Manchester Directors of Commissioning / Greater Manchester Chief Finance Officers (Delegated authority given to approve policy by Greater Manchester Joint Commissioning Board). • Commissioning Statement: Best practice guidelines section added.
1.1	24/01/2019	• Links updated as documents have all moved to a new EUR web address. • Commissioning Statement: *'Best Practice Guideline'* section moved to bottom of *'Commissioning Statement'*
1.2	01/08/2019	Clinical Exceptionality Section updated to read: *Clinicians can submit an Individual Funding Request (IFR) outside of this guidance if they feel there is a good case for exceptionality. More information on determining clinical exceptionality can be found in the Greater Manchester (GM) Effective Use of Resources (EUR) Operational Policy. Link to GM EUR Operational Policy*
1.3	08/10/2019	Policy Exclusions - Link to GMMMG guidance on FreeStyle Libre updated
2.0	20/11/2019	Policy reviewed by the GM EUR Steering Group and the following amendments were agreed:- Policy Inclusion Criteria The second paragraph has been reworded from: *Historic monitoring for reasons of improved management of an individual's diabetes either by themselves or the team caring for them is **NOT** covered by this policy and funding for these should be via a service development/business case.* To: *Using CGM to monitor and record glucose levels over time for the sole purpose of improving an individual's diabetes control (by themselves or by the team caring for them) when they do not meet NG17 or 18 is not commissioned and is **NOT** covered by this policy and funding for these should be via a service development/business case.* The following paragraph has been added: *Patients who have self-funded these devices will only be eligible for NHS funding if they meet the criteria.*

		Children and young people aged under 18 Section the following note has been removed:- **NOTE:** Children and young people with complex diabetes being managed by a specialised diabetic unit are covered by NHS England. The words highlighted below have been added to the following sentence Real-time CGM with alarm is commissioned for children and young people with type 1 diabetes, in line with NICE NG 18, who have The funding mechanism changed from: For all other cases including devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request. To: For all other funding applications including those for devices without alarms: Individual prior approval provided the patient meets the above criteria. Requests should be submitted with all relevant supporting evidence, which must be provided with the request. Patients on real-time CGM who do not meet the above criteria Section Second paragraph reworded from: *Patients already using real-time CGM (not on loan) who do not meet the above criteria should be able to continue using the device until they and their NHS clinician consider it appropriate to stop.* To: Patients, who are already using real-time CGM provided by the NHS (does not include "on loan" devices) who do not meet the above criteria should be able to continue using the device until they and their NHS clinician consider it appropriate to stop. Replacement devices will require an application clearly stating the case for exceptionality if they do not meet the criteria. Date of Review: Date amended to state: Five years from the date of the last review, unless new evidence or technology is available sooner.
2.1	16/06/2020	Equality and Equity Statement – GM EUR Policy Team email address updated.