Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER363
Topic:	Real-time continuous glucose monitoring of people with type 1 and 2 diabetes
Summary of findings:	Diabetes mellitus constitutes a metabolic condition in which glucose levels are unusually elevated. Real-time continuous glucose monitoring systems enable the continuous display of the glucose concertation on a screen, while also notifying the person with diabetes about glucose fluctuations. This topic exploration report summarises evidence on the clinical and cost effectiveness of real-time continuous glucose monitoring for people with type 1 and 2 diabetes, including children, young people, adults, and pregnant women. We identified four, recently updated, guidelines (NG17, NG28, NG18 and NG3) in diabetes produced by the National Institute for Health and Care Excellence (NICE). We also identified four NICE technology appraisals undertaken to support the updates on both guidelines respectively. These appraisals compared real-time continuous glucose monitoring compared to self-monitoring of blood glucose (usual care) and/or intermittently scanned continuous glucose monitoring for each population. Of these NICE appraisals, three were also accompanied with economic evaluations of these systems. We have also identified one SHTG (2020) adaptation on continuous glucose monitoring in pregnant women with type 1 diabetes based on guidance produced by HTW (2021) as well as a MedTech innovation briefing (MIB233) developed by NICE (2020a), which will not be discussed in this evidence overview, but are included in the literature search results for completeness.

Introduction and aims

Diabetes mellitus constitutes a metabolic condition in which glucose levels are unusually elevated. There are four main diabetes classifications: (1) type 1 diabetes, (2) type 2 diabetes, (3) gestational diabetes mellitus, and (4) other diabetes types due to specific causes. Diabetes mellitus can lead to life-threatening consequences if it is not managed appropriately.

Self-monitoring of blood glucose is the most common blood glucose monitoring system, involving the measurement of capillary glucose via a blood glucose meter. Continuous glucose monitoring constitutes a newer method for assessing glucose levels, including (1) intermittently scanned continuous glucose monitoring (i.e., flash), and (2) real-time continuous glucose monitoring systems. The former is a method in which the glucose levels are measured continuously by a sensor, however the results are accessible only when the sensor is scanned by a reading device. Real-time continuous glucose monitoring system enables the continuous display of the glucose concertation on a screen, while also notifying the person with diabetes regarding glucose fluctuations. The information displayed can be also downloaded to a computer or similar device.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of real-time continuous glucose monitoring systems for people with diabetes type 1 or 2 (including children and pregnant women).

Evidence overview

Evidence standards

Real-time continuous glucose monitoring is a digital health technology and was determined to be a Tier C technology according to the [Evidence Standards Framework for Digital Health Technologies](#). Technologies within this classification are serve as interventions. If the continuous glucose monitoring device (or supporting app) automatically shares patient data with healthcare professionals or similar, then it would meet the 'active monitoring' classification, for which randomised controlled trials are recommended as the best evidence (NICE 2022a).

Guidance and guidelines

We identified four guidelines in diabetes produced by the National Institute for Health and Care Excellence (NICE):
- NICE (2015c): Type 1 diabetes in adults: diagnosis and management (NG17)
- NICE (2015d): Type 2 diabetes in adults: management (NG28)
- NICE (2015a): Diabetes (type 1 and type 2) in children and young people: diagnosis and management (NG18)
- NICE (2015b): Diabetes in pregnancy: management from preconception to the postnatal period (NG3)

The first three were recently updated in March 2022, while the fourth was updated in December 2020 based on four different technology appraisals performed by the NICE guideline development team. Across all studies included in these appraisals, the primary and secondary outcomes varied.

Type 1 diabetes in adults: diagnosis and management (NG17)
NG17 guidance (NICE 2015c) recommends that adults with type 1 diabetes should be offered the choice of real-time continuous glucose monitoring based on their individual characteristics, preferences, needs, and the functionality of the device available. NICE (2015c) also recommends that if several devices meet the individual's needs and preferences, the device with the lowest cost should be offered.

The evidence review for NG17 included 16 studies on real-time continuous glucose monitoring (NICE 2022b). Of these studies, three compared real-time continuous glucose monitoring and intermittently scanned continuous glucose monitoring (n = 354), while 13 compared real-time continuous glucose monitoring and standard self-monitoring of blood glucose (n = 1,399). They found that real-time continuous glucose monitoring showed effects in time in, below and above range, changes in glucose control target (HbA1c), glycaemic variability and hypoglycaemia compared with standard self-monitoring of blood glucose and intermittently scanned continuous glucose monitoring (NICE 2022b).

Type 2 diabetes in adults: management (NG28)
NG28 guidance recommends considering real-time continuous glucose monitoring as an alternative to intermittently scanned continuous glucose monitoring for adults with insulin-treated type 2 diabetes, if it is available for the similar or lower cost. NICE (2015d) also recommends that in case the individual person is offered real-time continuous glucose monitoring system, but cannot or does not want to use it, self-monitoring of blood glucose should be offered.

The evidence review for NG28 included eight studies focusing on real-time continuous glucose monitoring (NICE 2022d). Different populations were included in these studies comparing real-time continuous glucose monitoring with self-monitoring of blood glucose; of these studies, three included adults who used insulin only (n = 260), one included adults who did not use insulin (n = 30) and four included mixed population (n = 284). They found that real-time continuous glucose monitoring showed low to moderate effects in HbA1c, changes in body mass index, and severe hypoglycaemia compared with standard self-monitoring of blood glucose (NICE 2022d).

Diabetes (type 1 and type 2) in children and young people: diagnosis and management (NG18)
NG18 guidance recommends offering real-time continuous glucose monitoring to all children and young people with type 1 diabetes, combined with education to support them, their carers, and families on its usage. NICE (2015a) also recommends that the offer should be based on their individual characteristics, preferences, needs, and the functionality of the devices available, while in case the child or young person cannot or does not want to use it, self-monitoring of blood glucose should be offered.

The evidence review for NG18 included five studies comparing on real-time continuous glucose monitoring with self-monitoring of blood glucose (n= 418) (NICE 2022c). They found that real-time continuous glucose monitoring showed low to moderate effects in HbA1c, severe hypoglycaemia, and quality of life compared with standard self-monitoring of blood glucose (NICE 2022c).

Diabetes in pregnancy: management from preconception to the postnatal period (NG3)
NG3 guidance recommends offering real-time continuous glucose monitoring to all pregnant women with type 1 diabetes to support them meet their pregnancy blood glucose targets, while also improving neonatal outcomes (NICE 2015b).

The evidence review for NG3 included three studies (NICE 2020b); of these studies two compared real-time continuous glucose monitoring and self-monitoring of blood glucose (n= 479), while three compared real-time continuous glucose monitoring with intermittently scanned continuous glucose monitoring (n= 186). They found that there was no statistical significant difference in HbA1c and severe hypoglycaemia between real-time continuous glucose and self-monitoring of blood glucose (NICE 2015b, NICE 2020b).

We have also identified one SHTG (2020) adaptation on continuous glucose monitoring in pregnant women with type 1 diabetes based on guidance produced by HTW (2021), which will not be discussed in this evidence overview but is included in the literature search results for completeness.

Economic evidence

Both NICE NG17, NG28 and NG3 included de novo cost-utility analyses comparing real-time continuous glucose monitoring and flash glucose monitoring. Based on a threshold of £20,000 per QALY, base case results showed that real-time continuous glucose monitoring was not cost effective for type 1 diabetes (£24,400 per QALY) or type 2 diabetes (£45,791 per QALY) compared to self-monitoring of blood glucose. Based on a threshold of £30,000, real-time continuous glucose monitoring would be considered cost-effective for type 1 diabetes.

Regarding diabetes in pregnancy, the base case reported that flash glucose monitoring dominates both continuous glucose monitoring and self-monitoring of blood glucose, but that the difference between continuous and flash glucose monitoring was very small. Sensitivity analyses exploring just continuous glucose monitoring versus self-monitoring of blood glucose determined that continuous glucose monitoring would be very likely cost effective (i.e., with an ICER of ≤£20,000 per QALY) compared to self-monitoring of blood glucose.

Additionally, we have identified a MedTech innovation briefing (MIB233) developed by NICE (2020a), which will not be discussed in this evidence overview, however is included in the literature search results for completeness.

Areas of uncertainty

NICE has recently updated their guidelines on continuous glucose monitoring systems for type 1 and 2 diabetes for several populations (i.e., children, young people, adults, and pregnant women). All these updated guidelines have been supported by evidence reviews and economic analyses. Consideration would be needed as to how additional HTW appraisal could add value alongside the recent NICE recommendations.

This exploration report gives an overview of evidence on continuous glucose monitoring for all diabetes populations. Were this topic to be considered for fuller appraisal, additional refinement of the population and research question of interest may be required.

Literature search results

Health technology assessments and guidance

HTW. (2021). Continuous glucose monitoring systems for managing diabetes in pregnant women. Guidance GUI012. Health Technology Wales. Available at: https://healthtechnology.wales/wp-content/uploads/2019/10/GUI012-Continuous-glucose-monitoring-in-pregnant-women-with-type-1-diabetes-English-3.pdf [Accessed 11 May 2022].

NICE. (2015a). Diabetes (type 1 and type 2) in children and young people: diagnosis and management. NICE guideline NG18. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng18 [Accessed 11 May 2022].

NICE. (2015b). Diabetes in pregnancy: management from preconception to the postnatal period. NICE guideline NG3. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng3 [Accessed 11 May 2022].

NICE. (2015c). Type 1 diabetes in adults: diagnosis and management. NICE guideline NG17. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng17 [Accessed 11 May 2022].

NICE. (2015d). Type 2 diabetes in adults: management. NICE guideline NG28. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng28 [Accessed 11 May 2022].

NICE. (2020a). Dexcom G6 for real-time continuous glucose monitoring. Medtech innovation briefing MIB233. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/advice/mib233 [Accessed 11 May 2022].

NICE. (2020b). Diabetes in pregnancy: management from preconception to the postnatal period - Continuous glucose monitoring. Evidence Review NG3: Appendix [A]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng3/evidence/a-continuous-glucose-monitoring-pdf-8955770797 [Accessed 13 May 2022].

NICE. (2022a). Evidence standards framework for digital health technologies. Corporate document ECD7. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/corporate/ecd7 [Accessed 10 Aug 2022].

NICE. (2022b). Type 1 diabetes in adults: diagnosis and management - Evidence reviews for continuous glucose monitoring in adults with type 1 diabetes. Evidence Review NG17: Appendix [B]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng17/evidence/b-continuous-glucose-monitoring-in-adults-with-type-1-diabetes-pdf-11013435182 [Accessed 11 May 2022].

NICE. (2022c). Type 1 diabetes in children and young people: diagnosis and management - Evidence reviews for continuous glucose monitoring in children and young people with type 1 diabetes. Evidence Review NG18: Appendix [B]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng18/evidence/b-continuous-glucose-monitoring-in-children-and-young-people-with-type-1-diabetes-pdf-11011942190 [Accessed 13 May 2022].

NICE. (2022d). Type 2 diabetes in adults: diagnosis and management - Evidence reviews for continuous glucose monitoring in adults with type 2 diabetes. Evidence Review NG28: Appendix [C]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng28/evidence/c-continuous-glucose-monitoring-in-adults-with-type-2-diabetes-pdf-11013297805 [Accessed 13 May 2022].

SHTG. (2020). Continuous glucose monitoring in pregnant women with type 1 diabetes. SHTG Adaptation 01. Scottish Health Technologies Group. Available at: https://shtg.scot/our-advice/continuous-glucose-monitoring-in-pregnant-women-with-type-1-diabetes/ [Accessed 11 May 2022].

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Concepts used:	diabetes (type 1 or type 2); adults; children; continuous glucose monitoring or CGM; self-monitoring blood glucose or SMBG or fingerstick; intermittently scanned continuous glucose monitoring or isCGM; glucose control target or HbA1c; hypoglyca?mia; hyperglyca?mia; glucose level*