Technoleg Iechyd Cymru
Health Technology Wales

HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 004-2 (July 2021)

Freestyle Libre flash glucose monitoring for the management of diabetes

HTW Guidance:

The evidence supports the routine adoption of Freestyle Libre flash glucose monitoring to guide blood glucose regulation in people with diabetes who require treatment with insulin.

The use of Freestyle Libre flash glucose monitoring in these people improves the proportion of time that the blood glucose is in target range and reduces time in hypo and hyperglycaemia.

Health economic modelling indicates that the use of Freestyle Libre flash glucose monitoring is a cost effective intervention compared to finger-prick self monitoring of blood glucose with incremental cost effectiveness ratios (ICERs) of £4,706 and £13,137 per QALY for type 1 and type 2 diabetes, respectively.

Why did Health Technology Wales (HTW) appraise this topic?

Maintaining the blood glucose concentration as close as possible to the normal range is an important objective for successful diabetes care since this helps to minimize short and long term complications. Regular blood glucose measurements are essential throughout the day for many people with diabetes, particularly those receiving insulin treatment, to guide treatment and nutrition decisions and to avoid the potentially serious consequences of blood glucose being too low (hypoglycaemia) or too high (hyperglycaemia). The standard means of monitoring blood glucose involves finger-prick testing (self-monitoring of blood glucose, SMBG). The Freestyle Libre flash glucose monitoring (FLFGM) technology provides an alternative to this by measuring the glucose level in subcutaneous tissue using a disposable sensor applied to the upper arm. Glucose levels recorded by the sensor are accessed by scanning over the sensor using either a dedicated reader or a mobile phone app. This means that a 'snapshot' as well as a trend in blood glucose can be obtained to guide decision-making.

HTW originally issued Guidance on FLFGM in November 2018. HTW Guidance is periodically updated when necessary. Following consultation with stakeholders, HTW agreed it was appropriate to issue updated Guidance, since there has been a substantial change in the available evidence since the original Guidance was published.

The status of HTW guidance is that NHS Wales should adopt this guidance or justify why it has not been followed. HTW will evaluate the impact of its guidance.

Evidence Summary

Refer to Evidence Appraisal Report 004-2 (EAR044-2) for a full report of the evidence supporting this Guidance.

- The EAR aimed to identify and summarise evidence that addresses the following question: What is the clinical and cost effectiveness of flash glucose monitoring in people with diabetes? This rapid review used evidence from randomised controlled trials (RCTs), existing evidence reviews, and non-randomised trials if limited outcome data from RCTs was available.
- Seven RCTs compared flash glucose monitoring to SMBG in people with type 1 or type 2 diabetes, the majority of whom were treated with insulin. All of the studies used the Freestyle Libre device (either Freestyle Libre or Freestyle Libre 2) and it was noted that the functionality of these two device iterations in terms of blood glucose measurement and monitoring is not significantly different. Overall, the results suggest FLFGM is beneficial in terms of improving time spent in target glucose range (and thus avoiding episodes or hypo- or hyperglycaemia), although it should be noted that not all trials found conclusive evidence of a difference between the two interventions. The evidence also suggests people who use FLFGM are able to check their glucose more frequently by scanning the device than those who use SMBG. For other outcomes (glycosylated haemoglobin levels, quality of life, and device-related adverse events) there was no convincing evidence of a difference between FLFGM and SMBG.
- Large-scale audits of real-world evidence suggest a reduction in paramedic callouts, hospital admissions, visits to diabetes/endocrine specialists and primary care visits following initiation of FLFGM over follow up times of 7.5 to 14 months. However, this evidence is of lower certainty than the evidence derived from RCTs.
- Evidence from three cost-utility analyses identified in the literature showed the potential for FLFGM to be cost-effective in cost per QALY terms. However, there was uncertainty around key assumptions in the analyses, such as the inclusion of a process-related improvement in quality of life associated with using flash glucose monitoring.
- A cost-utility analysis developed by HTW aimed to provide a more conservative estimate of the cost-effectiveness of FLFGM since it was based only on reductions in non-severe hypoglycaemic events and SMBG usage. The results suggest that FLFGM is a cost effective intervention compared to usual care with incremental cost effectiveness ratios (ICERs) of £4,706 and £13,137 per QALY for type 1 and type 2 diabetes, respectively. Sensitivity analysis showed that the key areas of uncertainty were the baseline SMBG testing frequency and the quality of life benefits associated with reducing non-severe hypoglycaemic events.
- The appropriate mechanism for patient engagement was determined and the patient perspective was considered where possible. A written patient submission from Diabetes UK Cymru was included in the appraisal. A literature search was also undertaken to report experiences, perspectives and opinions of patients with this condition and their experiences of blood glucose monitoring.

Appraisal Panel considerations

- The Appraisal Panel heard from a representative of Diabetes UK Cymru, and from clinical experts, that management of diabetes can be very challenging for some people who need to monitor their blood glucose regularly. Specifically, people with diabetes can feel overwhelmed by managing their condition and the challenges of regular blood glucose monitoring using SMBG can be a major contributory factor to this. Experts explained that the consequences of uncontrolled blood glucose levels include the immediate risks of hypoglycaemic events, which are frightening and potentially dangerous, as well as a wide range of long-term diabetic complications which can be disabling. The Appraisal Panel concluded, therefore, that the use of a novel technology to optimize blood glucose regulation is likely to have potentially important clinical benefits especially if it is easy to use and allows for more frequent assessment of blood glucose levels.
- The Appraisal Panel discussed the evidence on the clinical effectiveness of flash glucose monitoring (see Evidence Summary, above) and noted that all of the relevant studies used the Freestyle Libre device (either Freestyle Libre or Freestyle Libre 2) and this is the only FLFGM technology that is commercially available for use by patients in the UK. The clinical experts advised that patients included in RCTs are not necessarily entirely representative of those that they manage in their day-to-day clinical practice and that the results of observational studies are also relevant to understanding the potential impact of FLFGM on clinical and healthcare system outcomes. For example, patients who either choose not to or are unable to regularly perform SMBG are unlikely to be included in RCTs and yet they may, potentially, have the most to gain from an alternative technology-based approach such as FLFGM. The Appraisal Panel concluded that while the decision-making emphasis would be placed mostly on the results of the RCTs, it was also important to consider the results of observational studies as well, especially those that had been undertaken in the UK in which the results were of particular relevance to the UK healthcare system.
- The Appraisal Panel noted that while most of the published evidence compared FLFGM with SMBG, there are a smaller number of studies that compared FLFGM with real-time continuous glucose monitoring. The Panel concluded, however, that there was insufficient evidence from these studies on which to base any firm conclusions about the comparative clinical effectiveness of these two technologies. Furthermore, the clinical experts stated that in Wales, real-time continuous glucose monitoring is not widely used to monitor blood glucose, and is restricted, instead for use in very specific groups of people with diabetes such as those who are pregnant. The Appraisal Panel concluded, therefore, that the comparison of FLFGM with SMBG is most relevant in determining the clinical and cost effectiveness of flash glucose monitoring in this assessment.
- The Appraisal Panel concluded from the RCTs that compared FLFGM with SMBG, that there is convincing evidence of improvements in the time spent in target blood glucose range and in biochemical hypo or hyperglycaemia in patients using FLFGM. They also noted, however, that this was not necessarily translated into consistent reductions in glycosylated haemoglobin or a reduction in clinically important hypoglycaemic events, although the latter were infrequently reported in the studies. On the other hand, the Panel noted from the real-world data that was reported in the observational studies, that there was improvement in important outcomes with FLFGM such as healthcare utilisation including paramedic callouts and hospital admissions. While it was acknowledged that the results of these studies alone are associated with uncertainty, the Appraisal Panel concluded that the results are influential since they corroborate the potential for important clinical benefits through the use of FLFGM.
- The Appraisal Panel considered the economic analysis developed by HTW, which showed FLFGM to be cost effective on the basis of reductions in non-severe hypoglycaemic events and SMBG use. This was noted to be a conservative analysis since it did not consider further potential clinical and healthcare benefits suggested in the real-world observational studies

(such as reductions in hospital admissions for hypoglycaemic and in hyperglycaemic events). Sensitivity analysis showed that the inclusion of such benefits would further improve the cost effectiveness of flash glucose monitoring.

- Based on the clinical and cost effectiveness evidence, the Appraisal Panel concluded that the evidence supports the routine adoption of FLFGM for people with diabetes (of any type) who require treatment with insulin. It was noted that there are a range of additional specific scenarios in which FLFGM may also potentially offer benefit, such as:
    - people who cannot use current forms of glucose monitoring, or for whom use may be distressing, such as those with dementia, learning disabilities or needle phobias;
    - people who need extra care or assistance with glucose monitoring, such as children or the elderly;
    - people who need a course of intensive glucose monitoring in order to assist treatment decisions.
- While the Appraisal Panel noted that there is no published evidence reporting the impact of FLFGM in these groups of patients, they concluded that this technology offers a potential means by which glucose monitoring may be offered to cohorts of patients in whom SMBG may not be currently be undertaken or is not feasible. Further data on the use of FLFGM in these cohorts would be welcome.
- The Appraisal Panel also noted that FLFGM may not be suitable for all people with diabetes that require insulin and noted, for example, that some patients have experienced intolerable adverse reactions as a result of sensor wear, while others may not be able to tolerate the sensation of continuously wearing the sensor (such as people with autism).

Responsibilities for consideration of this Guidance

Health Technology Wales (HTW) was established by Ministerial recommendation[1,2] to support a strategic, national approach to the identification, appraisal and adoption of non-medicine health technologies into health and care settings. The HTW Appraisal Panel comprises senior representation from all Welsh boards with delegated authority to produce guidance 'from NHS Wales, for NHS Wales'. The status of HTW guidance is 'adopt or justify'. There is an expectation from Welsh Government that HTW guidance is implemented with adoption regularly audited by HTW.[3]

The guidance in this document is intended to assist Welsh care system decision makers to make evidence-informed decisions when determining the place of health technologies and thereby improve the quality of care services.

The content of this HTW guidance was based upon the evidence and factors available at the time of publication. An international evidence base was reviewed and external topic experts and HTW committee members consulted to contextualise available evidence to Wales. Readers are asked to consider the generalisability of the evidence reviewed to NHS Wales and that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. It is acknowledged that evidence constitutes only one of the sources needed for decision making and planning.

This guidance does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

No part of this guidance may be used without the whole of the guidance being quoted in full. This guidance represents the view of HTW at the date noted. HTW guidance is not routinely updated. It may, however, be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the guidance given.

Standard operating procedures outlining HTW's evidence review methods and framework for producing its guidance are available from the HTW website.

Acknowledgements. HTW would like to thank the individuals and organisations who provided comments on the draft Evidence Appraisal Report or HTW guidance.

Declarations of interest were sought from all reviewers. All contributions from reviewers were considered by HTW's Assessment Group. However, reviewers had no role in authorship or editorial control and the views expressed are those of Health Technology Wales.

Chair, Health Technology Wales Appraisal Panel

1. National Assembly for Wales, Health and Social Care Committee. Access to medical technologies in Wales. December 2014.
2. Response to Recommendations from the Health & Social Care Committee: Inquiry into Access to Medical Technologies in Wales. February 2015.
3. Gething, V. Letter to all Health Board Chairs re Funding for Sacral Nerve Stimulation in Wales. VG_01655_17. September 2017.