Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report [1]

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	TER556
Topic	Point-of-care blood glucose monitoring systems for diagnosis and management of hypoglycaemia in neonates
Summary of findings	One of the most common and critical metabolic issues for neonates is hypoglycaemia. It is often asymptomatic and can lead to neurological damage, seizures, permanent damage and death if untreated. Early diagnosis and management is therefore critical. No technology assessments or systematic reviews were identified that specifically referred to point-of-care blood glucose monitoring tests for the diagnosis and management of hypoglycaemia in neonates. There is limited, low quality evidence on the effectiveness of point-of-care blood glucose monitoring systems for diagnosis and management of hypoglycaemia in neonates. Evidence appears to suggest that the accuracy of these systems may be acceptable, but there are a lack of patient outcomes reported. It is unclear whether the use of point-of-care blood glucose monitoring systems in neonates would result in the improvement of important clinical outcomes, such as hospitalisation and mortality. No economic evaluations of point-of-care blood glucose monitoring systems in neonates were identified. Further research and economic evaluations are required to evaluate the clinical and cost-effectiveness of point-of-care blood glucose monitoring systems for diagnosis and management in neonates.

[1] Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg
Translation of published technical HTW documents from English into Welsh

Introduction and aims

One of the most common and critical metabolic issues for neonates is hypoglycaemia. It is often asymptomatic and can lead to neurological damage, seizures, permanent damage and death if untreated. Early diagnosis and management is therefore critical.

The British Association of Perinatal Medicine (BAPM) provided a framework for practice on the identification and management of neonatal hypoglycaemia in the full-term infant (2017). The framework stipulates that ward-based blood gas biosensors should be considered the reference standard for measuring blood glucose based on accuracy and speed of result availability. BAPM state that blood gas analysers produce glucose results as a calculated 'plasma glucose equivalent' concentration that should agree with laboratory plasma glucose results in the majority of cases, and they have the advantage of accessibility and speed in most maternity and newborn facilities.

The topic proposer has suggested that the view of The National Point of Care Testing Strategy Group is that appropriate hand-held capillary blood glucose devices should be an option for blood glucose monitoring in neonates; that they recommend their use as the method of choice, whilst also maintaining the option for the use of blood gas analysers for capillary whole blood glucose measurement. The topic proposer has also highlighted that using point-of-care systems reduces the sample volume by a clinically significant amount, making the process less traumatic for the neonate and potentially increasing the success rate of sampling and obtaining a valid test result.

Health Technology Wales researchers searched for evidence on clinical and cost-effectiveness of point-of-care blood glucose monitoring systems for diagnosis and management of hypoglycaemia in neonates.

Evidence overview

Secondary evidence

No technology assessments or systematic reviews were identified that specifically referred to point-of-care blood glucose monitoring tests for the diagnosis and management of hypoglycaemia in neonates.

Primary Evidence

The current International Organization for Standardization (ISO) standard 15197:2013 for in vitro diagnostic test systems details the requirements for blood glucose monitoring systems for self-testing (ISO, 2013). HTW researchers excluded older (≤2013) primary studies which used the superseded standard 15197:2003 (with less stringent accuracy criteria and a lack of the evaluation of the influence of factors such as haematocrit; ISO, 2003).

A multicenter study in the US (Nichols et al. 2021) evaluated the performance of the Roche Accu-Chek® Inform II point-of-care blood glucose monitoring system compared with the perchloric acid hexokinase comparator method on the Roche Cobas® 6000 analyser in critically ill patients (n=476), including neonates (n=100). For the latter population, the proportions of results within evaluation boundaries 1 and 2, respectively, were 84% and 98% for arterial samples, and 96% and 100% for heel-stick samples. The authors reported that clinical evaluation demonstrated high specificity and sensitivity, with low risk of potential insulin-dosing errors.

Kim and Yoon (2021) evaluated three i-SENS glucometers (BAROzen H Expert plus, CareSens PRO, and CareSens H Beat) and the ACCU-CHEK® Inform II glucometer. Leftover capillary blood samples from 319 neonates were analysed, using the YSI 2300 STAT Plus Analyzer as a reference. Acceptable accuracy was reported by the authors based on ISO standard 15197:2013.

Sheen et al. (2023) carried out a cross-sectional study in Taiwan to evaluate the accuracy of two wireless glucometers that link to mobile devices (Bayer CONTOUR PLUS and CONTOUR PLUS ONE) when used as point-of-care devices for blood glucose monitoring in neonates (n=114) and critically ill adults (n=106). Both glucometers reportedly had good precision, and all

Evidence overview

findings met the reference criteria of the within-lot results. The accuracy criteria specified by ISO standard 15197:2013 were met by both glucometers for all neonate venous blood measurements. An earlier study by Dietzen at al. (2015) evaluated older COUNTOUR systems, concluding that they exceeded ISO standard 15197:2013 and Clinical and Laboratory Standards Institute (CLSI) criteria in neonatal blood samples.

A Japanese study by Wada et al. (2014) evaluated the performance of the Nova StatStrip point-of-care blood glucose monitoring system and the self-monitoring blood glucose device, Terumo Medisafe Mini in screening for neonatal hypoglycaemia. A total of 222 samples were analysed from 213 neonates. StatStrip results were more closely aligned to those of the blood gas analyser ABL825 (at all levels of glucose) than the Medisafe Mini.

Lockyer et al. (2014) evaluated point-of-care glucose analysers against the central laboratory analysis of glucose using the Vitros 5600. The Nova StatStrip glucometer demonstrated an excellent coefficient of variation (< 5%) for glucose across the entire analytical measurement range. The StatStrip also had good concordance with the central laboratory (Bland–Altman plots r^2=0.01), while Roche Accu-check Inform had poorer correlation (Bland–Altman plots r^2=0.46). The StatStrip had minimal to no interference from haematocrit levels or maltose. Similarly, Tendl et al. (2013) reported that StatStrip values correlated well with those from the reference blood gas analyser across a wide glucose concentration range and were not affected by haematocrit levels. In contrast, Kitsommart et al. (2013) concluded from a prospective cross-sectional study of 172 neonate venous blood samples that the StatStrip and the SureStep Flex both have limited use compared to plasma glucose. They suggest that the devices can only be employed as screening tools in at-risk neonates with an appropriate, predetermined cut-off level. Mean (SD) plasma glucose in the study was 2.12 (0.45) mmol/L (range, 1.11-3.06 mmol/L). Mean (1.96SD) glucose differences of the StatStrip versus SureStep Flex were 0.21 (0.70) mmol/L and -0.04 (0.78) mmol/L, respectively. Sensitivity and negative predictive value (NPV) at 2.8mmol/L was 94.7 % and 86.1% respectively for Statstrip, compared to SureStep 100% values at the same cut-off level. Accuracy of both devices was not affected by haematocrit and bilirubin levels.

Point-of-care testing using the B Braun Glucometer and the Hemocue Glucose 201+ Analyser was compared to centralised testing in the neonatal intensive care unit (NICU) in a study (n=73) by Reddy et al. (2014). Blood glucose values (100.2 + 48.4) from the B Braun Glucometer were significantly higher (p=0.003) when compared to laboratory plasma glucose values (76.95 + 45.99) and those from the HemoCue Glucose 201+ Analyser (82.9 + 51.4). No significant difference was observed with the HemoCue Glucose 201+ Analyser compared to laboratory testing. The authors concluded that the HemoCue Glucose 201+ Analyser appears to be a suitable point-of-care blood glucose measurement device in neonates on both capillary and venous blood samples, as it showed a good correlation with central laboratory values without significant interference from haematocrit.

Economic evaluations

HTW researchers did not identify any economic evaluations on point-of-care blood glucose monitoring for diagnosis and management of hypoglycaemia in neonates.

Areas of uncertainty

- There is limited, low quality evidence on the effectiveness of point-of-care blood glucose monitoring systems for diagnosis and management of hypoglycaemia in neonates. Evidence focuses on accuracy, with a lack of patient outcomes reported.
- It is unclear whether the use of point-of-care blood glucose monitoring systems in neonates would result in the improvement of important clinical outcomes, such as hospitalisation and mortality.
- No economic evaluations of point-of-care blood glucose monitoring systems in neonates were identified.

Areas of uncertainty
• Further research and economic evaluations are required to evaluate the clinical and cost-effectiveness of point-of-care blood glucose monitoring systems in neonates.

Literature search results

Health technology assessments, guidance, guidelines and standards

British Association of Perinatal Medicine. (2017). Identification and management of neonatal hypoglycaemia in the full term infant - Framework for practice, 2017. Available at: https://www.bapm.org/resources/40-identification-and-management-of-neonatal-hypoglycaemia-in-the-full-term-infant-2017 [Accessed 25 June 2024].

International Organization for Standardization. (2013). ISO 15197:2013: In vitro diagnostic test systems — Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus; Edition 2; reviewed 2018. Available at: https://www.iso.org/standard/54976.html [Accessed 26 June 2024].

International Organization for Standardization. (2003). ISO 15197:2003: In vitro diagnostic test systems — Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus; Edition 1. Available at: https://www.iso.org/standard/26309.html [Accessed 26 June 2024].

Evidence reviews and economic evaluations

No relevant evidence found

Individual studies

Dietzen DJ, Nenninger DA, Simmons DA, et al. (2015). Analytic characteristics of three Bayer contour blood glucose monitoring systems in neonates. Journal of Diabetes Science and Technology. 9(2): 257-61. doi: https://doi.org/10.1177%2F1932296814557669.

Kim HN and Yoon SY. (2021). Comparative study of i-SENS glucometers in neonates using capillary blood samples. Clinical Chemistry and Laboratory Medicine. 59(6): 1133-41. doi: https://doi.org/10.1515/cclm-2020-1367.

Kitsommart R, Ngerncham S, Wongsiridej P, et al. (2013). Accuracy of the StatStrip versus SureStep Flexx glucose meter in neonates at risk of hypoglycemia. European Journal of Pediatrics. 172(9): 1181-6. doi: https://doi.org/10.1007/s00431-013-2019-2.

Lockyer MG, Fu K, Edwards RM, et al. (2014). Evaluation of the Nova StatStrip glucometer in a pediatric hospital setting. Clinical Biochemistry. 47(9): 840-3. doi: https://doi.org/10.1016/j.clinbiochem.2014.01.004.

Nichols JH, Brandler ES, Fantz CR, et al. (2021). A multicenter evaluation of a point-of-care blood glucose meter system in critically ill patients. Journal of Applied Laboratory Medicine. 6(4): 820-33. doi: https://doi.org/10.1093/jalm/jfab005.

Reddy VRS, Sumathi ME, Gowda YCB et al. (2014). Comparison of point of care (POC) testing of glucose by B Braun Glucometer and Hemocue Glucose 201+ Analyser versus centralised testing in Neonatal Intensive Care Unit (NICU). Journal of Clinical and Diagnostic Research. 8(7): PC10-3. doi: https://doi.org/10.7860/jcdr/2014/8666.4538.

Sheen YJ, Wang JM, Tsai PF, et al. (2023). Accuracy of point-of-care blood glucometers in neonates and critically ill adults. Clinical Therapeutics. 45(7): 643-8. doi: https://doi.org/10.1016/j.clinthera.2023.05.005.

Tendl KA, Christoph J, Bohn Aet al. (2013). Two site evaluation of the performance of a new generation point-of-care glucose meter for use in a neonatal intensive care unit. Clinical Chemistry and Laboratory Medicine. 51(9): 1747-54. doi: https://doi.org/10.1515/cclm-2012-0864.

Wada Y, Nakamura T, Kaneshige M, et al. (2015). Evaluation of two glucose meters and interference corrections for screening neonatal hypoglycemia. Pediatrics International. 57(4): 603-7. doi: https://doi.org/10.1111/ped.12543.

Ongoing research

No ongoing studies that have recently closed or are due to complete in the next 6-12 months were identified.

Date of search	June 2024
Concepts used	Accu-Check; blood glucose; Contour; hypoglycaemia; hypoglycemia; infant; neonatal; neonate; point-of-care test (POCT); StatStrip.

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	**Are point-of-care blood glucose monitoring systems clinically and cost-effective for diagnosis and management of hypoglycaemia in neonates?**

	Inclusion criteria	Exclusion criteria
Population	Neonates	Adults Other paediatric populations?
Intervention	Point-of-care blood glucose monitoring systems	
Comparison/ Comparators	Conventional blood glucose analysers (not point-of-care)	
Outcome measures	Accuracy Time to diagnosis Complications, duration of hospital stay, hospitalisations, mortality Health related QoL Resource use Economic outcomes	

Proposed specialities	**Blood and immune system; endocrine, nutritional and metabolic; health service organisation and delivery; paediatrics**