



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:

1. Inform discussions on new topics received by HTW.
2. Determine the quantity and type of evidence available on a topic.
3. Assess the topic against HTW selection criteria.

Topic:	Point-of-care procalcitonin testing for the assessment and treatment of sepsis in children
Topic exploration report number:	TER009
Referrer:	Martin Edwards, Cardiff and Vale University Health Board
Topic exploration undertaken by:	Health Technology Wales

Aim of Search

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of point-of-care procalcitonin testing in the assessment and treatment of sepsis in children.

Summary of Findings

The search identified one UK technology appraisal published by NICE (Diagnostics Guidance 18) in 2015, along with several other systematic reviews and economic evaluations studying procalcitonin testing in the diagnosis of sepsis. However, these varied in terms of the age of the populations studied, the setting in which they were used, and the exact type of test used. Most notably, NICE DG18 only assessed laboratory-based procalcitonin testing: point-of-care tests were not included in the scope of the assessment. Further investigation would be needed to establish which sources of evidence would be relevant to this topic, and whether these differ substantially from the evidence used in NICE DG18.

Technology appraisals

NICE DG18 was published in 2015 and assessed the clinical and cost effectiveness of using laboratory-based (but not point of care) procalcitonin testing to guide antibiotic therapy in people (of any age) with confirmed or highly suspected sepsis in intensive care, or people presenting to the emergency department with suspected bacterial infection. The recommendations state that “The procalcitonin tests ... show promise but there is currently insufficient evidence to recommend their routine adoption in the NHS.” The use of procalcitonin testing was assessed separately in children, but no age-specific recommendations were made.

Systematic reviews

Several systematic reviews were identified assessing either the diagnostic accuracy of procalcitonin testing in the diagnosis of sepsis, and/or the use of procalcitonin testing to guide subsequent treatment in bacterial infections or suspected sepsis. Four reviews (Pontrelli 2017; Tripella 2017; Yo 2012; Thompson 2012) studied children and four reviews (Chiesa 2015; Hedegaard 2015; Vouloumanou 2011; Yu 2010) studied neonates specifically. All of the most recent reviews only assessed the diagnostic performance of the test, and did not report health outcomes after PCT-guided treatment. Several other reviews included adults as well as children: the most recent (Shafiq, 2017) reached similar conclusions to NICE DG18: PCT-guided treatment reduced duration of antibiotic treatment, but did not improve health outcomes (mortality, duration of stay, ICU admission rates). None of the reviews specifically studied point of care testing.

Economic evaluations

Two economic evaluations were identified, both of which assessed procalcitonin testing for the assessment of sepsis and to guide subsequent decision making about antibiotic treatment. None of these studied children or point of care testing specifically. One evaluation (Westwood 2015) was conducted from the UK NHS perspective as part of NICE DG18 and was informed by a concurrent systematic review. The second evaluation was conducted from the perspective of the Canadian healthcare system and published in 2011.

Conclusions

Evidence exists about the clinical and cost-effectiveness of procalcitonin testing for the diagnosis of sepsis and to guide subsequent antibiotic therapy. However, the majority of evidence is not specific to children or to point of care testing. NICE DG18 evaluated procalcitonin testing in all age groups in 2015 (this assessment did not include point of care tests). The exploratory search did not identify any sources of secondary evidence published subsequent to this guidance that are likely to alter the conclusions.

Areas of Uncertainty

It is unclear whether sufficient evidence exists to assess the use of procalcitonin testing specifically as a point-of-care test in children. It is not clear whether it would be appropriate or feasible to extrapolate evidence from the wider evidence base to this specific scenario.

Feasibility of Technology Assessment

HTW's Assessment Group concluded to progress this topic to Evidence Appraisal. The findings will be published as Evidence Review EAR006, which will also outline the agreed inclusion criteria for the evidence review.

Brief literature search results

Resource	Results
<p>SIGN</p> <p>NICE (guidelines, technology appraisals, diagnostics guidance, interventional procedures, medical technologies)</p>	<p>We did not identify any relevant results from this source.</p> <p>NICE Diagnostics Guidance DG18. Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay). October 2015. https://www.nice.org.uk/guidance/dg18</p>
<p>CRD database</p>	<p>Economic evaluations</p> <p>Deliberato RO, Marra AR, Sanches PR, Martino MD, Ferreira CE, Pasternak J, Paes AT, Pinto LM, dos Santos OF, Edmond MB. Clinical and economic impact of procalcitonin to shorten antimicrobial therapy in septic patients with proven bacterial infection in an intensive care setting. <i>Diagn Microbiol Infect Dis.</i> 2013 Jul;76(3):266-71. doi: 10.1016/j.diagmicrobio.2013.03.027. Epub 2013 May 25. PMID: 23711530.</p> <p>Systematic reviews</p> <p>Yo CH, Hsieh PS, Lee SH, Wu JY, Chang SS, Tasi KC, Lee CC. Comparison of the test characteristics of procalcitonin to C-reactive protein and leukocytosis for the detection of serious bacterial infections in children presenting with fever without source: a systematic review and meta-analysis. <i>Ann Emerg Med.</i> 2012 Nov;60(5):591-600. doi: 10.1016/j.annemergmed.2012.05.027. Epub 2012 Aug 22. PMID: 22921165</p> <p>Systematic reviews with economic evaluation</p> <p>Westwood M, Ramaekers B, Whiting P, Tomini F, Joore M, Armstrong N, Ryder S, Stirk L, Severens J, Kleijnen J. Procalcitonin testing to guide antibiotic therapy for the treatment of sepsis in intensive care settings and for suspected bacterial infection in emergency department settings: a systematic review and cost-effectiveness analysis. <i>Health Technol Assess.</i> 2015 Nov;19(96):v-xxv, 1-236. doi: 10.3310/hta19960</p>
<p>evidence.nhs.uk/</p>	<p>Systematic reviews</p> <p><i>Clin Microbiol Infect.</i> 2015 May;21(5):474-81. Jan 14. The diagnostic accuracy of procalcitonin for bacteraemia: a systematic review and meta-analysis. Hoeboer SH. https://www.ncbi.nlm.nih.gov/pubmed/25726038</p>

	<p>A meta-analysis to assess usefulness of procalcitonin-guided antibiotic usage for decision making. Shafiq N. 2017. https://www.ncbi.nlm.nih.gov/pubmed/29512600</p> <p>Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. Schuetz, 2017 https://doi.org/10.1016/S1473-3099(17)30592-3</p> <p>AHRQ. Systematic review of Procalcitonin-Guided Antibiotic Therapy. 2012 https://effectivehealthcare.ahrq.gov/topics/procalcitonin/research</p> <p>Thompson M, Van Den Bruel A, Verbakel J, Lakhanpaul M, Haj-Hassan T. Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care. Health Technol Assess 2012;16(15). https://doi.org/10.3310/hta16150</p> <p>Vouloumanou 2011. Serum procalcitonin as a diagnostic marker for neonatal sepsis: a systematic review and meta-analysis. https://doi.org/10.1007/s00134-011-2174-8</p> <p>Wacker C, Prkno A, Brunkhorst FM, Schlattmann P. Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. Lancet Infectious Diseases 2013; 13(5): 426-435. http://dx.doi.org/10.1016/S1473-3099(12)70323-7</p> <p>Yu Z, Liu J, Sun Q, Qiu Y, Han S, Guo X. The accuracy of the procalcitonin test for the diagnosis of neonatal sepsis: a meta-analysis. Scandinavian Journal of Infectious Diseases 2010; 42(10): 723-733. http://dx.doi.org/10.3109/00365548.2010.489906</p> <p>BMC Infect Dis. 2017. Accuracy of serum procalcitonin for the diagnosis of sepsis in neonates and children with systemic inflammatory syndrome: a meta-analysis. Pontrelli G. https://www.ncbi.nlm.nih.gov/pubmed/28438138</p> <p>Cochrane Database of Systematic Reviews. Effectiveness and safety of procalcitonin evaluation for reducing mortality in adults with sepsis, severe sepsis or septic shock. 2017. DOI: 10.1002/14651858.CD010959.pub2</p>
<p>Medline <i>We searched for systematic reviews and other sources of secondary evidence</i></p>	<p>Systematic reviews Trippella G, Galli L, De Martino M, Lisi C, Chiappini E. Procalcitonin performance in detecting serious and invasive bacterial infections in children with fever without apparent source: a</p>

systematic review and meta-analysis. *Expert Rev Anti Infect Ther*. 2017 Nov;15(11):1041-1057. doi: 10.1080/14787210.2017.1400907. Epub 2017 Nov 15. PMID: 29103336.

Chiesa C, Pacifico L, Osborn JF, Bonci E, Hofer N, Resch B. Early-Onset Neonatal Sepsis: Still Room for Improvement in Procalcitonin Diagnostic Accuracy Studies. *Medicine (Baltimore)*. 2015 Jul;94(30):e1230. doi: 10.1097/MD.0000000000001230. PMID: 26222858; PMCID: PMC4554116.

Hedegaard SS, Wisborg K, Hvas AM. Diagnostic utility of biomarkers for neonatal sepsis--a systematic review. *Infect Dis (Lond)*. 2015 ar;47(3):117-24. doi: 10.3109/00365548.2014.971053. Epub 2014 Dec 18. Review. PubMed PMID: 25522182.

Prkno A, Wacker C, Brunkhorst FM, Schlattmann P. Procalcitonin-guided therapy in intensive care unit patients with severe sepsis and septic shock--a systematic review and meta-analysis. *Crit Care*. 2013 Dec 11;17(6):R291. doi: 10.1186/cc13157. Review. PubMed PMID: 24330744; PubMed Central PMCID: PMC4056085.

Wacker C, Prkno A, Brunkhorst FM, Schlattmann P. Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. *Lancet Infect Dis*. 2013 May;13(5):426-35. doi: 10.1016/S1473-3099(12)70323-7. Epub 2013 Feb 1. Review. PubMed PMID: 23375419.

Meem M, Modak JK, Mortuza R, Morshed M, Islam MS, Saha SK. Biomarkers for diagnosis of neonatal infections: A systematic analysis of their potential as a point-of-care diagnostics. *J Glob Health*. 2011 Dec;1(2):201-9. PubMed PMID: 23198119; PubMed Central PMCID: PMC3484777.

Yu Z, Liu J, Sun Q, Qiu Y, Han S, Guo X. The accuracy of the procalcitonin test for the diagnosis of neonatal sepsis: a meta-analysis. *Scand J Infect Dis*. 2010 Oct;42(10):723-33. doi: 10.3109/00365548.2010.489906. PubMed PMID: 20840003.

Systematic reviews with economic evaluation

Westwood M, Ramaekers B, Whiting P, Tomini F, Joore M, Armstrong N, Ryder S, Stirk L, Severens J, Kleijnen J. Procalcitonin testing to guide antibiotic therapy for the treatment of sepsis in intensive care settings and for suspected bacterial infection in emergency department settings: a systematic review and cost-effectiveness analysis. *Health Technol Assess*. 2015 Nov;19(96):v-xxv, 1-236. doi: 10.3310/hta19960. PMID: 26569153; PMCID: PMC4781547.

Heyland DK, Johnson AP, Reynolds SC, Muscedere J. Procalcitonin for reduced antibiotic exposure in the critical care setting: a systematic review and an economic evaluation. *Crit Care Med.* 2011 Jul;39(7):1792-9. doi: 10.1097/CCM.0b013e31821201a5. Review. PubMed PMID: 21358400.

Other studies

Wilke MH, Grube RF, Bodmann KF. The use of a standardized PCT-algorithm reduces costs in intensive care in septic patients - a DRG-based simulation model. *Eur J Med Res.* 2011 Dec 2;16(12):543-8. PubMed PMID: 22112361; PubMed Central PMCID: PMC3351898.

Date of search:

April 2018

Concepts used:

procalcitonin; PCT; sepsis, bacterial infections