

Review protocol for the effectiveness of serum procalcitonin measurement to guide decision making in people aged 16 or over, people aged less than 16, and pregnant or recently pregnant people.

ID	Field	Content	Developer comments (delete before publication)	QA comments (delete before publication)
1.	Review title	The effectiveness of serum procalcitonin measurement to guide decision making in the early management of people with suspected sepsis who are aged 16 or over, aged less than 16, or are pregnant or recently pregnant.		
2.	Review question	What is the clinical and cost effectiveness of serum procalcitonin measurement with standard care to support decision making regarding the early treatment of suspected sepsis compared to standard care alone?		
3.	Objective	To determine the clinical and cost effectiveness of using serum procalcitonin measurement alongside standard care to support decision making regarding the early treatment of suspected sepsis.		
4.	Searches	<p>The following bibliographic databases will be searched:</p> <ul style="list-style-type: none"> • Medline ALL (Ovid platform) • Embase (Ovid platform) • Cochrane Database of Systematic Reviews (Wiley platform) • Cochrane Central Register of Controlled Trials (CENTRAL, Wiley platform) • Epistemonikos (for systematic reviews-only) 		

		<p>Reference lists for any relevant systematic reviews identified will be checked for additional primary studies. The guideline committee or other stakeholders will be asked for details of any additional, relevant studies they may be aware of.</p> <p>The full search strategies for all databases will be published as an appendix to the final evidence review.</p>		
5.	Condition or domain being studied	Suspected sepsis		
6.	Population	<p>People with suspected sepsis</p> <ul style="list-style-type: none"> • people aged 16 or over (NG253), • people aged under 16 (NG254) • people of any age who are pregnant or have recently been pregnant *(NG255) <p>*Someone is considered to have recently been pregnant:</p> <ul style="list-style-type: none"> • in the 24 hours following a termination of pregnancy or miscarriage that occurred before 24 weeks gestation • for 4 weeks after a termination of pregnancy or miscarriage that occurred after 24 weeks gestation • for 4 weeks after giving birth. <p>Settings: Emergency department and in-hospital settings</p> <p>Exclusion:</p>		

		<ul style="list-style-type: none"> • People with neutropenic sepsis • People already receiving IV antibiotics 		
7.	Intervention	Treatment decisions made using serum procalcitonin measurement available for use in the NHS plus standard care.		
8.	Comparator	Treatment decisions based on standard care at the time and setting the study was conducted in, without procalcitonin testing. This may be based on other microbiological tests, early warning scores, and/or clinical intuition.		
9.	Types of study to be included	<p>Published full-text papers:</p> <ul style="list-style-type: none"> • RCTs • If insufficient RCTs*: <ul style="list-style-type: none"> ○ Non-randomised controlled trials/Prospective cohort studies that have adjusted for the following covariates in their analysis when there are differences between groups at baseline: <ul style="list-style-type: none"> ○ Age ○ Sex ○ Race ○ Renal function (eGFR/CKD stage) ○ Severity of illness (SOFA score/APACHE II score) ○ Comorbidities (e.g. CKD, Chronic lung disease, CVD, metabolic derangements) ○ Immune and inflammatory status (e.g. CRP, WBC, immunosuppression) 		

		<ul style="list-style-type: none"> ○ Vitamin D level <p>*Non-randomised studies will be considered for inclusion if insufficient RCT evidence is available for guideline decision making. Sufficiency will be judged taking into account factors including number/quality/sample size of RCTs, outcomes reported and availability of data from subgroups of interest.</p> <p>Systematic reviews of relevant primary study designs will be searched for and used as a source of primary studies in this review but will not be included as studies in the review, and no data extraction of those reviews will be undertaken.</p> <p>Only published full-text papers will be included.</p>		
10.	Other exclusion criteria	<ul style="list-style-type: none"> • Animal studies • Editorials, letters, news items and commentaries • Conference abstracts and posters • Registry entries for ongoing clinical trials or those that contain no results • Theses and dissertations • Papers not published in the English language. • Preprints 		
11.	Context	<p>Procalcitonin is an indirect marker of bacterial infection, released in response to pro-inflammatory stimuli. Measuring its levels in serum can indicate infection severity and the likelihood of systemic infection or sepsis. This can be used to guide decisions on whether to initiate antibiotics.</p>		

		There has previously been a healthtech guidance review published in 2015 (Procalcitonin testing for diagnosing and monitoring sepsis HTG386) which found insufficient evidence at the time to recommend PCT tests.		
12.	Primary outcomes	<p>People aged 16 or over:</p> <ul style="list-style-type: none"> • Time to initiation of IV antibiotics • Duration of IV antibiotic treatment • Mortality within 30 days <p>People aged under 16:</p> <ul style="list-style-type: none"> • Time to initiation of IV antibiotics • Duration of IV antibiotic treatment • Mortality within 30 days <p>People of any age who are pregnant or have recently been pregnant:</p> <ul style="list-style-type: none"> • Time to initiation of IV antibiotics • Duration of IV antibiotic treatment • Mortality within 30 days (including maternal and neonatal/foetal mortality) • Neonatal adverse events: preterm birth, low birth weight, neonatal infection and neonatal sepsis 		
13.	Secondary outcomes	<p>People aged 16 or over:</p> <ul style="list-style-type: none"> • Length of hospital stay • Admission to ICU within hospital stay • Severity of disease (using scoring systems such as SOFA, SAPS II, APACHE II) • HRQoL 		

		<p>People aged under 16:</p> <ul style="list-style-type: none"> • Length of hospital stay • Admission to ICU within hospital stay • Severity of disease (using scoring systems such as pSOFA) • HRQoL <p>People of any age who are pregnant or have recently been pregnant:</p> <ul style="list-style-type: none"> • Length of hospital stay • Admission to ICU within hospital stay • Severity of disease (using scoring systems such as SOFA, SAPS II, APACHE II) • Neonatal admission to NICU or Special Care Baby Unit 		
14.	Data extraction (selection and coding)	<p>All references identified by the searches and from other sources will be uploaded into EPPI R5 and de-duplicated.</p> <p>Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol.</p> <p>Dual sifting will be performed on at least 10% of records; 90% agreement is required.</p> <p>Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary.</p> <p>Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study</p>		

		<p>excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.</p>		
15.	Risk of bias (quality) assessment	<p>Quality assessment of individual studies will be performed using the following checklists:</p> <ul style="list-style-type: none"> • Cochrane RoB tool v.2 for RCTs and quasi-RCTs • Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies <p>The quality assessment will be performed by one reviewer, and this will be quality assessed by a senior reviewer.</p>		
16.	Strategy for data synthesis	<p>Intervention review:</p> <p>Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where possible, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted, and data will be presented as risk</p>		

		<p>ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes.</p> <p>Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic. Alongside visual inspection of the point estimates and confidence intervals, the following criteria will be used to assess heterogeneity: no serious $I^2 = <40\%$; serious $I^2 = 40-60\%$; very serious $I^2 = >60\%$. Where I^2 is 80% or above, the data will not be pooled. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis, then a random effects model will be used for meta-analysis, or the data will not be pooled.</p> <p>Publication bias will be investigated using a funnel plot when there are 10 or more studies in an analysis.</p> <p>The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/</p> <p>Importance and imprecision of findings will be assessed against minimally important differences (MIDs). MIDs for each outcome are detailed in the</p>		
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		<p>methods supplement for this guideline. If no MIDs are available (published or consensus based or the guideline committee cannot define MIDs) optimal information size (OIS) will be calculated utilising NICE's OIS calculators and OIS will be used to assess imprecision.</p>		
17.	Analysis of sub-groups	<p>Evidence will be stratified by:</p> <ul style="list-style-type: none"> • people aged 16 or over (NG253), • Older adults (aged over 65) • people aged under 16 (NG254) • Older children (aged 11-16), younger (aged 5-11) and very young (aged 4 and under) people of any age who are pregnant or have recently been pregnant (NG255) • Pre- and post- partum <p>The 3 committees formed for each of the guidelines will make separate recommendations for each group which will update and be published in the 3 respective guidelines.</p> <p>Where evidence is stratified or there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.</p>		
18.	Type and method of review	Intervention review		

19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	January 2026		
22.	Anticipated completion date	TBC		
23.	Stage of review at time of this submission	<ul style="list-style-type: none"> • Preliminary searches – Not started, • Piloting of the study selection process – Not started • Formal screening of search results against eligibility criteria – Not started, • Data extraction – Not started, Started or Started and completed • Risk of bias (quality) assessment – Not started, • Data analysis – Not started 		
24.	Named contact	<p>5a. Named contact NICE</p> <p>5b Named contact e-mail SepsisUpdate@nice.org.uk</p> <p>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance</p>		
25.	Review team members	<ul style="list-style-type: none"> • Technical advisor: Robby Richey • Senior technical analyst: James Jagroo • Technical analyst: Michellie Young • Health economics adviser: Eric Slade 		

		<ul style="list-style-type: none"> Information specialist: Lynda Ayiku 		
26.	Funding sources/sponsor	This systematic review is being completed by NICE which receives funding from the Department of Health and Social Care.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual . Members of the guideline committee are available on the NICE website: [NICE guideline webpage] .		
29.	Other registration details	None		
30.	Reference/URL for published protocol	NA	We don't think the protocol will be	

			published on PROSPERO	
31.	Dissemination plans	<p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. 		
32.	Keywords	Procalcitonin; sepsis; PCT assay; pregnancy		
33.	Details of existing review of same topic by same authors	NA		
34.	Current review status	Ongoing		
35.	Additional information	None		
36.	Details of final publication	www.nice.org.uk		