National Institute for Health and Care Excellence

Suspected sepsis: recognition, diagnosis and early management

Technical appendices for procalcitonin guided decision making

NICE guideline NG51

Technical data underpinning evidence review J

June 2026
Draft for consultation

Contents

Appendix A - Review protocols

Effectiveness review protocol

The review protocol was pre-registered. The full protocol can be found at:
https://www.nice.org.uk/guidance/indevelopment/gid-ng10467/documents

Economic review protocol

ID	Field	Content
1.	Review title	The effectiveness (clinical and cost effectiveness) of serum procalcitonin measurement to guide decision making in the early management of people aged 16 or over, people aged less than 16, and pregnant or recently pregnant people with suspected sepsis. The three populations will be addressed as separate review questions and will inform the update of the related guidance for people with suspected sepsis: • people aged 16 or over (NG253), • people aged under 16 (NG254) • people of any age who are pregnant or have recently been pregnant (NG255)
2.	Objective	To identify economic studies for all relevant review questions covering the three populations of interest. The review questions aim to determine the clinical and cost effectiveness of serum procalcitonin measurement alongside standard care, to support decision-making for the early treatment of suspected sepsis, compared with standard care alone in the aforementioned three populations.
3.	Inclusion criteria	• Populations, interventions and comparators must be as specified in the effectiveness review protocol. • Relevant comparative economic study design: cost–utility analysis, cost–effectiveness analysis, cost–consequences analysis, comparative cost analysis. • Decision analytic model-based or within-trial economic analyses. • OECD countries (except USA). • Healthcare and personal social services cost perspective. • Only including analyses where effectiveness evidence is included in clinical review, which may include non-randomised studies if trial evidence is insufficient. • Studies published from 2016 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs. High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making. Not all studies meeting the inclusion criteria will therefore necessarily be used in decision-making - see Review strategy below for details.
4.	Exclusion criteria	• Conference posters or abstract only studies – these do not provide sufficient information for quality assessment.

		• Studies published before 2016 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs. • Studies from non-OECD countries or the USA – these are considered unlikely to be applicable to the UK NHS setting due to substantial differences in healthcare delivery and unit costs. • Within-trial economic analyses based on studies that have been excluded from the clinical review. • Economic model analyses based exclusively on studies that have been excluded from the clinical review. • Non-comparative economic analyses including cost-of-illness studies. • Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility). • Non-English language papers. • Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of sepsis. • Studies comparing costs of branded vs generic forms of the same medicine. • Studies only focussing on productivity losses or gains.
5.	Search strategy	An economic study search will be undertaken using question-specific terms. For search details see appendix B below.

6.	Review strategy	• Studies meeting the inclusion and exclusion criteria will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist in appendix H of Developing NICE guidelines: the manual.
		• The NICE economic evaluation checklist assesses:
		  ○ Applicability to the NICE guideline decision making context with consideration of the NICE reference case relevant to the guideline. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness.
		  ○ Methodological limitations.
		• The aim is to present the best available economic evidence to inform committee decision-making in the context of the guideline, the current UK NHS setting and NICE methods. Therefore, the health economist may not present all studies that meet inclusion criteria. Studies that are deemed not applicable or have very serious methodological limitations should not inform committee decision-making. If recent high quality, UK cost-utility analyses are available for a question, it is often not deemed informative to present studies that are less applicable or lower quality such as older UK analyses or analyses from other countries. A similar principle is deemed to apply more generally when considering applicability and methodological limitations. Some specific examples are given below:
		  ○ If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version.
		  ○ If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent.
		  ○ If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older studies, unless they address a different subpopulation or other specific issue.
		  ○ If a UK model that includes all interventions in the decision space is available it may be reasonable not to present studies that only include

		individual or fewer interventions, if the analysis is sufficiently applicable and of good methodological quality.
		• Quality and relevance of effectiveness data used in the economic analysis: the more closely the clinical effectiveness data used in the economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.
		• Hierarchy of economic evaluation evidence based on quality assessment
		  ○ 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making.
		  ○ Directly or partially applicable combined with minor or potentially serious limitations (other than 1). Discretion over whether these are presented and used in decision-making, depending on the availability of more relevant evidence.
		  ○ 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making.
		
		The health economist will make a decision based on the relative applicability and quality of the available evidence for each question, in discussion with the guideline committee if required. All decisions will be transparently reported in the evidence report. Studies that are presented to the committee and used in decision-making when formulating recommendations will be included in the summary tables and will have an evidence extraction. Other studies may not be presented to the committee in detail but will be listed, with the reason for not being presented to the committee and thus not used in decision-making being provided. Committee members can review and query the decision not to present studies with the health economist and will be provided with full details of these studies where requested.

1

Appendix B - Literature search strategies

Background and development

Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches. The MEDLINE strategies below were quality assured (QA) by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

This search report is based on the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess "low-probability" matches. All decisions made for the review can be accessed via the deduplication history.

Prior work

The search terms for the sepsis population from '(A) Evidence reviews for stratifying risk of severe illness or death from sepsis' in NG51 (Jan 2024) were used to inform the population terms for the search strategy.

Search limits and other restrictions

Formats

Limits were applied in adherence to standard NICE practice (as set out in the Identifying the evidence chapter of the manual) and the eligibility criteria listed in the review protocol to exclude:

- 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.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:

> Dickersin K, Scherer R & Lefebvre C. (1994) Systematic reviews: identifying relevant studies for systematic reviews. *BMJ*, 309 (6964), 1286.

Date limits

No date limits were applied, in adherence to the review protocol.

Search filters and classifiers

Effectiveness searches

Systematic reviews filters:

Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. *BMC Medical Research Methodology,* 12(1), 51.

- In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.
- In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.

Randomised controlled trials filters:

The MEDLINE RCT filter was McMaster Therapy – Medline - "best balance of sensitivity and specificity" version.

The standard NICE modifications were used: the MeSH heading *randomized controlled trial/*, which is equivalent *to randomized controlled trial.pt* was exploded to capture newer, narrower *terms equivalence trial/ and pragmatic clinical trial*. The free-text term *randomized.mp* was also changed to the (more inclusive) alternative *randomi?ed.mp.* to capture both UK and US spellings.

Haynes RB et al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. *BMJ*, 330, 1179-1183.

The Embase RCT filter was McMaster Therapy – Embase "best balance of sensitivity and specificity" version.

Wong SSL et al. (2006) Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. *Journal of the Medical Library Association*, 94(1), 41-47.

Observational studies filters:

The terms used for observational studies are standard NICE practice that have been developed in house.

OECD countries:

The MEDLINE and Embase searches were limited to evidence from Organisation for Economic Co-operation and Development (OECD) member states using the validated NICE filter.

The OECD countries filters were used without modification:

Ayiku L, Hudson T, Williams C, Levay P & Jacob C (2021). The NICE OECD countries' geographic search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. *Journal of the Medical Library Association*, 109(4), 583–589.

Cost effectiveness searches

In line with the review protocol, the sensitive version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.

> Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.

The following search filters were applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:

> Glanville J et al. (2009) Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE. Alberta: Canadian Agency for Drugs and Technologies in Health (CADTH)

Note: Several modifications have been made to these filters over the years that are standard NICE practice.

Effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	28/01/2026	Wiley	Issue 1 of 12, January 2026	375
Cochrane Database of Systematic Reviews (CDSR)	28/01/2026	Wiley	Issue 1 of 12, January 2026	2
Embase	28/01/2026	Ovid	Embase <1974 to 2026 January 26>	727 - SR/RCT 2841 - Observational

Epistemonikos	28/01/2026	https://www.epistemonikos.org/	Searched 28th Jan 2026	54 - Procalcitonin 27 - Brands
MEDLINE ALL	28/01/2026	Ovid	Ovid MEDLINE(R) ALL <1946 to January 27, 2026>	459 - SR/RCT 2095 - Observational

1 Search strategy history

2 Database name: MEDLINE ALL

Searches	
1	exp sepsis/ (154664)
2	sepsis.ti,ab. (139258)
3	blood-borne pathogens/ (3082)
4	(blood* adj2 (pathogen* or poison*)).ti,ab. (3773)
5	exp systemic inflammatory response syndrome/ (164018)
6	'systemic inflammatory response syndrome*'.tw. (6571)
7	sirs.ti,ab. (7431)
8	(septicaemi* or septicemi*).ti,ab. (23341)
9	((septic or cryptic) adj2 shock).ti,ab. (31511)
10	(pyaemi* or pyemi* or pyohemi*).ti,ab. (266)
11	(bacter?emi* or fung?emi* or parasit?emi* or vir?emi*).ti,ab. (79531)
12	(hypotension adj3 induced adj3 hypoperfusion).ti,ab. (7)
13	or/1-12 (316867)
14	exp Calcitonin/ (18787)
15	(procalcitonin* or calcitonin*).tw,kf. (40875)
16	((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)).tw,kf. (16538)
17	or/14-16 (55732)
18	13 and 17 (5268)
19	(MEDLINE or pubmed).tw. (444924)
20	systematic review.tw. (380779)
21	systematic review.pt. (317363)
22	meta-analysis.pt. (224165)
23	intervention$.ti. (249560)
24	or/19-23 (892884)
25	exp Randomized Controlled Trial/ (655367)
26	randomi?ed.mp. (1237938)
27	placebo.mp. (274861)
28	or/25-27 (1309167)
29	24 or 28 (1974401)
30	18 and 29 (532)
31	limit 30 to english language (486)
32	animals/ (7824856)

33	exp Animals, Laboratory/ (1023792)
34	exp Animal Experimentation/ (10833)
35	exp Models, Animal/ (704183)
36	exp Rodentia/ (3785108)
37	(rat or rats or mouse or mice or rodent*).ti. (1552659)
38	or/32-37 (7963657)
39	38 not humans/ (5514142)
40	31 not 39 (480)
41	letter/ (1324838)
42	editorial/ (747044)
43	news/ (233939)
44	exp historical article/ (418617)
45	Anecdotes as Topic/ (4748)
46	comment/ (1060420)
47	(letter or comment*).ti. (225500)
48	or/41-47 (3076554)
49	randomized controlled trial/ or random*.ti,ab. (1849216)
50	48 not 49 (3047958)
51	40 not 50 (477)
52	Observational Studies as Topic/ (11864)
53	Observational Study/ (190645)
54	Epidemiologic Studies/ (9731)
55	exp Case-Control Studies/ (1673459)
56	exp Cohort Studies/ (2845673)
57	Cross-Sectional Studies/ (574428)
58	Controlled Before-After Studies/ (795)
59	Historically Controlled Study/ (242)
60	Interrupted Time Series Analysis/ (2742)
61	Comparative Study.pt. (1972600)
62	case control$.tw. (183296)
63	case series.tw. (128557)
64	(cohort adj (study or studies)).tw. (435014)
65	cohort analy$.tw. (16700)
66	(follow up adj (study or studies)).tw. (61848)
67	(observational adj (study or studies)).tw. (217803)
68	longitudinal.tw. (401762)
69	prospective.tw. (852560)
70	retrospective.tw. (974994)
71	cross sectional.tw. (678227)
72	or/52-71 (6276886)
73	18 and 72 (2729)
74	limit 73 to english language (2438)
75	animals/ (7824856)
76	exp Animals, Laboratory/ (1023792)
77	exp Animal Experimentation/ (10833)
78	exp Models, Animal/ (704183)
79	exp Rodentia/ (3785108)

80 (rat or rats or mouse or mice or rodent*).ti. (1552659)

81 or/75-80 (7963657)

82 81 not humans/ (5514142)

83 74 not 82 (2416)

84 letter/ (1324838)

85 editorial/ (747044)

86 news/ (233939)

87 exp historical article/ (418617)

88 Anecdotes as Topic/ (4748)

89 comment/ (1060420)

90 (letter or comment*).ti. (225500)

91 or/84-90 (3076554)

92 randomized controlled trial/ or random*.ti,ab. (1849216)

93 91 not 92 (3047958)

94 83 not 93 (2395)

95 94 not 51 (2218)

96 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1484133)

97 "organisation for economic co-operation and development"/ (729)

98 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3743656)

99 european union/ (18835)

100 developed countries/ (21970)

101	or/97-100 (3760881)
102	96 not 101 (1389328)
103	51 not 102 (459)
104	95 not 102 (2095)

1 **Database name: Embase**

Searches
Database: Embase <1974 to 2026 January 26>
Search Strategy:
---
1 exp sepsis/ (405934)
2 sepsis.ti,ab. (224000)
3 bloodborne bacterium/ (2286)
4 (blood* adj2 (pathogen* or poison*)).ti,ab. (5045)
5 exp systemic inflammatory response syndrome/ (421877)
6 'systemic inflammatory response syndrome*'.ti,ab. (10093)
7 sirs.ti,ab. (13643)
8 (septicaemi* or septicemi*).ti,ab. (27849)
9 ((septic or cryptic) adj2 shock).ti,ab. (54053)
10 (pyaemi* or pyemi* or pyohemi*).ti,ab. (152)
11 (bacter?emi* or fung?emi* or parasit?emi* or vir?emi*).ti,ab. (114415)
12 (hypotension adj3 induced adj3 hypoperfusion).ti,ab. (9)
13 or/1-12 (552442)
14 *calcitonin derivative/ or *calcitonin/ or *procalcitonin/ (19169)
15 (procalcitonin* or calcitonin*).tw,kf. (58774)
16 ((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)).tw,kf. (32677)
17 or/14-16 (85484)
18 13 and 17 (10170)
19 (MEDLINE or pubmed).tw. (548280)
20 exp systematic review/ or systematic review.tw. (683502)
21 meta-analysis/ (396467)
22 intervention$.ti. (347578)
23 or/19-22 (1267741)
24 random:.tw. (2573896)
25 placebo:.mp. (651497)
26 double-blind:.tw. (332759)
27 or/24-26 (2884414)
28 23 or 27 (3752531)
29 18 and 28 (1141)
30 limit 29 to english language (1055)
31 animal/ (1749051)
32 nonhuman/ (8482851)
33 exp Animal Experiment/ (3499316)
34 exp Experimental Animal/ (933780)

35 animal model/ (2020252)
36 exp Rodent/ (4458795)
37 (rat or rats or mouse or mice or rodent*).ti. (1752766)
38 or/31-37 (11129702)
39 38 not human/ (7828106)
40 30 not 39 (1037)
41 letter.pt. or letter/ (1418655)
42 note.pt. (1034349)
43 editorial.pt. (859761)
44 (letter or comment*).ti. (269954)
45 or/41-44 (3377583)
46 randomized controlled trial/ or random*.ti,ab. (2718290)
47 45 not 46 (3338917)
48 40 not 47 (1029)
49 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6669069)
50 48 not 49 (752)
51 Clinical study/ (172005)
52 Case control study/ (249160)
53 Family study/ (26617)
54 Longitudinal study/ (270755)
55 Retrospective study/ (2002803)
56 comparative study/ (1153486)
57 Prospective study/ (1031723)
58 Randomized controlled trials/ (307764)
59 57 not 58 (1019168)
60 Cohort analysis/ (1547549)
61 cohort analy$.tw. (27011)
62 (Cohort adj (study or studies)).tw. (637774)
63 (Case control$ adj (study or studies)).tw. (201068)
64 (follow up adj (study or studies)).tw. (84929)
65 (observational adj (study or studies)).tw. (359379)
66 (epidemiologic$ adj (study or studies)).tw. (135876)
67 (cross sectional adj (study or studies)).tw. (463303)
68 case series.tw. (184381)
69 prospective.tw. (1403425)
70 retrospective.tw. (1630199)
71 or/51-56,59-70 (6798830)
72 18 and 71 (4914)
73 animal/ (1749051)
74 nonhuman/ (8482851)
75 exp Animal Experiment/ (3499316)
76 exp Experimental Animal/ (933780)
77 animal model/ (2020252)
78 exp Rodent/ (4458795)
79 (rat or rats or mouse or mice or rodent*).ti. (1752766)
80 or/73-79 (11129702)

81 80 not human/ (7828106)

82 72 not 81 (4876)

83 letter.pt. or letter/ (1418655)

84 note.pt. (1034349)

85 editorial.pt. (859761)

86 (letter or comment*).ti. (269954)

87 or/83-86 (3377583)

88 randomized controlled trial/ or random*.ti,ab. (2718290)

89 87 not 88 (3338917)

90 82 not 89 (4836)

91 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6669069)

92 90 not 91 (3411) - Observational studies results

93 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1998171)

94 exp "organisation for economic co-operation and development"/ (3900)

95 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (4155209)

96 european union/ (34785)

97 developed country/ (37603)

98 or/94-97 (4192750)

99 93 not 98 (1821781)

100	50 not 99 (727)
101	92 not 99 (3168)
102	101 not 100 (2841)

1 **Database name: Cochrane Database of Systematic Reviews (CDSR)**

Searches	
#1	MeSH descriptor: [Sepsis] explode all trees 6722
#2	sepsis:ti,ab,kw 15301
#3	MeSH descriptor: [Blood-Borne Pathogens] this term only 35
#4	(blood* near/2 (pathogen* or poison*)):ti,ab,kw 388
#5	MeSH descriptor: [Systemic Inflammatory Response Syndrome] explode all trees 7262
#6	systemic inflammatory response syndrome*:ti,ab,kw 1874
#7	sirs:ti,ab,kw 1027
#8	(septicaemi* or septicemi*):ti,ab,kw 1045
#9	((septic or cryptic) near/2 shock):ti,ab,kw 4417
#10	(pyaemi* or pyemi* or pyohemi*):ti,ab,kw 7
#11	(bacter?emi* or fung?emi* or parasit?emi* or vir?emi*):ti,ab,kw 7019
#12	(hypotension near/3 induced near/3 hypoperfusion):ti,ab,kw 2
#13	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 26443
#14	MeSH descriptor: [Calcitonin] explode all trees 926
#15	(procalcitonin* or calcitonin*):ti,ab,kw 4367
#16	((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)):ti,ab,kw 2271
#17	#14 or #15 or #16 5964
#18	#13 and #17 797
#19	"conference":pt or (clinicaltrials or trialsearch):so 883173
#20	#18 not #19 380

2 **Database name: Cochrane Central Register of Controlled Trials (CENTRAL)**

Searches	
#1	MeSH descriptor: [Sepsis] explode all trees 6722
#2	sepsis:ti,ab,kw 15301
#3	MeSH descriptor: [Blood-Borne Pathogens] this term only 35
#4	(blood* near/2 (pathogen* or poison*)):ti,ab,kw 388
#5	MeSH descriptor: [Systemic Inflammatory Response Syndrome] explode all trees 7262
#6	systemic inflammatory response syndrome*:ti,ab,kw 1874
#7	sirs:ti,ab,kw 1027
#8	(septicaemi* or septicemi*):ti,ab,kw 1045
#9	((septic or cryptic) near/2 shock):ti,ab,kw 4417
#10	(pyaemi* or pyemi* or pyohemi*):ti,ab,kw 7
#11	(bacter?emi* or fung?emi* or parasit?emi* or vir?emi*):ti,ab,kw 7019

#12	(hypotension near/3 induced near/3 hypoperfusion):ti,ab,kw	2
#13	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12	26443
#14	MeSH descriptor: [Calcitonin] explode all trees	926
#15	(procalcitonin* or calcitonin*):ti,ab,kw	4367
#16	((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)):ti,ab,kw	2271
#17	#14 or #15 or #16	5964
#18	#13 and #17	797
#19	"conference":pt or (clinicaltrials or trialsearch):so	883173
#20	#18 not #19	380

Cost-effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EcoLit	02/02/2026	Ovid	Econlit <1886 to January 22, 2026>	0
Embase	02/02/2026	Ovid	Embase <1974 to 2026 January 29>	639
International HTA Database	02/02/2026	International Network of Agencies for Health Technology Assessment.	Searched 2nd Feb 2026	9
MEDLINE	02/02/2026	Ovid	Ovid MEDLINE(R) ALL <1946 to January 30, 2026>	433

Database name: MEDLINE ALL

Searches	
1	exp sepsis/ (154724)
2	sepsis.ti,ab. (139398)
3	blood-borne pathogens/ (3082)
4	(blood* adj2 (pathogen* or poison*)).ti,ab. (3777)
5	exp systemic inflammatory response syndrome/ (164084)
6	'systemic inflammatory response syndrome*'.tw. (6572)
7	sirs.ti,ab. (7438)

8 (septicaemi* or septicemi*).ti,ab. (23352)

9 ((septic or cryptic) adj2 shock).ti,ab. (31553)

10 (pyaemi* or pyemi* or pyohemi*).ti,ab. (266)

11 (bacter?emi* or fung?emi* or parasit?emi* or vir?emi*).ti,ab. (79573)

12 (hypotension adj3 induced adj3 hypoperfusion).ti,ab. (7)

13 or/1-12 (317090)

14 exp Calcitonin/ (18793)

15 (procalcitonin* or calcitonin*).tw,kf. (40905)

16 ((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)).tw,kf. (16551)

17 or/14-16 (55768)

18 13 and 17 (5280)

19 Cost-Benefit Analysis/ (100111)

20 Quality-Adjusted Life Years/ (18872)

21 Markov Chains/ (17771)

22 exp Models, Economic/ (17160)

23 cost*.ti. (163363)

24 (cost* adj2 utilit*).tw. (9214)

25 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (343694)

26 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (57791)

27 (qualit* adj2 adjust* adj2 life*).tw. (21438)

28 QALY*.tw. (17513)

29 (incremental* adj2 cost*).tw. (20855)

30 ICER.tw. (7779)

31 utilities.tw. (10921)

32 markov*.tw. (37559)

33 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (61716)

34 ((utility or effective*) adj2 analys*).tw. (30483)

35 (willing* adj2 pay*).tw. (12471)

36 (EQ5D* or EQ-5D*).tw. (17443)

37 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (5278)

38 (european* adj2 quality adj3 ("5" or five)).tw. (927)

39 or/19-38 (599304)

40 Economics/ (27557)

41 exp "Costs and Cost Analysis"/ (285277)

42 Economics, Dental/ (1922)

43 exp Economics, Hospital/ (26414)

44 exp Economics, Medical/ (14480)

45 Economics, Nursing/ (4015)

46 Economics, Pharmaceutical/ (3175)

47 Budgets/ (12060)

48 exp Models, Economic/ (17160)

49 Markov Chains/ (17771)

50 Monte Carlo Method/ (35197)
51 Decision Trees/ (13014)
52 econom$.tw. (500321)
53 cba.tw. (11897)
54 cea.tw. (30311)
55 cua.tw. (1611)
56 markov$.tw. (37559)
57 (monte adj carlo).tw. (67997)
58 (decision adj3 (tree$ or analys$)).tw. (43870)
59 (cost or costs or costing$ or costly or costed).tw. (905789)
60 (price$ or pricing$).tw. (62908)
61 budget$.tw. (41399)
62 expenditure$.tw. (78079)
63 (value adj3 (money or monetary)).tw. (3765)
64 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (4891)
65 or/40-64 (1715955)
66 "Quality of Life"/ (317442)
67 quality of life.tw. (474840)
68 "Value of Life"/ (5854)
69 Quality-Adjusted Life Years/ (18872)
70 quality adjusted life.tw. (21033)
71 (qaly$ or qald$ or qale$ or qtime$).tw. (17702)
72 disability adjusted life.tw. (9501)
73 daly$.tw. (8671)
74 Health Status Indicators/ (24252)
75 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (34580)
76 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (3095)
77 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (9069)
78 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (44)
79 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (496)
80 (euroqol or euro qol or eq5d or eq 5d).tw. (21717)
81 (qol or hql or hqol or hrqol).tw. (91095)
82 (hye or hyes).tw. (79)
83 health$ year$ equivalent$.tw. (41)
84 utilit$.tw. (339277)
85 (hui or hui1 or hui2 or hui3).tw. (2309)
86 disutili$.tw. (769)
87 rosser.tw. (113)
88 quality of wellbeing.tw. (65)
89 quality of well-being.tw. (567)
90 qwb.tw. (223)
91 willingness to pay.tw. (11142)

92 standard gamble$.tw. (950)

93 time trade off.tw. (1563)

94 time tradeoff.tw. (273)

95 tto.tw. (1753)

96 or/66-95 (929551)

97 39 or 65 or 96 (2553213)

98 18 and 97 (659)

99 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1485122)

100 "organisation for economic co-operation and development"/ (729)

101 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3744475)

102 european union/ (18842)

103 developed countries/ (21976)

104 or/100-103 (3761706)

105 99 not 104 (1390301)

106 98 not 105 (637)

107 limit 106 to yr="2016 -Current" (457)

108 animals/ (7827166)

109 exp Animals, Laboratory/ (1024241)

110 exp Animal Experimentation/ (10826)

111 exp Models, Animal/ (704482)

112 exp Rodentia/ (3786164)

113	(rat or rats or mouse or mice or rodent*).ti. (1553058)
114	or/108-113 (7966087)
115	114 not humans/ (5515254)
116	107 not 115 (453)
117	letter/ (1325174)
118	editorial/ (747523)
119	news/ (233974)
120	exp historical article/ (418600)
121	Anecdotes as Topic/ (4748)
122	comment/ (1060496)
123	(letter or comment*).ti. (225645)
124	or/117-123 (3077440)
125	randomized controlled trial/ or random*.ti,ab. (1850706)
126	124 not 125 (3048884)
127	116 not 126 (449)
128	limit 127 to english language (433)

1 **Database name: Embase**

Searches	
1	exp sepsis/ (406287)
2	sepsis.ti,ab. (224182)
3	bloodborne bacterium/ (2287)
4	(blood* adj2 (pathogen* or poison*)).ti,ab. (5044)
5	exp systemic inflammatory response syndrome/ (422248)
6	'systemic inflammatory response syndrome*'.ti,ab. (10099)
7	sirs.ti,ab. (13646)
8	(septicaemi* or septicemi*).ti,ab. (27869)
9	((septic or cryptic) adj2 shock).ti,ab. (54099)
10	(pyaemi* or pyemi* or pyohemi*).ti,ab. (152)
11	(bacter?emi* or fung?emi* or parasit?emi* or vir?emi*).ti,ab. (114486)
12	(hypotension adj3 induced adj3 hypoperfusion).ti,ab. (9)
13	or/1-12 (552860)
14	*calcitonin derivative/ or *calcitonin/ or *procalcitonin/ (19181)
15	(procalcitonin* or calcitonin*).tw,kf. (58759)
16	((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)).tw,kf. (32707)
17	or/14-16 (85485)
18	13 and 17 (10175)
19	cost utility analysis/ (14899)
20	quality adjusted life year/ (43443)
21	cost*.ti. (221119)
22	(cost* adj2 utilit*).tw. (15479)
23	(cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (481622)

24 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (82559)
25 (qualit* adj2 adjust* adj2 life*).tw. (33061)
26 QALY*.tw. (32485)
27 (incremental* adj2 cost*).tw. (34427)
28 ICER.tw. (16264)
29 utilities.tw. (17596)
30 markov*.tw. (47457)
31 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (86047)
32 ((utility or effective*) adj2 analys*).tw. (46702)
33 (willing* adj2 pay*).tw. (18439)
34 (EQ5D* or EQ-5D*).tw. (35010)
35 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (7213)
36 (european* adj2 quality adj3 ("5" or five)).tw. (1344)
37 or/19-36 (775809)
38 exp Health Economics/ (1199879)
39 exp "Health Care Cost"/ (384891)
40 exp Pharmacoeconomics/ (272063)
41 Monte Carlo Method/ (61332)
42 Decision Tree/ (32224)
43 econom$.tw. (612567)
44 cba.tw. (15706)
45 cea.tw. (47865)
46 cua.tw. (2251)
47 markov$.tw. (47457)
48 (monte adj carlo).tw. (72633)
49 (decision adj3 (tree$ or analys$)).tw. (56823)
50 (cost or costs or costing$ or costly or costed).tw. (1229893)
51 (price$ or pricing$).tw. (86546)
52 budget$.tw. (55584)
53 expenditure$.tw. (106287)
54 (value adj3 (money or monetary)).tw. (5034)
55 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (10666)
56 or/38-55 (2716362)
57 "Quality of Life"/ (838629)
58 Quality Adjusted Life Year/ (43443)
59 Quality of Life Index/ (3636)
60 Short Form 36/ (50697)
61 Health Status/ (174837)
62 quality of life.tw. (793078)
63 quality adjusted life.tw. (32314)
64 (qaly$ or qald$ or qale$ or qtime$).tw. (32804)
65 disability adjusted life.tw. (11735)
66 daly$.tw. (11261)

67 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (58622)

68 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (3515)

69 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (14990)

70 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (87)

71 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (615)

72 (euroqol or euro qol or eq5d or eq 5d).tw. (40749)

73 (qol or hql or hqol or hrqol).tw. (167418)

74 (hye or hyes).tw. (224)

75 health$ year$ equivalent$.tw. (41)

76 utilit$.tw. (477540)

77 (hui or hui1 or hui2 or hui3).tw. (3920)

78 disutili$.tw. (1568)

79 rosser.tw. (158)

80 quality of wellbeing.tw. (110)

81 quality of well-being.tw. (696)

82 qwb.tw. (279)

83 willingness to pay.tw. (16542)

84 standard gamble$.tw. (1260)

85 time trade off.tw. (2337)

86 time tradeoff.tw. (332)

87 tto.tw. (2731)

88 or/57-87 (1668897)

89 37 or 56 or 88 (4169104)

90 18 and 89 (1513)

91 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp

southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (2000101)
92 exp "organisation for economic co-operation and development"/ (3915)
93 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (4156672)
94 european union/ (34800)
95 developed country/ (37612)
96 or/92-95 (4194238)
97 91 not 96 (1823590)
98 90 not 97 (1443)
99 limit 98 to yr="2016 -Current" (1047)
100 animal/ (1749497)
101 nonhuman/ (8488729)
102 exp Animal Experiment/ (3501651)
103 exp Experimental Animal/ (934468)
104 animal model/ (2021847)
105 exp Rodent/ (4460984)
106 (rat or rats or mouse or mice or rodent*).ti. (1753462)
107 or/100-106 (11136106)
108 107 not human/ (7832179)
109 99 not 108 (1037)
110 letter.pt. or letter/ (1419342)
111 note.pt. (1034802)
112 editorial.pt. (860265)
113 (letter or comment*).ti. (270043)
114 or/110-113 (3379172)
115 randomized controlled trial/ or random*.ti,ab. (2720973)
116 114 not 115 (3340473)
117 109 not 116 (1007)
118 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (6675569)
119 117 not 118 (667)
120 limit 119 to english language (639)

1 **Database name: EconLit**

Searches
1 [exp sepsis/] (0)
2 sepsis.ti,ab. (27)
3 [blood-borne pathogens/] (0)

4 (blood* adj2 (pathogen* or poison*)).ti,ab. (1)
5 [exp systemic inflammatory response syndrome/] (0)
6 'systemic inflammatory response syndrome*'.tw. (0)
7 sirs.ti,ab. (22)
8 (septicaemi* or septicemi*).ti,ab. (3)
9 ((septic or cryptic) adj2 shock).ti,ab. (2)
10 (pyaemi* or pyemi* or pyohemi*).ti,ab. (0)
11 (bacter?emi* or fung?emi* or parasit?emi* or vir?emi*).ti,ab. (8)
12 (hypotension adj3 induced adj3 hypoperfusion).ti,ab. (0)
13 or/1-12 (61)
14 [exp Calcitonin/] (0)
15 (procalcitonin* or calcitonin*).tw. (2)
16 ((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)).tw. (47)
17 or/14-16 (49)
18 13 and 17 (0)

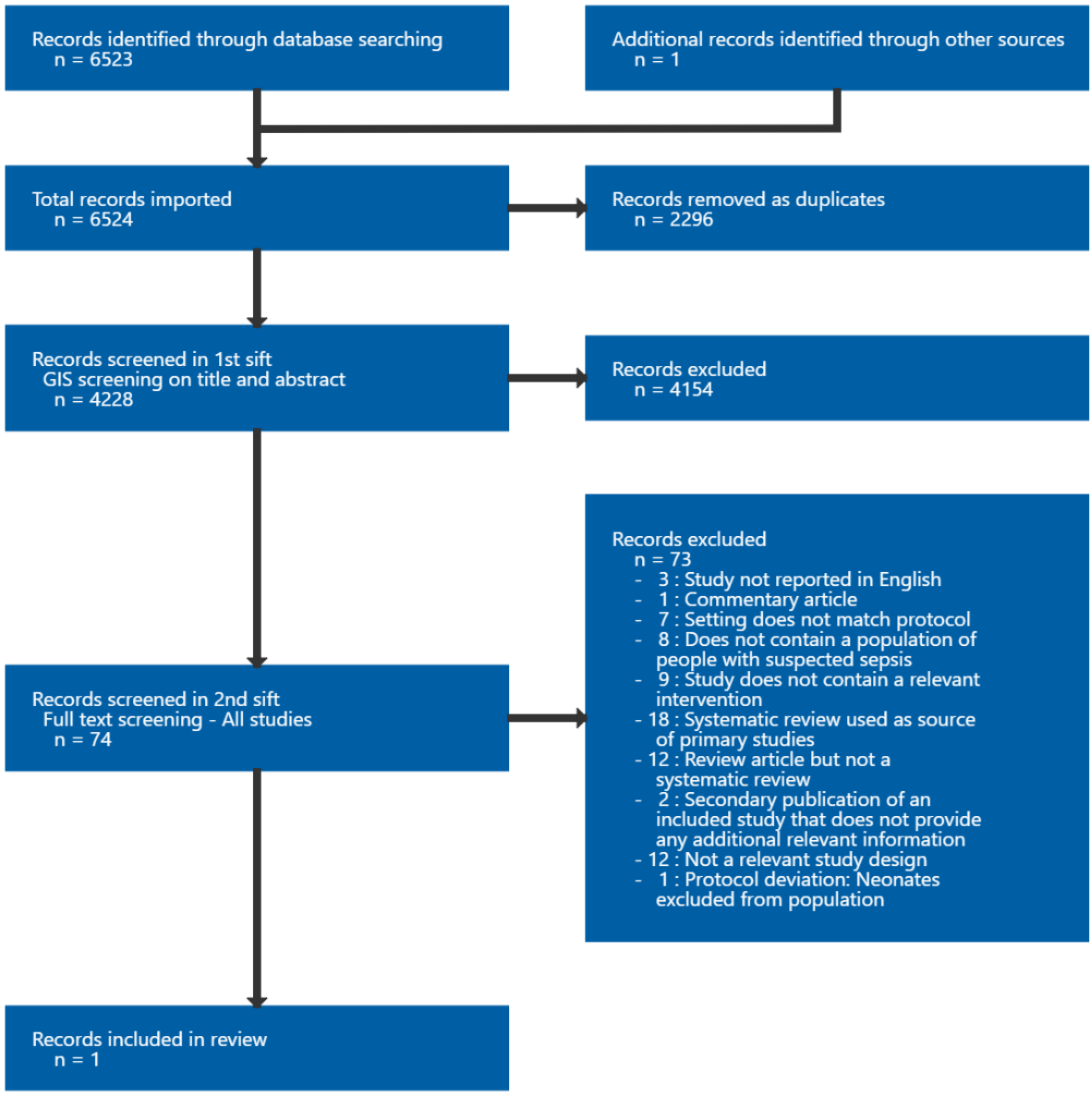
1 **Database name: International HTA Database**

Searches
(sepsis OR septi* OR crypti* OR pyaemi* OR pyemi* OR pyohemi* OR bacteremi* OR bacteraemi* OR fungemi* OR fungaemi* OR parasitemi* OR parasitaemi* OR viremi* OR viraemi* OR hypoperfusion* OR pathogen* OR poison*) AND (procalcitonin* OR calcitonin*) = 5 results (limited to English and 2016+)
(sepsis OR septi* OR crypti* OR pyaemi* OR pyemi* OR pyohemi* OR bacteremi* OR bacteraemi* OR fungemi* OR fungaemi* OR parasitemi* OR parasitaemi* OR viremi* OR viraemi* OR hypoperfusion* OR pathogen* OR poison*) AND ((PCT or ADVIA or Centaur or BRAHMS or Kryptor or Elecsys or LIAISON or VIDAS) and (assay* or immunoassay* or serum* or plasma* or test* or biomarker* or marker* or measur* or diagn*)) = 0 (limited to English and 2016+)

2
3
4

Appendix C - Study selection – effectiveness evidence

Figure 1 Effectiveness evidence study selection



Appendix D - Effectiveness evidence tables

Todd et al (2026)

Bibliographic Reference	Todd, S., Euden, J., Condie, J., Aston, S., Barlow, G., Brookes-Howell, L., Carman, J., Carrol, E. D., Gilbert, S., Howard, P., Hood, K., Inada-Kim, M., Llewelyn, M. J., Maboshe, W., McGill, F., Milosevic, S., Nsutebu, E., Schmidt, P., Tabner, A., Taylor-Robinson, D., Thomas, A., Thomas-Jones, E., Welters, I. D., Pallmann, P., & French, N., on behalf of the PRONTO trial team. (2026). Procalcitonin and NEWS2 evaluation for Timely identification of sepsis and Optimal use of antibiotics in the Emergency Department (PRONTO): A multi-centre, randomised, controlled, open-label, phase 3 trial. Pre-publication.

Study details

Trial registration number and/or trial name	PRONTO: ISRCTN54006056
Study type	Randomised controlled trial (RCT)
Study location	England and Wales, UK
Study setting	20 hospital EDs within 17 NHS Trusts or Health Boards
Study dates	November 2020 to November 2023
Sources of funding	National Institute for Health Research (NIHR)
Inclusion criteria	• Age 16 or over • Presenting to emergency department • Suspected sepsis
Exclusion criteria	• Already on intravenous antibiotics

	• Use of any chemotherapy agent associated with myeloablation/suppression • History of solid organ transplantation, allogeneic bone marrow or stem cell transplantation within 3 months prior • Patients known to require urgent surgical intervention (within the course of current admission) • Presence of an advance directive to withhold life-sustaining treatment
Intervention(s)	Clinical management based on NEWS2 score and PCT-guided risk assessment. Blood sample was obtained from either venous blood draw for testing using BRAHMS PCT-Direct and PathFast or capillary sampling via finger prick for testing using BRAHMS PCT-Direct only. The PCT test was used in combination with NEWS2 assessment using a guidance-only algorithm for clinicians, based on the NICE sepsis guideline (NG51) and associated NHS England guidance.
Comparator	Standard clinical management with risk assessment based on NEWS2 scoring. The algorithm for clinical management was based on the NICE sepsis guideline (NG51) and associated NHS England guidance.
Outcome measures	• Mortality [Time Frame: 28 days] • IV antibiotics initiation at 3 hours • Time until initiation of IV antibiotic therapy • Late IV antibiotic initiation: antibiotics commenced after 3 hours • Number of days on IV antibiotics • Number of days on any antibiotic • Number of days on broad-spectrum antibiotics (IV and oral) • ICU admission • Length of ICU stay • Length of hospital stay • Adverse antibiotic outcomes • Readmission to hospital within 90 days • Mortality within 90 days • Health utility measured using EQ-5D/5L at 28 and 90 days

Number of participants	From a total of 11,380 adults screened for eligibility, 7667 were randomised. 1657 participants withdrew, leaving 6010 eligible for analysis up to day 28. The primary analysis of the co-primary endpoints was conducted on 5453 participants (89·12%) with complete data on both IV antibiotic initiation at 3 hours and 28-day mortality; 2738 in the PCT-guided care arm and 2715 in the usual care arm.
Duration of follow-up	28 days and 90 days
Loss to follow-up	• 6010 participants were available for analysis up to day 28. • 5904 participants were available for analysis up to day 90.
Methods of analysis	The primary analysis was performed based on a modified intention-to-treat population, including all randomised consenting participants with available outcome data for both co-primary endpoints.

Abbreviations: NIHR= National Institute for Health and Care Research; NEWS2= national early warning score 2; PCT= procalcitonin; HRQoL= health related quality of life; EQ-5D/5L= European quality of life 5 dimensions 5 level version.

Study arms
Procalcitonin + NEWS2 (N = 2738)

Standard care (NEWS2) (N = 2715)

Characteristics
Arm-level characteristics

Characteristic	Procalcitonin + NEWS2 (N = 2738)	Standard care (NEWS2) (N = 2715)
% Female Nominal	50.7	50.1

Characteristic	Procalcitonin + NEWS2 (N = 2738)	Standard care (NEWS2) (N = 2715)
% Male Nominal	49.3	49.9
% Other Nominal	1	0
Age (years) Median (IQR)	72 (56 to 82)	73 (58 to 82)
Comorbidities – COPD (%) Nominal	22.8	22.7
Comorbidities - CKD (**%)** Nominal	13.6	13.7
Comorbidities - Heart failure (%) Nominal	12.3	13.9
Comorbidities - Ischemic heart disease (%) Nominal	10.5	11.6
Comorbidities - Stroke/TIA (%) Nominal	10.3	10.8
Comorbidities - Dementia (%)	9.2	9.8

Characteristic	Procalcitonin + NEWS2 (N = 2738)	Standard care (NEWS2) (N = 2715)
Nominal		
Comorbidities - Physical disability (%) Nominal	9.1	8.8
Comorbidities - Solid tumour malignancy (%) Nominal	7.5	7.5
Comorbidities - Myocardial infarction (%) Nominal	6.6	5.9
Comorbidities - Diabetes (%) Nominal	22.8	24
NEWS2 score - <=4 (%) Nominal	37.8	38.7
NEWS2 score - 5-6 (%) Nominal	26.9	26.5
NEWS2 score - >=7 (%) Nominal	35.2	34.8
Antibiotics within 14 days prior (%) Nominal	22.9	23.9

Critical appraisal - Critical Appraisal - Cochrane RoB 2.0 - RCT - Over 16s

Overall bias and Directness	Risk of bias judgement	Moderate *(Due to concerns about high attrition and therefore missing data, and about low adherence to the intervention.)*
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E - Forest plots

No meta-analysis was conducted, as there was only one study included.

Appendix F - GRADE summary

Table 1 Effectiveness evidence summary: Procalcitonin + standard care vs standard care dichotomous outcomes

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo	Risk difference with Procalcitonin + standard care vs standard care
Mortality within 30 days (measured on day 28)	5453 (1 RCT: PRONTO Todd 2026)	Low[a,b] **EV. OF BENEFIT**	RR 0.82 (0.72 to 0.93)	166 per 1,000	30 fewer per 1,000 (from 46 fewer to 12 fewer)
Time to initiation of IV antibiotics (number of patients who received antibiotics within 3 hours)	5453 (1 RCT: PRONTO Todd 2026)	Very low[a,b,c] **EV. OF NO EFFECT**	RR 1.00 (0.95 to 1.06)	482 per 1,000	0 fewer per 1,000 (from 24 fewer to 29 more)
Admission to ICU within hospital stay (number of patients admitted)	5842 (1 RCT: PRONTO Todd 2026)	Very low[a,b,c] **EV. OF NO EFFECT**	OR 1.19 (0.96 to 1.47)	56 per 1,000	10 more per 1,000 (from 2 fewer to 24 more)

Abbreviations: CI: confidence interval; **RR:** risk ratio; **OIS:** optimal information size

Explanations

a. Serious risk of bias in the evidence contributing to the outcome. The evidence came from a study at moderate risk of bias as per Cochrane RoB 2.0
b. Single study- downgraded once for inconsistency, as single study outcomes may otherwise receive favourable ratings for inconsistency by default.
c. Outcome was downgraded twice for imprecision because it did not reach OIS

Table 2 Effectiveness evidence summary: Procalcitonin + standard care vs standard care outcomes reported as medians (IQR)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)
Time to initiation of IV antibiotics (hours)	3839 (1 RCT: PRONTO Todd 2026)	Low[a,b] **EV. OF NO EFFECT**	HR 0.953 (0.9–1.02)
duration of IV antibiotic treatment (days)	5842 (1 RCT: PRONTO Todd 2026)	Low[a,b] **EV. OF NO EFFECT**	IRR 1.000 (0.937–1.068)
length of hospital stay (days)	5804 (1 RCT: PRONTO Todd 2026)	Low[a,b] **EV. OF NO EFFECT**	IRR 0.983 (0.933–1.036)

Abbreviations: CI: confidence interval; **HR:** hazard ratio; **OIS:** optimal information size; **IRR:** incidence rate ratio

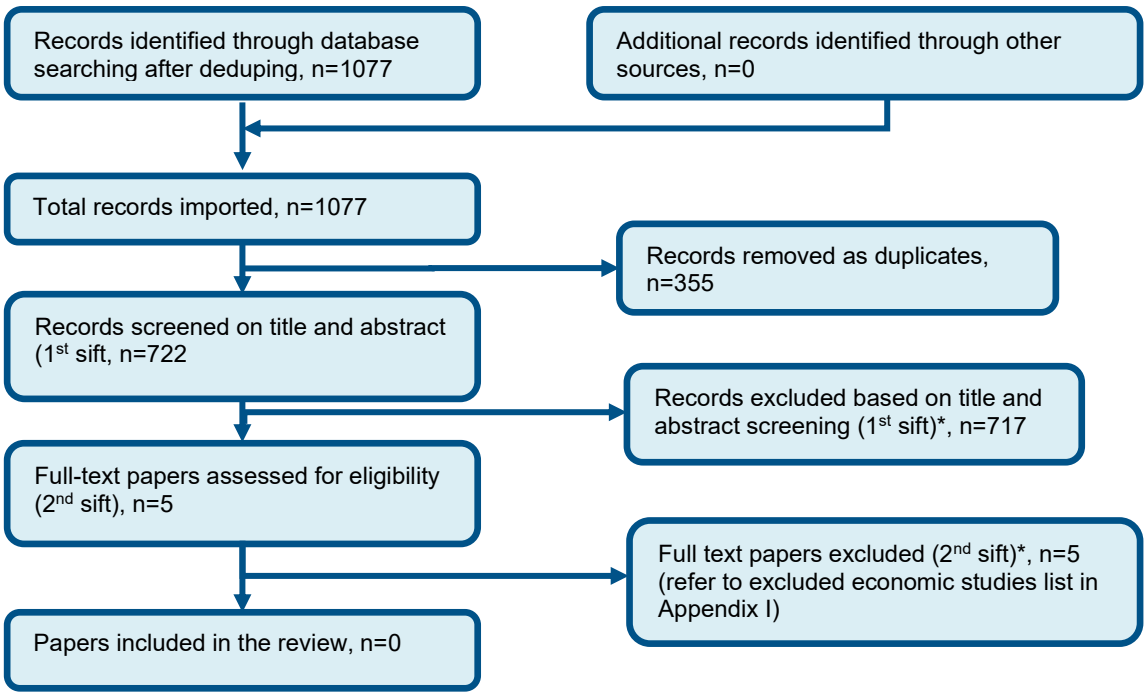
Explanations

a. Serious risk of bias in the evidence contributing to the outcome. The evidence came from a study at moderate risk of bias as per Cochrane RoB 2.0

b. Single study- downgraded once for inconsistency, as single study outcomes may otherwise receive favourable ratings for inconsistency by default.

Appendix G - Economic evidence study selection

Figure 2: Economic evidence study selection flow chart



Appendix H - Economic evidence tables

No evidence was identified which was applicable to this review question.

Appendix I - Excluded studies

Effectiveness

Table 2 Studies excluded from the effectiveness review

Study	Reason for exclusion
Abdelrahman, S.T., Omran, J.A., Del Castillo Miranda, J.C. et al. (2025) Point-of-Care Biomarkers in Pediatric Emergency Medicine: Advancing Rapid Diagnostics, Overcoming Limitations, and Shaping Future Innovations. Current Treatment Options in Pediatrics 11(1): 19	- Review article but not a systematic review
Andriolo, Brenda Ng, Andriolo, Regis B, Salomao, Reinaldo et al. (2017) Effectiveness and safety of procalcitonin evaluation for reducing mortality in adults with sepsis, severe sepsis or septic shock. The Cochrane database of systematic reviews 1: cd010959	- Systematic review used as source of primary studies
Anonymous (2007) Procalcitonin-Guided Antibiotic Therapy.	- Review article but not a systematic review *Book chapter*
Basitha, Kuntum, Sukardi, Rubiana, Farida Soenarto, Ratna et al. (2019) The value of procalcitonin in systemic inflammatory response syndrome after open-heart surgery for CHD. Cardiology in the young 29(11): 1335-1339	- Study does not contain a relevant intervention *No treatment decisions were based on PCT*
Bourika, Vasiliki; Rekoumi, Evangelia-Areti; Giamarellos-Bourboulis, Evangelos J (2025) Biomarkers to guide sepsis management. Annals of intensive care 15(1): 103	- Not a relevant study design *Review of diagnostic studies*
Branche, Angela, Neeser, Olivia, Mueller, Beat et al. (2019) Procalcitonin to guide antibiotic decision making. Current opinion in infectious diseases 32(2): 130-135	- Review article but not a systematic review
Cao, J and Sun, Y (2025) Assessment of the Efficacy of Procalcitonin, C-Reactive Protein, and Albumin Levels-guided Antibiotics Use in Sepsis. Mediterranean journal of hematology and infectious diseases 17(1)	- Study does not contain a relevant intervention *Mixed biomarkers used to guide treatment. Cannot isolate the effect of using PCT.*
Claessens, Y-E, Schmidt, J, Batard, E et al. (2010) Can C-reactive protein, procalcitonin and mid-regional pro-atrial natriuretic peptide measurements guide choice of in-patient or out-patient care in acute pyelonephritis? Biomarkers In Sepsis (BIS) multicentre study. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 16(6): 753-60	- Study does not contain a relevant intervention *No treatment decisions made using PCT*
De Oro, Nathalia, Gauthreaux, Maria E, Lamoureux, Julie et al. (2019) The Use of Procalcitonin as a Sepsis	- Not a relevant study design *Retrospective*

Study	Reason for exclusion
Marker in a Community Hospital. The journal of applied laboratory medicine 3(4): 545-552	
Elnajdy, Dina and El-Dahiyat, Faris (2022) Antibiotics duration guided by biomarkers in hospitalized adult patients; a systematic review and meta-analysis. Infectious diseases (London, England) 54(6): 387-402	- Systematic review used as source of primary studies
Farooq, Ayesha and Colon-Franco, Jessica M (2019) Procalcitonin and Its Limitations: Why a Biomarker's Best Isn't Good Enough. The journal of applied laboratory medicine 3(4): 716-719	- Review article but not a systematic review
Fazili, Tasaduq, Endy, Timothy, Javaid, Waleed et al. (2012) Role of procalcitonin in guiding antibiotic therapy. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists 69(23): 2057-61	- Review article but not a systematic review
Feng, Kun; Zhang, Tingwei; Hua, Ziyu (2025) Discontinuation of empirical antibiotics in suspected neonatal early-onset sepsis: a systematic review and meta-analysis. Pediatric research	- Systematic review used as source of primary studies
Freund, Yonathan, Delerme, Samuel, Goulet, Helene et al. (2012) Serum lactate and procalcitonin measurements in emergency room for the diagnosis and risk-stratification of patients with suspected infection. Biomarkers : biochemical indicators of exposure, response, and susceptibility to chemicals 17(7): 590-6	- Not a relevant study design *Prognostic*
Gai, L; Tong, Y; Yan, B-Q (2018) Research on the diagnostic effect of PCT level in serum on patients with sepsis due to different pathogenic causes. European review for medical and pharmacological sciences 22(13): 4238-4242	- Study does not contain a relevant intervention *No treatment decisions based on the pathogen identified*
Garnacho-Montero, Jose, Arenzana-Seisdedos, Angel, De Waele, Jan et al. (2017) To which extent can we decrease antibiotic duration in critically ill patients?. Expert review of clinical pharmacology 10(11): 1215-1223	- Systematic review used as source of primary studies
Georgopoulou, Antonia-Panagiota, Savva, Athina, Giamarellos-Bourboulis, Evangelos J et al. (2011) Early changes of procalcitonin may advise about prognosis and appropriateness of antimicrobial therapy in sepsis. Journal of critical care 26(3): 331e1-7	- Not a relevant study design *Single group observational study; no controls*
Goulet, H., Delerme, S., Madonna-Py, B. et al. (2024) Procalcitonin-based algorithm (ALGOPRO) for antibiotic and hospitalization decisions in adult patients with fever in the emergency department: a pilot study. Annales Francaises de Medecine d'Urgence 14(1): 17-25	- Study not reported in English
Gregoriano, Claudia, Wirz, Yannick, Heinsalo, Ashley et al. (2024) Procalcitonin-guided antibiotic treatment in patients with cancer: a patient-level meta-analysis	- Systematic review used as source of primary studies

Study	Reason for exclusion
from randomized controlled trials. BMC cancer 24(1): 1467	
Gupta, Simran; Klompas, Michael; Rhee, Chanu (2025) Reassessing Procalcitonin-Guided Antibiotic Therapy in Critically Ill Patients with Sepsis: Lessons from the ADAPT-Sepsis Trial. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America	- Setting does not match protocol *ICU*
Hassan, Junaid, Khan, Safeera, Zahra, Rukhe et al. (2022) Role of Procalcitonin and C-reactive Protein as Predictors of Sepsis and in Managing Sepsis in Postoperative Patients: A Systematic Review. Cureus 14(11): e31067	- Does not contain a population of people with suspected sepsis *Postoperative population already in hospital*
Heilmann, E., Gregoriano, C., Annane, D. et al. (2021) Duration of antibiotic treatment using procalcitonin-guided treatment algorithms in older patients: A patient-level meta-analysis from randomized controlled trials. Age and Ageing 50(5): 1546-1556	- Systematic review used as source of primary studies
Iankova, Irena, Thompson-Leduc, Philippe, Kirson, Noam Y et al. (2018) Efficacy and Safety of Procalcitonin Guidance in Patients With Suspected or Confirmed Sepsis: A Systematic Review and Meta-Analysis. Critical care medicine 46(5): 691-698	- Systematic review used as source of primary studies
James, Jemila; Tewari, Vishal Vishnu; Jain, Naveen (2021) Diagnostic Accuracy of Clinical Tool 'STOPS' and Serum Procalcitonin for Optimizing Antibiotic Therapy in Neonates Born at >= 28 Weeks of Gestation with Neonatal Sepsis. Mediterranean journal of hematology and infectious diseases 13(1): e2021019	- Not a relevant study design *Diagnostic*
Jeon, Kyeongman, Suh, Jae Kyung, Jang, Eun Jin et al. (2019) Procalcitonin-Guided Treatment on Duration of Antibiotic Therapy and Cost in Septic Patients (PRODA): a Multi-Center Randomized Controlled Trial. Journal of Korean medical science 34(14): e110	- Setting does not match protocol *ICU*
Ko, Young Hwii, Ji, Yoon Seob, Park, Sin-Youl et al. (2016) Procalcitonin determined at emergency department as na early indicator of progression to septic shock in patient with sepsis associated with ureteral calculi. International braz j urol : official journal of the Brazilian Society of Urology 42(2): 270-6	- Not a relevant study design *Prognostic study*
Koksal, Nilgun, Harmanci, Ramazan, Cetinkaya, Merih et al. (2007) Role of procalcitonin and CRP in diagnosis and follow-up of neonatal sepsis. The Turkish journal of pediatrics 49(1): 21-9	- Not a relevant study design *Diagnostic study*
Kundes, M F and Kement, M (2019) Value of procalcitonin levels as a predictive biomarker for sepsis in pediatric patients with burn injuries. Nigerian journal of clinical practice 22(7): 881-884	- Study does not contain a relevant intervention *PCT measurements were not used to guide treatement*

Study	Reason for exclusion
Kyriazopoulou, Evdoxia and Giamarellos-Bourboulis, Evangelos J (2022) Antimicrobial Stewardship Using Biomarkers: Accumulating Evidence for the Critically Ill. Antibiotics (Basel, Switzerland) 11(3)	- Systematic review used as source of primary studies
Kyriazopoulou, Evdoxia, Liaskou-Antoniou, Lydia, Adamis, George et al. (2021) Procalcitonin to Reduce Long-Term Infection-associated Adverse Events in Sepsis. A Randomized Trial. American journal of respiratory and critical care medicine 203(2): 202-210	- Does not contain a population of people with suspected sepsis *Confirmed sepsis in hospital before trial recruitment, rather than suspected sepsis*
Kyriazopoulou, Evdoxia, Stylianakis, Emmanouil, Damoraki, Georgia et al. (2025) Procalcitonin-guided early cessation of antibiotics prevents gut inflammation and preserves gut microbiome: Data from the PROGRESS controlled trial. International journal of antimicrobial agents 66(2): 107507	- Secondary publication of an included study that does not provide any additional relevant information
Lam, Simon W, Bauer, Seth R, Fowler, Robert et al. (2018) Systematic Review and Meta-Analysis of Procalcitonin-Guidance Versus Usual Care for Antimicrobial Management in Critically Ill Patients: Focus on Subgroups Based on Antibiotic Initiation, Cessation, or Mixed Strategies. Critical care medicine 46(5): 684-690	- Systematic review used as source of primary studies
Liu Y; Yang W; Wei J (2017) Guiding Effect of Serum Procalcitonin (PCT) on the Antibiotic Application to Patients with Sepsis. Iranian journal of public health 46(11): 1535-1539	- Study does not contain a relevant intervention *PCT used for later treatment, rather than early decisions*
Mahmutaj, Dafina, Krasniqi, Shaip, Braha, Bedri et al. (2017) The Predictive Role of Procalcitonin On the Treatment of Intra-Abdominal Infections. Open access Macedonian journal of medical sciences 5(7): 909-914	- Does not contain a population of people with suspected sepsis *Post surgical patients at risk of infection and sepsis*
Mann, Elizabeth A; Wood, Geri L; Wade, Charles E (2011) Use of procalcitonin for the detection of sepsis in the critically ill burn patient: a systematic review of the literature. Burns : journal of the International Society for Burn Injuries 37(4): 549-58	- Not a relevant study design *Diagnostic review*
Masiá, M, Padilla, S, Ortiz de la Tabla, V et al. (2017) Procalcitonin for selecting the antibiotic regimen in outpatients with low-risk community-acquired pneumonia using a rapid point-of-care testing: a single-arm clinical trial. PloS one 12(4): e0175634	- Does not contain a population of people with suspected sepsis *pneumonia with low risk of sepsis*
Mathur, N B and Behera, Bijaylaxmi (2019) Blood Procalcitonin Levels and Duration of Antibiotics in Neonatal Sepsis. Journal of tropical pediatrics 65(4): 315-320	- Study does not contain a relevant intervention *PCT measurements were not used to guide treatement decisions*
Meier, Marc A, Branche, Angela, Neeser, Olivia L et al. (2019) Procalcitonin-guided Antibiotic Treatment in Patients With Positive Blood Cultures: A Patient-level Meta-analysis of Randomized Trials. Clinical infectious	- Systematic review used as source of primary studies

Study	Reason for exclusion
diseases : an official publication of the Infectious Diseases Society of America 69(3): 388-396	
Mironov, P.I. and Lykov, A.V. (2010) Diagnostics and treatment of sepsis in the acute phase of severe heat injury. Khirurgiia: 22-24	- Study not reported in English
Muller, B. and Prat, C. (2006) Markers of acute inflammation in assessing and managing lower respiratory tract infections: Focus on procalcitonin. Clinical Microbiology and Infection 12(suppl9): 8-16	- Review article but not a systematic review
Nasir, I.A., Mele, H.U., Babayo, A. et al. (2015) Serum Procalcitonin Assay for Investigations and Clinical Management of Neonatal Sepsis: A Review. Journal of Pediatric Infectious Diseases 10(1): 3-11	- Review article but not a systematic review
Nobre, Vandack, Harbarth, Stephan, Graf, Jean-Daniel et al. (2008) Use of procalcitonin to shorten antibiotic treatment duration in septic patients: a randomized trial. American journal of respiratory and critical care medicine 177(5): 498-505	- Setting does not match protocol *ICU*
Oliveira, C.F., Botoni, F.A., Oliveira, C.R.A. et al. (2013) Procalcitonin versus C-reactive protein for guiding antibiotic therapy in sepsis: A randomized trial. Critical Care Medicine 41(10): 2336-2343	- Setting does not match protocol *ICU*
Papp, Marton, Kiss, Nikolett, Baka, Mate et al. (2023) Procalcitonin-guided antibiotic therapy may shorten length of treatment and may improve survival-a systematic review and meta-analysis. Critical care (London, England) 27(1): 394	- Systematic review used as source of primary studies
Peng, Fei, Chang, Wei, Xie, Jian-Feng et al. (2019) Ineffectiveness of procalcitonin-guided antibiotic therapy in severely critically ill patients: A meta-analysis. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases 85: 158-166	- Systematic review used as source of primary studies
Pepper, Dominique J, Sun, Junfeng, Rhee, Chanu et al. (2019) Procalcitonin-Guided Antibiotic Discontinuation and Mortality in Critically Ill Adults: A Systematic Review and Meta-analysis. Chest 155(6): 1109-1118	- Setting does not match protocol *Review of RCTs in ICU setting*
Porta, L., Liu, Y., Chen, P.-T. et al. (2025) GRADE-based procalcitonin guideline for emergency departments. American Journal of Emergency Medicine 89: 109-123	- Review article but not a systematic review
Prabhu, Malavika, Wilkie, Gianna, MacEachern, Mark et al. (2023) Procalcitonin levels in pregnancy: A systematic review and meta-analysis of observational studies. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics 163(2): 484-494	- Study does not contain a relevant intervention *Review of PCT levels in pregnant people, but PCT not used to guide treatment decisions.*

Study	Reason for exclusion
Pundiche, M., Sarbu, V., Unc, O.D. et al. (2012) [Role of procalcitonin in monitoring the antibiotic therapy in septic surgical patients]. Chirurgia (Bucharest, Romania : 1990) 107(1): 71-78	- Study not reported in English
Rafiq, Sonya, Shi, Chunhu, Ghosal, Shraboni et al. (2026) Clinical effectiveness of procalcitonin- or C-reactive protein-guided antibiotic discontinuation protocols for adult patients who are critically ill with sepsis: a rapid systematic review and meta-analysis. Anaesthesia	- Systematic review used as source of primary studies
Robati Anaraki, Mahmoud; Nouri-Vaskeh, Masoud; Abdoli Oskouie, Shahram (2020) Effectiveness of procalcitonin-guided antibiotic therapy to shorten treatment duration in critically-ill patients with bloodstream infections: a systematic review and meta-analysis. Le infezioni in medicina 28(1): 37-46	- Systematic review used as source of primary studies
Schuetz, P., Wirz, Y., Sager, R. et al. (2017) Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database of Systematic Reviews 2017(10): cd007498	- Systematic review used as source of primary studies
Schuetz, Philipp, Bolliger, Rebekka, Merker, Meret et al. (2018) Procalcitonin-guided antibiotic therapy algorithms for different types of acute respiratory infections based on previous trials. Expert review of anti-infective therapy 16(7): 555-564	- Systematic review used as source of primary studies
Schuetz, Philipp, Chiappa, Victor, Briel, Matthias et al. (2011) Procalcitonin algorithms for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms. Archives of internal medicine 171(15): 1322-31	- Systematic review used as source of primary studies
Schuetz, Philipp; Christ-Crain, Mirjam; Muller, Beat (2009) Procalcitonin and other biomarkers to improve assessment and antibiotic stewardship in infections--hope for hype?. Swiss medical weekly 139(2324): 318-26	- Review article but not a systematic review
Shafiq, Nusrat, Gautam, Vikas, Pandey, Avaneesh Kumar et al. (2017) A meta-analysis to assess usefulness of procalcitonin-guided antibiotic usage for decision making. The Indian journal of medical research 146(5): 576-584	- Systematic review used as source of primary studies
Sligl, Wendy I, Chen, Justin Z, Wang, Xiaoming et al. (2023) Antimicrobial stewardship, procalcitonin testing, and rapid blood-culture identification to optimize sepsis care in critically ill adult patients: A quality improvement initiative. Antimicrobial stewardship & healthcare epidemiology : ASHE 3(1): e107	- Commentary article
Sridharan, Prasanna and Chamberlain, Ronald S (2013) The efficacy of procalcitonin as a biomarker in the management of sepsis: slaying dragons or tilting at windmills?. Surgical infections 14(6): 489-511	- Review article but not a systematic review

Study	Reason for exclusion
Srinivasan, Arathi; Kumar, Nuthan; Scott, Julius X (2021) Evaluation of serum procalcitonin, serum interleukin-6, and interleukin-8 as predictors of serious infection in children with febrile neutropenia and cancer. Indian journal of cancer 58(2): 185-189	- Does not contain a population of people with suspected sepsis *neutropenia*
Stocker, Martin and Giannoni, Eric (2024) Game changer or gimmick: inflammatory markers to guide antibiotic treatment decisions in neonatal early-onset sepsis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 30(1): 22-27	- Review article but not a systematic review
Stocker, Martin; Hop, Wim C J; van Rossum, Annemarie M C (2010) Neonatal Procalcitonin Intervention Study (NeoPInS): Effect of Procalcitonin-guided decision making on duration of antibiotic therapy in suspected neonatal early-onset sepsis: A multi-centre randomized superiority and non-inferiority Intervention Study. BMC pediatrics 10: 89	- Protocol deviation: Neonates excluded from population
Stocker, Martin, van Herk, Wendy, El Helou, Salhab et al. (2017) Procalcitonin-guided decision making for duration of antibiotic therapy in neonates with suspected early-onset sepsis: a multicentre, randomised controlled trial (NeoPIns). Lancet (London, England) 390(10097): 871-881	- Protocol deviation: Neonates excluded from population
Sundara, Sri Vidya, Lu, Xinyu, Busmail, Hamide et al. (2025) C-reactive Protein Versus Procalcitonin in the Early Diagnosis of Neonatal Sepsis: A Systematic Review. Cureus 17(8): e90353	- Not a relevant study design *Diagnostic review*
Svoboda, Petr, Kantorova, Iona, Scheer, Peter et al. (2007) Can procalcitonin help us in timing of re-intervention in septic patients after multiple trauma or major surgery?. Hepato-gastroenterology 54(74): 359-63	- Setting does not match protocol *ICU*
Thongsamer, Piyanuch and Laoprasopwattana, Kamolwish (2022) Using procalcitonin levels to predict infection and reduce unnecessary antibiotic usage in febrile children aged 3-36 months. Journal of infection in developing countries 16(9): 1445-1449	- Does not contain a population of people with suspected sepsis *Sepsis was an exclusion criteria*
Tujula, Benita, Hamalainen, Sari, Kokki, Hannu et al. (2020) Review of clinical practice guidelines on the use of procalcitonin in infections. Infectious diseases (London, England) 52(4): 227-234	- Review article but not a systematic review
Ulm, Lena, Hoffmann, Sarah, Nabavi, Darius et al. (2017) The Randomized Controlled STRAWINSKI Trial: Procalcitonin-Guided Antibiotic Therapy after Stroke. Frontiers in neurology 8: 153	- Does not contain a population of people with suspected sepsis *Primarily a stroke cohort, 28% of which developed infection or sepsis*

Study	Reason for exclusion
van der Does, Y., Limper, M., Jie, K.E. et al. (2018) Procalcitonin-guided antibiotic therapy in patients with fever in a general emergency department population: a multicentre non-inferiority randomized clinical trial (HiTEMP study). Clinical Microbiology and Infection 24(12): 1282-1289	- Does not contain a population of people with suspected sepsis *Fever, but no suspicion of sepsis*
Velissaris, D, Zareifopoulos, N, Lagadinou, M et al. (2021) Procalcitonin and sepsis in the Emergency Department: an update. European review for medical and pharmacological sciences 25(1): 466-479	- Not a relevant study design *Diagnostic/prognostic review*
Venkatesh, B, Kennedy, P, Kruger, P S et al. (2009) Changes in serum procalcitonin and C-reactive protein following antimicrobial therapy as a guide to antibiotic duration in the critically ill: a prospective evaluation. Anaesthesia and intensive care 37(1): 20-6	- Setting does not match protocol *ICU*
Walker, Sarah, Harding, Irasha, Soomro, Kamran et al. (2022) An evaluation into the use of procalcitonin levels as a biomarker of bacterial sepsis to aid the management of intrapartum pyrexia and chorioamnionitis. AJOG global reports 2(3): 100064	- Study does not contain a relevant intervention *No treatment decisions were based on PCT results*
Waterfield, Thomas, Maney, Julie-Ann, Lyttle, Mark D et al. (2020) Diagnostic test accuracy of point-of-care procalcitonin to diagnose serious bacterial infections in children. BMC pediatrics 20(1): 487	- Not a relevant study design *Diagnostic*

Abbreviations: PCT= procalcitonin

Economic

Table 3 Studies excluded from the economic review

Study	Reason for exclusion
Collins, Curtis D, Brockhaus, Kara, Sim, Taeyong et al. (2019) Analysis to determine cost-effectiveness of procalcitonin-guided antibiotic use in adult patients with suspected bacterial infection and sepsis. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists 76(16): 1219-1225	- Non-protocol population *Intensive care unit patients with sepsis*
De Oro, Nathalia, Gauthreaux, Maria E, Lamoureux, Julie et al. (2019) The Use of Procalcitonin as a Sepsis Marker in a Community Hospital. The journal of applied laboratory medicine 3(4): 545-552	- Non-protocol population *People with diagnosed sepsis*
Geraerds, A J L M, van Herk, Wendy, Stocker, Martin et al. (2021) Cost impact of procalcitonin-guided decision making on duration of antibiotic therapy for suspected early-onset sepsis in neonates. Critical care (London, England) 25(1): 367	- Non-protocol population *Under 16s (will be included in under 16s review)*

Study	Reason for exclusion
Kip, Michelle M A, van Oers, Jos A, Shajiei, Arezoo et al. (2018) Cost-effectiveness of procalcitonin testing to guide antibiotic treatment duration in critically ill patients: results from a randomised controlled multicentre trial in the Netherlands. Critical care (London, England) 22(1): 293	- Non-protocol population *Critically ill intensive care unit patients with suspected or confirmed infection/sepsis, and receiving antibiotic treatment at admission*
Stevenson, Matt, Forsyth, Jessica E, Hossain, Anower et al. (2025) Cost-effectiveness of procalcitonin-guided antibiotic duration for hospitalized patients with sepsis. Critical care (London, England) 29(1): 508	- Non-protocol population *Patients (≥18 years) admitted to either a critical care or intensive care unit whose intravenous antibiotics for suspected sepsis had been initiated within 24 hours and likely to be continued for at least 72 hours were included in the trial.*

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Appendix J - Methods

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are outlined below.

Methods for combining studies

Meta-analysis was intended to be performed where there was no significant variation between studies or extremely serious heterogeneity (I2 ≥80%). As there was only one study for people aged 16 and over, the evidence could not be pooled for these separate populations. As a result, the studies were reported separately with no meta-analysis conducted.

Assessing imprecision

Using the optimal information size (OIS) approach recommended by GRADE Guidance 34, imprecision in dichotomous outcomes reported as risk ratio (RR) and odds ratio (OR) was evaluated based on the ratio of the upper to the lower boundary of the confidence interval (CI). A ratio greater than 3 for RR or greater than 2.5 for OR was considered very seriously imprecise. This was used to determine whether to downgrade twice for imprecision. Continuous outcomes were assessed based on whether N is greater than or equal to either OIS or 800.

Assessing clinical importance

For this review, there were no published, consensus based or commonly accepted minimally important differences (MIDs) available for any of the outcomes, nor were any identified by the guideline committee (GC). The GC agreed that all outcomes are serious outcomes, therefore they decided to use statistical significance to assess clinical importance. For all outcomes, we used the following decision rules to assess clinical importance:

(1) Evidence of benefit (**EV. OF BENEFIT**): where the point estimate is less than 1 (which is the null value for RRs and ORs) and the 95%

CI does not include 1, indicating a statistically significant reduction in the outcome compared to the comparison group.

(2) Evidence of disbenefit (**EV. OF DISBENEFIT**): where the point estimate is greater than 1 and the 95% CI does not include 1, indicating a statistically significant increase in the outcome compared to the comparison group.

(3) Uncertain effect (**UN. EFFECT**): where the point estimate is less than or greater than 1 and the 95% CI includes 1, indicating no statistically significant difference between groups.

(4) Evidence of no effect (**EV. OF NO EFFECT**): where the point estimate is 1 and the 95% CI includes 1, indicating no statistically significant difference between groups.

Note: The above categories are based on positive outcomes (i.e., where a large Point Estimate indicates better outcome). If outcomes are negative (i.e., where a large Point Estimate indicates worse outcome), then whether an intervention is considered to have a benefit or disbenefit should be switched.

Informative statements

Informative statements were developed by considering both clinical importance and the certainty of the evidence. They were adapted from GRADE Guidance 26. An example of how these statements were drafted is provided in the table below.

Effect estimate (clinical importance)	**Suggested statements (replace X with intervention, replace 'reduce/increase' with direction of effect, replace 'outcome' with name of outcome, replace Y with name of comparator).**
HIGH Certainty of the evidence (GRADE)	
Effect (Evidence of benefit or disbenefit)	The evidence shows that X reduces/increases [outcome] compared to Y.
Trivial, small unimportant effect or	The evidence shows that X results in little to no difference in [outcome] compared to Y.

no effect (Evidence of no effect)	
MODERATE Certainty of the evidence	
Effect (Evidence of benefit or disbenefit)	The evidence shows that X probably reduces/increases [outcome] compared to Y.
Trivial, small unimportant effect or no effect (Evidence of no effect)	The evidence shows that X probably results in little to no difference in [outcome] compared to Y.
Uncertain effect	The evidence is probably uncertain about the effect of X on [outcome] compared to Y.
LOW Certainty of the evidence	
Effect (Evidence of benefit or disbenefit)	The evidence suggests X reduces/increases [outcome] compared to Y.
Trivial, small unimportant effect or no effect (Evidence of no effect)	The evidence suggests that X results in little to no difference in [outcome] compared to Y.
Uncertain effect	The evidence is uncertain about the effect of X on [outcome] compared to Y. The evidence suggests that X does not reduce/increase [outcome] compared to Y, but the evidence is uncertain
VERY LOW Certainty of the evidence	
Any effect	The evidence is very uncertain about the effect of X on [outcome] compared to Y. X may reduce/increase/have little to no effect on outcome but the evidence is very uncertain.

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