

***Review protocol for clinical and cost effectiveness of different types of IV fluids in people under 16 with suspected sepsis.***

ID	Field	Content
1.	Review title	Clinical and cost effectiveness of type of IV fluids for resuscitation in people aged under 16 with suspected sepsis.
2.	Review question(s)	What is the most clinical and cost-effective intravenous fluid for resuscitation of people aged under 16 with suspected sepsis?
3.	Objective	To determine the clinical and cost effectiveness of different types of IV fluid for resuscitation in people aged under 16 with suspected sepsis.
4.	Searches	<p>The following databases will be searched:</p> <ul style="list-style-type: none"> <li>• Cochrane Central Register of Controlled Trials (CENTRAL)</li> <li>• Cochrane Database of Systematic Reviews (CDSR)</li> <li>• Embase</li> <li>• Epistemonikos</li> <li>• MEDLINE in process</li> </ul> <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> <li>• 2016</li> <li>• English Language</li> <li>• Human studies</li> <li>• Conference abstracts excluded</li> <li>• OECD countries</li> </ul> <p>The full search strategies will be reported in the final review in accordance with the PRISMA-S reporting guide.</p>

5.	Condition or domain being studied	Suspected sepsis
6.	Population	<p>Inclusion:</p> <ul style="list-style-type: none"> <li>Children and young people aged under 16 or over with suspected sepsis in acute hospital* and ambulance settings who require resuscitation in the first 6 hours of care.</li> </ul> <p>*this could include hospital at home/virtual wards</p> <p>Exclusion:</p> <ul style="list-style-type: none"> <li>Adults and young people over the age of 16</li> <li>People who are or have recently been pregnant</li> </ul>
7.	Intervention	<p><u>Type of IV Fluid – Specifically:</u></p> <p>Crystalloid –</p> <ul style="list-style-type: none"> <li>Ringer’s lactate (Hartmann’s)</li> <li>Plasmalyte A</li> <li>Plasma-lyte 148</li> <li>Normal Saline (0.9%)</li> </ul> <p>Colloid – albumin</p> <ul style="list-style-type: none"> <li>Human albumin solution</li> <li>Fresh frozen plasma (FFP)</li> </ul>
8.	Comparator	<p><u>Type of IV Fluid – Specifically:</u></p> <p>Crystalloid –</p> <ul style="list-style-type: none"> <li>Plasmalyte A</li> <li>Plasma-lyte 148</li> <li>Normal Saline (0.9%)</li> <li>Ringer’s lactate (Hartmann’s)</li> </ul> <p>Colloid – albumin</p>

		<ul style="list-style-type: none"> <li>• Human albumin solution</li> <li>• FFP</li> </ul>
9.	Types of study to be included	<ul style="list-style-type: none"> <li>• Systematic reviews of RCTs</li> <li>• RCTs</li> <li>• Cohort studies (prospective and retrospective) if no RCTs are identified.</li> </ul>
10.	Other exclusion criteria	<ul style="list-style-type: none"> <li>• All other study types for example conference abstracts, editorials/letters, studies not published in English and study pre-prints.</li> <li>• Studies reporting data without confidence intervals or data that cannot be used to calculate confidence intervals.</li> </ul>
11.	Context	<p>The previous update of the sepsis guideline that published in November 2024, resulted in the splitting of the guideline into 3 population specific guidelines (<a href="#">Suspected sepsis in under 16s: recognition, diagnosis and early management</a>; <a href="#">Suspected sepsis in pregnant or recently pregnant people: recognition, diagnosis and early management</a>; <a href="#">Suspected sepsis in people aged 16 or over: recognition, assessment and early management</a>). The recommendations for type of IV fluids for resuscitation in people aged under 16 with suspected sepsis were not considered in the most recent update and there insufficient detail in the current sepsis guideline for under 16s with suspected sepsis (<a href="#">NG 254</a>) to guide clinicians as to when to start and stop fluids, what volume and what type of fluid is appropriate. The current recommendations in this area are taken from the NICE guideline on <a href="#">Intravenous fluid therapy in children and young people in hospital</a>.</p>
12.	Primary outcomes (critical outcomes)	<ul style="list-style-type: none"> <li>• All cause mortality – in hospital and 30 days</li> <li>• Adverse events including but not limited to Acute Kidney Injury (AKI)</li> </ul>
13.	Secondary outcomes (important outcomes)	<ul style="list-style-type: none"> <li>• Length of hospital stay</li> <li>• Admission to ICU</li> <li>• Organ system dysfunction</li> <li>• Pulmonary oedema</li> </ul>

14.	Data extraction (selection and coding)	<p>All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see <a href="#">Developing NICE guidelines: the manual</a> section 6.2). Study investigators may be contacted for missing data where time and resources allow.</p> <p>Where appropriate, this review will make use of the priority screening functionality within the EPPI-reviewer software. At least 50% of the data set will be screened and we will stop screening after that if we screen more than 250 records without an include</p>
15.	Risk of bias (quality) assessment	<p>Risk of bias will be assessed using the Cochrane ROB-2 checklist for RCTs, ROBIS for systematic reviews and ROBINS-I for cohort studies as described in <a href="#">Developing NICE guidelines: the manual</a>.</p>
16.	Strategy for data synthesis	<p><b>Approach to meta-analysis</b></p> <p>Pairwise meta-analyses will be performed in Cochrane RevMan Web. A pooled relative risk will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event.</p> <p>A pooled mean difference will be calculated for continuous outcomes (using the inverse variance method) when the same scale will be used to measure an outcome across different studies. Where different studies presented continuous data measuring the same outcome but using different numerical scales these outcomes will be all converted to the same scale before meta-analysis is conducted on the mean differences. Where outcomes measured the same underlying construct but</p>

		<p>used different instruments/metrics, data will be analysed using standardised mean differences (SMDs, Hedges' g).</p> <p>Fixed effects models will be fitted unless there is significant statistical heterogeneity in the meta-analysis, defined as <math>I^2 \geq 50\%</math>, when random effects models will be used instead.</p> <p>Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically assess the potential for publication bias.</p> <p>GRADE will be used to assess the quality of any pair-wise analysis of outcomes. Outcomes using evidence from RCTs will be rated as high quality initially and downgraded from this point. Reasons for upgrading the certainty of the evidence will also be considered.</p>
17.	Analysis of sub-groups	<ul style="list-style-type: none"> <li>• Newborn babies under 28 days</li> <li>• Under 3 months old</li> <li>• Under 16's excluding newborn babies</li> </ul>
18.	Type and method of review	<input checked="" type="checkbox"/> Intervention
		<input type="checkbox"/> Diagnostic
		<input type="checkbox"/> Prognostic
		<input type="checkbox"/> Qualitative
		<input type="checkbox"/> Epidemiologic
		<input type="checkbox"/> Service Delivery
		<input type="checkbox"/> Other (please specify)
19.	Language	English

20.	Country	England		
21.	Anticipated or actual start date	TBC		
22.	Anticipated completion date	TBC		
23.	Stage of review at time of this submission	<b>Review stage</b>	<b>Started</b>	<b>Completed</b>
		Preliminary searches	<input type="checkbox"/>	<input type="checkbox"/>
		Piloting of the study selection process	<input type="checkbox"/>	<input type="checkbox"/>
		Formal screening of search results against eligibility criteria	<input type="checkbox"/>	<input type="checkbox"/>
		Data extraction	<input type="checkbox"/>	<input type="checkbox"/>

		Risk of bias (quality) assessment	<input type="checkbox"/>	<input type="checkbox"/>
		Data analysis	<input type="checkbox"/>	<input type="checkbox"/>
24.	Named contact	<p><b>5a. Named contact</b> TBC</p> <p><b>5b Named contact e-mail</b> TBC</p> <p><b>5e Organisational affiliation of the review</b> National Institute for Health and Care Excellence (NICE) and Centre for Guidelines – Professional team</p>		
25.	Review team members	<p>From the Centre for Guidelines:</p> <ul style="list-style-type: none"> <li>• Guideline lead: Robby Richey</li> <li>• Senior technical analyst: James Jagroo</li> <li>• Technical analyst: Rachel Gick</li> <li>• Health Economics Adviser: Eric Slade</li> <li>• Senior Information specialist: Lynda Ayiku</li> </ul>		
26.	Funding sources/sponsor	This systematic review is being completed by the guideline development team which receives funding from NICE.		
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 <a href="#">Developing NICE guidelines: the manual</a> . Members of the guideline committee are available on the NICE website: tbc
29.	Other registration details	N/A
30.	Reference/URL for published protocol	tbc
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: <ul style="list-style-type: none"> <li>• notifying registered stakeholders of publication</li> <li>• publicising the guideline through NICE's newsletter and alerts</li> <li>• 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.</li> </ul>
32.	Keywords	Under 16, Sepsis, Intravenous, IV, Fluids, mortality
33.	Details of existing review of same topic by same authors	This is a new review question that will update <a href="#">Suspected sepsis in under 16s: recognition, diagnosis and early management</a>
34.	Current review status	<input checked="" type="checkbox"/> Ongoing

		<input type="checkbox"/> Completed but not published <input type="checkbox"/> Completed and published <input type="checkbox"/> Completed, published and being updated <input type="checkbox"/> Discontinued
35.	Additional information	N/A
36.	Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>