Review protocol for clinical and cost effectiveness of different volumes and rates of IV fluids in pregnant and recently pregnant people with suspected sepsis.

ID	Field	Content
1.	Review title	Clinical and cost effectiveness of different volumes and rates of IV fluids for resuscitation in pregnant people with suspected sepsis.
2.	Review question(s)	What is the most clinically and cost-effective volume and rate of administration for IV fluid for resuscitation in pregnant people with suspected sepsis?
3.	Objective	To determine the clinical and cost effectiveness of different volumes and different rates of IV fluids for resuscitation in pregnant people with suspected sepsis
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • Epistemonikos • MEDLINE in process Searches will be restricted by: • 2016 • English Language • Human studies • Conference abstracts excluded • OECD countries The full search strategies will be reported in the final review in accordance with the PRISMA-S reporting guide.
5.	Condition or domain being studied	Suspected sepsis
6.	Population	Inclusion: • People with suspected sepsis who are or have recently been pregnant**, and who are in in-hospital* and ambulance settings *this could include hospital at home/virtual wards

		**Someone is considered to have recently been pregnant: • in the 24 hours following a termination of pregnancy or miscarriage • for 4 weeks after giving birth. Exclusion: • People who are not or who have not recently been pregnant
7.	Intervention	• boluses of x ml/kg bodyweight / x minutes
8.	Comparator	• boluses of x ml/kg bodyweight / at different rates
9.	Types of study to be included	• Systematic reviews of RCTs • RCTs • Cohort studies (prospective and retrospective) if no RCTs are identified.
10.	Other exclusion criteria	• All other study types for example conference abstracts, editorials/letters, studies not published in English and study pre-prints. • Studies reporting data without confidence intervals or data that cannot be used to calculate confidence intervals.
11.	Context	During the previous update of the sepsis guideline that published in January 2024, the committee indicated that there is insufficient detail in the current sepsis guideline to guide clinicians as to when to start and stop fluids, what volume and what type of fluid is appropriate. This was addressed for people aged 16 or over who are not or have not recently been pregnant in a recent update, so recommendations for pregnant people need to be updated to align with this.
12.	Primary outcomes (critical outcomes)	• Mortality (all cause, in hospital and at 30 days) • organ support (vasoactive drugs, mechanical ventilation, RRT) • signs that someone is not responding: tachycardia; level of consciousness; blood pressure decrease (clinical significance as defined by the study); respiratory rate; blood lactate; urine output; peripheral perfusion; blood gases • Fluid overload – hypervolemia as defined by the study • Adverse events including but not limited to AKI • Neonatal outcomes

13.	Secondary outcomes (important outcomes)	• Length of hospital stay • Admission to ICU • Length of ICU stay
14.	Data extraction (selection and coding)	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. 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 Developing NICE guidelines: the manual section 6.2). Study investigators may be contacted for missing data where time and resources allow. 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
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the Cochrane ROB-2 checklist for RCTs, ROBIS for systematic review and ROBINS-I for cohort studies as described in Developing NICE guidelines: the manual.
16.	Strategy for data synthesis	**Approach to meta-analysis** 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. 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 used different instruments/metrics, data will be analysed using standardised mean differences (SMDs, Hedges' g). Fixed effects models will be fitted unless there is significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$, when random effects models will be used instead.

		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. 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.		
17.	Analysis of sub-groups	People with heart failure prior to developing sepsis Post operative patients for example caesarean section		
18.	Type and method of review	☒	Intervention	
		☐	Diagnostic	
		☐	Prognostic	
		☐	Qualitative	
		☐	Epidemiologic	
		☐	Service Delivery	
		☐	Other (please specify)	
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	January 2026		
22.	Anticipated completion date	tbc		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐	☐
		Piloting of the study selection process	☐	☐
		Formal screening of search results	☐	☐

		against eligibility criteria		
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	**5a. Named contact** sepsisupdate@nice.org.uk **5b Named contact e-mail** sepsisupdate@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and Guideline Development Team B		
25.	Review team members	From the Centre for Guidelines: • Guideline lead: Robby Richey • Technical analysts: Michellie Young and Rachel Gick • Senior technical analyst: James Jagroo • Health Economist: Eric Slade • Senior Information specialist: Lynda Ayiku		
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 Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: tbc	
29.	Other registration details	N/A	
30.	Reference/URL for published protocol	N/A	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	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 Sepsis in pregnancy: recognition, diagnosis and early management	
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information	N/A	
36.	Details of final publication	www.nice.org.uk	