Trials

STUDY PROTOCOL

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Development of a core outcome set for neonatal septic shock management: a study protocol

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Abstract

Background Neonatal septic shock represents a critical and life-threatening condition that necessitates immediate and personalized interventions. Prior research endeavors have been undertaken to inform the optimization of neonatal septic shock management, yet substantial heterogeneity prevails in the selection, measurement, and reporting of outcomes across relevant studies. The heterogeneity in outcome selections and measures impedes the comparability of results and the synthesis of evidence, thus contributing to suboptimal utilization of research findings. This protocol presents the methodology for identifying and developing a *C*ore *O*utcome *S*et for *N*eonatal *S*eptic *S*hock Management (COS-NSS), intended for use in both research and routine clinical practice.

A rigorous four-stage approach will be employed to develop the COS-NSS. In Stage 1, a scoping review will be conducted to compile a list of currently reported outcomes for neonatal septic shock management. Stage 2 will involve an expert stakeholder meeting using a semi-structured discussion approach to elucidate all identified outcomes and outcome domains, as well as to gather any additional outcomes. Moving to Stage 3, a two-round e-Delphi survey involving a wide variety of stakeholders will be undertaken to elicit diverse perspectives on the level of importance assigned to each proposed outcome. Finally, in Stage 4, the results of the Delphi study will be discussed in a consensus meeting to determine and agree on the final list of outcomes that will constitute the COS-NSS.

Discussion The stagewise approach integrates research evidence with multi-stakeholder perspectives to establish standardized outcomes that would improve consistency across neonatal septic shock trials. The development and uptake of the COS-NSS will facilitate effective comparison of studies, allowing for study synthesis and generation of high-quality evidence, thus ultimately fostering enhanced medical care for neonates suffering from septic shock.

Trial registration Core Outcome Measures in Effectiveness Trials (COMET) Initiative database registration: 2766. Registered on July 19th, 2023.

Keywords Septic shock, Neonate, Outcomes, Core outcome set, Scoping review, Delphi, Consensus meeting, Protocol

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Background

Neonatal sepsis has been a considerable worldwide public health challenge, with an estimated incidence of 3.0 million cases annually [1]. Neonates with sepsis may progress into septic shock, characterized by inadequate tissue perfusion and systemic hypotension [2]. Timely interventions are needed to reverse this life-threatening condition of septic shock from the end-organ damage and mortality [2, 3]. Although the exact incidence remains unknown, a retrospective cohort study over 6 years documented septic shock in 1.3% of cases admitted to the neonatal intensive care unit (NICU) with a corresponding mortality rate peaking at 71% for extremely low birth weight (ELBW) neonates [4].

Many published studies have focused on the management of neonatal septic shock to minimize end-organ damage and mortality [4–7]. Nevertheless, substantial heterogeneity in the outcomes measured and reported across existing neonatal studies has prevented effective and meaningful comparisons and pooling of findings [8]. A Core Outcome Set (COS) represents an agreed collection of important outcomes identified through robust consensus methods involving key stakeholders [9]. The use of COS could facilitate the comparison, contrast, and combination of study results as appropriate, thereby mitigating waste in research [10]. The Core Outcome Measures in Effectiveness Trials (COMET) Initiative is an international organization that promotes the development and application of COS in clinical trials and other forms of health research. The initiative maintains a database of registered COS studies, which includes two protocols related to neonatal sepsis [11, 12]. However, neither of these protocols specifically targets neonatal septic shock [11, 12].

Neonatal septic shock represents an advanced and severe stage of neonatal sepsis, distinguishing itself from the initial condition in various aspects, including definitions, clinical presentations and management strategies, as well as the physiological parameters and patient outcomes that clinicians prioritize and rely upon for informed decision-making [2, 13]. In the context of neonatal septic shock, the management of hypotension and the provision of cardiovascular support are of paramount significance. The primary outcome measures used to evaluate treatment effectiveness in neonatal septic shock frequently focus on the time to vasoactive-free hemodynamic stability and organ dysfunction. In contrast, in neonatal sepsis, a greater emphasis is placed on effectively addressing and combating the underlying infection. These differences underscore the necessity of developing a COS tailored to neonatal septic shock to ensure that the most relevant and important outcomes are consistently measured and reported in research studies.

This paper outlines the protocol for developing a suite of *COS* for *N*eonatal *S*eptic *S*hock management (COS-NSS) by following rigorous methodological processes and involving key stakeholder groups. The publication of this protocol could foster transparency within the COS development process and might aid in mitigating potential bias.

Aim and scope

Aim

The aim of this study is to develop a COS for use in both academic research and routine clinical practice for the management of neonatal septic shock. The specific study objectives are as follows:

(1) To ascertain an inclusive list of potential outcomes through a scoping review and an expert stakeholder meeting.
(2) To prioritize outcomes from the perspective of key stakeholder groups through e-Delphi surveys and a consensus meeting.

Scope

The health condition focused on in the current study is neonatal septic shock. All neonates or infants who have received medical care for septic shock management in an inpatient neonatal care setting will be included, with no restrictions based on gestational age, and all interventions employed to manage septic shock will be encompassed. The COS is intended to be applicable in clinical trials regarding neonatal septic shock and, where appropriate, in observational research, benchmarking, auditing, quality improvement, and routine treatment of neonatal septic shock. We plan to involve the active participation of clinical experts, researchers, caregivers, methodologists, and policy makers in developing the COS to incorporate diverse perspectives and expertise to ensure the final outcome set is most relevant to all stakeholders.

Methods

Study design

The protocol outlines our methods employed to develop the COS-NSS. The methods have been informed by the COMET Initiative Handbook [10], the Core Outcome Set-STAndards for Development (COS-STAD) recommendations [14], and other relevant COS development studies [15–18]. The reporting of this protocol adheres to the recommendations of the Core Outcome Set-STAndardised Protocol Items (COS-STAP) Statement; the checklist can be found in Additional file 1 [19]. The COS development workflow will proceed in four stages, as shown in Fig. 1: (1) scoping review, (2) expert stakeholder meeting, (3) two-round e-Delphi survey, and (4)

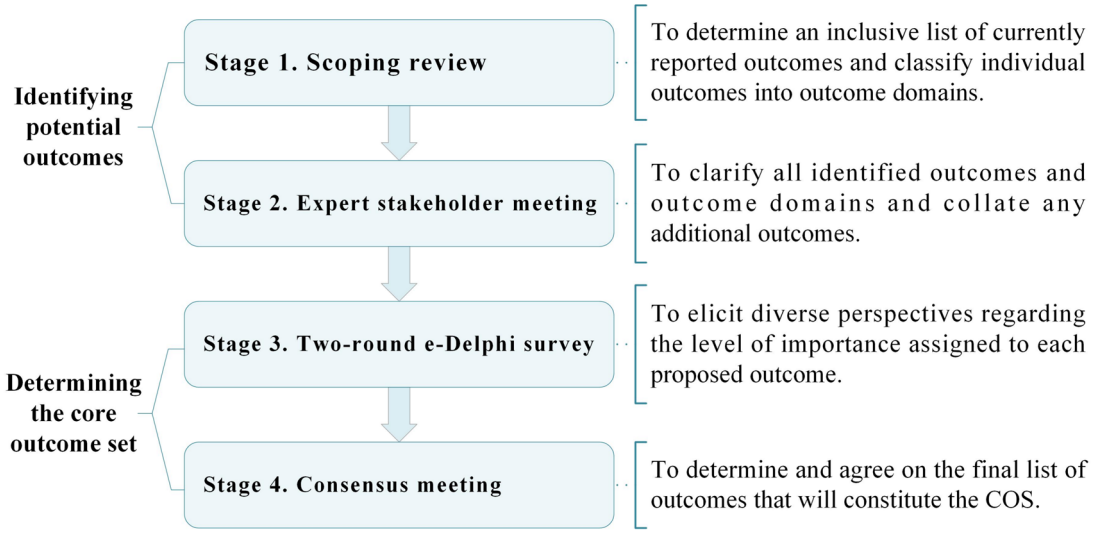

Fig. 1 Schematic overview of the core outcome set development workflow

consensus meeting. The study was prospectively registered with the COMET Initiative on July 19th, 2023, with study number 2766 (https://www.comet-initiative.org/Studies/Details/2766).

Study committees

A Study Management Group (SMG) representing a multidisciplinary skill set relevant to the study has been formed to account for the day-to-day project management. The SMG was chaired by one of the authors (JT) and composed of three leading clinicians specialized in either neonatal or pediatric critical care, two neonatal nursing specialists, two study coordinators with experience of literature review, qualitative research, and Delphi studies, two public research partners, and two experts in COS development. The members of the SMG will have a bimonthly meeting and as needed to guarantee the project progresses as planned.

A Study Advisory Group (SAG) will be formed to offer expert oversight and guidance throughout the COS development. The SAG members will be initially selected based on their scientific contributions and clinical influence in the field of neonatal septic shock. Subsequently, these selected members will be cordially requested to propose clinical and academic experts who possess the requisite knowledge and expertise to serve as members of the SAG. The SAG is anticipated to comprise 6 to 8 members, and these members' comments will be solicited primarily at three pivotal points during the study to (1) check the categorization and description of outcomes before applying the Delphi method, (2) review the structure and content of the list of items to be considered in the consensus process, and (3) confirm the final report following the consensus meeting.

Stage 1: scoping review

We will conduct a scoping review to determine an inclusive list of currently reported outcomes for the management of neonatal septic shock. Scoping reviews represent a form of knowledge synthesis that integrates diverse study designs to offer an overview or map of the evidence within a specific field [20]. The approach is valuable in comprehensively and inclusively synthesizing outcomes that have been measured and reported in the existing literature [21, 22]. This review will be guided by the research question: What outcomes have been investigated in research on neonatal septic shock management? The methodological framework proposed by Arksey and O'Malley [23], and further refined by the Joanna Briggs Institute [24], will be adhered to for conducting this scoping review. This process will be documented in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR) guidance [25].

Search strategy

We have conducted a systematic literature search of the PubMed, Embase (Ovid), and Cochrane Library databases from inception to May 03, 2023, to identify evidence describing and examining the neonatal septic shock management. The search strategies, combining MeSH and free-text terms to encapsulate patient populations (neonates, preterm infants, or infants with low birth weight) and the condition (septic shock), were initially developed by the first author, and subsequently reviewed by all authors. The complete search string for

each database can be found in Additional file 2. The bibliographies of all relevant articles were manually checked for additional eligible publications. ClinicalTrials.gov and the World Health Organization's International Clinical Trials Registry Platform (WHO ICTRP) have also been searched for relevant ongoing or recently completed studies. No restrictions were placed on language or year of publication throughout the electronic searches, and auto alerts of searches were set up to capture biweekly updates of new literature until completion of this review process.

Eligibility criteria

Table 1 displays the eligibility criteria for the scoping review, which were established following the "PCC" (Population, Concept, and Context) framework recommended by JBI [26]. Using this framework helps define the key components of the review and ensures clarity in identifying the relevant studies for inclusion.

Study selection and data extraction

After the removal of duplicates, four reviewers (ML, XL, YXL, and XG) diligently collaborated in an independent manner, applying the eligibility criteria first to titles and abstracts, and then to the full texts of all potential studies to ensure their relevance. The reviewers will continue working together for the data extraction process. Using a standardized form, the following data will be extracted where available from each study: identifier, design, setting, participant characteristics, reported outcomes, outcome measurement instruments, assessment time points, and respective outcome definitions as provided by the authors [10]. The extracted outcomes will be documented verbatim to guarantee authenticity and traceability from the source manuscript; any modifications made during extraction will be recorded [10]. Before data extraction, reviewers will undergo a brief training session to ensure consistency and reliability in the details extracted. Two other reviewers (YL and XW) will undertake a final check to ensure the dependable selection of studies and the reliable extraction of data and handle any disagreements that may arise during the process. As the objective of this review is to identify all reported outcomes regardless of study quality, a critique of the methodological quality is not deemed necessary.

Data analysis and presentation

The extracted data will be narratively synthesized to compile an inclusive list of currently reported neonatal septic shock outcomes, along with any associated outcome definitions and measurement instruments. Outcomes that assess the same overall concept but are defined or measured differently in various publications will be reconstructed under a single standardized outcome name. Subsequently, these outcomes will be categorized according to an established taxonomy, mapping outcomes to 38 domains within five core areas [10, 27]. In addition, an outcome matrix will be constructed using the open source ORBIT Matrix Generator to visually represent the frequency, consistency, and disparity of outcome reported across studies [28].

Stage 2: expert stakeholder meeting

After identification of the existing outcomes, we will proceed with an expert stakeholder meeting employing a semi-structured discussion approach to clarify all identified outcomes and outcome domains, while also collating any additional outcomes. This method will ensure that all essential aspects are adequately addressed, while granting stakeholders the flexibility to delve into specific topics.

Participants

A group of 12 to 15 national and international stakeholders will be actively engaged in this meeting, representing the following stakeholder groups: neonatologists, neonatal nursing specialists, neonatal surgeon, pediatricians, pediatric critical care physicians, infectious disease physician, physiotherapists, rehabilitation therapist, clinical neuropsychologists, and academical researchers specializing in the neonatal field. These stakeholder groups are

Table 1 The inclusion and exclusion criteria to identify the relevant studies

	Inclusion criteria	Exclusion criteria
Population:	Neonates (age 0 ~ 28 days) of any gestation or infants with a primary diagnosis of septic shock from any cause	Combined neonatal and pediatric patients but data not reported separately for neonates
Concept:	Studies that described or evaluated the effectiveness of various types of interventions to manage neonatal septic shock, using any outcomes, including both short-term outcomes within the neonatal period and long-term outcomes occurring in later life	Studies that failed to systematically measure a relevant outcome
Context:	Studies conducted in an inpatient neonatal care setting	—
Others	Peer-reviewed primary research studies of any study design, such as randomized controlled trials and observational studies	Case reports with less than three cases, diagnostical or screening studies, and studies with no full-text available

chosen to be broadly representative of healthcare professionals and academical researchers with practical experience and research expertise to offer valuable insights into neonatal septic shock outcomes identified in Stage 1. Healthcare professionals are required to have a minimum of 8 years of work experience in their current clinical field. Invitations to participate will be extended to them through national and international professional organizations and networks. Academical researchers will be identified based on their research outputs related to neonatal medicine, with a particular emphasis on neonatal septic shock. Patients and caregivers will not be included in this stage, as the primary focus is on facilitating discussions among expert stakeholders to clarify and refine the outcomes identified in the scoping review.

Procedures

All members of the stakeholder groups will be provided with the COMET plain language explanation of what constitutes an outcome and a COS [29], along with the identified outcomes and outcome domains, 3 days prior to the meeting's commencement. At the beginning of the meeting, the process for identifying, synthesizing, and categorizing outcomes will be explained to all participants, followed by a semi-structured discussion of the outcomes and outcome domains. The discussion will be moderated by two of the authors (JS and YH) who are experienced and adept at fostering dynamic and engaged participation. The topic guide for the semi-structured discussion as outlined in Table 2 will be piloted and updated if necessary. At the conclusion of the meeting, the outcome discussion results, along with any additional outcomes, will be presented back to participating stakeholders. They will be required to share any further thoughts on these outcomes and identify any potential overlaps or omissions. The entire semi-structured discussion will be audio-recorded.

After validating the outcomes from the expert stakeholder meeting, an inventory of potential outcomes, and their corresponding descriptions and categorizations, will be created by combining the results of the scoping review and the stakeholder meeting. This inventory will be subjected to review by the SAG to ensure the final list of outcomes is comprehensive and appropriate before commencing the Delphi process.

Stage 3: two-round e-Delphi survey

A Delphi exercise involving a wide variety of stakeholders will be undertaken to elicit diverse perspectives regarding the level of importance assigned to each proposed outcome. This exercise will entail two sequential rounds of e-Delphi surveys, utilizing online questionnaires populated with outcomes derived from the prior stages. The e-Delphi technique is chosen due to its efficiency, cost-effectiveness, and pragmatism in accommodating a large number of key stakeholders spread across a wide geographic dispersion [30]. This process will facilitate achieving a consensus on outcomes of importance through iterative evaluation and synthesis of participant responses. The Guidance on Conducting and REporting DElphi Studies (CREDES) will be followed to implement and document the Delphi exercise, ensuring the maintenance of methodological rigor [31].

Stakeholder selection

Three panels of stakeholders will be invited to participate in both rounds of the e-Delphi survey:

- Personal experience panel—parents and caregivers of neonates or infants treated for septic shock in an inpatient neonatal care setting. The personal experience panel will be incorporated to guarantee that the COS under development remains most relevant to neonatal patients and families.
- Neonatal panel—healthcare professionals and researchers involved in septic shock management in the neonatal period. This panel will include neonatologists, neonatal nursing specialists, neonatal surgeon, pediatricians, pediatric critical care physicians, infectious disease physician, physiotherapists, physician assistants, and research fellows.
- Non-neonatal panel—healthcare professionals and researchers responsible for follow-up after septic shock treatment beyond the neonatal period. This panel will include pediatricians, rehabilitation therapists, clinical neuropsychologists, physician assis-

Table 2 Topic guide for the semi-structured discussion

1	What aspects do you prioritize when providing treatment (or conducting clinical trials) for neonates diagnosed with septic shock?
2	What effect do you want to achieve through treatment (or clinical trial)?
3	What in your opinion are the most concerning issues faced by patients and caregivers?
4	What are your thoughts on the identified outcomes and outcome domains?
5	What suggestions do you have to ensure the outcomes inventory fully captures all important outcomes for neonatal septic shock management?

tants, and research fellows. Experts engaged in both neonatal and later care will only be included in the neonatal panel.

Sampling strategy of the stakeholders

The decision on the number of individuals to be included in a Delphi process is frequently a pragmatic choice [10, 32]. Our intention is to attain a sample size of 20 ~ 30 for personal experience panel and 30 ~ 40 for both the neonatal and non-neonatal panels to ensure adequate representation from each of the stakeholder panels. We will identify potential personal experience representatives for enrollment through the following channels: referrals from physicians and other healthcare providers, parent support networks, placement of advertisements on social media platforms and neonatal charity websites, as well as engagement with bloggers who address neonatal septic shock. Healthcare professionals in the neonatal and non-neonatal panels will be identified through national and international professional organizations and networks. Potential researchers will be selected based on their research outputs, identified through bibliographic analysis employing R studio 4.2.1 [33]. The bibliographic data will be procured from the Web of Science Core Collection database through searches for pertinent publications using keywords associated with neonatal septic shock. Author contact details will be sourced from academic papers or institutional websites to facilitate communication and recruitment. Individually tailored emails containing study information will be dispatched to all prospective participants, using specific language appropriate for each stakeholder group. Snowball sampling will also be utilized to augment the scale of stakeholders. Participants will be encouraged to forward study information to any colleagues they deem eligible and who may be interested.

The inclusion and exclusion criteria for participants

Table 3 presents the inclusion and exclusion criteria for participants in the e-Delphi surveys. Upon receiving the invitation, participants will be asked to provide brief responses concerning their biographic details, profession, and relevant experience to ascertain eligibility.

Delphi round 1 and data analysis

Round 1 of the e-Delphi survey will present outcomes organized by domain, with the arrangement of domains and outcomes within each domain randomized to mitigate response bias. The survey will undergo pilot testing to check the language's readability and face validity. This pilot phase will also inform the time frame required for the completion of each Delphi round.

Participants will be requested to score outcomes using a 9-point Likert scale, where ratings of 1 to 3 will be denoted as "not important," 4 to 6 as "important but not critical," and 7 to 9 as "critical" [34, 35]. Participants will also have the option to select "unclear" for any outcome that they find difficult to score in terms of importance. In the concluding section of the first-round survey, participants will encounter an open-ended question: "Which outcomes do you consider important but have not been covered in the questionnaire?" There will be no imposed limit on the number of additional outcomes that a participant can suggest.

The first round of the Delphi survey is scheduled to be over 4 weeks of duration. Reminder emails or messages will be sent 2 weeks after the initial contact. In case participants have not completed the questionnaire by the end of the 3rd week, they will receive another contact to remind them and inquire if they are facing any difficulties in completing the questionnaire or have decided to withdraw their participation. Participants who have not completed the questionnaire within 4 weeks from the round's initiation will be considered as not completed and will be excluded from the subsequent survey.

Table 3 The inclusion and exclusion criteria for participants

Parents/caregivers (should…)	• Be at least 18 years of age • Have a minimum of a high school's degree • Be immediate family members of the patients • Have provided direct care to neonates or infants treated for septic shock in an inpatient neonatal care setting within the past 3 years • Voluntarily agree to participate in the study
Healthcare professionals (should…)	• Have a minimum of a bachelor's degree • Have at least 8 years of work experience in their current clinical field • Have provided healthcare service to neonates or infants treated for septic shock
Academic researchers (should…)	• Have research interest encompassing neonatal medicine • Have published at least one clinical article on neonatal septic shock within the past 3 years

The response rate from each panel group will be recorded. The frequencies of the response options for each outcome will be documented, and the median score along with inter-quartile range (IQR) will be calculated, all stratified by stakeholder panel. Additional outcomes proposed by participants will undergo independent review by 2 SMG members to ensure they are new, distinct, and relevant to the scope of the COS. Disagreements will be resolved by consulting a third SMG member or discussion. Only outcomes that are deemed to be new and relevant will then be incorporated into round 2. The summarized response will be shared anonymously with participants in the subsequent round, enabling them to consider collective viewpoints before re-rating the outcomes. Reiterated reflection and scoring could function as a mechanism to harmonize diverse opinions and facilitate the attainment of a consensus.

Delphi round 2 and data analysis

Round 2 of the Delphi survey will be administered to participants who have completed round 1. All outcomes will be retained and carried forward to the second round. Participants will be presented with a graphical description of the rating distribution from the three different panels alongside their own ratings from round 1, with a brief explanation provided to ensure understanding of the presented information. This allows participants to thoroughly consider and contrast the perspectives of other stakeholder panels and their own before rescoring the outcomes. Subsequently, participants will be requested to rescore each outcome from the previous round, as well as provide scores for any newly proposed outcomes.

In case of non-response, follow-up emails or messages will be sent once a week, until a maximum of three follow-up attempts. If the response rate remains below 75%, we will extend the period for two additional weeks, allowing the Delphi survey to remain open to encourage further participation.

Data analysis employed in Round 1 will be repeated. In addition, the potential bias resulting from the loss of participants between rounds will be evaluated by comparing the median scores of participants who completed both rounds with those who only completed Round 1. Our definition of consensus following that of previous COS publications is given in Table 4 [10, 15, 16]. Outcomes that receive a score of 1 ~ 3 from more than 70% of participants and a score of 7 ~ 9 from less than 15% of participants will be considered to have met the criteria for "consensus out." Such outcomes will be removed from the outcomes list. The results of this second Delphi round will undergo review by the SAG before proceeding to the next stage, to determine the structure and content of the list of items to be considered in the consensus process.

Stage 4: consensus meeting

The results of the Delphi study will be discussed in a consensus meeting to determine and agree on the final list of outcomes that will constitute the COS. The meeting will be held for half a day in Chengdu City, Sichuan Province, China, and it may incorporate a blend of in-person and teleconference participation to enable the attendance of as many prospective participants as possible.

Participants

Participants who have completed all rounds of the e-Delphi survey will be requested to attend. The consensus group will consist of, at a minimum, four representatives each from neonatologists, neonatal nursing specialists, and pediatric critical care physicians; two representatives each from pediatricians, physiotherapists, rehabilitation therapist, clinical neuropsychologists, and academic researchers with expertise in neonatal care; and at least two representatives each from caregivers, methodologists, and policy makers. Participants will be recruited using the same processes described previously.

Procedures

The study background, objectives, a lay definition of an outcome and a COS, and the results obtained from each round of the Delphi survey will be shared with the participants in advance. The summarized responses from the final round, along with the comparison between stakeholder panels, will be presented and demonstrated at the beginning of the final consensus meeting. The focus

Table 4 Definition of consensus [10]

Consensus classification	Description	Definition
Consensus in	Consensus that outcome should be included in the core outcome set	≥ 70% of participants scoring as 7 ~ 9 AND < 15% of participants scoring as 1 ~ 3
Consensus out	Consensus that outcome should not be included in the core outcomes set	≥ 70% of participants scoring as 1 ~ 3 AND < 15% of participants scoring as 7 ~ 9
No consensus	Uncertainty about importance of outcome	Did not meet criteria for "consensus in" or "consensus out"

of the meeting will be placed on the outcomes for which "no consensus" is reached during the Delphi stage. Participants will be requested to anonymously re-score all the "no consensus" outcomes using the same 9-point Likert scale applied in the Delphi survey. Outcomes that meet consensus for inclusion in the COS will be those that receive a score of 7 ~ 9 from at least 70% of participants, and a score of 1 ~ 3 from less than 15% of participants at the consensus meeting (Table 4). Outcomes that have achieved "consensus out" in the Delphi stage will be excluded, while those achieving "consensus in" will be discussed and validated. If any participants express disagreement with an outcome that has been agreed upon for inclusion in the COS, further discussions will be arranged to address the concern during the consensus meeting. If necessary, the nominal group technique will be used to build consensus on controversial outcomes. Following the consensus meeting, outcomes reaching "consensus in" will be included in the finalized COS, when all others will be excluded. The SAG will carefully review the final list of outcomes constituting the COS-NSS, and where necessary, the descriptions and terminology of the outcomes will be adjusted to improve their clarity and comprehensibility.

Dissemination

Upon completion, the COS-NSS will be disseminated to raise awareness and promote its uptake. The study findings will be published in peer-reviewed international publications with an interest in neonatal septic shock, and the COS-NSS will be made freely available through the COMET Initiative website. We will also communicate our results through international conferences, professional societies, and our institution's social media platforms. In addition, all participants of the COS-NSS will be strongly encouraged to incorporate the COS-NSS into their future research endeavors and routine management of neonatal septic shock. It is also expected that they will advocate for the adoption of this COS among their colleagues and other prospective researchers.

Discussion

This study protocol outlines a four-stage systematic approach for the development of a COS for neonatal septic shock management. Specifically, we plan to use a scoping review and expert stakeholder meeting to create an inclusive list of potential outcomes. Subsequently, we will employ a two-round e-Delphi survey and a consensus meeting to reach consensus on the outcomes for inclusion in the finalized COS. This study protocol stands as the first COS registered on the COMET website to develop a suite of COS for neonatal septic shock. It is expected that this proposed COS-NSS will be consistently collected and reported in all clinical trials, benchmarking activities, practice audits, quality improvement initiatives, and other types of research related to neonatal septic shock management, as well as in routine treatment of neonatal septic shock. This will facilitate the comparison and contrast of studies, allowing for the synthesis of pertinent research and generation of high-quality evidence, thus ultimately fostering enhanced medical care for neonates afflicted by septic shock.

The main limitation of the study lies in the non-inclusion of former patients who received treatment for septic shock in a neonatal unit. This is because either this particular population is too young to articulate their thoughts effectively, or recruiting adults who experienced septic shock in infancy proves exceedingly challenging. Nonetheless, we will actively engage parents and caregivers of the neonatal patients to constitute the personal experience panel and represent their perspectives. Moreover, we do acknowledge the potential difficulty in reaching a diverse group of well-representative national and international participants, especially considering the necessity for a significant number of respondents during the Delphi rounds. To address this concern, a dataset comprising experts with specialized knowledge in neonatal septic shock will be constructed via bibliometric analysis performed using R studio 4.2.1 [33], and 2 members of the SMA will be appointed to assume full responsibility for establishing connections with and maintaining relationships with the selected participants. Additionally, this study will not be able to answer the questions of how to measure the outcomes included in the finalized COS-NSS or at what time point the outcomes should be measured. Further research will be warranted to address how to measure the outcomes and ascertain the appropriate timing of assessments.

In conclusion, we will rigorously adhere to established methodologies to ensure that the resulting COS-NSS is not only suitable and valued by all key stakeholders but also widely embraced in further research and routine clinical care. We anticipate that the development of the COS-NSS will contribute to the consistency of reporting clinical study outcomes, aid in mitigating reporting bias, and facilitate the auditing of clinical practices related to the management of neonatal septic shock in the future.

Trial status

As of the submission of this protocol manuscript, the literature search, screening, and selection process for the scoping review have been completed, and data abstraction from the selected literature is currently underway. The projected timeline for the completion of the scoping review is December 2023, with the finalization of the core outcome set expected by December 2024.

Abbreviations

COS	Core outcome set
COS-NSS	Core outcome set for neonatal septic shock management
COMET	Core Outcome Measures in Effectiveness Trials
COS-STAD	Core Outcome Set-STAndards for Development
COS-STAP	Core Outcome Set-STAndardised Protocol Items
SMG	Study Management Group
SAG	Study Advisory Group

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-024-08422-0.

Additional file 1: Core Outcome Set-STandards Protocol Items: The COS-STAP Statement Checklist.

Additional file 2: Search Strategies.

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Authors' contributions
JT, JS, YH, XW, and YL initially designed the study; subsequently, all authors participated in further conceptualizing and refining the study design. YL, XL, YXL, and ML formulated the protocol for the scoping review. YL, XG, YH, BL, and XW developed the Delphi protocol. YL, XL, XG, YXL, MRF, and ML wrote the first draft of the protocol manuscript. JT, JS, XW, BL, MRF, and YH revised and improved the manuscript. All authors have read and approved the final manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Ethical approval for the entire project has been granted by the Ethics Committee of West China Second University Hospital (No. 2023–085). Written informed consent will be obtained from all participants involved in semi-structured discussions, e-Delphi surveys, or consensus meeting. All procedures will be carried out in accordance with the principles stipulated by the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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