MRC-NIHR Trials Methodology Research Partnership: Webinar recording

Developing a Core Outcome Set for Neonatal Sepsis (NESCOS)

Presented, on behalf of the HRB TMRN, by:

Dr Petek Eylül Taneri (University of Galway)

13 March 2024

The slides are available below.

For any queries, please contact uktmn@nottingham.ac.uk

https://youtu.be/NOu0oq3XqrM

NESCOS

Ollscoil na Gaillimhe
University of Galway

Health Research Board
TMRN
Trials Methodology Research Network

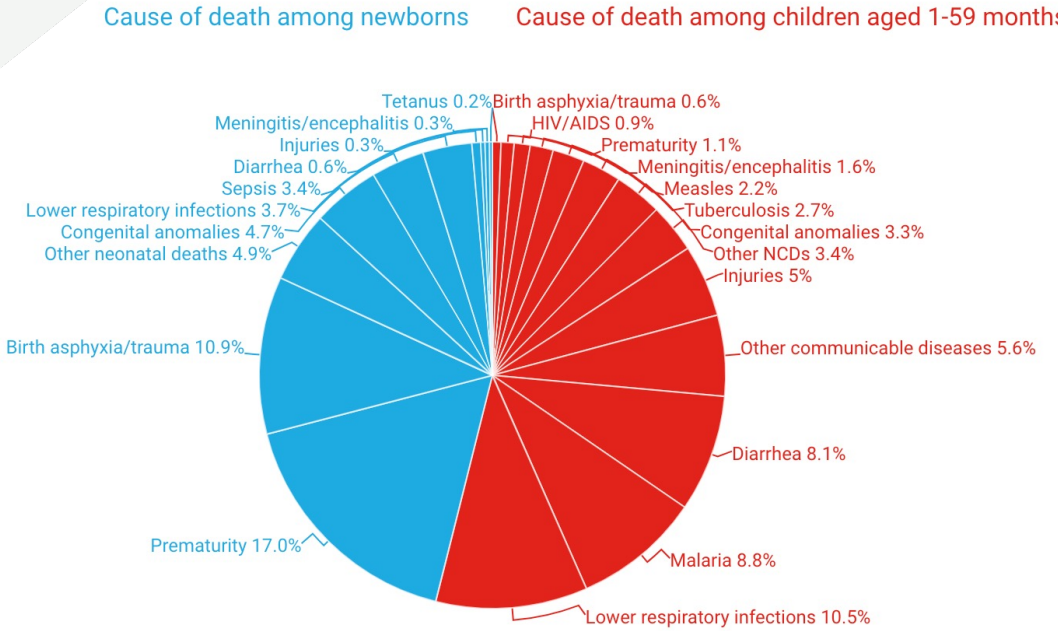
in4kids
Health Research Board
Irish Network for Children's Clinical Trials

Developing a Core Outcome Set for Neonatal Sepsis

Petek Eylül Taneri, MD, PhD

Postdoctoral researcher, University of Galway

Neonatal Sepsis



Download data

Source: Child and Adolescent Causes of Death Estimation (CA CODE) project (2023).
Note: Estimates are rounded and therefore may not sum up to 100%. NCDs = Non-communicable diseases.

- One of the leading causes of newborn death
- Mortality rate of 17% worldwide
- Preterm and very low birth weight neonates disproportionately effected
- Low-income countries experiencing a 3.5-fold increase and middle-income countries encountering a 1.8-fold increase

Challenges in Neonatal Sepsis Research

- Outcomes measured and reported in neonatal sepsis studies are significantly heterogeneous
- Complicating the process of drawing definitive conclusions, as a result it is hard to draw conclusions

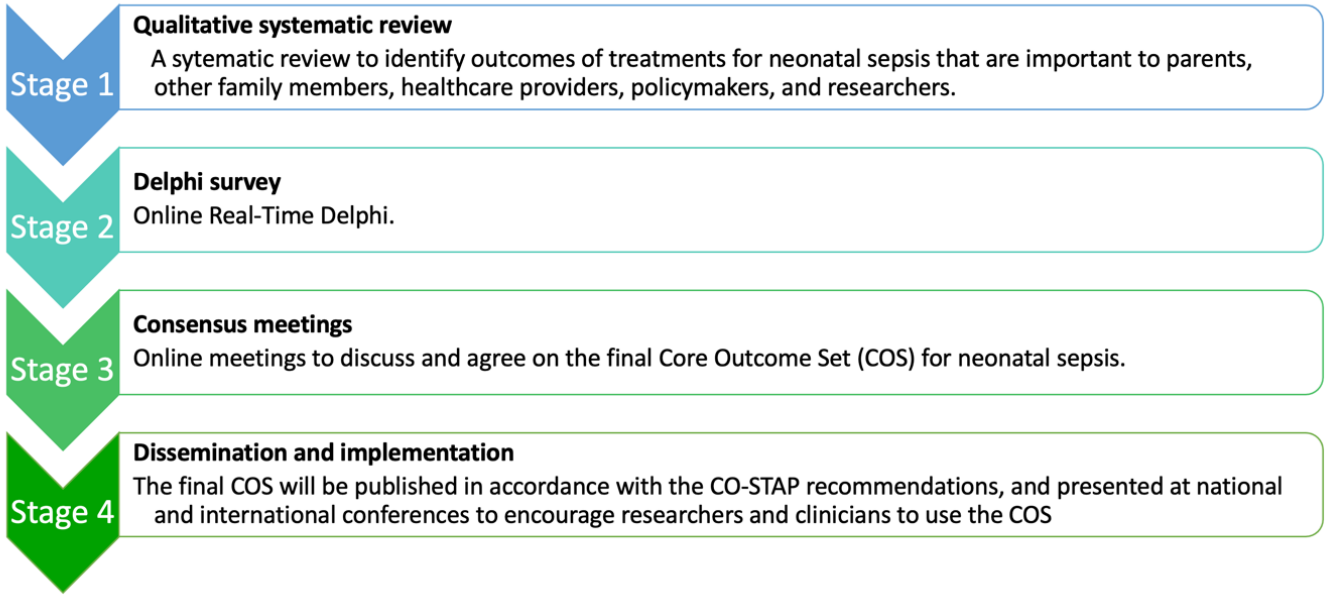
Why do we need a COS?

- Mitigating heterogeneity in the outcomes measured and reported
- Enhancing evidence synthesis by reducing outcome-reporting bias
- Ensuring that all trials contribute meaningful and uniform information
- *Core outcomes should be consistently collected, researchers may include other outcomes*

Aim of the project

«Develop a COS for research evaluating the effectiveness of neonatal sepsis treatments with our project called NESCOS (NEonatal Sepsis Core Outcome Set).»

Stages of our project



NESCOS

Study overview

- Ethics approval from the University of Galway Research Ethics Committee (Reference number: 2022.10.002)
- Registered on the Core Outcome Measures in Effectiveness Trials database (COMET)
- Participants' consent was obtained through standardised forms

OPEN ACCESS

STUDY PROTOCOL

Protocol for the development of a core outcome set for neonatal sepsis (NESCOS)

Petek Eylul Taneri, Jamie J. Kirkham, Eleanor J. Molloy, Linda Biesty, Richard A. Polin, James L. Wynn, Barbara J. Stoll, Niranjan Kissoon, Kondwani Kawaza, Mandy Daly, Aoife Branagan, Lívia Nagy Bonnard, Eric Giannoni, [···], Declan Devane

[view all]

Published: December 5, 2023 • https://doi.org/10.1371/journal.pone.0295325

Abstract

Stakeholder involvement

- The steering group included neonatologists, paediatricians, infectious disease specialists, obstetricians, microbiologists, midwives, neonatal nurses, researchers, academics, parents of newborns who had neonatal sepsis, and parent representatives
- Representation from low-, middle-, and high-income countries.
- ***Public research partners*** participated in the ***design and oversight*** of the COS development process

NESCOS

Stage 1: Qualitative Systematic Review

Background

Our aim is **to identify outcomes from qualitative research** on any intervention to prevent or improve the outcome of neonatal sepsis that are **important to parents, other family members, parent representatives, healthcare providers, policymakers, and researchers** as a part of the development of a Core Outcome Set (COS) for neonatal sepsis.

Methods

We conducted a systematic review of qualitative studies. Publications describing qualitative data relating to neonatal sepsis outcomes were included. Drawing on the concepts of thematic synthesis, text related to outcomes were coded and grouped. These outcomes were then mapped to the domain headings of an existing model relating to a COS for neonatal research.

Results

Out of 6,777 records screened, six studies were included. Overall, **19 outcomes were extracted** from the included studies. The most frequently reported outcomes were related to the domain of **outcomes related to parents** (6 outcomes, 32 %), individual organ systems such as the gastrointestinal system (5 outcomes, 26%), and outcomes related to healthcare workers (4 outcomes, 22%). The remaining outcomes were classified under the headings of general outcomes, miscellaneous outcomes, survival, and infection.

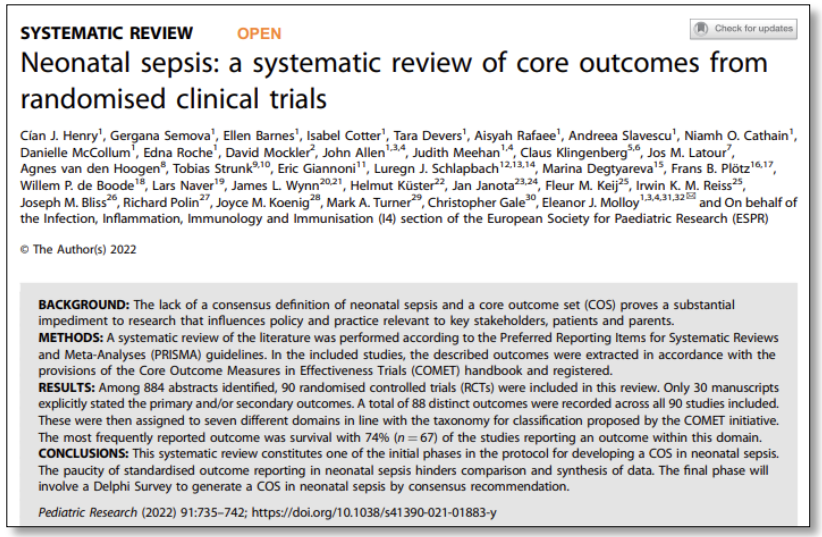
Conclusions

The outcomes identified in this review, are different from the outcomes reported in neonatal sepsis clinical trials, thus highlighting the importance of incorporating qualitative studies into COS development to encapsulate all relevant stakeholders' perspectives.

The outcomes and their domains that were extracted from the included studies

Domain	Outcome
Survival	Mortality
Respiratory	Tachypnea
Gastrointestinal	Necrotising enterocolitis
	Interrupted breastfeeding
Neurological	Seizures
	Quadriplegia
Infection	Antimicrobial use
Outcomes related to parents	Support for parents
	Parental bonding with their baby
	Parental involvement in care
	Parental competence on care
	Psychological wellbeing of the parents
	Economic burden to parents
Outcomes related to HCW	Effective caring relationship with parents
	Communication between parents and health care workers
	Job satisfaction of the health care workers
	Wellbeing of the health care workers
General Outcomes	Normality after discharge
Miscellaneous	Increased body temperature

NESCOS



SYSTEMATIC REVIEW OPEN

Check for updates

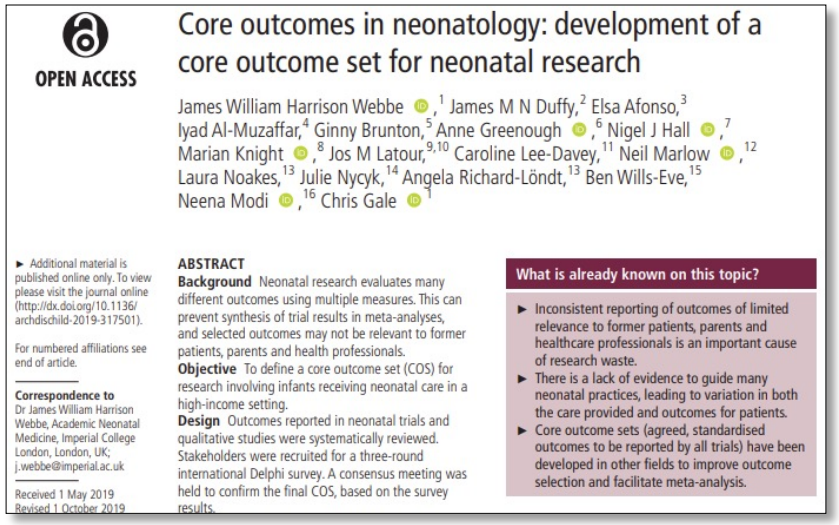
Neonatal sepsis: a systematic review of core outcomes from randomised clinical trials

Cían J. Henry[1], Gergana Semova[1], Ellen Barnes[1], Isabel Cotter[1], Tara Devers[1], Aisyah Rafaee[1], Andreea Slavescu[1], Niamh O. Cathain[1], Danielle McCollum[1], Edna Roche[1], David Mockler[2], John Allen[1,3,4], Judith Meehan[1,4], Claus Klingenberg[5,6], Jos M. Latour[7], Agnes van den Hoogen[8], Tobias Strunk[9,10], Eric Giannoni[11], Luregn J. Schlapbach[12,13,14], Marina Degtyareva[15], Frans B. Plötz[16,17], Willem P. de Boode[18], Lars Naver[19], James L. Wynn[20,21], Helmut Küster[22], Jan Janota[23,24], Fleur M. Keij[25], Irwin K. M. Reiss[25], Joseph M. Bliss[26], Richard Polin[27], Joyce M. Koenig[28], Mark A. Turner[29], Christopher Gale[30], Eleanor J. Molloy[1,3,4,31,32]✉ and On behalf of the Infection, Inflammation, Immunology and Immunisation (I4) section of the European Society for Paediatric Research (ESPR)

BACKGROUND: The lack of a consensus definition of neonatal sepsis and a core outcome set (COS) proves a substantial impediment to research that influences policy and practice relevant to key stakeholders, patients and parents.
METHODS: A systematic review of the literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. In the included studies, the described outcomes were extracted in accordance with the provisions of the Core Outcome Measures in Effectiveness Trials (COMET) handbook and registered.
RESULTS: Among 884 abstracts identified, 90 randomised controlled trials (RCTs) were included in this review. Only 30 manuscripts explicitly stated the primary and/or secondary outcomes. A total of 88 distinct outcomes were recorded across all 90 studies included. These were then assigned to seven different domains in line with the taxonomy for classification proposed by the COMET initiative. The most frequently reported outcome was survival with 74% ($n = 67$) of the studies reporting an outcome within this domain.
CONCLUSIONS: This systematic review constitutes one of the initial phases in the protocol for developing a COS in neonatal sepsis. The paucity of standardised outcome reporting in neonatal sepsis hinders comparison and synthesis of data. The final phase will involve a Delphi Survey to generate a COS in neonatal sepsis by consensus recommendation.

Pediatric Research (2022) 91:735–742; https://doi.org/10.1038/s41390-021-01883-y

Qualitative Systematic Review



OPEN ACCESS

Core outcomes in neonatology: development of a core outcome set for neonatal research

James William Harrison Webbe [1], James M N Duffy,[2] Elsa Afonso,[3] Iyad Al-Muzaffar,[4] Ginny Brunton,[5] Anne Greenough [6], Nigel J Hall [7], Marian Knight [8], Jos M Latour,[9,10] Caroline Lee-Davey,[11] Neil Marlow [12], Laura Noakes,[13] Julie Nycyk,[14] Angela Richard-Löndt,[13] Ben Wills-Eve,[15] Neena Modi [16], Chris Gale [1]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/archdischild-2019-317501).

For numbered affiliations see end of article.

Correspondence to
Dr James William Harrison Webbe, Academic Neonatal Medicine, Imperial College London, London, UK; j.webbe@imperial.ac.uk

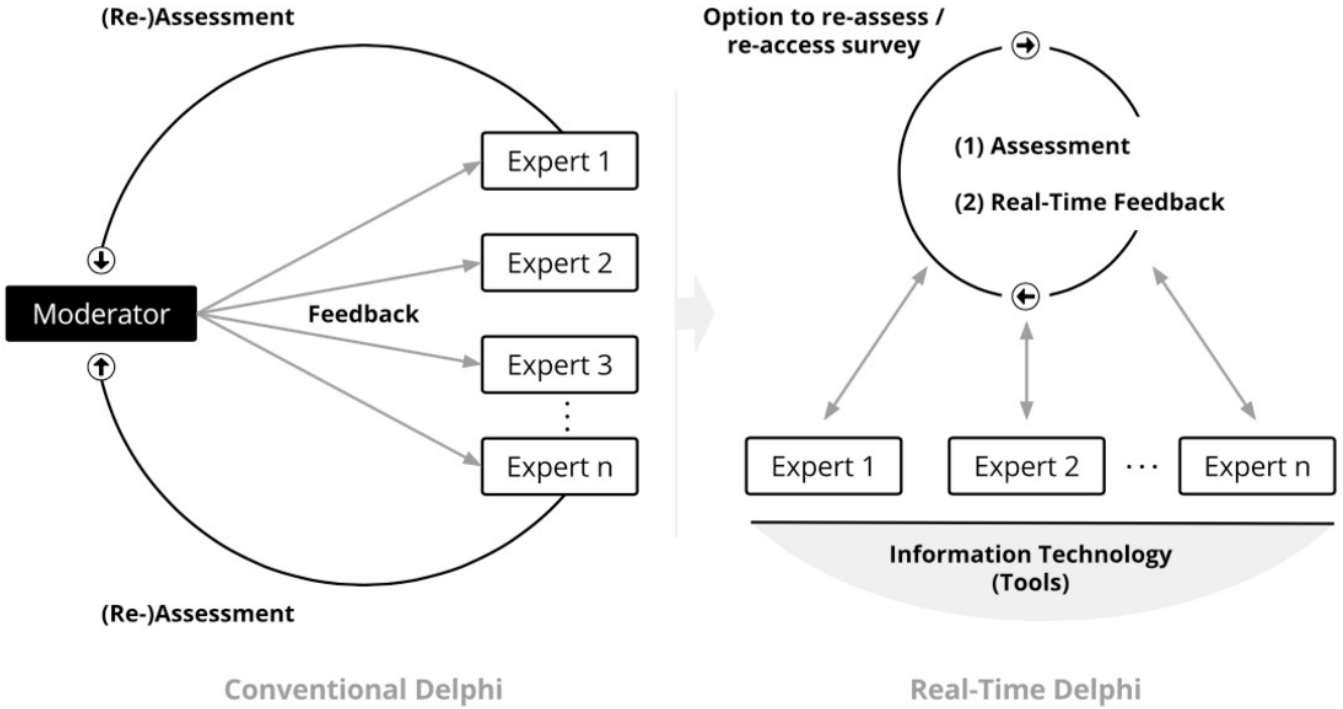
Received 1 May 2019
Revised 1 October 2019

ABSTRACT
Background Neonatal research evaluates many different outcomes using multiple measures. This can prevent synthesis of trial results in meta-analyses, and selected outcomes may not be relevant to former patients, parents and health professionals.
Objective To define a core outcome set (COS) for research involving infants receiving neonatal care in a high-income setting.
Design Outcomes reported in neonatal trials and qualitative studies were systematically reviewed. Stakeholders were recruited for a three-round international Delphi survey. A consensus meeting was held to confirm the final COS, based on the survey results.

What is already known on this topic?

- Inconsistent reporting of outcomes of limited relevance to former patients, parents and healthcare professionals is an important cause of research waste.
- There is a lack of evidence to guide many neonatal practices, leading to variation in both the care provided and outcomes for patients.
- Core outcome sets (agreed, standardised outcomes to be reported by all trials) have been developed in other fields to improve outcome selection and facilitate meta-analysis.

Stage 2: Real-Time Delphi Survey



NESCOS

Stage 2: Real-Time Delphi Survey

- Participants in the Delphi study were initially provided with **79 outcomes** derived from a systematic review of trials and a qualitative systematic review of outcomes previously utilized in studies on neonatal sepsis treatment.

- Participants were also asked to add additional outcomes that had not been listed but that they considered important.

- Two outcomes were added: **Infant's quality of life** & **Antibiotic resistance**

NESCOS

Stage 2: Real-Time Delphi Survey

- Participants were asked to rate the ***importance*** of each outcome ***from 1 (not important) to 9 (critical)***.

- We bring forward the outcomes that scored 7–9 by 70%, and 1–3 by less than 15% of participants across all stakeholder groups to consensus meetings

- When 50% or fewer participants score 7-9 in each stakeholder groups that outcome was excluded

NESCOS

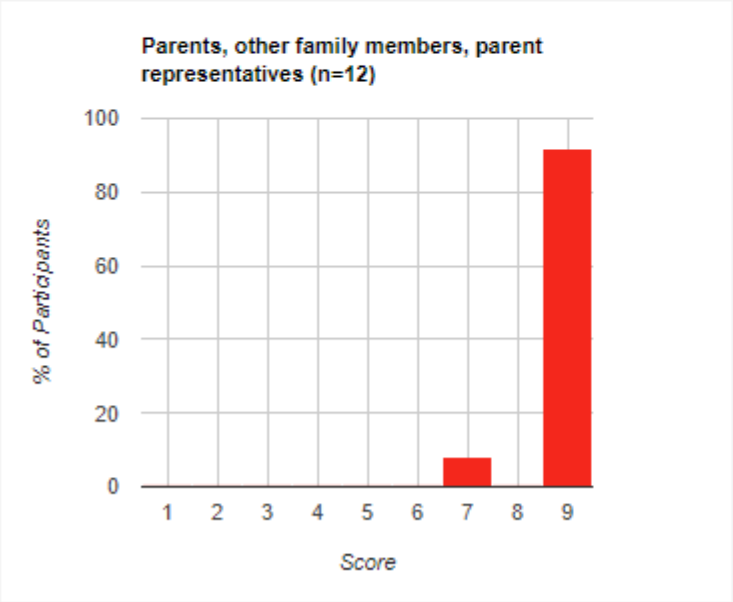
For each outcome, please rate the importance of the outcome for inclusion in a Core Outcome Set.

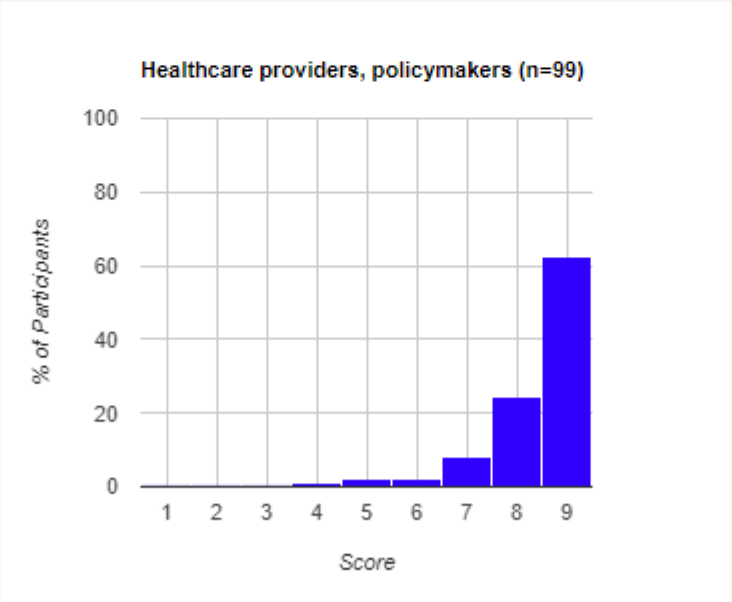
Infant's quality of life

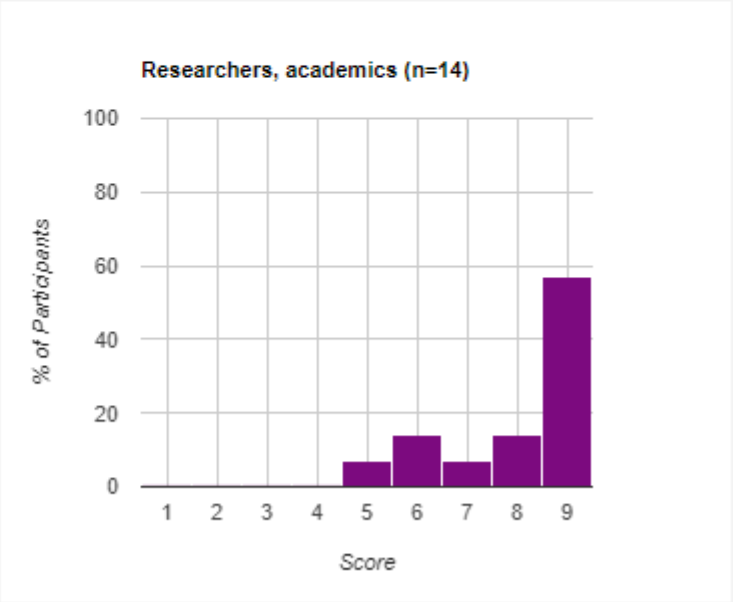
An infant's quality of life refers to their overall well-being, including physical and mental health, safety, comfort, and emotional development.

1 (not important) 2 3 4 5 6 7 8 9 (critical)

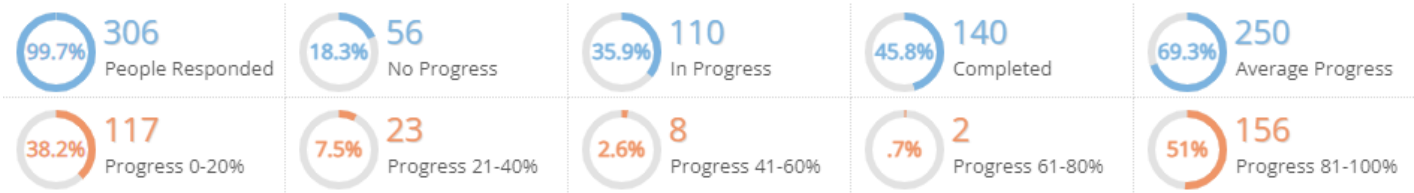
I don't know







Stage 2: Real-Time Delphi Survey



- In total ***55 outcomes*** remained following the Real-Time Delphi Survey.

- 140 participants completed the survey

- We included responses from each participant who evaluated a particular outcome, irrespective of whether they rated all outcomes.

Stage 3: Consensus Meetings

4th August 2023 (24 participants)

Neonatalogist	Poland
Neonatalogist	Ireland
Neonatalogist	UK
Neonatalogist	Ireland
Neonatalogist	Ireland
Neonatalogist	Ireland
Paediatrician	Barbados
Paediatrician	UK
Paediatrician	UK
Paediatrician	Pakistan
Neonatal nurse	Ireland
Neonatal nurse	Kenya
Midwife	Zambia
Obstetrician	Malawi
Obstetrician	UK
Microbiologist	Germany
Researcher	USA
Researcher	Ireland
Researcher	Turkey
Researcher	South Africa
PPI	Ireland
PPI	Canada
PPI	Switzerland
Epidemiologist	Switzerland

17th October 2023(25 participants)

Neonatalogist	Poland
Neonatalogist	UK
Neonatalogist	Ireland
Neonatalogist	Ireland
Neonatalogist	Ireland
Neonatalogist	Switzerland
Neonatalogist	Tanzania
Paediatrician	Barbados
Paediatrician	UK
Paediatrician	Zambia
Paediatrician	UK
Paediatrician	Uganda
Paediatrician	Ethiopia
Paediatrician	Gambia
Paediatrician	Burkano Faso
Neonatal nurse	Ireland
Midwife	Zambia
Obstetrician	Tanzania
Microbiologist	Germany
Researcher	USA
Researcher	Ireland
Researcher	Germany
PPI	Ireland
PPI	Hungary
PPI	Switzerland

15 out of the 25 participants in the second meeting had also been present during the first meeting.

Stage 3: Consensus Meetings

- If at least **80% of participants**, including at least one representative from each stakeholder group, vote in favour of an outcome, it was included in the COS.

- In total 55 outcomes were discussed, 9 outcomes (7 domains) were included in the final COS.

DOMAIN	OUTCOME
Survival	All-cause mortality
Respiratory	Need for invasive mechanical ventilation
Neurological	Brain injury on imaging
	Neurological status at discharge
Infection	Escalation of antimicrobial therapy
	Infections of the central nervous system
Developmental	Neurodevelopmental impairment
Outcomes related to parents	Quality of life
Miscellaneous	Multi-organ dysfunction

Stage 4: Dissemination and implementation strategy

- Publishing the results in an Open Access journal
- COMET database
- National and international conferences

As a result...

We developed a COS for studies investigating the effectiveness of treatments for neonatal sepsis.

NESCOS includes *outcomes relevant to key stakeholders*, including parents, families, caregivers, healthcare professionals, policymakers, and researchers, in various settings.

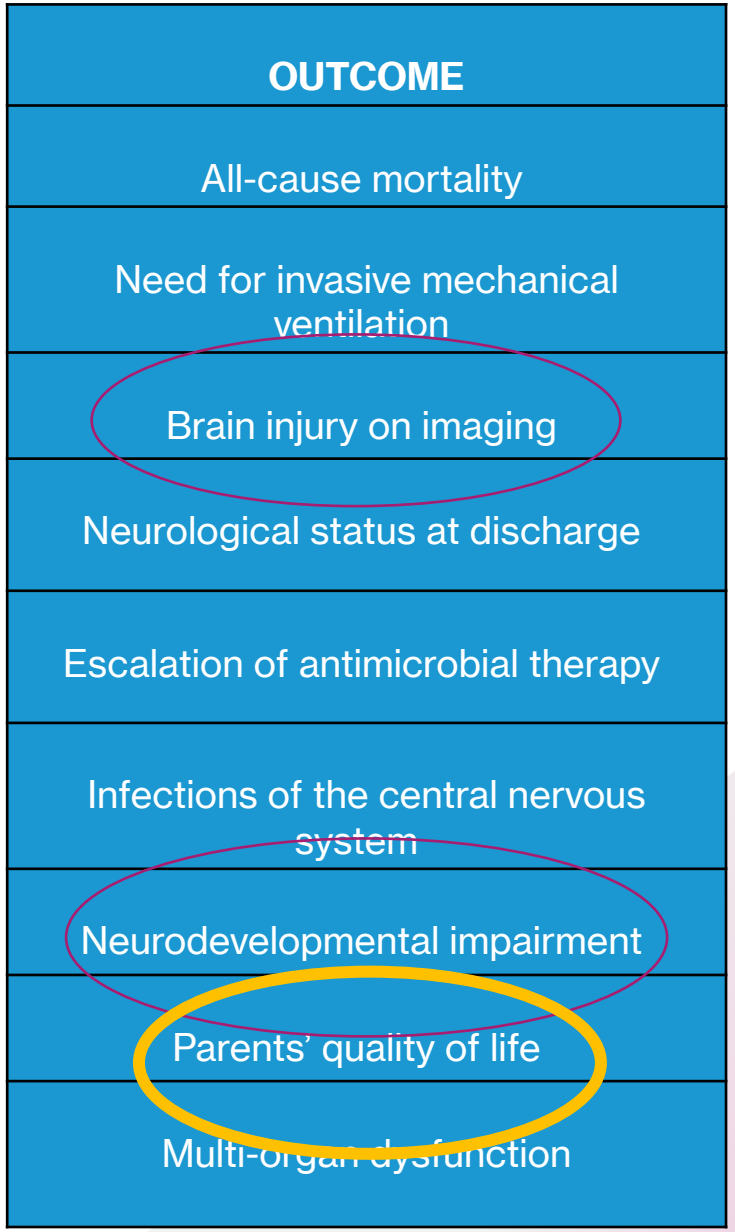
Discussion

- Our study focused on consensus about 'what' outcomes to measure in neonatal sepsis trials.
- The specifics of 'how' and 'when' to measure these outcomes remain critical areas for future research.
- COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) guidelines to ensure accurate and comprehensive outcome measurement.

NESCOS

Discussion

- Some outcomes may be difficult to measure (short-term vs. long-term)
- Feasibilty in under-resourced settings ?
- Studies in English & Key-stakeholders who can speak English
- RTD mainly disseminated in social media



NESCOS

Conclusion

- Adopting this COS should enhance consistency in outcome reporting and help reduce bias and variability in this research area.
- It would also enable more effective data synthesis.
- Future research endeavours must focus on establishing ***robust, standardised methods for measuring the outcomes*** we have identified within our COS.

THANK YOU!

Ollscoil na Gaillimhe
University of Galway

Health Research Board
TMRN
Trials Methodology Research Network

in4kids
Health Research Board
Irish Network for Children's Clinical Trials