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Core outcomes in neonatal encephalopathy: a qualitative study with parents

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ABSTRACT

Objective To identify the outcomes considered important to parents or caregivers of infants diagnosed with neonatal encephalopathy, hypoxic ischaemic encephalopathy or birth asphyxia in high-income and low- to middle-income countries (LMiCs), as part of the outcome-identification process in developing a core outcome set (COS) for the treatment of neonatal encephalopathy.

Design A qualitative study involving 25 semistructured interviews with parents or other family members (caregivers) of infants who were diagnosed with, and treated for, neonatal encephalopathy, hypoxic ischaemic encephalopathy or birth asphyxia.

Setting Interviews were conducted in high-income countries (HiCs) (n=11) by Zoom video conferencing software and in LMiCs (n=14) by phone or face to face.

Findings Parents identified 54 outcomes overall, which mapped to 16 outcome domains. The domains identified were neurological outcomes, respiratory outcomes, gastrointestinal outcomes, cardiovascular outcomes, motor development, cognitive development, development (psychosocial), development (special senses), cognitive development, development (speech and social), other organ outcomes, survival/living outcomes, long-term disability, hospitalisation, parent-reported outcomes and adverse events.

Conclusions This study provides insight into the outcomes that parents of infants diagnosed with neonatal encephalopathy have identified as the most important, to be considered in the process of developing a COS for the treatment of neonatal encephalopathy. We also provide description of the processes employed to ensure the inclusion of participants from LMiCs as well as HiCs.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Parents of newborn infants diagnosed and treated for neonatal encephalopathy, hypoxic ischaemic encephalopathy or birth asphyxia have extensive experience of caring for these infants.

⇒ Qualitative interviews are increasingly used in core outcome set (COS) development but little has been done to include participants from low- to middle-income countries (LMiCs).

WHAT THIS STUDY ADDS

⇒ This study highlights the outcomes that parents of infants diagnosed and treated for neonatal encephalopathy consider important to include in a COS.

⇒ Provides a transparent reporting of processes used to include parents from LMiCs in qualitative research contributing to COS development.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study was part of the process of developing a COS for use in trials and other studies for the treatment of neonatal encephalopathy.

INTRODUCTION

Neonatal encephalopathy is a condition of impaired neurological function that can occur in newborns. There can be many causes of neonatal encephalopathy including among others, infection, genetic or maternal risk factors, and a lack of oxygen supply to the brain of the infant.[1] Neonatal encephalopathy is associated with impaired respiratory functioning, depressed reflexes and tone, reduced level of consciousness and the occurrence of seizures.[2] The current leading treatment for neonatal encephalopathy is therapeutic hypothermia, which has been shown in randomised trials to reduce mortality and major disability in high-income countries (HiCs); however, mortality still occurred in some infants and only a borderline decrease in blindness and seizures was seen.[3] Moreover, in a low-income to middle-income country (LMiC) setting, therapeutic hypothermia did not reduce the risk of death or disability, and instead increased the likelihood of death in these infants.[4] This has resulted in studies of new treatments[5] and the

need to standardise the outcomes measured to allow for results to be compared and combined.

This qualitative study is a part of a larger study (COHESION) to develop a core outcome set (COS) for the treatment of neonatal encephalopathy.[6] A COS is a standardised list of outcomes considered to be the most important to all stakeholders (parents/caregivers, healthcare providers, researchers/academics), which should be measured as a minimum in all trials for a specific condition.[7]

The development of COSs involves a consensus process to prioritise outcomes for a particular condition. This process begins with identifying outcomes for the condition, usually by reviewing outcomes used in prior studies.[7 8] More recently, COS developers also identify outcomes important to patients through qualitative research.[9] Outcomes are then presented to stakeholders in an online Delphi survey to rate the importance of each outcome. The final COS is then agreed on at a consensus meeting.[5] According to Keeley *et al*[8] conducting qualitative research with patients, including parents of patients, to inform the list of outcomes should increase confidence that 'all potentially relevant outcomes' will be identified. Other benefits of incorporating qualitative methods for outcome identification in COS development include gaining a better understanding of 'why' outcomes are important to patients/parents of patients/caregivers. This context can strengthen outcomes and justify inclusion in the Delphi survey.[8] Plain language explanations for outcomes presented in the Delphi survey can also be informed by the language used by participants of the interviews.[8]

In addition to including parents/caregivers of infants with neonatal encephalopathy, it is important that previously under-represented parents/caregivers from LMiCs are involved in developing this COS. A review by Karumbi *et al* in 2021[10] found that in the 370 published COSs reviewed, only 20% had included participants from LMiCs. Temporal, cultural and resource disparities have been suggested as barriers for inclusion of LMiCs.[10] For a COS to have global relevance, more effort needs to be made to include the perspectives of patients from low-income and middle-income countries.

This study aims to identify the outcomes considered important to parents/caregivers of infants diagnosed with neonatal encephalopathy, hypoxic ischaemic encephalopathy or birth asphyxia in HiCs and LMiCs, as part of the outcome-identification process in developing a COS for interventions for the treatment of neonatal encephalopathy.

Previous qualitative studies exploring parents' experiences of their child receiving therapeutic hypothermia treatment have been conducted in the USA and Sweden.[11–14] However, the focus of COHESION is to develop a COS for all treatments of neonatal encephalopathy across all jurisdictions, for all treatments.[6] This prompted the team to conduct primary qualitative research, with participants from both HiC and LMiCs, as opposed to a systematic review of previous qualitative research, as had been done in other COS development.[15]

METHODS

This study is reported in line with reporting recommendations for qualitative research methods in COS development described by Jones *et al*.[16] (online data supplemental file 1) and Consolidated criteria for reporting qualitative research guidelines (COREQ) (online data supplemental file 2).

DESIGN

Using a qualitative design to underpin this inquiry allowed the research team to hear parents/caregivers speak to their experiences of an infant with neonatal encephalopathy and the outcomes they considered important to measure.

Participants

The eligibility criteria for inclusion in this study were that participants were over 18 years of age and a parent or other family member who care for, or have cared for, an infant that was diagnosed with, and received treatment for, neonatal encephalopathy, hypoxic-ischaemic encephalopathy or birth asphyxia (see standard operating procedure (SOP) online data supplemental file 3) and participant information leaflet (PIL) (online data supplemental file 4), these documents were developed by researchers and parent representatives on the COHESION Steering Group. The grade of brain injury was not included in the inclusion criteria. Participants' infants were not required to have been part of a trial for treatment. On consultation with colleagues in Kenya, 'birth asphyxia' was included in the inclusion criteria, in addition to neonatal encephalopathy, to account for diagnosis criteria used locally.

Patient and Public Involvement

Parent representatives are members of the COHESION Study steering group and contributed to the design, conduct and reporting of this study. Parent representatives contributed to all documentation relating to the recruitment of parents/ caregivers to interviews and the conduct and reporting of the interviews.

Recruitment strategy

We planned to interview 8–12 parents/caregivers in HiCs and 4–6 parents/caregivers in each LMiC participating in the study (Kenya and Pakistan), informed by the numbers interviewed in previous qualitative studies.[11–14] We were mindful that the concept of conceptual saturation[17] (ie, when no new outcomes were identified as the interviews and analysis progressed) would guide the final interview numbers.

We developed a strategy for preparatory work and recruitment in both HiCs and LMiCs as follows (figure 1):

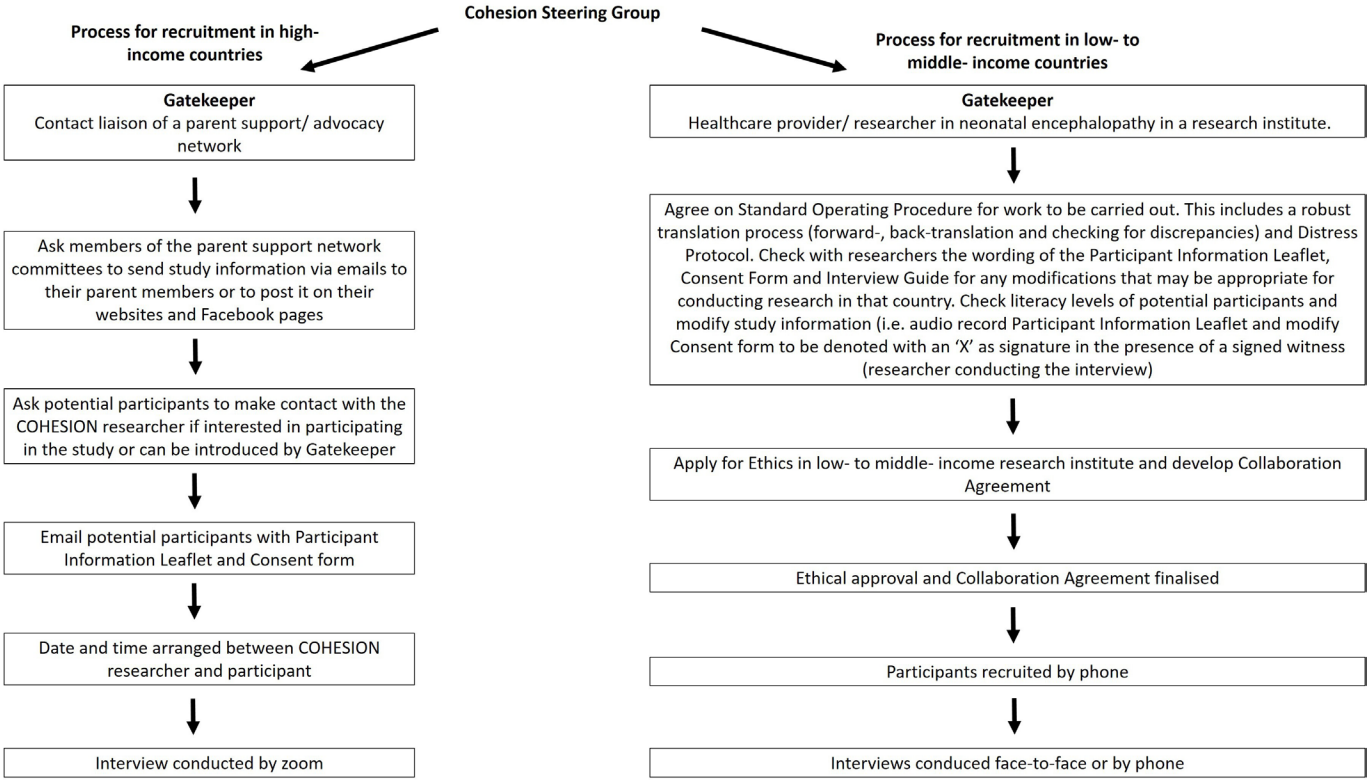

Figure 1 Strategy for recruiting parents/ caregivers of infants diagnosed with neonatal encephalopathy in HiCs and LMiCs.

High-income countries

For the HiCs, we used purposeful sampling[18] and developed a recruitment approach (figure 1) to recruit parents/caregivers. Gatekeepers were representatives of national and international parent support networks (see acknowledgements) to facilitate recruitment of parents/caregivers. Parents/caregivers were also recruited through the COHESION Study Facebook page where a recruitment video was uploaded and shared (https://www.facebook.com/100053069057849/videos/109673200811648/). The participant from India was also recruited in this way. Information (names and affiliations) on the researchers was provided in the recruitment of participants in all locations.

Low-income to middle-income countries

Gatekeepers were healthcare providers and/or researchers working in the area of neonatal encephalopathy. Gatekeepers in LMiCs used a purposeful and convenience sampling technique[14] and invited parents/caregivers who had engaged previously with local healthcare or research teams about neonatal encephalopathy/birth asphyxia (see figure 1).

Data collection

A semistructured interview guide (online data supplemental file 5) was developed for data collection in HiCs and LMiCs. The guide was informed by those used for qualitative interviews conducted in previous COS development,[19 20] and codeveloped with parent representatives and our colleagues in Kenya. Interviews were carried out between March 2020 and February 2021. Interviews were concept-elicitation interviews,[21] which enabled participants to elicit spontaneous responses based on their experiences. A Distress Protocol document (online data supplemental file 6) adapted from Draucker[22] was also available across all research sites. All interviews were conducted by experienced qualitative researchers. Colleagues involved in the interview process were academics and/or clinicians.

High-income countries

All interviews with participants from HiC countries (Ireland, Australia, the USA and the UK), and the interview with the participant from India, were conducted online by FQ and LB, in English, audio recorded and transcribed. Reflective notes were written during and after each interview (online supplemental table 1). Researchers in HiCs were not known to participants prior to recruitment.

Low-income to middle-income country

The SOP guided the processes of translating the PIL, consent form and interview guide to local dialects to ensure that participation was not restricted to English-speaking parents/caregivers. The translation process was guided by published principles of good practice[23 24] and is described in figure 2. One interview was conducted in English with a participant from India who was fluent in English. In keeping with the country classification by the World Bank, we describe the data from this participant with the LMiC interviews. Interviews in LMiC countries

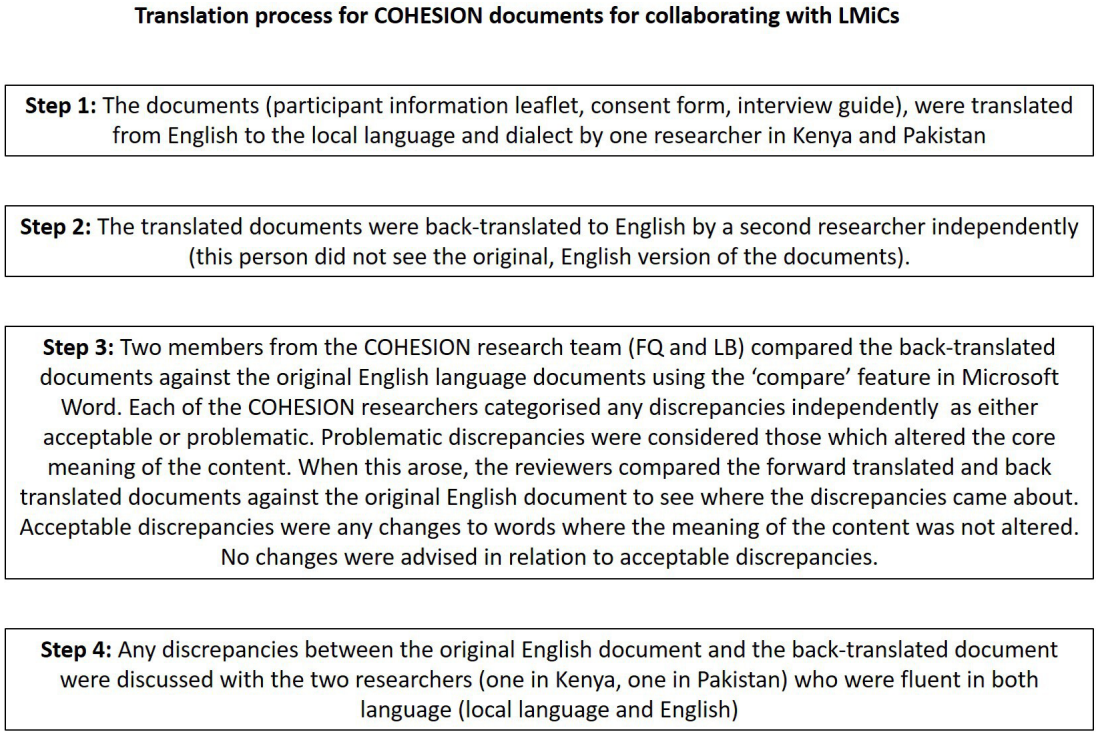

Figure 2 Translation process for COHESION parent interviews in LMiCs.

were conducted face to face or by phone by interviewers in the local language using the interview guide, audio recorded and transcribed by COO, CB, VK and SK (Kenya) and SA, MN and FT (Pakistan). The process for transcription and translation of interview scripts is outlined in figure 3.

Data analysis

Data analysis was carried out by FQ and LB using methods adopted by other COS developers,[25 26] based on the approach by Corbin and Strauss.[27] The transcripts were coded by (a) inductive coding, capturing definitive outcomes reported by the participants and (b) semantic coding, for references to outcomes inferred by the participants. This approach to coding was carried out for each interview independently, verified, and any differences were discussed before proceeding to the next stage. Similar codes (outcomes) were merged and deduplicated from interviews and grouped into higher-level

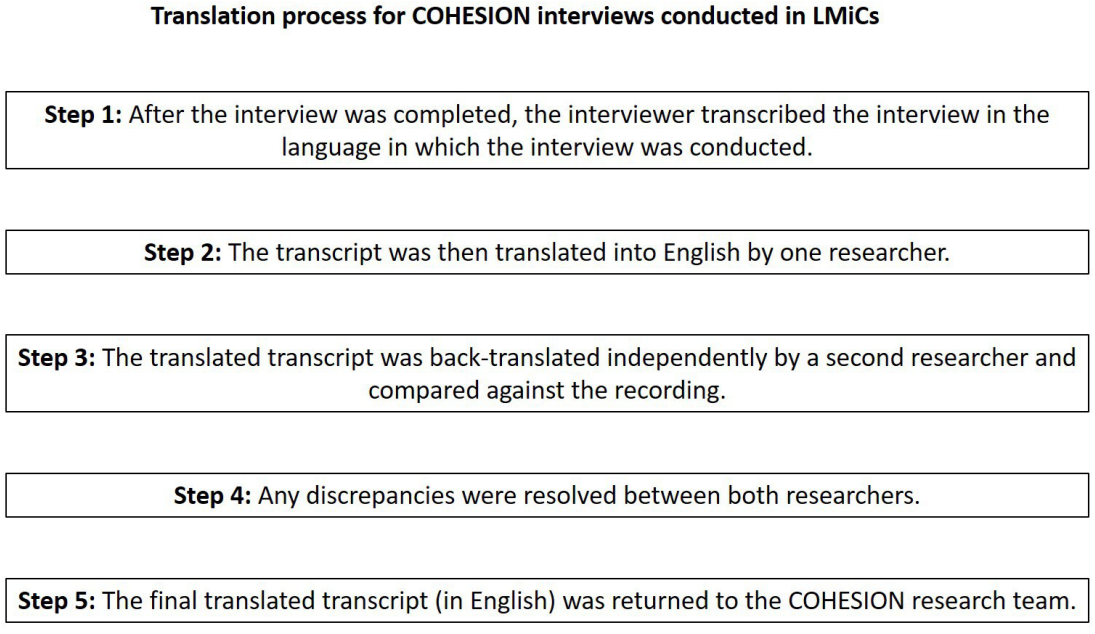

Figure 3 Translation processes for COHESION interviews conducted in LMiC.

thematic categories (outcome domains). The domain categorisation was largely based on domains used in previous similar COSs.[15 28]

The process of mapping direct quotes to outcomes and domains was not presented to participants but was presented to parent representatives and healthcare providers on the COHESION Steering Group for final verification and agreement, rather than presenting to participants.

Conceptual saturation[17] was assessed iteratively during the analysis and was reached by the interview 11 in HiCs, by interview 5 in Pakistan and by interview 8 in Kenya.

RESULTS

Interviews were carried out with 25 parents. The children of these parents ranged between 4 months at the time of interview and 17 years. Other parents initially showed interest but decided not to take part in the interviews due to the time, childcare and working from home commitments. The country breakdown is as follows: Ireland (n=8), Australia (n=1), the USA (n=1), the UK (n=1), India (n=1), Kenya (n=8) and Pakistan (n=5). The interviewees included twenty-one mothers and four fathers. Four of the infants of parents we interviewed had died. Fourteen children had received therapeutic hypothermia treatment and eleven received standard care. Twelve interviews were carried out by Zoom video conferencing; seven interviews face-to-face and six interviews by phone. Interviews took between 40 and 70 min.

Many of the outcomes mentioned and discussed by parents align with those previously measured in randomised trials of interventions for the treatment of neonatal encephalopathy.[29–31] Fifty-four outcomes were identified overall by parents as important to measure in the treatment of neonatal encephalopathy. These outcomes mapped to sixteen outcome domains (online supplemental table 1). We have included whether parents mentioned the outcomes in HiCs alone, LMiCs alone or both. Four unique outcomes were identified by parents in LMiCs, and seven unique outcomes were identified by parents from HiCs. The outcomes, noted under the domain headings, are presented in the online supplemental table 1. Twenty-one of the outcomes are unique to this study and were not identified in our ongoing systematic review of randomised trials and systematic reviews of randomised trials for the treatment of neonatal encephalopathy, these outcomes are indicated with an Asterix in the online supplemental table 1. These unique outcomes were mapped across eight domains: neurological outcomes, respiratory outcomes, gastrointestinal outcomes, motor development, development (speech & social), survival/living outcomes, long-term disability and parent-reported outcomes. Extracts from the interviews providing illustrative examples of the parents/family caregivers narratives are reported in table 1. This table provides illustrative examples of the definitive (and inferred) outcomes considered important to parents/caregivers.

DISCUSSION

Outcomes considered important to parents of infants with neonatal encephalopathy are largely unreported in trials evaluating treatments.[29–31] This qualitative study highlights the outcomes that these parents identified as most important in determining their child's health following treatment. Twenty-one outcomes were identified by parents as important to measure in the treatment of neonatal encephalopathy that were not measured in randomised trials of interventions for the treatment of neonatal encephalopathy, as identified by our ongoing systematic review. This highlights the need for inclusion of parents' perspectives in identifying important outcomes in the COS development process.

This study also highlights the need for qualitative data collection in COS development to be more inclusive of LMiCs. Although many outcomes were identified as important by parents from both LMiCs and HiCs, some were unique to either LMiC or HiC. While, the reasons for these differences in outcomes is beyond the scope of this work, all outcomes will be included in the next phase of the COS development.[6 32]

Using the processes we have reported to engage with gatekeepers in LMiCs, future COS developers have the opportunity to be more inclusive of the experiences and opinions of stakeholders on a given condition from both HiCs and LMiCs. In addition, using the translation processes described, language does not have to be a barrier for the inclusion of patients' opinions of important outcomes in COS development.

Strengths and limitations

The findings of this work contribute to an under-researched area. We chose not to present parents with a list of outcomes from the literature, a method that has been used in other qualitative work informing COS development.[20] This decision was pragmatic in that it was influenced by time frames of other work packages of this study. It also contributed to the iterative process underpinning the aim of this qualitative study that is, the focus was on the parents identifying outcomes they deemed important rather than offering comments on outcomes we presented to them. Parents will also be invited to participate in the next phase of this study, an online Delphi survey to prioritise outcomes and inform the final COS for use in future studies evaluating treatments for neonatal encephalopathy.

Having rigorous procedures in place, including developing an SOP and Distress Protocol helped ensure that similar processes were followed for all parents regardless of what country they were participating from.

A strength of this study was that fathers of infants with neonatal encephalopathy/birth asphyxia were also interviewed and contributed their unique experience

Table 1 Examples of illustrative quotes mapped to outcomes

Outcome identified	Illustrative quote	Participant details
Absence of neonatal reflexes	She told we cannot predict when he will be fine because when the pupillary reflex is not there, when other reflexes are not there. He's not responding to any of the treatment	Interview H, mother, (LMiC)
Gag reflex (absent)	They did a test to see if he had a gag reflex and he had no gag reflex	Interview A, mother, (HiC)
Swallow (absent)	I remember them saying to me that's a really good sign he can swallow	Interview E, mother, (HiC)
Sleep disorders	When you're a mum and she's sleeping four or four and a half hours between feeds you think it's great, you don't think or know that could be…a bad thing	Interview I, mother, (HiC)
Ability to breathe normally and unaided	He was able to breathe on his own he was kind of fighting it straight away. That was a good sign I suppose	Interview C, father, (HiC)
Need for neonatal resuscitation	He needed resuscitating while he was being warmed up twice while I was sitting there… that was terrifying	Interview E, mother, (HiC)
Meconium passage	Personally, I used to observe some problems on the baby. It got to a point that when he would pass stool, it had blood so for me I used to ask such questions because I thought it was related with the problem with the problem that he had	Interview S, mother, (LMiC)
Ability to undertake sport	Now he has no problems (motor development), he loves swimming, watching him in the water in the pool, watching him swimming around and having fun is fantastic	Interview E, mother, (HiC)
Heightened sensory sensitivity	They also told us that she could have a sensory condition where she'd be, where she mightn't want to be touched	Interview K, mother, (HiC)
Suffering	He was very uncomfortable and crying shaking cause obviously they were cooling him down	Interview D, mother, (HiC)
Parental involvement in care	She let me hold him earlier than I was meant to… my instinct was this can't be bad for him to be held by his mother	Interview D, mother, (HiC)
Parental attachment with their baby	I was in the post-surgery room and my son was in the Neonatal Intensive Care Unit. No-one was allowed to see my son except my husband	Interview H, mother, (LMiC)
Uncertainty for future well-being	I missed out on so much. I kept having to hug her and if she wasn't there or gone to Montessori or something I would have to get a pillow or something just to hug	Interview E, mother, (HiC)
Parental psychological impact of Neonatal Intensive Care Unit experience	I went back to my room and I was in some kind of shock. I remember my mum and dad came in and there were conversations I had with doctors that had been there at his birth, a lot of them came to see me over those couple of days and I have no recollection of speaking to them	Interview F, mother, (HiC)
Impact of child's condition on parents' relationship	Probably nearly caused our divorce. There were some very, very hard times	Interview E, mother, (HiC)
Financial burden of healthcare costs of care for infant on parents	Like financially to take her to the hospital. It brings a lot of trouble	Interview P, mother, (LMiC)
Parental ability to work	You don't go to work, you need to stay with the baby, to look after them. So it has effect	Interview Q, mother, (LMiC)
Impact of child's condition and Neonatal Intensive Care Unit experience on wider family (stress, disappointment, sadness, grief etc)	As a family, we are not as before, everyone is very down. It has caused a big impact in our life	Interview H, mother, (LMiC)
Effective communication between parents and healthcare providers	What's this mean? Numbers. What's a good number for this? What's a good range for that? And I just, I went deep. Every night I'd come home at ten o'clock, until two or three in the morning I'd be, numbers, what's that mean? HIE studies, outcomes, grading, HIE one, two, three, long-term prognosis, everything like you know, cerebral palsy, what comes with this. So it broke it down over a few weeks and I learned as much as I could	Interview J, father, (HiC)

HiC, high-income country; LMiC, low- to middle-income country.

of outcomes they considered to be important. A lack of inclusion of fathers was listed as a limitation of interviews carried out by Duffy *et al*.[25]

We must acknowledge the limitations of this study. The age range of participants children was broad (children ranged from 4 months to 17 years) at the time of these interviews. The eldest 'child' had taken part in a trial for therapeutic hypothermia and so this informed the higher age threshold. We are aware that the age range of the children may have modified parents experiences and observations. However, for the purposes of identifying outcomes as part of a COS development process, the diversity of outcomes at different age milestones is an important factor and ensures all relevant outcomes (short term and long term) are considered in deciding the final COS. We did not seek in-depth demographic information of the parents taking part in the interviews (eg, level of education, socioeconomic status etc). We acknowledged the parents by the World Bank classification of their country of residence in terms of income

status (see https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html). However, we suggest that further exploration of demographic data would be interesting.

This study was conducted during the COVID-19 pandemic. The multiple methods of recruitment reported were used as the recruitment took longer than planned, perhaps this could be aligned to the pandemic. Due to public health guidance and social distancing, some of the interviews were conducted via phone and not face to face as we had originally planned.

Including parents in this stage of COS development ensures that the outcomes presented in the next rounds of the COS development (ie, the Delphi survey) will present outcomes that are important to parents from HiC and LMiCs. Including parents in all stages of the COS development ensures the COS will be relevant to those in HiCs and LMiCs. This is particularly important as different treatments are being investigated and disparities have been shown in the effectiveness of treatments between HiC and LMiC populations.[3 4]

CONCLUSION

Our findings present outcomes identified by parents as important to measure and report in future trials for interventions for the treatment of neonatal encephalopathy. In addition to physiological/clinical outcomes measured by healthcare providers and researchers in studies, parents also highlighted outcomes of parental and familial involvement in the care of the infant and their overall well-being. This study also offers processes for the inclusion of participants from LMiCs in COS development. The next phase of COHESION Study will combine these outcomes with those from a systematic review of studies for the treatment of neonatal encephalopathy. Unique outcomes will be scored by stakeholders in an online consensus process called a Delphi survey. The final outcomes to include in the COS will be decided through discussion with stakeholders in online consensus meetings.[6]

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Contributors FQ, FHB, MD, DD, DMH, PH, TH, JJK, SM, EM, ENB, KW and LB conceived and designed this qualitative study. FQ, LB, PH, DD, MD, ENB, CB and COO contributed to the study design of the interview guide and SOP. FQ, LB, PH, DD, MD and ENB contributed to the study design of all other supplementary material including the Participant Information Leaflet and Distress Protocol. SA, FT, MN, CB, VK, COO and SK conducted the recruitment, interviews, transcription and translation in LMiCs. FQ and LB conducted the recruitment, interviews and transcription in HiCs. FQ and LB analysed the data. DD, PH and MB verified the data analysis. FQ and LB wrote the paper. FQ is the corresponding author and guarantor of this manuscript. All authors critically revised the manuscript. All authors reviewed and approved the final manuscript.

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Competing interests No, there are no competing interests.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Received

Ethics approval This study involves human participants and was approved by the National University of Ireland, Galway, Research Ethics Committee (REC) (Reference 19 April 2014). The Moi University/Moi Teaching and Referral Hospital Institutional Ethics Review Committee (IREC, reference IREC/2016/243, approval number: 0001874). Aga Khan University Ethics Research Committee (ERC) (Reference 2020-5263-14425). Participants gave informed consent to participate in the study before taking part.

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REFERENCES

1 Aslam S, Strickland T, Molloy EJ. Neonatal encephalopathy: need for recognition of multiple etiologies for optimal management. *Front Pediatr* 2019;7:142.
2 de Vries LS, Jongmans MJ. Long-term outcome after neonatal hypoxic-ischaemic encephalopathy. *Arch Dis Child Fetal Neonatal Ed* 2010;95:F220–4.
3 Jacobs SE, Berg M, Hunt R, *et al*. Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane Database Syst Rev* 2013;69:CD003311.
4 Thayyil S, Pant S, Montaldo P, *et al*. Hypothermia for moderate or severe neonatal encephalopathy in low-income and middle-income countries (helix): a randomised controlled trial in India, Sri Lanka, and Bangladesh. *Lancet Glob Health* 2021;9:e1273–85.
5 McAdams RM, Berube MW. Emerging therapies and management for neonatal encephalopathy-controversies and current approaches. *J Perinatol* 2021;41:661–74.
6 Quirke FA, Healy P, Bhraonáin EN, *et al*. Cohesion: core outcomes in neonatal encephalopathy (protocol). *Trials* 2021;22:125.
7 Williamson PR, Altman DG, Bagley H, *et al*. The comet Handbook: version 1.0. *Trials* 2017;18:280.
8 Keeley T, Williamson P, Callery P, *et al*. The use of qualitative methods to inform Delphi surveys in core outcome set development. *Trials* 2016;17:230.
9 Gorst SL, Gargon E, Clarke M, *et al*. Choosing important health outcomes for comparative effectiveness research: an updated review and user survey. *PLoS One* 2016;11:e0146444.
10 Karumbi J, Gorst SL, Gathara D, *et al*. Inclusion of participants from low-income and middle-income countries in core outcome sets development: a systematic review. *BMJ Open* 2021;11:e049981.
11 Lemmon ME, Donohue PK, Parkinson C, *et al*. Parent experience of neonatal encephalopathy. *J Child Neurol* 2017;32:286–92.
12 Nassef SK, Blennow M, Jirwe M. Parental viewpoints and experiences of therapeutic hypothermia in a neonatal intensive care unit implemented with Family-Centred care. *J Clin Nurs* 2020;29:4194–202.
13 Craig AK, James C, Bainter J, *et al*. Parental perceptions of neonatal therapeutic hypothermia; emotional and healing experiences. *J Matern Fetal Neonatal Med* 2020;33:2889–96.
14 Lemmon ME, Donohue PK, Parkinson C, *et al*. Communication challenges in neonatal encephalopathy. *Pediatrics* 2016;138:e20161234.
15 Webbe J, Brunton G, Ali S, *et al*. Parent, patient and clinician perceptions of outcomes during and following neonatal care: a systematic review of qualitative research. *BMJ Paediatr Open* 2018;2:e000343.
16 Jones JE, Jones LL, Keeley TJH, *et al*. A review of patient and carer participation and the use of qualitative research in the development of core outcome sets. *PLoS One* 2017;12:e0172937.
17 Francis JJ, Johnston M, Robertson C, *et al*. What is an adequate sample size? Operationalising data saturation for theory-based interview studies. *Psychol Health* 2010;25:1229–45.
18 Patton MQ. *Qualitative research and evaluation methods*. 3rd ed. Thousand Oaks, CA: SAGE publications, 2002.
19 Fish R, Sanders C, Williamson PR, *et al*. Core outcome research measures in anal cancer (CORMAC): protocol for systematic review, qualitative interviews and Delphi survey to develop a core outcome set in anal cancer. *BMJ Open* 2017;7:e018726.
20 Dadouch R, Faheim M, Juando-Prats C, *et al*. Development of a core outcome set for studies on obesity in pregnant patients (COSSOPP): a study protocol. *Trials* 2018;19:655.
21 Nabbout R, Auvin S, Chiron C, *et al*. Development and content validation of a preliminary core set of patient- and caregiver-relevant outcomes for inclusion in a potential composite endpoint for Dravet syndrome. *Epilepsy Behav* 2018;78:232–42.
22 Draucker CB, Martsolf DS, Poole C. Developing distress protocols for research on sensitive topics. *Arch Psychiatr Nurs* 2009;23:343–50.
23 Brelsford KM, Ruiz E, Beskow L. Developing informed consent materials for non-English-speaking participants: an analysis of four professional firm translations from English to Spanish. *Clin Trials* 2018;15:557–66.
24 Wild D, Grove A, Martin M, *et al*. Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (pro) measures: report of the ISPOR Task force for translation and cultural adaptation. *Value Health* 2005;8:94–104.
25 Duffy J, Thompson T, Hinton L, *et al*. What outcomes should researchers select, collect and report in pre-eclampsia research? A qualitative study exploring the views of women with lived experience of pre-eclampsia. *BJOG* 2019;126:637–46.
26 Gonçalves A-C, Marques A, Samuel D, *et al*. Outcomes of physical activity for people living with dementia: qualitative study to inform a core outcome set. *Physiotherapy* 2020;108:129–39.
27 Corbin JM, Strauss A. Grounded theory research: procedures, canons, and evaluative criteria. *Qual Sociol* 1990;13:3–21.
28 Healy P, Gordijn SJ, Ganzevoort W, *et al*. A core outcome set for the prevention and treatment of fetal growth restriction: deVeloping endpoints: the COSGROVE study. *Am J Obstet Gynecol* 2019;221:339.e1–339.e10.
29 Azzopardi D, Brocklehurst P, Edwards D, *et al*. The TOBY study. whole body hypothermia for the treatment of perinatal asphyxial encephalopathy: a randomised controlled trial. *BMC Pediatr* 2008;8:17.
30 Jacobs SE, Morley CJ, Inder TE, *et al*. Whole-Body hypothermia for term and near-term newborns with hypoxic-ischemic encephalopathy: a randomized controlled trial. *Arch Pediatr Adolesc Med* 2011;165:692–700.
31 Laptook AR, Shankaran S, Tyson JE, *et al*. Effect of therapeutic hypothermia initiated after 6 hours of age on death or disability among newborns with hypoxic-ischemic encephalopathy: a randomized clinical trial. *JAMA* 2017;318:1550–60.
32 Quirke FA, Healy P, Bhraonáin EN, *et al*. Multi-round compared to real-time Delphi for consensus in core outcome set (COS) development: a randomised trial. *Trials* 2021;22:142.

Correction: *Core outcomes in neonatal encephalopathy: a qualitative study with parents*

Quirke F, Ariff S, Battin M, *et al*. Core outcomes in neonatal encephalopathy: a qualitative study with parents. *BMJ Paediatrics Open* 2022;6:e001550. doi:10.1136/bmjpo-2022-001550

In the published version the term we have deleted the following sentence including the respective reference 17 and updated the sequence in reference section:

"Qualitative research focuses on understanding people's lives, experiences and what is important to them.[17]"

BMJ Paediatrics Open 2022;**6**:e001550corr1. doi:10.1136/bmjpo-2022-001550corr1

Data supplements

Data Supplement 1. Reporting recommendations for qualitative research methods in COS development

Table 1. Reporting recommendations for qualitative research methods in COS development, as developed by Jones *et al.* .

1	Research aims and relationship with broader COS development process	See section introduction
2	Sampling approach	See section methods
3	Type of data collection methods (e.g. interviews, focus groups, combination); content and derivation/ justification (e.g. topic guide)	See section data collection
4	Analytical approach and justification	See section data analysis
5	Sample characteristics and participants numbers	See section participants
6	Findings related to outcome domains (concordant with research aims)	See section results
7	Report approaches to ensuring rigour (e.g. multiple perspectives on the data, respondent validation) and consider reflexive content	See section data analysis and discussion
8	Discuss the strengths and limitations of the approach	See section strengths and limitations

Data Supplement 2. Standard Operating Procedure for LMiCs

Standard Operating Procedure (SOP) for COHESION Interviews in Low- to Middle-Income Countries

Who? Potential participants are parents whose infants have been diagnosed with and received treatment for neonatal encephalopathy or birth asphyxia, or other family members who may care for the infant. Infants will have been born at 35 weeks' gestation or later, where this can be confirmed or estimated, with a birth weight considered healthy for each location (preferably 2.5kg or above). We will recruit a minimum of 5-6 participants in each country.

Process for identifying participants

Steering Group members for COHESION, members with experience in the area of neonatal encephalopathy research, will identify Gatekeepers in each respective country. Gatekeepers will consist of researchers or healthcare professionals working in the area of neonatal encephalopathy. The Gatekeepers will act to identify potential participants through their local knowledge in their particular country.

Translation of information for recruitment of parents for whom English is not their first language

The following documents need to be translated from English to the local language in the area in which the interviews are being carried out:

- Participant Information Leaflet
- Consent Form
- Interview Schedule

Two researchers fluent in both English, and the local language and dialect of the region in which the interviews are taking place will support the translation of the above documents. One

of these individuals may be the research assistant conducting the interviews. The process for translating these documents is:

1. The documents are translated from English to the local language and dialect by one researcher.

2. The translated document is back-translated to English by a second researcher independently (this person will not have seen the original, English language version of the documents)

3. Two members from COHESION (FQ and LB) will compare the back-translated documents against the original English language documents using the "compare" feature in Microsoft word. Each will categorise any discrepancies independently as either acceptable or problematic. Acceptable discrepancies will be those where the meaning is not altered. Problematic discrepancies will be those, which alter the core meaning of the content. If this arises, the reviewers will compare the forward translated and back-translated documents against the original English document to see where the discrepancy arose.

4. Any discrepancies between the original English document and the back-translated document will be discussed with the two researchers who are fluent in both languages.

Audio recording of the Participant Information Leaflet: The researcher conducting the interviews will audio-record the translated Participant Information Leaflet and Consent form. This can then be played for potential participants who may have literacy challenges and ensure that adequate information is given to potential participants before consent is considered. Participants who agree to participate will sign (either through writing or annotating with an 'x' depending on literacy levels) the consent form and return it to the interviewer prior to commencing the interview. A copy of the signed consent form will be sent to the COHESION research team at the earliest opportunity.

Interviews

Research assistants or healthcare professionals with experience in interviewing will conduct the interviews. The interviewer will conduct the interviews in the native language using a structured interview schedule. All interviews will be audio recorded and recordings transcribed. The transcripts will be translated into English by one researcher. The translated transcript will be back-translated independently by a second researcher and compared against the recording. Any discrepancies will be resolved between both researchers. The final translated transcript (in English) will be returned to the COHESION research team.

The interviews will follow a semi-structured format, where participants will initially be prompted by open questions to encourage discussion, followed by additional questions, which will be informed by the *a priori* domains that emerge from the systematic review. The interview schedule may develop iteratively during the interview process.

Distress Protocol

We have developed a *Distress Protocol* document outlining steps for the interviewer to undertake in the event of the interviewee becoming distressed during the process of the interview. This is a separate document in English that does not need to be translated, as it intended for the interviewer to use.

Additional Information

Please note that the COHESION team will, subject to a priori agreement on costs, pay the interviewer and other researcher involved in translating the documents and interview transcripts, for their time and work for audio-recording the Participant Information Sheet and Consent Form, conducting the interviews and translating the transcripts back into English.

Data Supplement 3. Participant Information Leaflet

Consent form

COHESION (Core Outcomes in Neonatal Encephalopathy)

Participant Information Number: _____ (to be completed by researcher)

Declaration of the participant- please tick (□) the relevant box	YES	NO
I have read or have been read the participant information sheet for this interview and I understand the contents.		
I have had the opportunity to ask questions and all my questions have been answered to my satisfaction.		
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving reason and without any negative consequences.		
I agree to the interview being audio recorded.		
I agree that the audio recording of the interview will be stored securely in the National University of Ireland, Galway, for a period of seven years after the completion of this study.		

Storage and future use of information: I give my permission for information collected about me to be stored or electronically processed for the purpose of research and to be used in related studies or other studies in the future but only if the research is approved by a Research Ethics Committee.		
I give permission to be contacted in the future about other studies I may be interested in participating in.		

Participant name: _____

Participant signature: _____

Date: _____

Statement by the researcher/person taking consent

I have, to the best of my ability made sure that the participant understands what is involved in taking part in this study and that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Researcher / person taking consent:

Name of person taking consent: _____

Signature of person taking consent: _____

Date: _____

Data Supplement 4. Interview Guide

COHESION Interview Guide

Interview Schedule

I. Introduction

II. The participant will be reminded of the purpose of the COHESION study.

III. The participant will be given the opportunity to ask questions about the COHESION study.

IV. The participant will be asked if they are still willing to take part.

V. The participant will be asked if they agree to having the interview audio/video recorded.

VI. They will be asked to fill in the consent for and to sign it and to give to the signed form to the interviewer.

VII. In the case of interviews carried out by teleconference, they will be prompted to provide consent via email attachment of the signed consent form prior to commencement of the video/ audio interview.

VIII. The specific questions will be asked of the participant.

I. Introduction

You are very welcome to our interview session today and we are very grateful that you have taken the time to participate in our focus group session. This session is part of a study we are carrying out to develop a "Core Outcome Set". (May insert slot to show POPPIE video explaining core outcome sets in plain language). One of the main delays in the improvement and progression of care for patients

with a particular disease is the differences in what things researchers look at to see a treatment works or not. These 'things' are called outcomes. If different outcomes are measured in different trials, they can't be compared and this slows progress in knowing how to improve patient care. Another problem is that often the research carried out does not incorporate the values and opinions of patients and care-givers and often prioritises the values of clinicians. The development of our Core Outcome Set (COS) will:

- Standardise what should be measured in trials for treating Neonatal Encephalopathy (Birth Asphyxia).
- Incorporate the opinions of Parents and care-givers of children with Neonatal Encephalopathy (Birth Asphyxia) (and have an expertise which is often overlooked).

II. The participant will be reminded of the purpose of the COHESION study.

Our COS aims to find people's opinions on what measures they think are most important and that should be measured when doing research on treatments for Neonatal Encephalopathy (Birth Asphyxia). We will compile a list of outcomes that will then be used to develop a questionnaire which we will circulate to a wider group. We really want your experiences to influence these outcomes.

III. The participant will be given the opportunity to ask questions about the COHESION study.

Before we begin, have you any questions?

IV. The participant will be asked if they are still willing to take part.

We would like to take this opportunity before we begin to make sure you are still happy to take part in this interview. If at any stage you'd like a break (or the questions asked are too difficult to answer), please just let us know.

V. *The participant will be asked if they agree to having the interview audio/video recorded.*

We'll be recording this interview (sound and/or video) and storing the recording safely until the study is complete. We will not mention names or anything that individually identifies you in anything we do.

If you do not wish for the interview to be video recorded we can offer audio recording instead.

VI. *Participants will be asked to fill in the consent form, sign it and give the signed form to the interviewer.*

VII. *In the case of interviews carried out by tele/videoconference, participants will be asked sent the consent form by email prior to commencement of the video/ audio interview.*

VIII. *The specific questions will be asked of the participant.*

1*	*Why do you think your baby was admitted to the NBU/ NICU?*
2*	(Ask about their experience of their child (relation/ child they care for) being told of their diagnosis of Neonatal Encephalopathy)

	Do you know what diagnosis your son/daughter was given? Can you explain?
3*	*What treatment options were offered to your baby and how did you decide about undergoing treatment?* What information did parents/caregivers want about the treatment their child would be receiving, and what factors did they consider when deciding on treatment options
4*	*What treatment did your baby receive while in hospital?*
5	*What treatment did your baby receive after discharge from hospital?*
6*	*What effects has the treatment had/ is having?* Prompt for areas such as (physical health, mental health, effects on family/ relationships, developmental milestones etc.) Ask what parents/caregivers would consider the worst side effect their infant has experienced
7	*Does your baby have any lasting illness or problems? If yes what are they?*
8*	*What are your concerns for your child for the future?*

9	*Is there any information you wished you had received in hospital that you did not get? What?* i.e. were they given any information leaflets/ websites at the time of diagnosis or treatment
10	*Did the explanation and information given about the treatment your child received match your real experience?*
11*	*Is there any information or advice your healthcare provider shared with you that you do not agree with and/or feel was important?*
12*	If I say I am studying health outcomes, what does a health outcome mean to you? *How would you describe an **outcome**?* (In their own words)
13*	*What outcomes do you think are important to measure to give an idea of the health/ progress of your child?*
14*	*What matters most to you about the health of your baby?*
15*	*What about the impact of your baby's health on you?*
16*	*What about the impact of your baby's health on the other members of your family?*

17*	*In the research, researchers and doctors have looked into (**insert list of outcomes derived from systematic review**)* *What are your thoughts?* *Is there anything else you would like to add?*

Note: *Where the question has an asterix (*), these questions should be prioritised and must be asked; Where the question does not have this asterix, these questions are supplementary questions that could be used where additional participant prompting is required.*

Data Supplement 5. Distress Protocol for COHESION interviews

Signs indicative of stress that may occur during the interview process	**Procedure when participant displays signs of distress and questions to determine level of distress**	**Response or behaviour of participant in response to questions**	**Is the participant displaying signs of strong emotional distress and/or is there a concern for their safety? (YES/NO)**	**Is there a cause to believe the participant may be in danger? (YES/NO)**
Participant informs interviewer that they are experiencing a high level of distress.	1. Stop the interview. 2. Offer support to the participant and allow then time recover. 3. Determine the level of distress through the following questions: a. Would you like to share what you are thinking? b. Would you like to share how you are feeling?			

	c. Do you feel you are able to continue with this interview? d. Would you like to end this interview? e. Do you feel you would be able to go on about your day as normal after this interview? (For Interviewer): Do you think that the participant is experiencing emotional distress beyond what would be expected from this interview?			
Participant shows signs of emotional distress (e.g. crying, becoming agitated, loss of concentration etc.)	1. Stop the interview. 2. Offer support to the participant and allow then time recover. 3. Determine the level of distress through the following questions: a. Would you like to share what you are thinking?			

	b. Would you like to share how you are feeling? c. Do you feel you are able to continue with this interview? d. Would you like to end this interview? e. Do you feel you would be able to go on about your day as normal after this interview? 4. (For Interviewer): Do you think that the participant is experiencing emotional distress beyond what would be expected from this interview?			

Actions for the Interviewer:

1. If the distress displayed by the participant is what would be expected in an interview on this sensitive topic;

offer the participant support and the option to:

a. Stop the interview.

b. Give the participant a break from the interview.

c. Continue the interview.

2. If the distress displayed by the participant is **beyond** what would be expected in an interview such as this on a sensitive topic;

   a. Encourage the participant to follow up with his/her GP for support.

   b. Provide the participant with the number of the emergency room at the nearest hospital (location specific) and encourage the participant to make contact with this service if their distress is increased in the hours/days/weeks following the interview.

   c. Indicate that you (the interviewer), with the participant's permission, will follow up with/ contact the participant on the day following the interview.

   d. Notify the PI/Lead Researcher of the steps undertaken and the recommendations given to the participant.

3. If the distress displayed by the participant indicates they may be in immediate danger;

   a. Contact the local authorities, unless a family member can transport the participant to the nearest hospital.

   b. Indicate that you (the interviewer), with the participant's permission, will follow up with/ contact the participant on the day following the interview.

   c. Notify the PI/Lead Researcher of the steps undertaken and the recommendations given to the participant.

Supplementary Table. Inductive codes, outcome domains and outcome domain categories mapped.

Outcome Domain Categories	**~~Outcome Domains~~ ~~(~~Outcomes proposed for Delphi~~)~~**	**Inductive code**	**Descriptive notes on Domain**	**HiC or LMiC**
Neurological Outcomes	Electroencephalogram (EEG) abnormalities	Brain Activity	Parents recalled the importance of measurements relating to brain injury and seizure activity being discussed with them in the NICU. Parents spoke of the significance they placed on neonatal reflexes. They described how healthcare providers looked for responses, tone and changes in reflexes to judge their baby's response to treatment. Being able to swallow or gag was also noted by parents as a welcome sign. Parents across both HiC and LMiCs spoke of their baby's sleeping. For some, sleeping too much was regarded as something associated with illness; others were concerned that their baby was not sleeping enough or had a disturbed sleep pattern. Many of the parents were unsure what was "normal", what they should expect and took their cues from the comments offered by health care providers.	HiC & LMiC
	Neonatal seizures	Seizures		HiC & LMiC
	Brain Injury on imaging	Brain Injury		HiC & LMiC
		Brain Abnormalities		HiC & LMiC
	Severity of encephalopathy	Absent pupillary reflex		LMiC
		Consciousness		HiC & LMiC
		Opening eyes		HiC & LMiC
		Brain Function		HiC
		Being active/responsive		HiC & LMiC
	Absence of Neonatal Reflexes*	Neonatal reflex/reflexes absent (asymmetrical tonic neck reflex, Babinski reflex, grasp reflex Moro reflex, rooting reflex, step reflex, Galant reflex)		HiC & LMiC
	Sleep Disorders*	Sleep difficulties/ Sleeplessness		HiC
		Sleepiness/ over sleepiness		HiC & LMiC

	Normal tone	Tone (ability to support head, neck,)		HiC & LMiC
		Ability to practise "tummy time"		HiC
	Gag reflex (absent)*	Gag reflex (absent)		HiC & LMiC
	Swallow (absent)*	Swallow (absent)		HiC & LMiC
		Need for suctioning (unable to handle secretions)		HiC & LMiC
Respiratory Outcomes	Ability to breathe normally and unaided*	Breathing ability	Parents spoke of the importance of their child breathing normally, without struggle, and unaided, without the need for breathing machines. They also spoke of the need for their infant to be resuscitated as frightening and made them realise the seriousness of their child's condition and health.	HiC & LMiC
		Breathing abnormality		LMiC
		Ability to breathe unaided		HiC
		Coughing		LMiC
	Need for neonatal resuscitation*	Need for adrenaline		HiC
		Need for resuscitation		HiC & LMiC
	Oxygen requirement	Continuous positive airway pressure (CPAP) requirement		HiC & LMiC
		High-flow oxygen requirement		HiC
		Oxygen requirement		HiC & LMiC
		Low-flow oxygen requirement		HiC

		Oxygen saturations		HiC
	Need for mechanical ventilation	Mechanical ventilation requirement		HiC & LMiC
		Respirator requirement		HiC & LMiC
		Need for intubation		HiC
		Extubation		HiC & LMiC
		Need for a tracheostomy tube		HiC
Gastrointestinal Outcomes	Feeding intolerance	Vomiting	Parents spoke of their concern for their infant's intolerance to feeding, indicated by vomiting. Independence in feeding was also a worry, and parents discussed whether their infant was able to be fed by their mouth or if they needed to be fed using a tube as a strong concern for their infant's quality of life. The ability of the infant to pass meconium normally and not having blood in the stool was a particular concern of parents in LMiCs	HiC & LMiC
	Meconium passage*	Ability to pass stool		LMiC
		Ability to digest food		HiC
	Oral feeding ability	Ability to feed		HiC & LMiC
		Feeding difficulties		LMIC
		Ability to eat by mouth		HiC
		Ability to breastfeed		HiC
		Ability to suck		HiC
		Intravenous (i.v.) fluid requirement		HiC & LMiC

	Need for tube feeding	Need for nasogastric tube feeding		HiC & LMiC
		Need for percutaneous endoscopic gastrostomy (PEG) feeding		HiC
Cardiovascular Outcomes	Abnormal changes in heart rate or rhythm	Heart rhythm/ electrical activity	Parents spoke of the monitors connected to their baby which measured the activity of the heart. They remembered the sounds it made and the doctors and nurses recording information from it. An outcome uniquely identified by HiC parents was the risk of clotting, and the potential need for transfusion described to them by the doctor while their baby was being treated in the NICU.	HiC & LMiC
		Arrhythmia		HiC
		Bradycardia		HiC
	Coagulopathy	Need for platelet transfusion		HiC
Motor Development	General Gross Motor ability	Movement – Absent	Reference was made to their infant's mobility and strength in their legs and arms. For some parents, this went beyond their child's ability to stand unaided or to grasp something in their hand; they also identified outcomes associated with childhood games and with activities they saw as 'normal' for other children. Parents of children who were school-aged recalled the importance of their child's motor development in their ability to undertake sport with other children their age, which was unique to these interviews.	HiC
		Movement (moving fingers, hands, arms, legs, twitching)		HiC
		Ability to crawl		HiC & LMiC
		Ability to walk/ run		HiC & LMiC
		Ability to roll over		HiC & LMiC
		Ability to jump		HiC

		Ability to stand		HiC & LMiC
		Ability to stand independently		HiC
		Ability to bear weight		HiC
		Ability to kneel		HiC
		Ability to sit		HiC & LMiC
		Pulling to standing		HiC
		Ability to reach		HiC
		Weakness in hand/ hands		HiC
		Weakness in arm/arms		HiC
		Weakness in leg/ legs		HiC
		Weakness in body		LMiC
		Reduced mobility in arm/arms		HiC
		Reduced mobility in hand/hands		HiC
		Reduced mobility in foot/ feet		HiC
		Ability to grasp/ pick up objects		HiC & LMiC
		Coordination/ Balance		HiC
		Ability to hold objects		LMiC

	Ability to undertake sport*	Ability to kick a ball		HiC & LMiC
		Ability to undertake sport		HiC
Cognitive Development	General cognitive ability	General cognitive ability	General cognitive ability was a concern for parents of infants of various ages, this included learning difficulties and the need for educational support at school-age.	HiC & LMiC
		Cognitive disability		LMiC
		Learning difficulties		HiC & LMiC
		Need for educational support		HiC
Development (Psychosocial)	Psychological development	Ability to cry	Psychological development was highlighted as important by many parents, including the child's ability to display emotions and connect with others in a meaningful way. Behavioural issues were a concern for parents of HiCs and not LMiCs.	HiC & LMiC
		Smiling		HiC & LMiC
		Happiness		HiC & LMiC
		Laughing		HiC & LMiC
		Being upset		HiC & LMiC
		Being overwhelmed		HiC
		Anxiety (child)		HiC
		Ability to play		HiC &

				LMiC
		Need for Social and Emotional support		HiC
		Social withdraw (child)		HiC
		Peer and family relationships		HiC
	Behavioural issues	Behavioural issues		HiC
Development (Special Senses)	Visual impairment	Visual Impairment	Many parents highlighted the ability to see and hear as something they were concerned about in their child's development. Parents were also concerned for their child having a sensory condition whereby they would become distressed when faced with bright lights loud noises, certain tastes, smells or touch. The child's ability to communicate through speech and sound was also critical for parents.	HiC & LMiC
		Sensory reaction (to light)		HiC & LMiC
		Ability to recognise people/ objects		LMiC
	Hearing Impairment	Hearing impairment		HiC & LMiC
		Reaction to sound/ voices		LMiC
	Heightened sensory sensitivity	Sensitivity to light		HiC & LMiC
		Sensitivity to smell		HiC
		Sensitivity to taste		HiC
		Behaviour in response to a sensory sensitivity		HiC

Development (Speech & Social)	Ability to make noises/ verbalise*	Ability to make noises	The child's ability to communicate either through speech, noises or gestures was critical to parents.	HiC
		Ability to verbalise		HiC & LMiC
	Speech delay	Speech Delay		HiC & LMiC
		Ability to talk		HiC & LMiC
		Need for Speech and Language Therapy		HiC
	General communication ability	Need to learn sign language		HiC
		Ability to communicate needs		HiC & LMiC
Other Organ Outcomes	Renal Dysfunction	Pass urine	Renal dysfunction was discussed by parents in HiCs only. Contrastingly, hypoglycaemia was only highlighted as important by parents in LMiCs.	HiC
	Hypoglycaemia	Hypoglycaemia		LMiC
Survival/ Living Outcomes	Growth	Weight	Outcomes such as growth, survival, and full recovery from acute illness were described by parents as clear and important indications of how well their child responded to treatment. Survival was considered one of the most important outcomes. Several parents spoke of their infant's passing, and other parents spoke of this as a constant concern they had for their	HiC & LMiC
		Growth		HiC & LMiC
	Survival	Death		HiC & LMiC
		Brain death		LMiC

	Suffering*	Suffering	child when receiving treatment in the Neonatal Intensive Care Unit (NICU). Parents spoke of the suffering of their infant while receiving treatment in the NICU and how they viewed it as important to consider. Speaking of their infant being distressed and suffering in the NICU was difficult for parents to discuss, highlighting the importance of this outcome as an indication to parents of their child's health	HiC
		Pain		HiC
	Full recovery from acute illness	Time to clinical improvement		LMiC
		Recovery/ Reaction to treatment (being stable, consciousness)		HiC & LMiC
		Reduction in dose of medication		HiC
		Discontinuation of treatment		HiC & LMiC
		Symptom-free/ illness-free survival		HiC & LMiC
		Normality after discharge		HiC & LMiC
Patient-reported outcome	Quality of life	Quality of life	Overall quality of life of their child was also considered critical for parents in showing if the treatment their baby received had worked or not.	HiC & LMiC
Long-term Disability	Cerebral Palsy	Cerebral Palsy	Both the diagnosis of epilepsy in the child and the need for ongoing occupational therapy were considered important indicators of improvement following treatment. The diagnosis of cerebral palsy was a concern raised by parents in HiCs alone.	HiC
	Epilepsy	Epilepsy		HiC & LMiC
	Need for Occupational Therapy*	Need for Occupational Therapy		HiC & LMiC
Hospitalisation	Duration of neonatal stay	Admission to the Neonatal Intensive Care Unit (NICU)/	The length their baby was in the NICU being treated and the requirement to re-visit	HiC &

		Newborn Unit (NBU)	the hospital later in their child's life gave parents an indication of their child's health following treatment.	LMiC
		Duration of hospitalisation		HiC
		Discharge from hospital		HiC
	Re-admission in childhood	Follow-up care/appointments		HiC & LMiC
		Re-hospitalisation		LMiC
Parent-reported outcomes	Parental Involvement in care*	Ability to hold baby	This domain identified a number of outcomes relating to the parent(s) of the infant receiving treatment and how they should be considered in the overall care of their child.	HiC & LMiC
		Ability to touch baby		HiC & LMiC
		Ability to dress baby		HiC
		Ability to bathe baby		HiC
		Ability for parents to change baby's nappy		HiC
		Ability to provide care for baby		LMiC
		Support from HCPs on how to care for the baby		HiC
	Parental attachment with their baby*	Separation from baby (while in the Neonatal Intensive Care Unit)		HiC & LMiC
	Parental sense of loss of normal*	Sense of loss		HiC

	Uncertainty for future wellbeing*	Uncertainty for future wellbeing		HiC & LMiC
	Parental psychological impact of Neonatal Intensive Care Unit (NICU) experience*	Parental Psychological Impact of Neonatal Intensive Care Unit experience		HiC & LMiC
		Sleep deprivation		HiC
		Parent's feeling of being a burden/ out of place in Neonatal Intensive Care Unit		HiC
	Emotional impact on parents	• Trauma • Depression • Anxiety • Devastation • Worry • Grief • Guilt		HiC & LMiC
	Impact of child's condition on parents' relationship*	Impact on parents' relationship		HiC
	Financial burden of health care costs of care for infant on parents*	Impact on parents' ability to work		LMiC
	Parental ability to work*	Impact on parents' ability to work		LMiC
	Impact of child's condition and Neonatal Intensive Care Unit experience on wider family	Impact on wider family (stress, disappointment, sadness, grief etc.)		LMiC

	(stress, disappointment, sadness, grief etc.)*	Support from family/ friends	Parents described their experience of communicating with healthcare providers when their baby was receiving treatment in the NICU. Some parents had positive experiences and other parents wished their experience had been better. Parents discussed the importance of being told different information and at different times during their child's treatment. Parents also described how communication could have been improved.	HiC & LMiC
		Having visitors in the hospital		HiC
		Having family members (extended) hold the baby		HiC
	Effective communication between parents and HCPs*	Communication regarding diagnosis of infant		HiC & LMiC
		Communication regarding treatment (options)/ explanation of treatment		HiC & LMiC
		Communication regarding need for treatment		HiC
		Communication regarding tests being carried out while the baby was in the Neonatal Intensive Care Unit		HiC & LMiC
		Communication regarding cause of diagnosis		HiC & LMiC
		Communication regarding follow-up care		HiC & LMiC
		Communication regarding progress of the baby		HiC & LMiC
		General communication with		HiC

		parents (overuse of jargon)		
		Communication regarding the prognosis of the baby (expected outcome/ future)		HiC & LMiC
		Communication regarding how to care for the infant (tube feeding, special needs, seizure identification etc.)		HiC & LMiC
		Communication and positive support for parents		LMiC
		Need for counselling and communication		LMiC
Adverse Events	Adverse events	Skin Rashes	Side effects related to treatment were a concern of parents in LMiCs alone.	LMiC
		Fever		LMiC
		Blood in stool		LMiC

*Indicates outcomes that were identified by parents but were not identified in our ongoing systematic review of randomised trials and systematic reviews of randomised trials of interventions for the treatment of neonatal encephalopathy.

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