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A Core Outcome Set for the prevention and treatment of fetal GROwth restriction: deVeloping Endpoints: The COSGROVE study

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Title: A **C**ore **O**utcome **S**et for the prevention and treatment of fetal **GRO**wth restriction: de**V**eloping **E**ndpoints: The COSGROVE study.

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Condensation: COSGROVE has identified which 22 core outcomes should be included in all future trials in fetal growth restriction.

Short Title: COSGROVE- Core Outcome Set for Fetal Growth Restriction

AJOG at a Glance:

A.Why was this study conducted?

Systematic evaluation of the evidence from clinical trials is often difficult because of variation in the outcomes measured and reported. The development and implementation of core outcome sets for use in clinical trials improves the efficiency of trials, minimizes research waste and reporting bias - and ultimately ensures that evidence is readily available for policy and practice.

B. What are the key findings?

The COSGROVE study identified 22 outcomes grouped under four domains: maternal (n=4); fetal (n=1); neonatal (n=12), and childhood (n=5), that should be measured and reported in all future trials of prevention or treatment of fetal growth restriction.

C. What does this study add to what is already known?

This core outcome set for fetal growth restriction will enable future trials to measure similar, meaningful outcomes, and ensure findings from different studies can be compared and combined.

Abstract

Background Fetal growth restriction refers to a fetus that does not reach its genetically predetermined growth potential. It is well recognized that growth restricted fetuses are at increased risk of both short and long-term adverse outcomes. Systematic evaluation of the evidence from clinical trials of fetal growth restriction is often difficult because of variation in the outcomes measured and reported. The development of core outcome sets for fetal growth restriction studies would enable future trials to measure similar, meaningful outcomes

Objective To develop core outcome sets for trials of prevention or treatment of fetal growth restriction.

Study Design Delphi consensus study.

Population An international group of health care providers, researchers, academics and maternity service users with informed opinions or known expertise in fetal growth restriction .

Methods A comprehensive literature review was conducted to identify outcomes reported in studies of prevention or treatment of fetal growth restriction. All outcomes were presented for prioritization to key stakeholders (135 health care providers, 68 researchers/academics and 35 members of the public) in three rounds of online Delphi Surveys. A priori consensus criteria were used to reach agreement on the final outcomes for inclusion in the core outcome set at a face-to-face meeting with five health care providers, five researchers/academics and six maternity service users.

Results In total, 22 outcomes were included in the final core outcome set. These outcomes were grouped under four domains: maternal (n=4); fetal (n=1); neonatal (n=12), and childhood (n=5).

Conclusions The COSGROVE study identified a large number of potentially relevant outcomes and then reached consensus on those factors that – as a minimum – should be measured and reported in all future trials of prevention or treatment of fetal growth restriction. This will enable future trials to measure similar, meaningful outcomes, and ensure findings from different studies can be compared and combined.

Key words Fetal growth restriction, Small for Gestational Age, pregnancy, trials, randomised, newborn, mortality, morbidity, core outcomes.

Introduction

Fetal growth restriction (FGR) is a condition of suboptimal growth of the fetus in utero with heterogeneous causes. It is associated with increased risks of perinatal morbidity and mortality, including fetal hypoxia, birth asphyxia, prematurity, stillbirth and neonatal death (1) (2). Long after birth with FGR, this group of infants is at higher risk of poor growth, metabolic and cardiovascular disorders and neurodevelopmental delay (3) (4). The scientific community has undertaken detailed research into the causes, consequences, prediction and prevention of FGR. However, these efforts have been impeded by a lack of consensus on the diagnosis of FGR; what exposure variables should be measured; and what outcomes collected (5). Thus, although interventions for preventing and treating FGR have been studied, the resulting evidence is often difficult to interpret because of differences in inclusion, case selection, definitions and reporting of outcomes. Such heterogeneity results in difficulties not only of direct comparisons between studies, but also renders aggregating data amongst trials difficult. This means that evidence synthesis and meta-analysis is unsatisfactory. This in turn limits the reliability of evidence to guide health care decisions.

These challenges could be mitigated if it was possible to agree, in advance, what study data should be collected. We have previously reported on a consensus procedure for the antenatal diagnosis of FGR (6), the diagnosis of FGR in the newborn period (7), and a minimum reporting set of study variables for FGR research studies (8). In this study we aim to develop consensus among international stakeholders on a set of core outcomes that should be used in trials that evaluate (a) preventative or (b) therapeutic interventions for FGR. COS represent an agreed standard set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of healthcare; they are also

suitable for use in cohort studies, clinical audit, and other research methods (9). By standardizing a minimum set of outcomes across trials the potential for evidence synthesis is maximized, and this improves the efficiency of trials, minimizes research waste and reporting bias - and ultimately ensures that evidence is readily available for policy and practice.

Methods

The protocol of the COSGROVE study (**C**ore **O**utcome **S**et for **GRO**wth restriction; de**V**eloping **E**ndpoints), is described in detail elsewhere (10). In brief, in order to build consensus from relevant stakeholders, a systematic review of outcomes was first conducted to identify all potential outcomes collected in studies of FGR. Following this, the outcomes identified were presented to stakeholders for prioritization in a modified Delphi study. Finally, the prioritized list of outcomes was discussed in a face-to-face meeting and consensus reached on which outcomes would be included in the final COS. Two separate procedures were initially conducted – one for prevention and another for treatment of FGR; however, the results from these separate consensus procedures were almost identical, and suggested that combining the two was appropriate; therefore a single COS was created.

The design was guided by The Core Outcome Set-STAndards for Development (COS-STAD) (11). We report the findings of the COSGROVE study in accordance with the COS-STAR Statement reporting criteria (12) and guidance from The COMET (Core Outcome Measures in Effectiveness Trials) Initiative (13). The study was registered prospectively with COMET

(registration number 689, available online at http://www.comet-initiative.org/studies/details/689/).

Identification of relevant outcomes

We conducted a comprehensive search of the published literature including previous trials and systematic reviews of trials to identify potential outcomes. We searched the Cochrane Central Register of Controlled Trials, EMBASE, and Medline from inception to June 2017 for randomised controlled trials and systematic reviews evaluating any potential intervention for prevention or treatment of FGR. The review highlighted a significant lack of standardization in what outcomes are measured and reported. The outcomes from this review were grouped into the following domains: maternal; fetal; neonatal; childhood, and patient reported quality of life, with sub-categories as appropriate.

Participants

In order to reflect the perspectives of a variety of international stakeholders with informed opinions or known expertise in FGR, we accessed potential participants through mass invitational emails, electronic discussion lists, professional organizations and social media. Invitees were encouraged to forward the invitation to others who they regarded as having appropriate experience to capture as broad expertise as possible. We used purposeful sampling to approach eight groups of stakeholders: 1) users of maternity services (women and their partners) or their representative advocacy group; 2) midwives; 3) obstetricians; 4) pediatricians/neonatologists; 5) family doctors; 6) ultra-sonographers; 7) policy makers, and 8) individuals with specific expertise/interest in research or perinatal care related to FGR.

These groups were later combined into 3 groups: health care providers; researchers/academics, and maternity service users. This was done to present findings by stakeholder groups in the Delphi Manager platform (http://www.comet-initiative.org/delphimanager/) used for the COS development. We provided potential participants with an explanatory email and a video (https://youtu.be/yqAvHJcs2Rg) outlining the need for the study, the principles of a COS and participant involvement. Individuals who wished to participate were then asked to click on a link to register for the study and indicate their consent to receive the Delphi survey.

Ethical approval for the study was obtained from the Medical Ethics Review Committee of the University of Groningen.

Modified Delphi Study

We conducted a 3-round modified Delphi study using the web based DelphiManager system (http://www.comet-initiative.org/delphimanager/). Each round had a response closing date 21 days after the date of distribution of the survey, with regular email reminders to non-responders. A short questionnaire seeking relevant participant demographic data including stakeholder group and country of residence was presented in the first round.

The round 1 survey presented the outcomes identified in the review. Each outcome was explained in plain English using explanations from patient information leaflets where available. Participants were asked to rate each outcome for FGR prevention and treatment separately on a 9-point Likert-scale, with higher values representing increased importance for inclusion in the COS, or to select an 'unable to score' category. Participants were given

the option to add up to two further 'new' outcomes that they considered important or relevant for inclusion in COS (13). Only participants who had completed the first round were invited to participate in round 2.

The round 2 survey presented all outcomes from round 1 again. In round 2, in addition to presenting each participant's individual round-1 score, results for each separate stakeholder group were also presented numerically as proportions. Using the same 9-point Likert scale, round 2 participants were then asked to re-rate each outcome taking into consideration their own initial response and the responses from the separate stakeholder groups. At this point, participants were also asked if they would be able and willing to attend a subsequent planned face-to-face consensus meeting. Only those participants who had completed rounds 1 and 2 were invited to participate in round 3.

In round 3, survey participants were presented with outcomes from round 2 that were rated as important for inclusion, defined as scoring 7-9 on Likert scale by at least 70% of all respondents and rated as of limited importance (1-3 on Likert scale) by 15% or less of all respondents. These consensus criteria for round 3 were decided a priori based on the total number of outcomes remaining after round 2, and on guidance in The COMET Handbook (13) and COS-STAD (11).

Following round 3 outcomes were then classified as 'consensus in' (≥70% participants scoring as 7–9 and <15% scoring as 1–3), 'consensus out' (≥70% scoring as 1–3 and <15% scoring as 7–9) or 'no consensus' (anything else). We agreed our consensus criteria for inclusion a priori based on guidance in The COMET Handbook (13) and COS-STAD (11).

Consensus meeting

Consensus on the final outcomes to be included in the COS was achieved through a face-to-face full day meeting on April 18th 2018 in Brighton UK. The meeting was moderated by an independent chair (JK) and the consensus panel comprised sixteen participants, from a variety of countries, representing the stakeholder groups who had volunteered in their Delphi survey or who had been purposefully sampled for their expertise by the COSGROVE working group. They were maternity service users (n=6), healthcare providers including midwives, obstetricians, neonatologists and family physicians (n=5) and researchers/academics in FGR (n=5). All participants were asked to vote on each outcome as 'yes' or 'no' for inclusion in the final COS following a period of discussion on each listed outcome. The consensus criterion used at the meeting to determine whether an outcome should be in the final COS was defined as 70% or more of the consensus meeting participants scoring it 'yes'. The participants were also asked to consider whether each outcome was uniquely a prevention outcome, uniquely a treatment outcome or an outcome for both prevention and treatment. Anonymous voting was facilitated by participants using Poll Everywhere (www.polleverywhere.com). Members of the COSGROVE working Group attended as observers only.

Results

The review of the literature identified 238 different outcomes for prevention and treatment of FGR (14). Following the removal of duplicate outcomes, the combination of similar outcomes and the clarification of outcome terminology by the COSGROVE team, 103 outcomes remained. For example: cord pH arterial, cord PO_2 arterial, cord PCO_2 arterial, cord BE arterial, cord pH venous, cord PO_2 venous, cord PCO_2 venous and cord lactate all

became the outcome 'Umbilical cord blood gases'. Grouping different outcome assessments into a single category referring to an outcome in this manner is recommended in the COMET Handbook (13) as is the subsequent classification of those outcomes under overarching domains. We considered using the taxonomy of outcomes discussed by Dodd et al (15) but found that the domains maternal, fetal, neonatal, childhood and patient-reported, with appropriate subdomains, were more appropriate to our needs. As there was significant overlap in the outcomes for prevention and treatment, we decided to present the 103 outcomes twice in the round 1 Delphi survey; participants were asked to rate them from a prevention perspective first and then from a treatment perspective.

Two hundred and thirty eight relevant stakeholders from 36 different countries registered to participate in COSGROVE and received the first survey. The round 1 survey was completed by 180 people (76%), of whom 59% (n=105) were health care providers, 29% (n=53) were researchers/academics and 12% (n=22) were maternity service users.

The round 2 survey again presented the 103 outcomes twice. Some new outcomes had been suggested by participants in round 1. After evaluation these were all judged to be either covered by the outcomes presented already or suggested by one person only; therefore, in keeping with the a priori decisions in the study protocol (10), no new outcomes were added after round 1. Round 2 was completed by 65% (118/180) of those who had completed the first survey: 58% (n=69) health care providers, 36% (n=42) researchers/academics and 6% (n=7) maternity service users. At the end of round 2, the number of outcomes was reduced by applying our pre-specified consensus criteria.

The round 3 survey presented 34 prevention outcomes and 35 treatment outcomes for rating. Round 3 was completed by 91% (107/118) of those who had completed the second survey. The stakeholder groups represented in the 3rd round were 59% (n=63) health care providers, 35% (n=37) researchers/academics and 6% (n=7) maternity service users. At the end of round 3, we again applied a priori consensus criteria to decide which outcomes to bring forward to the consensus meeting. As no outcome met the criteria for "consensus out", 34 prevention outcomes and 35 treatment outcomes were brought forward for discussion at the face-to-face consensus meeting.

Following the consensus meeting 22 outcomes were included in the final COS for the treatment or prevention of FGR, under four domains: maternal (n=4); fetal (n=1); neonatal (n=12), and childhood (n = 5). Given almost complete overlap, the consensus panel participants concluded that all 22 outcomes were suitable for both prevention and treatment; consequently a single COS for the prevention and/or treatment of FGR was arrived at (Table 1). Outcomes that were removed or combined following discussion (e.g. stillbirth and intrapartum death were combined into stillbirth) are listed in Supplementary table 2 (S2).

Table 1: Final COS to be included in all studies of FGR

Discussion

Main Findings

COSGROVE developed a COS for FGR using robust consensus methodology to capture the views and opinions of an international group of multiple stakeholders, including patients.

The final COS includes 22 outcomes grouped under four domains. It is important that a COS represents the *minimum* number of outcomes that should be reported in all trials in a specific area. The list is not exhaustive and additional outcomes can be freely reported if deemed relevant (9). The list is suitable not only for trials but also for cohort studies, studies of diagnostic accuracy or service evaluation.

Our effort is an international collaboration between research groups aiming to standardize research, monitoring and management for FGR. There is a growing recognition of the need for standardizing outcome sets for trials (11) (16) (17). Although there is an extensive list of planned/ongoing and completed COS in the health area 'pregnancy and childbirth' on the COMET website (www.comet-initiative.org/studies/search), there is currently no published COS for FGR. This study fills that deficit. Effective dissemination will now be required to ensure uptake of the COS. Dissemination through the CROWN initiative will enable us to disseminate widely to the relevant community (17). We hope that our COS for FGR will be adopted into future clinical trials with the ultimate goal of informing clinical practice.

The number of survey rounds varies across COS development procedures with most containing 2 or 3 rounds (18). We decided to have 3 rounds due to the number of outcomes presented, and believe that this number of iterations was necessary.

While the modified Delphi process allowed participants to consider the importance of the outcomes independently, the consensus meeting provided an opportunity for collaborative discussion to reach consensus on the outcomes. The equal representation of stakeholder groups across the participants ensured that the meeting was collaborative and inclusive and the voice of the public was not overshadowed by that of research academics and

practitioners, and anonymous electronic voting was used. Participants were measured and reasonable in searching for acceptable compromises to reach consensus.

Strengths and limitations

We used COMET guidance (13) (19) to inform our methodological choices when developing this COS. The process employed (literature review, modified Delphi survey and consensus meeting) is a well-established and widely-used consensus process. However, we do acknowledge that methods to develop COS vary (20) and there are limitations in the evidence underlying the methodology. For example, no validation step is recommended in the process to ask the stakeholders who completed round 3 whether they agree or not with the final COS.

The initial long-list of outcomes presented in the survey was derived from a comprehensive search of the relevant literature. We adhered to standard systematic searching and selection strategies. We limited our search to published clinical trials and systematic reviews of trials as our timelines did not allow review of qualitative research studies. In addition we only included English language papers as we did not have the resources for translating non-English papers. However, we believe that given the large number of papers reviewed, and the large, international panel of participants who were able to add outcomes as part of the open questions of the survey, the likelihood of missing relevant outcomes is very small. The fact that no additional outcomes were added to round 2 strengthened the value of this approach. We acknowledge these pragmatic decisions as potential limitations.

We identified key stakeholders to capture a representative and diverse range of opinions. This is important to ensure that the outcomes included in the resulting COS are relevant,

applicable, important and acceptable to those affected by FGR (21) (22) (23) (24). Including members of the public presents unique challenges (25); so, although an acceptable number of maternity service users initially registered to take part, a relatively small number completed all three rounds of the survey. However, their contribution was rich, generous, insightful and very well informed and they were equally and fairly represented at the consensus meeting. We are convinced, following our engagement with members of the public that their involvement in COSGROVE was meaningful, important and relevant.

Another aspect of diversity is ensuring geographical representation. It is recognized that internationally developed core outcome sets have more validity and are easier to implement into clinical research worldwide (9). Because of this, we were not only mindful of the total number of participants (13) (26), but also ensured a "global" coverage of opinions.

Interpretation

The final COS contains 22 outcomes to be measured in all future trials in FGR. We acknowledge that considering that, this is a minimum amount of outcomes to be reported it may be considered excessive. This is an unavoidable feature of this particular clinical area which represents outcomes for both mother and baby. This is consistent with other core outcome sets in women's and newborn health with outcome numbers varying considerably from 11 to 48 (27). The outcomes are divided into a more manageable number within the maternal, fetal, neonatal and childhood domains. In addition, many of the outcomes are overlapping. For example, gestational age, preterm birth and extremely preterm birth are reported separately. This reflects the independent importance of the distribution of

gestational age in a study population and also the proportion of preterm (or extremely preterm) births. This is an example of an easy win: these proportions can be readily calculated by researchers of primary studies, but are impossible to work out without access to individual data. By reporting them in primary studies, data synthesis is facilitated enormously. There is also overlap between outcomes and baseline characteristics. As an example, pre-eclampsia may be a baseline characteristic in one study and an outcome in the same study or another. This is, indeed, reflected by the fact that hypertensive disorders of pregnancy are also in the previously defined Minimum Reporting Set (8). Obviously, different interventions (e.g. early delivery) may also reduce the co-appearance of pre-eclampsia and its morbidities.

Long-term follow-up outcomes included in this COS may present difficulties for some trials. However, the consensus was that studies must examine not only short-term neonatal outcomes but also long-term development (28). It is notable that most research funding is limited to 2-3 year programs; in perinatal health this is incompatible with best practice: as an example, measuring childhood outcomes following interventions given in early pregnancy means a longer term approach is needed. We hope that the views expressed by our international group of stakeholders will translate into research practice by encouraging funders to look beyond the short-term and allow for the design of trials that ensure long-term follow up, even if these are not reported on in the initial publications. A good example of this is the TRUFFLE trial where initial short-term outcomes were published as a cohort, and the primary outcome of long-term follow when this became available later (29) (30).

COSGROVE has been developed to guide researchers on what to measure; however, it does not tell researchers *how* to measure or when to measure, and further work will be required

to determine the most appropriate approach. We acknowledge that there may be outcomes in our COS that require further research work around broader definitions. Some of the outcomes are well defined in the literature and have a recognised method on 'how' to measure (e.g., HIE staging), while others do not (e.g., need for resuscitation).

Conclusion

International research collaboration is needed to achieve progress in improving outcomes of mothers and their children. Although adverse outcomes in pregnancy are catastrophic, they are fortunately rare. This means that studies need to be large, and data synthesis of individual trials is a key component needed to advance our field. This challenge can only be met if there is agreement and standardization of definitions, exposures and outcomes. We have gathered an international group of stakeholders to agree upon and standardize the core set of outcomes that, as a minimum, should be collected in all future trials in FGR. We call on funders, researchers and the scientific community to adopt COSGROVE into future clinical trials in FGR with the ultimate goal of improving health outcomes.

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The COSGROVE team members acknowledge with gratitude the stakeholders who attended the final consensus meeting and voted on the outcomes.

Disclosure of interests

The authors declare that they have no competing interests.

Contribution to Authorship

All authors (PH, SG, WG, IB, AB, AK, LK, FB, MD, JK, DD & AP) made substantial contributions to conception and design for the Core Outcome Set. PH, SG, DD and AP drafted the manuscript. All authors (PH, SG, WG, IB, AB, AK, LK, FB, MD, JK, DD & AP) commented on revisions to draft versions of the manuscript. All authors (PH, SG, WG, IB, AB, AK, LK, FB, MD, JK, DD & AP) read, commented on and approved the final manuscript. All authors are members of the overall COSGROVE study team.

Details of Ethics Approval and consent to participate

Ethical approval was obtained for the COSGROVE study from the Medical Ethics Review Committee of the University of Groningen (reference number: METc 2016.660). Participation in the Delphi surveys and consensus meeting was optional and each participant gave informed consent.

Availability of data and material

The datasets used and/or analyzed during the COSGROVE study will be held by the COSGROVE team at patricia.healy@nuigalway.ie

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Table 1: Final COS to be included in all studies of FGR

Domain	Outcome Retained by Consensus (22)
Maternal	Preeclampsia
	Eclampsia
	Maternal mortality (death)
	Mode of birth
Fetal	Stillbirth/livebirth
Neonatal	Gestational age at birth
	Preterm birth (delivery before 37 weeks' gestation)
	Extremely preterm birth (delivery before 28 weeks' gestation)
	Birth weight
	Birth weight less than the 10th percentile
	Birth weight less than the 3rd percentile
	Need for mechanical ventilation
	Bronchopulmonary dysplasia/ Chronic lung disease
	Necrotizing enterocolitis
	Neonatal seizures
	Hypoxic Ischemic Encephalopathy
	Neonatal death

Childhood	Cognitive impairment
	Motor impairment
	Cerebral palsy
	Hearing Impairment
	Visual Impairment

Supplementary Table 1(S1): FGR outcomes presented in the Delphi Survey

Domain	Outcome
1: Maternal outcomes	
1.1: Maternal disease pregnancy related	Pregnancy (gestational) hypertension
	Preeclampsia
	HELLP Syndrome
	Eclampsia
	Renal impairment
	Development of thrombotic disease
	Abnormal Uterine Artery Doppler
	Placental abruption
1.2: Maternal care needs	Admission to high dependency unit (HDU) or intensive care unit (ICU)
	Length of hospital stay
	Cost of hospital stay
	Days from diagnosis to delivery
1.3: Maternal delivery outcomes	Induction of Labour
	Mode of birth
	Maternal mortality (death)
1.4: Maternal	Postpartum hemorrhage

postpartum outcomes	
	Postpartum infection
1.5: Maternal biochemical values	Abnormal serum biomarkers (e.g. antigenic factors, placental growth factor, HCG, Pregnancy-associated plasma protein-A)
1.6: Placental findings	Placental weight
	Abnormal placental histology
	Birthweight: placental weight ratio
2: Fetal/neonatal outcomes	
2.1: Fetal ultrasound findings	Abnormal biophysical profile score
	Abnormal fetal Doppler assessment
	Oligohydramnios
2.2: Fetal outcomes	Abnormal fetal scalp pH in Labour
	Abnormal CTG during Labour
	Miscarriage
	Stillbirth
	Intrapartum death
	Meconium stained amniotic fluid
2.3: Neonatal birth outcomes	Livebirth
	Apgar score at 5 min
	Apgar score at 10 min

	Abnormal umbilical cord blood gases
	Gestational age at birth
	Preterm birth (delivery before 37 weeks' gestation)
	Extremely preterm birth (delivery before 28 weeks' gestation)
	Birth weight
	Birth weight less than the 10th percentile
	Birth weight less than the 5th percentile
	Birth weight less than the 3rd percentile
	Low birthweight (LBW)
	Very low birthweight (VLBW)
	Extremely low birth weight (ELBW)
	Birth length
	Head Circumference
	Growth restriction of the newborn
2.4: Neonatal Care Outcomes	Length of hospital stay
	Admission to high dependency (SCBU) or intensive care unit (NICU)
	Length of high dependency (SCBU) or intensive care unit (NICU)stay
	Cost of hospital stay
	Readmission after discharge home
2.5: Neonatal immediate	Need for neonatal resuscitation

and short-term outcomes	
	Need for any non-invasive respiratory support
	Intubation
	Need for mechanical ventilation
	Need for surfactant
	Respiratory Distress Syndrome
	Bronchopulmonary dysplasia/ Chronic lung disease
	Neonatal sepsis
	Necrotizing enterocolitis
	Neonatal seizures
	Abnormal Thompson/Sarnat score
	Hypoxic Ischemic Encephalopathy
	Need for therapeutic hypothermia (cooling)
	Hyperbilirubinaemia requiring intervention
	Hypoglycemia
	Hypothermia
	Thrombocytopenia
	Periventricular leukomalacia
	Intraventricular Hemorrhage
	Patent ductus arteriosus
	Retinopathy of prematurity
	Feeding Difficulties requiring supplemental enteral feeding
	Feeding Difficulties requiring supplemental parenteral feeding

	Circulatory dysfunction requiring pressor support
	Hypothyroidism requiring substitution treatment
	Discharge weight
	Fat mass at discharge
	Congenital anomalies
	Chromosomal malformations
	Neonatal death
	Exclusive breast-feeding
2.6: Neonatal long-term outcomes	Accelerated growth
	Body Mass Index (BMI)
	Waist circumference
	Ponderal index measurements
	Childhood fat mass / body composition
	Bayley Scales of infant development
2.7: Neonatal neurologic developmental outcomes	Cognitive impairment
	Motor impairment (excluding cerebral palsy)
	Cerebral palsy
	Deafness
	Blindness
	Need for special educational support
	Executive function

	Mental illness
	Attention-deficit hyperactivity disorder
3. Patient-reported outcomes	Maternal satisfaction with care
	Difficulties in maternal and child bonding
	Maternal Post-traumatic stress disorder (PTSD)
	Maternal Depression
	Maternal Anxiety

Supplementary Table 2 (S2): Outcomes removed or combined at the consensus meeting

	Outcome Removed by Consensus (14)
Maternal	HELLP Syndrome
Fetal	Abnormal fetal Doppler assessment
	Intrapartum death (Combined with Stillbirth)
Neonatal	Umbilical cord blood gases
	Apgar score at 5 min
	Admission to high dependency (SCBU) or intensive care unit (NICU)
	Birth weight less than the 5th percentile
	Need for neonatal resuscitation
	Respiratory Distress Syndrome
	Neonatal sepsis
	Periventricular leukomalacia
	Intraventricular Hemorrhage
	Congenital anomalies
	Chromosomal malformations