

## OBSTETRICS

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



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**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 that are measured and reported. The development of core outcome sets for fetal growth restriction studies would enable future trials to measure similar meaningful outcomes.

**OBJECTIVE:** The purpose of this study was to develop core outcome sets for trials of prevention or treatment of fetal growth restriction.

**STUDY DESIGN:** This was a Delphi consensus study. A comprehensive literature review was conducted to identify outcomes that were reported in studies of prevention or treatment of fetal growth restriction. All outcomes were presented for prioritization to key stakeholders (135 healthcare providers, 68 researchers/academics, and 35 members of the public) in 3 rounds of online Delphi surveys. A priori consensus criteria were used to reach agreement on the final outcomes for in-

clusion in the core outcome set at a face-to-face meeting with 5 healthcare providers, 5 researchers/academics, and 6 maternity service users.

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

**CONCLUSION:** The Core Outcome Set for the prevention and treatment of fetal GROwth restriction: deVeloping Endpoints 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 to ensure that findings from different studies can be compared and combined.

**Key words:** core outcome, fetal growth restriction, gestational age, pregnancy, trial

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 death and includes fetal hypoxia, birth asphyxia, prematurity, stillbirth, and neonatal death.<sup>1,2</sup> Long after birth with FGR, this group of infants is at higher risk of poor growth, metabolic and cardiovascular disorders, and neurodevelopmental delay.<sup>3,4</sup> 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.<sup>5</sup> Thus, although interventions for the prevention and treatment of 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 the aggregation of data among trials difficult. This means that evidence synthesis and metaanalysis is unsatisfactory, which in turn limits the reliability of evidence to guide healthcare decisions.

These challenges could be mitigated if it were possible to agree, in advance, about which study data should be collected. We previously have reported on a consensus

procedure for the antenatal diagnosis of FGR,<sup>6</sup> the diagnosis of FGR in the newborn period,<sup>7</sup> and a minimum reporting set of study variables for FGR research studies.<sup>8</sup> In this study, we aimed to develop consensus among international stakeholders on a set of core outcomes that should be used in trials that evaluate (1) preventative or (2) therapeutic interventions for FGR. Core outcome sets (COSs) 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 audits, and other research methods.<sup>9</sup> By standardizing a minimum set of outcomes across trials, the potential for evidence synthesis is maximized, which improves the efficiency of trials, minimizes research waste and reporting bias, and ultimately ensures that evidence is readily available for policy and practice.

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## AJOG at a Glance

**Why was this study conducted?**

Systematic evaluation of the evidence from clinical trials is often difficult because of variation in the outcomes that are 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.

**Key findings**

The COSGROVE study identified 22 outcomes that are grouped under 4 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.

**What does this add to what is known?**

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

**Methods**

The protocol of the COSGROVE study (Core Outcome Set for GROWth restriction; deVELOping Endpoints) is described in detail elsewhere.<sup>10</sup> In brief, to build consensus from relevant stakeholders, a systematic review of outcomes was first conducted to identify all potential outcomes that are collected in studies of FGR. After this, the outcomes that were 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 a consensus was reached on which outcomes would be included in the final COS. Two separate procedures were conducted initially (1 for prevention and another for treatment of FGR); however, the results from these separate consensus procedures were almost identical and suggested that combining the 2 was appropriate; therefore, a single COS was created.

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

prospectively with the Core Outcome Measures in Effectiveness Trials initiative (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 that included 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 randomized controlled trials and systematic reviews that evaluated any potential intervention for the 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 subcategories as appropriate.

**Participants**

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. To

capture as broad a field of expertise as possible, invitees were encouraged to forward the invitation to others whom they regarded as having appropriate experience. We used purposeful sampling to approach 8 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) ultrasonographers, (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: healthcare 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/delphi-manager/>), which was used for the COS development. We provided potential participants with an explanatory email and a video (<https://youtu.be/yqAvHJcs2Rg>) that outlined the need for the study, the principles of a COS, and the 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 Delphi-Manager 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 nonresponders. A short questionnaire that sought relevant participant demographic data that included 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 with 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 2 further “new” outcomes that they considered important or relevant for inclusion in COS.<sup>13</sup> 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. 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 rerate each outcome taking into consideration their own initial response and the responses from the separate stakeholder groups. At this point, participants were also asked whether 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  $\leq 15\%$  of all respondents. These consensus criteria for round 3 were decided a priori based on the total number of outcomes that remained after round 2 and on guidance in the COMET Handbook<sup>13</sup> and COS-STAD.<sup>11</sup>

After round 3, outcomes were then classified as “consensus in” ( $\geq 70\%$  participants scoring as 7–9 and  $< 15\%$  scoring as 1–3), “consensus out” ( $\geq 70\%$  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<sup>13</sup> and COS-STAD.<sup>11</sup>

### 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 18, 2018, in Brighton, UK. The meeting was moderated by an independent chair (J.K.), and the consensus panel comprised 16 participants, from a variety of countries, who represented the stakeholder members who had volunteered in their Delphi survey or who had been sampled purposefully for their expertise by the COSGROVE working group. They were maternity service users ( $n=6$ ), healthcare providers (midwives, obstetricians, neonatologists and family physicians;  $n=5$ ), and researchers/academics in FGR ( $n=5$ ). After a period of discussion on each listed outcome, all participants were asked to vote on each outcome as “yes” or “no” for inclusion in the final COS. The consensus criterion that was used at the meeting to determine whether an outcome should be in the final COS was defined as  $\geq 70\%$  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.poll.everywhere.com](http://www.poll.everywhere.com)). Members of the COSGROVE working group attended as observers only.

### Results

The review of the literature identified 238 different outcomes for the prevention and treatment of FGR.<sup>14</sup> After 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<sub>2</sub> arterial, cord PCO<sub>2</sub> arterial, cord BE arterial, cord pH venous, cord PO<sub>2</sub> venous, cord PCO<sub>2</sub> venous, and cord lactate all became the outcome “umbilical cord blood gases.” Grouping different outcome assessments into a single category that refers to an outcome in this manner is recommended in the COMET Handbook,<sup>13</sup> as is the subsequent classification of those outcomes under

overarching domains. We considered using the taxonomy of outcomes discussed by Dodd et al<sup>15</sup> but found that the domains maternal, fetal, neonatal, childhood, and patient-reported, with appropriate subdomains, were more appropriate to our needs. Because there was significant overlap in the outcomes for prevention and treatment, we decided to present the 103 outcomes (Supplementary Table 1) 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 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 healthcare 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 1 person only; therefore, in keeping with the a priori decisions in the study protocol,<sup>10</sup> 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% healthcare providers ( $n=69$ ), 36% researchers/academics ( $n=42$ ), and 6% maternity service users ( $n=7$ ). 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% of those who had completed the second survey (107/118). The stakeholder groups represented in the 3<sup>rd</sup> round were 59% ( $n=63$ ) healthcare 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

TABLE

**Final core outcome set to be included in all studies of fetal growth restriction**

| Domain    | Outcome                                                   |
|-----------|-----------------------------------------------------------|
| Maternal  | Preeclampsia                                              |
|           | Eclampsia                                                 |
|           | Maternal death                                            |
|           | Mode of birth                                             |
| Fetal     | Stillbirth/livebirth                                      |
| Neonatal  | Gestational age at birth                                  |
|           | Preterm birth (delivery at <37 weeks gestation)           |
|           | Extremely preterm birth (delivery at <28 weeks gestation) |
|           | Birthweight                                               |
|           | Birthweight <10th percentile                              |
|           | Birthweight <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                                         |

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consensus meeting. Because 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.

After the consensus meeting, 22 outcomes were included in the final COS for the treatment or prevention of FGR under 4 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 determined (Table). Outcomes that were removed or combined after discussion

(eg, stillbirth and intrapartum death were combined into stillbirth) are listed in [Supplementary Table 2](#).

### Comment

#### Main findings

COSGROVE developed a COS for FGR with robust consensus methods to capture the views and opinions of an international group of multiple stakeholders that included patients. The final COS includes 22 outcomes grouped under 4 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 reported freely if deemed relevant.<sup>9</sup> The list is suitable not only for trials

but also for cohort studies, studies of diagnostic accuracy, or service evaluation.

Our effort was an international collaboration between research groups that aimed to standardize research, monitoring, and management for FGR. There is a growing recognition of the need for standardizing outcome sets for trials.<sup>11,16,17</sup> Although there is an extensive list of planned/ongoing and completed COS in the health area of “pregnancy and childbirth” on the COMET website ([www.comet-initiative.org/studies/search](http://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 the uptake of the COS. Dissemination through the Core Outcomes in Women’s and Newborn Health initiative will enable us to disseminate widely to the relevant community.<sup>17</sup> 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.<sup>18</sup> We decided to have 3 rounds because of the number of outcomes presented and believe that this number of iterations was necessary.

Although 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 that the voice of the public was not overshadowed by that of research academics and practitioners; 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 to inform our methods choices when developing this COS.<sup>13,19</sup> The process that was used

(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<sup>20</sup> and that there are limitations in the evidence underlying the method. 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 because our timelines did not allow review of qualitative research studies. In addition, we included only English language papers because 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 that were included in the resulting COS are relevant, applicable, important, and acceptable to those affected by FGR.<sup>21–24</sup> Inclusion of members of the public presents unique challenges<sup>25</sup>; so, although an acceptable number of maternity service users initially registered to take part, a relatively small number completed all 3 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, after our engagement with members of the public,

that their involvement in COSGROVE was meaningful, important, and relevant.

Another aspect of diversity is ensuring geographic representation. It is recognized that internationally developed core outcome sets have more validity and are easier to implement into clinical research worldwide.<sup>9</sup> Because of this, we were not only mindful of the total number of participants<sup>13,26</sup> but also were ensured of 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 that 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 11–48.<sup>20</sup> 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 not only can be calculated readily by researchers of primary studies but also 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, preeclampsia may be a baseline characteristic in 1 study and an outcome in the same study or another. This is reflected, indeed, by the fact that hypertensive disorders of pregnancy are also in the previously defined Minimum Reporting Set.<sup>8</sup> Obviously, different interventions (eg, early delivery) may also reduce the coappearance of preeclampsia 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.<sup>27</sup> It is notable that most research funding is limited to 2- to 3-year programs; in perinatal health, this is incompatible with best practice (eg, measuring childhood outcomes after 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 (The Trial of Randomized Umbilical and Fetal Flow in Europe) trial in which initial short-term outcomes were published as a cohort and the primary outcome of long-term follow up when this became available later.<sup>28,29</sup>

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 (eg, hypoxic ischemic encephalopathy staging), although others do not (eg, need for resuscitation).

### Conclusion

International research collaboration is needed to achieve progress in the improvement of 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; 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 on 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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SUPPLEMENTARY TABLE 1

## Fetal growth restriction outcomes presented in the Delphi Survey

| Domain                                  | Outcome                                                                                                                                         |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| 1: Maternal                             |                                                                                                                                                 |
| 1.1: Maternal disease pregnancy related | Pregnancy (gestational) hypertension                                                                                                            |
|                                         | Preeclampsia                                                                                                                                    |
|                                         | HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome                                                                      |
|                                         | Eclampsia                                                                                                                                       |
|                                         | Renal impairment                                                                                                                                |
|                                         | Development of thrombotic disease                                                                                                               |
|                                         | Abnormal uterine artery Doppler scan                                                                                                            |
|                                         | Placental abruption                                                                                                                             |
| 1.2: Maternal care needs                | Admission to high dependency unit or intensive care unit                                                                                        |
|                                         | Length of hospital stay                                                                                                                         |
|                                         | Cost of hospital stay                                                                                                                           |
|                                         | Days from diagnosis to delivery                                                                                                                 |
| 1.3: Maternal delivery outcome          | Induction of labor                                                                                                                              |
|                                         | Mode of birth                                                                                                                                   |
|                                         | Maternal death                                                                                                                                  |
| 1.4: Maternal postpartum outcome        | Postpartum hemorrhage                                                                                                                           |
|                                         | Postpartum infection                                                                                                                            |
| 1.5: Maternal biochemical value         | Abnormal serum biomarkers (eg, antigenic factors, placental growth factor, human chorionic gonadotropin, pregnancy-associated plasma protein-A) |
| 1.6: Placental finding                  | Placental weight                                                                                                                                |
|                                         | Abnormal placental histologic condition                                                                                                         |
|                                         | Birthweight: placental weight ratio                                                                                                             |
| 2: Fetal/neonatal                       |                                                                                                                                                 |
| 2.1: Fetal ultrasound finding           | Abnormal biophysical profile score                                                                                                              |
|                                         | Abnormal fetal Doppler assessment                                                                                                               |
|                                         | Oligohydramnios                                                                                                                                 |
| 2.2: Fetal outcome                      | Abnormal fetal scalp pH in labor                                                                                                                |
|                                         | Abnormal CTG (Cardiotocograph) during labor                                                                                                     |
|                                         | Miscarriage                                                                                                                                     |
|                                         | Stillbirth                                                                                                                                      |
|                                         | Intrapartum death                                                                                                                               |
|                                         | Meconium-stained amniotic fluid                                                                                                                 |

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(continued)

SUPPLEMENTARY TABLE 1

## Fetal growth restriction outcomes presented in the Delphi Survey (continued)

| Domain                                         | Outcome                                                   |
|------------------------------------------------|-----------------------------------------------------------|
| 2.3: Neonatal birth outcome                    | Livebirth                                                 |
|                                                | Apgar score at 5 minutes                                  |
|                                                | Apgar score at 10 minutes                                 |
|                                                | Abnormal umbilical cord blood gases                       |
|                                                | Gestational age at birth                                  |
|                                                | Preterm birth (delivery at <37 weeks gestation)           |
|                                                | Extremely preterm birth (delivery at <28 weeks gestation) |
|                                                | Birthweight                                               |
|                                                | Birthweight <10th percentile                              |
|                                                | Birthweight <5th percentile                               |
|                                                | Birthweight <3rd percentile                               |
|                                                | Low birthweight                                           |
|                                                | Very low birthweight                                      |
|                                                | Extremely low birthweight                                 |
|                                                | Birth length                                              |
|                                                | Head circumference                                        |
|                                                | Growth restriction of the newborn infant                  |
| 2.4: Neonatal care outcome                     | Length of hospital stay                                   |
|                                                | Admission to high dependency or intensive care unit       |
|                                                | Length of high dependency or intensive care unit stay     |
|                                                | Cost of hospital stay                                     |
|                                                | Readmission after discharge home                          |
| 2.5: Neonatal immediate and short-term outcome | Need for neonatal resuscitation                           |
|                                                | Need for any noninvasive 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)                |
|                                                | Hyperbilirubinemia that requires intervention             |
|                                                | Hypoglycemia                                              |
|                                                | Hypothermia                                               |
|                                                | Thrombocytopenia                                          |

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(continued)

SUPPLEMENTARY TABLE 1

## Fetal growth restriction outcomes presented in the Delphi Survey (continued)

| Domain                                         | Outcome                                                           |
|------------------------------------------------|-------------------------------------------------------------------|
|                                                | Periventricular leukomalacia                                      |
|                                                | Intraventricular hemorrhage                                       |
|                                                | Patent ductus arteriosus                                          |
|                                                | Retinopathy of prematurity                                        |
|                                                | Feeding difficulties that require supplemental enteral feeding    |
|                                                | Feeding difficulties that require supplemental parenteral feeding |
|                                                | Circulatory dysfunction that requires pressor support             |
|                                                | Hypothyroidism that requires substitution treatment               |
|                                                | Discharge weight                                                  |
|                                                | Fat mass at discharge                                             |
|                                                | Congenital anomalies                                              |
|                                                | Chromosomal malformations                                         |
|                                                | Neonatal death                                                    |
|                                                | Exclusive breastfeeding                                           |
| 2.6: Neonatal long-term outcome                | Accelerated growth                                                |
|                                                | Body mass index                                                   |
|                                                | Waist circumference                                               |
|                                                | Ponderal index measurements                                       |
|                                                | Childhood fat mass/body composition                               |
|                                                | Bayley Scales of infant development                               |
| 2.7: Neonatal neurologic developmental outcome | 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 outcome                    | Maternal satisfaction with care                                   |
|                                                | Difficulties in maternal and child bonding                        |
|                                                | Maternal posttraumatic stress disorder                            |
|                                                | Maternal depression                                               |
|                                                | Maternal anxiety                                                  |

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| SUPPLEMENTARY TABLE 2                                                                           |                                                                            |
|-------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Outcomes removed or combined at the consensus meeting                                           |                                                                            |
| Domain                                                                                          | Outcome                                                                    |
| Maternal                                                                                        | HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome |
|                                                                                                 |                                                                            |
| Fetal                                                                                           | Abnormal fetal Doppler assessment                                          |
|                                                                                                 | Intrapartum death (combined with stillbirth)                               |
| Neonatal                                                                                        | Umbilical cord blood gases                                                 |
|                                                                                                 | Apgar score at 5 minutes                                                   |
|                                                                                                 | Admission to high dependency or intensive care unit                        |
|                                                                                                 | Birthweight <5th percentile                                                |
|                                                                                                 | Need for neonatal resuscitation                                            |
|                                                                                                 | Respiratory distress syndrome                                              |
|                                                                                                 | Neonatal sepsis                                                            |
|                                                                                                 | Periventricular leukomalacia                                               |
|                                                                                                 | Intraventricular hemorrhage                                                |
|                                                                                                 | Congenital anomalies                                                       |
|                                                                                                 | Chromosomal malformations                                                  |
| Healy et al. COSGROVE: Core Outcome Set for Fetal Growth Restriction. Am J Obstet Gynecol 2019. |                                                                            |