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KEYWORDS: consensus; core outcome set; Delphi consensus; fetal growth restriction; multiple pregnancy

CONTRIBUTION

What are the novel findings of this work?
This work brought together all relevant stakeholders to assess the outcomes reported in the existing literature on selective fetal growth restriction. Stakeholder consensus was achieved on 11 core outcomes that are of key importance for reporting in studies evaluating treatments for selective fetal growth restriction.

What are the clinical implications of this work?
The core outcome set developed through this process should be used by researchers evaluating interventions for selective fetal growth restriction. To maximize the utility of this set, a further consensus approach to defining the outcomes and outcome measures will be undertaken.

ABSTRACT

Objective *Selective fetal growth restriction (sFGR) occurs in monochorionic twin pregnancies when unequal placental sharing leads to restriction in the growth of just one twin. Management options include laser separation of the fetal circulations, selective reduction or expectant management, but what constitutes the best treatment is not yet known. New trials in this area are urgently needed but, in this rare and complex group, maximizing the relevance and utility of clinical research design and outputs is paramount. A core outcome set ensures standardized outcome collection and reporting in future research. The objective of this study was to develop a core outcome set for studies evaluating treatments for sFGR in monochorionic twins.*

Methods *An international steering group of clinicians, researchers and patients with experience of sFGR was established to oversee the process of development of a core outcome set for studies investigating the management of sFGR. Outcomes reported in the literature were identified through a systematic review and informed the design of a three-round Delphi survey. Clinicians, researchers, and patients and family representatives participated in the survey. Outcomes were scored on a Likert scale from 1 (limited importance for making a decision) to 9 (critical for making a decision). Consensus was defined* a priori *as a Likert score of* ≥ 8 *in the third round of the Delphi survey. Participants were then invited to take part in an international meeting of stakeholders in*

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which the modified nominal group technique was used to consider the consensus outcomes and agree on a final core outcome set.

Results *Ninety-six outcomes were identified from 39 studies in the systematic review. One hundred and three participants from 23 countries completed the first round of the Delphi survey, of whom 88 completed all three rounds. Twenty-nine outcomes met the* a priori *criteria for consensus and, along with six additional outcomes, were prioritized in a consensus development meeting, using the modified nominal group technique. Twenty-five stakeholders participated in this meeting, including researchers (*n = *3), fetal medicine specialists (*n = *3), obstetricians (*n = *2), neonatologists (*n = *3), midwives (*n = *4), parents and family members (*n = *6), patient group representatives (*n = *3), and a sonographer. Eleven core outcomes were agreed upon. These were live birth, gestational age at birth, birth weight, intertwin birth-weight discordance, death of surviving twin after death of cotwin, loss during pregnancy or before final hospital discharge, parental stress, procedure-related adverse maternal outcome, length of neonatal stay in hospital, neurological abnormality on postnatal imaging and childhood disability.*

Conclusions *This core outcome set for studies investigating the management of sFGR represents the consensus of a large and diverse group of international collaborators. Use of these outcomes in future trials should help to increase the clinical relevance of research on this condition. Consensus agreement on core outcome definitions and measures is now required. Copyright © 2019 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Clinical uncertainty regarding the optimal management strategy of selective fetal growth restriction (sFGR) in monochorionic twin pregnancies persists, particularly for cases presenting at very early gestational ages. Intrauterine demise in sFGR (with a shared placenta) seems less predictable than in fetal growth restriction associated with placental insufficiency of an individual placenta in dichorionic twins or singletons, and additionally carries the unique additional risk of acute fetofetal transfusion after the death of one twin, which may cause death or neurological injury in the cotwin[1]. Available options include expectant monitoring or active fetal intervention including selective termination using a variety of techniques, fetoscopic laser treatment or termination of the whole pregnancy[2]. A recent systematic review and meta-analysis comparing these management options reported data from over 700 pregnancies affected by sFGR[3]. Many studies were excluded because of classification, and meta-analysis of several key outcomes, for example neurological morbidity, intrauterine death and preterm birth, was limited by variation in outcome reporting and measurement in the included studies[3,4]. Such variation in outcome selection, collection and reporting has been observed across women's health[5,6].

Given the high potential for morbidity and mortality in sFGR, there is a need for robust guidance and, given the rarity of this condition, it is critical that diagnostic criteria and reported outcomes are consistent across trials. Consensus on diagnosis, classification and outcomes is key to the generation of high-quality studies amenable to comparison and meta-analysis[4,7]. Incorporating agreed variables helps to avoid wasted effort and, equally importantly, needless exposure to trial participation for women and babies affected by sFGR.

Core outcome sets are groups of outcomes that can be collected and reported consistently and are selected by consensus[6]. The development of a core outcome set requires taking into account the perspective of all relevant stakeholders[8,9]. Core outcome sets should include outcomes relevant to clinical practice and the outcomes in the set should also reflect both harmful and beneficial aspects of a treatment, especially in the case of twins, in which benefit to one twin may often be associated with harm to the other. Additionally, components of a core outcome set should be defined clearly and be amenable to standardized measurement. The aim of this study was to develop a core outcome set for studies investigating the management of sFGR.

METHODS

The development of this core outcome set for sFGR was planned in accordance with the methodology recommended in the Core Outcomes Measures in Effectiveness Trials (COMET) handbook 1.0[8] and the methods of the International Consortium for Health Outcomes Measurement[10], and drew upon the experience of the steering group in developing other core outcome sets in women's health[11–14]. The detailed protocol has been published previously[15]. Details of this core outcome set are included in the COMET database (registration number 998) and further details are available at www.comet-initiative.org. From the guidelines of the National Research Ethics Service, it was established that ethical approval is not required for this project.

Steering group

An international steering group of key experts in the fields of fetal medicine, management of multiple pregnancies and fetal growth restriction, pediatricians, neonatologists, and midwives was established to guide the development of the core outcome set. Parents and non-clinical stakeholders were identified through the Twin and Multiple Birth Association (TAMBA). The steering group determined the scope of the core outcome set and defined the methodology and recruitment strategies.

Definition of terms

In the development of this core outcome set, the steering group agreed to use the recently published consensus diagnostic criteria for sFGR[2]. This requires either the solitary finding of estimated fetal weight (EFW) $< 3^{rd}$ centile in one twin or at least two out of four of the following: (1) EFW $< 10^{th}$ centile in one twin, (2) abdominal circumference $< 10^{th}$ centile in one twin, (3) EFW discordance $\geq 25\%$, and (4) umbilical artery Doppler pulsatility index $> 95^{th}$ centile in the smaller twin.

Systematic review of variation in outcome reporting in selective fetal growth restriction

In order to establish outcomes reported in the existing literature and investigate the degree of variation in outcome reporting, a systematic review of published trials of interventions for sFGR was performed. The protocol for the systematic review was registered prospectively on PROSPERO (international prospective register of systematic reviews; registration number: CRD42018092697). The methodology followed the reporting guidelines for meta-analyses and systematic reviews of randomized controlled trials, as outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[16].

Details of the search methods have been reported previously[4]. Briefly, the Cochrane Central Register of Controlled Trials, EMBASE and MEDLINE were searched from inception to February 2018 for randomized controlled trials, non-randomized studies and observational studies evaluating any potential intervention for monochorionic twin pregnancies affected by sFGR. Abstracts and full texts were screened by two reviewers (R.T. and F.S.) and studies meeting the inclusion criteria were assessed using a purposively constructed data extraction form.

The population was all monochorionic twin pregnancies complicated by sFGR. For this initial review, we accepted the authors' definition of sFGR given that the consensus diagnostic criteria had been published only recently. Interventions included any intervention used for the treatment of sFGR. Comparators included any comparator treatment used for sFGR interventions. Outcomes were all outcomes reported in the included studies investigating sFGR. A comprehensive inventory of these outcomes was developed, with outcomes organized initially into six broad categories: offspring mortality, pregnancy outcomes, procedure-related outcomes, fetal outcomes, neonatal outcomes and childhood outcomes. We used descriptive statistics to characterize the included studies, mapping the reporting of maternal, fetal, neonatal and childhood outcomes across the included studies.

Consensus development using Delphi technique

The outcomes identified in the systematic review were taken into consideration by the steering group in designing a Delphi survey in order to achieve convergence of opinion on the key outcomes to be included in the core outcome set. After reviewing these outcomes, the steering group were invited to add any outcomes that they felt were potentially relevant but had not been reported in previously published studies. Outcomes were defined in lay terms for the Delphi questionnaire, in keeping with prior core outcome set development or existing published patient information. The survey was developed using established online software (DelphiManager, University of Liverpool, UK) appropriate for the delivery of online Delphi surveys relating to core outcome set development[17,18]. The survey invited participants to score each outcome using a nine-point Likert scale from 1 (limited importance for making a decision) to 9 (critical for making a decision), developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group and commonly used in core outcome set development.

Key stakeholder groups identified by the steering committee included clinicians (obstetricians, fetal medicine specialists, neonatologists and midwives), researchers, and patients or parents of patients who had been affected by sFGR. Potential participants from these stakeholder groups were identified from the researchers and clinicians whose studies were identified during the systematic review, professional networks such as the Royal College of Obstetricians and Gynaecologists and the International Society for Twin Studies, personal contacts of the steering group and through TAMBA. Participants were invited by email to respond to the web-based Delphi survey. Each participant was allocated a unique identifier in order to anonymize their responses.

The survey was first piloted with representatives of the key stakeholder groups and then disseminated to all invited participants. Before commencing the survey, participants were asked to provide demographic data and state whether they self-identified as either a healthcare professional, researcher, or parents and family of patients. The first and second rounds were open for responses for 2 weeks and the third and final round was open for 3 weeks. Personalized reminders were sent to participants to prompt completion of data entry during each round. During the first round, participants were invited to suggest additional outcomes to be considered for inclusion in the subsequent round of the survey. Participants received feedback on their own responses and the overall responses of the group in the previous round (Figure 1).

Analysis of Delphi survey results

The Delphi survey response results and demographic details were analyzed using spreadsheet software (Microsoft Excel 16.13.1, Microsoft Corp., Redmond, WA, USA). Consensus was defined according to pragmatic criteria by the steering group, as described in the study protocol, as any outcome achieving a median score of ≥ 8 in the third round. After the third round, results were reported as the number of outcomes meeting the

Outcome 52. Preterm birth
Baby born before 37 weeks of pregnancy.

		Not important (%)			Important but not critical (%)			Critical (%)	
Stakeholder	**Number**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Healthcare professional	57	0	0	4	13	0	56	21	3	3
Researcher	18	0	0	0	0	8	67	18	2	5
Parent or carer	28	0	0	0	4	14	48	30	4	0
→ Please rescore		□	□	□	□	□	□	□	□	□

Figure 1 Example of outcome presented in round two of Delphi survey for consideration for inclusion in core outcome set for studies evaluating management of selective fetal growth restriction. Percentage of participants scoring outcome from 1 to 9 on Likert scale is presented. Shaded column highlights participant's score from Round 1 of survey.

a priori definition for consensus. All outcomes meeting this criterion were taken forward as potential core outcomes for discussion.

Face-to-face stakeholder consensus development meeting

A modified nominal group technique was used in the final stage of achieving consensus on core outcomes for use in studies of interventions in sFGR[19]. This structured discussion technique allows all opinions to be considered from the start, encourages equal participation and allows the identification of divergence in opinion between different groups in a safe way[20]. This technique has been used successfully in the development of a number of core outcome sets[11,21]. Those who participated in the initial Delphi survey were invited to attend a half-day face-to-face consensus development meeting, held in London, UK. Participants unable to attend in person or via teleconference were invited to contribute their views through structured interviews prior to the consensus meeting. Parents and non-clinical participants were offered the opportunity to clarify the study background and purpose, the Delphi results and the outcome terms used.

The meeting was chaired by an experienced facilitator. The meeting opened with an initial briefing on the purpose and scope of the meeting, and the results of the systematic review and Delphi survey were presented. Participants were asked to engage in an initial period of idea generation in small groups or pairs before moving on to a 'round robin', sharing their priority outcomes[22]. Participants were able to suggest additional potential core outcomes. They were asked to identify both the most and least important outcomes for inclusion in the final core outcome set. During this discussion, outcomes were separated into three categories: (1) those that should be included in the final core outcome set; (2) those for which opinion was divided; and (3) those that should not be included in the final core outcome set. Participants were asked to discuss outcome terminology, simplify the similar or poorly worded outcomes and remove duplicates.

On considering the outcomes for which opinion was divided, participants were asked to consider the relative importance of different outcomes in relation to each other, the overall balance between common and rare outcomes, the breadth of the outcome set and the feasibility of measurement and reporting of the outcomes. Specifying measurement and reporting tools for the included outcomes was beyond the scope of this meeting. After discussion, consensus was ultimately reached on a group of core outcomes.

RESULTS

Systematic review of variation in outcome reporting

The literature search yielded 1859 records. Two independent reviewers (F.S., R.T.) evaluated 61 potentially relevant studies and identified 39 studies that met the inclusion criteria. Details of the included studies have been reported previously[4]. Thirty (77%) studies evaluated a single intervention: expectant management ($n = 20$; 51%), selective reduction ($n = 8$; 21%), and fetoscopic laser surgery ($n = 2$; 5%). Eight (20%) studies evaluated two different interventions in the same study. One study (3%) evaluated all three interventions.

Included studies reported 96 different outcomes that were organized into six domains: fetal, neonatal and perinatal mortality (12 outcomes), pregnancy and childbirth (15 outcomes), procedure-related (seven outcomes), fetal (13 outcomes), neonatal (36 outcomes), and childhood (13 outcomes) (Table 1).

Delphi survey results

One hundred and three participants from 23 countries completed the first round of the Delphi survey, 92 completed the second round and 88 completed the final round (Table 2). The demographics of the participants are shown in Table S1. There were seven women who had experienced sFGR in pregnancy, seven relatives of people affected by sFGR, 52 fetal medicine specialists,

Table 1 Variation in outcomes reported across 39 studies evaluating interventions for selective fetal growth restriction

Outcome	*Studies (*n*)*
Fetal, neonatal and perinatal mortality	
Miscarriage	6
Termination of pregnancy	10
Intrauterine fetal death overall	27
Intrauterine fetal death per twin	21
Double intrauterine fetal death	13
Live birth overall	22
Live birth per twin	10
Neonatal mortality overall	26
Neonatal mortality per twin	9
Perinatal mortality	8
Perinatal mortality per twin	8
Perinatal survival	19
Fetal outcome	
Middle cerebral artery Doppler	4
Ductus venosus Doppler	5
Umbilical artery Doppler	8
Neurological morbidity in surviving twin following cord occlusion	4
Other	7
Pregnancy and birth outcome	
Preterm prelabor rupture of membranes	11
Mode of delivery	12
Gestational age at delivery	39
Preterm delivery	14
Other	8
Procedure-related outcome	
Membrane septostomy	3
Intrauterine infection	5
Procedure-to-delivery time interval	3
Other	7
Neonatal outcome	
Birth weight	35
Apgar score	7
Intertwin birth-weight discordance	14
Intraventricular hemorrhage	20
Periventricular leukomalacia	18
Retinopathy of prematurity	2
Hypertrophic cardiomyopathy	2
Respiratory distress syndrome	8
Intubation and mechanical ventilation	3
Necrotizing enterocolitis	8
Sepsis	6
Neonatal intensive care unit admission	6
Other	12
Childhood outcome	
Cognitive impairment	6
Motor impairment	6
Visual impairment	3
Hearing impairment	3
Behavioral disorder	4
Blood pressure	1
Other	1

19 obstetricians, eight midwives, four neonatologists or pediatricians, and five researchers, while one participant chose not to disclose their stakeholder group. Fifty-six discrete outcomes identified in the systematic review and by the steering committee were included in the first round and a further seven outcomes were suggested by participants and added to the second and third rounds. After the third round, 29 outcomes met the *a priori* definition for consensus (Table 2). The results of the Delphi survey according to stakeholder group are shown in Table S2.

Face-to-face consensus development meeting

All participants in the Delphi survey were invited to attend a face-to-face consensus meeting in London, either in person or via teleconference. Nineteen people participated directly in the consensus development meeting, with another four participants contributing via teleconference. Two people with experience of sFGR took part in structured interviews prior to the meeting and their input was presented to the meeting by the researcher who interviewed them. Participants included three researchers, three fetal medicine specialists, two obstetricians, three neonatologists, four midwives, six parents and twins, three patient group representatives, and a sonographer. The 29 consensus and six additional outcomes were discussed in the meeting. These six additional outcomes included four that were entirely new (parental stress; disability; separation of twins; death of surviving twin after loss of cotwin) and two that grouped together multiple smaller outcomes already included in the Delphi survey (loss during pregnancy or prior to hospital discharge; procedure-related adverse outcomes (failure of procedure, procedure-to-delivery interval, placental abruption, life-threatening hemorrhage, sepsis, maternal death)). Three outcomes were reformulated or condensed from other outcomes. The group agreed on 11 core outcomes (Table 3). The meeting agreed additionally that, when relevant, each outcome should be reported for each baby (both the smaller and the larger twin).

DISCUSSION

Summary of study findings

A group of 103 multi-disciplinary stakeholders from 23 countries developed a core outcome set for sFGR in monochorionic twin pregnancy. Ninety-six outcomes identified from a systematic review of the existing literature were reduced to 29 consensus outcomes using a modified Delphi method. Using the modified nominal group technique, a consensus development meeting prioritized 11 core outcomes across five domains (mortality, pregnancy, procedure, and neonatal and childhood outcomes) (Table 3).

There is significant variation in outcome reporting in the published literature relating to sFGR. Although most studies reported gestational age at delivery and birth weight, only 22/39 (56%) studies reported live birth. Few studies reported neonatal and childhood morbidity. During core outcome set development, parents highlighted the importance of these outcomes. No study reported on measures of parental stress or childhood disability as defined by the World Health Organization, which are new outcomes included in this core outcome set.

Strengths and limitations

The strengths of this study include the use of validated consensus-building methodology, incorporating Delphi

Table 2 Results of Delphi survey aimed at developing core outcome set for studies evaluating interventions for selective fetal growth restriction (sFGR)

	Round 1		*Round 2*		*Round 3*	
Outcome	*Responses* (n)	*Median score*	*Responses* (n)	*Median score*	*Responses* (n)	*Median score*
Fetal, neonatal and perinatal mortality						
Miscarriage	103	8	92	8	88	9
Termination of pregnancy	103	7	92	7	88	7.5
Intrauterine death/stillbirth	103	9	92	9	88	9
Live birth	103	9	92	9	88	9
Neonatal death (death ≤ 28 days postpartum)	103	9	92	9	88	9
Perinatal death (death in pregnancy or ≤ 7 days postpartum)	103	9	92	9	88	9
Infant death	103	9	92	9	88	9
Fetal outcome						
Fetal neurological morbidity	103	9	92	9	88	9
Fetal heart abnormality	103	7	92	7	88	7
Disease progression	103	8	92	9	88	9
Pregnancy and birth outcome						
Delivery of growth-restricted twin indicated when there is no indication for delivery of cotwin	—	—	92	8	88	7
Prelabor rupture of membranes	101	7	91	6	88	6
Mode of delivery	102	6	91	6	88	6
Gestational age at delivery	102	9	91	9	88	9
Preterm delivery	101	8	91	9	88	9
Postpartum depression	101	6	91	6	88	6
Gestational diabetes or pre-eclampsia complications	101	6	91	6	88	6
Chorioamnionitis	101	7	91	7	88	6
Procedure-related outcome						
Unintentional membrane separation	101	7	91	6	88	6
Unintentional septostomy	101	7	91	6	88	6
Maternal length of stay in hospital	101	6	91	6	88	6
Failure of procedure/treatment	101	8	91	8	88	8
Procedure-to-delivery interval	101	7	91	8	88	8
Intensive care unit admission	—	—	91	8	88	8
Maternal death	101	9	91	9	88	9
Placental abruption	101	8	91	8	88	8
Life-threatening bleeding (hemorrhage)	101	9	91	9	88	9
Neonatal outcome						
Birth weight	102	7	91	8	88	9
Apgar scores	102	6	91	6	88	6
Intertwin birth-weight discordance	102	7	91	8	88	8
Intraventricular hemorrhage	102	8	91	9	88	9
Periventricular leukomalacia	102	8	91	9	88	9
Retinopathy of prematurity	102	7	91	7	88	6
Hypertrophic cardiomyopathy	102	7	91	6	88	6
Respiratory distress syndrome	102	7	91	7	88	7
Intubation and mechanical ventilation	102	7	91	7	88	6
Necrotizing enterocolitis	102	8	91	8	88	7
Sepsis (severe infection)	102	7	91	8	88	7
Admission to neonatal unit	102	7	91	7	88	7
Length of stay in neonatal unit	102	7	91	7	88	7
Ventriculomegaly	102	7	91	7	88	7
Cystic lesion	102	8	91	9	88	8
Other neurological imaging abnormality	102	7.5	91	8	88	8
Persistent pulmonary hypertension	102	7	91	7	88	7
Congenital heart disease	102	7	91	7	88	6
Anemia at birth	102	6	91	6	88	6
TAPS at birth	102	7	91	7	88	7
Chronic lung disease/bronchopulmonary dysplasia	102	8	91	8	88	7
Pneumonia	102	6	91	6	88	6
Pulmonary hypoplasia	102	7	91	7	88	7
Feeding difficulty	—	—	91	6	88	6
Histopathological evidence of sFGR	—	—	91	5	88	6
Neonatal renal failure	—	—	91	7	88	7

Continued over.

Table 2 *Continued*

Outcome	Round 1		Round 2		Round 3	
	Responses (n)	*Median score*	*Responses* (n)	*Median score*	*Responses* (n)	*Median score*
Childhood outcome						
Neurocognitive developmental impairment	101	8	91	9	88	9
Motor impairment	101	8	91	9	88	9
Visual impairment	101	7	91	8	88	8
Hearing impairment	101	7	91	7	88	8
Behavioral disorder	101	7	91	7	88	8
Hypertension	101	6	91	6	88	6
Cerebral palsy	101	9	91	9	88	9
Cardiovascular disorder	101	7	91	7	88	7
Autism spectrum disease	0	—	91	6	88	6
Receptive and expressive language disorder	0	—	91	7	88	6

Outcomes were scored on nine-point Likert scale, from 1 (limited importance for making decision) to 9 (critical for making decision). TAPS, twin anemia–polycythemia sequence.

Table 3 Agreed core outcome set for studies reporting management of selective fetal growth restriction (sFGR) in monochorionic twin pregnancy

Core outcomes for sFGR
1. Live birth
2. Gestational age at birth
3. Birth weight
4. Intertwin birth-weight discordance
5. Death of surviving twin after death of cotwin
6. Loss during pregnancy or before final hospital discharge (miscarriage, stillbirth, termination of pregnancy, neonatal death, perinatal death)
7. Parental stress
8. Procedure-related adverse outcome (failure of procedure, procedure-to-delivery interval, placental abruption, life-threatening hemorrhage, sepsis, maternal death)
9. Length of stay in hospital (neonatal)
10. Neurological abnormalities on postnatal imaging
11. Childhood disability (as described in WHO ICF[30]: disabilities is umbrella term, covering impairments, activity limitations and participation restrictions; impairment is problem in body function or structure; activity limitation is difficulty encountered by individual in executing task or action; participation restriction is problem experienced by individual in involvement in life situations)

ICF, International Classification of Functioning, Disability and Health; WHO, World Health Organization.

and nominal group techniques to converge many potential outcomes into a focused, clinically important set of core outcomes. The participants in this study were international, from 23 countries. Although participants were classified according to their self-reported identities, many participants had multiple perspectives that informed the discussion, with several clinicians having an interest in research, many participants having experience of pregnancy and parenting beyond their professional roles, several parents having engaged previously with research, and one of the clinicians being a twin. The key to reducing research waste and answering the most important clinical questions is to center the end users of research, i.e. families needing care in complicated pregnancies, in the design and development of new research[23]. We have adhered to this principle in the development of this core outcome set; patients and patient representative groups, notably TAMBA and the Multiple Births Foundation, were involved throughout the design, conduct and dissemination of this study.

Although the collaborating group was international and multidisciplinary, it was limited by being dominated by professionals from Europe and North America. The survey was not available in other languages or in an offline format, and some potential participants may have been unable to take part. Balancing the widest possible participation against what is feasible with available resources, we feel that the collaborator group included a broad range of perspectives. The bias relating to the large number of healthcare professionals applies primarily to the Delphi rounds, since the participants in the final meeting were proportionately more balanced between professionals, researchers, and parent and family representatives, reducing possible bias in the final core outcome set.

In developing this core outcome set, we adopted a simple and pragmatic definition of consensus *a priori*. There are no accepted optimal criteria for consensus in Delphi surveys, so we have reported our results according to this definition.

Clinical and research implications

Although this core outcome set will form the basis of future research in sFGR, clear definitions and measurement instruments need to be provided for each outcome. For example, the outcome 'neurological abnormalities on postnatal imaging' should be specified clearly. The

measurement instrument (ultrasound and/or MRI) is understood, but the outcome definition must specify the timing of imaging and the findings of significance. The intention was to include all findings associated with an increased risk of long-term sequelae, but it was beyond the scope of this meeting to define precisely this outcome. Equally, the outcome of parental stress was considered by both clinicians and families to be relevant particularly in pregnancies affected by sFGR in which management options involve difficult choices that can prioritize one twin over the other. Assessment of parental stress should be considered by researchers, but the choice of measurement instrument must maximize the utility of this outcome within the research setting. There are established tools that have been used to investigate parental psychological effects in similar situations, e.g. a survey administered to parents after fetoscopic surgery for congenital diaphragmatic hernia[24] or after laser for twin-to-twin transfusion syndrome[25,26].

Agreeing the measurement instruments for use with this core outcome set will follow the recommendations of the Consensus-based standards for the selection of health measurement instruments (COSMIN) initiative[27]. A literature search will examine formal definition development studies, guidelines, systematic reviews and trials for existing definitions and measurement instruments. These will then be quality assessed using the COSMIN criteria. A panel of healthcare professionals, researchers, and parents and families with experience of sFGR will review existing definitions and measures identified and agree on those that should be used in the reporting of these core outcomes in future research.

Use of this core outcome set in the future will help focus sFGR research on the outcomes of importance to all stakeholders, prevent selective outcome reporting and facilitate high-quality evidence synthesis[28]. Over 80 journals in the field of women's health have joined the Core Outcomes in Women's and Newborn's Health (CROWN) initiative to promote the implementation of core outcome sets. Researchers will need to meet core outcome reporting requirements in order to publish their work in these key journals, which will motivate the rapid adoption of core outcome sets across the field of women's health[29].

The existence of a core outcome set does not limit researchers to reporting only these outcomes. It may be appropriate to collect and report other outcomes related to the specific scope of a study. We have included neonatal and childhood outcomes in the set because of the strong interest from many relevant stakeholders and a clear deficiency in this area in published literature, but it might be necessary for a study to initially report short-term outcomes while awaiting longer-term data.

Conclusion

This core outcome set for studies reporting the management of sFGR in monochorionic pregnancies has been developed using a rigorous systematic review of the existing literature and a robust consensus development study. This core outcome set should inform the design and reporting of future studies on sFGR and promote high-quality evidence synthesis.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Demographics of participants in Delphi survey

Table S2 Results of Delphi survey aimed at developing core outcome set for studies evaluating interventions for selective fetal growth restriction, according to stakeholder group

Appendix S1 Members of the International Collaboration to Harmonise Outcomes for Selective Fetal Growth Restriction (CHOOSE-FGR).