BMJ Open

Balancing key stakeholder priorities and ethical principles to design a trial comparing intervention or expectant management for early-onset selective fetal growth restriction in monochorionic twin pregnancy: FERN qualitative study

Tracy Karen Mitchell ,[1] Mariana Popa ,[1] Richard Edmund Ashcroft ,[2] Smriti Prasad ,[3,4] Andrew Sharp ,[5] Christine Carnforth,[6] Mark Turner ,[5] Asma Khalil ,[3,7] Natasha Fenwick ,[8] Shauna Leven,[9] The FERN study team, Kerry Woolfall [1]

To cite: Mitchell TK, Popa M, Ashcroft RE, *et al*. Balancing key stakeholder priorities and ethical principles to design a trial comparing intervention or expectant management for early-onset selective fetal growth restriction in monochorionic twin pregnancy: FERN qualitative study. *BMJ Open* 2024;**14**:e080488. doi:10.1136/bmjopen-2023-080488

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2023-080488).

Received 02 October 2023
Accepted 16 July 2024

For numbered affiliations see end of article.

Correspondence to
Doctor Tracy Karen Mitchell; Tracy.Mitchell@Liverpool.ac.uk

ABSTRACT

Objectives As part of the FERN feasibility study, this qualitative research aimed to explore parents' and clinicians' views on the acceptability, feasibility and design of a randomised controlled trial (RCT) of active intervention versus expectant management in monochorionic (MC) diamniotic twin pregnancies with early-onset (prior to 24 weeks) selective fetal growth restriction (sFGR). Interventions could include laser treatment or selective termination which could lead to the death or serious disability of one or both twins.

Design Qualitative semi-structured interviews with parents and clinicians. Data were analysed using reflexive thematic analysis and considered against the Principles of Biomedical Ethics.

Participants and setting We interviewed 19 UK parents experiencing (six mothers, two partners) or had recently experienced (eight mothers, three partners) early-onset sFGR in MC twin pregnancy and 14 specialist clinicians from the UK and Europe.

Results Participants viewed the proposed RCT as 'ethically murky' because they believed that the management of sFGR in MC twin pregnancy should be individualised according to the type and severity of sFGR. Clinicians prioritised the gestational age, size, decrease in growth velocity, access to the placental vessels and acceptability of intervention for parents. Discussions and decision-making about selective termination appeared to cause long-term harm (maleficence). The most important outcome for parents and clinicians was 'live birth'. For clinicians, this was the live birth of at least one twin. For parents, this meant the live birth of both twins, even if this meant that their babies had neurodevelopmental impairment or disabilities.

Conclusions All three pregnancy management approaches for sFGR in MC twin pregnancy carry risks and benefits, and the ultimate goal for parents is to receive individualised care to achieve the best possible outcome for both twins. An RCT was not acceptable to parents or clinicians or seen as ethically appropriate. Alternative study designs should be considered to answer this important research question.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study provides in-depth insight into the experiences of families who had different outcomes, including bereavement, resulting from their selective fetal growth restriction (sFGR) complicated monochorionic twin pregnancy, as well as specialist clinicians managing sFGR pregnancies.
⇒ Data analysis was informed by the biomedical ethical principles which provided insight into the challenging ethics of running the proposed study in a randomised fashion.
⇒ Parents had experience of being offered the pregnancy management options that are proposed for the randomised controlled trial due to being recruited via hospital sites (currently pregnant) and social media (pregnant within the last 3 years).
⇒ An ethicist was involved in the analysis of findings.
⇒ Limited to participants who could speak English.

INTRODUCTION

Around a third of twin pregnancies share a placenta (monochorionic (MC) twins);[1] this poses unique difficulties for pregnancy management including selective fetal growth restriction (sFGR) where one twin grows significantly slower than the other. sFGR

Table 1 Management options offered in the UK to women with a monochorionic twin pregnancy complicated by selective fetal growth restriction (sFGR)

Expectant management	Involves close monitoring of the twins. Expectant management aims to balance the risks of continuing the pregnancy and prematurity against the risk of intrauterine demise of the sFGR twin, which can then lead to the death of, or neurological damage in, the larger twin.
Selective termination of the sFGR twin	A procedure with bipolar cord coagulation or radiofrequency ablation or selective laser photocoagulation to block the blood flow through the umbilical cord from the placenta to the smaller twin. The sFGR twin dies which allows the larger twin to continue growing and gain maturity, hopefully delivering at a normal gestation. This procedure may also protect the larger twin from death or neurological damage.
Fetoscopic laser treatment	Placental laser photocoagulation to close the connections between the babies in the placenta with the aim of balancing the blood supply to both babies. This is likely to be a complex surgery and may worsen outcomes for the sFGR twin.

sFGR, selective fetal growth restriction.

affects between 10% and 15% of MC twin pregnancies.[2] Despite advances in antenatal care, sFGR in MC twin pregnancy is associated with preterm birth, stillbirth, neonatal death[3–5] and neurodisability, including cerebral palsy.[4 6 7] Early-onset sFGR, occurring before 24 weeks gestation, is less common but poses greater risk to the fetus and substantial management difficulties due to the distance from viability and the need to account for the welfare of both twins.[5] One study investigating 119 pregnancies (n=75/63% early onset sFGR and n=44/37% late onset sFGR) showed that in early-onset sFGR, survival of one (n=62/82.7%) or both twins (n=55/73.3%) were lower compared with late-onset sFGR (one twin n=42/95.5%; both twins n=39/88.6%).[8]

There is a lack of high-quality evidence on the best way to manage sFGR in twin pregnancies, leading to uncertainty among clinicians about clinical management and how best to discuss options with parents to help them make difficult decisions about management. Depending on where parents live and which clinician they see,[4] the three options offered in the UK are expectant management, selective termination of the sFGR twin and laser treatment (see table 1).

A randomised control trial (RCT) could provide clinicians and parents with evidence to inform decisions about the management option that would have the most favourable outcome for MC twin pregnancies with early-onset sFGR. There are, however, many challenges for a potential RCT in this situation, including a low incidence of the condition, uncertainty about clinician equipoise, parents' information needs and preferences and whether it is ethically acceptable to randomise women to expectant management or active intervention, which may lead to serious disability or the death of one or both twins.

METHODS

Study design

The FERN study[9] involved three work packages, including (1) prospective UK multicentre observational study, (2) qualitative study, (3) international survey[10] and consensus meeting. This paper presents the findings of the qualitative work package 2 phase of the study. The aim of work package 2 was to explore parents' and clinicians' perspectives on how the future clinical trial should be designed (including recruitment and consent approaches and the design of research materials), the factors that influence parents' and clinicians' decision-making and the acceptability of a future clinical trial.

Following ethics approval (REC reference: 20/SW/0156), we conducted online or telephone interviews with English-speaking women and their partners (where applicable) in the UK who were experiencing early-onset sFGR in MC twin pregnancy (or with experience in the last 3 years), and English-speaking clinical staff involved in the management of MC twin pregnancies in the UK and Europe, to explore their views on the feasibility, acceptability and design of a proposed RCT, with one 'watch and wait' expectant management arm, and two intervention arms: (1) selective termination of the sFGR twin and (2) laser treatment, for early-onset sFGR in MC twin pregnancy. Interviews were conducted between September 2022 and March 2023.

We used previous research[11 12] to develop the parent, partner and clinician participant information sheets (PIS) (see online supplemental files 1-3), while ongoing study findings were used to develop parent and clinician interview topic guides (see online supplemental files 4-5) as part of an iterative process. Interview topic guides included questions on the experience of management of MC twin pregnancies that were complicated by sFGR, decision-making processes, proposed trial design, information materials, trial acceptability, willingness to randomise/be randomised, prioritised outcomes and clinician training needs. The consolidated criteria for reporting qualitative research (COREQ) checklist[13] was used to aid reporting (see online supplemental file 6).

Patient and Public Involvement and Engagement (PPIE)

Our PPIE members include six coapplicants: Michelle Watson, Jessica Mendoza, Danielle Harding and Joel Marsden (two with personal experience of sFGR in MC twin pregnancy) and Natasha Fenwick and Shauna Leven from Twins Trust (https://twinstrust.org), which is a registered charity who support parents through every milestone of their journey with twins, triplets or more. The PPIE members were involved in the grant development, design, recruitment for, conduct, progress and/or

findings of the FERN study; and/or as members of the study oversight/steering committee; and/or attended the work package 3 Key Stakeholder meeting in London (3 July 2023) and/or reviewing and providing input on draft research information materials for this qualitative study and reviewing drafts of this manuscript.

Recruitment and sampling procedure

Based on previous qualitative feasibility studies,[11 14] we anticipated that we would need to interview 15–25 parents and clinicians to reach information power,[15] which is the point at which data address the study aims; sample variance[13] (e.g.,, parents offered expectant management or intervention, bereaved and non-bereaved parents and clinicians in favour of intervention and expectant management); our reflexive and interpretive approach to theory and analysis[16 17] and sufficient quality of interview dialogue.[15] We planned to hold additional focus groups if divergence in opinion was observed in interview data, but these were not required. Parents were recruited via work package 1 hospital sites and social media (Facebook and Twitter, with the support of Twins Trust).

Eligibility screening and conduct

Research midwives at hospitals (n=5/17) involved in work package 1 checked eligibility and approached parents with FERN study information, which included details of the qualitative study. MP (female, Social Scientist) or TKM (female, Social Scientist) contacted parents who had registered interest to participate in an interview to arrange a convenient time for an online or telephone interview (according to their preference). For social media recruitment, MP and TKM responded to parents' expressions of interest to take part in an interview in sequential order. Once eligibility had been confirmed, parents were emailed a copy of the Parent PIS which explained what would happen during their interview (see online supplemental file 7). Once parents confirmed their continued interest, they were then sent a proposed trial PIS and the core outcome measures list (see online supplemental file 8), derived from a review of the literature and Core Outcome set for this population.[18]

TKM and MP contacted work package 1 site clinicians and attendees at the International Society of Ultrasound in Obstetrics and Gynaecology World Congress 2022 to invite them to take part in an interview. Clinicians who expressed an interest in taking part were sent the Practitioner PIS, proposed Inclusion and Exclusion Criteria (see online supplemental file 9), and the same outcome measures list that was sent to parents before interview.

TKM and MP facilitated parent and clinician interviews using the topic guides.[19] Interviews stopped when information power[15] was reached. Parents then received a £30 Amazon voucher via email to compensate them for their time.

Analysis

MP and TKM conducted the analysis with oversight from KW (female, Social Scientist) and RA (male, Ethicist). Digital audio recordings of interviews were transcribed verbatim by a professional transcription company (UK Transcription, Brighton, UK). Transcripts were checked for accuracy and identifiable information were

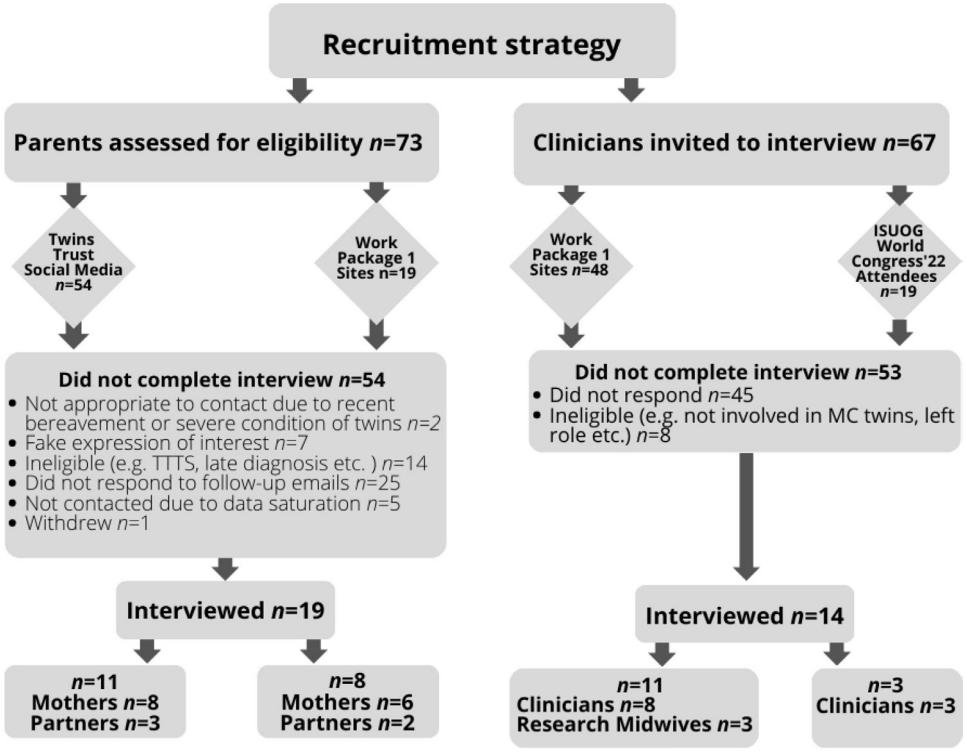

Figure 1 Participant recruitment. MC, monochorionic.

Table 2 Parent characteristics

Parent characteristics (n=19)	
Hospital* where pregnancy was managed	Intervention sites (sites that perform selective termination or fetoscopic laser treatment for sFGR) (n=8)
	Local/referral sites (sites who do not perform selective termination or fetoscopic laser treatment for sFGR and refer to the above hospital sites) (n=5)
Gestation when sFGR diagnosed	16, 18, 20 and 22 weeks but noted (not diagnosed) in some as early as 12 weeks
Pregnancy management route taken	Expectant management (n=19)
Other management options offered	Selective termination (n=5, 3 families) Laser treatment (n=2, one initially for Twin-to-Twin Transfusion Syndrome)
Pregnancy outcome	Not known (n=8, 6 families-site parents, so pregnant at the time of the interview)
	Both twins lived (n=8, 6 families) Twin born with neurodevelopmental impairment (n=1)
	Both twins died (n=3, 2 families)
Country of residence	England (n=18)
	Scotland (n=1)
Ethnic group	Asian (n=2)
	Black Caribbean (n=1)
	Mixed Other (n=1)
	White British (n=15)

*Some mothers were cared for at multiple hospitals.
sFGR, selective fetal growth restriction.

anonymised before being imported into NVivo V. 12 Plus software,[20] which was used to assist the organisation and coding of data. Reflexive thematic analysis was broadly interpretive and inductive.[17] MP, TKM and KW met regularly to discuss interpretation and develop the coding framework. Outcome measures prioritised as being most important were given a score of 13, second most important a score of 12, third most important a score of 11 and so on down to a score of one. Outcomes were then ranked. Findings were considered against the Adapted Theoretical Framework of Acceptability (ATFA) for paediatric trials[11 21] and Principles of Biomedical Ethics[22 23] (in particular, autonomy, justice, beneficence and non-maleficence) and synthesised using a symbiotic empirical ethics approach[24] to produce normative conclusions (e.g.,, should a randomised controlled trial be conducted?)

FINDINGS

Participant recruitment

Seventy-three parents registered interest in taking part in an interview (figure 1). Recruitment was closed at the point of information power.[15] Nineteen parents (14 mothers, 5 partners representing 28 babies and 14 families) took part in an online (n=11) or telephone (n=8) interview. Characteristics of the 19 parents and their pregnancy are shown in table 2.

Sixty-seven clinicians were invited to an interview. Recruitment was closed when 14 clinicians had taken part in an online (n=10) or telephone (n=4) interview (see table 3). Interviews with clinicians lasted between 53 and 83 min (mean=62 min), whilst parent interviews lasted between 47 and 106 min (mean 68 min).

Six interlinked themes will now be presented, which highlight the importance that parents and clinicians place on answering the research question and considering the practical and ethical challenges of conducting the proposed clinical trial.

An important question to answer

Parents and clinicians indicated that the proposed trial would answer an important research question to guide clinical practice and discussions with parents:

> I think it's great that you're doing something to help parents make decisions … there wasn't really a lot of information … that me and my wife could find. (P14, partner, social media)

> (Parents require) figures, so percentiles … because the science that is available at the moment is a bit contradicting and, in some aspects, also not always fitting to current practice. (C14, doctor)

Participants spoke of the need for evidence to alleviate the psychological distress that comes with making the 'traumatic' (P2, bereaved mother, social media), 'impossible decisions' (P1, bereaved partner, social media) about whether to go down the expectant management or intervention route, and for clinicians to confidently counsel parents about which route to take (C3, doctor). Clinicians stated that they 'sometimes counsel too pessimistic'

Table 3 Clinician characteristics

Clinician characteristics (n=14)	
Roles	Involved in the clinical management of sFGR (n=11, including: Professors, Consultants or Specialists/Subspecialists in Obstetrics, Gynaecology, Multiple Pregnancy and/or Fetal Medicine)
	Research midwives (n=3)
Country where practising	England and Northern Ireland (n=11)
	The Netherlands (n=2)
	Germany (n=1)
Hospital sites	Intervention sites (n=7)
	Local/referral sites (n=7)
Involvement in the clinical management of sFGR	Between 2 and 6 years (n=4)
	Between 15 and 18 years (n=4)
	>20 years (n=5)
	N/A (e.g., research midwife, n=1)
Experience recruiting to trials	<2 years (n=2)
	Between 2 and 6 years (n=2)
	Between 10 and 15 years (n=4)
	>20 years (n=4)
	Not known (n=2)

NA, not applicable; sFGR, selective fetal growth restriction.

and are 'ashamed' that they cannot provide parents with the right information specific to their pregnancy:

> I sometimes am ashamed of that I have to say to parents, in this modern, developed world in which medicine can treat, let's say, metastasis of melanomas with immune therapy, we cannot predict what the outcome is of their specific pregnancy complication. (C14, doctor)

Pregnancy management decision-making as 'traumatic' when outcomes include death or serious disability of one or both twins

We began parent interviews exploring clinical practice and the pregnancy management route experienced. All parents had their pregnancy managed expectantly. Nine parents (six families) had considered selective termination and laser treatment options, yet described how their decision to decline intervention was informed by clinicians explaining how there were positive indicators of life (e.g., blood flow), which gave parents hope for the survival of both babies.

> She (clinician) said, You can terminate little twin and focus on just having one baby, but because she had also said that all the internal blood flow was normal, that was an option which we said we weren't going to take. (P12/13 joint interview, pregnant mother, site)

> I don't see why if we've got this far we can't get further (…) I only need to make it to 28 weeks for them to be able to be born, even if it is very prematurely … I kind of felt like I didn't want to do too much action. I felt protective of the pregnancy in a sense I didn't want to do anything to upset it. (P11, mother, social media).

Although clinicians believed that parents should lead decision-making about whether to intervene, it was clearly evident in parent interviews (and compounded by whether their twins lived or died) that such decisions were traumatising, causing much distress and burden. They spoke of feeling disconnected from their surroundings, with bereaved parents stating 'that some people end up being diagnosed with PTSD after having to make difficult decisions around their babies' (P8, bereaved mother, social media). One mother who went on to have two healthy babies described her smaller twin as having 'a life that wouldn't need to be lost' (P9, mother, social media).

> We went away for a couple of hours, sat in the car … crying … because we had been presented with these options and had no idea, and no one seemed to have any idea what was the best one to do. That was quite traumatic. (P2, bereaved mother, social media)

> I feel like when it hit 24 weeks and I was being asked to make decisions about whether to keep a baby or not, I almost wasn't able to clearly… I felt very separate from my…. almost disassociated from myself. I felt very separate from what was going on just because I'd been so detached. It was a really weird experience. (P11, mother, social media)

Clinicians highlighted how the timing of intervention is difficult due to the changing and unpredictable nature of sFGR in MC twin pregnancy:

> We can only offer selective reduction (termination) up to a certain gestation, usually 24 weeks. It's a tricky one, because you think, 'Well, in two weeks' time, it is highly likely that the ductus venosus is going to become abnormal … By then, I may not have the option of offering them a selective reduction. And then, what if it dies?' … And so, you can end up in this very difficult situation. If you don't offer it early enough … but then you end up in this situation where you're 24 to 25 weeks, you can't offer a selective reduction, because technically, it's not possible … I think that is the really difficult decision for them, because then it is an impact on their life or the life of that child. I mean, accepting death is so difficult, but looking after a child with a disability is a different ballgame altogether. So, it is those things that I think are very difficult for parents to weigh up. (C8, Doctor)

As well as the long-term impact of having conversations about selective termination, clinicians and parents were worried about the 'devastating' scenario where 'it's possible that one could've made a wrong decision … based on a worst-case scenario' (P17, mother, site).

The challenge of diagnosing an unpredictable condition in the context of a trial

Clinicians emphasised that every pregnancy is different and that there are many factors that determine their decision-making to recommend expectant management or active intervention. Clinicians' decision-making was described as being 'on a case-by-case basis' (C12, doctor) and informed by multiple factors, including the severity and type of sFGR (as determined by Dopplers), as shown in Gratacós *et al* (2007) three types classification of sFGR[25 26] (see table 4).

Other factors that determine clinicians' decision-making to recommend expectant management, active intervention or early delivery were: the gestational age at diagnosis; the 'size of the' affected twin (C12, doctor); 'the speed of growth decreases' (C14, doctor) 'where the placenta is'/placental vessels are (C14, doctor)/'accessibility to the smaller twin' (C7, doctor); and the perceived acceptability of intervention for parents. Furthermore, intervention in sFGR pregnancy 'really varies according to … the centre where the patient is seen' (C1, doctor), 'the culture … (and) general consensus … of the population (area or country) and how they see things' (C10, doctor), the knowledge and experience of, and how the individual clinician articulates the benefits and risks of pregnancy management options. These factors also contributed to clinicians' suggestions for additions or amendments to the proposed inclusion and exclusion criteria (see online supplemental file 10).

While there was some variance in clinician's preferred management approach, most clinicians stated they would not discuss intervention options early in the pregnancy, particularly for type I sFGR, and would 'see again always … in one week's time, just to see how things evolve' (C2, doctor).

Parents described being told that their condition could correct itself or change from a more severe type to one with a more favourable outcome:

> Like my consultant said, it's a weekly thing. Today's appointment is good, but we don't know if it's going to get worse or better next week. So, that was made very clear. (P17, pregnant mother, site)

When parents reflected on their discussions in these situations, they said they had relied on the clinician's advice. However, this posed difficulties for parents who were faced with contradictory advice from different clinicians:

> He (consultant) reached out to one guy in Germany and one guy in the USA, and he said that one of them went, 'Why on earth would you intervene? There's no proof that this works. Why would you do that?' The

Table 4 Gratacós *et al* (2007) classification of sFGR

Pregnancy course	Description according to the Doppler finding of end-diastolic flow in the umbilical artery of the smaller twin	Potential outcomes
Type I	Persistently positive	At the lower end of the spectrum of severity. Type I has the best outcome in terms of mortality and morbidity (neurological damage) and is unlikely to require active intervention or early delivery
Type II	Persistently absent or reversed	Type II has worst prognosis. More severe, progressive deterioration that leads to considering active intervention or delivery in 90% of cases (earlier delivery may prevent mortality of one or both twins, but increases the risk of morbidity)
Type III	Intermittently absent or reversed	Better outcomes than type II cases, but still a highly unpredictable clinical course in terms of mortality and morbidity of both twins, requiring active intervention or early delivery in 10.8% of cases

sFGR, selective fetal growth restriction.

other guy went, 'Why on earth wouldn't you do it? There's something available to you. Why wouldn't you intervene if you think there's a big problem?' (P1, bereaved partner, social media).

Parents require clear information about risks and potential outcomes to make informed decisions as to whether to take part in the proposed RCT

When asked what would make an RCT like FERN more acceptable, parents said that they would want reassurance from their consultant that (hypothetically) taking part would 'have no greater adverse outcome if we do this than if we didn't do it?' (P1, bereaved partner, social media) 'because it's such a … not invasive. Invasive is the wrong word. But it's not, like, an observational study. It could actually affect what happened' (P2, bereaved mother, social media).

Parents would require information and statistics about potential outcomes for each trial arm to decide whether or not to take part:

> I don't even know whether this exists, but potentially, statistics of how successful expectant management would be, how successful interventions are. So, the science behind each of the choices in simple numbers, so that it's in black and white, easy to see how positive each of the outcomes are. (P4, mother (one twin with neurodevelopmental disability), social media).

Nevertheless, most parents and clinicians agreed that selective termination as a trial arm was not acceptable. While parents said that a trial comparing laser treatment with expectant management would be more acceptable because 'you weren't necessarily selectively choosing which baby would have to be terminated' (P9, mother, social media), some clinicians said that they were 'not a fan of laser because I think we have to be honest that we don't have any pathophysiological argument to say that it will improve the outcome' (C2, doctor). Another clinician said that it would be unethical not to provide parents with the evidence about outcomes of laser treatment in sFGR:

> It would be unethical … (to) not provide parents with the … current evidence (that) shows that they're more likely to take a baby home if they have a selective reduction, compared to if they had a laser. (C8, doctor)

The proposed RCT was viewed by parents and clinicians as 'ethically murky'

While recognising the importance of answering the question about which management option is most effective for sFGR in MC twin pregnancy, our findings suggest that conducting an RCT comparing expectant management to active intervention would not be acceptable to parents, who view the proposed study as 'ethically murky' (P3, pregnant mother, site). Most parents clearly stated that they would not participate in an RCT with active intervention and expectant management as trial arms because they would not want the fate of their babies' lives being left to a randomisation process:

> If we were approached, I would be a straight 'No!' straightaway… Just reading the treatment sections (in the proposed participant information sheet), like the options of treatments, the termination treatments were definitely, immediately, I was like, 'Okay, no!' It was an immediate 'No!' That was it!. (P18, partner of pregnant mother, site)

Parents were clear that they would drop out of the proposed trial if they were randomised to a trial arm that they were not comfortable with, particularly if their pregnancy course was type I:

> If it were us, I would've gone with it but if I was put into a category that I didn't agree with I would've pulled out. Going back to the whole severity level of the pregnancy on a scale of one to ten, then being randomly put into category B which is termination, if you were on the less severe end of the spectrum you might look at that and think, 'I'm not happy with that!'. (P6, partner, social media).

Indeed, clinicians raised ethical concerns about randomising women to a trial arm, especially selective termination, that might not be appropriate to their individual case. Decision-making was informed by the severity and type of sFGR (see table 4):

> It very much depends on the type of selective fetal growth restriction, whether it's Type I or Type II … or Type III … We know that outcome for Type I is good without intervention. Outcome for Type II with abnormal ductus venosus is bad without intervention … Type II … deteriorates much faster and in a predictable way. And Type III can go on for a long, long time, but it's an unpredictable, sudden loss. (C8, doctor)

'Live birth', 'childhood disability' and 'neurodevelopmental impairment' were the most important outcome measures for parents and clinicians

Parents and clinicians were asked to consider a list of 13 potential outcomes sent prior to interview and were asked if there were any additional outcomes that they felt were missing.

The ranking of outcomes prioritised by parents can be seen in table 5, and the ranking of outcomes prioritised by clinicians in table 6. Outcome measures prioritised as being most important were given a score of 13 and those ranked least important were given a score of one.

The most important outcome for the proposed trial for parents and clinicians was live birth which, for clinicians, meant the survival of one of the twins and for parents meant the survival of both twins, even if it meant that the twins had neurodevelopmental impairment:

Table 5 Parent ranking of outcomes

Weighted ranking	Outcome	Weighted score	No. (& %) parents/18*
1	Live birth	234	18 (100)
2	Childhood disability†	96	9 (50)
3	Neurodevelopmental impairment†	89	8 (44)
4	Gestational age at birth	72	8 (44)
5	Child quality of life†	66	7 (39)
6	Birth weight	61	6 (33)
7	Loss during pregnancy or before final hospital discharge†	60	6 (33)
8	Death of surviving twin after death of co-twin†	54	5 (28)
9	Procedure-related adverse outcome	32	4 (22)
10	Intertwin birth-weight discordance	31	5 (28)
11	Parental stress†	30	7 (39)
12	Parent quality of life†	18	3 (17)
13	Length of stay in hospital	12	3 (17)

*As P19, pregnant mother, site is missing data.
†Most parents ranked the three outcomes of 'Childhood disability', 'Neurodevelopment impairment' and 'Child quality of life' equally and suggested that they be grouped together. Parents also ranked and suggested that the two outcomes of 'Loss during pregnancy or before final hospital discharge' and 'Death of surviving twin after death of co-twin' be grouped together. Additionally, the two outcomes of 'Parental stress' and 'Parent quality of life' were ranked together by parents, who suggested that they be grouped together.

Table 6 Clinician ranking of outcomes

Weighted ranking	Outcome	Weighted score	No. (& %) of clinicians/12*
1	Live birth (of at least one twin)	125	13 (93)
2	Neurodevelopmental impairment†	84	13 (93)
3	Childhood disability† (follow-up until at least 8 years old)	73	13 (93)
4	Death of surviving twin after death of co-twin†	67	10 (71)
5	Gestational age at birth (include short and long-term consequences of prematurity here or under new outcome 'Neonatal morbidity', which is currently missing)	66	11 (79)
6	Loss during pregnancy or before final hospital discharge+ (Define—does this mean one or two losses and does this include whether death is due to termination of pregnancy?)	66	10 (71)
7	Procedure-related adverse outcome+ (include premature rupture of membranes, pregnancy loss and injury to the fetus)	61	10 (71)
8	Birth weight (centile)	55	10 (71)
9	Intertwin birth-weight discordance	51	9 (64)
10	Parent quality of life†	50	7 (50)
11	Parental stress†	40	9 (64)
12	Length of stay in hospital†	36	9 (64)
13	Child quality of life†	36	7 (50)

*As C8 and C12 are missing data.
†Clinicians stated that the two outcomes of 'Neurodevelopment impairment' and 'Childhood disability' should be composite as they are unable to separate these outcomes from each other. Clinicians also suggested that the two outcomes of 'Death of surviving twin after death of co-twin' and 'Procedure-related adverse outcome' are unable to be separated and should be composite. Additionally, clinicians stated that the four outcomes of 'Parent quality of life', 'Parental stress', 'Length of stay in hospital', and 'Child quality of life' are composite and should be grouped together.

> I remember saying I would have preferred to have two alive children with … a bit of cognitive impairment … (or) disabilities than two dead ones or one dead one (P11, mother, social media).

Neurodevelopmental impairment and disability, which were the next most important outcome measures for parents and clinicians, had been presented to the participants as two separate measures. However, participants spoke of how these outcomes, together with the child's quality of life (which was an important outcome measure to parents), overlap and could be measured together:

> They (outcomes) all come under the same umbrella for us. Because as a result of his neurological impairment, he has got childhood disabilities and then that affects his quality of life. (P4, mother (one twin with neurodevelopmental disability), social media)

Parental stress was ranked as one of the least important outcomes (weighted 11 most important for parents and clinicians). Participants spoke of how stressful going through a high-risk pregnancy was for families, and as stress is 'almost like a given' (P15, pregnant mother), they would not consider this an important outcome to be measured in the proposed RCT.

Almost half of clinicians, unprompted, said that 'neonatal morbidity' meaning 'all of the complications that can arise in the neonate, while the neonate did not actually die' (C6, doctor) was a missing outcome, with one clinician saying that that neonatal morbidity is an outcome that is included in other UK sFGR and neonatal trials.

> In other UK trials of sFGR and neonatal trials, there is actually quite a long list of neonatal morbidity outcomes or indicators that should be included in this list. (C1, doctor).

Suggestions for longer term (and missing) outcome measures were made by both clinicians and parents, such as, importantly, including 'some sort of measurement of parental experience or any regret or anything to do with their decision-making' (C3, doctor) for trial participation, parent emotional well-being and living with the choices made (e.g., post-traumatic stress disorder and suicide risk), as demonstrated by this mother's powerful question:

> Did they (parents) survive emotionally … after the decisions … to terminate one of these kids? … (Did) parents … go and kill themselves because they have made the wrong decision? How the hell do you, as a mother, cope? (P16, pregnant mother, site)

Clinicians spoke of how 'parents will always remember that they were offered a termination' (C8, doctor) and 'are (still) traumatised by mentioning the option of cord occlusion' when their child is followed up at age 8 years:

> It is so difficult, and that still, at the age of eight years, they (parents) look at the twins and they think frequently about one of them that they had, that they could end up in a situation that they had chosen cord occlusion …. (C14, doctor)

The proposed RCT is 'like mission impossible' and an alternative study design is required

After considering the proposed trial, participants stated that the FERN study would not be acceptable nor practical to conduct 'in a randomised fashion' (C2, doctor) as the risk of distress and burden for parents and harm or death to one or both twins would be too great. Applying our findings to the Principles of Biomedical Ethics[22 23] (see online supplemental file 11) and ATFA for paediatric trials[11 21] (see online supplemental file 12) and synthesising them using a symbiotic empirical ethics approach[24] clearly support our findings that the proposed RCT would not be ethical or acceptable for clinicians or parents. As one parent said: 'You can't be ethical basically, I don't think … It is almost like the mission impossible and you just need to find a way to kind of … There will be damage basically, you can't avoid it, there is no way, there is no other way' (P18, partner, site).

Some parents and clinicians suggested consideration should be given to other study designs that are more acceptable and still scientifically valid. One parent asked, 'Is there another way of doing it? … Perhaps, for example, could those who are already going to have these managements, then base it on that, instead of selecting at random?' (P5, mother, social media). Cohort studies were proposed by clinicians as an option 'where patients are counselled in a similar way and then depending on what's technically possible and also on patient preferences, you document an outcome in a uniform way. I think that's the only way to do that' (C2, doctor).

DISCUSSION

To our knowledge, this qualitative study is the first to explore parents and clinicians' views on the acceptability and feasibility of conducting an RCT of active intervention versus expectant management in MC twin pregnancy with early-onset sFGR. To navigate the ethical issues with the proposed RCT, we drew on the ethical principles of autonomy, justice, beneficence and non-maleficence proposed by Beauchamp and Childress[22] and involved an ethicist (RA) in the analysis of findings.

Our findings suggest that an RCT comparing active intervention versus expectant management would not be acceptable, seen as ethical to parents and clinicians, nor feasible to conduct. One of the main challenges to conducting the proposed RCT related to the different types, severity and clinical uncertainty around the diagnosis and management of sFGR in MC twin pregnancies. A recent retrospective study that assessed the accuracy of diagnosis of sFGR with Doppler ultrasound in MC twin pregnancies between 14 and 26 weeks of gestational age, in 280 pregnant women (118 with sFGR), found that

second trimester Doppler and ultrasound measurements could correctly identify 74.5% of sFGR twins.[27] However, the study did not report on the three types of sFGR, which correspond with different clinical behaviour, patterns and outcomes[25] (see table 4). Type I and III sFGR have a better outcome than type II (albeit that type III has a highly unpredictable clinical course in terms of mortality and morbidity of both twins, requiring active intervention or early delivery in 10.8% of cases).[25 26] Consequently, while all parents and clinicians spoke about the need for high-quality information to inform decision-making and were supportive of a study that aims to answer the FERN research question, many strongly opposed having selective termination as a trial arm, feeling that it would be unethical to randomise women with type I and type III sFGR to a trial arm 'directly killing'[28] their sFGR twin.

Similarly, although parents in our study considered laser treatment to be more acceptable as a trial arm than selective termination, because they believed that this pregnancy management option would minimise the risk of harm to the sFGR twin (and they would not be 'directly killing'[28] their sFGR twin), this was in contradiction with clinicians' views on laser treatment as a trial arm. Whilst laser treatment is a common and effective option for Twin-to-Twin Transfusion Syndrome,[29] the evidence to support it as an effective therapy for sFGR is currently lacking. Clinicians felt that it would be unethical to not provide parents with the evidence that shows that they are more likely to take a baby home if they have a selective termination, compared to if they have laser treatment.

Furthermore, our findings suggest it would be unethical, and in conflict with the Hippocratic Oath promise of 'first, do no harm' and the fundamental ethical principles of non-maleficence and beneficence,[30] to randomise women with type I and type III sFGR, who would potentially not require intervention, to receiving laser treatment intervention. A mother with type II sFGR that may require active intervention could potentially be randomised to the expectant management arm of the proposed RCT. The ethical principles of non-maleficence and beneficence demand that patients be offered care that minimises risks. However, in the proposed FERN RCT, acting for the rights of one twin diminishes the rights of the other twin, which is in opposition to the ethical principle of individual autonomy for both twins[31] and, depending on opinion about when a fetus becomes a child with a right to life, survival and development, the United Nations Convention on the Rights of the Child.[32] This poses issues as, for the women in our study who ultimately gave birth to two healthy babies, terminating the life of their sFGR twin/both twins would have been, as one mother said, 'a life that wouldn't need to be lost'. Therefore, clinicians must be clear about the benefits and risks of each pregnancy management option when counselling parents, especially as parents ranked survival of both twins as the most important outcome. Our findings also highlight the importance of the long-term measurement of parent well-being and any regret to do with their decision-making, even though long-term parent related outcomes of trial participation are rarely collected.[33]

We also found that clinicians' practice varied regarding active intervention and the timing of discussion with parents about this (depending on the culture of the population in the area that they are practising in). This has implications for the proposed RCT, as some parents would not typically need to discuss active intervention. Although clinicians believed that parents should lead decision-making about pregnancy management in line with the biomedical ethical principle of autonomy,[22 34 35] it was clearly evident that even the offering of selective termination and suggestion that parents should make a decision, which was traumatic for parents and potentially caused long-term harm, is in breach of the non-maleficence biomedical ethical principle, regardless of outcome or pregnancy management route taken. One parent spoke of having feelings of dissociation during the conversation, which puts into question whether parents will truly have the capacity to make an informed consent decision about the proposed RCT. This finding demonstrates the difficulties in balancing the biomedical ethical principles of autonomy, beneficence and non-maleficence, as well as the need to answer an important research question to inform future clinical practice to improve outcomes for such challenging pregnancies. Shea argues the need for specification and balancing to determine the relative weight of conflicting principles.[34] Ultimately, the psychological long-term impact for parents of having to make a decision that may result in the death or severe damage to one or both twins must be considered, and parents must be counselled in a way that helps them to manage feelings of guilt, grief and mental health distress. This recommendation is relevant to future clinical practice as well as studies they may be conducted in the future.

Conclusion

Our findings have shown that parents and clinicians do not consider an RCT comparing active intervention versus expectant management to be acceptable or ethical for the management of MC twin pregnancies complicated by sFGR. Drawing on findings from the wider FERN study, as well as the barriers identified in this study to both recruitment and retention, alternative study designs such as an international multicentre observational cohort study or propensity score matching should be considered to address this important research question. Parents value clear information about potential risks and outcomes to make better informed decisions and clinicians wish to be in a better position to counsel parents appropriately. As we have shown, care should be taken when counselling parents as the impact of such clinical discussions can have long-lasting effects on parents, regardless of outcome.

Strengths and limitations of this study

This study provides insight into how parents and clinicians would respond to being invited to participate in an RCT investigating active intervention versus expectant

management of MC twin pregnancies complicated by sFGR. The primary strength of the study is the recruitment of parents whose experiences varied in terms of pregnancy outcomes. The sample included bereaved families who had lost both twins, those who had two healthy twins, a case where the co-twin had neurodevelopmental impairment and women who were currently experiencing an MC pregnancy complicated by sFGR and their partners. This last group, in particular, provided insight into how women and their partners might respond to being asked to participate in a definitive trial. Another strength of this study was the involvement of an ethicist in the analysis of findings. Several factors that would help with the design of a future study that does not include randomisation were identified. Our findings can help clinicians reflect on how best to carry out pregnancy management conversations with women to ensure that they are aware of the risks and benefits of each option.

One of the study limitations was that only parents who had their pregnancy managed expectantly took part in an interview (although six families had been offered active intervention). Thus, we cannot conclude that our results accurately reflect the views of women who experienced selective termination or laser treatment intervention. The sample consisted primarily of families of White British ethnicity and all interviews were conducted with English-speaking participants. The views, experiences and understanding of the decision-making parents are asked to make should be explored with families via an interpreter. Although research samples should always reflect the diversity in the population studied, this is particularly important in this study where parents will have to make decisions that include the termination of one of their twins. As demonstrated by our findings, pro-life or pro-choice views on selective termination can be influenced by cultural and religious backgrounds.[36 37] Interviews were conducted over the telephone or online which may have impacted on possible eye contact or development of rapport. However, our previous research and other studies have reported that telephone interviews are preferred over face-to face interviews when discussing delicate topics or balancing childcare responsibilities.[38]

Author affiliations
[1]Public Health, Policy and Systems, University of Liverpool, Liverpool, UK
[2]School of Law, City University of London, London, UK
[3]Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust, London, UK
[4]Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[5]Department of Women's and Children's Health, University of Liverpool, Liverpool, UK
[6]Clinical Directorate Professional Services, University of Liverpool, Liverpool, UK
[7]Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK
[8]Research and Resources Officer, Twins Trust, London, UK
[9]Twins Trust, Woking, Surrey, UK

X Tracy Karen Mitchell @trakmitch

Acknowledgements We would like to thank collaborators: David Howe, Edward Johnstone, Lawrence Impey, Ahmet A Baschat, Jan Deprest, Liesbeth Lewi, Kurt Hecher and Enrico Lopriore and Kevin Southern and Alex Astor who had supporting roles on the NIHR application. Special thanks are extended to our Patient and Public Involvement and Engagement (PPIE) members and coapplicants, Natasha Fenwick and Shauna Leven from Twins Trust, and Keith Reed, Michelle Watson, Isabella O'Connor, Jessica Mendoza, Danielle Harding and Joel Marsden for their involvement in the design, conduct, progress and findings of the feasibility study and the development and conduct of the proposed trial. Special thanks are also extended to Natasha Fenwick and Shauna Leven from Twins Trust for their support with recruitment to the study and, similarly, to Principal Investigators/Coprincipal Investigators: Carolyn Bailie, Alexandra Viner, Andrew Breeze, Angelo Cavallaro, Anoop Rehal, Dilly Anumba, Elena Greco, Elisabeth Peregrine, George Attilakos, Hiran Samarage, Koon Loong Chan, Mark Denbow, Martin Maher, Nashwa Eltaweel, Rajeswari Parasuraman, Renata Hutt, Sharmila Sivarajan, Shireen Meher, Surabhi Nanda, Therese Hannon, Tommy Mousa, Linden Stocker, Luxmi Velauthar, Rosemary Townsend and Sarah Newell. Finally, we wish to express our immense gratitude to the parents and staff who took part in interviews, without whom, these findings would not have been made.

Contributors TKM and MP are joint first authors. AK, AS, REA, MT, CC, NF, SL and KW were coapplicants and involved in the conception and design of the study. TKM and MP collected the data. MP and TKM analysed and interpreted the data with oversight from KW and REA. TKM and MP drafted the article and REA, SP, AK and KW critically revised it for important intellectual content. TKM, AS, MP, REA, SP, AK, NF and KW gave approval of the version to be published. TKM, MP and KW agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. TKM is responsible for the overall content as guarantor, and accepts full responsibility for the finished work and the conduct of the study, had access to the data, and controlled the decision to publish. We would like to thank Research Coordinator, Tracey Ricketts; Coapplicants: Andy Healey, Baskaran Thilaganathan, Brigitte Vollmer, Jamie Kirkham, Jane Sandall, Karen Wilding, Louise Hardman, Richard Jackson, Richard Ashcroft, Shakila Thangaratinam and Zarko Alfirevic who were part of the study management group

Funding The FERN study was funded by the National Institute for Health Research Health Technology Assessment Programme (project number NIHR128596). Work package 2, presented here, was coordinated by the University of Liverpool. The views and opinions expressed here are those of the authors and do not necessarily reflect those of the HTA Programme, NIHR, NHS or the Department of Health. The funders had no role in the collection, analysis and interpretation of data or in the decision to submit this article for publication.

Competing interests National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme grant payments were made to the institutions of all authors (except REA, NF and SL). TKM and MP employment roles were funded by the NIHR HTA programme grant payment made to their institution.

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

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by South West—Cornwall and Plymouth Research Ethics Committee (Reference number: 20/SW/0156). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. The data sets generated and analysed for this study are not publicly available due to participants being from a small, specialised population, which creates ethical and privacy concerns about being too identifiable.

ORCID iDs
Tracy Karen Mitchell http://orcid.org/0000-0003-0014-8016
Mariana Popa http://orcid.org/0009-0006-9237-4094
Richard Edmund Ashcroft http://orcid.org/0000-0001-6065-4717
Smriti Prasad http://orcid.org/0000-0003-2329-4470
Andrew Sharp http://orcid.org/0000-0003-3396-7464
Mark Turner http://orcid.org/0000-0002-5299-8656
Asma Khalil http://orcid.org/0000-0003-2802-7670
Natasha Fenwick http://orcid.org/0000-0002-3232-163X
Kerry Woolfall http://orcid.org/0000-0002-5726-5304

REFERENCES

1 Twinstrust. Identical or non-identical? 2023. Available: https://twinstrust.org/information/pregnancy-and-birth/finding-out/identical-or-non-identical.html
2 Rustico MA, Consonni D, Lanna M, *et al*. Selective intrauterine growth restriction in monochorionic twins: changing patterns in umbilical artery doppler flow and outcomes. *Ultrasound Obstet Gynecol* 2017;49:387–93.
3 Cheong-See F, Schuit E, Arroyo-Manzano D, *et al*. Prospective risk of stillbirth and neonatal complications in twin pregnancies: systematic review and meta-analysis. *BMJ* 2016;354:i4353.
4 Townsend R, D'Antonio F, Sileo FG, *et al*. Perinatal outcome of monochorionic twin pregnancy complicated by selective fetal growth restriction according to management: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2019;53:36–46.
5 Townsend R, Khalil A. Fetal growth restriction in twins. *Best Pract Res Clin Obstet Gynaecol* 2018;49:79–88.
6 Khalil A, Thilaganathan B. Selective fetal growth restriction in monochorionic twin pregnancy: a dilemma for clinicians and a challenge for researchers. *Ultrasound in Obstet & Gyne* 2019;53:23–5.
7 Sharp A, Cornforth C, Jackson R, *et al*. Maternal sildenafil for severe fetal growth restriction (STRIDER): a multicentre, randomised, placebo-controlled, double-blind trial. *Lancet Child Adolesc Health* 2018;2:93–102.
8 Wang Y, Shi H, Wang X, *et al*. Early- and late-onset selective fetal growth restriction in monochorionic twin pregnancy with expectant management. *J Gynecol Obstet Hum Reprod* 2022;51:102314.
9 Khalil A. FERN: intervention or expectant management for early onset selective fetal growth restriction in monochorionic twin pregnancy, 2023. Available: https://www.liverpool.ac.uk/life-course-and-medical-sciences/research/groups/fern-study/?
10 Prasad S, Khalil A, Kirkham JJ, *et al*. Diagnosis and management of selective fetal growth restriction in monochorionic twin pregnancies: A cross-sectional international survey. *BJOG* 2024.
11 Deja E, Peters MJ, Khan I, *et al*. Establishing and augmenting views on the acceptability of A paediatric critical care randomised controlled trial (the FEVER trial): A mixed methods study. *BMJ Open* 2021;11:e041952.
12 O'Hara CB, Canter RR, Mouncey PR, *et al*. A qualitative feasibility study to inform a randomised controlled trial of fluid bolus therapy in septic shock. *Arch Dis Child* 2018;103:28–32.
13 Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. *Int J Qual Health Care* 2007;19:349–57.
14 Deja E, Roper L, Tume LN, *et al*. Can they stomach it? Parent and practitioner acceptability of a trial comparing gastric residual volume measurement versus no gastric residual volume in UK NNU and picus: a feasibility study. *Pilot Feasib Stud* 2021;7:49.
15 Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: guided by information power. *Qual Health Res* 2016;26:1753–60.
16 Angen MJ. Evaluating interpretive inquiry: reviewing the validity debate and opening the dialogue. *Qual Health Res* 2000;10:378–95.
17 Braun V, Clarke V. Reflecting on reflexive thematic analysis. *Qual Res Sport Exerc Health* 2019;11:589–97.
18 Townsend R, Duffy JMN, Sileo F, *et al*. Core outcome set for studies investigating management of selective fetal growth restriction in twins. *Ultrasound Obstet Gynecol* 2020;55:652–60.
19 Mays N, Pope C. Assessing quality in qualitative research. *BMJ* 2000;320:50–2.
20 Ltd QIP. NVivo (version 12). 2018.
21 Sekhon M, Cartwright M, Francis JJ. Acceptability of health care interventions: Atheoretical framework and proposed research agenda. *Br J Health Psychol* 2018;23:519–31.
22 Beauchamp TL, Childress JF. *Principles of biomedical ethics*. 8th edn. Oxford: Oxford University Press, 2019.
23 Beauchamp T, Childress J. *principles of biomedical ethics*: marking its fortieth anniversary. *Am J Bioeth* 2019;19:9–12.
24 Frith L. Symbiotic empirical ethics: A practical methodology. *Bioethics* 2012;26:198–206.
25 Gratacós E, Lewi L, Muñoz B, *et al*. A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery doppler flow in the smaller twin. *Ultrasound in Obstet & Gyne* 2007;30:28–34.
26 Buca D, Pagani G, Rizzo G, *et al*. Outcome of monochorionic twin pregnancy with selective intrauterine growth restriction according to umbilical artery doppler flow pattern of smaller twin: systematic review and meta-analysis. *Ultrasound in Obstet & Gyne* 2017;50:559–68.
27 Wang Y, Zhang A, Stock T, *et al*. The accuracy of prenatal diagnosis of selective fetal growth restriction with second trimester doppler ultrasound in monochorionic diamniotic twin pregnancies. *PLoS ONE* 2021;16:e0255897.
28 Thomson JJ. A defense of abortion. In: Schüklenk U, Singer P, eds. *Bioethics: an anthology*. 4th edn. Hoboken, New Jersey: WILEY Blackwell, 2021: 31–41.
29 Van Der Veeken L, Couck I, Van Der Merwe J, *et al*. Laser for twin-to-twin transfusion syndrome: a guide for endoscopic surgeons. *Facts Views Vis Obgyn* 2019;11:197–205.
30 Askitopoulou H, Vgontzas AN. The relevance of the hippocratic oath to the ethical and moral values of contemporary medicine. part II: interpretation of the hippocratic oath-today's perspective. *Eur Spine J* 2018;27:1491–500.
31 Wright L. *Twins and what they tell us about who we are*. New York: John Wiley & Sons, Inc, 1997.
32 UNCRC. *The United Nations convention on the rights of the child*. UNICEF, 1989.
33 Farmer N, Hillier M, Kilby MD, *et al*. Outcomes in intervention and management of multiple pregnancies trials: A systematic review. *Eur J Obstet Gynecol Reprod Biol* 2021;261:178–92.
34 Shea M. Principlism's balancing act: why the principles of biomedical ethics need a theory of the good. *J Med Philos* 2020;45:441–70.
35 Hėbert PC, Rosen W. *Doing right. A practical guide to ethics for medical trainees and physicians*. 4th edn. Ontario, Canada: Oxford University Press, 2020.
36 Cantens B. *A critical introduction to the ethics of abortion: understanding the moral arguments / by Bernie Cantens*. London: Bloomsbury Academic, an imprint of Bloomsbury Publishing Plc, 2019.
37 Kaczor C. *The ethics of abortion: women's rights, human life, and the question of justice*. New York: Routledge, 2022. Available: https://www.taylorfrancis.com/books/9781003305217
38 Farooq MB, de Villiers C. Telephonic qualitative research interviews: when to consider them and how to do them. *MEDAR* 2017;25:291–316.

Participant Information Sheet

FERN: Intervention or Expectant Management for Early Onset Selective Fetal Growth Restriction in Monochorionic Twin Pregnancy

We are inviting women pregnant with twins to take part in a research study. Before you decide whether or not to take part it is important for you to understand why the research is being performed and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of our research team will go through the information sheet with you and answer any questions you may have. Please take time to decide whether or not you wish to take part.

Thank you for reading this.

Why are we doing the study?

The UK has approximately 11,000 twin pregnancies per year with a third of these sharing a placenta (monochorionic (MC) twins). MC twin pregnancy presents extra risks to both the mother and the babies, with some babies dying during pregnancy or shortly after birth. Often this is due to a complication called selective Fetal Growth Restriction (sFGR), where one twin is smaller than the other. sFGR affects one in seven MC twin pregnancies in the UK although we know less about pregnancies where this happens early (before 24 weeks).

There are three main ways of managing MC twin pregnancies with sFGR: 1) a watch and wait approach (also called expectant management), 2) a procedure that blocks the umbilical cord from the smaller twin to the placenta and causes the loss of the smaller twin (also known as selective termination), and 3) a laser that can be used to completely separate the twins' circulations. All of which present significant risks (death and severe disability) to one or both twins.

At present there is a lack of evidence to tell us the best way of managing sFGR in MC twin pregnancies. Currently, women and their partners are offered different management options depending on where they live and who they see. It is also clear that there are gaps in what we know about sFGR.

To be able to find the best way to manage these pregnancies there is much need for a clinical trial comparing management options. Before running a trial, we need to understand things like how many twin pregnancies would be needed to run the trial and whether parents would think such a trial is acceptable. We also need to work out which management options would be the best to use and what outcomes would be important.

To do this we would like you and your birth partner (if applicable) to allow us to access your health records and collect data on your pregnancy. We would also like to hear about your pregnancy experience and discuss your views and opinions on a potential future clinical trial (qualitative interview), for example do you think such a trial is a good idea and would you be happy to take part.

Participant Information Sheet

Why have I been chosen?

We are inviting all women aged 18 years and older who are currently pregnant (16 - 23 weeks) with an MC twin pregnancy complicated by sFGR or have had an sFGR affected MC twin pregnancy in the last 3 years to take part in this study.

Do I have to take part?

It is up to you to decide whether or not to take part in this study. If you decide to take part - you will be asked to sign a consent form. You will be free to withdraw from the study at any time, without giving a reason. If you decide not to take part – this will not affect the care you or your family receives in any way.

What will happen to me if I take part?

There are two parts to this study, data collection and qualitative interviews. If you are currently pregnant, you can decide to take part in either the data collection aspect or the interview aspect. If you wish, you could decide you would like to take part in both. If you are not currently pregnant but have had an MC twin pregnancy complicated by sFGR in the last 3 years you will be invited to take part in an interview.

If you agree to take part in the data collection aspect of this study, you will be asked to give your permission (consent) for your health records to be accessed by the research team. After your consent has been provided, we will look at your records and collect data related to you and your babies during your pregnancy. This data will include information on the management option chosen for your pregnancy and how your pregnancy progressed. If you take part in this aspect of the study, you will not need to do anything other than give us permission to collect your data. The care you receive will not be affected in any way.

If you agree to take part in an interview, you will be asked to provide your contact details so that a member of the research team can get in touch with you to arrange a convenient date and time for the interview to happen. Your birth partner (if applicable) can also take part in an interview if they wish. If you have any questions about this part of the study, please contact Dr. Kerry Woolfall (Tel: 0151 794 4634, Email: k.woolfall@liverpool.ac.uk). Your interview can be carried out over the telephone, online (via Microsoft Teams or Zoom) or face to face (in line with the latest government guidance on COVID-19), whichever you prefer. It will last approximately 40 minutes and will be arranged at a time that is suitable for you. Before your interview starts you will be asked to give your permission for your conversation to be recorded. This is so that we have a record of your consent if you are having a telephone or online interview. It will also allow us to analyse the information you provide to us at a later date. Due to your experience during pregnancy you may find some parts of the interview upsetting. You are free to decline to answer any questions you do not wish to or to stop the interview at any point. Your interview will be carried out by experienced researchers and any distress will be treated with care and compassion.

Participant Information Sheet

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information collected about you and your babies will be handled in confidence. Any information you provide will only be looked at by the research team and will be stored securely. Your information will be coded, and no personal data will be available to the researchers. With your consent, your GP will be notified of your participation in the study.

How will you use my data?

How will you use information about me?
We (study sponsor – the University of Liverpool) will need to use information from you and from your medical records for this research project.

This information will include your initials, date of birth, NHS number, name, contact details (telephone number and email address), and the first part of your postcode. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are my choices about how my information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can I find out more about how my information is used?
You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to legalservices@liverpool.ac.uk, or
- by ringing us on 0151 795 0523.

Participant Information Sheet

What are the possible benefits of taking part?

Taking part in this study will have no direct benefit to you or your partner (if applicable). It will however, in the long-term, result in a better understanding of the outcomes for sFGR in MC twin pregnancies managed in a variety of ways. This will not only benefit women in terms of counselling as to which pregnancy management option to choose, but will also provide the much needed evidence to design and conduct a future clinical trial comparing these management options. The ultimate goal of such a trial is to establish the best possible way to manage MC twin pregnancies complicated by sFGR.

What are the possible risks of taking part?

Taking part in this study presents no direct risks to you and your partner (if applicable). All the information you provide to us will be collected, stored and used in compliance with data protection regulations (GDPR) and the study will be conducted in accordance with ethical and legal practices.

What will happen if I don't want to continue in the study?

You are free to withdraw from the study at any time, without explanation. The care you or your family receives will not be affected in any way. If you withdraw from the study we will not collect any further information from you. We will however keep and use any information you have already provided.

What will happen to the results of the research study?

It is intended that once the study is complete the results will be used to establish whether a future clinical trial comparing different management options for sFGR in MC twin pregnancies is both feasible and acceptable. We will also use the information you provide to us to help with the design of the trial.

Where can I get further information or discuss any problems?

If you have any questions or concerns about any aspect of this study, please contact a member of the research team (Email Mariana on M.Popa2@liverpool.ac.uk; Tracy on Tracy.Mitchell@liverpool.ac.uk; or Kerry on k.woolfall@liverpool.ac.uk). If your concerns are not resolved, you can visit the Patient Advisory Liaison Services (PALS) by asking at your hospital reception. If you should need additional support to help with any distress arising from your pregnancy you can contact either the Twins Trust (email: support-team@twinstrust.org or telephone: 01252 332 344) or your GP.

Who is organising and funding the research?

The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme is funding this study (Reference: HTA-128596) and Professor Asma Khalil is the study Chief Investigator. The study is sponsored by The University of Liverpool and is managed by the Harris Wellbeing of Women Research Centre, University of Liverpool.

Participant Information Sheet

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed for ethical considerations and given a favourable opinion by members of the South West – Cornwall and Plymouth Research Ethics Committee.

Contact for further information.

Should you have any further queries regarding this study, please contact:

Professor Asma Khalil, Chief Investigator, University of Liverpool / Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool, L8 7SS. Email: fern1@liverpool.ac.uk Tel: 0151 795 9565.

Participant Information Sheet

FERN: Intervention or Expectant Management for Early Onset Selective Fetal Growth Restriction in Monochorionic Twin Pregnancy

Birth partner interviews

We are inviting the birth partners of women pregnant with twins to take part in a research study. Before you decide whether or not to take part it is important for you to understand why the research is being performed and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of our research team will go through the information sheet with you and answer any questions you may have. Please take time to decide whether or not you wish to take part.

Thank you for reading this.

Why are we doing the study?

The UK has approximately 11,000 twin pregnancies per year with a third of these pregnancies sharing a placenta (monochorionic (MC) twins). MC twin pregnancy presents extra risks to both the mother and the babies, with some babies dying during pregnancy or shortly after birth. Often this is due to a complication called selective Fetal Growth Restriction (sFGR), where one twin is smaller than the other. sFGR affects one in seven MC twin pregnancies in the UK although we know less about pregnancies where this happens early (before 24 weeks).

There are three main ways of managing MC twin pregnancies with sFGR: 1) a watch and wait approach (also called expectant management), 2) a procedure that blocks the umbilical cord from the smaller twin to the placenta and causes the loss of the smaller twin (also known as selective termination), and 3) a laser that can be used to completely separate the twins' circulations. All of which present significant risks (death and severe disability) to one or both twins.

At present there is a lack of evidence to tell us the best way of managing sFGR in MC twin pregnancies. Currently, women and their partners are offered different management options depending on where they live and who they see. It is also clear that there are gaps in what we know about sFGR.

To be able to find the best way to manage these pregnancies there is much need for a clinical trial comparing management options. Before running a trial, we need to understand things like how many twin pregnancies would be needed to run the trial and whether parents would think such a trial is acceptable. We also need to work out which management options would be the best to use and what outcomes would be important.

To try to do this we would like to hear about your and your partners pregnancy experience and find out your views and opinions on a potential future clinical trial by inviting you to take part in an interview.

Participant Information Sheet

Why have I been chosen?

We are inviting birth partners of women aged 18 years and older who are currently pregnant (16 - 23 weeks) with an MC twin pregnancy complicated by sFGR or have had an sFGR affected MC twin pregnancy in the last 3 years to take part in this study.

Do I have to take part?

It is up to you to decide whether or not to take part in this study. If you decide to take part - you will be asked to sign a consent form. You will be free to withdraw from the study at any time, without giving a reason. If you decide not to take part – this will not affect the care you or your family receives in any way.

What will happen to me if I take part?

If you agree to take part in the study, you will be asked to provide your contact details so that a member of the research team can get in touch with you to arrange a date for your interview. If you have any questions about the study, please contact Dr. Kerry Woolfall (Tel: 0151 794 4634, Email: k.woolfall@liverpool.ac.uk). Your interview can be carried out over the telephone, online (via Microsoft Teams or Zoom) or face to face (in line with the latest government guidance on COVID-19), whichever you prefer. It will last approximately 40 minutes and will be arranged at a time that is suitable for you. Before your interview starts you will be asked to give your permission for your conversation to be recorded. This is so that we have a record of your consent if you are having a telephone or online interview. It will also allow us to analyse the information you provide to us at a later date. Due to your experience during pregnancy you may find some parts of the interview upsetting. You are free to decline to answer any questions you do not wish to or to stop the interview at any point. Your interview will be carried out by experienced researchers and any distress will be treated with care and compassion.

How will you use my data?

How will you use information about me?
We (study sponsor – the University of Liverpool) will need to use information from you for this research project.

This information will include your initials, name, contact details (telephone number and email address), and the first part of your postcode. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Participant Information Sheet

What are my choices about how my information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can I find out more about how my information is used?
You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to legalservices@liverpool.ac.uk, or
- by ringing us on 0151 795 0523.

What are the possible benefits of taking part?

Taking part in this study will have no direct benefit to you or your partner. It will however, in the long-term, result in a better understanding of the outcomes for sFGR in MC twin pregnancies managed in a variety of ways. This will not only benefit women in terms of counselling as to which pregnancy management option to choose, but will also provide the much needed evidence to design and conduct a future clinical trial comparing these management options. The ultimate goal of such a trial is to establish the best possible way to manage MC twin pregnancies complicated by sFGR.

What are the possible risks of taking part?

Taking part in this study presents no direct risks to you and your partner. All the information you provide to us will be collected, stored and used in compliance with data protection regulations (GDPR) and the study will be conducted in accordance with ethical and legal practices.

What will happen if I don't want to continue in the study?

You are free to withdraw from the study at any time, without explanation. The care you or your family receives will not be affected in any way. If you withdraw from the study we will not collect any further information from you. We will however keep and use any information you have already provided.

What will happen to the results of the research study?

It is intended that once the study is complete the results will be used to establish whether a future clinical trial comparing different management options for sFGR in MC twin pregnancies is both feasible and acceptable. We will also use the information you provide to us to help with the design of the trial.

Participant Information Sheet

Where can I get further information or discuss any problems?

If you have any questions or concerns about any aspect of this study, please contact a member of the research team (Email Mariana on M.Popa2@liverpool.ac.uk; Tracy on Tracy.Mitchell@liverpool.ac.uk; or Kerry on k.woolfall@liverpool.ac.uk). If your concerns are not resolved, you can visit the Patient Advisory Liaison Services (PALS) by asking at your hospital reception. If you should need additional support to help with any distress arising from your pregnancy you can contact either the Twins Trust (email: support-team@twinstrust.org or telephone: 01252 332 344) or your GP.

Who is organising and funding the research?

The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme is funding this study (Reference: HTA-128596) and Professor Asma Khalil is the study Chief Investigator. The study is sponsored by The University of Liverpool and is managed by the Harris Wellbeing of Women Research Centre, University of Liverpool.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed for ethical considerations and given a favourable opinion by members of the South West – Cornwall and Plymouth Research Ethics Committee.

Contact for further information.

Should you have any further queries regarding this study, please contact:

Professor Asma Khalil, Chief Investigator, University of Liverpool / Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool, L8 7SS. Email: fern1@liverpool.ac.uk Tel: 0151 795 9565.

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

FERN: Intervention or Expectant Management for Early Onset Selective Fetal Growth Restriction in Monochorionic Twin Pregnancy

Practitioner interviews and focus group

We are inviting you to take part in a research study. Please take time to read the following information and ask us if there is anything that is unclear or if you would like further details about the study (contact details overleaf).

Why are we doing the study?

At present, there is a lack of evidence to inform the best way of managing Selective Fetal Growth Restriction (sFGR) in monochorionic (MC) twin pregnancies, particularly where this happens early in pregnancy (before 24 weeks). Currently, women and their partners are offered different management options depending on their geographical location and their clinical team. It is also clear that there are gaps in our knowledge in terms of sFGR.

There is a need for a clinical trial comparing different management options for sFGR. Before conducting a trial however, several factors such as the number of twin pregnancies needed to power the trial and whether women and clinicians think such a trial is acceptable and would be willing to participate need to be determined. We also need to establish the best management options to use and the most important outcomes.

We are conducting the FERN feasibility study with the aim of addressing these questions in order to establish the feasibility and design of a clinical trial. We would like to invite you to take part in an interview with one of our team. We may also conduct focus groups with MC twin parents and clinicians if interviews show differences in opinion about the study.

Why have I been chosen?

As you are involved in the care of sFGR in MC twins your views on a potential future clinical trial are important.

What will happen if I take part?

We will ask you to register your interest in taking part in either an interview or a focus group. The email invitation outlines which type of interview we are recruiting to at this point in time. Interviews will take place by telephone, online (via Microsoft Teams or Zoom) or face to face for participants in the North West (in line with the latest government guidance on COVID-19) and will be arranged at your convenience. Interviews will take about 40 minutes. Focus groups will take place online or in a private meeting room at one of the participating FERN research sites (in line with the latest government guidance on COVID-19). The focus group will take about 60 minutes and involve 8-10 site healthcare professionals. All interviews and focus groups will be conducted by the University of Liverpool FERN study team.

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

What will I be asked about?

Interviews and focus groups will explore your views on:

- trial design, including views on active intervention and expectant management, randomisation, outcomes, and approach to recruitment and consent, including consent decision making and length and content of trial information materials,
- factors influencing parent and clinician decision-making when potential outcomes include death or serious disability of one or both twins, and
- acceptability of a future trial, including potential barriers to recruitment, consent decisions, trial procedures, equipoise; inclusion / exclusion criteria and training needs.

How will you use my data?

How will you use information about me?
We (study sponsor – the University of Liverpool) will need to use information from you for this research project.

This information will include your initials, name, and contact details (telephone number and email address). People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are my choices about how my information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can I find out more about how my information is used?
You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.liverpool.ac.uk/legal/data_protection/
- by sending an email to legalservices@liverpool.ac.uk, or
- by ringing us on 0151 795 0523.

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

What are the possible benefits and risks of taking part?

This qualitative component of the FERN study is very low risk. Should you want to discuss any aspect of the study, please contact Kerry Woolfall (details below). Findings of this study will be used to inform the design of a future clinical trial. We cannot promise that you or the families you work with will benefit directly from this study, but many people find that taking part in studies of this sort is useful because they have a chance to reflect and air their views.

Who is involved in this study?

The National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme is funding the study (Reference: HTA-128596) and Professor Asma Khalil is the FERN study Chief Investigator. The study is sponsored by The University of Liverpool and managed by the Harris Wellbeing of Women Research Centre, University of Liverpool. Dr Kerry Woolfall (University of Liverpool) is leading this qualitative component.

What if there is a problem?

Any complaint about the conduct of this study, the way you have been dealt with during the study or any possible harm you might suffer will be addressed. If you have a concern about any aspect of this study, then please speak to a member of the FERN study team who will do their best to answer your questions (see contact details below). If you remain unhappy and wish to complain formally, then you can do this through the NHS Complaints Procedure. Details can be obtained from your employer.

Contact for further information.

If you have any further questions about the interviews or focus groups, please contact:

Dr. Kerry Woolfall, Qualitative Lead, University of Liverpool, Block B Waterhouse Building, 3 Brownlow Street, Liverpool, L69 3GL. Email: k.woolfall@liverpool.ac.uk Tel: 0151 794 4634.

Or

Professor Asma Khalil, Chief Investigator, University of Liverpool / Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool, L8 7SS. Email: fern1@liverpool.ac.uk Tel: 0151 795 9565.

Topic guide for interviewing mothers and birth partners (SOCIAL MEDIA)

Introduction, obtaining consent and any questions

Demographics

- For administration reasons please could you tell me your:
  DOB *(check that they are over 18 years)*,
  Occupation,
  First part of post code,
  Ethnic background,
  How many children do you have and their ages?
  Where you saw the study advertised?

Monochorionic (MC) Pregnancy Experience

If known: My notes from when you registered interest in taking part in this interview state that you had identical twins in (*insert month and year*). Is that correct?

- Please tell me a little bit about your pregnancy?
- When were you admitted to hospital? *(Prompt confirm gestation in weeks)*
- At what point where you made aware that there may be a problem with your pregnancy and that one of your twins was smaller than the other? *(explore how and when this was explained).*
- Who spoke to you about the problem with your pregnancy?
- Can you recall what they told you?
- How did the doctor explain the options you had at that point in time?
  (Explore: What the options were and at what timepoint these were presented? (e.g. Wait and see, selective termination [cord occlusion] or laser treatment- note only one option may have been presented so amend prompts below accordingly).
  - How were you feeling at that point in time?
  - What information was presented to you at that point in time to help to inform your decision? *(e.g. written information or numbers/probabilities of survival)*
  - Where any potential risks discussed for the options presented? *(if so, what risks were discussed for the options presented?)*
  - Where any potential benefits discussed for the options presented? *(if so, what advantages or benefits were discussed for the options presented?)*
  - Did you discuss potential options with anyone else?
  - What type of things did you consider when making the decision about which option to take?
- Could you tell me what happened next? *(Leave this to parent to discuss and tell as much as they would like. Ultimately, we need survival information (may already have this from background question) and how child/children are now).*

FERN Study (refer to draft information sheet)

Have you had chance to look at the draft participant information sheet I sent to you for the proposed FERN study? (If no- read through sheet with parent)

Based on the participant information sheet please describe your understanding of what the FERN study is aiming to do?

What are your initial thoughts about this proposed study?

Would you have any concerns about the FERN study? *(Prompt: after exploring concerns- would you raise these concerns with the nurse or doctor?)*

Would you have any questions about the FERN study?

Looking at the information sheet, are there any parts of the study design that you think parents may find difficult to understand? *(explore language/jargon).*

Are there sections of the information sheet which you would prioritise when making your decision about whether or not to consent? *(Prompt: were there any parts of the information sheet that stood out to you in terms of influencing your decision as to whether or not you would like to take part?)*

Is there anything you would find useful when deciding whether or not you would like to take part?)

What kind of support do you think you would need when deciding whether to participate or not in the trial?

Who else would you need to talk to before making your decision? *(doctors, midwives, research nurses, partner, other family members, friends?)*

Would there be any other information that you would need to help make this decision?

Would you have given your permission to take part in the FERN study?... Could you tell me a bit more about your reasons for this?

How would you feel if you were randomised to 'watch and wait' (expectant management) in the proposed FERN trial?

How would you feel if you were randomised to receive cord occlusion (selective termination) in the proposed FERN trial?

How would you feel if you were randomised to receive laser treatment in the proposed FERN trial?

[If cord occlusion doesn't seem like a viable option], How would you feel if the study were to only have two options – 'watch and wait' and laser treatment? Would this make you more likely to hypothetically take part in the trial?

When do you think is the best time to approach a family to discuss the FERN Study? *(Prompt: we are suggesting within 24 hours)*

How much time would you need to consider the information before making a decision about the FERN Study?

Who do you think would be the best person to approach a family and when should this person go back or call the family again? *(look into where potential participants would be).*

Outcomes

As we have discussed, in the FERN study we want to find out the best way to manage monochorionic (MC) twin pregnancies.

To do this we will collect information *on (read through outcome measures list sent prior to interview).* By collecting information on these main things, we hope to find out which approach to managing MC twin pregnancies should be used in the future. These are called outcome measures.

It is important that we include outcome measures that matter to parents.

Thinking about your pregnancy what would you hope the outcome of your pregnancy management would be? (*Prompt: what effect would the approach to managing your pregnancy have to be most effective?*

- What would you be looking for as an indicator that your pregnancy was being managed well?
- What do you think about the outcome measures (*re-cap measures in the list provided*)?
- Is there another outcome measure that you think is important to families which we should be collecting information about in the FERN Study? (*prompt: present identified outcome measures based on responses to first two questions*)

Recap on outcomes measured and ask them to put in order of importance *(e.g. So far, you have mentioned x outcomes, X, Y & Z. Which would you say is the most important for this study? Second most important for this study?)*

Finally, is there anything else you would like to say about this proposed new study?

INTERVIEW TOPIC GUIDE FOR PRACTITIONERS

FERN: Intervention or Expectant Management for Early Onset Selective Fetal Growth Restriction in Monochorionic Twin Pregnancy

Introductions and obtaining consent for audio recording

Section 1. Role and Background

1.1 Please tell me what your role is
1.2 How long have you been involved in the clinical management of sFGR?
1.3 How much, if any, experience do you have in recruiting to clinical trials?

Section 2: Current Practice

2.1 Could you please describe to me what your usual practice is for the management of sFGR in MC twin pregnancies with early-onset (prior to 24 weeks) sFGR?
Prompt: explore responses in reference to the management options in the box above. Explore: which options are preferred or most commonly used by you / your unit. If a particular option isn't used explore why (e.g. personal preference, not current practice on unit, or any barriers such as resources to provide a particular option)
2.2 What factors do you consider when making decisions about which management option would be most appropriate for individual patients?
Explore: what influences your decision making when death or serious disability of one or both twins are potential outcomes?
2.3 Who do you consult with when making these decisions?
Explore: which clinical colleagues
2.4 At what point/when do you think is the best time to approach mothers/partners to discuss management options with them?
2.5 I'm sure these are very difficult conversations to have with mothers / partners. Do you or your colleagues present a number of options for them to consider?
Explore: which management options do you present them with? Explore, which and what information is provided in these discussions
2.6 How do you present the benefits and risks of each option presented/what wording do you use? *(identify the wording used to present the risks and benefits of the three (if applicable) options)*
2.7 Could you tell me if there is anything that mothers and partners tend to prioritise when making a decision about pregnancy management options?
2.8 What questions do they ask?
2.9 Do they need any support or additional information when making this decision?

Section 3: Role and Involvement in the FERN Feasibility Study

3.1 Have you been involved in the WP1 – collecting prospective data on the management and clinical outcomes of MC pregnancies complicated by sFGR? ***(If no go to Section 3.6 - questions about inclusion and exclusion criteria)***
3.2 Which elements of this work package have you been involved in? Explore: screening patients, consenting patients

If screening:
3.3 Could you talk me through the screening process?
3.4 Have any potential participants been missed? Please elaborate
3.5 Do you think the screening process could be improved if we moved to a full trial comparing intervention versus expectant management of sFGR in MC twin pregnancy? (Yes/No) *Discuss potential challenges to screening or systems that have been put in place to assist screening.*

Inclusion and Exclusion Criteria

3.6 Do you have any comments or suggested changes for proposed inclusion and exclusion criteria that we sent you by email? Do you have this to hand?

Mitchell TK, *et al. BMJ Open* 2024; 14:e080488. doi: 10.1136/bmjopen-2023-080488

INTERVIEW TOPIC GUIDE FOR PRACTITIONERS

3.7 Are there patients you think we should definitely **NOT** include in this proposed trial? *Explore who, why or why not*

Section 4: Defining Management Options (section to be informed and developed in light of any key WP1 findings of relevance)

I have a few questions about your unit's clinical management for these pregnancies

4.1 How often do you repeat the ultrasound in these pregnancies (e.g. once or twice/week)?

4.2 What is the gestation at delivery?

4.3 What are the triggers for delivery or intervention?

4.4 If you do need to intervene, which form of intervention do you use, selective termination or laser treatment? (if not clear, ask)

4.5 What determines your choice of a particular intervention?

CONSULTANTS ONLY

4.6 What is your management protocol if complications occur:

a) single intrauterine death (IUD) if the pregnancy is managed expectantly,

b) Single IUD if the pregnancy was treated by laser,

c) Preterm Premature Rupture Of Membranes (PPROM) if the pregnancy was treated by laser or cord occlusion,

d) the pregnancy developed twin anaemia polycythemia sequence (TAPS),

e) the pregnancy developed TAPS after laser or cord occlusion.

4.7 Does your personal clinical management of such pregnancies differ from your unit's management protocol?

Explore: how and examples of what informs decision making

Section 5. Acceptability and Trial design

Check if the participant is familiar with the proposed trial design:

Women aged 18 years and older who are pregnant (16-23 weeks) with an MC twin pregnancy complicated by sFGR will be invited to participate in the FERN study. If they agree to take part in the study we will use a computer to decide at random which management option 1), 2) or 3) is followed.

1) Expectant: close monitoring but no active intervention. This carries a risk of death of the smaller twin. Death of the smaller twin may result in demise of the larger twin (40%) or disability (30%).

2) Selective termination of the smaller twin. This may protect the larger baby from harm if the smaller twin were to subsequently die. However, termination may not be acceptable to some parents.

3) Selective placental laser photocoagulation of connecting vessels. This is likely to be a complex surgery where Laser is used to close the connections between the babies in the placenta. It may worsen outcomes for the smaller twin.

5.1 Given the proposed trial arms, how acceptable would you find expectant management (e.g. close monitoring but no active intervention) of the sFGR twin as a trial arm?
Explore reasons including anything that would make this arm of the trial more or less acceptable

5.2 At the moment, the trial is exploring selective termination and laser treatment as two separate intervention arms. How acceptable would you find selective termination (e.g. cord occlusion) of the sFGR twin as a trial arm?
Explore reasons including anything that would make this arm of the trial more or less acceptable.

5.3 How acceptable would you find selective laser treatment as a trial arm? *Explore reasons including anything that would make this arm of the trial more or less acceptable*

5.4 How acceptable do you think it is that the decision about which treatment option in the intervention arm is made by a consultant or the parent?

5.5 Would you be willing to randomise women to the proposed FERN RCT?
Explore: any concerns about randomising patients to either expectant management or active intervention being different from how they would personally manage such pregnancies.
The following is informed by the discussion around the acceptability of the trial design, especially If proposed trial/trial arms do not seem acceptable:

5.6 Is there an alternative trial design that you'd suggest?

Mitchell TK, *et al. BMJ Open* 2024; 14:e080488. doi: 10.1136/bmjopen-2023-080488

INTERVIEW TOPIC GUIDE FOR PRACTITIONERS

Section 6. Parents discussion

6.1 Considering the suggested trial design, how do you think mothers / partners will react to being asked to participate in the FERN RCT?
6.2 How long do you think mothers / partners will need to consider trial participation?
6.3 What timeframe (post screening) do you think we should approach mothers / birth partners about trial participation? *Explore: minimum and maximum time frames*
6.4 Would you have any concerns about discussing this RCT with mothers and partners?

Section 7. Training and Resources for the Proposed FERN RCT

7.1 Is there anything specific that you would suggest we include in the FERN site training package?
7.2 Do you envisage any potential barriers to training staff for the proposed FERN RCT?
7.3 Are there any particular resources or other support that you would need to deliver the proposed FERN RCT at your site?

Section 8: Outcomes

Ask participants to refer to the list of outcomes sent prior to the interview.
8.1 Are there any outcomes that you think are important that are not included in the list?
8.2 What do you think would be an appropriate primary outcome for the proposed FERN RCT? *Explore: reasons and alternatives*
8.3 What secondary outcomes would you suggest we measure?
8.4 Considering the outcomes we have just discussed what order would you rank them in, starting with the most important outcomes to measure for this trial and then working down.

Section 9: Overall acceptability

9.1 Overall how acceptable do you think it is to conduct a randomised controlled trial (RCT) exploring active intervention and expectant management for sFGR in MC twins?
Explore answers and rationale
9.2 How do you think you would feel if you were involved in this trial?
Explore: any concerns about decisions about active intervention or expectant management being taken away from them as an individual.
5.7 Do you think a trial exploring active intervention and expectant management is practically possible to conduct? Yes / no *Explore: reasons*, Prompt: logistics and potential solutions

Section 10: Anything Additional

Before we finish, is there anything you think is important for us to know if we conducted the proposed FERN RCT which we have not already covered?

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			4
Personal characteristics			4
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	4
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	4
Occupation	3	What was their occupation at the time of the study?	4
Gender	4	Was the researcher male or female?	4
Experience and training	5	What experience or training did the researcher have?	
Relationship with participants			S. Files 1-5, 7-9
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	S. Files 1-5, 7-9
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	S. Files 1-5, 7-9
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	4-5
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	4
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	4-6
Sample size	12	How many participants were in the study?	5-6
Non-participation	13	How many people refused to participate or dropped out? Reasons?	5
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	5-6
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	N/A
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	6
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	4;S.Files1-5,7-9
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	N/A
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	5
Field notes	20	Were field notes made during and/or after the inter view or focus group?	N/A
Duration	21	What was the duration of the inter views or focus group?	6
Data saturation	22	Was data saturation discussed?	4-5
Transcripts returned	23	Were transcripts returned to participants for comment and/or	N/A

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			5
Data analysis			
Number of data coders	24	How many data coders coded the data?	N/A
Description of the coding tree	25	Did authors provide a description of the coding tree?	5
Derivation of themes	26	Were themes identified in advance or derived from the data?	5
Software	27	What software, if applicable, was used to manage the data?	4
Participant checking	28	Did participants provide feedback on the findings?	
Reporting			7-13
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	7-14
Data and findings consistent	30	Was there consistency between the data presented and the findings?	7-13
Clarity of major themes	31	Were major themes clearly presented in the findings?	7; 13
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

THANK YOU FOR TAKING THE TIME TO READ AND CONSIDER THE DRAFT PROPOSED RCT INFORMATION SHEET. TO BE USED IN CONJUNCTION WITH THE INTERVIEW TOPIC GUIDE PARENT VERSION 1.0 26082020

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

FERN: Intervention or Expectant Management for Early Onset Selective Fetal Growth Restriction in Monochorionic Twin Pregnancy

We are inviting women pregnant with twins to take part in a research study. Before you decide whether or not to take part it is important for you to understand why the research is being performed and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of our research team will go through the information sheet with you and answer any questions you may have. Please take time to decide whether or not you wish to take part.

Thank you for reading this.

Why are we doing the study?

The UK has approximately 11,000 twin pregnancies per year with a third of these sharing a placenta (monochorionic (MC) twins). MC twin pregnancy presents extra risks to both the mother and the babies, with some babies dying during pregnancy or shortly after birth. Often this is due to a complication called selective Fetal Growth Restriction (sFGR), where one twin is smaller than the other. sFGR affects one in seven MC twin pregnancies in the UK although we know less about pregnancies where this happens early (before 24 weeks).

There are three main ways of managing MC twin pregnancies with sFGR: 1) a watch and wait approach (also called expectant management), 2) a procedure that blocks the umbilical cord from the smaller twin to the placenta and causes the loss of the smaller twin (also known as selective termination), and 3) a laser that can be used to completely separate the twins' circulations. All of which present significant risks (death and severe disability) to one or both twins.

At present there is a lack of evidence to tell us the best way of managing sFGR in MC twin pregnancies. Currently, women and their partners are offered different management options depending on where they live and who they see. It is also clear that there are gaps in what we know about sFGR.

To be able to find the best way to manage these pregnancies there is much need for a clinical trial comparing management options.

Why have I been chosen?

We are inviting all women aged 18 years and older who are currently pregnant (16 - 23 weeks) with an MC twin pregnancy complicated by sFGR.

THANK YOU FOR TAKING THE TIME TO READ AND CONSIDER THE DRAFT PROPOSED RCT INFORMATION SHEET. TO BE USED IN CONJUNCTION WITH THE INTERVIEW TOPIC GUIDE PARENT VERSION 1.0 26082020

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

Do I have to take part?

It is up to you to decide whether or not to take part in this study. If you decide to take part - you will be asked to sign a consent form. You will be free to withdraw from the study at any time, without giving a reason. If you decide not to take part – this will not affect the care you or your family receives in any way.

What will happen to me if I take part?

There are three main ways of managing MC twin pregnancies with sFGR: 1) a watch and wait approach (also called expectant management), 2) a procedure that blocks the umbilical cord from the smaller twin to the placenta and causes the loss of the smaller twin (also known as selective termination), and 3) a laser that can be used to completely separate the twins' circulations. All of which present significant risks (death and severe disability) to one or both twins.

If you are currently pregnant and you agree to take part in the study we will use a computer to decide at random which management option 1), 2) or 3) is followed.

1) Expectant: close monitoring but no active intervention. This carries a risk of death of the smaller twin. Death of the smaller twin may result in demise of the larger twin (40%) or disability (30%).
2) Selective termination of the smaller twin. This may protect the larger baby from harm if the smaller twin were to subsequently die. However, termination may not be acceptable to some parents.
3) Selective placental laser photocoagulation of connecting vessels. This is likely to be a complex surgery where Laser is used to close the connections between the babies in the placenta. It may worsen outcomes for the smaller twin.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information collected about you and your babies will be handled in confidence. Any information you provide will only be looked at by the research team and will be stored securely. Your information will be coded, and no personal data will be available to the researchers. With your consent, your GP will be notified of your participation in the study.

THANK YOU FOR TAKING THE TIME TO READ AND CONSIDER THE DRAFT PROPOSED RCT INFORMATION SHEET. TO BE USED IN CONJUNCTION WITH THE INTERVIEW TOPIC GUIDE PARENT VERSION 1.0 26082020

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

How will you use my data?

How will you use information about me?
We (study sponsor – <<insert Sponsor name>> will need to use information from you and from your medical records for this research project.

This information will include your initials, date of birth, NHS number, name, contact details (telephone number and email address), and the first part of your postcode. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no one can work out that you took part in the study.

What are my choices about how my information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can I find out more about how my information is used?
You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to legalservices@liverpool.ac.uk, or
- by ringing us on 0151 795 0523.

THANK YOU FOR TAKING THE TIME TO READ AND CONSIDER THE DRAFT PROPOSED RCT INFORMATION SHEET. TO BE USED IN CONJUNCTION WITH THE INTERVIEW TOPIC GUIDE PARENT VERSION 1.0 26082020

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

What are the possible benefits of taking part?

The results of this study will benefit women for counselling as to which management option is best for the smaller and larger twin; both short-term (such as risk of death during pregnancy or in the neonatal period or risks of prematurity) or long-term (such as the risk of disability in the surviving babies).

Taking part will also result in a better understanding of the outcomes for sFGR in MC twin pregnancies managed in a variety of ways and will benefit women in terms of counselling as to which pregnancy management option to choose in the future.

The ultimate goal of this study is to establish the best possible way to manage MC twin pregnancies complicated by sFGR.

What are the possible risks of taking part?

Taking part in this study presents a possible risk to the babies mainly (risk of death whether during pregnancy or the neonatal period, risk of prematurity including the risk of disability) and the mother (likely to be small and related to the surgery, e.g. fetoscopic Laser surgery or selective termination of the smaller twin). Surgical risks include risk of bleeding, infection or injury to internal organs, but as the surgery is usually performed using minimally invasive techniques, the risks are likely to be small.

All the information you provide to us will be collected, stored and used in compliance with data protection regulations (GDPR) and the study will be conducted in accordance with ethical and legal practices.

What will happen if I don't want to continue in the study?

You are free to withdraw from the study at any time, without explanation. The care you or your family receives will not be affected in any way. If you withdraw from the study we will not collect any further information from you. We will however keep and use any information you have already provided.

What will happen to the results of the research study?

It is intended that once the study is complete the results will be publication in peer reviewed journals, presented in national and international scientific meetings and shared with pregnant women through social platforms and the Twins Trust website.

THANK YOU FOR TAKING THE TIME TO READ AND CONSIDER THE DRAFT PROPOSED RCT INFORMATION SHEET. TO BE USED IN CONJUNCTION WITH THE INTERVIEW TOPIC GUIDE PARENT VERSION 1.0 26082020

(To be printed on Hospital Trust headed paper)

Participant Information Sheet

Where can I get further information or discuss any problems?

If you have any questions or concerns about any aspect of this study, please contact a member of the research team on <<insert telephone number>>. If your concerns are not resolved, you can contact the Patient Advisory Liaison Services (PALS) on <<insert telephone number>>. You can also visit PALS by asking at your hospital reception. If you should need additional support to help with any distress arising from your pregnancy you can contact either the Twins Trust (<<insert email address / telephone number>>) or your GP.

Who is organising and funding the research?

<<insert Funder name>> is funding this study and Professor Asma Khalil is the study Chief Investigator. The study is sponsored by <<insert Sponsor name>> and is managed by the <<insert Research Centre name>>.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed for ethical considerations and given a favourable opinion by members of the <<insert REC name>> Research Ethics Committee.

Contact for further information.

Should you have any further queries regarding this study, please contact:

Professor Asma Khalil, Chief Investigator <<insert contact details>>

FERN: Outcomes

THIS INFORMATION WILL BE EXPLAINED TO YOU FULLY DURING YOUR INTERVIEW

- An outcome measure refers to **'what'** should be measured in a research study to find out whether a treatment is effective.
- Studies often have a number of outcome measures to determine whether a treatment is effective.
- Researchers or doctors often suggest what outcomes should be measured in a research study. However, they do not always fully understand what it's like to be the mother or partner of a mother who has a problem with their pregnancy. That is why it's important we ask parents/guardians what outcomes they think a research study should measure to determine whether a treatment is effective.
- Below is a list of outcomes that might be useful to measure. During your interview, we will ask you what you think about the outcome measures on this list.
- It's not a test! We just want to make sure we include outcomes that are important to parents and children.

Mitchell TK, *et al. BMJ Open* 2024; 14:e080488. doi: 10.1136/bmjopen-2023-080488

- Live birth (baby is breathing or shows any other evidence of life such as beating of the heart, voluntary muscles are moving, and umbilical cord is pulsating at birth)
- Gestational age at birth (the period of time between conception and birth)
- Birth weight
- Intertwin birth-weight discordance
- Death of surviving twin after death of cotwin
- Loss **during** pregnancy **or before** final hospital discharge (miscarriage, stillbirth, termination of pregnancy, neonatal death, perinatal death)
- Parental stress
- Procedure-related adverse outcome (failure of procedure, procedure-to-delivery interval, placental abruption, life-threatening haemorrhage, sepsis, maternal death)
- Length of stay in hospital (neonatal)
- Neurodevelopment impairment / Cognitive ability (how your baby's brain develops and functions)
- Childhood disability (for example, growth, breathing, hearing, visual and gross motor impairments, activity limitations and participation restrictions)
- Child quality of life
- Parent quality of life

Inclusion and exclusion criteria

Inclusion Criteria:

- Monochorionic diamniotic twin pregnancy
- Diagnosis of sFGR (estimated fetal weight (EFW) of one twin <10th centile + EFW discordance >25%)
- Gestational age at diagnosis between 16+0 - 23+6 weeks based on ultrasound
- Informed consent given by the participant and consent form completed and signed

Exclusion Criteria:

- Singleton pregnancies
- Maternal age under 18 years
- Other MC complications; twin to twin transfusion syndrome (TTTS), twin anaemia polycythaemia sequence (before enrolment), other rare complicated MC twin pregnancies, such as twin reversed arterial perfusion syndrome
- Known karyotype abnormality at enrolment
- Known major fetal structural abnormality at enrolment, defined as a lethal, incurable or curable severe abnormality with a high risk of residual handicap
- Indication for immediate delivery
- Pre-term pre-labour rupture of membranes before enrolment
- Women who lack the capacity to give informed consent
- Any medical or psychiatric condition which compromises the woman's ability to participate

Clinician suggestions for additions or amendments to the proposed FERN inclusion and exclusion criteria

Clinician suggestions for additions or amendments to the proposed inclusion criteria		
Inclusion criteria should include:	**Women with Type II sFGR only**	*'I wouldn't take part in it for Type I'* (C3, Doctor). *'I wouldn't agree with offering them intervention if they were Type I sFGR'* (C8, Doctor). *'Expectant management is typically the best option for Type I sFGR. Intervention (in the form of selective termination) is typically the best for Type II sFGR, and … is typically the best for Type III sFGR'* (C2, Doctor). *'Type I would never be an indication for doing a cord coagulation because it's a good prognosis, as long as you have positive flow in the umbilical artery of the smaller foetus. But on the other hand, in Type II, it's quite well predictable when there is foetal deterioration, because you can do it via extensive monitoring, and you look at the foetal circulation… Certainly, Type II would be the one which would qualify most or is most convincing if you decide to do cord coagulation… But if there is persistent reverse flow in the umbilical artery, or zero flow from a very early stage onwards, then the situation is different. It's a very high risk that the smaller baby will die at a certain point. And that's what you want to… So uncontrolled death, let's say, that's one you would like to avoid by doing the study, because the theory would be, or the hypothesis, that it's better to do it in a controlled way by cord coagulation. It's better for the surviving, for the second twin, the normally growing twin. And, at the end of the day, you accept the loss of the smaller twin for the sake of the bigger twin'* (C13, Doctor).
	Women with an abnormal ductus venosus Doppler (and carefully consider how the timing of diagnosis can impact the outcome):	*'For the ones where I'm pretty sure that the baby is going to die, that's your ductus venosus A wave absent or reversed, I think it's right that the parents should be able to choose in those situations'* (C8, Doctor). *'I would be stricter on the degree of Doppler abnormalities in the smaller baby regarding ___and umbilical artery and the timing of onset. Yeah, like when there's a big difference when you first diagnose at 23^{+6} weeks or whether it's already there at 16 weeks. So, we know that the earlier, the worse the outcome'* (C2, Doctor). *'If you put … ductus venosus, DV Doppler. This is a severity criteria but actually the children with abnormal ductus venosus are at the highest risk'* (C10, Doctor).
Amend these inclusion criteria:	**Estimated fetal weight of one twin to be less than the 3rd Centile** (rather than less than the 10th centile):	*'Move… to less than the third centile… to catch the more severe cases'* (C8, Doctor). *'Maybe you should say, "One twin below the third centile," because then you are sure that it is really a tiny one, or making the estimated foetal weight [discordance] bigger'* (C14, Doctor).

	Estimated fetal weight discordance to be more than 40% (not more than 25%):	*'I think the other thing that they should consider adding in the inclusion criteria is the degree of growth discordance, because I think that is where the real uncertainty is. So, for example, if you've got, at 18 weeks, a 40% growth discordance, then it is more likely to deteriorate, the Dopplers are more likely to deteriorate quicker. So, maybe specifying the degree of growth discordance, and maybe more than 40% or more, yeah, at that gestation, because I think there is a dilemma there in terms of clinical management'* (C8, Doctor). *'If it's a severe Type II, then the discordance doesn't matter. Like, in my opinion, I think it's not so much the discordance that matters. I think you can easily take also more than a 20% difference in estimated foetal weight. It's more the Dopplers that matter. So, I would be less strict on the estimated foetal weight'* (C2, Doctor).
	Split estimated fetal weight/weight discordance into two groups – those with mild and those with severe.	*'The main problem I foresee: that in the current inclusion criteria a milder and a very severe group are merged together. If you want to offer laser, I would say that you should offer that, but it is an interesting thing to offer in the milder group'* (C14, Doctor).
	The **gestational age at diagnosis should be between 18^{+0} [or 20]** (not 16^{+0}) **and 23^{+6} [or 27^{+6}] weeks** based on ultrasound:	To account for abnormal Dopplers that you can get at 16 weeks *'just because of an early gestation effect'* and *'to try and maybe rule out and try and be more specific that we've got the right group of patients and growth-restricted foetuses with Type II selective IUGR'* (C8, Doctor). *'I would advocate [the inclusion criteria to be] at least … 20 weeks… and second measurement… [and] a little bit more focused to slightly more severe [sFGR]* (C14, Doctor). And *'maybe with the chance to recruit right up to 27^{+6}'* (C11, Midwife).
Clinician suggestions for additions to the proposed exclusion criteria/Defining current proposed exclusion criteria carefully		
Exclusion criteria should include	**Diagnosis of Type I sFGR**	*'I think most Type I and Type III cases do well without any treatment. So, yeah, I think the criteria are not… These are not severe enough'* (C2, Doctor). *'Definitely Type I, because I really don't think it's fair to offer those women that can actually… Where the pregnancies can go on for weeks and weeks, to offer them an intervention that puts them at risk of miscarriage. I think we'll be doing harm there. So, I think Type I should be an exclusion criterion… I certainly wouldn't be offering intervention for Type I IUGR''* (C8, Doctor).

		'It might be difficult to offer it if it is Type I was normal Doppler in a smaller baby' (C1, Doctor). *'Type I would never be an indication for doing a cord coagulation because it's a good prognosis, as long as you have positive flow in the umbilical artery of the smaller foetus… so I would never randomise to cord occlusion… because they have a good prognosis'* (C13, Doctor).
	Diagnosis of Type III sFGR	*'I think most Type I and Type III cases do well without any treatment. So, yeah, I think the criteria are not… These are not severe enough'* (C2, Doctor). *'I've looked after a number of Type III's, and I find that I can usually take both babies to 28 weeks, 26 to 28, where they're both viable… the chances of survival are very good at 28 weeks, but I've monitored them like a hawk… I've not lost a single baby earlier than that, that I've looked at for type three. So, with my own experience with Type III, I wouldn't offer it for Type III'* (C8, Doctor). *'And it's similar with class [Type] III, because our experience also has been described in longitudinal observational studies, that they had a very good chance to get on until 30/32 weeks, because they have this arterial anastomosis, which seems to be good for them, let's say it like that. And therefore, I would be hesitant to randomise them'* (C13, Doctor).
	Bleeding in pregnancy	*'Bleeding in pregnancy, so bleeding increases the risk of … miscarriage, and I'm not sure it's fair to put those patients through that'* (C8, Doctor).
	Women with a BMI of over 40	*'I suppose if you were doing a bipolar cord occlusion or an RFA it is- I don't know. I don't do those, so I don't know how technically difficult it is. But I don't know whether a BMI over 40 would make it tricky'* (C3, Doctor).
Define these exclusion criteria more carefully:	**Twin to twin transfusion syndrome (TTTS)**	*'We have found clinically often there can be a bit of a combination of both'* TTTS and sFGR (C3, Doctor). *'Sometimes it is a little bit of a grey area between twin-to-twin and selective IUGR. So, … the two conditions may concur concurrently. I think about a third of selective IUGR babies, twins, also have*

		superimposed twin-to-twin transfusion' (C7, Doctor).
	Known karyotype abnormality at enrolment	*'I think with monochorionic twins, selective foetal growth restriction is more likely to be secondary to placental problems, rather than karyotypic abnormality. So, I wouldn't make an amniocentesis or a karyotype a requirement'* (C8, Doctor).

Application of FERN qualitative (WP2) findings to the Principles of Biomedical Ethics (Beauchamp and Childress, 2019)

Biomedical ethics principle	Clinician views	Parent views
Respect for Patient Autonomy - Supporting parents' decision making and giving parents the freedom to choose how their pregnancy is managed	Although clinicians might support parents with their decision making, their background and culture can impact parent autonomy. Parents find it ethically challenging to terminate the life of one or both their twins. *'I think ethically, if the women are consenting to that and are fully informed, I don't think there's too much of a problem there ethically, because the pregnancies are very, very high risk. And I think as long as the women are fully informed and have had a big discussion with the clinician, which they will do, then I think that's probably okay'* (C5, midwife) – but the trouble is 'Veracity' because there is a paucity of evidence available about outcomes for Type I and Type III sFGR. *'I think including a third arm of selective termination would exclude a lot of people, I think they wouldn't necessarily take part if that was one of the arms. That arm of selective termination may be the barrier to some people signing up to the trial… termination is not an option for… Asian or ethnic minority population'* (C7, doctor) or parents from Ireland: '*the culture … [and] general consensus … of the population [area or country] and how they see things'* (C10, doctor). *'But I think culturally women are still quite- And I am sure it will change with time, but I know if we offer feticide to women with fetal abnormality a lot of them just will continue the pregnancy rather than them having the feticide procedure'* (C3, doctor). Parents *'struggle with … the decision to actually actively choose to terminate the life of one baby… [even] when trying to save the life and optimise the outcome of the other baby'* (C8, doctor).	Parents felt (or were told by clinicians) that they were unequipped to make decisions about which pregnancy management route to take. Parent were not always given all the management options. Although parents would have the choice in whether to participate in the RCT or not, they would be randomised to a pregnancy management option which they would not choose and which goes against autonomy. Parents can feel pushed into making decisions within the legal timeframe for termination: *'If they are given an option, every woman has the right to decide which option they take. I just feel, for me, that the prerequisite or the criteria probably should be thought about a little bit more. It should be based on individual cases, how you select it, as opposed to randomly, any woman that has this diagnosis'* (P19, mother, site). *'We went back into the hospital and then I think they had realised that, probably because we had been gone so long, I don't know, that maybe we were not equipped to make this decision… 'She had opportunity to say, "Actually I think this is the wrong course" [expectant management]. Because they said, "You can change your mind. You've got up until 26 weeks to change your mind." We still had a few weeks, even though I think we probably wouldn't have wanted to push it. I don't know'* (P2, bereaved mother, social media). *'At that point the consultant was like, "We're going to run out of time for you to have anything done. If you do want to do selective termination, you need to do that now'* (P11, mother, social media). *'One of those options is choosing to have an abortion, which I know a lot of people feel very strongly about. I don't think I'd participate. I'd rather feel like I was getting the balanced view*

		from your doctors and your consultants about what they think will be the best option for you and your individual circumstances, rather than it being random' (P3, mother, currently pregnant, site). *'I think one of the options they also gave us was, "You don't have to come in and have scans, you can just say goodbye and not have a conversation with us again until birth." They obviously, at that point, said, "We don't recommend that one in particular," but that was still given as an option, of, "You don't have to do any of this that we're talking about. It's your body, your children, etc., you can do what you would like to do"'* (P14, partner, social media).
Beneficence - Doing their best to save the lives of one or both babies	Clinicians indicated that they wanted to save the lives of at least one, but preferably both babies – Live birth was the top ranked outcome for clinicians and parents. The proposed trial will answer an important research question to guide clinical practice and discussions with parents*:* *'I have had patients come to me who were offered a selective termination within somebody from the team, and I felt that it was a different type of selective IUGR. So, somebody thought it was Type II but I thought it was Type III, and I would manage Type III differently… Somebody in the team thought it was Type II, which deteriorates much faster and in a predictable way. And Type III can go on for a long, long time, but it's an unpredictable, sudden loss. So, I have scanned a patient like that, where I was asked for a second opinion, and I said that, "This is Type III and I wouldn't offer a termination." I wouldn't offer a termination… And we took them to 26-plus weeks, and they delivered the twins, both alive, and I get pictures from them still, and they're so grateful. And they do say that, that, "Oh, we were offered a termination, but actually, you said that it was okay and we just carry on. And we're so grateful to you that both our babies are here today""'* (C8, doctor).	Parents wanted to save the lives of both babies – Live birth was the top ranked outcome for parents and clinicians. '*I knew that if we intervened Twin 2 would almost certainly die. But we did decide, they seemed to think he wasn't going to survive anyway so we sort of came to the decision that we had a responsibility to Twin 1 to do what was best for him*' (P2, bereaved mother, social media). *'I think I would need statistics to show me that it was better for the bigger baby, that their chances of being born healthy were significantly better if the cord occlusion took place. I think because my smaller twin was always really healthy, that would've always been a no from us. But had our smallest twin shown signs of being poorly or showing signs of not being compatible with life once they were born, that would've made a difference'* (P4, mother, social media).
Justice - Supporting parents and their babies' legal rights, allocating resources,	Selective termination of smaller twin does not support that twin's legal right. There is not enough evidence to show the risks of intervention to the larger twin:	'*By sacrificing those babies who might have survived in order to increase the chance of future babies surviving it feels wrong to me'* (P18, partner, site).

equal respect, non-discrimination	'*Most centres would go for cord coagulation of the smaller twin. But, on the other hand, that means that, by default, by definition, this means mortality for this pregnancy of 50%. It's foetal mortality, because it's like controlled feticide. And therefore…Well, it would be possible, it is also ethically and legally possible in [European Country], but we also have the experience that there is still a higher than 50% double survival rate in selective foetal growth restriction, if you have conservative monitoring. So why would you do a selective cord coagulation in the first place? The main argument for doing a cord coagulation is that it may prevent damage to the surviving foetus, because you have closed the vascular circulation of that foetus. But, on the other hand, no trial so far has ever shown that the neurological morbidity is lower after cord coagulation of the surviving twins than if you have conservative management, which may include intrauterine foetal death of one of the twins and then the other one is at risk as well*' (C13, doctor).	'*I knew that if we intervened Twin 2 would almost certainly die. But we did decide, they seemed to think he wasn't going to survive anyway so we sort of came to the decision that we had a responsibility to Twin 1 to do what was best for him'* (P2, bereaved mother, social media) – parents ended up going with expectant management, lost both twins.
Non-Maleficence - Not harming parents or their babies	Every case needs managing differently. Some clinicians felt strongly that the trial inclusion criteria should only include women with Type II sFGR and women with an abnormal umbilical artery Doppler Types I and III generally do not require intervention. A clinician (C8, doctor) recalled that they gave a second opinion on a colleague's recommendation for selective termination and found that the sFGR was type III, and not type II, so recommended expectant management. The family had two healthy children and send photographs to them every year thanking them for not terminating the life of their smaller twin who is healthy (see quote in 'Beneficence'). Similarly, to reduce harm to parents, discussions regarding the different management options should be tailored to each individual depending on the severity of their pregnancy, because even the mention of selective termination causes long-term harm to parents: *'But what you also see, if patients are rational and can cope with these kinds of things, that is a good approach, but you also see, in our hospital, we do a lot of follow-up visits also at the age of four, eight and twelve years old. Then, still, people are telling to the psychologists who do, they also do Bayley Scales testing and that kind of thing, that the mentioning of the option of cord occlusion was one of the worst things*	Evidence of potential long-term harm to parents by them being offered and even considering selective termination of one of their twins. Regret for a bereaved mother for not choosing the selective termination option. Regret for the mother of two healthy twins that they even considered selective termination: *'Did they [parents] survive emotionally… after the decisions… to terminate one of these kids? … I am not going to go and kill myself because I have made the wrong decision? ... How the hell do you, as a mother, cope? I don't want to think about it. Not even close to wanting to think about it. But it is one of those questions you have to ask yourself*" (P16, Mother, site). One mother, who had initially decided to take the intervention route but had been told by the consultant to *'do nothing'* and whose twins had both gone on to die in utero at just over 26 weeks, said that *'if there had been conclusive evidence that had said intervention was the better option, I would have done it. I would have gone back the next day and done it'* (P2, bereaved mother, social media). On the other hand, a mother who had Type II sFGR (from which she understood, and from what a clinician also said was the type *'that has the most negative outcomes'* (P9, mother, social media) *'without intervention [when] abnormal ductus venosus'* (C8, doctor) who

	that happened to them in the monitoring of the pregnancy. So, I think, as FMFs, because those people are with the paediatrician, of course, we don't see those patients back again. As FMF, we should take this into account. Those patients who are traumatised by mentioning the option of cord occlusion, they say, they report back, that every time they entered the hospital – and it was sometimes far later – we, as the doctors, already thought that there was a forgotten option, if you understand what I mean, but the patient, the parents themselves, felt that every time they visited the hospital the doctor could say that one of the babies had to die' (C14, doctor).	was not given a choice and was put onto the expectant management route and whose twins were both born and remain healthy and free of any disability at 17 months old said *'if I'd been selected into the cord occlusion [selective termination], it's a [her smaller twin's] life that, potentially, wouldn't need to have been lost there'* (P9, mother, social media); a healthy baby's life would have been ended.
Fidelity - Being loyal and providing parents with support throughout their pregnancy and the post-natal period; being worthy of a patient's trust	Clinicians monitor their patients *'like a hawk'* and are *'really invested in them':* *'Type III, I would want to consider that carefully, and I'd probably want to have a discussion with other experts in terms of their experience. But, I'm uncomfortable offering it to Type III's from my own limited experience, and Type III is less common, but where I have looked after the Type III's, I've taken them to 28 weeks and delivered two live babies. And the chances of survival are very good at 28 weeks, but I've monitored them like a hawk. So, it is just, you take ownership of the patient and you become really invested in them, but then, it's very fulfilling and good for them if you can deliver two live babies'* (C8, doctor).	Parents want clinicians to express their views in order to support the patient in making a decision that would give them the best outcome in their situation. Parents also have trust that clinicians will manage the pregnancy according to need: '*I think I would've always trusted what a consultant had recommended, potentially with a second opinion. I wouldn't have been against it if that was what would've been best. It's not something I'm completely against if that is what would give us the best outcome, then that's what we would've done'* (P4, mother, social media).
Veracity - Being honest and truthful with parents; not presenting parents with misleading information	Clinician data suggests that there is a lack of evidence-based information that can be provided to parents to inform their decision making about trial participation and expectant management versus intervention outcomes. Clinicians gave conflicting advice to women: *'I have had patients come to me who were offered a selective termination within somebody from the team, and I felt that it was a different type of selective IUGR. So, somebody thought it was type two but I thought it was type three, and I would manage Type III differently… Somebody in the team thought it was Type II, which deteriorates much faster and in a predictable way. And Type III can go on for a long, long time, but it's an unpredictable, sudden loss. So, I have scanned a patient like that, where I was asked for a second opinion, and I said that, "This is Type III and I wouldn't offer a termination." I wouldn't offer a termination…* (see rest of quote in 'Beneficence')*'* (C8, doctor).	Parents need to be presented with enough information about the study, risk and benefits, and reassurance around the ethics of it. *'I guess reassurance that it had been approved as safe research to be doing and ethical. Reassurance about how my information and data would be used. Then, yes, I guess a really clear rationale for why it is needed, especially because it's such a… Not invasive. Invasive is the wrong word. But it's not like an observational study. It could actually affect what happened… What happens to your babies'* (P2, bereaved mother, social media). *'What I like about this [proposed trial] information sheet is it actually says things that I never knew. 'Close monitoring, but no active intervention this carries a risk death to the smaller twin. Death to the smaller twin may result in demise of the*

	'The data that we have now… comes from different observational studies with their own risks of bias' (C2, doctor). *'I think a trial will be important because I think the literature is very biased'* (C1, doctor). *'We don't really have that information … about outcomes… at the minute… and you can't predict that really [for Type I and Type III sFGR]'* (C3, doctor).	*larger twin, 40%...' I didn't know that, that's helpful… That's helpful to actually know that'* (P11, mother, social media).
Confidentiality and privacy	Laws on abortion changing but culturally, patients still continue with the pregnancy in some areas where abortion laws were in place until recently: *'The abortion laws have changed here. So, we now would offer feticide. But I think culturally women are still quite-'* (C3, doctor).	*'I guess reassurance that it had been approved as safe research to be doing and ethical. Reassurance about how my information and data would be used'* (P2, bereaved mother, social media).

Application of FERN qualitative (WP2) findings to the Adapted Theoretical Framework of Acceptability (Deja et al., 2021*; Sekhon et al., 2018)

Construct & definition	Fully met for parents?	Fully met for clinicians?
Affective attitude: *How an individual feels about the intervention.*	**No:** Most parents clearly stated that they would not consent for their child to take part in the FERN RCT. The few that would hypothetically agree to participate would withdraw if not happy with allocated arm. *'Why would it be done in that way rather than giving people the balanced options and then finding out the outcomes of each one or has that already been done? ... Overall, I think it is a bit worrying to be randomly choosing someone. That's the ethical side of things, randomly choosing someone to have a certain* loss *would be something I'd be concerned about'* (P3, mother, social media).	**No** Whilst seeing the merit of doing an RCT, most clinicians did not find the proposed FERN RCT acceptable overall and '*wouldn't take part […] We have ethics raised about lots of different studies and we work through them most of the time, but I don't think we could work through this one'* (C11, Doctor). RCT acceptable if inclusion criteria changed: *'I would say yes, it is acceptable with the confinement to the very severe growth restriction, which we have discussed, which is type II'* (C13, doctor). However, this is still problematic if someone requiring intervention is allocated to expectant management.
Burden: *The perceived amount of effort that is required to participate in the intervention.*	**No:** Having to decide which pregnancy management option to take was described by parents as traumatic. Adding the option of a study to an already stressful situation may add to the burden: *'I think it would be really helpful to not have that couple of hours crying in the car, because we had been presented with these options and had no idea, and no one seemed to have any idea what was the best one to do. That was quite traumatic'* (P2, bereaved mother, social media). Moreover, some parents spoke of the added burden of feeling like they *'disappointed'* (P14, partner, social media) the clinician or as if they are *'bad people'* for not participating: *'It's removing that guilt away from the parent, I think, as well. If they don't go ahead [with the trial/allocated arm], then firstly, it doesn't make them bad people if they don't want to make that choice. That's alright, you don't have to make that choice [to participate in the study]. You can go with your gut instinct and do what you think is best for you and your babies'* (P12, mother, social media, joint interview).	**Depends** on site and the management options they offer (i.e., patients randomised to intervention at a referral site would need to be referred to a tertiary hospital – hence reducing the burden on the referral hospital who would have instead expectantly managed the pregnancy on site).

Ethicality: *The extent to which the intervention has a good fit with an individual's value system*	**No:** Timing of approach, mentioning of selective termination causes harm, personal and cultural views of selective termination *'In a way it is contradictory, it is opposite courses, like you want to be ethical but it is almost like an impossible task to be ethical, so it is more like… You can't be ethical basically, I don't think. Am I making sense? It is almost like the mission impossible and you just need to find a way to kind of… There will be damage basically, you can't avoid it, there is no way, there is no other way'* (P18, Partner, site). '*Regret on if you were put in the bracket of selective termination, that's never an option for any parent, never, that's not a decision you can… It's not fair really, isn't it? It's borderline abortion in my eyes, I don't think I'd like that'* (P6, Partner, social media).	**No:** Some clinicians had concerns about causing *'harm'* to babies and parents. They felt that pregnancy management should be individualised. Clinicians spoke of how their patients' values would make the selective termination arm unacceptable to them: *'[Town] has a very high rate of Asian or ethnic minority population, termination is not an option for them'* (C7, doctor). *'But I think culturally women are still quite- And I am sure it will change with time, but I know if we offer feticide to women with fetal abnormality a lot of them just will continue the pregnancy rather than them having the feticide procedure'* (C3, doctor). '*I would not start a conversation because it is not acceptable for me first of all, and I don't think it is acceptable for anybody, as I said not ethical to be randomised to kill your own child. So, just imagine to ask a computer to decide for you which child will survive. (Laughter). Or which child will be brain damaged, that is not… They [parents] have to decide what they do, so you give them percentages, you give them risk factors in a particular scenario'* (C10, Doctor).
Intervention coherence: *The extent to which the participant understands the intervention and how it works.*	**No:** Clear and understandable trial materials but uncertain about understanding that laser treatment arm is not selective termination or the risks and benefits of either intervention option. If randomised to intervention, parents would drop out (especially for selective termination). *'I feel quite conflicted about it. I think it's [the proposed RCT is] really needed and I really, really want there to be research like this that's been done, because I think it would have been really helpful for us. Even if it hadn't led to Twin 1 surviving, I don't know, I think if there is research found that intervention was more effective, had better outcomes and there was good evidence to show that I think we would have chosen to do it, and then Twin 1 might have survived' (*P2, bereaved mother, social media).	**No:** Clinicians understand the intervention and how it works, however, clinicians cannot agree on the risks and benefits of each intervention due to limited evidence. *'Well, that's almost impossible to predict because emotionally it is a very difficult situation for the parents. But I think, in that situation, what we just have defined, when we would randomise, you can clearly tell the parents, with all honesty, that there's equipoise. We don't know. We don't know what's better'* (C13, doctor).
Opportunity costs: *The extent to which benefits, profits, or*	**No:** Although a few parents would hypothetically consent to their child taking part in the trial for altruistic purposes (to answer the research question and help families in the future), parents would want to go down the pregnancy management route that their clinician recommended and that they felt they had a choice in.	**No:** Clinicians prefer expectant management for types I and III sFGR and intervention (especially selective termination over laser treatment to increase the likelihood of parents taking a baby home) for type II sFGR with abnormal Dopplers. This would mean that, in the context of the proposed trial, they would have to give up their beliefs and values if

values must be given up to engage in the intervention.	Whilst most parents preferred the expectant management arm of the trial, some spoke of how they would find selective termination acceptable only in severe cases and would want to go down that route if that's what the clinician recommended (i.e., if their condition was severe, they wouldn't want to be in the expectant management arm): '*I think if I was pregnant with twins again and had the same problem I would take part in a study like this, because I would want to be part of helping there to be better research. But I would not hesitate to withdraw if I felt that I was assigned to an option that I didn't think was going to give us the best outcome for our babies'* (P2, bereaved mother, social media).	their patient was randomised to an arm that was not the best option for that individual pregnancy. *'That is why we have expectant management as the default. And, also, from a pathophysiological perspective, you don't expect laser to improve the outcome. And also, if you look at the literature, that's also what comes out of it. So, most of the time you lose the smaller baby and if you're really unlucky, then you lose the bigger baby, and then you have an even bigger problem'* (C2, doctor). Clinicians would be selective about who they recruit to the trial. They would not randomise women with type I or III sFGR to selective termination when that family would have a chance to take two healthy babies home because these types generally have more favourable outcomes: *'… [But], especially in…the greater growth… [Type] III situations, you are frequently surprised by how well the small ones keep growing'* (C14, doctor).
Perceived effectiveness: *The extent to which the intervention is perceived likely to achieve its purpose.*	**No:** Differences in pregnancy management are already happening and practice varies; Timing of approach and mentioning intervention especially sensitive: *'I feel like when it hit 24 weeks and I was being asked to make decisions about whether to keep a baby or not, I almost wasn't able to clearly… I felt very separate from my…. almost disassociated from myself. I felt very separate from what was going on just because I'd been so detached. It was a really weird experience. It's funny, even when I gave birth I hadn't really… It wasn't until I saw them that I was like, oh my gosh, I'm having babies'* (P11, mother, social media).	**No:** Clinicians would not be happy to randomise women with Types I and III sFGR to the intervention arm, and similarly would not be happy to randomise women with Type II sFGR with abnormal Dopplers to the expectant management arm. Differences between evidence on the effectiveness of laser or selective termination. *'Parents … [are] more likely to take a baby home if they have a selective reduction, compared to if they had a laser'* (C8, doctor). '*There's a big difference between laser and cord occlusion… I don't think laser has… that's a little bit the issue that I don't believe in laser as a treatment for selective foetal growth restriction, unless you see that the smaller baby is going to die and the parents do not opt for, or they cannot, mostly because of religious beliefs, go for a selective reduction'* (C2, doctor). *'I think it is probably true that the cord occlusion is potentially the option to maximise the chance of having one healthy child, which is maybe potentially avoiding the risk of significant prematurity. However, I think that might be the method for only the cases where maybe there are abnormal Dopplers. Because I think where the Doppler of the smaller*

		baby is normal, I think it is reasonable to offer expectant management' (C1, doctor).
Self-efficacy: *The participant's confidence that they can perform the behaviour(s) required to participate in the intervention.*	**No:** Whilst the parent information leaflet provides clear and understandable information, most parents reported that they were under a lot of stress during initial meetings and found it difficult to comprehend the information that was presented to them. *'It was like really top-line understanding of what the next thing could look like, which, in fairness, is probably best because it's so much information to take in initially, anyway, that I probably wouldn't have heard what she was saying, even though I was listening'* (P15, mother, site).	**No:** Most clinicians did not believe that they can perform the behaviours required to participate in the RCT. Clinicians do not think that the FERN trial is practically possible to conduct in a randomised fashion because management of MC twin pregnancy with sFGR requires an individualised approach, due to the many factors that influence their decision making, and parents need to be provided with high quality evidence to inform their decisions, which is currently lacking. *'What I want to say, and tried to say from the beginning, is we cannot randomise them ourselves, they [parents] will decide the management and then we can put them in that category to reach to some conclusions at the end. But we cannot randomise them, so they have to decide what they want to do'* (C10, doctor).
Trust*: *The extent to which the parent / guardian trusts those delivering the intervention to put the needs of patient before the requirements of the study.*	**Yes:** Parents trusted the opinions of clinicians. However, this makes the proposed RCT difficult to carry out if the clinician has strong opinions on management options or if parents receive conflicting information from different clinicians. *'Being really honest, I think we probably would've done [hypothetically consented to take part in the RCT]. But if we'd got the randomised option and we were like, "This doesn't feel right," and our consultant is going, "Oh, oh, oh, oh," we might've dropped out'* (P1, bereaved partner, social media). *'He [consultant] reached out to one guy in Germany and one guy in the USA, and he said that one of them went, "Why on earth would you intervene? There's no proof that this works. Why would you do that?" The other guy went, "Why on earth wouldn't you do it? There's something available to you. Why wouldn't you intervene if you think there's a big problem?'* (P1, bereaved partner, social media).	N/A