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Full length article

Fluidity of Equipoise in a Multi-Centred Pilot RCT: Influences on Clinician Decision-Making in Offering Trial Entry

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ABSTRACT

Objectives: The embedded Qualitative Process Evaluation (QPE) within the CSTICH- Pilot RCT explored facilitators and barriers to recruitment within the Pilot. This study reports a secondary analysis of the overarching theme of *Fluidity of Equipoise* and the influences on individual and community clinical equipoise around the use of Emergency Cervical Cerclage (ECC).

Study design: RCT recruitment assumes clinical equipoise and is defined as genuine uncertainty about an intervention. The ability of trial recruiters to convey this equipoise is also key to participant recruitment and fully informed consent. This exploratory qualitative process evaluation used semi-structured interviews with healthcare professionals (HCPs) involved in trial recruitment. Interviews were audio-recorded, transcribed, and analysed using codebook thematic analysis.

Results: 23 HCPs were interviewed. Clinical equipoise around the use of ECC was variable and influenced by a multitude of factors including: (1) obstetric history; (2) gestation; (3) standard site practice, and (4) HCPs previous experiences of ECC. We have interpreted this variability as 'fluidity of equipoise'.

Conclusions: Clinical equipoise around complex pregnancy related conditions was fluid and influenced by the complexities of obstetric histories and gestation at presentation. Equipoise of HCPs involved in trial recruitment should be considered carefully as it can impact the nuances of recruitment, particularly in more challenging trials such as CSTICH-2. Study-specific documents and training can be used to increase staff and patient awareness of uncertainty in the evidence base for interventions under investigation. Further research is needed around the potential consequences of equipoise fluidity.

Introduction

Second trimester miscarriage and very early preterm birth is a multifactorial complex condition [1]. Women often with no previous history or identifiable risk factors can present in emergency situations with cervical dilatation and exposed, unruptured foetal membranes in the *peri*-viable gestation period [1,2]. Management of premature cervical dilatation is complex and the evidence for interventions to prevent premature birth is limited; the placement of Emergency Cervical Cerclage (ECC) in attempt to keep the cervix closed is sometimes considered [2]. There is limited evidence on the feasibility, complications, risks, and benefits of this type of cerclage [3]. NICE guidelines [4] suggest ECC may be considered as a potential management option, recommending a randomised trial or a well conducted cohort study to evaluate ECC. This contrasts with the well-established use of cervical cerclage (CC) in the non-emergency setting to prevent preterm birth in women based on their obstetric history of ultrasound findings of a short cervix [5].

The C-STICH2 pilot RCT aimed to recruit women presenting with cervical dilatation, between 16 and 27 + 6 weeks of pregnancy to either standard care for that site e.g., expectant management (with adjuncts such as bed rest, antibiotics, progesterone) or ECC. The C-STICH2 pilot incorporated a Qualitative Process Evaluation (QPE) designed to explore

Abbreviations: CC, Cervical Cerclage; ECC, Emergency cervical cerclage; RCT, Randomised Controlled Trial; QPE, Qualitative Process Evaluation; SC, Standard Care; QTA, Qualitative Thematic Analysis; NIHR, National Institute for Health Research; HCPs, Healthcare Professionals; QRT, Qualitative Research Team; EM, Expectant Management; ROM, Rupture of Membranes; SIVs, Site Initiation Visits.

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the acceptability to potential participants and healthcare professionals involved in recruitment of the pilot trial and trial processes and use these findings to inform and optimise recruitment strategies in the future main phase trial.. [3]. The reporting of the wider QPE findings, including women's perceptions of ECC and the offering of ECC in the context of an RCT are described elsewhere [6]. Within the full QPE paper [6] three super-ordinate themes were identified through data analysis, which influenced trial offering by HCPs: *a complex obstetric history*, *the influence of gestation* and *fluidity of equipoise*. Here we specifically report a further in-depth exploration of the Fluidity of Equipoise theme, namely variations in equipoise within and across the clinical community, how this influenced trial offering within the CSTICH-2 Pilot, and potentially the acceptability of the intervention for HCPs.

RCT recruitment assumes both that clinical equipoise exists, in which clinical equipoise if usually referred to as "a state of genuine uncertainty on the relative value of two approaches being compared in a trial" [7].. The ability to convey this equipoise is also key to participant recruitment and fully informed consent [8]. Various types of equipoise may be considered to exist [10], and can be described as (A1, Table 1):

The concept of equipoise as a pre-requisite for RCTs then seems to imply that it is, or can be, a fixed idea or standpoint for the investigation of the intervention or approaches under investigation.

Trials of surgical interventions are considered particularly challenging to recruit to and manage in terms of active *versus* passive management and the implications of the placebo effect [8]. Active management, specifically in relation to CSTICH-2 and other similar maternity setting trials, is that in which something is 'done', i.e., a surgical intervention is used. This is as opposed to passive management, i.e., expectant management. Which may involve medication including antibiotics, or other physical interventions (e.g., tilted bed rest), but without a surgical intervention. RCTs have not been regularly used in pregnancy and maternity care and are considered to be challenging, reasons for this including complexities around ethics and recruitment [12]. Maternal-fetal surgery trials may have competing ideologies around randomisation, relating to balancing the primary benefit of the surgery to the foetus with a lack of risk to the pregnant participant [13].

This article specifically focusses on how clinician equipoise was interpreted with the CSTICH-2 QPE, alongside implications for RCT recruitment and future practice and research. The QPE of the CSTICH-2 Pilot aimed to:

> "qualitatively explore the feasibility, acceptability and appropriateness of the trial and intervention for women and healthcare professionals (HCPs)."

Study aims

This paper reports a secondary analysis of the QPE data from the CSTICH2 pilot RCT QPE, which focussed on *fluidity of equipoise* and the influences on offering entry into the trial. This study specifically aimed to explore and describe how clinical equipoise was understood and operationalised as reported by HCPs involved in recruitment to the CSTICH-2 Pilot trial,

Table 1
Definitions of Equipoise.

Equipoise type	Definition
Clinical Equipoise	Defined as "a state of genuine uncertainty on the relative value of two approaches being compared in a trial." Fried, C, 1974 in (7).
Personal Equipoise	The investigator or HCP has no preference for one of the available interventions (5)
Community (or Clinical) Equipoise	Describes a lack of consensus within the clinical community around a specific treatment (8).
Proxy Equipoise	Describes an individual's reference to a senior HCPs preference for an intervention as opposed to their own assessment (9).

Methods

The QPE was designed to explore eligible participants' understanding of and satisfaction with C-STICH2 trial processes and the acceptability of ECC in the context of trial randomisation. The methods related to the QPE design and methodological approach, and data collection, and analysis approaches are described in detail in previous publications [3,6], the reporting in this paper should be considered in relation to the findings and reporting of these two previous publications.

Participant eligibility

HCPs eligibility was contingent on their involvement in approaching, or caring for women who were approached, about C-STICH2 participation at the point of a diagnosis of cervical dilatation between 16 and 27 + 6 weeks of pregnancy. This involvement may have been during a direct approach to potential participants, discussions around eligibility, or facilitating consent for randomisation. HCPs had to be named on the CSTICH-2 site delegation logs.

Participant recruitment

Eligible HCPs were approached directly by the Qualitative Research Team to participate in an interview. This approach occurred following screening or successful recruitment of participants into either CSTICH-2 and/or the QPE (A3, Fig. 1). Approach was made via e-mail contact to elicit interest in participation in interview and accompanied by brief information about the interview. Where clinicians were willing to participate, potential participants were then sent (also via e-mail) the full HCP Participant Information Leaflet, a background questionnaire, for the purposes of both sampling and data collection, and a consent form. Consent was sought electronically and verbally reconfirmed for all interviewees for the purposes of the audio recording.

Approaches about interview participation were made to 17 senior clinicians, and 15 midwives. Of these, 2 senior clinicians were ineligible (n = 1) or did not respond to contact within the recruitment period (n = 1). 2 further clinicians declined participation due to workload constraints, and 2 midwives did not respond to initial contact (n = 1) or agreed to participate but then did not respond to further contact for scheduling interviews (n = 1). Contact was initiated and then re-attempted up to a maximum of three times for each participant, depending on previous responses.

Data collection

Semi-structured interviews were held with HCPs. Interview transcripts were analysed inductively as the QPE data collection progressed. Semi-structured interviews in healthcare research are used to allow for in-depth discussion exploring participant's experiences or understanding of specific phenomena, within the structure of a pre-determined set of objectives set by the research team [14].

The interview guide explored experiences and views on approaching potential participants for trial recruitment, and their thoughts and experiences on the use of ECC and EM in the context of randomisation, including personal, clinical, and community equipoise. The guides were refined iteratively by the research team as interviews progressed. All participants completed demographic questionnaires which also informed subsequent sampling approaches.

Data analysis

Interviews were recorded and transcribed verbatim by a specialist transcription company in accordance with the principles of GDPR and

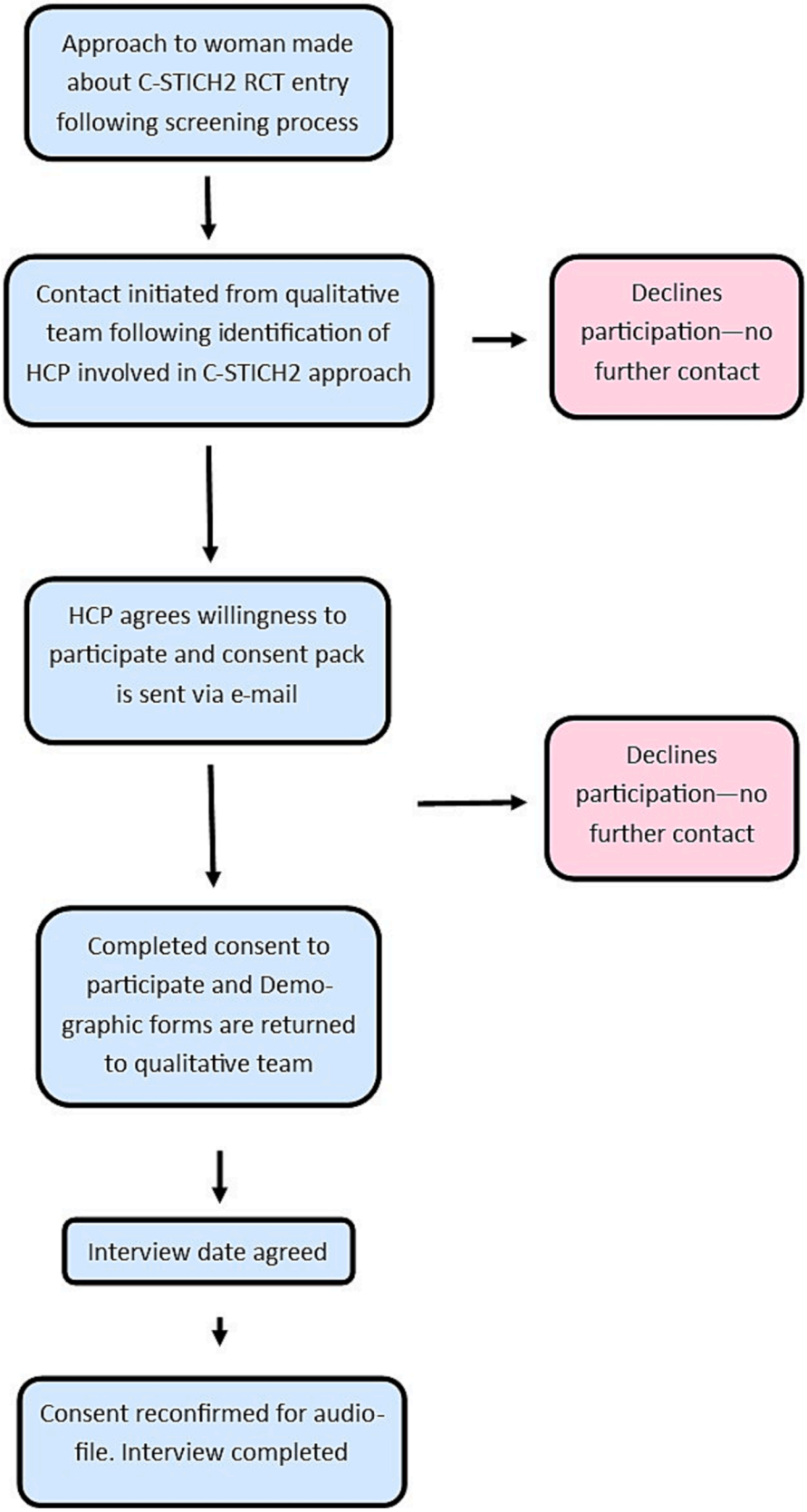

Fig. 1. Recruitment pathway HCP.jpg.

confidentiality. Transcripts were checked against the recording for accuracy, and identifying characteristics were removed as appropriate.

Transcripts were uploaded to NVivo (QSR International Pty Ltd, 2019) to facilitate data analysis. Codebook Qualitative Thematic Analysis (QTA) was used to inductively explore and elucidate themes within the data following the guidelines described by Braun and Clarke [15]. Inductive approaches search for patterns within the data, whilst also allowing for unexpected findings to be considered. This is described further in Fig. 2 (A4, Fig. 2).

The transcript data were interpreted to generate themes from these analyses. These themes described the perceived acceptability and feasibility of the CSTICH-2 Trial for HCPs. The wider findings from the QPE are reported elsewhere [6]. Further inductive analysis of transcript data was undertaken to explore the *Fluidity of Equipoise* theme in relation to offering trial entry.

Demographic data were entered into SPSS Statistics (IBM 2017) and analysed using descriptive statistics.

This paper reports the secondary analysis of data related to the *Fluidity of Equipoise* theme identified in the wider CSTICH-2 QPE Findings.

Findings

Participant recruitment

Interviews took place with 10 midwives and 13 senior clinicians from 13 recruiting sites. Of the 23 interviews, 16 were undertaken via telephone and 5 were completed face-to-face. Demographic characteristics of HCP are described in Table 2 (A2, Table 2). Average interview duration was 49 min (range 29 min– 63 min).

Fluidity of equipoise

Three superordinate themes were previously identified and described from the CSTICH-2 QPE as the main influencing factors on HCPs willingness to offer trial participation. These were *a complex obstetric history,* the *influence of gestation* and *Fluidity of equipoise.* These themes were shown to interact with and influence each other and are described in detail elsewhere [6].

For people with *a complex obstetric history*, clinicians perceived that some people were carrying pregnancies that were especially precious or

Table 2
Demographic information for HCPs recruited into the CSTICH-2 QPE.

Characteristic	Midwives = n (%)	Senior Clinicians = n (%)
	Total n = 10	Total n = 13
Age (years)		
25–34	3 (30)	–
35–44	5 (50)	8 (61)
45–54	1 (10)	3 (23)
55 – 59	1 (10)	2 (15)
60+	–	–
Ethnicity		
Arab	1 (10)	–
Any other white background	–	1 (8)
Mixed: White and Asian	1 (10)	–
White (English/Welsh/Scottish/ Northern Irish/ British)	8 (80)	12 (92)
Gender		
Female	10 (100)	8 (62)
Male	–	5 (38)
Years since qualification		
0–9	5 (50)	–
10–19	–	8 (62)
20–24	3 (30)	1 (8)
25+	2 (20)	4 (31)
Years in role		
1–3	7 (70)	5 (38)
4–6	1 (10)	3 (23)
7–10	1 (10)	–
11–14	1 (10)	4 (31)
15+	–	1 (8)
Annual births at site		
<5000	2 (20)	1 (8)
5000–7500	4 (40)	7 (53.8)
7600 – 9900	–	1 (7.7)
10,000 +	4 (40)	4 (30.8)
Experience of caring for women with this condition		
Daily	–	–
Weekly	1 (10)	3 (23)
Monthly	–	3 (23)
1–2 x yr	1 (10)	1 (8)
3–4 x yr	4 (40)	5 (38)
Other	4 (40)	1 (8)

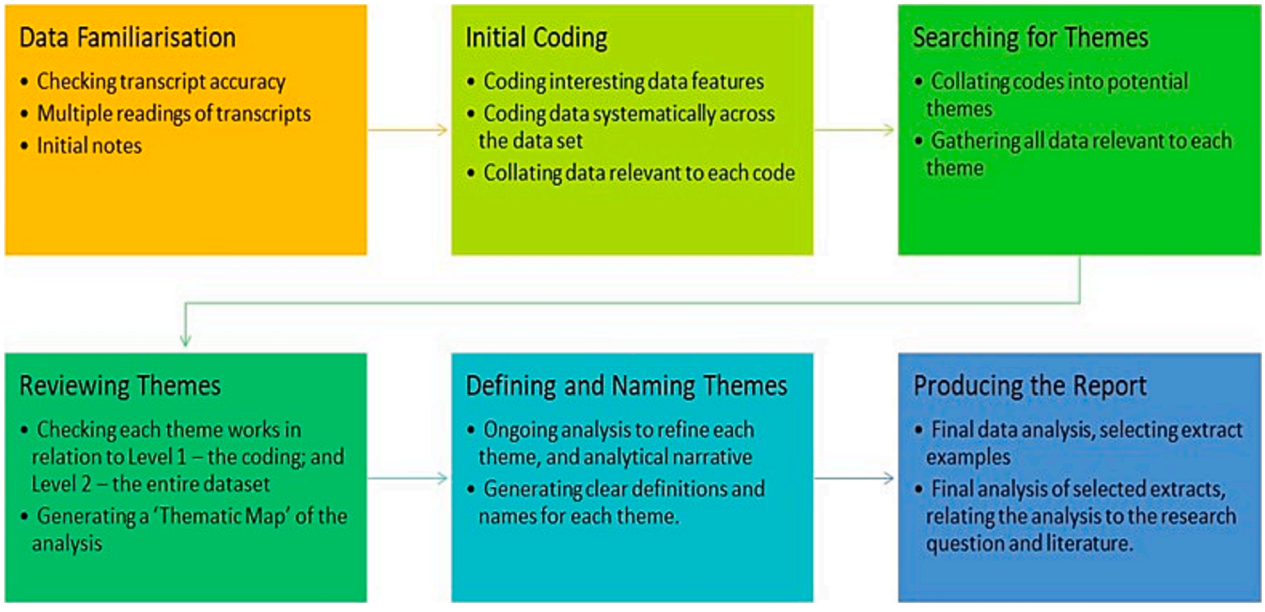

Fig. 2. Codebook Thematic Analysis.jpg.

hard to achieve, e.g., pregnancy after multiple miscarriages or following neonatal death or stillbirth. The authors agree that most pregnancies are just as precious and wanted, however where parents have struggled with infertility, stillbirths, neonatal deaths or multiple miscarriages, when receiving a premature cervical dilatation diagnosis in a subsequent pregnancy, which then put this pregnancy 'at risk' the randomisation element of the CSTICH-2 Pilot RCT was perceived to carry an additional risk of withholding what the clinician deemed as the 'appropriate' course of action.

The *influence of gestation* described how equipoise changed depending on the gestation at diagnosis. Earlier gestations (i.e., between 18 and 22 weeks) were perceived as being on the cusp of viability, and therefore certain to, or likely to result in a pregnancy loss. Thus, offering an ECC would give hope in a hopeless situation. At later gestations (especially after 24 weeks) neonatal outcomes are better, and thus ECC was considered to potentially increase the risk of earlier birth or pregnancy loss compared to expectant management.

This article focuses on further exploration of the theme of the *fluidity of equipoise* (information published elsewhere [6]. The previous analysis described how the three over-arching themes interacted with each other. This secondary, more detailed analysis has highlighted how elements of the themes of *a complex obstetric history* and *the influence of gestation* were embedded within this *Fluidity of Equipoise* theme. We interpreted the concept of equipoise as being fluid because it was dynamic and flexible and was shown to be dependent on multiple influencing factors. Equipoise was fluid depending on the specific circumstances of the person presenting with this diagnosis, including this individual's previous obstetric history and their gestation at the point of diagnosis of premature cervical dilatation.

Further influencing factors were related to clinician's ECC experience, the influence of lead clinicians at sites on standard site practice, circumstances specific to the pregnant person and this pregnancy; and the clinical situation at diagnosis..

Clinician equipoise was shown to be influenced by several factors which are described in Fig. 3 (A4, Fig. 3) and include:

- Obstetric history
- Influence of gestation
- Before viability (<22 weeks)
- Threshold of viability (22–24 weeks)
- Beyond 24 weeks
- Standard site practice
- HCP previous experiences of ECC

Clinical equipoise was influenced by several factors which were specific to either the accepted standard practice at site or the HCP and their level of experience with ECC.

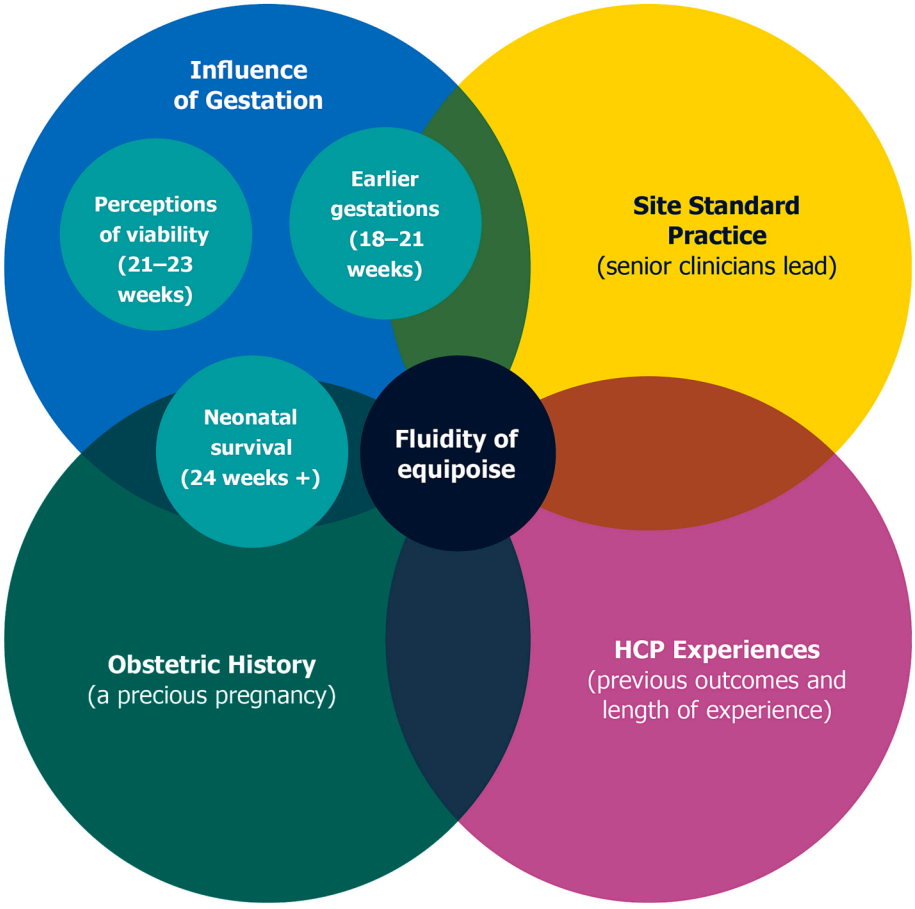

Fig. 3. Influences on Equipoise.jpg.

Equipoise and obstetric history

Individual equipoise was influenced by assumptions about a woman's perceived preferences. In some cases, HCPs appeared to make assumptions that a potential participant would prefer one management option above another, based on their obstetric history or gestation. This may have influenced decision making about trial offering and the language used about risks and benefits.

> *"I think they [women] seem to be in two schools, there's either one that just wants to throw everything at it or one that is just, you know what it's not meant to be, and I don't know whether that's a demographic thing, if they've had ten miscarriages or this is an IVF pregnancy it's almost like their last-ditch attempt" (C08 –Senior Clinician)*

Where a pregnancy was considered more complex, already high-risk, or especially precious, perhaps following a history of pregnancy loss, HCP may have considered that active management was preferable to expectant. This context may have led HCPs to draw the conclusion that offering the trial was not appropriate. This was frequently predicated on the idea that for a precious, precarious pregnancy an ECC would be beneficial.

> *"He [the senior consultant] was alluding to that she wouldn't necessarily be appropriate because she's quite an older lady herself, and this is a very desperate pregnancy, … but I said we need to talk to her about it still because she is eligible, and she can say no…" (C14 – Research Midwife)*

Equipoise and gestation

Earlier gestations seemed to be perceived as being at such high risk that even an intervention with unclear benefits and risks was believed to be worthwhile considering.

> *"At 18/19 weeks and we've got nothing to lose really, because if they've got exposed membranes they are probably going to deliver quite soon anyway, so we might as well try and put a suture in, give her the best chance possible." (C13 – Senior clinician)*

HCP perceptions of gestations > 20 weeks also influenced the time at which decisions about both ECC and trial offering were made. Gestations past 24 weeks, were less likely to be gestations at which ECC was offered either outside or within the context of the trial linked to standard site practice. This was explained by the perceived improvements in neonatal care.

> *"Because our neonatal unit is so good, I think our unit policy is that in terms of we wouldn't try and put a rescue suture in at that gestation [24 weeks]" (C09 – Senior Clinician)*

Equipoise and standard site practice

Within sites, individual HCP equipoise was influenced by standard site clinical practice, this referred to what was considered to be 'standard site practice' in relation to ECC within that site for pregnant people who attend and receive this unexpected diagnosis, outside of the CSTICH-2 Pilot. This 'standard site practice' was shown to influence the likelihood of parents being approached about the trial and illustrated example of both community and proxy equipoise. Clinicians who were more junior, or who had less experience of discussing ECC as part of clinical practice were more likely to be influenced by both standard practice at site which was often based on senior clinician preferences for practice. This was true for junior clinicians and midwives who did not have specific expertise in ECC and premature cervical dilatation management who respected the experience of senior colleagues who had more understanding of the condition and its management; and described what could be interpreted as proxy equipoise, where assumptions about management of this diagnosis were based on more senior staff preferences. This variation in 'standard site practice' therefore led to variations in equipoise across sites, where different sites had different 'standard site practice' in relation to ECC as part of the management plan offering and placement of an ECC outside of the CSTICH-2 trial.

> *"I feel really respectful of their clinical judgement, and that I think because I know them, how they work, I feel like that is a big part of opinion on how… what happens in [this area]. So, my feeling is really it's a balanced judgement, and somebody just wouldn't put a stitch in just for the sake of giving it a try if they didn't really feel like it was beneficial." (C22 – Research Midwife)*

HCPs who had ECC experience were also influenced by previous outcomes of expectant vs active management decisions, and this often changed how they viewed ECC specific to the clinical presentation in front of them, and therefore, how likely they were to offer trial entry.

> *"If it's clear that they have got an infection I wouldn't want to put a stitch in, I really wouldn't want to do that. If it's somebody who has had maybe a full dilatation section previously, or they'd got some kind of uterine anomaly, or they have had a bit of their cervix taken away and it's likely to be some kind of functional cervix problem then I would be much more inclined to put a stitch in." (C05 - Senior Clinician)*

Where 'standard site practice' involved offering ECC to women presenting with this condition (which itself would have been dependent on gestation and other contraindicating factors), placement of ECC was less likely to have been offered as optional or using language which invites discussion inclusive of the availability of other management options. In the context of offering trial entry, this was highlighted in the wider QPE findings [6] and referred to as 'pre-priming'. 'Pre-priming' described how eligible pregnant parents were told they would be seeing a consultant to talk about having a stitch, prior to discussion about the lack of evidence base, uncertainty and being offered CSTICH-2 entry.

> *"I think probably before the trial if somebody had presented, I think probably we wouldn't necessarily… I might not have seen it, but I think the initial counselling probably would have been this is happening, we could give you a stitch do you want to try it?" (C28 – Research midwife)*

This variation between ECC or expectant management being offered as standard site practice, also contributed to variations in equipoise between sites. This was a function of proxy equipoise which was dependent on the experiences and opinions of senior lead clinicians, and varied between sites in relation to lead clinical teams at each site.

Equipoise and HCP previous experience of ECC

Equipoise was shown to be fluid for individual HCPs based on their previous knowledge, and experiences of ECC. Despite identifying that they did not have a 'good' answer for the question around success of ECC, many senior HCPs with experience of ECC placement felt they would look for patterns, and frequently used 'what happened last time' to inform decision making about ECC placement outside of the trial.

> *"I totally acknowledge that we don't know what the right thing to do is, and as I say I think each situation almost needs assessing uniquely, and that's where people that have an interest in prematurity probably have a part to play rather because we then see it more commonly and we've had that experience to be able to know whether this is worth going for or these can just sit and watch and wait."*

This fluidity in clinician's equipoise then influences the likelihood of offering trial entry, in the context of the CSTICH-2 Pilot RCT. HCPs described how they would make decisions about trial entry, and/or ECC placement, based on how a person's clinical situation reflected previous situations, and therefore whether offering trial entry, and potentially ECC would result in 'success' based on what had happened last time. This was also related to the current clinical presentation at the point of diagnosis, i.e., degree of cervical dilatation.

> *"How you look at women for a rescue cerclage does get influenced by what has happened in the last few you have done […] you try to pick out of what you have done which are the ones that are going to work, and*

which aren't. The more you do the more you realise there probably aren't any rules, but I am still looking for rules." (C02 – senior clinician)
"the outcome […] that we have seen over the last few months stick in your head and I think if you have a very positive outcome for either management process then I think that does stick in your head. But I think if three out of three ladies have gone to theatre, had a stitch and ruptured their membranes then that is in your mind." (C24 – senior clinician)

Perceptions of success of ECC placement and outcomes also influenced equipoise and contributed to *fluidity of equipoise* in the context of the presentation of the pregnant person at diagnosis and their clinical situation. HCPs described how they had some confidence in ECCs as a potentially successful treatment, but the uncertainty lay around who the ECC would be successful for, and under which clinical situations.

"We have nothing much to go on, we don't have any markers that can tell us how likely they are to go into labour, when they are likely to go into labour, you have to go on clinical judgement, and that's very difficult, and it has to be you have to counsel people, provide them with really good up to date local data about what their risks are." (C05 – senior clinician)

Discussion

Main findings

Evidence from the C-STICH2 QPE indicates that even when there is community equipoise across the clinical body, actual offering of trial entry at a site level is influenced by clinician's personal equipoise. Equipoise varied across the study sites, both within sites and between sites. Within site equipoise was influenced by individual clinicians' experiences of placing previous ECC, and between site equipoise was influenced by senior clinicians usual offering of treatment for this condition, which influenced standard site practice. This equipoise was demonstrated to be fluid based on individual obstetric history, gestation at different time points within an individual pregnancy and in how the condition presents.

Clinician decision making about offering trial entry to women who were eligible for the trial was influenced by multiple factors, many of which were interlinked. Decision-making about trial offering was influenced by experiences of similar situations and the attendant previous outcomes, gestation at presentation and a women's personal obstetric history in the lead up to this pregnancy where they were presenting 'at risk' (see A6, Fig. 4). Fig. 4 describes how each factor which influences fluidity of equipoise may influence the likelihood of offering trial entry in one direction or another, depending on the specific influencing factor.

Standard clinical practice at sites is often led by a small number of senior clinicians. Thus, site equipoise may be influenced by these HCPs perceived stance on an intervention under investigation. Where some HCPs prefer one treatment or have had successful outcomes recently when using a treatment, and feel that a specific intervention, in this case ECC, is in a woman's best interest to maintain this pregnancy a decision was often made to not offer the trial to women.

Interpretation

Research in maternity is challenging due to the ethical considerations surrounding the health of mother and foetus [14]. Previous well publicised medical interventions which caused harm to developing foetuses where appropriate safeguarding and testing had not been in place [15,16], led to much needed tighter restrictions on investigatory medical interventions in pregnancy. Despite legislation now actively encouraging equitable access to clinical trials for women [17] only a small number of registered clinical trials involve drugs in pregnancy, and of those only a small number focus on maternal and fetal health

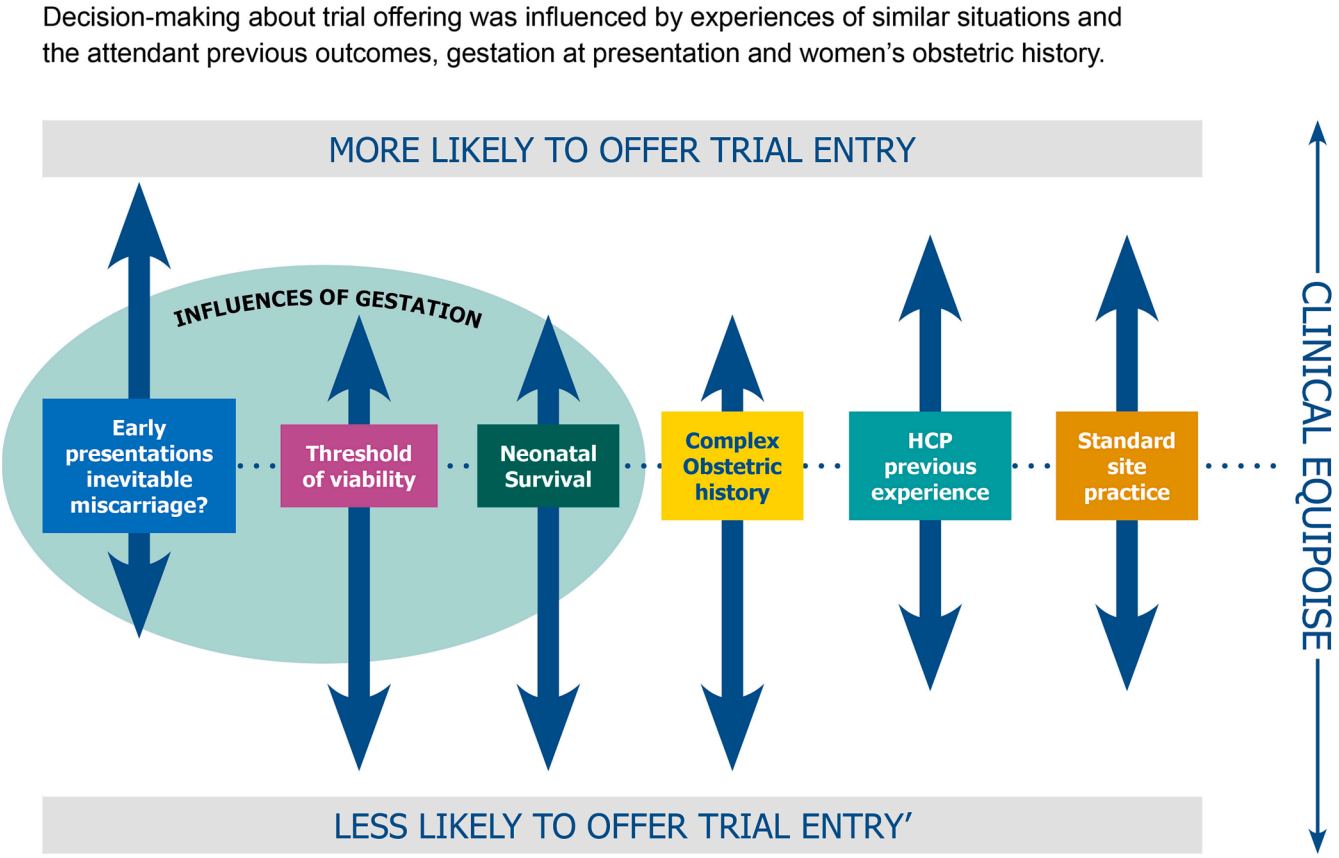

Fig. 4. Fluidity of Equipoise and trial offering.jpg.

outcomes [18].

Surgical trial recruitment is considered more complex due to perceptions around preferences – either from HCPs or potential participants [5]. Where HCPs have a treatment preference, they may choose to not offer trial entry removing decision-making capacity from women and other pregnant people. This was shown here where although clinical equipoise was indicated within the community, at a site level, and for individual HCPs, decision making varied around offering trial entry. HCPs may also use language and terminology about the interventions which convey their own preferences. Where this happens within sites, HCPs with less experience of the intervention or population group may default to a position of proxy equipoise [9] and thus site equipoise is affected, and the likelihood of pre-priming around one intervention is higher [4]. Pre-priming, as identified above, was used here to refer to the process of introducing one intervention as the standard or superior action prior to discussing the trial and therefore influencing participation.

Trials are at increased risk of low(er) recruitment where clinical equipoise is in doubt or where a rare condition may mean a lack of experience in one intervention arm, across the clinical body [19]. According to Miller and Joffe [20] RCTs and equipoise are both a necessity, without which a robust evidence-base supporting the use of complex interventions as standard care will not exist. We have shown that ECC may already be in use as standard care based on clinician experience and preference despite the lack of consensus in the evidence-base.

Equipoise is considered necessary to offer ethical participation in clinical trials [9]. In maternity care pregnant parents are not the sole focus of the healthcare experience as they are likely to feel responsibility for ensuring the continuation of the pregnancy, and the safety of their baby [21]. Parental decision-making around trial entry and acceptance of randomisation has been shown to be influenced by multiple factors [22–26]. The same model of influences has until recently not been as well described for HCPs tasked with recruiting pregnant participants into RCTs [11]. However, we have shown that for many experienced HCPs equipoise is fluid and varies depending on not only their level of experience of the intervention in question, but also specific to the clinical history of the presenting potential participant and the unfolding clinical situation at that time.

Strengths and limitations

The focus on only recruiting HCPs who were enrolled on delegation logs, at sites which were part of the CSTICH-2 Pilot means that data capture has focused on those sites in which the clinicians perceived they had equipoise and that the site staff would be willing and able to recruit into CSTICH-2. This was because the QPE focus was on trial processes of CSTICH-2 Pilot and the feasibility and acceptability of CSTICH-2 as an RCT. The findings around fluidity of equipoise may be relevant in other settings, where ECC is either always, or never offered, but further work would be needed to confirm this. Similarly, the fluidity of equipoise which we identified here may also be relevant for other complex/surgical interventions which have a poor evidence base but are accepted as standard practice in some areas.

The qualitative research team worked independently from the NHS and the main clinical trial leads, which may have encouraged participants to speak more freely, thus allowing the gathering of rich in-depth data within the qualitative interviews. No observation of consent processes or trial entry discussions were included in the data collection for CSTICH-2 QPE. Thus, how these discussions took place is based on HCP and participant recall. Other work has shown that this recall during research interviews may not accurately reflect real-world situations. [7].

The QPE resulted in the participation of a wide range of HCPs (n = 23), including both midwives (n = 10) and consultants (n = 13) across multiple trusts (n = 11) all of whom operate within varied local policies on ECC use. HCP participants had a range of understanding and experience of ECC as a procedure. This captured a more accurate snapshot of both current provision for ECC as well as variations in standard site practice across the UK.

Practical recommendations

Embedding QPEs as an integral part of pilot RCTs are potentially an effective way of exploring the perceived and experiential barriers and facilitators to trial offering and subsequent recruitment for sensitive and complex questions which are being answered using RCTs.

Well designed and balanced participant information leaflets for the intervention or treatment in question are sometimes a useful learning point for staff where standard site practice may be led by senior clinicians. These may be used in conjunction with trial offering decision support tools, for example, HCP approach infographic, to support an equipoise informed approach.

Continued and supportive relationships between the trial management team and the recruiting sites may result in changes to clinician equipoise where individuals may not have equipoise or where it is fluid. Using training materials and encouraging sites in recruitment, combined with sharing best practice from sites who are recruiting well, may all also influence increases in and consistency of equipoise.

Conclusion

Despite preliminary indications of equipoise which are often collected via surveys of clinical networks, experiences of recruitment into maternal or sensitive RCTs may not reflect the nuances of trial offering in practice.

Randomised trials focused on questions aimed at complex or rare participant groups or conditions rely on community, clinical and personal equipoise of recruiting clinicians in order to successfully recruit participants, and therefore gather enough data to answer the trial question. It may be important to consider contextual aspects of equipoise for the recruiting clinician body prior to pilot trial set-up, increasingly the likelihood of increased and consistent equipoise.

Not all HCPs at each study site, including those who are on the delegation log will have a full understanding of the complexities of some of the interventions, or the expected outcomes or current evidence base. Site initiation visits, and study documentation can be a key method of describing and disseminating information around the current evidence base relating to interventions which are being investigated within trials. Study documentation and Site Initiation Visits, including participant information leaflets and staff training which describe uncertainties around the evidence base may support more informed discussions between recruiting staff and potential participants. Not only can this information as provided by the lead study team be key to disseminating information around the current evidence-base related to the intervention under investigation, but they can also support recruiters when discussing participation in trials.

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CRediT authorship contribution statement

Eleanor Molloy: Formal analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing, Conceptualization, Visualization. **Nicole Pilarski:** Project administration, Writing – original draft, Writing – review & editing. **Katie Morris:** Funding acquisition, Project administration, Supervision, Validation, Writing – review & editing. **Victoria Hodgetts-Morton:** Funding acquisition, Investigation, Supervision, Writing – review &

editing. **Laura Jones:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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