CLINICAL STUDY PROTOCOL

Full Study Title: The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the **C**ircle **o**f **S**ecurity **I**ntervention for mothers in perinatal mental health services.

Short Study title / Acronym: The COSI Study

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This protocol describes the COSI Study trial and provides information about procedures for enrolling participants to the trial. The protocol should not be used as a guide for the treatment of other participants; every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study, but centres enrolling participants for the first time are advised to contact the Trial Coordination centre to confirm they have the most recent version. Problems relating to this trial should be referred, in the first instance, to the Trial Coordination centre.

This trial will adhere to the principles outlined in the International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines. It will be conducted in compliance with the protocol, the Data Protection Act 2018 and other regulatory requirements as appropriate.

ABBREVIATIONS

AFNCCF	Anna Freud National Centre for Children and Families
AE	Adverse Event
ASQ-3 & SE	Ages and Stages Questionnaire-3 & Socio-Emotional
CI	Chief Investigator
CORE-10	Clinical Outcomes in Routine Evaluation-10
CORE-OM	Clinical Outcomes in Routine Evaluation – Outcome Measure
COS-P	Circle of Security – Parenting
CRF	Case Report Form
CSRI	Client Service Receipt Inventory
CTQ-SF	Childhood Trauma Questionnaire-Short Form
DERS	Difficulties in Emotion Regulation Scale
DMEC	Data Monitoring and Ethics Committee
EbE	Expert by Experience
eCRF	Electronic Case Report Form
EQ-5D-5L	EuroQoL- 5 Dimension
HRA	Health Research Authority
HTA	Health Technology Assessment
ICF	Informed Consent Form
ICTU	Imperial Clinical Trials Unit
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
PBQ	Postpartum Bonding Questionnaire
PIS	Participant Information Sheet
PMHS	Perinatal Mental Health Service

QA	Quality Assurance
QC	Quality Control
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
SSP	Strange Situation Procedure
TMG	Trial Management Group
TSC	Trial Steering Committee
UoH	University of Huddersfield

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1. TRIAL SUMMARY

Title

The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the Circle of Security Intervention for mothers in perinatal mental health services.

Objectives

The aim of the research is to conduct a Randomised Controlled Trial (RCT) to test whether the Circle of Security-Parenting Programme (COS-P), a brief group therapy intervention, will reduce maternal mental health symptoms in mothers accessing specialist NHS community perinatal mental health services (PMHS) compared to treatment as usual (TAU). We will also explore whether the intervention improves emotion regulation difficulties, maternal sensitivity, mother-infant bonding, attachment security, social support, and has an impact on infant development. Additionally, the project aims to examine whether the intervention is acceptable to participants and NHS staff, whether it is cost-effective or not, and whether there is value of information associated with the trial results.

Design

The study will be a multi-centre, individually randomised controlled trial, in which outcome assessors will be blind to intervention allocation and women are randomised to either:

1. COS-P plus TAU in a PMHS – the 'intervention' delivered in groups size 4-6.
2. TAU in a PMHS – the 'control'. Treatment in a PMHS is defined by a national service specification [1].

Sample Size

Three hundred and sixty-nine participants will be recruited from NHS PMHS in England for the RCT (n=246 for the intervention arm, n=123 for the control arm).

Inclusion/Exclusion Criteria

Inclusion criteria for the study are women or birthing parents who:

1. Are accessing a community PMHS from one of the recruiting sites.
2. Have a child aged 0-12 months with no severe illness or developmental disorder.

3. Score 1.1 or more as their average score on the Clinical Outcomes in Routine Evaluation-10 (CORE-10) [2].
4. Score 12 or more on the Postnatal Bonding Questionnaire (PBQ) [3].
5. Are aged at least 18 and are willing and able to give informed consent.
6. Are able to attend groups without being under the influence of substances.

Birthing parents who do not identify as women are also eligible to take part in the trial and although the term women has been used throughout this protocol, any reference concerning participation should be understood to include any birthing parents.

Exclusion criteria for the study are women who:

1. Do not meet the inclusion criteria.
2. Do not have a minimum of conversational English.
3. Have received COS-P previously.
4. Are experiencing active psychosis.

Intervention / Main Study Procedures

Participants will be randomly allocated to either the intervention or control arm of the study. Those allocated to the intervention arm of the study will receive COS-P, a brief, 10-session group therapy programme delivered over 10 weeks, alongside TAU. Participants allocated to the control group will receive TAU only. Follow-up data will be collected at 3-, 7-, and 12-months after baseline.

Outcome Measures

(i) Primary Outcome Measure

- Clinical Outcomes in Routine Evaluation – Outcome Measure (CORE-OM) [4]

(ii) Secondary Outcome Measures

- Postpartum Bonding Questionnaire (PBQ) [3]
- The Difficulties in Emotion Regulation Scale (DERS) [5]
- Ages and Stages Questionnaire-3 & Socio-emotional (ASQ-3 & SE) [6, 7]
- Sensitivity Scales [8]
- Strange Situation Procedure (SSP) [9]

- EuroQol- 5 Dimension (EQ-5D-5L) [10]
- Client Service Receipt Inventory (CSRI) [11]
- CORE-6D [12]
- Childhood Trauma Questionnaire-Short Form (CTQ-SF) [13]
- Adverse Events Questionnaire

2. BACKGROUND

Perinatal mental health difficulties are a significant public health concern in England, affecting up to 20% of new mothers [14]. Untreated perinatal mental health difficulties cost £8.1 billion per birth cohort, with 72% of this cost attributed to adverse impacts on the child [14]. Although multifactorial in origin, impact on the child arises in part from changes in the quality of the mother-infant relationship when a mother is mentally unwell. The government has responded with a £365 million service transformation programme to ensure that women with moderate to severe mental illness in the perinatal period (in pregnancy and the first postnatal year) can access evidence-based interventions in a timely manner. This programme of work has led to the establishment of NHS community perinatal mental health services (PMHS) in every CCG in England. Building on this, the NHS Long Term Plan prioritises the expansion of evidence-based psychological therapies within PMHS. PMHS need clinically effective and cost-effective psychological interventions that target both maternal mental health symptoms and the quality of the mother-infant relationship. However, the evidence base for such interventions in the perinatal setting is poor with the most recent National Institute for Health and Care Excellence (NICE) guidance for antenatal and postnatal mental health describing substantial gaps for interventions that can be delivered in a group format, can work trans-diagnostically, and those that target both symptoms of perinatal mental health difficulties and the quality of the mother-infant relationship [15].

However, some psychological interventions are showing preliminary efficacious findings and are already being adopted widely by psychologists working in NHS community PMHSs. One of these interventions is COS-P [16]. COS-P aims to address several gaps in the current evidence base including:

(a) working trans-diagnostically with a range of perinatal mental health difficulty presentations;
(b) targeting both symptoms of perinatal mental health difficulties and mother-infant relationship quality; and
(c) being delivered in a group format.

An unpublished survey conducted by the national NHS England/Improvement Mental Health & Strategy Transformation team in 2019 that explored which psychological interventions were offered found that COS-P is already being delivered in a quarter of the

country's PMHS (although not in any of the sites associated with this study). However, COS-P has not yet been rigorously evaluated in England and in the context of PMHS. We therefore propose to conduct a definitive trial of COS-P to determine its clinical and cost-effectiveness as an intervention offered to this population.

2.1 Rationale for the Study

Women entering PMHS often present with multiple mental health difficulties and comorbidities [17,18], making it difficult for clinicians to select the most appropriate intervention as NICE guidelines predominantly use a single diagnostic framework [15], e.g. high-intensity CBT for moderate to severe depression. However, there is growing evidence for trans-diagnostic models of psychopathology, which suggest that many mental disorders are manifestations of a small number of core underlying features [19]. A large body of research indicates that emotion regulation difficulties are one of these core trans-diagnostic symptoms [20,21], which underlines the importance of developing and testing treatments that target emotion regulation for individuals who present with multiple mental disorders.

Emotion regulation is a particularly relevant intervention target in the postnatal period as it impacts both mother and infant. A key early developmental task is an infant's acquisition of skills for regulating their emotional states. Mothers play a key role in helping with this, and in turn supporting the infant's brain development [22]. There is strong evidence that perinatal mental health difficulties can disrupt this process. For example, it has been found that mothers with emotion regulation problems [23] and difficulties thinking about their baby's thoughts and feelings (reflective functioning) [24] are more likely to experience bonding problems. Therefore, research is needed to examine the effectiveness of treatments that address transdiagnostic constructs such as emotion regulation, particularly in PMHS.

There has been very little research examining the effectiveness of interventions that target both perinatal mental health and bonding difficulties; particularly in relation to mothers of infants under 12 months, or critically with mothers with complex and severe perinatal mental health difficulties who are accessing PMHS. Where research has taken place, studies often have had very small sample sizes, poor-quality methodology and were conducted in the United States [25-27].

COS-P [16] aims to address this trans-diagnostic gap. COS-P focuses on building a mother's relationship capacities (e.g., emotion regulation and reflective functioning), rather than on behavioural techniques, making it potentially effective for simultaneously addressing maternal psychopathology and mother-infant bonding. Currently, PMHSs assess and treat perinatal mental health and bonding difficulties separately. It could therefore be cost-effective and potentially more acceptable to both patients and staff to deliver an intervention that addresses both needs.

2.2 Intervention: Circle of Security-Parenting

2.2.1 The Evidence Base

A 2016 meta-analysis of COS programmes found a total of 10 eligible studies and concluded [28]:

- A medium effect for reduction in maternal depressive symptoms.
- A large effect for improving maternal self-efficacy.
- A medium effect for improving child attachment security.

However, very few of these studies were RCTs. Since this review, four trials have evaluated the effectiveness of the COS-P intervention [29, 30,31,32] with sample sizes of 141, 52, 221, and 72 respectively. Again, the conclusions that can be drawn from these studies are limited by their small sample sizes. Although there has been no published research evaluating the use of COS-P in England, the intervention has been running in many PMHS across the country. The research team have worked with these sites and preliminary outcome data indicates a mean decrease in emotional dysregulation and a significant improvement in parenting efficacy by the end of the intervention. The qualitative feedback from both facilitators and participants has shown high levels of acceptability and feasibility.

2.2.2 The Model

The COS-P intervention is based on psycho-educational, cognitive-behavioural and psychodynamic theories and techniques. The treatment is a group intervention to support social support and peer connection and is typically delivered by qualified psychologists to up to six parents. It is divided into eight treatment modules that are delivered via ten 90-

min sessions weekly. The first session will be delivered in a face-to-face format, and the remaining sessions will be delivered remotely online. Where possible, PMHS are encouraged to run at least one additional session in a face-to-face format. Interpreters will be present during group sessions (both online and face-to-face) to assist women with low levels of English where necessary. The eight modules will be delivered throughout these sessions as follows:

Group Session	Manual modules & corresponding themes
1	1 (Welcome to Circle of Security Parenting)
2	2 (Exploring Our Children's Needs All The Way Around the Circle)
3	3 ("Being With" on the Circle) 4 ("Being With" Infants on the Circle) 5 (The Path to Security) 6 (Exploring Our Struggles) 7 (Rupture and Repair in Relationships)
4	
5	
6	
7	
8	
9	
10	8 (Summary and Celebration)

Each module contains a series of clips that are viewed and discussed during the session. The clips are of mother-child interactions, as well as of previous COS-P participants reflecting on what they learned about their own parenting from COS-P. The modules include topics such as the basic concepts of attachment, responding to children's affective states, reflecting on caregiving struggles, noticing mean (hostile), weak (helpless), and gone (neglecting) parenting (see the logic model below for more details on the intervention and its mechanisms of change).

2.2.3 COSI Study Logic Model

LOGIC MODEL
Circle of Security Parenting for mothers in perinatal mental health services

1. TARGET: Who is the intervention for?

- Patients of specialist community perinatal mental health services (cPMHS) and their infants

2. INTERVENTION: What is the intervention?

COS-P is based on psychoeducational, cognitive-behavioural and psychodynamic theories and techniques. It consists of eight treatment modules delivered in weekly 90-min sessions to groups of 6-8 parents. It employs the followings strategies:

- Provide mothers with an engaging and coherent model of children's developmental needs and their role as caregiver, teaching them to accurately observe children's needs.
- Create a secure base/safe haven relationship with mother
- Help mothers reflect on what they are doing (or not) to meet children's needs.
- Promote mothers' reflection on how their experience of being parented informs their parenting
- Co-regulate mothers' emotional experience and promote caregivers reflection on the co-regulation of their infant's emotions

3. CHANGE MECHANISMS: How and why does the intervention work?

- Increases mothers' awareness of their infant's needs & their role as caregiver, accepting responsibility as a secure base/safe haven, increasing parental self-efficacy.
- Decreases caregiver negative attributions about self and infant, increasing empathy and positive attributions about themselves and their infant. This improves self-esteem as well as increased secure base/safe haven caregiving behaviour.
- Increased reflection on their own and their infant's needs, thoughts and feelings, allows mothers to be more emotionally available to their child, decreasing maternal insensitivity and increasing child secure base/safe haven behaviour
- Increased appreciation for how their past informs their parenting and experience of co-regulating maternal emotional experience increases maternal emotion regulation, increasing emotional availability to infant and maternal sensitivity
- Above increase quality of parent-infant relationship, leading to increased child emotion regulation and longer term mental health and resilience

4. OUTCOMES: what differences will it make?

Experience of COS-P intervention

- Positive experience of group intervention focused on mother-infant relationship within context of cPMHS

Maternal outcomes

- Decrease in maternal mental health symptoms (CORE-OM)
- Increase in maternal emotion regulation (DERS)
- Increase in Quality of Life (EQ-5D)
- Increase in social support (MSPSS)

Mother-infant relationship quality

- Increased maternal sensitivity (NICHD Sensitivity Scales)
- Decrease in parent-infant relationship difficulties (PBQ)
- Increase in infant attachment security (Strange Situation)

Infant outcomes

- Improvement in global (ASQ-3) and socio-emotional development (ASQ:SE-2)

5. MODERATORS: what factors will influence the change process?

- **Parent engagement** – willingness of mothers to attend, to attend all sessions and to participate in activities and share
- **Fidelity to the intervention model/ group facilitator skills** – how closely the therapists keep to the COS-P model through high quality specialist training and supervision
- **Implementation issues** – ensuring therapist's time for preparation and delivery

2.3 Risk / Benefit Assessment

The substantial benefit from the research will be evidence of whether or not COS-P is a clinical or cost-effective intervention for new mothers with complex and severe mental health difficulties that can be delivered in PMHS. The impact of the research will include:

1. **Improved knowledge:** The proposed research will add substantially to the evidence for the effectiveness of psychological interventions that target both maternal psychopathology and mother-infant relationship difficulties for perinatal mothers, an area which is consistently highlighted in NICE guidelines and governmental policy. The research will add to existing knowledge of the developmental pathways leading to mother-infant relationship difficulties and of the mechanisms implicated in the prevention of these difficulties.

2. **Potential to improve clinical outcomes for mothers and their children:** If effective in treating maternal psychopathology and mother-infant relationship difficulties, the intervention will lead to improved short- and long-term outcomes for mothers and their children across a range of domains, including improved psychiatric, educational and physical health outcomes.

3. **Potential to positively impact the NHS and society:** The COS-P intervention we are testing has the potential to be used widely across all PMHS in the country given the established gaps in evidence-based provision that it has the potential to fill, i.e., group work and mother-infant relationship difficulties. The treatment and prevention of maternal psychopathology and mother-infant relationship difficulties in the perinatal period are areas of key concern to the NHS, but there is a lack of consistency in the availability of intervention programmes and no clear pathway for access to evidence-based and cost-effective interventions. The evidence from the proposed study could make a substantial contribution towards addressing this area of concern to the NHS. It will fit well within current NHS services, and if rolled out successfully will make a considerable impact on reducing the costs of perinatal mental health difficulties to both the NHS and wider society, through reduced burden on the health, social, educational and criminal justice systems

Potential barriers to implementation are discussed below together with how to overcome them.

- **Intellectual property.** The intellectual property for COS-P is held by COS International. No restrictions exist on the right to use the materials of the COS-P intervention, and no costs are associated with its use from the creators or their organisation, other than the costs to train in the intervention (see section 7.1.1 for further information).

- **Cost and availability of COS-P training.** The 4-day training costs are £645 (£161.25 per day) per intervener. We have done a horizon scan of the market for similar training and concluded that the cost of the training is significantly below average, and all the NHS sites involved in the trial confirmed they thought it was an acceptable amount for a NHS service to afford for their staff to attend. Additionally, there are a number of accredited trainers that are based across the UK, and trainings are held at regular intervals in a range of locations throughout the year, so access to training is will not be a barrier.

- **Workforce.** Having the workforce available to train up in COS-P following the trial results is a potential barrier. However, the NHS Long Term Plan Implementation Framework indicates a substantial increase in psychologists and other therapists in PMHS. Furthermore, if effective the intervention will fill a gap in service provision that PMHS services have told our research team they both need and want for the women accessing their service.

- **Influencing decision makers.** Our choice of primary outcome was intentionally chosen as it is one of the most widely used outcome measures in secondary care mental health services, including PMHS, and as such, is familiar to service managers, as well as local and national commissioners. It is also compatible with the national Mental Health Service Dataset. In this way, we hypothesise that any changes detected on it as a result of this trial will be highly compelling to key decision-making stakeholders and have the potential to positively impact clinical practice. We will use our multi-modal dissemination plan above to share the outcomes of the trial in an innovative way. Furthermore, Dr Camilla Rosan previously led the national perinatal

mental health transformation programme at NHS England and is the Secretary for the British Psychological Society's (BPS) Faculty of Perinatal Psychology, and as such has unparalleled access to both front-line NHS perinatal psychologists as well as PMHS service managers and commissioners. The findings of this trial will be shared with these key stakeholders and decision makers through the twelve NHS England Strategic Clinical Networks for Perinatal Mental Health and their corresponding annual conferences, listservs and newsletters.

3. OBJECTIVES AND OUTCOME MEASURES

3.1 Primary Objective

The primary objective of this research is to conduct a RCT to test whether a brief group intervention (COS-P) will reduce maternal mental health symptoms in mothers accessing specialist community PMHS compared to TAU.

3.2 Secondary Objectives

The secondary objectives of this research are as follows:

1. To explore whether COS-P improves emotion regulation difficulties, maternal sensitivity, mother-infant bonding, attachment security and social support.
2. To examine whether COS-P has an impact on infant development.
3. To explore whether COS-P is acceptable to participants and NHS staff.
4. To examine whether COS-P is cost-effective or not.
5. To investigate whether there is value of information associated with the trial results.

3.3 Primary Outcome Measure

The primary outcome will be the Clinical Outcomes in Routine Evaluation – Outcome Measure (CORE-OM) averaged over 3, 7 and 12 months [4].

3.4 Secondary Outcome Measures

The secondary outcomes at 3, 7 and 12 months are as follows:

- Postpartum Bonding Questionnaire (PBQ) [3].
- The Difficulties in Emotion Regulation Scale (DERS) [5].
- Ages and Stages Questionnaire-3 & Socio-emotional (ASQ-3 & SE) [6, 7].
- Sensitivity Scales [8].
- Strange Situation Procedure (SSP) [9] (12-month timepoint only).
- EuroQol- 5 Dimension (EQ-5D-5L) [10].
- Client Service Receipt Inventory (CSRI) [11].
- CORE-6D [12].
- Childhood Trauma Questionnaire-Short Form (CTQ-SF) [13] (Baseline only).
- Adverse Events Questionnaire. A pre-specified Adverse Event of interest is the start of social care involvement for the family.

In addition to these secondary outcome measures, the following data will be collected 3-months after baseline:

- Short Experience Survey (participants allocated to the intervention arm of the study only).
- Qualitative interviews with a subsample of participants allocated to the intervention arm of the study.

The study would also like to understand the factors and barriers influencing the decision not to take part in the trial to ensure that participation is as accessible as possible. As such, women who decline to take part in the study will be asked to complete a short survey about their decision. Some women who are assigned to the intervention arm do not begin the COS group programme, referred to here as 'non-starters'. The study would like to understand the factors and barriers relating to this and non-starters will therefore be asked to complete a short three-question survey about their decision, administered via Qualtrics.

- The study will also use focus groups to collect the views and experiences of NHS Staff members involved in the delivery of COS-P groups in the Trial; individual interviews will be offered to practitioners who are due to leave their role prior to the focus groups taking place.

3.5 Summary Table of Objectives and Outcome Measures

Objectives	**Outcome Measure(s)**	**Timepoint(s) of evaluation of this Outcome Measure (if applicable)**
Primary Objective To test whether a brief group intervention (COS-P) will reduce maternal mental health symptoms in mothers accessing specialist community PMHS compared to TAU.	CORE-OM	Data will be averaged over 3, 7 and 12 months. Timepoint of evaluation is screening, baseline, 3-months, 7-months, and 12-months after baseline.

Secondary Objectives To explore: 1. Whether COS-P improves emotion regulation difficulties, maternal sensitivity, mother-infant bonding, attachment security and social support. 2. Whether COS-P has an impact on infant development. 3. Whether COS-P is acceptable to participants and NHS staff. 4. Whether COS-P is cost-effective or not. 5. Whether there is value of information associated with the trial results.	• PBQ • DERS • ASQ-3 & SE • SSP • EQ-5D-5L • CSRI • CORE-6D • CTQ-SF • Adverse Events Questionnaire • Views and experiences via surveys, interviews and focus groups	Participant outcome measures will be collected at each time point (3, 7 and 12 months) separately, with time point of most interest at 12 months. Within the intervention arm, participants' views and experiences will be gathered by surveys at 3-months after baseline. At this timepoint, a subsample of participants will be invited to a qualitative interview. NHS staff focus group data will be conducted and evaluated after staff have been involved with several COS-P groups; this will be scheduled after the majority of recruitment blocks have taken place (approximately month 31 of the study). To maximise learning, individual interviews will be offered sooner to any practitioners who have facilitated at least one group and are leaving their role prior to the focus groups.

4. STUDY DESIGN

This study is a RCT taking place across England. Participants will be randomly allocated to either the intervention or control group of the study.

4.1 Design

The study is a multi-centre, individually randomised controlled trial with a 2:1 randomisation ratio, in which outcome assessors will be blind to intervention allocation and women are randomised to either:

1. COS-P plus TAU in a PMHS – the 'intervention' delivered in groups size 4-6.
2. TAU in a PMHS – the 'control'. Treatment in a PMHS is defined by a national service specification [1].

To note, alternative trial designs were reviewed by the CTU, including cluster randomisation as a means of managing contamination, but were not on balance recommended, which is supported by a recent review on managing contamination in trials [33]. Contamination will be strictly managed via good trial conduct and analysis methodology.

The trial sites within the study will be community PMHS in the following NHS Trusts:

1. Cheshire and Wirral Partnership NHS Trust
2. North West Boroughs Healthcare NHS Foundation Trust
3. Merseycare NHS Foundation Trust
4. Northumberland, Tyne & Wear NHS Trust
5. South West Yorkshire Partnership NHS Trust
6. Tees, Esk and Wear Valleys NHS Foundation Trust
7. Northampton Healthcare NHS Foundation Trust
8. Sussex Partnership NHS Foundation Trust
9. Devon Partnership NHS Trust

4.2 Internal Pilot

An internal pilot will be included to assess recruitment rate by site, adherence to the intervention, fidelity to intervention, time to starting the intervention in the active arm, number and type of 'treatment as usual' received in control and active arm, and overall trial retention. This information will be reviewed 12 months after recruitment has started. For full details please see section 8.

5. PARTICIPANT ENTRY

There will be two groups of participants involved in this study: women accessing PMHS (secondary care mental health services), and the NHS staff members working at these services.

5.1 Study Setting and Population

PMHS Patients

The first group of participants will include 369 patients of PMHS, and a child aged 0-12 months. From the annual NHS Benchmarking reports on PMHS, we are aware of the demographic breakdown of women that attend services, for example that 13% of women are non-White British [17], and we would seek to reflect this ethnic diversity within the trial sample and in our recruitment strategies.

1. Inclusion Criteria

Women and other birthing parents who:

1. Are accessing a community PMHS from one of the recruiting sites.
2. Have a child aged 0-12 months with no severe illness or developmental disorder.
3. Score 1.1 or more as their average score on the CORE-10 [2].
4. Score 12 or more on the Postnatal Bonding Questionnaire PBQ) [3].
5. Are aged at least 18 and are willing and able to give informed consent.
6. Are able to attend groups without being under the influence of substances.

2. Exclusion Criteria

Women and other birthing parents who:

1. Do not meet the inclusion criteria.
2. Do not have a minimum of conversational English.
3. Have received COS-P previously.
4. Are experiencing active psychosis.

NHS Staff Members

The second group of participants involved in the study will be the approximately 20 NHS staff members working at the PMHS involved in the trial. These staff members will be trained as COS-P International Interveners as part of the study and be responsible for the delivery of COS-P groups within the trial. These participants will be invited to take part in the qualitative intervention evaluation aspects of the study. Staff members were chosen to be trained in COS-P according to the following criteria.

1. Inclusion Criteria

NHS staff members who:

1. Are currently working in one of the PMHS involved in the trial.
2. Trained and experienced in the delivery of psychological interventions.
3. Have capacity to undertake the time commitment associated with the COS-P training and group delivery within their current role.
4. Are preferably experienced in delivering group therapy sessions.

2. Exclusion Criteria

NHS staff members who do not meet the inclusion criteria.

6. PROCEDURES AND MEASUREMENTS

Participants will be recruited from PMHS at the trial sites. Women accessing these services will be screened by staff at the PMHS during standard screening meetings (e.g.

intake assessments, review meetings) and referred to the research team if eligible. Women screened from existing caseload can also be referred to the research team if eligible. The research team will invite these women to participate in the full study, provide information regarding the trial, and obtain informed consent. Participants will be randomly allocated to either the intervention or control arm of the study.

NHS staff members to be trained as COS-P facilitators will be identified by their service. They will receive training and support to deliver the COS-P groups within the trial.

6.1 Identification and Recruitment of Participants

PMHS Patients

Trial recruitment will take place in seven x four-week recruitment blocks that will be equally spaced across the recruitment period. During these recruitment blocks, information about the trial will be publicised widely among clinical colleagues working in all 9 PMHS sites. Members of the research team will present plans for the study at local clinical meetings and continue to visit sites on a regular basis to remind them about the study.

With the support of the local CRN, PMHS staff will approach women about the trial during standard screening meetings (e.g., intake assessments, review meetings). We will aim to use standard intake assessment visits as primary recruitment pathways, but women in PMHS can also be recruited outside of these standard visits. Staff members completing these screening meetings will not be involved in the intervention delivery; however, it is probable that they will be involved in the delivery of TAU at some sites. Those women that score 1.1 or more as their average score on the Clinical Outcomes in Routine Evaluation – 10 (CORE-10; [2]) and 12 or more on the Postnatal Bonding Questionnaire (PBQ; [3]) will be given a printed Participant Information Sheet (PIS) and leaflet about the study and asked to provide verbal consent to be contacted by a member of the research team to discuss this information further (this will be done via an interpreter for women who require this). The PIS will contain information on the aims of the study, benefits and risks of taking part, consent and withdrawal processes, data storage and confidentiality processes, ethical approval and sponsor information, and payment arrangements for participation. The study leaflet will provide a shorter overview of the study. The PIS and study leaflet will be translated for women who do not speak English to ensure inclusivity.

The contact details and raw CORE-10 and PBQ scores of those who provide verbal consent will be shared with the research team via email (this will only be shared with the research assistant who has an honorary NHS contract with the service). The research assistant will review the information provided by the service to confirm eligibility and contact the individual. Participants who do not meet the eligibility criteria will also be contacted and informed of this.

Women who do not provide verbal consent to be contacted with the study team will be asked to complete a short survey about their decision. The survey was created in collaboration with the study's Expert by Experience (EbE) panel and includes one question about factors/barriers which may have influenced the women's decision. The PMHS staff member who completed the screening will ask the women to complete this and share the completed survey with the Trial Manager who will then upload this information to the database.

NHS Staff Members

NHS staff members at each of the trial sites will be identified by their service, either by nomination or putting themselves forward. Verbal consent to share the staff member's contact details with the research team and COS International will be obtained by the Site Lead at that service. These staff members will then be contacted by the Trial Manager and consent for contact details to be stored will be collected.

6.2 Informed Consent

The process of obtaining informed consent in all scenarios will be conducted in accordance with the requirements of Research Ethics Committee guidance, the Declaration of Helsinki and Good Clinical Practice.

6.2.1 PMHS Patient Participants

Obtaining informed consent will follow a stepped process as follows:

1. **Getting in touch.** All women who provided verbal consent to being contacted by a member of the COSI Study research team and met the eligibility criteria will be contacted by a member of the research team to share an electronic version of the PIS

and to arrange a time to discuss the study further. Where necessary, the PIS will be translated into alternative languages.

2. **Decision making.** The COSI Study research team member will encourage potential participants to spend as much time as they want asking questions about the study and considering whether they want to take part. Where necessary, an interpreter will join these discussions to assist women who do not have a high level of English. In all instances potential participants will have at least 24 hours before deciding whether they wish to take part in the study.

3. **Consent.** Informed (digital) consent to the trial will be taken either before, or during, the baseline data collection visit with families. Participants will already have received study information by email and will have had the opportunity to ask the research team questions over the phone. Following this discussion, the research assistant will confirm if the participant wishes to continue with the study. If so, the baseline data collection visit will be scheduled and the participant will be sent a unique link to provide digital informed consent via Microsoft Forms. If any participants do not complete the consent form before the baseline visit, the trained research assistant will take the participant through each of the clauses on the consent form and record their informed consent via Microsoft Forms. The consent form will be translated into alternative languages where necessary, and an interpreter will join these discussions with the participant if required. As part of this appointment, the research assistant will check eligibility and conduct a mental health capacity assessment (as trained by the AFNCCF) to ensure the woman is able to provide consent. All women will be informed that they will be able to withdraw from the study at any time and this will not impact their care.

4. **Records.** A copy of the PIS and informed consent form (ICF) will be shared with the women via email for their records. The ICF will be downloaded from Microsoft Forms in a PDF format for this purpose. An electronic copy of the PIS and ICF will also be provided to the participant's service to be included in their site service record. This will be shared with the relevant service by the Research Assistant between NHS email accounts.

Interviews

At approximately 3-months after baseline , a selection of women allocated to the intervention arm of the study will be invited to take part in an additional interview about their experiences of COS-P. Informed consent for the interview will be obtained via the following steps:

1. **Identification.** At the 3-month follow-up, participants within the intervention arm of the study will be asked to complete an experience survey via Qualtrics, linked to the main dataset via the unique trial ID number. This survey will include items asking whether they would be interested in taking part in an interview. We will invite a subsample of completers and all non-completers of the COS-P groups to take part in an interview. Non-completers are defined as those who attended less than six of the ten COS-P group sessions or were 'uninvited' from the group by a COS facilitator (e.g. due to concerns about attendance, following usual clinical approaches to group programmes). We recognise that non-completers may face greater barriers to participation and when contacting them about their feedback, we will highlight that they are able to take part in an interview even if they choose not to complete a survey.

2. **Contact**. A selection of women who express an interest in taking part in the interview and agree for their details to be shared with the UoH will be contacted by a member of the research team using the participant's contact details (telephone or email). A PIS about the interview will be shared, and a time to discuss the study further will be arranged. Where necessary, the PIS will be translated into alternative languages.

3. **Decision making.** The researcher will encourage the participant to spend as much time as they want asking questions about the study and considering whether they want to take part. If required, an interpreter will join the discussions with the participant to assist in answering any questions.

4. **Consent.** Informed consent to the interview will be provided by participants providing digital informed consent via Microsoft Forms. Where necessary, the consent form will be translated into alternative languages. The researcher will then schedule the interview to take place remotely or in-person, according to participant preferences and current restrictions.

5. **Records.** A copy of the electronic ICF will be shared with participants via email for their records. The ICF will be downloaded from Microsoft Forms in PDF format for this purpose.

6.2.2 NHS Staff Members

Informed consent will be obtained from the trained facilitators to join the study as participants..

1. **Contact**. Verbal consent will be obtained by the Site Lead for these staff members' contact details to be shared with the research team for the purpose of sharing additional information about the study, and with COS International to schedule the COS-P training. The COSI Study research team will contact these staff members to obtain consent for their contact details to be stored for the purpose of the trial.

2. **Study Information**. Following the verbal consent and training of these staff members, the facilitators in the trial will be provided with a participant information sheet regarding joining the study. The information sheet will outline the requirements for fidelity coaching, fidelity coding (including video recordings of COS-P sessions), and the storage of this data. Staff members will be given the opportunity to ask any questions about the study, their participation, and the intervention.

3. **Consent**. Informed consent to the trial will be collected by the research team when the site opens. This will be collected digitally via Microsoft Forms.

4. **Records**. An electronic copy of the PIS and ICF will be given to the staff members for their records. The ICF will be downloaded from Microsoft Forms in PDF format for this purpose.

Focus Groups

Staff members participating in the trial (including those who are delivering the COS-P groups or managing/supervising group delivery) will be invited by research staff at the UoH to join a focus group regarding their experiences of COS-P (see section 6.8.4 for full details). This will follow the below procedure:

1. Contact. The research team will share the PIS and ICF for the focus group with staff members.

2. Decision making. Staff members will be provided with an opportunity to ask any questions about the focus group over the phone.

3. Consent. Written informed consent will be obtained prior to the beginning of the focus group. This will be collected digitally via Microsoft Forms.

4. Records. An electronic copy of the PIS and ICF will be given to the participants for their records. The ICF will be downloaded from Microsoft Forms in PDF format for this purpose.

Where practitioners are due to leave their role prior to the focus groups taking place, they will be invited to take part in an individual interview about COS-P, following the same procedure as outlined above and using the same topics as will be used in the focus groups.

6.3 Screening and Pre-randomisation Evaluations

Participants will be asked to complete the following screening measures during their routine screening appointment at the trial site PMHS:

1. **Postpartum Bonding Questionnaire (PBQ) [3]**

   The PBQ is a 25-item self-administered measure designed to provide an early indication of disorders within mother-infant relationships, through the assessment of a mother's feelings and attitudes towards her infant. This measure is frequently used in research on mother-infant bonding with postpartum populations [34-36] and has demonstrated acceptable reliability and reasonable validity [37]. The impaired bonding sub-scale is the PBQ general factor used for identifying a general problem in the mother-infant relationship.

2. **Clinical Outcomes in Routine Evaluation- 10 (CORE-10) [2]**

   The CORE-10 is a 10-item, session-by-session, monitoring tool with items covering various mental health difficulties. The CORE-10 has been shown to have

good psychometric properties with good internal reliability (0.90) and is routinely used with people presenting common mental health properties in primary care settings.

Where required, these measures will be completed with the assistance of an interpreter. Those that score 1.1 or more as their average score on the CORE-10 (i.e. raw score of 11 or more) plus 12 or more on the PBQ will be given basic information about the study and asked to provide verbal consent to be contacted by a local researcher. A member of the COSI Study research team will follow up with these women and invite them to participate in the full study. Informed consent will be obtained during the initial assessment visit. Once the baseline assessment has been completed and the recruitment block at the site is full, the participant will be randomly allocated to one of the study arms.

6.4 Randomisation and Blinding

6.4.1 Randomisation

Consenting participants who meet the eligibility criteria and consent to take part will be randomly allocated to one of two arms by a web-based randomisation system (integrated within the trial RedCAP system) in a 2:1 intervention:TAU ratio. Participants will be recruited in 'cohorts' to be allocated to an active group in a timely manner. Randomisation will be stratified by site and recruitment cohort. This ratio is used to ensure that intervention delivery is not delayed by the time to accumulate sufficient numbers to be allocated to the group intervention for delivery to take place. Randomisation will take place once the recruitment block at the site is full.

6.4.2 Blinding

Researchers who obtain follow-up data from the participants will be blinded to participants allocation. This will be ensured by participants being identified by a unique trial ID only, in addition intervention data will not be shared with the researchers. To minimise the risk of unblinding within the research team during data collection visits, the following steps will be taken:

1. All participant communications confirming the data collection visits will include a reminder that the researcher needs to remain blinded and a request for the participant to withhold this information during the visit.

2. At the beginning of the data collection visit, the researcher will reiterate the above information to the participant.
3. Participants allocated to the intervention arm of the study will be reminded during the first COS-P group sessions that the researchers need to be kept blinded.
4. Researchers will not be able to view participant's group allocation within the REDCap database.

In the event that a member of the research team is unblinded during a data collection visit, this will be immediately reported to the Trial Manager. This researcher will not complete any further data collection visits with the participant whose group allocation has been unblinded.

Participants, the Site Principal Investigator (PI) and COS-P facilitators will not be blinded and will be informed of participant's allocation by the Trial Manager via email.

6.5 Visit Schedule PMHS Patients

The below visit schedule will be used for women within the study. The research team will ensure that for those in the intervention arm of the study, there is no more than 4 weeks between the baseline timepoint and the first COS-P group. As such, the time between screening and baseline visits is not standardised and will vary between participants.

	Screening	**Baseline**	**COS-P Group (intervention arm only)**	**3-month f/u**	**7-month f/u**	**12-month f/u**
Informed consent *(20 mins)*	X	X				
CORE-10 *(8 mins)*	X					
Inclusion & exclusion criteria *(10 mins)*		X				
Demographics *(10 mins)*		X				
Randomisation *(5 mins)*		X				
CORE-OM *(8 mins)*		X		X	X	X
PBQ *(5 mins)*	X	X		X	X	X

CTQ-SF *(8 mins)*		X				
DERS *(15 mins)*		X		X	X	X
ASQ-SE *(15 mins)*		X		X	X	X
ASQ-3 *(15 mins)*		X		X	X	X
Sensitivity Scales *(10 mins)*		X		X	X	X
CSRI *(15 mins)*		X		X	X	X
EQ-5D-5L *(8 mins)*		X		X	X	X
CORE-6D *(2 mins)*		X		X	X	X
COS-P Groups *(10 sessions)*			X			
SSP *(40 mins)*						X
Adverse Events *(5 mins)*		X		X	X	X
Short Experience Survey *(10 mins)*			X			
Qualitative Interviews *(60 mins)*			X			
Time per visit	**33mins**	**137mins**	**970mins**	**85mins**	**98mins**	**125mins**

6.6 Visit Schedule for NHS Staff Members

	After Recruitment Ends (approx. Sept. 2023)
Staff Focus Groups (90-120 mins) or interview (60 mins, where leaving their role before this point)	X
Time per visit	**120 mins**

6.7 Follow-up

Follow-up data collection visits with parent participants will take place 3-, 7-, and 12-months after baseline. The visits will take place as close to these time points as possible, and within a visit window of +/- 1 month. Participants will receive follow-up communications (e.g., email, text, and phone call) regarding the scheduling of the data collection visit if there has been no response. If a response has still not been received following the third

communication, an email will be sent to the participant confirming that we will contact them at the next data collection timepoint.

At each timepoint, the data collection visit will take place remotely with the self-reported measures completed by the participant online. If the participant is unable to complete the measures online, a member of the research team will assist with this. The Strange Situation Procedure (SSP) (completed at the 12-month follow up) will be completed at a research centre and so participants will need to travel to this location to complete this task.

6.8 Measures

Data (except for the qualitative aspects) will be collected on an Electronic Data Capture (EDC) system developed using the REDcap system, incorporating the trial database and randomisation system. This will be a web-based EDC comprising a full GCP-compliant audit trail and stored on a secure server at Imperial College London.

6.8.1 Demographics

We will collect contextual factors including:

- Maternal characteristics (e.g., mental health presentation, ethnicity, non-English speaking background).
- Pregnancy details (e.g., complications experienced, delivery type, previous pregnancies).
- Infant characteristics (e.g., gender, age and first-born status).

6.8.2 Primary Outcome Measure

Clinical Outcomes in Routine Evaluation – Outcome Measure (CORE-OM) [4]

The CORE-OM is a 34-item measure of psychological distress. The CORE-OM is one of the most widely used outcome measures in secondary care mental health services, including specialist community PMHS, and as such is familiar to service managers, as well as local and national commissioners. It is also compatible with the national Mental Health Service Dataset. The CORE-OM has strong internal consistency (0.75-0.95) and convergent validity with other measures of mental health difficulties (e.g. the Symptom Checklist-90-Revised, p =.88) [38]. The CORE-OM has been reported as acceptable in both clinical and non-clinical populations [38]. The CORE-OM total change score we are using of 5 (mean item change of 0.147), was strongly endorsed

by our Expert by Experience panel as being meaningful.

6.8.3 Secondary Outcome Measures

- **Postpartum Bonding Questionnaire (PBQ) [3]**
  The PBQ is a 25-item self-administered measure designed to provide an early indication of disorders within mother-infant relationships.
- **The Difficulties in Emotion Regulation Scale (DERS) [5]**
  The DERS is a self-report measure of perceived maternal emotion regulation ability.
- **Ages and Stages Questionnaire-3 & Socio-emotional (ASQ-3 & SE) [6, 7]**
  The ASQ-3 is a tool for assessing and screening global infant development in communication, motor and cognitive areas. The ASQ:SE-2 focuses specifically on social and emotional behaviours.
- **Sensitivity Scales [8]**
  The Sensitivity Scales are an observational measure of maternal sensitivity from infancy up to 24 months. The scales require training, but the team has extensive experience in its use and can readily provide the necessary training.
- **Strange Situation Procedure (SSP) [9]**
  The Strange Situation Procedure is the gold standard assessment of attachment security in infancy. The research team has extensive experience in administering this protocol. Participants will be asked to wear a heart rate monitor during this tasks and State Space Grids coding grids will be used to evaluate co-regulation of emotion.
- **EuroQol- 5 Dimension (EQ-5D-5L) [10]**
  The EQ-5D-5L is a preference-based health-related quality of life measure to compute QALYs for economic evaluation.
- **Client Service Receipt Inventory (CSRI) [11]**
  The CSRI collects information about health service usage, such as participants' use of health and social care services, accommodation and living situation, income, employment and benefits.
- **CORE-6D [12]**
  The CORE-6D is a 2-dimensional health state classification system derived from the CORE-OM consisting of a unidimensional 5-item emotional component and physical item.

- **Childhood Trauma Questionnaire-Short Form (CTQ-SF) [13]**
  The CTQ-SF is a 28-item version of the Childhood Trauma Questionnaire [39] used as a screening measure for maltreatment histories.
- **Adverse Events Questionnaire**
  Adverse Events and Serious Adverse Events (e.g., eye strain from online measures) will be reported via a short questionnaire. A specific AE of interest is the start of social care involvement for the family.

6.8.4 Qualitative Data

At 3 months, the intervention arm participants will complete a short questionnaire designed for the trial in collaboration with the Expert by Experience (EbE) panel regarding acceptability, including barriers and facilitators to use, for the purpose of helping to understand contextual factors at the practitioner level, system level and for women, including with consideration of parent demographics. The survey will be made available for self-completion online via Qualtrics but can be completed with a member of the research team if the participant wishes. The survey will additionally be used to help identify the interview sample, including asking about interest in taking part in an interview.

Individual semi-structured interviews will take place with approximately 20-30 completers from the intervention arm of the study and offered to all ‘non-completers’, defined as women who attended less than six of the ten COS-P group sessions or were ‘uninvited’ from the group by a COS facilitator (e.g. due to concerns about attendance, following usual clinical approaches to group programmes). Interviews with women will explore the acceptability of the intervention, including barriers and facilitators to use. Interview schedules will be developed in collaboration with the EbE panel and piloted before use. Focus groups with PMHS staff will examine staff views of the intervention and experiences of delivery, following a topic guide based on the study aims. Interviews are anticipated to each last approximately 1 hour and focus groups approximately 1.5-2 hours. All will be audio/audio-visually recorded and transcribed verbatim. Interviewers, including EbE researchers, will receive specialist training in preparation for data collection and will be supervised by Dr Zoe Darwin. All aspects of the qualitative work will explore contextual factors which may influence the effectiveness and acceptability of the intervention at practitioner level, system level and for women. For example, contextual

factors at the group or system level include site differences, mode of treatment delivery and group size.

6.8.5 Trial Delivery

Regarding mode of delivery, we have prepared for the eventuality of delivering the trial in different ways, responsive to the pandemic and reviewed in collaboration with NIHR in June 2021. Due to the ongoing pandemic, the trial will be delivered via a mixed delivery approach as follows:

1. **COS-P Groups** The majority of COS-P sessions will be delivered remotely online via Microsoft Teams or Zoom. Services will be asked to deliver the first session of each group face-to-face, and at least one other session face-to-face where possible.
2. **Data Collection.** The data collection visits will take place remotely online via Microsoft Teams. Ahead of each data collection visit, participants will be emailed a link which allows the questionnaires to be completed directly into REDCap. Participants will be invited to complete as many of these questionnaires as they wish prior to the visit. The Research Assistant will then complete the remaining measures and the sensitivity scales observational task with the participants during the visit. All assessments will be completed in this manner except for the Strange Situation Procedure, which will be administered face-to-face. For the baseline data collection visit, the link to the online questionnaires will not be shared with participants until informed consent has been received.

6.9 Participant Reimbursement

Participants will receive a £10 voucher per assessment visit as reimbursement for their time. An additional £20 voucher will be provided as reimbursement for participants who take part in the interviews.

7. INTERVENTION

7.1 The Circle of Security-Parenting (COS-P)

The COS-P intervention is based on psycho-educational, cognitive-behavioural and psychodynamic theories and techniques. The treatment is a group intervention to support

social support and peer connection and is typically delivered by qualified psychologists to up to 6 parents. It is divided into 8 treatment modules that are delivered in 10 sessions that will each last between 90-120 minutes. Each module contains a series of clips that are viewed and discussed during the session. The clips are of mother-child interactions, as well as of previous COS-P participants reflecting on what they learned about their own parenting from COS-P. The modules include topics such as the basic concepts of attachment, responding to children's affective states, reflecting on caregiving struggles, noticing mean (hostile), weak (helpless), and gone (neglecting) parenting (see the logic model in section 2.2.3 for more details on the intervention and its mechanisms of change).

Each group will be delivered by one trained, supervised, NHS health professional working in specialist community PMHS, predominantly doctorate level clinical and counselling psychologists. The key role of the therapists will be to develop a trusting relationship with the participants in the treatment arm, and to deliver the treatment in 10 sessions in accordance with the manual. They will be supervised, and the treatment will be monitored closely for fidelity to the manual.

The COS-P groups will be predominantly delivered remotely online using Microsoft Teams or Zoom. However, the first session of each group will be delivered face-to-face in local, accessible community group rooms, such as in children centres, libraries, and hospital antenatal education settings. Each service will also be encouraged to deliver at least one other session face-to-face where possible. Where required, an interpreter will join the COS-P group sessions (both online and face-to-face) to assist women who do not have a high level of English.

7.1.1 Intellectual Property of the Intervention

The intellectual property for COS-P is held by COS International. No restrictions exist on the right to use the materials of the COS-P intervention, and no costs are associated with its use from the creators or their organisation, other than the costs to train in the intervention. The research will trial COS-P in a version that is delivered to women with perinatal mental health difficulties who are accessing a PMHS. No third-party licenses are required to carry out the proposed research to the best of our knowledge, and COS International are aware of the proposed study and involved to provide consultation and fidelity coaching to all the trial interveners.

It is not expected that any foreground IP will be developed as a result of the trial, however any foreground IP relating to the Circle of Security (e.g., a perinatal adaption of the intervention) will be not be owned by the sponsor or any partners as background IP lies with COS International. Any foreground IP relating to scientific results of the trial will be co-owned by the sponsor (the AFNCCF) and partners.

7.1.2 Treatment Fidelity

Each therapist will be trained by accredited COS International trainers. As part of this training, all trial interveners will be given a clear 10-session group delivery manual and protocol to follow. As part of becoming a therapist on the trial, they will also undertake 20-hrs of fidelity coaching, involving 10x 2-hours sessions throughout the delivery of their first group, i.e., after each of the 10 sessions in one group intervention. Fidelity during the trial will be monitored in three ways:

1. The interveners will use the standard COS documenting procedure to record, after each session, parental and infant responses, any significant events, and the interventions they had used. These follow a structured scheme and help the intervener identify key moments in each session where supervision and support may be required.

2. Each session of each intervener's third group is video recorded. Independent trained coders will review 20% of the available recorded sessions following the fidelity protocol recommended by the developers (still in development). Coders rate adherence to the manualised content, as well as the competence with which the material is delivered by the intervener, during all scheduled (i.e., required) and recommended (i.e., optional) breaks (i.e., during any times in which video is not being shown). Adherence to the manual is assessed independently of competence. A criterion of 75% is used to ensure that the treatment administered meets the standards of fidelity required for a valid trial. While competence in delivery is also rated there is no minimum criteria for competence as reliability of competence ratings in this treatment, as in many other similar interventions, is too low.
    - Competence is rated on a 1-5 scale:

- 1 - Very poor. The therapist handled this in an unacceptable, even ‘toxic’ manner.
- 2 - Poor. The therapist handled this poorly (e.g., showing clear lack of expertise, understanding, competence, or commitment, inappropriate timing, unclear language).
- 3 - Adequate/Good Enough. The therapist handled this in a manner characteristic of an ‘average’, ‘good enough’ therapist.
- 4 - Good. The therapist handled this in a manner slightly better than ‘average.’
- 5- Excellent. The therapist demonstrated a high level of excellence and mastery in this area.

3. Trial interveners receive a minimum of monthly clinical supervision sessions at each of the sites by three expert therapists trained in parenting interventions and COS-P. Using information from 1. and 2. supervisors will identify learning and teaching opportunities that serve to improve both adherence to the manual and competence in delivery.

7.2 Treatment as usual (TAU)

Participants in both groups will continue to access TAU. TAU in PMHSs is organised and defined by a national service specification [1]. Despite this, there will be a degree of variability in what women receive which may change over time as PMHSs receive more NHS England funding as part of the NHS Long Term Plan expansion [40]. To support our understanding of TAU, during the study set up stage, we will comprehensively map TAU in each of the sites by conducting a series of face-to-face structured interviews with PMHS clinicians working in each of the local recruitment sites. We will then cross-reference and group the sites against the PMHS service taxonomies that have been developed by the ESMI-II study team (NIHR Award ID:17/49/38). This will allow us to later use these different taxonomies for comparison with the intervention arm.

To verify TAU, we will also collect data from all participants on concurrent use of health services (via a standardised measure: Client Service Receipt Inventory [11]), including number of sessions offered, the location where they were provided, and which healthcare (or other non-healthcare) professionals provided the care. We will therefore be able to

describe TAU in some detail.

7.3 Permanent Discontinuation of Study Intervention and Withdrawal from Study

1. Permanent Discontinuation of Study Intervention

Participants may discontinue the study intervention for the following reasons:

- At the request of the participant.
- Adverse event/ Serious Adverse Event.
- If the investigator considers that a participant's health will be compromised due to adverse events or concomitant illness that develop after entering the study.

2. Withdrawal from Study

Withdrawal from the study refers to discontinuation of study intervention and study procedures and can occur for the following reasons:

- At the request of the participant
- Loss to follow-up
- Adverse event/ Serious Adverse Event
- If the investigator considers that a participant's health will be compromised due to adverse events or concomitant illness that develop after entering the study.

Should a participant decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible and participants will be encouraged to continue to provide outcome data except in exceptional circumstances or loss to follow-up. Withdrawn participants will not be replaced.

7.4 Procedures for Withdrawal from Study

If a participant withdraws from the study intervention or from further follow-up visits, this will be documented in the participant records and Case Report Form (CRF) including the reason for withdrawal, whether study data collected up to that point can be used and whether further follow-up can be conducted.

Main Trial Data

Upon withdrawal, participants personal information (e.g., contact details) will be deleted.

Any data collected as part of the trial up to the point of withdrawal will be retained unless otherwise stated by the participant. If an NHS staff member delivering COS-P groups as part of the trial decides to withdraw from the study, the recordings of COS-P sessions which they have delivered will be deleted upon request.

If a participant is allocated to the intervention arm of the study and chooses to withdraw, they will be invited to continue with the COS-P group sessions if they wish.

Qualitative Interviews and Focus Groups

If participants choose to withdraw during the interview, participants will be asked what they wish to happen to the data provided up to the point of withdrawal. Participants can choose to withdraw their data up to one month after the interview has been completed.

If participants choose to withdraw during the focus group, they will be asked what they wish to happen to the data provided up to the point of withdrawal. Due to the nature of focus groups, information provided during group discussion cannot be completely withdrawn however direct quotes can be removed.

8. INTERNAL PILOT

An internal pilot will evaluate 5 criteria across all sites, which will be reviewed at month 23, 12 months after recruitment started. The aim of the internal pilot is to review the trial data at an early stage in the study to ensure that the trial is able deliver on its objectives within the planned timetable and budget. In line with the recommendations in Avery et al [41], a green/amber/red traffic light system will be used to advise progression from the internal pilot to the main trial.

Criteria overseen by the Trial Steering Committee (TSC) with discussion with the funder include:

1. Recruitment rate overall and by trial site; and
2. Retention to the trial at 3 months (additionally follow-up at 7 & 12 months will be monitored throughout by DMEC)

TSC progression criteria	Recruitment Criteria*	Retention Criteria
RED: Do not progress to main trial	Average recruitment per recruitment cohort** is less than 3 per site (58%)	Retention at 3 months is less than 50%
AMBER: Explore methods to increase recruitment and/or retention	Average recruitment per recruitment cohort is between 3 (58%) and 5.2 (100%) per site	Retention at 3 months is between 50% and 95%***
GREEN: progress to main trial	Average recruitment per recruitment cohort >= 5.2 per site (100%)	Retention at 3 months is greater than or equal to 95%*

*all sites will be held to the same criteria

** This trial does not have monthly recruitment. Recruitment will take place in seven periodic 4-week recruitment cohorts.

***5% missing at 3 months is incorporated

Criteria overseen for the intervention arm by the Data Monitoring and Ethics Committee (DMEC; who will be unmasked to data by arm) are:

1. Average time to first intervention session from randomisation;
2. Adherence to the planned intervention sessions by participants; and
3. Fidelity of delivery of the intervention by healthcare professionals.

The DMEC's assessment will be based on a credible intervention dose being received, contamination issues and monitoring in prescribing of 'treatment as usual' therapies in the control arm that would be cause for concern. Their recommendation will be at their

discretion and with evaluation across the multiple outcomes, but they will however be provided the above framework to assist their decision-making.

DMEC subjective review criteria	Time to first intervention	Adherence to the planned intervention	Fidelity of delivery
RED: Recommend not to progress to main trial	Average time >8 weeks	Average dosage < 4 sessions	Fidelity < 50%
AMBER: Recommend changes to operational aspects of the main trial	Average time is between 4 and 8 weeks	Average dosage is between 4 and 6 sessions	Fidelity is assessed as between 50-75%
GREEN: progress to main trial with no changes	Average time is < 4 weeks	Average dosage > 6/10 sessions	Fidelity is assessed as > 75%

If the trial progresses beyond the pilot the DMEC will continue to monitor these outcomes throughout the trial. See section 13.3 for further details.

8.1 OUTCOMES OF INTERNAL PILOT

- **Recruitment Rates**

Recruitment rates per recruitment cohort per sites and overall will be collated by the Trial Manager.

- **Retention Rates**

Retention rate to the trial overall at the 3-month follow-up from each site will be collated by the Trial Manager.

- **Time to First COS-P Session in the Intervention Arm**

The average time between randomisation of participant and delivery of the first COS-P session (for those allocated to the intervention arm of the study) will be collated by the Trial Manager.

- **Adherence to the Planned Intervention**

Adherence to the planned intervention will be assessed via video recordings of each session of the third COS-P group delivered by each intervener. These recordings will be reviewed by independent coders according to a fidelity protocol issued by the intervention developers. A criterion of 75% is used to ensure that the treatment administered meets the standards required for a valid trial.

- **Fidelity of Delivery**

Fidelity during the trial will be monitored in three ways:

1. The interveners will use the standard COS documenting procedure to record parental and infant responses, any significant events, and interventions used at the end of each session. This procedure follows a structured scheme to help identify any areas where supervision/support may be needed.
2. Each session of the intervener's third group will be video recorded and reviewed by independent coders according to a fidelity protocol issued by the intervention developers to assess fidelity and competence.
3. Interveners are supported in monthly supervision sessions at each of the sites by three expert therapists trained in parenting interventions and COS-P. Using information from 1. and 2. supervisors will identify learning and teaching opportunities that serve to improve both adherence to the manual and competence in delivery.

Full details on how fidelity will be measured in the trial can be found in section 7.1.2.

9. SAFETY REPORTING

9.1 Adverse Event (AE)

An AE is any untoward medical occurrence which does not necessarily have a relationship with the trial treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or diseases temporally associated with the trial treatment, whether considered related to the trial treatment or not.

AEs which do not fall under this definition but are considered of particular relevance to this trial will be classified as 'Social AEs'. These include safeguarding issues, information relating to children being placed in foster care, incidents of violence towards research staff or health professionals, and reports of domestic abuse.

9.2 Adverse Event Recording

Adverse events are not anticipated but will be monitored by the research team. At each time-point, participants in both arms will complete the same short questionnaire regarding any adverse events (both physical and social) which are experienced. This questionnaire will ask whether the participant has experienced the following 'solicited adverse events':

- Self-harm/concerns about self-harm
- An increase in mental health difficulties/symptoms leading to inpatient care
- Involvement of social care in the participant's family
- Eye strain following screen use for study activities (e.g., completion of online measures and data collection visits)
- Musculoskeletal/back pain following screen use for study activities (e.g., completion of online measures and data collection visits)
- Headaches following screen use for study activities (e.g., completion of online measures and data collection visits)
- Accidents involving the participant's infant during online data collection visits

Adverse events that are not considered related to the study intervention or procedures and that are not one of the solicited adverse events listed above, will not be recorded.

Unsolicited related adverse events (both physical and social) may also be reported during data collection visits. The study team may also be informed of related adverse events through the participant's PMHS (e.g., removal of child).

All related adverse events and serious adverse events will be reported to the Chief Investigators, Trial Steering Committee (TSC) and Data Monitoring and Ethics Committee (DMEC) and reviewed by the independent PSC.

(i) Severity of Adverse Events

Severity of Adverse Events will be assessed by the study Principal Investigator according to the following definitions:

Mild: Awareness of event but easily tolerated.
Moderate: Discomfort enough to cause some interference with usual activity.
Severe: Inability to carry out usual activity.

(ii) Causality of Adverse Events

Causality of Adverse Events will be assessed by the study Principal Investigator according to the following definitions:

Unrelated: No evidence of any causal relationship.
Unlikely: There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial treatment). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).
Possible: There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial treatment). However, the influence of other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant treatments).
Probable: There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Definite: There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.

9.3 Serious Adverse Events (SAE)

(i) Definition of SAE

A SAE is defined as any event that:

- Results in death,
- Is life-threatening*,

- Requires hospitalisation or prolongation of existing inpatient's hospitalisation**,
- Results in persistent or significant disability or incapacity, or
- Is a congenital abnormality or birth-defect.

* "Life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
** "Hospitalisation" means any unexpected admission to a hospital department. It does not usually apply to scheduled admissions that were planned before study inclusion or visits to casualty (without admission).

Medical judgement should be exercised in deciding whether an adverse event/reaction is serious in other situations. Important adverse events/reactions that are not immediately life-threatening, or do not result in death or hospitalisation but may jeopardise a participant or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious.

9.4 Reporting of SAEs

Only SAEs which are related to the study and unexpected will be reported to the sponsor as detailed in the study-specific Safety reporting instructions.

The SAE report will be recorded on the CRF. SAEs will be followed up until they are resolved.

Active monitoring of participants after the end of the trial is not required, but if the investigator becomes aware of safety information that appears to be related to the trial, involving a participant who participated in the study, even after an individual participant has completed the study, this should be reported to the Sponsor.

1. Definition of Related and Unexpected SAEs

A Related or Unexpected SAE is an Adverse Event that is classed as serious, is suspected to be caused by the trial treatment and is unexpected i.e. not listed as an 'unexpected SAE' in this protocol.

2. Reporting of SAEs that are Related and Unexpected

All Related and Unexpected SAEs will be notified to the Research Ethics Committee (REC) and the Sponsor within 15 days of the Chief Investigator becoming aware of the event. Follow up of participants who have experienced a Related or Unexpected SAE will continue until recovery is complete or the condition has stabilised.

9.4.1 Annual Reporting of SAEs

Annual safety reporting will be included in the Annual Progress reports submitted to the Sponsor and the Research Ethics Committee, on the anniversary of Ethics approval each year. The Annual Progress Report will detail all SAEs recorded.

9.5 Reporting Urgent Safety Measures

If any urgent safety measures are taken the Chief Investigator/Sponsor shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant REC of the measures taken and the circumstances giving rise to those measures.

10. STATISTICAL ANALYSES

10.1 Sample Size and Power Considerations

The primary outcome will be a measure of maternal psychopathology assessed using CORE-OM [11]. Measurements will be taken at baseline, 3-, 7- and 12-months. A change in CORE-OM of 5 has been proposed as a meaningful improvement and a reliable change that exceeds that which might be expected by chance [15]. In a 2009 study, Morrell [42] reported that in a sample of women with Edinburgh Postnatal Depression Scale (EPDS) scores ≥ 12 (i.e., women with perinatal mental health difficulties), the mean score on the CORE-OM had a standard deviation of 0.5. A change in total score of 5 equates to an average mean item change of 0.147. In order to estimate a reasonable expected correlation between observations on the same subject, we used unpublished clinical audit data. This contained CORE-OM scores for 71 women entering a specialist community perinatal mental health service - pre and post intervention.

Based on this data we make the assumption that the correlation between measurements within subject will be 0.35.

With 104 in the control arm and 208 (N=312) in the intervention arm we will have 90% power to detect a minimally clinically important average mean item change of 0.147, assuming a SD of 0.5, three repeated measurements with a correlation of 0.35, using 5% significance threshold. Previous small trials have reported 15-20% missing at follow up [29, 30] by the end of the trial. In the current trial, participants will be rigorously followed up and those who have at least one post randomisation measurement will be included in the analysis. We therefore assume it will be reasonable to obtain one post-randomisation measurement of the primary outcome in at least 90% and therefore will factor in 10% missing. As the intervention is delivered in groups there is potential for clustering of the outcomes in the active arm. We do not have reliable data to inform us what the intra-cluster correlation (ICC) coefficient in this context will be. However, even if the ICC were large (>0.05) as the intervention group size is small the effect will be limited, it is not expected this clustering will greatly affect the results. To protect against any potential affect in the absence of information we have inflated the sample size by an additional 5% to take into account the potential for one- arm clustering and use appropriate modelling to adjust the standard deviation in the analysis.

Taking into account the potential for clustering (5%) and missing data (10%), we will aim to **recruit a total of 369 women (n=246 and n= 123 per arm)**. This was calculated using the time-averaged difference test in the PASS statistical software.

For the embedded qualitative component, we have estimated interviewing approximately 20-30 completers, which is consistent with other HTA-funded process evaluations [e.g. ISRCTN12655391, ISRCTN34701576]. The sample size will be guided by principles of data saturation. With non-completers and with focus groups with staff, we will use total population sampling, i.e. inviting all members of those groups.

10.2 Planned Recruitment Rate

We aim to recruit a total of 369 women in seven x 4-week recruitment blocks in each of the sites over a 20-month period. Based on this, we have calculated that we will need to screen 1262 women during this time, which draws the most conservative data from

previous trials and published studies on recruitment (65% of women consenting to be screened, 75% meeting the screening criteria, and 60% consenting to be randomised across the study period) [e.g., 29,30].

Across the sites between 20-76 assessments are completed every month/4-week recruitment block, with a total of 435 across all sites per recruitment block. We will aim for a minimum of 6 women to be randomised per site per each 4-week recruitment block on a 2:1 ratio (45-54 women across all sites per recruitment block) (maximum block size will be 120). As the women accessing the 9 PMHS sites far exceeds the participants we would need to consent and screen, this makes recruitment theoretically highly feasible.

10.3 Statistical Analysis

All analyses will follow the intention to treat principle for all efficacy outcomes.

10.3.1 Analysis Populations

The primary analysis will aim to estimate the treatment policy estimand, and we will use the intention-to-treat principle including all participants who undergo randomisation and have at least one post-randomisation measure (3-month, 7-months, 12-months). As a result of this inclusion the number of participants missing from the primary analysis model is expected to be low.

A safety population consisting of all participants who attend at least one session of the assigned intervention will be used for the analysis of adverse events. For participants in the TAU arm of the trial, this will be defined as any participant randomised to TAU as per the intention to treat the population.

10.3.2 Internal Pilot

Internal pilot outcomes will be summarised and presented overall and by trial site and recruitment cohort, where appropriate. In addition, where relevant, summaries by treatment arm will be presented. Specifically:

- The number of participants recruited per recruitment cohort at each site will be calculated as the percentage of the target number of 5.2 participants per

recruitment cohort per site. At the end of the pilot period if the mean recruitment figure across recruitment cohorts for each site is ≥100% (≥5.2 participants) we are in the green zone and the advice is to progress to main trial (if other progression criteria are also in green zone), if the mean figure across recruitment cohorts at each site is ≥58% and <100% we are in the amber zone and the oversight committees should discuss with investigators methods to increase recruitment, and if the mean figure across recruitment cohorts for each site is <58% (<3 participants) we are in the red zone and the advice is not to progress to the main study.

- Retention will be calculated as the proportion of recruited participant retained at 3 months. At the end of the pilot period if the overall percentage retained is ≥95% we are in the green zone and the advice is to progress to main trial (if other progression criteria are also in green zone), if the percentage retained is ≥50% and <95% we are in the amber zone and the oversight committees should discuss with investigators methods to increase retention, and if the percentage retained is <50% the advice is not to progress to the main study. Overall retention summaries will be used by the TSC to assess progression criteria and summaries by trial site will be presented for information. Additional by treatment arm summaries will be presented for DMC consideration only.

For the intervention arm only for consideration by the DMEC:

- Time-to-first intervention session from randomisation will be presented via Kaplan-Meier estimates plotted with confidence interval and the overall median time to first intervention session will be reported. If the overall median time to first intervention is <4 weeks the advice is to progress to main study (if other progression criteria are also satisfied), if ≥4 weeks and ≤8 weeks the DMEC should discuss with investigators methods to reduce the time between randomisation and first intervention, and if >8 weeks the advice is not to progress to the main study. Summaries by trial site will also be presented for information.

- The overall mean number of sessions per participant will be calculated and will be reported. If the overall mean number of sessions completed is >6 the advice is to progress to main study (if other progression criteria are also satisfied), if ≥4 and ≤6 the DMC should discuss with investigators methods to increase adherence to the

intervention, and if >8 the advice is not to progress to the main study. Summaries by trial site will also be presented for information.

- Overall fidelity will be measured using a fidelity coding protocol recommended by the programme developers (still in development). The competency of interveners will be rated on a 1-5 scale and will be reported. All 10 sessions of each intervener's third COS-P group will be recorded, and 20% of these sessions (two sessions per intervener) will be reviewed for fidelity. Fidelity will be defined by a high threshold (e.g. 3 or 4) which will be confirmed when the protocol is finalised. If fidelity is met over >75% across all cohorts, we are in the green zone and the advice is to progress to main trial (if other progression criteria are also satisfied), if the percentage fidelity is ≥50% and ≤75% we are in the amber zone and the DMC should discuss with investigators methods to increase fidelity to the intervention, and if the percentage fidelity is <50% the advice is not to progress to the main study. Summaries by trial site will also be presented for information.

10.3.3 Baseline Analysis

Baseline characteristics will be summarised by treatment arm and overall using suitable measures of central tendencies; for continuous data (means and medians), variability (standard deviation, SD) and interquartile range (IQR); for categorical data (frequencies and proportions). The flow of participants through the trial and trial results will be reported according to Consolidated Standards of Reporting Trials (CONSORT; see the uploaded documents).

10.3.4 Primary Outcome Measure Analysis

We will use a mixed effects linear regression model to estimate the mean difference in CORE-OM between arms averaged over 3, -7 and 12-months and a Bayesian mixed effects linear regression model using minimally informative priors. From the Bayesian model we will obtain the posterior probability of the intervention being superior to TAU, as well as the posterior probability of treatment effect exceeding the pre-specified MCID of 5 points in the CORE-OM averaged over 3, 7 and 12 months.

In the mixed effects linear regression model participants and recruitment cohort in the intervention arm to account for group clustering in one arm will be included as random

intercepts with fixed effects for intervention arm, site, and baseline CORE-OM, infant sex, infant age, infant first born status. [43]. The mean-difference in CORE-OM between arms averaged over 3, 7, and 12 months with accompanying 95% confidence intervals and p-value will be presented.

A Bayesian mixed effects linear regression model will be fitted and follow the same form as the frequentist mixed effects linear regression model described above. We will use minimally informative (large variance) normal priors for regression coefficients and inverse-gamma priors for the error variance and for the variance of random intercepts which have been chosen to be uninformative. Post-estimation commands will be used to obtain the posterior probabilities that the mean difference exceeds 0 and the MCID of 5 points. Model convergence will be investigated for the parameters of primary interest, specifically the treatment effect estimate using graphical diagnostics.

The intervention effect will also be estimated at 3, 7, and 12-months using a Bayesian mixed effects linear regression model with a model including, 7 and 12-month time points and adding a time-by-intervention arm interaction into the above mixed effects model.

The analysis using mixed effects linear regression model will be valid under a missing at random (MAR) assumption. If the proportion of participants that have no post-randomisation measures is above 5%, we will conduct an additional analysis using controlled multiple imputation to examine the impact of Missing Not At Random (MNAR).

We will also undertake supplementary analysis to estimate the intervention effect in those that received the intervention sessions as planned. This will be undertaken using a counterfactual approach where we will initially define a ‘complier’ (complier Y/N) as an individual who attends at least 60% (i.e. 6 of the 10) of the intervention sessions. We will also examine alternative definitions of a ‘complier’ estimating the effect of attending an increasing number of session (1-10)**.**

If the primary analysis indicates a treatment effect then we will undertake a mediation analysis to explore the mechanisms underlying the intervention using a structural equation modelling approach. Variables to be included as potential mediators include maternal sensitivity (as measured by the Sensitivity Scales), emotion regulation (as measured by the DERS), and life changes (e.g., the start of social care for the family) and relationship

status (as measured by the demographic questionnaire and CSRI). See the statistical analysis plan for full details.

10.3.5 Subgroups

Pre-specified subgroup analysis will be performed for the primary outcome to explore the uniformity of the treatment effect by adding a treatment-by-subgroup interaction term to the primary analysis model (or test for trend where appropriate) for the following:

- history of mental health difficulties (type of mental health difficulty, i.e., depression, anxiety, OCD, personality difficulties, trauma, psychosis, bi-polar, other; age of onset of mental health difficulties, i.e., 18-24, 25-34, 35-44,45-54, 55+; whether mental health difficulties experienced before first child, i.e., yes/no)
- experienced childhood maltreatment (CTQ scoring: Non-low; low-moderate moderate-severe; severe-extreme)
- geographical area (as measured by county, i.e., Cheshire, Merseyside, Tyne & Wear, Northumberland, County Durham, Cumbria, West Yorkshire, North Yorkshire, Northamptonshire, Sussex)
- age (18-24, 25-34, 35-44, 45-54, 55+)
- race (categories include White (British, Irish, Other White Background), Black or Black British (Caribbean, African, Other Black Background), Asian or Asian Background (Indian, Pakistani, Bangladeshi, Other Asian Background), Chinese or Other Ethnic Group)
- deprivation (as measured by personal gross income, yearly categories are: “Under £7,785”, “£7,786-£10,635”, “£10,636-£14,504”, “£14,505-£20,394”, and “More than £20,395”)
- first child (yes or no)
- relationship status (single, in a relationship (cohabiting), in a relationship (not cohabiting), married, civil partnership, separated, divorced, widowed).

10.3.6 Secondary Outcome Measure Analysis

Analysis of the secondary efficacy outcomes will be undertaken following the same framework as the primary outcome model with a time-by-intervention interaction using appropriate generalised linear models. For each continuous outcomes including the DERS, PBQ, ASQ-3, ASQ, SE and the Sensitivity Scales, a mixed effects linear regression model will be fitted as described above for the primary outcome. Trajectories of

the predicted estimates with accompanying 95% confidence intervals from the mixed effects models over time will also be displayed graphically.

Any secondary binary outcomes will be analysed using a generalized linear model fitted with a binomial distribution and logit link function and treatment effects will be reported as odds ratios with 95% confidence intervals.

Any secondary categorical outcomes will be analysed using a generalized linear model fitted with a binomial distribution and ologit link function for ordered categorical responses and the mlogit link function for unordered categorical responses and treatment effects will be reported as odds ratios (ologit model) or relative risk ratios (mlogit model) with 95% confidence intervals.

For the analysis of any time-to-event outcomes treatment effects will be modelled using a proportional hazards time-to-event model and Kaplan-Meier estimates will also be plotted with confidence intervals for each treatment arm with extended at-risk tables [44].
In addition, we will also undertake supplementary analysis on the secondary outcomes to estimate the intervention effect in those that received the intervention sessions as planned as outlined in the primary outcome analysis.

Information on adverse events (AEs) will be collected from a survey administered at each data collection timepoint, as well as any unsolicited reports made by participants outside of these timepoints. Physical adverse events will be coded using the MedDRA coding dictionary. AEs will be summarised at the Preferred Term level and System Organ Class level. Social adverse events will be coded using terms chosen by the study investigators. Kaplan Meier plots will be used to examine rates of withdrawals by arm due to any AE. The number of participants requiring social care involvement for the family will be tabulated by arm and Kaplan-Meier plots will be used to examine the time to social care involvement by arm. This specific AE will be collected via the adverse events questionnaire items completed at each data collection timepoint. All AEs will be tabulated by arm and severity for the number of participants with at least one adverse event and the number of adverse events. We will also calculate odds ratios and incident rate ratios and their 95% CIs for binary and count AE outcomes at SOC level using logistic regression and Zero-Inflated Poisson model or negative Binomial model, following the same framework as the primary analysis model using appropriate generalized linear models with adjustments. The results from these models will be presented graphically along with the raw counts using visual approaches such as the dot plot [45].

A detailed statistical analysis plan will be written prior to first data extraction from the database and will detail all analysis models and model checks to be performed.

Qualitative Data

Survey Data

Response rates and descriptive data on the demographics of respondents will be summarised in order to describe the sample of respondents. These data and responses to closed questions, will be subject to basic descriptive statistics including frequency counts and cross-tabulation. Responses to open-ended survey questions will be analysed using content analysis which involves generating descriptive codes summarising text responses and counting the frequency of those codes within the dataset.

Interviews and Focus Groups

The qualitative data collected during focus groups and interviews regarding participant and intervener experiences will be transcribed verbatim by a confidentiality-bound professional transcription service. The data will be managed using NVivo and analysed using the Braun and Clarke thematic analysis approach [46]. Initially, a selection of the transcripts will be independently coded line-by-line by a qualitative sub-team (including OR, PPI Co-A; ZD, Co-A) to generate initial codes and search for candidate themes. These will be reviewed and refined in a face-to-face meeting before undertaking further coding of subsequent transcripts. To promote rigour, we will use peer debriefing, with the researchers scrutinising each other's interpretations and searching for disconfirming evidence. The emerging themes will be discussed with the EbE panel to ensure credibility and relevance for service users. We will explore alternative interpretations by revisiting transcripts, and refining the analysis supported by a series of remote and face-to-face discussions, until a satisfactory analysis is reached with agreement of final themes. Anonymised quotations will be used to illustrate the themes and a detailed audit trail will be recorded, summarising the development of themes.

Economic Analysis

We will perform a within-trial economic evaluation comparing the costs and outcomes of the intervention group (COS-P) versus the treatment as usual. We will assess the cost of implementing and delivering the intervention (e.g. cost of each session, including video projection, practitioner psychologist time) and the cost of the treatment as usual. We will identify and measure health care resources use (e.g. GP consultations, psychological

consultation, medications etc.) through the CSRI [11] and using standard unit costs (PSSRU, BNF, tariffs etc.). The base case perspective will be the one of the UK NHS and Personal Social Services. Outcomes will be measured using the EQ-5D-5L questionnaire [10] (but we will also explore translating the CORE-OM [4] and CORE-6D [12] into utility) to generate QALYs for the 12-month follow-up. The economic evaluation will estimate the incremental cost per QALY associated with COS-P. Net monetary benefit of the intervention and TAU will be assessed using the NICE lower and upper threshold. If there is a significant outcome effect, a decision analytic model will be used to extrapolate the results over the longer term. Sensitivity analysis will be performed to control for uncertainty in the parameters and data.

11. REGULATORY, ETHICAL AND LEGAL ISSUES

11.1 Declaration of Helsinki

The investigator will ensure that this study is conducted in full conformity with the seventh revision of the 1964 Declaration of Helsinki act.

11.2 Good Clinical Practice

The study will be conducted in accordance with the guidelines laid down by the International Conference on Harmonisation for Good Clinical Practice (ICH GCP E6 guidelines).

11.3 Research Ethics Committee (REC) Approval

1. Initial Approval

Prior to the enrolment of participants, approval from the Research Ethics Committee (REC) was obtained. REC approval included the conduct of the study at named sites, the trial protocol, participant information sheet and consent form, questionnaires, interviews, any other written information that will be provided to the participants, and any advertisements that will be used during the study.

2. Approval of Amendments

Any amendments to the protocol and information provided to participants will be submitted to the Sponsor and REC for approval prior to implementation. An assessment of whether the amendment is substantial or non-substantial will be made prior to submitting the amendment for review. Substantial amendments may only be implemented after written REC approval has been obtained whereas non-substantial amendments can be implemented without written approval from the REC.

Amendments that are intended to eliminate an apparent immediate hazard to participants may be implemented prior to receiving Sponsor or REC approval. However, in this case,

approval must be obtained as soon as possible after implementation.

The trial team, in collaboration with the Sponsor will assess whether a proposed amendment is substantial or non-substantial. For each proposed amendment, a revised version of the protocol will be prepared using tracked changes, a new version number assigned and the revised document will be reviewed and approved by Protocol Development Group and Sponsor prior to submission to the REC and Health Research Authority (HRA). The amended protocol will be sent to participating sites for local approval to be granted and the approved version will be shared with all staff involved in the trial.

11.4 Annual Progress Reports

Annual Progress Reports will be submitted to the Research Ethics Committee (REC) and the Sponsor on an annual basis, on the anniversary of REC approval. The Annual Progress Report will also detail safety information and all SAEs recorded.

11.5 End of Trial Notification

The REC will be informed about the end of the trial within 90 days of the final follow-up visit taking place.

11.6 HRA approval

Approval for the study to be conducted within each participating NHS site will be obtained from the NHS Health Research Authority (HRA) prior to starting the study.

The HRA and all participating sites will be notified of all protocol amendments to assess whether the amendment affects the institutional approval for each site.

11.7 Other Required Approvals

Ethical Approval will be required from University of Huddersfield, School of Psychology ethics committee. The ethics committee have already been consulted during the set-up stage of the study and have reviewed and approved all participant-facing documents (PIS and ICF) and information included in the IRAS regarding qualitative data collection, storage and analysis.

11.8 Non-Compliance and Serious Breaches

All protocol deviations and protocol violations will be reported via the eCRF/CRF and reviewed by the Chief Investigator and reported to the ICTU QA manager on a monthly basis. Protocol violations will be reported to the Sponsor. An assessment of whether the protocol deviation/violation constitutes a serious breach will be made.

A serious breach is defined as a breach of the conditions and principles of GCP in connection with a trial or the trial protocol, which is likely to affect to a significant degree:

- The safety or physical or mental integrity of the UK trial participants; or
- The overall scientific value of the trial

The Sponsor will be notified within 24 hours of identifying a likely Serious Breach. If a decision is made that the incident constitutes a Serious Breach, this will be reported to the REC within 7 days of becoming aware of the serious breach.

11.9 Insurance and Indemnity and Sponsor

The AFNCCF holds negligent harm and non-negligent harm insurance policies which apply to this study. The AFNCCF would be covered for it's legal liability for the management, design and conduct of research in the COSI trial (Policy number: 02/CHA/0342841).

NHS Trusts provide indemnity against clinical risk for all work carried out on its behalf. In England, indemnity is provided through the Clinical Negligence Scheme for Trusts (CNST), which is administered by NHS Resolution.

11.10 Trial Registration

The study will be registered on the ISRCTN database in accordance with requirements of the International Committee of Medical Journal Editors (ICMJE) regulations. Any protocol amendments will also be registered there.

11.11 Informed Consent

All adult research participants (mothers of the infants in the study) will digitally sign and date an Informed Consent Form (ICF) before any trial specific procedures are performed. Participants will be asked to provide verbal consent to be contacted by the research team

following eligibility screening at their PMHS, followed by written consent to participate in the full study. The mother of the child will also provide consent for their infant to participate in the study, including their child being audio and video recorded.

At the 3-month follow-up of the study, a selection of participants within the intervention arm of the study will be invited to take part in an additional interview. Informed consent for these interviews will be collected separately at this timepoint.

For full information regarding the procedures to obtain informed consent, please see section 6.2.

11.12 Contact with General Practitioner and Health Visitor

With the consent of the participant, the research team will inform the participant's (and infant's) General Practitioner and Health Visitor by digital letter that the participant is taking part in the study. Information to this effect is included in the Participant Information Sheet and Informed Consent Form. A copy of the letter will be filed in the Investigator Site File.

11.13 Participant Confidentiality

The investigator must ensure that the participant's confidentiality is maintained. On the CRF or other documents submitted to the Sponsors, participants will be identified by a participant ID number only. Documents that are not submitted to the Sponsor (e.g., signed informed consent form) should be kept in a strictly confidential file by the investigator.

All audio-visual recordings made by the research team will be immediately uploaded to a secure digital platform that will be supported by the Sponsor. These recordings will be stored pseudoanonymously according to each participants' study ID. All temporary video stored on video cameras will be deleted and permanently removed immediately after each session, once the video has been uploaded to the secure digital platform (e.g., a secure and private Microsoft Teams Channel).

The investigator shall permit direct access to participants' records and source document for the purposes of monitoring, auditing, or inspection by the Sponsor, authorised representatives of the Sponsor, NHS, Regulatory Authorities and RECs.

11.14 Data Protection and Participant Confidentiality

The investigators and study site staff will comply with the requirements of the Data Protection Act 2018 concerning the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

11.15 End of Trial

The end of the trial will be defined as the last data capture for the last participant recruited.

11.16 Study Documentation and Data Storage

The investigator will retain essential documents until notified by the Sponsor, and for at least ten years after study completion, in accordance with Sponsor requirements. Participant files and other source data (including copies of protocols, CRFs, original reports of test results, correspondence, records of informed consent, and other documents pertaining to the conduct of the study) will be kept for the maximum period of time permitted by that institution. Documents will be stored in such a way that they can be accessed/data retrieved at a later date. Consideration will be given to security and environmental risks.

No study document will be destroyed without prior written agreement between the Sponsor and the investigator. Should the investigator wish to assign the study records to another party or move them to another location, written agreement must be obtained from the Sponsor.

12. DATA MANAGEMENT

12.1 Source Data

Source data will include: participant files, consent forms, and other documents pertaining to the conduct of the study. Trial therapist and Research Assistant records including paper questionnaires completed during study assessments will also be included.

12.2 Language

CRFs will be in English. All written material to be used by participants must use vocabulary that is clearly understood.

12.3 Database

Data will be collected on an Electronic Data Capture (EDC) system developed using the REDcap system, incorporating the trial database and randomisation system. This will be a web-based EDC comprising a full GCP-compliant audit trail, stored on a secure server at Imperial College London. Questionnaire data will be collected via tablets provided by the study and will automatically be uploaded to REDcap.

Access will be restricted to trained staff with unique password-protected accounts. Identifiable data will not be recorded in the eCRF and participants will be identified by a unique trial ID only.

12.4 Data Collection

Personal information (e.g. contact details) will be collected when participants provide informed consent to participate in the full study. This information will be held by the AFNCCF on a secure, encrypted drive, and only be accessible by the Trial Manager and all research team members involved in data collection.

Questionnaire data will be collected at baseline, 3-, 7-, and 12-months post baseline, and will be collected on an Electronic Data Capture (EDC) system developed using the REDcap system. This will be a web-based EDC comprising a full GCP-compliant audit trail, stored on a secure server at Imperial College London. Serious Adverse Events will be signed electronically by the CI (or delegate) within REDcap.

The video recordings of mother-infant interactions will be recorded during the above data collection visits. Video recordings of the Strange Situation Procedure will be collected as part of the 12-month follow up. Access will be restricted to trained staff with unique password-protected accounts.

Identifiable data will not be recorded in the eCRF and participants will be identified by a unique trial ID only. During the trial, access to paper and electronic data will be restricted to authorised trial staff. Records will be held securely in locked offices and in the case of electronic audio and video data, these will be held on encrypted drives only with secure backup.

Qualitative data from semi-structured interviews will also be collected (as per section 6.8.4). The interviews will be audio / audio visually recorded and transcribed verbatim. The recordings and transcripts will be encrypted and stored on a secure server at the UoH. The recordings and transcripts will be temporarily stored on the secure server of the professional confidentiality-bound transcription service to enable them to transcribe the data. The company is GDPR compliant and will securely delete these files once the transcripts have been downloaded to the secure server at the UoH.

The survey will be administered using Qualtrics and the unique trial ID will be used when completing the survey, enabling linkage with the other data (e.g. demographics, site ID, number of sessions attended). Data that is extracted from Qualtrics will be stored in Box at the UoH and managed using relevant software (Excel/SPSS and NVivo). Qualtrics is GDPR compliant and has provided written consent to store and process data securely within the EU.

Focus groups with staff delivering the intervention will also be completed. The focus groups will be audio / audio visually recorded and transcribed verbatim. The recordings and transcripts will be stored on a secure server at the UoH.

Hard copies of data sheets linking the participant identification number to the person's contact details will be kept securely in the Investigator Site File, in a locked filing cabinet in a locked office at the AFNCCF, accessible only to key research team members.

12.5 Archiving

All trial documentation, including that held at participating sites and the trial coordinating centre, will be archived for a minimum of 10 years following the end of the study.

Personal Information

Participant's postcode will be collected at the beginning of the study. This is a requirement for any referrals to local adult and child safeguarding boards in the event of a safeguarding concern. This information will be deleted when participants leave the study (either upon completion of the study or withdrawal), and will not be included in the pseudonymised dataset shared with ICTU or for analyses.

Qualitative Data

All recordings and personal data collected for the interviews and focus groups will be destroyed at the end of the study. All other information relating to the qualitative data collection will be destroyed 10 years after the completion of the study.

13. STUDY MANAGEMENT STRUCTURE

13.1 Trial Steering Committee

A Trial Steering Committee (TSC) has been convened to oversee the progress and conduct of trial, including the first two criteria of the internal pilot. Membership of the committee includes an independent chair, independent statistician, independent PPI member, independent experts including experts by experience, and representatives of the study team. The TSC will meet at the start of the project to agree their Terms of Reference and review the protocol. Thereafter they will meet annually at a minimum.

13.2 Trial Management Group

A Trial Management Group (TMG) consisting of the Co-Principal Investigators, Co-applicants, Senior Statistician, Operations Manager, Trial Manager and EbE panel members will be convened. The TMG will be responsible for day-to-day management of the study. The TMG will meet regularly during the set-up phase of the trial and approximately 3-4 times a year thereafter.

13.3 Data Monitoring and Ethics Committee

The Data Monitoring and Ethics Committee (DMEC) will be fully independent and oversee safety of the trial and the last three criteria of the internal pilot (see section 8). Membership of the DMEC includes a chair, statistician, an expert and EbE member. The DMEC will meet at the start of the project to agree their Charter and review the protocol and will then meet annually at a minimum with meetings taking place prior to the TSC to facilitate reporting from DMEC to TSC.

The TSC and DMEC will be conducted in accordance with NIHR guidelines on Oversight Committees.

13.4 Expert by Experience (EbE) Panel

An EbE panel of women who have received treatment at one of the trial sites has been created to review and advise on various aspects of the research. The panel will be chaired by Lani Richards, a co-applicant of the trial, who has also liaised with other organisations working with parents accessing perinatal services to increase inclusivity. Panel members

will be comprised of women who have accessed PMHS and/or COS-P groups. All EbE involved in the study will be encouraged and supported to develop their knowledge and skills through personalized role descriptions and development plans. Practical support, expenses, and access to training will be provided, and they will be remunerated for their time in accordance with recommendations from INVOLVE (£150 per day). The panel will meet every month for the first 6 months of the research project, and thereafter once every 3 months. Panel members will also work outside regular meetings on specific pieces of work to improve the relevance, acceptability, and impacts of the research. Throughout the project, we will consult with the Panel for the input. The Panel will review its activity and achievements on an annual basis according to predetermined Terms of Reference, with any suggested changes to be agreed in consultation with the TSC.

EbE co-applicant

The study has an EbE Lead and Co-A (Ms. Lani Richards). She has been extensively involved in the development and refinement of the study proposal. In the study, she will be responsible for chairing an EbE panel, train to become an EbE researcher and support the qualitative data collection and analysis and will attend all the quarterly TMG meetings.

EbE panel

The panel have already advised on research protocols, recruitment, engagement, and retention strategies; and co-designed documents for participant use including information sheets and consent forms. Throughout the project, we will consult with the Panel for their input, and will involve them in the following activities: reviewing ethics application prior to submission; designing and reviewing documents for participants including consent forms and information leaflets; advising on strategies to maximise recruitment, engagement and retention; advising on culturally and ethnically relevant issues as necessary; elaborating on ambiguities in emerging research findings; advising on research reports; selecting specific outlets for dissemination; designing and producing summary reports for current and potential service users, including the research participants; and designing and producing interactive dissemination workshops.

EbE researchers

The EbE panel particularly highlighted the importance of using EbE researchers in order to enhance the quality of the information collected, as EbE researchers are likely to be better placed to explain data-gathering approaches, facilitate the free disclosure of sensitive

information, and facilitate trust and rapport. A sub-group of the EbE panel will be formed to be involved with data analysis and interpretation, through a series of meetings where emerging findings will be shared to invite alternative interpretations and consider together the learning from the study and its implications. Our EbE Co-A will be involved as an EbE researcher with data collection (including assisted survey completion and focus groups) and with aspects of data analysis. The EbE panel will receive training from the AFNCCF concerning EbE involvement in research, confidentiality, handling potentially emotive issues in a sensitive manner, safeguarding, and introduction to research (including trials and qualitative research). They will be retrained by the AFNCCF at regular 6 monthly intervals throughout the study. Overall coordination and monitoring of their role will rest with the Trial Manager, with additional support from the Dr Zoe Darwin (Co-A with oversight for qualitative component of the study).

13.5 Early Discontinuation of the Study

The Data Monitoring and Ethics Committee (DMEC) for the trial will prepare a charter outlining their responsibilities and planned interim analyses.

If a decision to discontinue the trial prematurely is reached, a notification will be sent to the Research Ethics Committee within 15 days of the end date. The Trial Management Group will assess how participants should be informed and whether follow-up visits to the families that have been recruited to the study should continue.

13.6 Risk Assessment

A study-specific risk assessment will be performed prior to the start of the study to assign a risk category of ‘low’, ‘medium’ or ‘high’ to the trial. Risk assessment will be carried out by the ICTU QA Manager in collaboration with the Trial Manager and the result will be used to guide the monitoring plan. The risk assessment will consider all aspects of the study and will be updated as required during the course of the study.

13.7 Monitoring

The study will be monitored periodically by the Trial Manager to assess the progress of the study, verify adherence to the protocol, ICH GCP E6 guidelines, and to review the completeness, accuracy and consistency of the data.

Monitoring procedures and requirements will be documented in a Monitoring Plan.

COS-P interveners will report on intervention fidelity in terms of the delivery of key components of the programme as well as reporting on global adherence to the manual. Compliance will be assessed by the clinical supervisor in supervisory sessions.

13.8 Quality Control and Quality Assurance

Quality Control will be performed according to ICTU internal procedures. The Sponsor may also complete financial and data protection Quality Control Monitoring. The study may be audited by a Quality Assurance representative of the Sponsor and/or ICTU. All necessary data and documents will be made available for inspection.

The study may be subject to inspection and audit by regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd Edition).

13.9 Peer Review

The Trial was independently reviewed by two experts in this field (Drs Paul Ramchandani and Rafael Gafoor) and a group of EbEs as part of the adoption process to the ICTU. The Trial also received a NIHR HTA peer review. All feedback provided was recorded and incorporated into the Trial design.

13.10 Publication and Dissemination Strategy

Irrespective of outcome, the study will result in a number of a publications and other outputs to disseminate the findings of the research. The TMG will be responsible for approval of the main manuscript prior to submission for publication. Authorship of presentations, reports, and/or peer-reviewed journal articles related to the study will be in the name of the collaborative group. The final NIHR report will name local co-ordinators as well as those involved in central co-ordination and trial management.

Publications and dissemination activities will include:

- NIHR report
- A Clinical Study Report summarising the study results will be prepared and submitted to the REC within a year of the end of study.
- Presentations at national and international conferences to audiences of health professionals, policy makers and researchers relevant to the field of public mental health, perinatal and infant mental health, maternity care, and psychological

practice.

- Publishing open-access articles in high-impact peer-reviewed journals, as well as less academic practitioner journals with high readerships.
- Writing policy briefings and reports, engage the What Works Centres, and promoting through the All Party Parliamentary Group on 1001 critical days.
- Providing continuous updates and presentations through local and national NHS England Perinatal Mental Health Strategic Clinical Network meetings.
- Working with the AFNCCF's communication team to develop an online presence on social media.
- Providing research summaries in newsletters and on websites e.g. through the Maternal Mental Health Alliance, Early Years Foundation.
- Working with the EbE panel to present findings on support forums, parent events, and through high profile service user blogs and social media platforms.

At the end of the study, participants will be able to request a copy of the results of the study from the investigator at that site. A summary of results will also be provided through other formats including animation, study newsletters, podcasts, and social media blogs.

Information concerning the study, processes, scientific data or other pertinent information is confidential and remains the property of the Sponsor. The investigator may use this information for the purposes of the study only. It is understood by the investigator that the Sponsor will use information developed in this clinical study and, therefore, may disclose it as required to other clinical investigators. In order to allow the use of the information derived from this clinical study, the investigator understands that he/she has an obligation to provide complete test results and all data developed during this study to the Sponsor. Verbal or written discussion of results prior to study completion and full reporting should only be undertaken with written consent from the Sponsor. Therefore, all information obtained as a result of the study will be regarded as confidential, at least until appropriate analysis and review by the investigator(s) are completed.

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15. REVISION HISTORY

Version	Date	Summary of changes
1.0	26/08/2021	First version
2.0	14/12/2021	Amendment Submission

SIGNATURE PAGE 1 (CHIEF INVESTIGATOR)

The signature below constitutes approval of this protocol by the signatory, on behalf of the Protocol Development Group, and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol including all statements regarding confidentiality.

Study Title: The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the **C**ircle **o**f **S**ecurity **I**ntervention for mothers in perinatal mental health services.

Protocol Number: COSI010321

Signed: _____

Prof Peter Fonagy
Chief Investigator

Date: 31st August

SIGNATURE PAGE 2 (DEPUTY CHIEF INVESTIGATOR)

The signature below constitutes approval of this protocol by the signatory, on behalf of the Protocol Development Group, and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol including all statements regarding confidentiality.

Study Title: The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the **C**ircle **o**f **S**ecurity **I**ntervention for mothers in perinatal mental health services.

Protocol Number: COSI010321

Signed: _____

Dr Camilla Rosan
Deputy Chief Investigator

Date: 31st August 2021

SIGNATURE PAGE 3 (SPONSOR)

The signatures below constitute approval of this protocol by the signatory.

Study Title: The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the **C**ircle **o**f **S**ecurity **I**ntervention for mothers in perinatal mental health services.

Protocol Number: COSI010321

Signed: _____

Dr Camilla Rosan
Head of Early Years Programme
Anna Freud National Centre for Children and Families

Date: 31st August 2021

SIGNATURE PAGE 4 (STATISTICIAN)

The signatures below constitute approval of this protocol by the signatory.

Study Title: The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the **C**ircle **o**f **S**ecurity **I**ntervention for mothers in perinatal mental health services.

Protocol Number: COSI010321

Signed: _____

Dr Victoria Cornelius
Senior Statistician
Imperial College London

Date: _____

SIGNATURE PAGE 5 (PRINCIPAL INVESTIGATOR)

The signature of the below constitutes agreement of this protocol by the signatory and provides the necessary assurance that this study will be conducted at his/her investigational site according to all stipulations of the protocol including all statements regarding confidentiality.

Study Title: The COSI study: a multi-site randomised controlled trial (RCT) to explore the clinical and cost effectiveness of the **C**ircle **o**f **S**ecurity **I**ntervention for mothers in perinatal mental health services.

Protocol Number: COSI010321

Address of Institution: _____

_____

_____

Signed: _____

Print Name and Title: Dr Ruth O'Shaughnessy_____

Date: _____