Trial of Healthy Relationships Initiatives for the Very Early-years (THRIVE): A three-arm randomised controlled trial for mothers identified as vulnerable in pregnancy and their babies who are at risk of high maltreatment.

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1. Aims and objectives

The overarching aim of *THRIVE* is to rigorously evaluate, using a three-arm randomised controlled trial, the impact of two parenting interventions against routine antenatal care or care as usual (CAU). In particular, *THRIVE* will assess whether women who receive either Enhanced Triple P for Baby (ETPB) or Mellow Bumps (MB) in addition to Care As Usual (CAU) experience improved mental health and wellbeing and develop positive, interactive and attuned mother-child relationships. The trial will also assess whether children whose mother received ETPB or MB show reduced incidence of child maltreatment and improved language development and socio-emotional wellbeing.

The primary research questions that will be addressed by *THRIVE* are:

1) Do participants receiving ETPB or MB show significantly lower anxiety, depression and outwardly directed irritability compared to those receiving CAU when their babies are 6 months old?

2) Do women who receive ETPB or MB show more sensitive interactions with their babies compared to those receiving CAU when their babies are 6 months old?

The secondary research questions that will be addressed by *THRIVE* are:

3) Do any benefits to maternal mood, sensitive interaction style and quality of life continue or emerge when the women's infants are 18 months old?

4) Do infants whose parents receive ETPB or MB show more cooperative behaviour signs than those whose parents received CAU?

5) Do ETPB or MB lead to changes in the number of children flagged as 'at risk' on the social services risk register, under a child protection plan, taken into local authority care or attending accident and emergency?

6) Do ETPB or MB lead to an improvement in the socio-emotional development of children at 30 months old?

7) Do ETPB or MB lead to an improvement in language development in children at 18 and 30 months?

8) Do ETPB or MB lead to an improvement in longer term educational and health outcomes for children?

9) Are either ETPB or MB cost-effective for the NHS or society more broadly, in the long-term?

10) Do differences in programme fidelity; practitioners' characteristics and motivation; mothers' engagement; the intervention mechanisms; and contextual factors affect mother and infant outcomes.

11) Does fathers' involvement or support affect mothers' engagement with ETPB or MB?

2. Background

2.1 Existing research

A recent UNICEF report, which compared 21 high-income countries across six dimensions of child and adolescent wellbeing, found that the UK was ranked worst, and obtained the lowest scores for three of these six dimensions (family and peer relationships, behaviours and risks, and subjective wellbeing). [1] Thus, there is an urgent need for improvement in children's health and wellbeing in the UK. "There is powerful new evidence from neuroscience that the early years of development from conception to age six, particularly for the first three years, set the base for competence and coping skills that will affect learning, behaviour and health throughout life." [2] Furthermore, nature and nurture interact in a way that can be harmful to the foetuses/babies of stressed mothers. Women who are vulnerable in pregnancy (for instance, due to domestic abuse, mental health issues, an addiction, having been in care) are likely to be more anxious, depressed and produce higher levels of cortisol than women who are not vulnerable. Evidence is growing that depression, stress and anxiety in pregnant women can i), create adverse epigenetic modifications to the foetus in utero that permanently affect the baby's response to stress [3, 4] and, ii) independently disrupt the mother's ability to be sensitive to her baby. [5] Both these pathways may adversely affect the mother-infant interaction. Thus, most postnatal interventions may not be able to undo some of the damage sustained by infants due to their mother's and/or parents' maladaptive coping in adverse circumstances during pregnancy.

Poor mother-child interaction and maternal mental health strongly predict child maltreatment [6, 7] and are highly prevalent among mothers identified as vulnerable in pregnancy. [7] In addition, poor mother-child interaction and maltreatment predict a disadvantaged trajectory for children in terms of their future social, emotional, cognitive development and health. [8-10] One of the early distinctive features of children from disadvantaged social backgrounds in general, and of those from very stressed or abusive backgrounds in particular, is that they commonly have very limited language skills. [11-16] Although the nature of the deficit is complex, it is assumed that the nature of the verbal input, interaction and range of positive learning experiences, whether in book reading or outside the home, is limited. [17-20] Although factors affecting early child development are very complex, there is reasonable evidence from the British Cohort Study that delayed language ability at school entry can have long term adult outcomes such as poor literacy, mental health and employment. [21] Recent research using the ALSPAC dataset has suggested that the early communication environment has a specific effect on early language development in the second year of life, over and above generic social risk, and language in turn is closely associated with performance on the Foundation Stage profile at school entry. [22] Thus, it is reasonable to see early language as a critical lynch pin between the infant's earliest experiences and their later achievements. Mother-baby/infant interactions that facilitate secure future attachments enable infants to be placed on improved pathways for their overall development, including language. Furthermore, sensitive mother-infant interactions are characterised by reciprocal communication from an early stage, which again facilitate language but also significantly reduce the risk of maltreatment thought to be due to mothers perceiving their infants as co-operating with them.

Evidence demonstrates that early intervention is more cost-effective than intervening later, and most effective in the antenatal period.[23] The evidence for the effect of early child development on health and wellbeing in later life is robust and widely accepted, and early childhood interventions, such as the High/Scope Perry Preschool Project,[24] the USA Family Nurse Partnership (FNP)[25], the Carolina Abecedarian Project [26] and the Chicago Child-Parent Programme [27] have had positive effects on a number of child development domains and on wellbeing and life success in adulthood. It is appropriate to exemplify this using the long-term results of the FNP trial [25], as it shares some

similarities to the interventions we are proposing to evaluate. FNP targeted vulnerable mothers (albeit their definition was tighter than ours, for instance, they only worked with first time mothers), and started antenatally. The FNP intervention group received antenatal and postnatal home visits from trained nurses until their child was two years old. When the children reached adolescence the intervention group (relative to the controls) were less likely to run away from home, had fewer convictions, fewer lifetime sexual partners, smoked less, drank less alcohol, and their parents reported fewer behavioural problems. The long-term impact of the FNP is currently being evaluated in the UK [28]. However, short-term UK results have shown an improvement in maternal sensitivity and infant cooperation (as evidenced by video-tape analysis using the CARE Index), and an improvement in the identification of infants in need of child protection. The FNP intervention costs society £3,246 more than standard treatment. [25, 29]

2.2 Rationale for current study

Despite the considerable observational evidence summarised to date there is little rigorous, UK-based evidence on the effectiveness of psychosocial parenting interventions delivered during the antenatal and early postnatal period. Whilst the evidence for the short-term effects of FNP in the UK appears to be robust, the intervention is expensive to implement, costing £3246 more per patient than routine care, is delivered on a one-to-one basis and may not be generalisable to different groups of vulnerable mothers, for instance those who are not first time mothers or teenagers. Therefore, the *THRIVE* trial aims to explore if participating in a group-based antenatal and early postnatal parenting intervention improves maternal and infant outcomes more than CAU. In particular, we aim to investigate if receiving an antenatal and early postnatal parenting intervention in addition to CAU can improve maternal mental health, mother-infant relationships and child language development relative to receiving routine antenatal care alone.

2.3 Pilot Studies

THRIVE has been informed by two pilot studies conducted with women from similar socio-demographic backgrounds and diagnostic histories to those who will be recruited to the *THRIVE* trial.

2.3.1 Baby Triple P Open Prospective Trial

A three-arm open prospective trial, conducted by Dr. Anja Wittowski and Prof. Rachel Calam, compared the effectiveness of Baby Triple P and routine postnatal care against baby massage plus routine postnatal care in order to assess which, if any intervention, is most effective at improving outcomes of mother and child. In particular, the trial assessed whether women who received Baby Triple P alongside routine postnatal care showed significant improvements in mental well-being, maternal sensitivity, parenting confidence and perceived relationship with their baby than women who received baby massage with routine postnatal care. 60 women diagnosed with postnatal depression and admitted to the Mother and Baby Unit in Manchester were recruited to the trial and allocated to receive either Baby Triple P and routine care, or Baby Massage and routine care. Due to the possibility of women discussing their care plans and causing contamination between arms of the trial, an open prospective trial design was used in which Baby Triple P plus routine care were offered for a period of time, and then withdrawn so that Baby Massage and Triple P could be evaluated. All participants completed questionnaires on mood, bonding and parenting confidence prior to the interventions beginning. These questionnaires were then repeated after completion of the two conditions, and at 6 and 12 months follow up assessments. Video-recordings of mother-infant interaction were also made to allow for the quality of mother-infant relationships to be assessed using the CARE Index [30].

The Baby Triple P Open Prospective Trial has informed *THRIVE* by establishing procedures for the handling and coding of video-recordings of mother-infant interaction.

2.3.2 Mellow Bumps RCT

A three-armed randomised controlled trial, conducted by Prof. Phil Wilson and Dr. Lucy Thomson, Dr. Marion Henderson and Dr. Jane White, compared the effectiveness of Mellow Bumps (MB) against Chillout-In-Pregnancy (CHiP) and the routine antenatal care (CAU) received during pregnancy in order to assess which, if any intervention, was most effective at improving the outcomes of mother and child. The primary outcome measure was anxiety as measured by the Adult Wellbeing Scale. Participants who were identified by community midwives as having additional health and social care needs in pregnancy (SNiPs criteria) were invited to take part in the project. The interventions took place when they were between 20 and 30 weeks pregnant. In total 35 women were recruited and randomized in groups of six to one of three conditions: MB (designed to reduce maternal anxiety and improve maternal sensitivity) Chillout-In-Pregnancy (designed to reduce maternal anxiety only) or CAU. All participants were asked to complete questionnaires and give saliva samples (for cortisol assay) before the interventions began. The questionnaires were repeated on completion of the intervention and at a follow up occurring 8-12 weeks after birth. Consent was also sought to take saliva samples (for cortisol assay) from the baby before and after a routine blood test taken the baby was five days old.

The MB RCT has informed *THRIVE* by providing insight into recruitment, retention, and the handling and coding of video-recordings of mother-infant interaction. In terms of recruitment, the pilot study was conducted in the same NHS Health Board areas that *THRIVE* is being undertaken in, and recruited women using the same NHS Greater Glasgow & Clyde Special Needs in Pregnancy (SNiP) criteria. This has enabled the *THRIVE* team to build up local area contacts and understanding of the challenges of recruiting "hard to reach" and vulnerable women during pregnancy.

The MB RCT managed to retain about two-thirds of the women recruited for an average of six months (26.86 weeks, range 19-34, SD 4.6) from consent. To date 68% (n=21) of those who completed the baseline line measures (n=31) have completed measures at the three time points. Remuneration (£20 shopping voucher) was offered to participants at the last data collection point. In the *THRIVE* trial women will be provided with a £15 shopping voucher upon completion of each of the three outcome questionnaires. In addition, we plan to provide the women with a toiletry kit to take into hospital with them for the birth of their child and a baby bib with the THRIVE logo on it when the baby is 6 months. The MB RCT has also provided valuable insights into the retention of practitioners involved in delivering the interventions. Learning from these, *THRIVE* has successfully applied for funding from the Chief Scientist Office (Scotland) to provide the NHS with funds for each participant successfully recruited to *THRIVE.* These funds will allow the NHS to provide "backfill" for practitioners involved in the delivery of the interventions, as well as recoup 75-90% of the costs associated with the delivery of the interventions to each participant.

Finally, *THRIVE* has benefited from the piloting of video-recordings of mother-infant interaction with the target population.

2.4 The interventions

Two interventions will be evaluated by *THRIVE.* These are Enhanced Triple P for Baby (ETPB) and Mellow Bumps (MB). All women receiving these interventions will also receive their routine antenatal care (see 2.5 for details).

2.4.1 Enhanced Triple P for Baby (ETBP)

ETPB was developed at the Parenting and Family Support Center (PFSC) at the University of Queensland, Australia and is provided as a service to families by Triple P

International. The efficacy and effectiveness of Triple P interventions delivered in five different levels of intensity have been demonstrated in numerous studies and randomised trials. [31, 32]

ETPB is informed by social learning theory. It consists of four antenatal group sessions and up to four postnatal telephone consultations with a further four individual, one hour sessions in order to ameliorate ongoing maternal psychological distress in this group. ETPB sessions take from 30 minutes (telephone) to two hours (group) and the intervention averages around 14 hours in total. ETPB's emphasis is on families and includes fathers, with very practical content around expectations and skills to meet the challenges of becoming a parent whilst ideally maintaining a happy family or at least reducing family discord. In the first two sessions mothers and their partners are introduced to positive parenting ideas and asked to reflect on their expectations about parenthood and knowledge of infant development. Then they are provided with guidance on to how to respond to common infant problems (i.e., crying, fussing) and how to interact with their infants in a nurturing, positive environment. They are then introduced to a range of 'survival skills' for dealing with psychological distress and how this impacts on their ability to appropriately interact with others, including their infants. The final two group sessions focus on partner support and strategies for positive communication in order to ensure practical and emotional support, facilitate adjustment to parenthood and reduce marital stress and social isolation. The four postnatal sessions allow the woman/parents to practice these coping strategies and techniques once their baby is born. The foci for these sessions are determined by the parents who are encouraged to become their own coach throughout (and have their own workbook). The enhancement of coping is provided in the final individual sessions to ensure the amelioration of distress.

2.4.2 Mellow Bumps (MB)

MB was developed by Mellow Parenting. Trial data for Mellow Parenting programmes is encouraging. [33] MB is underpinned by attachment theory and designed to target women who have are have additional health and social care needs in pregnancy. It involves seven antenatal group sessions (each two hours, i.e. 14 hours in total), focuses on mothers, although fathers are invited to one session; and the content focuses on encouraging nurturing, engagement and synchrony between mother and baby. In each session, a topic is raised that relates to maternal wellbeing. This includes healthy eating, exercise, relaxation and having fun for the mothers as well as exploring barriers to good parenting and sources of support which will benefit the mother and the baby. The infancy foci are the competencies of infants, infant brain development and the significance of very early interaction for shaping this development. The group dynamics and the development of safe relationships within the group play a key role in allowing mothers to address their current emotional state and its modulation. All activities are designed to require only the minimal literacy, with the emphasis on activity, viewing videos and discussion.

2.5 The control

All women recruited to the trial will receive Care as Usual. Participants in NHS Greater Glasgow & Clyde will receive care in line with NHS Greater Glasgow & Clyde's Special Needs in Pregnancy protocol. [7] Participants in NHS Ayrshire & Arran will receive care in line with NHS Ayrshire & Arran's Vulnerable Families guidelines. A Pre-Birth Case Conference may be arranged, between weeks 28-32 of the pregnancy, which may be followed by either a Child Protection Case Conference Post-Birth or a Post-Birth Planning Meeting. The CAU group will not be offered group based parenting interventions such as ETPB or MB, although contact with health visitors, Parent's and Children Together (PACT) teams and any relevant specialist services such as the Community Addictions Team will be available.

3. Study design and methods

3.1 Setting

The *THRIVE* trial will recruit participants from NHS, Social Care and Voluntary organisations located within the catchment areas of NHS Greater Glasgow and Clyde and NHS Ayrshire and Arran Health Boards.

3.2 Participants

The *THRIVE* trial will collect data from women who have been identified by a health or social care professional as having additional health and social care needs in pregnancy, their partners, and health and social care professionals.

Women who have additional health and social care needs

Women who are identified, by a health or social care professional, as having additional health and social care needs in pregnancy wil be invited to take part in this project. NHS Greater Glasgow and Clyde's Special Needs in Pregnancy guidelines will be used as inclusion criteria. Women should be between 20 and 30 weeks pregnant at the start of the group intervention. Women who do not meet the criteria, or who have passed 30 weeks of pregnancy prior to the interventions beginning will not be recruited to the trial. If a woman is receiving any other antenatal parenting interventions beyond CAU then they would also be excluded as this would have potential to affect the results of the study. Women who miscarry after recruitment or during the delivery of the interventions will naturally no longer be included in the trial. Such situations will be handled with extreme sensitivity.

Women who are known schedule 1 offenders or are living with a known schedule 1 offender AND have a Child Protection Order (CPO) that states the child will be removed at birth will be excluded from the study. Where a CPO is not in place the women can be recruited to the trial, but we will seek advice from their midwife or referring professional to determine whether or not participation in the trial would be appropriate. In addition, women who have active psychosis or have limited comprehension of spoken or written English will be excluded from the study as both could affect the women's ability to consent, participate and engage with the interventions. There are two other situations in which we would consider excluding a woman from the trial. These are women who are experiencing complex homelessness and women with severe mental health problems, other than active psychosis. The recruitment of women in these situations will be carefully considered based upon the research team's confidence to i), retain and maintain contact with women experiencing complex homelessness, and ii), whether the mental health symptoms being experienced would negatively affect a woman's ability to consent, participate and engage with the interventions.

Partners of women participating in the THRIVE trial

Partners of women who are allocated to the ETPB or MB arms of the *THRIVE* trial will be invited to accompany participants to either all (ETPB) or one (MB) of the intervention sessions. Male partners will also be invited to participate in a linked PhD study, funded by the MRC, which aims to explore the effects of partners on mother-child interaction, mother's participation in trial and the men's perceptions of fatherhood. The men do not have to be the biological father of the woman's baby in order to participate in the PhD study on fatherhood.

Health and social care practitioners

Practitioners who are recruited to deliver ETPB or MB programmes will be invited to complete questionnaires and participate in qualitative interviews about their experiences of being trained in and delivering the interventions. Additionally, health and social care professionals involved in the recruitment of women to the *THRIVE* trial will be invited to participate in qualitative interviews about their experiences of participating in the trial.

3.3 Recruitment

Permission to recruit participants to the *THRIVE* trial has been granted by the relevant NHS heads of service.

Women who have additional health and social care needs

The recruitment of women to the trial will commence in late summer 2013. In total, 500 women identified by the SNiPs protocol as having additional health and social care needs will be recruited to the trial over a two year period. Recruitment will be undertaken by health and social care professionals during routine care. This will involve them explaining the trial to the women, and referring those women who express an interest in participating to the research team who will then contact the women in order to consent them to the trial.

Partners of women participating in the THRIVE trial

Women who agree that their male partners can be contacted about the linked PhD study will be asked to provide them with a postal questionnaire that can be returned using a pre-paid envelope. At the back of the questionnaire there will be a tear of slip that men can complete and return if they are interested in participating in two semi-structured qualitative interviews about their attitudes to fatherhood, parenting and their partner's participation in the *THRIVE* trial. Male partners may also be directly approached by members of the research team about participation in the semi-structured interviews whilst attending ETPB or MB group sessions, or during a home visit to a participating woman.

Health and social care practitioners

Advertisements for 36 health and social care practitioners to deliver the ETPB and MB interventions will be placed by NHS Greater Glasgow and Clyde and NHS Ayrshire and Arran Health Boards. After the practitioners have been recruited, we plan to randomly allocate them to either the ETPB or MB arms of the trial. However, as some practitioners may already have experience delivering ETPB or MB it might not be feasible to use a fully randomised design as that could introduce contamination between arms of the trial. To avoid contamination we will allocate those practitioners to the intervention in which they have experience. We will still randomly allocate the other practitioners. Although employed to deliver the interventions, the practitioners will also be participants in the trial, with quantitative and qualitative data collected about their experiences of being trained in and delivering the interventions. In addition health and social care professionals (n=20) involved in the recruitment of women to the project will also be asked to participate in qualitative interviews about their experiences.

3.4 Design

THRIVE is a three-arm randomised controlled trial, and is supplemented by a full process and health economics evaluation.

Randomised controlled trial

Participating women with additional health and social care needs in pregnancy will be randomised into intervention and control arms after baseline data has been collected. The three arms will be treated identically in terms of data collection. The randomisation will be conducted by colleagues at the Robertson Centre for Biostatistics, University of Glasgow using randomised permuted blocks, with stratification for parity (number of children), severity of psychiatric symptoms and history of substance dependency. For every 12 participants randomised: two will receive CAU, five will receive ETPB and five will receive MB. The women will then be contacted and informed of their group allocation and, where appropriate, invited to attend the ETPB or MB group sessions. There will be two follow ups; these will be conducted when the women's children are aged six and 18 months.

The *THRIVE* trial has been powered based upon the proposed primary outcomes. These are maternal mental wellbeing and mother-child interaction. In particular, *THRIVE* aims to assess whether women receiving ETPB or MB show:

1) significantly lower anxiety, depression and outwardly directed irritability compared to those receiving CAU when their babies are 6 months old.

2) significantly higher maternal sensitivity scores in mother-infant interactions (compared to those receiving CAU when their babies are 6 months old).

Maternal mental wellbeing will be measured using the Hospital Anxiety and Depression (HADS) and the outwardly directed irritability (I) questions from the Adult Wellbeing Scale (HADS+I), whilst mother-infant interaction quality (MIIQ) will be measured using the observer-rated child-centred component of the CARE index. Both of these measures are well established and validated.

The efficacy of ETPB and MB will be analysed at a significance level of 2.5% in order to maintain an overall Type I error rate of 5%. Two analyses, performed in a hierarchical fashion so no further p-value adjustment is necessary, will be undertaken. Analysis 1 will compare the two intervention groups (ETPB and MB) with CAU. If a positive result, at a significance level of 2.5%, is found then Analysis 2 will compare ETPB and MB. If Analysis 1 does not give a positive result, the focus of subsequent analyses will shift from testing whether ETPB and MB achieved different outcomes and determining which, if any, intervention was effective.

In order to have 90% power to detect an effect size of less than 0.5 for Analysis 1 and 0.4 for Analysis 2 requires 157 participants in both the ETPB and MB groups. Comparing these 314 subjects with CAU in Analysis 1 can be achieved with only 63 participants in the CAU group. Therefore, 377 participants are required. Due to the trial purposively recruiting women who are vulnerable in pregnancy, we decided to opt for a cautious attrition rate (25%) to minimise risk to the trial. To allow for 25% attrition at first follow up, 500 participants will be randomised.

The mother-centred primary outcome is the HADS+I. No data are available on the standard deviation (SD) of this measure in a comparable population. However, data from a similar sample of vulnerable mothers suggest the mean value on the Outwardly Directed Irritability (I) subscale of the Adult Wellbeing Scale (AWS) to be 4.7 points with a SD of 2.7.[34] Department of Health (DoH) Guidelines indicate that scores of 8 or more have a problem on this scale, with 5-7 being borderline; given the above mean and SD, we would expect 15% of mothers to have scores of 8 or more, and a further 38% to lie in the borderline range.[35] An effect size of 0.5 points (Analysis 1) would represent a mean difference of 1.35 points between the active intervention groups and CAU, and would results in a reduction in the clinical range to 6%, and in the borderline range to 28%. In addition, the anxiety subscale of the HADS has been found to have a SD of roughly 4.8 points in a population of non-vulnerable mothers-to-be. [36] Effect sizes of 0.5 and 0.4 would therefore represent differences in mean HADS anxiety score of 2.4 and 1.9 points, which clinicians would consider to be clinically significant.

The child-centred primary outcome is the observer-rated child-centred component of the CARE index (Mother-Infant Interaction Quality, MIIQ) has a SD of approximately 3 points. A score in the range 0-2 suggests the need for psychotherapy for the parent, 3-4 suggests the need for a lesser parental intervention and score of 5-6 suggest the need for parental education only, whilst a score of 7 or over is considered normal. For Analysis 1, an effect size of 0.5 corresponds to a difference in mean MIIQ scores between the active interventions and CAU of 1.5 points; for Analysis 2, an effect size of 0.4 would

equate to a 1.2 point difference, either of which would represent a clinically relevant difference. [28]

Although we have powered the study at 90%, we will also have good power to detect smaller effect differences. For example, we will have 80% power to detect an effect size of 0.35 between the two active interventions (Analysis 2), corresponding to a difference of 1.05 points on the MIIQ.

Process evaluation
In order to interpret the trial outcomes and to answer secondary research questions related to process, a process evaluation will be conducted. The process evaluation has three main components which are designed to investigate the fidelity of programme delivery; practitioners' characteristics, perceptions and motivation; mothers' engagement; the importance of different intervention components; and contextual factors facilitating or inhibiting delivery and participation.

Health economics evaluation
Health Economics and Health Technology Assessment (HEHTA) at the University of Glasgow has been commissioned to undertake a comprehensive economic evaluation. The majority of applied economic evaluations in the area of home visiting and parenting (many of which have been conducted in the USA) [37-40] have suffered from diverse economic objectives and methodological problems including the lack of a societal perspective and limited cost analysis. The *THRIVE* evaluation will assess the costs and outcomes associated with the delivery of each intervention and CAU from the NHS and Personal Social Services (PSS) perspective favoured by the National Institute for Health and Clinical Excellence (NICE). A broader societal perspective will be adopted to allow for the possibility of costs and outcomes beyond the NHS and PSS such as housing, education, employment and justice.

3.5 Data collection

3.5.1 Outcome data

Outcome data will be collected from women at three time points. Baseline questionnaire data will be collected after the 12th week of pregnancy, whilst follow up data will be collected six and 18 months after childbirth. In addition, video-recordings of mothers interacting with their infants in a caring situation such as feeing or during play will be made when the infants are six and 18 months old.

The following questionnaire data will be collected:
Baseline questionnaire
Includes questions on the reason for vulnerability in pregnancy; socio-demographic characteristics; previous childbirth history and parity; psychological distress, depression and anxiety, measured using the BSI-53 and HADS+I; women's health, measured using the EQ-5D; health in pregnancy; attitudes towards parenting; relationship with partner/father of child; and, recollections of childhood and childhood trauma.

First follow up questionnaire
Includes questions on childbirth experience; depression and anxiety, measured using the HADS+I; women's health, measured using the EQ-5D; antenatal care history; health after pregnancy; child's health and development; attitudes towards parenting; parenting self-efficacy; relationship with partner; peer, partner and family support; child's relationship with father.

Second follow up (18 months after childbirth)
Includes questions on depression and anxiety, measured using the HADS+I; women's health, measured using the EQ-5D; child's health and development; attitudes towards

parenting; parenting self-efficacy; relationship with father; peer, partner and family support; child's relationship with partner; child's learning environment; child's language development, measured using the sure start language questionnaire.

3.5.2 Process data

Process evaluation data will be collected from women identified as having additional health and social care needs during pregnancy, practitioners involved in the delivery of ETPB and MB, practitioners involved in the recruitment of women to the trial and the partners of the women.

Women who have additional health and social care needs

Women receiving ETPB or MB will be asked to complete a pre- and post-intervention questionnaire about their expectations and experiences of participating in the group sessions. The pre-intervention questionnaire will be completed at the beginning of the first session, whilst the post-intervention questionnaire will be completed within two weeks of the last antenatal group session being delivered. During the intervention programmes, we will seek permission from the women to physically observe or video-/audio-record a sample of the sessions in order to assess the fidelity of intervention delivery and the quality of practitioner-participant interaction.

33 women (ETPB n=14, MB n=14, CAU n=5) will then be invited to participate in a semi-structured interview about their experiences of participating in the trial and the support that they have received during pregnancy, including their experiences of ETPB, MB and CAU. The same sample of women will be interviewed 6 months after the birth of their child in order to explore the perceived lasting effects of the intervention upon their parenting. We anticipate that further women will be identified by the THRIVE steering group and data monitoring committee to participate in semi-structured interviews to explore issues arising from the trial, this number will not exceed 30 women. These will be identified by the THRIVE steering group and data monitoring committee, and will be dependent upon the timing of emerging issues. A nested purposive sample of young women with a history of being looked after and accommodated by local authorities (n=33) will also be invited to answer additional questions, as per the request of our funders, to explore the parenting experiences of young people who are in/have been in the care system.

Partners of women participating in the THRIVE trial

The male partners of women participating in *THRIVE* will be provided with postal questionnaires via their partner or a member of the research team. These will include questions on sociodemographic background; relationship with partner; feelings about partner's pregnancy, motherhood, fatherhood and parenting; and, recollections of childhood and childhood trauma. In addition, up to 40 men will be invited to participate in two semi-structured interviews about the effects of fathers on mother-child interaction, mother's participation in trial and the men's perceptions of fatherhood.

Health and social care practitioners involved in ETPB and MB delivery

All practitioners delivering ETPB and MB will be asked to complete a questionnaire at three time points: pre-training, immediately post-training and following 12 months experience delivering the interventions. This will include information on their experience and qualifications, experience working with families, experience running parenting groups (including any previous training that they have undertaken to deliver groups), their perceived level of confidence and proficiency in running parenting groups in general and the specific intervention in particular. 18 practitioners, 9 per intervention, will be invited to participate in a semi-structured interview about their expectations of training; motivation for participating in the study; views on the specific parenting intervention and the need for fidelity; expectations of delivering the interventions; history working with,

and perceptions of, families and vulnerable groups; previous training in parenting programs; and, expectations of supervision during delivery of interventions. The same practitioners will be interviewed after they have 12 months experience delivering ETPB or MB.

As previously noted, we will ask permission to observe the delivery of ETPB and MB using researcher observation or audio-/video-recordings. At the end of each session the practitioners will be asked to complete protocol adherence checklists. These will be requested from Mellow Parenting and Triple P to assess fidelity of programme delivery. Practitioners will receive routine supervision from practitioners more experienced in delivering ETPB or MB during intervention delivery. All supervisors recruited to the study will be asked to participate in two semi-structured interviews (before delivery of the first groups; 12 months after intervention delivery has begun) with the research team about their experiences of providing supervision.

Health and social care practitioners involved in recruiting women to the *THRIVE* trial
A geographically representative sample of 20 health and social care practitioners involved in the recruitment of women to the trial will be invited to participate in a semi-structured interview about their experiences of recruiting women to the trial, and the decisions that they make in relation to the inclusion/exclusion criteria provided. The sample of midwives invited to participate in the interview will be stratified by recruitment rates to allow us to compare the experiences of those with high and low recruitment rates. In addition to the semi-structured interviews outlined previously, practitioners involved in the recruitment of women to the THRIVE trial may be asked to participate in semi-structured interviews to explore issues arising from the trial. The samples sizes and the issues to be explored will be identified by the THRIVE steering group and data monitoring committee, and will be dependent upon the timing of emerging issues. Examples of topics that might be explored include attrition and difficulties recruiting specific types of women.

3.5.3 Health economics data
All women participating in the trial will be asked to keep a service use diary throughout their pregnancy and after their child is born. This will record attendance at NHS, social care, local authority and voluntary organisations for both mother and child. The diary will collect data at two time points: 1) between baseline and 6 months post birth, and 2) between 6 and 18 months post birth.

Consent will be sought from all women participating in the trial for linkage of mother and infant data with routinely collected NHS health data, educational, social care and justice records. This will include asking permission to use the mother's and baby's NHS Community Health Index (CHI) number for data linkage using the NHS Greater Glasgow and Clyde Safe Haven service. This data will be used to allow the health economics evaluation to assess the broader societal costs associated with receiving ETPB, MB and CAU.

3.6 Data Analysis
3.6.1 Primary and secondary statistical outcomes
Baseline-adjusted linear regression analysis (ANCOVA) will be used to compare primary statistical outcomes between intervention groups. Similar methods will be used for other outcomes (using data transformation and alternative regression methods, depending on the distribution of each outcome). Regression models will be extended to investigate the effects of baseline characteristics and the potential moderating effects of these variables and other measures of intervention compliance. Repeated measures methods will be applied to outcomes collected at more than one post-baseline assessment. Missing data will not be imputed in the first instance, but the sensitivity of key results will be assessed

under alternative assumptions regarding missing values, such as imputation with the baseline value or with the average response in the alternative group. Multiple imputation, based on predictive regression models of study outcomes on baseline and intermediate outcome measures, will also be explored to account for the additional uncertainty in estimates of intervention effect differences due to missing outcome data. Whilst outcomes may exhibit clustering in the intervention arms of the study, due to being delivered in a group setting, this clustering will not be present in the CAU arm, and the anticipated benefits of the two interventions are expected to act in part through the group dynamic. Accordingly, since randomisation is performed at the individual, rather than at the group level, we will not make adjustment for the clustering of outcomes in the main analyses. We will, however, explore the extent of clustering of outcomes within each treatment arm as secondary analyses, in order to evaluate potential explanatory factors for any group-level variability in outcomes.

3.6.2 Analysis of video tapes

Video-recordings of mother-infant interaction will be analysed by researchers at the University of Manchester. These researchers will be blinded to the conditions that participants have been allocated, and will code the quality of mother-infant interactions using the CARE index [30] and the Mellow Parenting Observation System [41].

3.6.3 Health economics data

Up-to-date unit costs will be attached to quantities of resource used to generate mean costs per study participant. The incremental costs and benefits of the treatment arms will be reported within an incremental cost-effectiveness ratio (ICER) where appropriate. Costs to participants and families will be examined as part of a sensitivity analysis. The cost-effectiveness will be assessed by comparing the additional costs associated with each of the interventions with the outcomes achieved in the study and those achievable in the longer term. These longer term outcomes will be assessed by linking the short term outcomes identified in the study to longer term impacts on health and wellbeing for both mother and child via relationships identified from the literature. Economic resource use forms developed for the economic evaluation carried out by McIntosh et al 2009 [29] for the Economic Evaluation of an intensive home visiting programme for vulnerable families were used as templates for the service use questionnaire and data collection forms. Diaries completed by the study participants will be used as an 'aide memoir' to inform the economic resource use data collection at the follow up points. The inclusion of the EQ-5D generic outcome measure will also allow the estimation of a cost-utility analysis (preferred evaluative technique of NICE). In line with current guidance, discount rates of 3.5% for costs and benefits will be applied where appropriate. Sensitivity analysis will be carried out on the perspective adopted as well as key cost-drivers and outcomes. As per recent economic evaluation guidance, missing data will be predicted as a function of relevant baseline covariates. [42]

The economic evaluation will incorporate available trial linked data, project cost and outcome data from baseline, 6 and 18 months and up to 30 months follow up. The cost-effectiveness will be assessed by comparing the additional costs associated with each of the interventions to the outcomes achieved in the study and those achievable in the longer term. The trial aims at collecting a number of long term variables including health measures, educational outcomes, children on the at-risk register, and children taken into care and attending Accident & Emergency departments. Based on the availability of such routine data, longer term economic outcomes will be assessed by linking the short term outcomes identified in the study to potential longer term impacts on health and wellbeing for both mother and child via trial extrapolation methods including economic modeling techniques.[46] However, given the well-recognised limited nature of this exercise in terms of assumptions required to link intermediate costs and outcomes to long term economic costs and outcomes, relationships identified from the literature will

also be used to guide and strengthen modelling scenarios and form the basis of a more robust, evidence-based long term modelling exercise. This long term modelling exercise will contain a base case scenario and incorporate a significant number of sensitivity analyses to allow for the likely variation around long term costs and outcomes. Hence, the long term model will be based on the best data available at the time, including short and long term trial outcomes, routinely available linked data, as well as best evidence from the published literature. In doing so, an evidence-based, realistic picture of likely cost effectiveness from a societal perspective over the long term will be generated. This approach fits with guidance of the methods for the economic evaluation of public health interventions. [47]

3.6.4 Process evaluation data

Qualitative interviews conducted with practitioners, women participating in the trial and their partners will be audio recorded and transcribed. An initial coding schedule will be piloted with a representative sample of transcripts. A revised schedule incorporating emergent themes will then be used to code all the data, using NVivo.

4 Trial Management

NHS Greater Glasgow and Clyde Health Board will be the sponsor of the *THRIVE* trial. A steering committee and data monitoring committee will be established to provide independent expert advice.

5 Ethical Considerations

Ethical approval for *THRIVE* will be sought from the NHS's West of Scotland Research Ethics Service.

5.1 Informed consent

Women identified as having additional health and social care needs in pregnancy by health and social care professionals, as per NHS Greater Glasgow & Clyde Special Needs in Pregnancy criteria, will be recruited and consented to the study after the 12th week of pregnancy. The consent procedure will clearly explain all aspects of the study, and seek consent not only for participation in the study but also for the linkage of mother and infant data with routinely collected NHS health data, educational, social care and justice records. This will include asking permission to use the mother's and baby's NHS Community Health Index (CHI) number for data linkage using the NHS Greater Glasgow & Clyde's Safe Haven service. We will seek permission where applicable for the partners/fathers to be contacted in relation to a complementary MRC-funded PhD studentship. We will also seek permission to store the women's contact details on file so that we can re-contact them in the future should we be able to secure additional funding to follow up mother and child outcomes over a longer period. Informed consent will also be sought from practitioner participating in research elements.

5.2 Participation in the research

We anticipate there will be minimal risk to the women participating in the study. Our quantitative data collection procedure consists of completing repeat questionnaires with trained researchers who have enhanced disclosure from Disclosure Scotland and who have experience of working with vulnerable groups. The questions being asked are well established and are not known to be problematic. All researchers will follow NHS guidance relating to patient confidentiality and protection, including child protection procedures. The same risks are present in conducting qualitative interviews with participants. All interviewers will have experience conducting qualitative interviews and working with vulnerable populations. Additionally, the researchers will have contact details for the women's health and social care professionals and will be able to contact them should they become concerned about women participating in the study. All

researchers will also carry a "useful contacts" sheet that can be used to signpost the women to relevant services should they request information about services.

5.3 Participation in the interventions

Since we will be working with vulnerable women at a sensitive period in their lives, some activities such as being asked to reflect upon past experiences may have the potential to cause distress. However, we believe that this risk is minimal as both interventions are designed to reduce stress through positive action and the development of coping strategies. In addition, the group facilitators will have undergone training to work with this group of woman and will be able to provide empathetic support and direct the woman to appropriate services when necessary. The group dynamics may help to reduce stress/distress to participants by providing a supportive and considerate atmosphere in which issues can be discussed. This will be laid out in the group rules and will be carefully monitored by the group facilitators. Additionally, the interventions will be delivered by trained facilitators who will be able to provide pastoral support and signposting to services should women require additional support.

The delivery of ETPB and MB within group settings carries a risk that participants might choose to discuss issues raised with others outside of the group setting. As the focus of the group sessions is more on activities and active discussion rather than disclosing personal histories, we believe the risk of this occurring is low. Nevertheless, to promote respect and confidentiality amongst participants the intervention facilitators will work with them to establish group rules about confidentiality, especially in relation to social media. Finally, as part of the process evaluation we will seek permission to audio or video record a sample of the group sessions, but will only record if permission is granted by all participants.

5.3 Access to routine services

Participation in the research will not affect women's access to health and social care. All women will continue to receive their maternity care plan during and after pregnancy, and no care will be withheld due to participation in the study. The research team will ask permission from the women to notify their GP and/or other relevant health/social care worker of their participation in the research. All of the women will be told during the consent process that if a significant risk of harm to themselves or their baby/child(ren) is identified, the research team will notify their GP and/or other relevant health/social care professional(s).

5.4 Privacy of routinely held records and data linkage

All data linkage will be initiated by the Robertson Centre for Biostatistics (RCB) using the NHS Greater Glasgow and Clyde's Safe Haven that has been developed to support secondary research use of clinical data. Data from NHS Ayrshire and Arran will also be required and access to these data via a Safe Haven will become available during the life of the THRIVE trial. If this doesn't occur then the research team will seek permission from ISD Scotland to link NHS records for NHS Ayshire & Arran's patients into the Safe Haven. In addition to accessing routine NHS datasets we will ask permission from the participants to access routinely held social care, education, police and judiciary records about them and their child. We will request that these data are linked within the NHS Greater Glasgow & Clyde's Safe Haven during the life of the trial. Should this data not be made available during the lifespan of the trial the research team will liaise with the RCB to identify methods of linking this data in a manner that does not compromise patient confidentiality and privacy. The research team understands that data linkage at the individual level is sensitive and raises issues of privacy and will ensure that all data linkage undertaken adheres to the standards outlined by ISD Scotland. In addition, the

NHS Greater Glasgow & Clyde's Safe Haven is subject to a local privacy advisory committee that will ensure that that privacy risks at the individual patient level are minimised.

5.5 Storage and anonymisation of confidential data

All data collected will be stored securely in accordance with MRC Best Research Practice Guidelines in either locked filing cabinets or password-protected databases accessible only by main research and survey office staff. Identifying information will be held separately at all times from non-identifying information. No names will be retained on any mother, father or practitioner questionnaires. Unique ID codes, and corresponding barcodes, will be used to identify all participants in order to link them throughout the study and identifying information linking participants to ID numbers will be stored securely in a database accessible only by main research and Survey Office staff and held separately from participant questionnaire responses.

All of the data collected as part of the study will only be accessible to members of the research team, with the following exceptions: quantitative data collected from participants will be securely transferred to the Robertson Centre for Biostatistics (RCB) for data entry and cleaning; qualitative interview data and recordings of intervention delivery sessions will be transcribed by an external transcription agency; video-recordings of mother-infant interaction will be securely transferred to the University of Manchester for observer-rated coding using the CARE Index and the Mellow Parenting Observation System. In all cases data sharing and confidentiality agreements will be established per MRC regulations. All of the data collected as part of the study will be anonymised.

Permission will be sought from participants for archiving purposes during trial consent, and the trial consent form will notify participants that their and their child's data will be made available to the funders in anonymised form.

Abbreviations

ANCOVA:	Analysis of Covariance
AWS:	Adult Wellbeing Scale
BSI-53:	Brief Symptom Inventory – a short version of Symptom Checklist-90-Revised: Measures the severity of any psychological distress across nine dimensions
CAU:	Care as Usual
CHI:	Community Health Index
CPO:	Child Protection Order
CSO:	Chief Scientist Office
EQ-5D:	EuroQol 5 Dimensions: a standardised instrument used as a generic measure of health
ETPB	Enhanced Triple-P for Baby
FNP:	Family Nurse Partnership
GP:	General Practitioner
HADS+I:	Hospital Anxiety and Depression Scale enhanced by the outwardly-directed irritability questions from the Adult Wellbeing Scale
HEHTA:	Healthy Economics and Health Technology Assessment
ICER:	Incremental Cost-effectiveness Ratio

MB:	Mellow Bumps
MIIQ	Mother-Infant Interaction Quality
MRC:	Medical Research Council
NHS:	National Health Service
NICE:	National Institute for Health and Clinical Excellence
RCB	Robertson Centre for Biostatistics
RCT:	Randomised Controlled Trial
SD:	Standard deviation
SNiP:	Special Needs in Pregnancy
SPHSU:	Social and Public Health Sciences Unit
THRIVE:	Trial of Healthy Relationships Interventions in the Very Early years

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