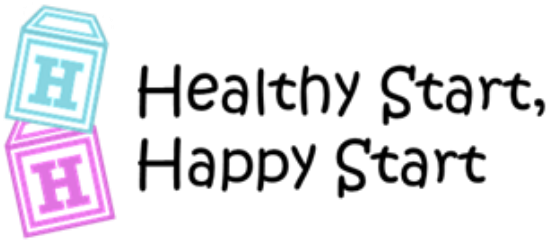
CLINICAL TRIAL PROTOCOL



Study Title: Preventing enduring behavioural problems in young children through early psychological intervention: Healthy Start, Happy Start

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ABBREVIATIONS

AE	Adverse Event
CA-SUS	Child and Adolescent Service Use Schedule
CI	Chief Investigator
CBCL	Child Behaviour Checklist
DMEC	Data Monitoring and Ethics Committee
eCRF	Electronic Case Report Form
GAD7	Generalized Anxiety Disorder 7
ICF	Informed Consent Form
ICTU	Imperial Clinical Trials Unit
PIS	Patient Information Sheet
PMG	Project Management Group
Pre-PACS	Preschool Parent Account of Child's Symptoms
PHQ-9	Patient Health Questionnaire 9
QA	Quality Assurance
RDAS	Revised Dyadic Adjustment Scale
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
SSAR	Suspected Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
TSC	Trial Steering Committee
VIPP-SD	Video-Feedback Intervention to Promote Positive Parenting and Sensitive Discipline

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1. TRIAL SUMMARY

TITLE	Preventing enduring behavioural problems in young children through early psychological intervention: Healthy Start, Happy Start
OBJECTIVES	**Primary objective** To undertake a randomised controlled trial to evaluate whether compared to treatment as usual, a brief parenting intervention (Video Feedback to Promote Positive Parenting and Sensitive Discipline) leads to lower levels of behavioural problems in young children who are at high risk of developing these difficulties. **Secondary objective** To undertake an economic evaluation to assess the cost-effectiveness of the intervention compared to treatment as usual.
DESIGN	Randomised, parallel, two-arm controlled trial
SAMPLE SIZE	300 (150 in each arm)
STUDY POPULATION	Parents/caregivers of children aged 12-36 months and their infants
ELIGIBILITY CRITERIA	**Inclusion criteria** 1. Parents aged ≥ 18 years 2. Child aged between approximately 12-36 months 3. Child scores in the top 20% for behavioural problems on the Strengths and Difficulties Questionnaire (SDQ), based on population norms 4. Written informed parental/carer consent **Exclusion criteria** 1. Child or parent has severe sensory impairment, learning disability, or language limitation, which is sufficient to preclude participation in the trial. 2. Siblings participating in trial 3. Families participating in active family court proceedings 4. Parent/carer is participating in another closely related research trial and/or is currently receiving an individual video-feedback based intervention.
TREATMENT	Video-Feedback Intervention to Promote Positive Parenting and Sensitive Discipline (VIPP-SD)
PRIMARY ENDPOINT	Assessment of severity of behavioural problems using the Pre-PACS interview at five months post-randomisation
SECONDARY ENDPOINTS	1. Child Behaviour assessed by the CBCL questionnaire 2. Child Behaviour assessed by the Strengths and Difficulties Questionnaire (SDQ) 3. Parental sensitivity in interactions with their child. 4. Parental mood assessed by the Parent Health Questionnaire 9

	5. Parental anxiety assessed by the GAD-7 6. Couple functioning assessed by the Revised Dyadic Adjustment Scale 7. Parenting practice assessed by the Parenting Scale 8. 8. Resource use using a modified version of the Child and Adolescent Service Use Schedule (CA-SUS)

2. INTRODUCTION AND RATIONALE

Behavioural problems affect 5-10% of children, and children with established behavioural problems have significantly worse outcomes through childhood and into adult life. They have an increased risk of psychiatric disorders, antisocial behaviour and criminality, drug and alcohol misuse, educational failure and physical ill health. As well as these high levels of difficulties and unhappiness for young people and their families, there are also large costs incurred by society through the health, social care and criminal justice systems.

A key risk factor for the development of behavioural problems is the quality of the parental care that children receive: low levels of sensitive parenting and greater use of harsh discipline have been causally linked to the development of behavioural problems. Interventions which work with parents and carers to improve their parenting have been found to reduce child behavioural problems, and intervening early in children's lives has the potential to be particularly effective in improving outcomes, as well as having beneficial effects for parental health and wellbeing.

Most research to date has focussed on older children, when behavioural problems are more established, and thus more difficult to treat. Interventions have also focussed predominantly on mothers, with very few interventions involving fathers or a second caregiver, despite accumulating evidence that interventions involving two parents or caregivers can be more effective than those engaging just one. The proposed intervention (VIPP-SD) has a developing evidence base as an early preventive intervention (16-20) and has the potential to be delivered widely across the NHS as part of an early intervention programme. Young children and their carers have regular contact with the NHS, yet evidence is needed to ensure that resources are directed in the most effective manner. The trial has been designed to provide this evidence, as the first large randomised controlled trial to test whether an early video feedback intervention (ViPP-SD) is an effective and cost-effective approach to reducing behavioural problems in at-risk young children. It addresses an area of key concern to the NHS and represents an opportunity to reduce the burden of behavioural problems on individuals, families and society. If shown to be effective, the intervention could be delivered widely across the NHS to parents and carers of young children at risk of behavioural problems as part of community based services.

There are a number of systematic reviews (25-28) and policy-relevant reviews (29-31, 40) of this field. These highlight that intervening early in children's lives can be particularly effective in improving child outcomes, with evidence from three areas of research: i) trials that have tested interventions with parents of young children or with expectant parents (27,

32-34); ii) epidemiological work pointing to the potential importance of the earliest years of development in setting the trajectory for later outcomes (35-36), and iii) economic studies demonstrating the increased opportunities and cost returns achieved by effective early intervention (29, 37).

Some key early interventions for behavioural problems have been identified (27-28), including those which show promise for intervention on a wide scale. The Family Nurse Partnership (32) is being used across the UK and shows promise, but it is focussed on a limited target group and, as the Harvard Policy Review (30) points out: “No single program approach or mode of service delivery has been shown to be a magic bullet”.

Alternative and complementary approaches are still needed, and Video Feedback (ViPP-SD) is a compelling alternative because it has already been evaluated and shown to improve mother-infant interaction (a key pathway for behavioural problems) (16-19), with initial evidence of improvement in child behaviour (20). Research also suggests that including two parents/caregivers in interventions, particularly fathers, may lead to increased efficacy (25, 38-39).

The ViPP intervention has been developed and evaluated in a systematic way, including six randomised controlled trials in different settings and with different groups of families. It has an evidence base for early preventive intervention with effects shown on parental sensitivity in parent-child interactions, positive parental discipline practices and child behaviour (16-20).

The intervention is derived from an understanding of attachment theory (41), whereby the promotion of sensitive parenting improves the relationship that children have with their primary caregiver. It begins with a core series of four sessions that aim to enhance the parent’s capacity to identify the child’s exploratory behaviour and attachment cues and to respond to them appropriately (1). Each session also includes an explicit focus on parental discipline strategies, based on the video recordings of the interactions with their own child. This incorporates aspects of social learning theory (42), with a focus on increasing positive and reducing aversive interactions. Overall, the intervention represents a powerful combination of the insights from the attachment and social learning perspectives (43).

The case for early preventive intervention is becoming increasingly established. The 2012 Chief Medical Officer’s report, ‘Our Children Deserve Better: Prevention Pays’ (40), clearly highlights the social and economic benefits of early, preventive interventions in child health. The report focusses particularly on the need for interventions to improve the early parent-child relationship, as a way of reducing the risk of psychiatric disorder in children. However, it is essential that proposed early interventions are shown to be effective and cost-effective. This is the first RCT to test VIPP-SD in a UK setting. VIPP-SD has the potential to be an effective and cost-effective early intervention for behavioural problems.

3. AIMS, HYPOTHESIS AND OBJECTIVES

3.1. Aim

To evaluate the effectiveness and cost-effectiveness of a brief early parenting intervention, designed to prevent enduring behavioural problems in young children aged 12-36 months old.

3.2. Primary hypothesis

Among children with high levels of behavioural problems aged twelve to thirty-six months, adding a brief video-feedback parenting intervention (ViPP-SD) to treatment as usual will reduce enduring behavioural problems measured at five months post-randomisation, using the Pre-PACS interview.

3.3. Secondary hypotheses

i. Among children with high levels of behavioural problems aged twelve to thirty-six months, adding a brief video-feedback parenting intervention (ViPP-SD) to treatment as usual will reduce enduring behavioural problems measured at two years post-randomisation, using the Pre-PACS interview.

ii. Among children with high levels of behavioural problems aged twelve to thirty-six months, adding a brief video-feedback parenting intervention (ViPP-SD) to treatment as usual will reduce enduring behavioural problems measured at five months and two years post-randomisation, using the Child Behaviour CheckList (CBCL) and Strengths and Difficulties Questionnaire (SDQ), completed by parents/carers and the SDQ completed by a nursery carer/teacher.

iii. Among children with high levels of behavioural problems aged twelve to thirty-six months, adding a brief video-feedback parenting intervention (ViPP-SD) to treatment as usual will result in higher levels of parental sensitivity in parent-child interactions, measured at 5 months.

iv. Among children with high levels of behavioural problems aged twelve to thirty-six months, adding a brief video-feedback parenting intervention (ViPP-SD) to treatment as usual will provide a cost effective use of resources.

4. OBJECTIVES

1. To undertake a randomised controlled trial to evaluate whether, compared to treatment as usual in the NHS, a brief parenting intervention (Video Feedback to Promote Positive Parenting and Sensitive Discipline) leads to lower levels of behavioural problems in young children who are at high risk of developing these problems.
2. To undertake an economic evaluation to assess the cost-effectiveness of the intervention compared to treatment as usual.

5. OUTCOME MEASURES

5.1. Primary endpoint

Assessment of severity of behavioural problems using the Pre-PACS interview at five months post-randomisation

5.2. Secondary endpoints

1. Child Behaviour assessed by the CBCL questionnaire
2. Strengths and Difficulties Questionnaire (SDQ)
3. Parental sensitivity in interactions with their child.
4. Parental mood assessed by the Patient Health Questionnaire 9 (PHQ9)
5. Parental anxiety assessed by the Generalized Anxiety Disorder 7 (GAD7)
6. Parental couple functioning assessed by the Revised Dyadic Adjustment Scale (RDAS)Parenting practice assessed by the Parenting Scale
7. Resource use using a modified version of the Child and Adolescent Service Use Schedule (CA-SUS)

6. STUDY DESIGN

The study is a two-arm, parallel group, researcher-blind, randomised controlled trial (RCT), to test the clinical and cost effectiveness of a video-feedback intervention (ViPP-SD) for parents of young children (12-36 months) at risk of behavioural difficulties. The trial will involve 300 families, who will be randomly allocated into one of two groups:

(1) The intervention group, who will receive the video-feedback intervention (described below) (n=150) plus treatment as usual

(2) Treatment as usual (control group) (n=150)

7. TRIAL INTERVENTION

7.1. ViPP-SD

ViPP-SD is a home-based intervention, delivered over six sessions at approximately fortnightly intervals, which shows high levels of parental acceptability. Each session involves filming parent-child interactions and giving parents feedback based on these video clips. Adaptations have been made to account for treatment delivery to two parents/caregivers.

The intervention will be delivered by trained, supervised health professionals, predominantly health visitors. They will deliver the intervention in research participants' homes (or another location according to participant preference). 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 6 sessions in accordance with the manual. They will be supervised, and the treatment will be monitored closely for fidelity to the manual by the clinical supervisor (and a proportion will be taped and assessed by an independent researcher trained in the intervention).

- Four core sessions: these aim to enhance the parent's capacity to identify the child's exploratory behaviour and attachment cues and to respond to them appropriately
- Two booster sessions: these are spaced one month apart, and the key messages are repeated using continuing video interaction material at each session

Therapists responsible for delivering the intervention will be trained by the developers of ViPP-SD and will undertake supervised clinical practice before becoming a therapist on the trial.

7.1.1. Treatment Fidelity

Each therapist will be trained by an accredited VIPP trainer, and will undertake supervised clinical practice before becoming a therapist on the trial.

In order to determine treatment fidelity, the therapist will be asked to document, for each session, whether they delivered key components of the treatment as well as reporting on global adherence to the manual. All sessions will additionally be audio recorded to enable assessment of fidelity (on a random proportion) by independent raters. Preparatory work for the sessions, notes from sessions and the audio recordings will be used during monthly supervision with the lead clinical supervisor in the study, with oversight and regular review from the lead investigators.

7.2. Usual care

Participants in both groups will continue to receive their usual care. Usual care may include a range of services such as the following:

- health visitor services
- GP advice
- early intervention mental health services linked to children's centres
- parenting advice and support sessions

Data on concurrent use of health services will be collected including number of sessions offered, where they were provided, and which healthcare (or other non-healthcare) professionals provided the care.

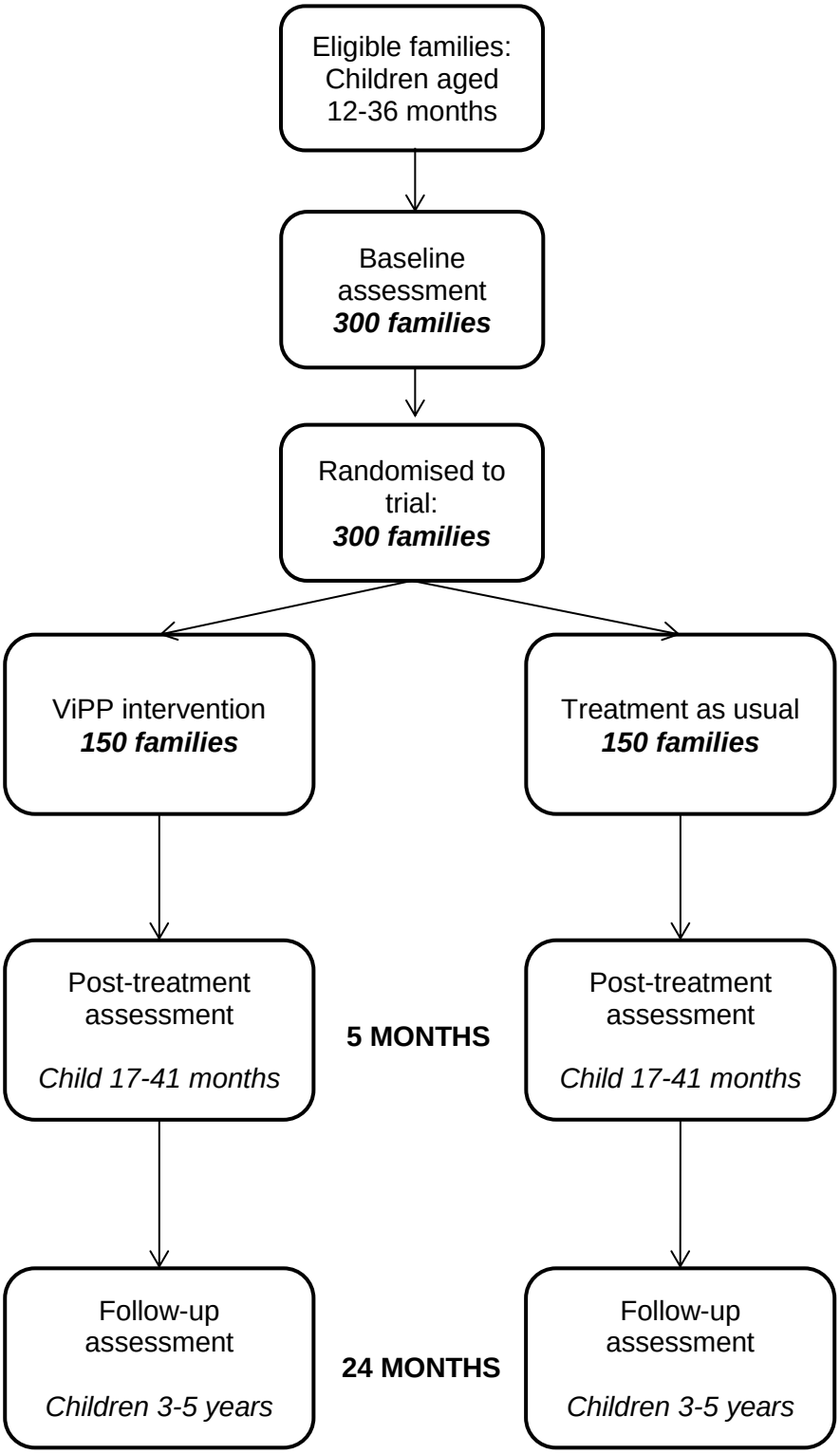
7.3. Qualitative interviews with families

A proportion of families who receive treatment will also be invited to participate in a semi-structured qualitative interview to share information about their experiences of the VIPP intervention. A separate protocol provides further detail on this sub-study.

7.4. Qualitative interviews with therapists

Therapists delivering the treatment will be invited to participate in a semi-structured qualitative interview to share information about their experiences delivering the VIPP intervention. A separate protocol provides further detail on this sub-study.

8. FLOW CHART


Eligible families: Children aged 12-36 months
Baseline assessment ***300 families***
Randomised to trial: ***300 families***
ViPP intervention ***150 families***
Treatment as usual ***150 families***
Post-treatment assessment *Child 17-41 months*
5 MONTHS
Post-treatment assessment *Child 17-41 months*
Follow-up assessment *Children 3-5 years*
24 MONTHS
Follow-up assessment *Children 3-5 years*

9. EARLY DISCONTINUATION OF THE STUDY OR WITHDRAWAL OF INDIVIDUAL PARTICIPANTS

9.1. 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. The charter will also define whether any stopping rules should be implemented for the trial.

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 Project 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.

9.2. Withdrawal of Individual participants

Participants may discontinue the intervention or withdraw from the study for the following reasons:

- At the request of the child's family
- 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

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

10. STUDY POPULATION

Children aged 12-36 months with behavioural problems and their parents/carers.

10.1. Eligibility criteria

10.1.1. Inclusion criteria

1. Parents aged ≥ 18 years
2. Child aged between 12-36 months
3. Child scores in the top 20% for behavioural problems on the Strengths and Difficulties Questionnaire (SDQ), based on population norms.
4. Written informed parental consent

10.1.2. Exclusion criteria

1. Child or parent has severe sensory impairment, learning disability, or language limitation, which is sufficient to preclude participation in the trial.
2. Siblings participating in the trial
3. Families participating in active family court proceedings
4. Parent/carer is participating in another closely related research trial and/or is currently receiving an individual video-feedback based intervention.

11. STUDY PROCEDURES

11.1. Phase 1

Potential participants will be recruited from NHS health services via health visiting services, child and adolescent mental health services, GP services**,** and through links with children's centres and similar community services for families (such as family support services, libraries, and one o'clock clubs) working within the four NHS study sites (Camden, Hillingdon, Islington, Oxfordshire). Other sites may be added as needed, subject to approval. Participants will be parent/s accessing these services already, therefore will already be known to local services.

Health visitors will recruit families to take part in the study at the routine 12 and 24-month health reviews. Clinicians and practitioners in other settings will recruit families when they are referred for support. These identified clinicians will be able to support recruitment by either signposting parents to the study, passing on screening packs**,** or by completing the screening stage of recruitment themselves. Members of the research team and clinical research network (CRN) support staff will also support recruitment of families on site in health visiting services and other venues.

Potential participants will be approached to take part in the screening process, via a questionnaire measure of child behaviour difficulties (The Strengths and Difficulties Questionnaire, SDQ) as well as providing some brief contact details which will enable the research team to make contact following screening and basic demographic variables (relationship to child, age, ethnicity, and educational attainment). The SDQ is a short questionnaire that is widely used in clinical practice assessing parental perception of child difficulties. This questionnaire is well validated and is widely used in clinical practice and research. Those scoring in the top 20% on population norms will then be invited to participate in the full study.

This screening questionnaire will be presented to participants as a pack, together with an invitation letter, an information sheet, consent form, and a freepost envelope regarding taking part in Phase 1 of the study (the screening stage of the recruitment). The written information will explain that they have the opportunity to discuss any questions with the health professional/CRN support staff member/or member of the research team, or call a member of the research team to discuss the study over the phone or email, using contact details contained on the information sheet. It will also be made clear that they will be able to withdraw their consent at any time and that they are providing consent to complete the screening questionnaire only, and not the full study (Phase 2).

The screening questionnaire pack will either be sent to participants as an enclosure in a standard letter being sent regarding the service (e.g. an invitation to attend a 12 or 24 month health review)**,** a separate mailshot if preferred by the service**,** or handed to potential participants when they attend the service. Those participants that received the screening questionnaire in the post will be invited (via written information in the pack) to return it to their healthcare professional at their subsequent appointment. They will also have the option of returning it directly to the research team in the post using an enclosed freepost envelope or filling it in online via a link to a secure website contained in the information sheet.

Those participants that are given the screening questionnaire pack in person when they attend the service, will have the opportunity to complete the SDQ and consent form whilst

at the service, or they will be asked to complete the questionnaire and consent form to return by post or in person when next using the service or electronically using the link provided in the information sheet. Members of the research team or CRN support staff will also visit community centres such as children's centres and one o'clock clubs (e.g. during play, activity, information, and training sessions), with permission from management, to disseminate screening packs to families and where appropriate support families in completing the screening questionnaire, in line with the procedures outlined above. Screening packs will also be made available to families by staff in these settings and in GP practices.

Recruitment will also be supported via poster advertisements and flyers in these health and family service settings, as well as other community venues which cater for families (e.g., GP practices, libraries, nurseries, activity groups) and mailshots from these services. All poster/flyer adverts will contain an email address and phone number for parents to call if they are interested in taking part in the study. Recruitment will also be conducted via social media (facebook and twitter) and relevant online websites designed to support parents of young children, such as 'Netmums' and 'Mumsnet'. Information about the study will also be displayed on specific websites linked to the research team (e.g. http://www.ppod.org.uk). All information posted online will replicate that contained in the study's posters or leaflets. Information will also be provided through adverts in print media and on community radio stations, which will signpost families to the study team.

Those parents that see recruitment information or have been signposted to the study (e.g. via posters and leaflets displayed in health settings, or on internet advertisements) and therefore make contact directly with the research team will be provided with the same screening information pack to complete and return, if they so wish. It is estimated that in excess of 5,000 families will need to be screened in order to enrol the target sample of 300 participants in the trial.

11.2. Phase 2

Following screening, participants who score in the top 20% of population norms will be contacted by a member of the research team to see if they would like to participate in the full study.. For those that are selected, they will be contacted by phone and a date will be arranged for a member of the research team to visit them at home to complete the first assessment visit. At this stage it will be ascertained whether there are two parents in the family and whether both would like to take part.

This first assessment visit will take approximately 90 minutes with each family. During this visit the research team will provide additional written and verbal information about the study, and will allow participants to ask any questions about the study. The purpose of the study will be explained, as well as the procedures participants will be asked to complete. Participants will be informed that they can withdraw from any aspect of the home visits, and from the overall study at any time. The randomisation process will also be explained, so participants are aware that they will be randomly allocated to one of the two groups.

11.3. Blinding

Researchers assessing study outcomes will be blinded to randomised allocation. Participants (i.e. parents and their children) will be informed of their randomised allocation.

In the event of a severe adverse event the Chief Investigator will be notified and may be informed of the randomised allocation.

11.4. Randomisation

Randomisation lists (one per site) will be prepared by a statistician using 1:1 allocation (ViPP intervention vs treatment as usual) and appropriate block sizes and uploaded on to InForm (the study electronic data capture system) prior to the start of the study. Eligible subjects will be allocated online to the next available treatment code in the appropriate randomisation list.

Randomisation will be stratified by treatment centre and by willingness and availability of both parents to be involved (versus one only).

11.5. Follow-up visits

Follow-up assessments will be undertaken in the family home by research assistants who are blind to treatment allocation, at a time convenient for the family.

Participants will be contacted by the research team prior to the visit time or the first post-treatment assessment and they will be sent a thank you note (via post or email) following this assessment. The thank you note will include a reminder of the later follow up arrangements and a request to contact the research team if their contact details change.

Participants will then be contacted one month prior to the planned final follow up at 2 years post randomisation to arrange a suitable time and place for the assessment. Where parents incur travel costs, these will be reimbursed.

11.6. Assessment Visit Schedule

	Baseline	5 month f/u	24 month f/u
Visit	**1**	**2**	**3**
Day/Week/Month		Month 5 post randomisation (+/- 3 weeks)	Month 24 post randomisation (+/- 4 weeks)
Informed consent	X		
Inclusion & exclusion criteria	X		
Demographics and medical history	X		
AUDIT-C	X	X	X
Randomisation	X		
SDQ	X	X	X
CBCL	X	X	X
GAD-7	X	X	X
Pre-PACS interview	X	X	X
PHQ-9	X	X	X
Revised Dyadic Adjustment Scale	X	X	X
Parenting Scale	X	X	X
CA-SUS	X	X	X
Parent-Child interactions	X	X	X
Feedback questionnaire		X	
Serious adverse events	X	X	X

11.7. ViPP-SD Visit Schedule

	VIPP Intervention Schedule[a]					
Visit	**1**	**2**	**3**	**4**	**5**	**6**
Day/Week/Month	Day 14-28 (+/- 7 days) post randomisation	Visit 1 plus 14 days (+/-7 d)	Visit 2 plus 14 days (+/-7 d)	Visit 3 plus 14 days (+/-7 d)	Visit 4 plus 21 days (+/-7 d)	Visit 5 plus 21 days (+/-7 d)

Note. [a]*Visit schedule is a guide for optimal treatment delivery, variation is expected given the pragmatic context of the trial.*

11.8. Measures

11.8.1. Pre-PACS

The primary outcome measure will be an assessment of the severity of the child's behavioural problems using a structured investigator-led interview of a parent or caregiver (the Preschool-PACS), at five and twenty four months after randomisation (the child will be

aged 3-5 years at this later assessment point).Where two parents/caregivers are participating in the trial the Pre-PACS will be completed by the parent who identifies as being the primary caregiver. The Pre-PACS is a semi-structured assessment of child behaviour problems, administered by trained interviewers, which yields a score for behavioural problems based on investigator judgement. To determine pre-PACS scores, caregivers are asked to recall and describe detailed examples of their child's behaviour over the last week in a range of settings (e.g., in the home, with peers, and in public settings such as the supermarket). The parent is also asked about how representative the behaviour is of the past 4 months (to ensure the example is typical and characteristic of the child). The interviewer then rates the severity and frequency of the symptoms on the basis of their professional/clinical judgement and written definitions and thresholds of the behaviours, validated according to clinical practice. Symptoms are rated for frequency and severity on two subscales, one measuring ADHD/Hyperkinesis, and the other measuring conduct problems and antisocial behaviours.

The Pre-PACS has high inter-rater reliability and good construct validity, and has been used in previous clinical trials (e.g., 11-14). Interviewers will be blind to allocation. Semi-structured interviews are the gold-standard measure for most psychiatric disorders. They are more objective as they use investigator-based criteria for scoring symptoms, and are thus less prone to parental biases, which are seen when using parent-reported questionnaires. All PPACS interviews will be recorded for reliability purposes. Recordings will be assessed periodically to avoid drift and ensure that the measure remains robust to rater and respondent bias.

11.8.2. CBCL

The Child Behavior Checklist (45), which is a robust and widely-used questionnaire, will be used as child behaviour is the main outcome of interest.

Each question asks about a specific behaviour and a score is given (0 = Not True, 1 = Somewhat or Sometimes True, 2 = Very True or Often True). For behavioural problems (externalising problems) it yields an overall score, as well as specific subscales for attention problems and aggressive behaviours. The CBCL is a well-validated questionnaire, which has been extensively used in previous substantive clinical trials. The CBCL will be completed by one or two parents/caregivers depending on their participation in the trial.

11.8.3. SDQ

The SDQ (Strengths and Difficulties Questionnaire) is a robust and reliable measure of child behaviour. The SDQ will be used as a screening questionnaire, where those scoring in the top 20% on population norms will be eligible to take part in the trial.

The questionnaire is made up of 25 items that make up 5 subscales (5 items per subscale). The subscales include conduct problems, hyperactivity-inattention, emotional symptoms, peer problems and pro-social behaviour. Each question asks about a specific behaviour and is rated as 0 = Not True,1 = Somewhat True or 2 = Certainly True (items 1,4,9,17 and 20 make up the pro-social behaviour score, which is reverse scored). The combined scores of the subscales (not including the pro-social behaviour subscale), can be combined to generate an overall difficulties score which can range from 0-40. Higher scores in the overall difficulties scale indicate increased difficulties. The scoring for the pro-social behaviour scores are reversed, and range of scores between 0-10. The lower

scores on this subscale indicate increased difficulties. The SDQ will be completed by one or two parents/caregivers depending on their participation in the trial, in addition to a nursery teacher or carer who knows the child well. Almost all of the children will be in some form of non-parental care or schooling by the age of 3-5 years (the age at final follow-up) and previous response rates in studies from nursery and preschool teachers have been excellent (97% in the FCCC study15). This will provide an independent report of the child's behaviour, in addition to the semi-structured interview and questionnaire measures completed by parents.

11.8.4. RDAS

The Revised Dyadic Adjustment Scale (RDAS) is a reliable and valid measure of relationship adjustment. This 14 item scale consists of three subscales: dyadic consensus, dyadic satisfaction and dyadic cohesion. A total DAS score is obtained by summing all items of the questionnaire. Scores range from 0 to 69, where higher scores indicate greater relationship satisfaction, and lower scores greater relationship distress. The RDAS will be completed by one or two parents/caregivers depending on their participation in the trial and relationship status.

11.8.5. Patient Health Questionnaire 9

The Patient Health Questionnaire 9 is a widely used and reliable measure of depression severity. The measure is made up of nine statements, each corresponding to one of the 9 DSM-IV criteria for depression. Each statement is scored on the frequency the responder has experienced each problem over the past two weeks. Scores range from Not at all = 0, Several days = 1, More than half the days = 2 or Nearly every day = 3, and a total score is obtained by summing all items of the questionnaire. Scores range from 0-27, with higher scores indicating more severe depression. The PHQ-9 will be completed by one or two parents/caregivers depending on their participation in the trial.

11.8.6. Parenting Scale

The Parenting Scale is a reliable and valid measure of dysfunctional discipline practices in parents. This will be assessed on each parent separately (when both parents are available). The Parenting Scale will be completed by one or two parents/caregivers depending on their participation in the trial.

11.8.7. CA-SUS

A modified version of the Child and Adolescent Service Use Schedule (CA-SUS) will be used in the trial. The CA-SUS has been developed and successfully employed in previous evaluations with young people (e.g. 48-49), including pre-school children (50). Where two parents/caregivers are participating in the trial the PPACS will be completed by the parent who identifies as being the primary caregiver.

11.8.8. GAD-7

A seven item anxiety disorder questionnaire that has been extensively used in research as a general measure of anxiety in adults.The GAD-7 will be completed by one or two parents/caregivers depending on their participation in the trial.

11.8.9. AUDIT-C

The Alcohol Use Disorders Identification Test - Consumption (AUDIT-C) is an abbreviated version of the original AUDIT (a 10-item screening questionnaire used to detect and identify signs of hazardous, harmful, or dependent drinking). The AUDIT-C, consisting of questions 1-3 of the AUDIT, solely encompassing the consumption items, and as such will be used to obtain information regarding parents' alcohol consumption. Individual question scores range from 0-4, making the overall possible score total range from 0-12. An overall score of 5 or above on the AUDIT-C indicates increasing or higher risk drinking.

11.8.10. Parental sensitivity

Parental sensitivity will be rated based on video recorded parent-child interactions, using a standardised rating scale, by raters blinded to group allocation.

11.8.11. Feedback questionnaire

A brief feedback questionnaire will be given to parents at the 4-month follow-up visit. This is closely based on those previously used in ViPP studies in the United Kingdom. Questions explore participant satisfaction and experience of the intervention's helpfulness, enjoyableness, relevance, and format.

12. SAFETY REPORTING

12.1. Adverse Event (AE)

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

12.2. Severity of Adverse Events

Severity of AEs will be assessed 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, including play for infants and children

12.3. Causality of Adverse Events

Causality of AEs, i.e. relationship to the trial treatment, will be assessed 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 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 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.

12.4. Serious Adverse Events (SAE)

12.4.1. Definition of SAE

An SAE is defined as any adverse 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
- *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 apply to scheduled admissions that were planned before study inclusion or visits to an accident and emergency department (without admission).

*** "Congenital abnormality or birth defect" will not be applicable for this trial as all participants will be children aged 12 – 36 months.

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.

12.4.2. Reporting of SAEs

Due to the low risk nature of this study, AEs that do not meet the above Seriousness criteria will not be collected during the study.

Rapid reporting of all SAEs occurring during the study must be performed as detailed in SAE reporting instructions. SAEs will be reported via the eCRF within 24 hours of becoming aware of the event. All reported SAEs will be reviewed by the Chief Investigator (or designee) within 2 working days of receiving notification of the SAE report. The SAE review will be recorded on the eCRF.

SAEs will be followed up until they are resolved.

If the investigator becomes aware of safety information that appears to be related to the treatment, involving a participant who participated in the study, even after an individual participant has completed the study, this should be reported to the Sponsor.

12.5 Definition of a Serious Adverse Reaction (SAR)

A SAR is defined as a SAE that is judged to be related to the trial treatment.

12.6 Definition of Unexpected and Related Serious Adverse Events

A Related and Unexpected Serious Adverse Events 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 'expected SAE' in this protocol.

12.6.1 Reporting of Related and Unexpected Serious Adverse Events

All Related and Unexpected Serious Adverse Events will be notified to the Research Ethics Committee (REC) and the Sponsor within 15 days of becoming aware of the event.

Follow up of participants who have experienced a Related and Unexpected Serious Adverse Event should continue until recovery is complete or the condition has stabilised.

12.7 Annual reporting of SAEs

Annual safety reporting will be included in the annual progress report sent to the REC, on the anniversary of Ethics approval each year.

13. STATISTICAL ANALYSES

13.1. Sample Size and power considerations

The total sample size will be 300 participants.

If losses to follow-up are 20%, this leaves 120 participants per group with follow-up data. We would then have 80% and 90% power to detect standardised effect sizes of 0.36 and 0.42 respectively, at the 5% significance level. In addition, we have stated that our analysis will adjust for baseline behavioural score, research centre and age of child, which will increase power, probably to over 90% for the 0.36 effect size (since such adjustment will reduce the residual error variance in our model). (Kahan and colleagues (2014) found that covariate adjustment for 1 to 4 variables in trials increased power from 80% to a median of 93% power in their sample of 12 outcomes assessed across 8 studies.)

We have conservatively allowed for a potential drop-out rate of 20% because of the longer follow-up time in the proposed study, even though previous intervention studies detailed below have maintained retention rates of over 90% at follow-up.

The pooled effect size for all randomised controlled trials to date that have used the same video feedback intervention (ViPP) is 0.46 (Bakermans-Kranenburg, 2013, personal correspondence). Other relevant literature for interventions for behavioural problems, predominantly in slightly older children, yield higher effect size estimates. In the systematic reviews undertaken for the most recent NICE guidance on conduct disorders in children and young people (5), the pooled effects for parent-focussed interventions yielded estimated effect sizes of 0.69 standard deviations for researcher-rated outcome (the main outcome measure in the proposed study), and 0.54 for parent-rated outcome. In a study of the Incredible Years programme in 2-9 year olds (6) effect sizes ranged from 0.48-0.78. In

the SPOKES trial (7) of intervention for parents of 6 year olds, the effect size for behavioural outcomes was 0.52 SD difference between the treatment and control group. Where parenting programmes have been rolled out across the UK (8-9) similar effect sizes have been found, albeit in non-randomised designs (effect sizes ranged from 0.44-0.71).

13.2. Data Analysis

The primary analysis will be by intention to treat (ITT). Histograms and box-plots will be used to assess the distributional assumptions and to check for possible outliers. Log transformations will be applied, where appropriate, in order to render the outcomes distributions closer to the Normal. Bootstrap techniques will be used if this does not achieve reasonable normality, to the extent that this may influence the properties of the regression analysis. The relationship between the outcomes and other variables will be explored graphically, using scatter plots and box-plots. Continuous variables that follow an approximately Normal distribution will be summarised using the mean and standard deviations. Skewed variables will be summarised using the median and inter-quartile range. Categorical variables (binary and ordinal and multinomial) will be presented in terms of frequencies and percentages.

Before starting the data analysis, the level, pattern and likely causes of the missingness in the baseline variables and outcomes will be investigated by forming appropriate tables. This information will be used to determine whether the level and type of missing data has the potential to introduce bias into the analysis results or reduce substantially the precision of estimates for the proposed statistical methods. The primary outcome, externalizing behaviour (Pre-PACS), will be analysed at follow-up using linear regression analysis (after checking regression assumptions), adjusting for treatment centre, parental willingness to participate (one or two parents), for infant's baseline behaviour and for infant's age at randomisation. Sensitivity analyses will be undertaken, based on assuming that missing outcomes are the worst possible, or the best possible, in different randomisation groups. If these show that conclusions may differ based on missing values, then supplementary multiple imputation for missing values will be undertaken. These analyses will account for results of any losses to follow-up insofar as they pertain to differences in measured variables (i.e. under the assumption of missing at random). This will enable us to effectively incorporate information gleaned from earlier follow-up times when the final follow-up outcome is absent. This will be done by incorporating outcomes at earlier time points into the predictive model for the multiple imputation of the outcome at 2 year follow-up. Secondary outcome variables will be analysed similarly.

Categorical outcome variables will be presented by treatment group, and compared using logistic/ ordered logistic regression adjusted as per linear regression above.

A detailed statistical analysis plan will be prepared and signed off prior to any interim analyses.

13.3. Economic analysis

13.3.1. Short-term cost-effectiveness

Short-term assessment of cost-effectiveness will take the NHS/Personal Social Services perspective preferred by NICE (23), and will include all hospital and community based health and social services provided for the child over the course of the trial. Data will be recorded in interview with parents at baseline, end of intervention and follow-up

assessments using a modified version of the Child and Adolescent Service Use Schedule (CA-SUS), developed and successfully employed in previous evaluations with young people (e.g. 48-49), including pre-school children (50). Data on intervention contacts and other resources will be collected directly from health visitor records and indirect time (time spent on preparation, supervision, administration, travel etc) will be estimated using questionnaires completed by each health visitor delivering the intervention. National unit costs will be applied to all services (51-52), with the exception of the ViPP intervention, which will be costed using a micro-costing approach (53).

Two short-term economic evaluations will be undertaken:

i) cost-effectiveness analysis using the primary outcome measure of the trial (Pre-PACS)
ii) cost-consequences analysis, outlining the costs alongside all secondary outcome measures in order to explore potential economic impacts of the intervention more broadly. No method of direct estimation of health-related quality of life, and thus quality adjusted life years (QALYs), currently exists for infants and pre-school children, so it is not possible to undertake a cost-utility analysis at this stage. However, the feasibility of using modelling to explore longer-term cost-utility will be explored, as described below.

For the cost-effectiveness analysis, incremental cost-effectiveness ratios will be reported and uncertainty explored using cost-effectiveness acceptability curves (54-56).

13.3.2. Long-term cost-effectiveness

The economic implications of behavioural problems are long-term in nature, with childhood behaviour problems being linked to later delinquency and criminality and affecting future mental health status and education and employment outcomes (57-58). Longer term outcomes will be explored using decision analytic modelling, following methods applied in similar research (59).

Data from the trial will be supplemented with data from a systematic literature review, which takes a broader perspective, additionally including education and criminal justice sector resources, the cost of criminal activity and productivity losses. In terms of outcomes, where data allow, effectiveness estimates in the trial will be linked to estimates of health-related quality of life scores, to support a cost-utility analysis. The Strengths and Difficulties Questionnaire (SDQ) (21) will be used for this purpose, as there are known datasets containing SDQ and utility scores (e.g. 22). The SDQ, completed by parents, is suitable for children aged 3 years and upwards, the age of the proposed population at final follow-up. However, the systematic review may highlight alternative outcomes that can be mapped onto utility scores, so this will be finalised during the course of the study.

Decision analysis will be used to model data from the proposed trial plus existing data on costs, outcomes and probabilities from published studies (24, 60). The most suitable modelling framework in which to carry out the analysis will be selected, dependent upon the results of the proposed study. In cases where individuals can be regarded as independent and interaction between them is not an issue in terms of the course or progression of an illness, as is the case in the current population, either a decision tree or a Markov model is appropriate (61). Decision trees are limited by their fairly simplistic representation of reality and they can often become unwieldy as attempts are made to make them sufficiently complex to model real-world scenarios. A Markov model may

provide a useful alternative since they are better able to deal with more complicated structures and are often used when costs and outcomes need to be considered over longer periods of time. The final choice between these two frameworks will be informed by the findings of the naturalistic study.

The cost-effectiveness of the ViPP versus control groups will be analysed using incremental analysis and probabilistic sensitivity analysis. It is necessary for models to build in uncertainty estimates for the probability, cost and outcome parameters used. In this model it is likely that variability, heterogeneity and uncertainty will be important and will therefore need to be incorporated. Because many of the model parameters will be based on real data from the proposed RCT study, it will be possible to use regression models and appropriate assumptions regarding the statistical distribution of the data to handle the uncertainty (24). The model will initially be run over two years, in line with the data to be collected in the trial. However, secondary analysis will explore longer time periods, dependent on data availability.

14. PATIENT AND PUBLIC INVOLVEMENT (PPI)

The views of parents of young children with behavioural problems have been considered during the development of this protocol. Parents will play a significant role in helping to conduct the study, monitor study progress and disseminate study findings.

In previous trials of the ViPP-SD intervention, parents fed back that it would be useful to have support earlier on in their children's lives, before behavioural problems become established. Repeated feedback from mothers has also suggested that they are keen for their partners to be involved in interventions and that fathers appreciate involvement. Two participants from the previous pilot studies will provide ongoing input into the trial.

Feedback from participants and service users has influenced the protocol in the following ways:

i) Plan to take pragmatic approach to the delivery of the intervention, focusing on ensuring engagement with the primary caregiver, but also actively trying to involve both parents/carers if possible;
ii) assessment and therapy sessions will be held in participants' homes and will be flexibly timed, offering evening and weekend sessions where necessary;
iii) the intervention format is more flexible so that sessions can be held with an individual parent or with parents/carers together.

A Parent Advisory Group (PAG) will be set-up to oversee study progress throughout the duration of the trial. There will also be two service users on the Trial Steering Committee. Members of the PAG will be asked to comment on participant information before the start of the study and will also be sent a draft version of the full study report, summary reports of the study findings for participants, and all other aspects of the dissemination strategy.

15. REGULATORY, ETHICAL AND LEGAL ISSUES

The study will be conducted in accordance with the Declaration of Helsinki, the Data Protection Act and the guidelines laid down by the International Conference on Harmonisation for Good Clinical Practice (ICH GCP E6 guidelines).

15.1. Research Ethics Committee (REC) Approval

Approval from a multi-centre Research Ethics Committee (REC) will be obtained prior to the start of the trial. REC approval will include the trial protocol, parent 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.

15.2. Approval of Amendments

Any amendments to the protocol and information provided to participants will be submitted to the Sponsor and the 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.

15.3. Addition onto trial register

The trial protocol will be registered on clinicaltrials.gov in accordance with the International Committee of Medical Journal editors (ICMJE) requirements. Any protocol amendments will also be registered there.

15.4. Annual Progress Reports

A progress report will be submitted to the REC on an annual basis, on the anniversary of REC approval. The progress report will also include details of safety information.

15.5. End of Trial Notification

A notification of the end of the trial will be submitted to the REC within 90 days of the final follow-up visit taking place

15.6. NHS Health Research Authority Study Approval

Approval for the study to be conducted within NHS sites will be obtained from the NHS Health Research Authority.

15.7. Informed Consent

All adult research participants (parents of the children in the study) will sign and date an Informed Consent Form (ICF) before any trial specific procedures are performed. Participants will be asked to provide written consent twice: written**/**electronic consent to complete the screening questionnaire and, if eligible, written consent to participate in the full study.

Health visitors will recruit families to take part in the study at the routine 12 and 24-month health reviews. Clinicians in other settings will recruit families when they are referred for support. Members of the research team and clinical research network support staff will also support recruit families on site in health visiting services.

Potential participants will be initially approached to complete a screening questionnaire. This screening questionnaire will be presented to participants as a pack, together with an

information sheet and consent form regarding taking part in the screening stage of the recruitment. The screening questionnaire pack will either be sent to participants as an enclosure in a standard letter being sent regarding the service (e.g. an invitation to attend a 12 or 24 month health review), a separate mailshot if preferred by the service, or handed to potential participants when they attend the service.

Those participants that received the screening questionnaire in the post will be invited (via written information in the pack) to return it to their healthcare profession at their subsequent appointment. The written information will also explain that they will have ample time to discuss any questions they have about the screening stage of the study at their next appointment, and withdraw their consent at any time. It will be made clear to participants that they are providing consent to complete the screening questionnaire only, and not the full study.

Those participants that are given the screening questionnaire pack in person when they attend the service, and then go on to consent to take part in the screening, will have the opportunity to complete the SDQ and consent form whilst at the service, or they will be asked to complete both the questionnaire and consent form to return by post, in person when next using the service, or electronically using the link provided in the information sheet.

Those parents that see recruitment information or have been signposted to the study (e.g. via posters and leaflets displayed in health settings, or on internet advertisements) and therefore make contact directly with the research team will be provided with the same screening information pack to complete and return, if they so wish. Members of the research team or clinical research network support staff will also visit community centres such as children's centres and one o'clock clubs (e.g., during play, activity, information, and training sessions), with permission from management, to disseminate screening packs to families and where appropriate support families in completing the screening questionnaire, in line with the procedures outlined above.

The researcher involved in consenting participants to the study will encourage them to spend as much time as they want asking questions about the study and considering whether they want to take part. In all instances potential participants will have at least 24 hours before deciding whether they wish to take part in the study.

Following screening, participants who score in the top 20% of population norms will be contacted by a member of the research team to see if they would like to participate in the full study. If verbal consent is given, a date will be arranged for one or two members of the research team to visit them at home to complete the first assessment visit. Written consent to the trial will be taken at the initial assessment home visit with families. Participants will already have received study information by post or email and will have had the opportunity to ask the study team questions over the phone. At the visit a trained research assistant will take the participants through each of the clauses on the consent form and participants will record their written consent. A copy of the information sheet and ICF will be given to the parents for their records and a further copy stored in the participant file.

Study participants will be asked to give up their time to take part in study assessments and to complete study questionnaires. Baseline assessment takes approximately 90 minutes, with a shorter period for the follow up assessments. All participants will be offered an honorarium following the assessments.

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

15.8. Contact with General Practitioner and Health visitor

It is the investigator's responsibility to inform the child's General Practitioner and Health Visitor by letter that the child is taking part in the study provided the child's parent agrees to this, and information to this effect is included in the Participant Information Sheet and Informed Consent Form. A copy of the letters should be filed in the Investigator Site File.

15.9. Patient Confidentiality

The investigator must ensure that the participant's privacy is maintained. On the eCRF or other documents submitted to the Sponsors, participants will be identified by a trial 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 audiovisual recordings made by the research team will be immediately uploaded after each session via a secure digital platform that will be supported by the Sponsor, Imperial College London. These audiovisual recordings will be backed up on an external hard drive that will be password protected and accessible only to specific members of the research team. The audiovisual recordings will be stored anonymously according to each family's 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.

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 and the REC.

16. END OF TRIAL

The end of the trial will occur when the final participant recruited has completed the 24-month follow-up visit.

17. ADMINISTRATIVE MATTERS

17.1. Source Data

Trial therapist and Research assistant records including paper questionnaires and measures completed during study assessments.

17.2. Language

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

17.3. Data collection and management

Data will be collected on an electronic Case Report Form (eCRF) developed using the InForm system. The eCRF will include the randomisation system and database. This will

be a web-based eCRF comprising a full GCP-compliant audit trail, stored on a secure server. 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. Instructions for completion of the eCRF will be provided in a separate eCRF manual.

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, accessible only to key research team members.

17.4. Study Documentation and Data Storage

The investigator will retain essential documents until notified by the Sponsor, and at least for ten years after study completion, in accordance with Sponsor requirements. Participant files and other source data (including copies of protocols, questionnaires, 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 the 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 will be obtained from the Sponsor.

All audiovisual recordings made by the research team will be immediately uploaded after each session via a secure digital platform that will be supported by the Sponsor, Imperial College London. These audiovisual recordings will be backed up on an external hard drive that will be password protected and accessible only to specific members of the research team. The audiovisual recordings will be stored anonymously according to each family's 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.

17.5. Study Management Structure

17.6. Trial Steering Committee (TSC)

A Trial Steering Committee (TSC) will be established to oversee the conduct of the study. TSC will comprise the lead investigators, an independent chair, additional independent members and two user representatives. The TSC will meet prior to the start of the study and every six months during recruitment and annually during follow-up, or as required throughout the duration of the trial. Reports from each meeting will be submitted to the trial funder.

17.7. Data Monitoring and Ethics Committee (DMEC)

An independent Data Monitoring and Ethics Committee (DMEC) will be established to oversee safety of the trial. The DMEC will review SAE reports and key data as required. The DMEC will develop, in agreement with the investigators and TSC, a charter outlining their responsibilities, planned interim analyses and operational details. The DMEC will meet prior to the start of the trial to agree the charter.

17.8. Project Management Group (PMG)

The Project Management group will be responsible for overseeing management of the study and operational issues. The PMG will meet every 2 months during the set-up phase of the trial and every 6 months thereafter. Membership will include the Chief Investigator, key investigators, the Trial Manager and Trial Statistician.

17.9. Patient Advisory Group (PAG)

At establishment of the study we will set up a Parent Advisory Group of service users drawn from clinical services in London, including two previous research participants who will also serve on the Trial Steering Group. The Parent Advisory Group will help us develop material for publicising the study and design the Patient Information Sheet that we would use. The clinical service in Westminster, where the Chief Investigator is a consultant, already has well established parent advisory groups for a range of different advisory functions.

17.10. Target organisations

NHS services for young children and linked children's centres in the UK.

17.11. Monitoring

The study will be monitored periodically by the Trial Manager or Trial Monitor to assess the progress of the study, verify adherence to the protocol, ICTU SOPs, 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.

Therapists will report on fidelity in terms of the delivery of key components of the treatment as well as reporting on global adherence to the manual. Compliance will be assessed by the clinical supervisor in supervisory sessions. In addition, a random proportion of the audio recordings will be assessed by an independent assessor who is trained in the intervention.

17.12. Quality Control and Quality Assurance

Quality Control and Quality Assurance will be performed according to ICTU procedures. The ICTU QA Manager will conduct a risk assessment prior to the start of the study to assign a risk category to the trial. The monitoring plan will be developed in accordance with the outcome of the Risk Assessment. The study may be audited by a Quality Assurance representative of the Sponsor or ICTU. All necessary data and documents will be made available for inspection.

17.13. Publication policy

The results from the trial will be submitted for publication in a peer-reviewed journal irrespective of the outcome. The Trial Steering Committee will be responsible for approval

of the main manuscript prior to submission for publication. At the end of the study, children's parents will be able to request a copy of the results of the study from the investigator at that site.

Authorship of presentations and reports related to the study will be in the name of the collaborative group. The final follow-up study results paper will name local co-ordinators as well as those involved in central co-ordination and trial management.

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SIGNATURE PAGE 1 (Chief Investigator)

The signature below constitutes approval of this protocol by the signatory 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: Preventing enduring behavioural problems in young children through early psychological intervention: Healthy Start, Happy Start

Protocol Number: Protocol number

Signed: _____

Dr Paul Ramchandani

Date: _____

SIGNATURE PAGE 2 (SPONSOR)

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

Study Title: Preventing enduring behavioural problems in young children through early psychological intervention: Healthy Start, Happy Start

Protocol Number: Protocol number

Signed: _____

Name of Sponsor's Representative
Title
Sponsor name

Date: _____

SIGNATURE PAGE 3 (STATISTICIAN)

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

Study Title: Preventing enduring behavioural problems in young children through early psychological intervention: Healthy Start, Happy Start

Protocol Number: Protocol number

Signed: _____

Name of Statistician
Title
Organisation/Company

Date: _____

SIGNATURE PAGE 4 (PARTICIPATING INSTITUTIONAL APPROVAL)

The signature below constitutes approval 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: Study title

Protocol Number: Protocol number

Address of Institution: _____

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Signed: _____

Print Name and Title: _____

Date: _____

SIGNATURE PAGE 5 (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: Preventing enduring behavioural problems in young children through early psychological intervention: Healthy Start, Happy Start

Protocol Number: Protocol number

Address of Institution: _____

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Signed: _____

Print Name and Title: _____

Date: _____