Treatment of Child Anxiety Disorder in the Context of Maternal Anxiety: A Randomised Controlled Trial

Trial Acronym: MACh (i.e. mother and child anxiety treatment study)

RATIONALE: The outcome from CBT for children with anxiety disorders is highly variable. A major factor contributing to this is likely to be the presence of maternal anxiety and the associated disturbances in mother-child interactions and maternal behaviours. Where parental anxiety has been addressed in treatment research it has been difficult to assess its contribution to child outcome. Similarly, where therapeutic measures to address parent-child interactions have been included, it has not been possible to determine the specific role of such measures in the treatment package employed.

The trial is a three-arm RCT which aims to determine the extent to which treatments of maternal anxiety and mother-child interactions enhance standard cognitive behaviour therapy for children (CCBT) who have anxiety disorders in the context of maternal anxiety disorder (a group who currently show a poor response to treatment). Index children will receive CCBT with either additional treatment for maternal anxiety or specific measures to address features of mother-child interactions; and their outcome will be compared to that of children receiving standard individual CCBT (together with appropriate control conditions)

A. Background

Childhood Anxiety Disorders

Anxiety disorders are the most common form of psychopathology in children. They have a significant adverse impact on children's general socio-emotional functioning and commonly persist into adulthood.

Treatments of childhood anxiety disorders

Following advances in the development of successful cognitive behavioural therapies (CBT) for adult anxiety disorders (e.g. Clark & Fairburn, 1996), CBT for child anxiety disorders has now been developed. Although there is still some uncertainty over the optimal form of such intervention, recent systematic reviews of outcome research indicate that the general CBT approach produces significant therapeutic benefit in this patient group. However, it is clear from these reviews, and from the individual treatment trials, that outcome is highly variable,

with a significant proportion of patients retaining their anxiety diagnoses following treatment (i.e. 16-61%; James, Soler & Wetherall, 2006).

Predictors of Treatment Outcome

There has been little research into the factors that predict response to CBT in anxious children, although, in addition to severity of child anxiety, two factors are likely to be especially significant: anxiety in the mother, and features of mother-child interactions.

i. Anxiety in mothers.

It has been known for some time that the rate of anxiety disorder amongst the parents of anxious children is raised (Last et al, 1987; Last et al, 1991), but the extent of this elevation has been uncertain and the implications for treatment outcome of child anxiety have not been fully considered. Recent research of our own has addressed this issue. In a consecutive series of children referred for treatment of an anxiety disorder, two thirds of the mothers were found to have a current DSM-IV anxiety disorder (with no elevated rate of current disorder amongst the fathers), almost three times the base rate (Cooper et al, 2006). Furthermore, follow up of the children after treatment revealed a significant association between child response and level of maternal anxiety (Cooper et al, in press).

ii. Mother-child interactions

Specific features of mother-child interactions have been implicated in the maintenance of child anxiety, in particular, an over-controlling and over-protective maternal style (see Rapee, 1997; Wood et al, 2003) and associated maternal cognitions and expectations about child competence (Creswell et al, 2006). Notably, strong associations have been found between level of maternal anxiety and both maternal behaviours (e.g. Whaley et al, 1999; Bogels & van Melick, 2004) and maternal expectations of child competence (Wheatcroft & Creswell, 2007). It appears that the disturbances in mother-child interactions which serve to maintain child anxiety are, at least in part, themselves driven by maternal anxiety. These conclusions are supported by the findings of further research by our group. We have been conducting a prospective study of 250 infants born to mothers with anxiety disorders and control mothers to investigate the intergenerational transmission of anxiety disorders. Recent data from both this study (Murray et al, 2007), and from an associated experimental study (DeRosnay et al, 2006), have shown that a lack of both appropriate modelling and support, both features of mothers with anxiety disorders, are associated with the development of anxiety in offspring.

Implications for optimal treatment outcomes

In so far as CBT treatments of child anxiety disorder commonly require the day-to-day prosecution of treatment regimes to be managed by the mother (e.g. mothers are typically required to model positive responses to fear provoking stimuli and to prompt and reinforce their child's positive responses), the mother's own anxiety and the associated disturbances in mother-child interactions are likely to militate against optimal treatment delivery. Although the CBT treatments developed to date for the treatment of child anxiety do acknowledge the importance of both parental anxiety and parenting (e.g. Barrett et al, 1996; Mendlowitz et al, 1999; Nauta et al, 2003; Spence et al, 2000), there has been no systematic evaluation of an intervention in which both maternal anxiety and mother-child interactions are specifically addressed. There is, therefore, a need for the development and evaluation of a CBT treatment for child anxiety disorder in which maternal anxiety and associated disturbances in mother-child interactions are systematically targeted.

Rationale for the trial

The outcome from CBT for children with anxiety disorders is highly variable. Major factors contributing to this are likely to be the presence of maternal anxiety and associated disturbances in mother-child interactions and maternal behaviours. Where parental anxiety has been addressed in treatment research (e.g. Barrett et al, 1996; Mendlowitz et al, 1999; Nauta et al, 2003; Spence et al, 2000), for several methodological reasons, it has been difficult to assess its contribution to child outcome. It is notable, however, that in the single study in which treatment of parental anxiety was systematically varied, child anxiety outcome was better where therapeutic measures to address parental anxiety symptoms were included (Cobham et al, 1998). Whilst this is a finding of critical importance, since the treatment did not significantly alter levels of parental anxiety it remains unclear what aspect of the treatment effected the clinical improvement in the children. Similarly, where therapeutic measures to address parent-child interactions have been included (e.g. Wood et al, 2006), it has not been possible to determine the specific role of such measures in the complex treatment package employed. A controlled trial in which both factors – treatment of maternal anxiety and measures to address mother-child interactions - are systematically varied, would produce data of both clinical utility and scientific importance.

Research Questions

In an RCT for child anxiety occurring in the context of maternal anxiety, the principal questions are:

1. Is the impact of child CBT (CCBT) enhanced by first providing CBT to the mother for her own anxiety?
2. Is the impact of CCBT enhanced by the addition of therapeutic measures designed to improve mother-child interactions?

Secondary questions are:

a. Is sustained improvement in child anxiety significantly associated with a reduction in maternal anxiety?

b. Is sustained improvement in child anxiety significantly associated with improvements in maternal modelling, encouragement, over-controlling/over-protective behaviour, and associated cognitions?

B. Summary

The aim of the trial is to establish the relative effectiveness of treatments of (i) maternal anxiety and (ii) key features of mother-child interactions for children with anxiety disorders who have a mother with current anxiety disorder. All treatments will be in addition to individual Cognitive Behaviour Therapy administered to all children.

Patients who consent to join the trial (participants) will be randomised to one of three conditions: (i) Child Cognitive Behaviour Therapy (CCBT) plus Cognitive Behaviour Therapy for Maternal Anxiety (MCBT); (ii) CCBT plus treatment targeting the Mother-Child Interaction (MCI), (iii) CCBT plus control conditions (see below).

Condition	**CCBT+MCBT**	**CCBT+MCI**	**CCBT**
Standard child treatment	CCBT (child: 8 sessions)	CCBT (child: 8 sessions)	CCBT (child: 8 sessions)
Treatment of maternal anxiety	MCBT (mother: 8 sessions)	Counselling control (mother: 2 sessions)	Counselling control (mother: 8 sessions)
Treatment of mother-child interactions	Family Health Control (child and mother: 2 sessions; mother: 2 sessions)	MCI (child and mother: 2 sessions; mother: 8 sessions)	Family Health Control (child and mother: 2 sessions; mother: 2 sessions)
Total therapist	Child: 8 sessions	Child: 8 sessions	Child: 8 sessions

contact	Mother: 10 sessions Child and mother: 2 sessions	Mother: 10 sessions Child and mother: 2 sessions	Mother: 10 sessions Child and mother: 2 sessions

CCBT: Individual CBT for child anxiety; MCBT: Individual CBT for maternal anxiety; MCI: Mother-child interaction treatment

C. Eligibility

The trial is open to children with a current primary diagnosis of a major anxiety disorder (Generalised Anxiety Disorder, Social Phobia, Separation Anxiety Disorder, Panic Disorder/Agoraphobia, Specific Phobia, as long as co-morbid with another anxiety disorder) whose mother also has a current major anxiety disorder.

1. Inclusion Criteria

Child:

(i) Aged 7 to 12 years;

(ii) Primary diagnosis of DSM-IV generalised anxiety disorder, social phobia, separation anxiety disorder, panic disorder/agoraphobia or specific phobia (if co-morbid with another anxiety disorder).

Mother:

(i) Primary carer;

(ii) Current maternal DSM-IV anxiety disorder.

2. Exclusion Criteria

Participants will not be eligible if the following criteria are met.

Child:

(i) Significant physical[1] or intellectual impairment (including ASD)[2];

(ii) Current prescription of psychotropic medication (or, if psychotropic medication is prescribed, it should have been at a stable dose for at least one month with agreement to maintain that dose throughout the study);

[1] Where physical disability would impede treatment delivery (e.g. significant speech/ hearing impairment).

[2] Significant intellectual impairment will be determined by children being registered within local learning disability services. Children will be excluded if they have a current diagnosis of an Autistic Spectrum Disorder (ASD). In case of undiagnosed ASD, a preliminary assessment will be made at the initial assessment (see Section S).

(iii) Previously received six or more sessions of systematically administered Cognitive-Behaviour Therapy for an anxiety disorder;

Mother:

(i) Significant intellectual impairment[3];

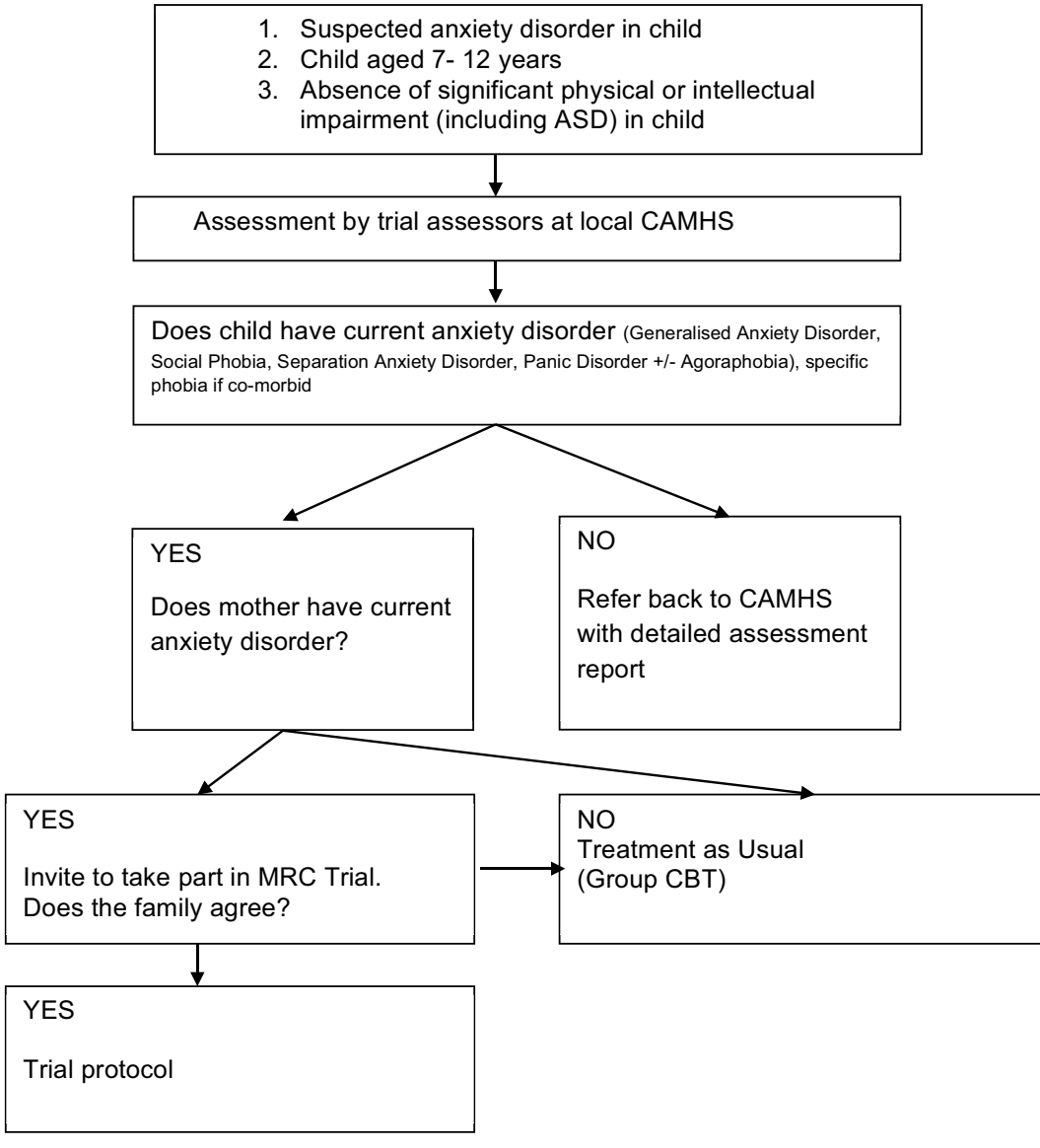
(ii) Severe comorbid disorder (e.g. severe major depressive disorder, psychosis, substance/alcohol dependence);

(ii) Prescription of psychotropic medication (Or, if psychotropic medication is prescribed, it should have been at a stable dose for at least one month with agreement to maintain that dose throughout the study);

[3] Significant intellectual impairment will be determined by the mother being registered within local learning disability services.

D. Trial Procedures

1. ***Recruitment schedule***



2. Treatment Interventions

There will be two stages of treatment intervention in the trial:

(1) Individual Cognitive Behavioural Treatment for maternal anxiety (MCBT), or control

a. Individual CBT for maternal anxiety

This will consist of an eight session (one hour each) intervention for mothers delivered by a clinical psychologist (or equivalent) over eight-weeks. Sessions will take place in the participants' local CAMHS, within their home, or at the University of Reading. The CBT programme will follow a manualised transdiagnostic treatment for adult anxiety disorders (Shafran, unpublished manuscript).

b. Control: Supportive Counselling

This will consist of either two or eight sessions (one hour each) of supportive counselling (see figure 1), delivered by a clinical psychologist (or equivalent) over eight-weeks. Sessions will take place in the participants' local CAMHS, within their home, or at the University of Reading. The supportive counselling programme will follow a manualised treatment (Borkovec & Costello, 1993).

(2) Individual Cognitive Behavioural Treatment for child anxiety (CCBT) with Mother Child Interaction treatment (MCI) or control

Individual CBT for child anxiety

All participating children will receive an eight session (one hour each) intervention based on the Cool Kids programme (Rapee, 2000), delivered by a clinical psychologist (or equivalent) over eight-weeks. Sessions will take place in the participants' local CAMHS, within their home, or at the University of Reading.

a. Mother-Child Interaction Treatment

This intervention consists of 10 sessions: eight with the mother alone and two with the mother and child together. This is a novel intervention which specifically targets anxiogenic features of mother-child interactions. Specifically it aims to enhance maternal cognitions associated with child competence, reduce maternal overcontrol/overprotection, and enhance maternal warmth and encouragement. This is achieved through a combination of specific materials from existing family interventions for childhood anxiety (Rapee & Wignall, 2000; Wood et al, 2006) and video-feedback techniques developed and piloted by the trial investigators (Stein et al, 2006; Creswell et al, in press). This intervention is provided by a clinical psychologist (or equivalent) in parallel with the CCBT sessions. Sessions will generally take place in the participants' local CAMHS, within their home, or at the University of Reading. The two mother and child sessions will be conducted within the laboratory at the

University of Reading, as these involve the mother and child completing structured tasks which are video-recorded for feedback purposes.

b. Control: Family Lifestyle Management

This will consist of four sessions, two with the mother alone and two with the mother and child together. These sessions will focus on promoting a healthy lifestyle with a focus on family diet and exercise, based on existing packages applied within school settings (British Dietetic Association, 2003). This intervention is provided by a clinical psychologist (or equivalent) in parallel with the CCBT sessions. Sessions will generally take place in the participants' local CAMHS, within their home, or at the University of Reading.

For all treatment conditions, therapists will routinely rate the extent to which participants adhere to the intervention (e.g. completion of in-session and homework exercises, session attendance).

How the second stage interventions run in parallel is illustrated in Section R.

E. Randomisation

Following confirmation of eligibility and informed consent, participants will be randomised to treatment condition. Randomisation will be performed centrally by facsimile contact at the Centre for Statistics in Medicine, Oxford (CSM). This will be performed/coordinated by the Trial Statistician. The randomisation programme will include a minimisation algorithm to ensure balanced allocation of participants across the three treatment groups for the following potential prognostic factors: child age, child gender, type of child anxiety disorder (GAD, Social Phobia, SAD, Other) and baseline severity (ADIS Clinician Severity Rating) of child and mother's primary anxiety disorder. To reduce the possibility of outcome measure events occurring after randomisation and before treatment, intervention will start within 2 weeks of randomisation.

F. Routine Care Outside of the Trial

Participants (mothers and children) will be asked not to engage in other psychological interventions during the course of the trial. They will also be asked not to initiate psychotropic medication and if psychotropic medication is prescribed, this should have been at a stable dose for at least one month with agreement to maintain that dose throughout the study. Referrers (Local CAMHS) and General Practitioners will be informed of this requirement.

G. Serious and Unexpected Adverse Events

There are no adverse side-effects of the interventions being delivered. Successful treatment of anxiety may involve some distress, however this will be managed and contained by qualified clinical psychologists, receiving regular expert supervision. Although substantial clinical benefits are anticipated from the interventions, some children and mothers can be expected to not respond to the interventions. Where children continue to meet criteria for a current anxiety disorder at the six month post treatment assessment, they will be invited to participate in a group intervention for anxious children or referred back to their local CAMHS team following clinical review and liaison. If other significant difficulties emerge these will be discussed with referrer from the local CAMHS team.

H. Assessment of Outcome

1. Primary outcomes

The primary outcome is child anxiety (assessed both categorically [i.e. diagnosis] and continuously [i.e. symptoms]). Diagnostic status will be assessed by the ADIS for DSM-IV: C/P administered to both the mother and child. Assessors will be blind to treatment condition. Assessors' beliefs about treatment condition will be formally assessed. Child anxiety symptoms will be assessed using questionnaires (SCAS; Spence, 1998) administered to the child, the mother and the child's teacher. These measures will be administered post-treatment, and at 6 and 12 month follow-up assessments.

2. Secondary outcomes

Maternal anxiety will be assessed categorically using the ADIS (DSM-IV) and continuously using questionnaires (i.e. DASS, Lovibond & Lovibond, 1995; PSWQ, Meyer et al, 1990; SIAS and SPS, Mattick & Clark, 1998). These measures will be administered post-treatment, and at 6 and 12 month follow-up assessments.

Maternal interactive behaviours will be assessed by filming the mother assisting the child perform an anxiety provoking task and applying standardised ratings of anxiogenic behaviours (i.e. modelling, lack of encouragement, overcontrol/overprotection). Interactive behaviours will be coded by independent, trained, reliable raters. Coders will be blind to the purpose and conditions of the trial. Maternal cognitions will be assessed by a standardised interview. These measures will be conducted at the post-treatment assessment.

See Section S for a full assessment schedule.

3. Health Economic Assessment

An economic evaluation will be undertaken integral to the main trial. The evaluation will adhere to guidelines for good economic evaluation practice as outlined in the reference case by Gold et al (1996). The economic analysis will estimate the incremental cost and effectiveness of each of CCBT/MCBT and CCBT/MCI in relation to the control group as well as their relative costs. Patient level resource use data, including all health and social care costs (staff costs for provision of CCBT, MCBT, MCI, and the control interventions, GP costs, referrals, and other relevant services identified) as well as leisure and productivity estimates for the parents will be collected within trial forms and valued using appropriate unit costs. Staff training costs and the costs of staff supervision will also be identified and allocated pro-rata. The outcome measure for the cost-effectiveness analysis will be the ADIS as well as a measure of 'days off school avoided'. In line with recent recommendations from the National Institute for Health and Clinical Excellence (NICE) the economic evaluation will also include generic quality of life instruments, the child friendly EuroQol EQ-5D (EuroQol, 1990; Hennesy & Kind, 2002) and HUI2 outcome measure (Feeny et al, 1995), on which normative data are available. Measures of the impact of anxiety disorders will also be included, using questionnaires administered to the child and mother (CAIS; Langley et al, 2004) and teacher (School Adjustment/ Teacher Report Form; Achenbach, 1986). These instruments will be administered at baseline, following treatment and at 6 and 12 months follow up.

I. Power and Sample Size

A total sample size of 210 pairs of anxious children with anxious mothers will be recruited into the trial. This sample size is based on calculations relating to the primary outcome of child anxiety diagnosis for the principal questions.

i. Efficacy of CCBT/MCBT:

Comparison of Group 1 and the Control Group. To detect an absolute difference of 30% in success (i.e. absence of child anxiety diagnosis) post-treatment for CCBT/MCBT compared with control (40% to 70%), with 90% power at the 5% significance level (two sided) would require 56 patients per treatment group. This difference is based on reported effect of CBT with parental anxiety management in children where at least one parent had high anxiety (Cobham et al, 1998).

ii. Efficacy of CCBT/MCI:

Comparison of Group 2 and the Control Group. Assuming that the response to treatment in the control group is 40% (from Cobham et al, 1998) and the minimum clinical difference in response due to MCI is 30%, 56 patients per group are required to enable us to detect this difference with 90% power at the 5% significance level.

Thus, 56 patients are required in each of the three randomised groups. Accounting for a 20% loss to follow up would require 210 children in total to be recruited to the study. No formal comparison will be made between Groups 1 and 2 (CCBT/MCBT and CCBT/MCI). The sample size has been estimated as if two independent trials were conducted, with no adjustment for multiple testing, as recommended by Machin et al (1997).

A difference of 30% in the proportion of anxiety-free children following completion of the treatment is considered to be the minimum that would be clinically worthwhile taking into account the increased resources required and change to service delivery that would be required if either of these interventions were found to be effective and implemented in practice.

J. Data Management

Data management will be consistent with MRC Guidelines for Good Clinical Practice in Clinical Trials (MRC, 1998) and with the Data Protection Act (1998). Principal investigators will ensure that all personnel are familiar and comply with the MRC guidelines, particularly section 5.9 ‘Data handling and record keeping’ and section 7 ‘Documentation’.

1. Identifying information

After providing consent, participants will be given a unique, sequential, study identifier. This will be used for randomisation and data entry purposes.

2. Data entry

Data will be entered in to desktop computers, fitted with SPSS for Windows v13 as standard allowing for an immediate interactive message to be displayed if an invalid data entry is made. The Trial Manager will arrange appropriate quality assurance checks.

3. Backing up of data

Immediately after every episode of data entry, data will be backed up onto a portable USB drive, which will be securely stored locally. These files will be backed up on to a password-protected system on a weekly basis. A hard copy will be printed and stored locally compliant with Data Protection Act (1998).

K. Data Analysis

The principal comparisons will be performed on an intention-to-treat basis. The results from the trial will be presented as comparative summary statistics (difference in proportion of anxiety-free children or mean anxiety level) with 95% confidence intervals. The analysis and reporting of results will follow the general principles of Consolidated Standards of Reporting Trials (CONSORT; Moher et al, 2001).

The primary analysis will focus on the effect of the intervention following completion of treatment (post-treatment/16 week assessment). Analysis of the 6 and 12 month outcome data will utilize all outcome assessments (post treatment, 6 and 12 months) using multilevel repeated measures analysis, to establish maintenance of change.

Child anxiety diagnosis (ADIS for DSM-IV C/P): The proportion of anxiety-free children in the two groups following treatment will be compared using the Chi squared test. Testing for a treatment effect after adjustment for minimisation factors will be conducted using multiple logistic regression.

Child anxiety symptoms: Change in anxiety scores following treatment will be analysed using multiple linear regression with baseline score and minimisation factors entered as covariates. We will formally assess the distribution of the change in anxiety scores for evidence of departure from normality. If necessary, data will either be transformed or analysed using a non-parametric equivalent. Change in anxiety scores at 6 and 12 months will be analysed using a multilevel repeated measures analysis, adjusted for baseline anxiety score and minimisation covariates.

The secondary research questions will be explored using univariate tests (e.g. Chi squared test, t-test and correlation) to examine whether the particular factors identified are associated with sustained improvement in child anxiety. Multiple logistic and linear regression will be adopted to investigate the independent factors predictive of sustained improvement in child anxiety.

A comprehensive statistical analysis plan will be produced prior to any data being seen.

L. Management Structure

1. Trial Management

The Trial Management Group (TMG) comprises the five grant holders, the clinical director (LW) and the Trial Manager (RG). The group will meet periodically throughout the trial as requested by the Principal applicant (PJC).

The day to day administration of the trial will be the overall responsibility of the principal applicant (PJC) who will monitor all aspects of recruitment, treatment and assessment, as well as the budget.

The child anxiety clinics will be under the direction of the Clinical Director (LW). She will coordinate all clinical referrals, and, together with her assistant, carry out initial clinical assessments of all referred children. Where both child and mother are found to have a current anxiety disorder, the trial manager (RG) will recruit to the trial and, in liaison with the trial statistician (NA), will ensure randomisation to treatment condition and assign to the appropriate therapists. The Trial Manager will also coordinate and supervise the maternal and child assessments. Assessment and coding of the mother-child interactions will be the under the supervision of Professor Lynne Murray.

Professor Roz Shafran (Reading) will train and supervise the adult therapists providing treatment to mothers. The therapists providing the non-directive counseling (control condition) will be supervised by an experienced counseling practitioner and supervisor to ensure adherence to protocol. The Clinical Director (LW) will supervise the two child therapists delivering CCBT to the children and the mother-child interaction treatment as well as the healthy lifestyle sessions (control). Professor Alan Stein will provide supervision to Dr Willetts on the interaction treatment.

The Trial Manager (RG) will have responsibility for the data file which will be handed over to the Trial statistician for analysis. The Trial Manager will also liaise with Dr McIntosh to ensure that all health economic data are collected appropriately.

2. Trial Steering Committee (TSC)

Overall responsibility for the trial will lie with the Trial Steering Committee comprising: Professor Jonathon Hill (Chair), Dr Gavin Malloch (MRC), Dr Natasha Conner and Vicky Taylor (Berkshire Healthcare NHS Foundation Trust), Dr Pasco Fearon (Reading) and a consumer representative. Their function is to maintain the overall integrity of the trial, to receive and consider reports from both the Trial Management Group and IDMEC and take action if appropriate. The Trial Steering Committee will meet before the trial is initiated and then every 6 months throughout the trial.

3. Independent Data Monitoring and Ethics Committee (IDMEC)

The Independent Data Monitoring and Ethics Committee will be chaired by Professor Jonathon Geddes (Oxford). Other members are Dr Craig Ramsay (Aberdeen) and a representative from Berkshire Healthcare NHS Foundation Trust). The Trial statistician will also attend meetings to present reports. The IDMEC will monitor: recruitment to the trial, protocol adherence and serious adverse events as well as the difference between trial treatments on the primary outcome measures. The IDMEC will consider reports prepared by the Trial Statistician and any other relevant studies published during the timeframe of the trial. Recommendations of IDMEC will be passed on to the Chair of the Steering Committee. The Data Monitoring and Ethics Committee will meet throughout the trial as determined by the Chair.

M. Indemnity

University of Reading indemnity will apply:

i. To meet the potential legal liability of the University of Reading for harm to participants arising from the management and design of the research.

ii. To meet the potential legal liability of the investigators/collaborators arising from harm to participants in the conduct of the research.

iii. For payment of compensation in the event of harm to the research participants where no legal liability arises.

N. Ethics

Berkshire Local Research Ethics Committee has given a favourable opinion of this study (07/H0505/156), as has the University of Reading Research Ethics Committee (07/48). All aspects of the study will be conducted in line with MRC Guidelines for Good Clinical Practice in Clinical Trials (MRC, 1998).

O. Informed Consent

Information about the trial will be provided to both the mother and child in person from the Clinical Director (LW) as well as in written information. A copy will be provided for the participants to keep. Written consent will be obtained from parents by the Clinical Director (LW). Assent will be obtained from children. Following treatment completion, participants will be asked whether they would be happy for video-taped material to be used for teaching and training purposes. Where participants agree, separate written consent will be obtained.

P. Publications and Ancillary Studies

1. Publications

A meeting of the Trial Management Group will be held on completion of the study to allow discussion of the main results among the collaborators. The results will then be presented to a combined meeting of the TSC and IDMEC for comment. Public presentations pertaining to the main trial must not be made without the prior agreement of the Trial Management Group.

2. Ancillary studies

Ancillary studies will be conducted by Dr Cathy Creswell (MRC Clinician Scientist Fellowship, Reading), Mr Ray Percy (PhD student, Reading) and Dr Thalia Eley (Institute of Psychiatry, London), in collaboration with Peter Cooper. The protocols for these studies will be referred to the Trial Steering Committee, whose responsibility is to safeguard the integrity of the trial, for final approval. Any further proposals for ancillary studies should initially be referred to the Trial Management group for consideration. Studies considered appropriate by the TMG will then be submitted to the TSC for final approval. In principle it is preferable for the trial to be kept as simple as possible with few further add-on studies.

Q. Proposed Timetable

Main tasks	Proposed timetable
Finalise protocols	May- November 2007
Submit Ethics & Trust approval	August 2007
Register Trial Receipt of MRC award In post: Cathy Creswell (Trial Manager; MRC) Lucy Willetts (Clinic Manager; NHS/MRC)	1 September 2007
Ethics Outcomes	November 2007
Invite referrals from East and West Berks (establish wait-list for assessments)	September- December 2007

Recruit remaining University & Trust staff Establish satellite clinics Convene Trial Steering Committee and IDMEC	
Training University and Trust staff	January – February 2008
Initiation of assessments	January 2008
Initiation of treatment	March 2008
Recruitment ends	30 August 2010
Treatments end	31 January 2011
Trials end	30 June 2012

Recruitment assessments will be conducted from January 2008 until end of August 2010 (32 month), therefore we aim to recruit 6-7 new cases to the trial every month.

R. Stage 2 Treatment (CCBT/MCI/FH) Outline

Week		CCBT (child 8 sessions)	MCI (mother 8; mother& child 2)	FH (mother 2; mother & child 2)
1	Session 1	Introduction- 1. Getting to know each other 2. Psychoeducation	Mother 1. Introduction-psycho-education and rationale.	Mother 1. Introduction-healthy family lifestyle
2	Session 2	1. Update & review 2. How I feel depends	Mother 1. Update & Review	

		on what I think; Detective Thinking	2. Promoting autonomy (i):Self-help skills: giving choices, allowing struggle, attention (ii) Feedback on video from research assessment: highlight parental positive impact on child through autonomy granting, encouragement, modelling, cognitions re child coping)	
3	Session 3	1. Update & review 2. How I feel depends on what I think; Detective Thinking Practice	Mother 1. Update & Review 2. Promoting autonomy (i) Alternative strategies: managing child's anxious thoughts	
4	Session 4A	1. Update & review 2. Rewards	Mother 1. Update & review 2. Promoting autonomy: encouraging brave behaviour; inc CALM strategy (reflective listening, selective attention , planned	Mother & Child Family diet

			ignoring), positive encouragement (verbal and nonverbal), modelling brave behaviours	
4	Session 4B		Mother & Child Video Task: setting up an exposure hierarchy	
5	Session 5	1.Update &review 2. Problem solving	Mother 1. Update & Review 2. Video feedback (to highlight successful autonomy granting). 3. Promoting autonomy: Family problem-solving	
6	Session 6A	1. Update & review 2. Practice	Mother 1. Update and review 2. Promoting autonomy: New roles	Mother & Child Family exercise
6	Session 6B		Mother & Child Challenging task	
7	Session 7	1. Update & review 2. Practice	Mother 1. Update & Review *2.* Video feedback (to highlight successful autonomy granting, modelling, encouragement (verbal/nonverbal), positive cognitions re	

			child coping).	
8	Session 8	1. Update & review 2. You did it	Mother 1. Update & Review 2. You did it- what helped? Future plans/ Relapse Prevention	Mother Healthy family lifestyle Review and summary

S. Assessment Schedule

l clinical assessment Conducted within local CAMH service	Structured clinical interviews: 1. Anxiety Disorders Interview Schedule-Child/Parent version (ADIS-C/P) 2. Anxiety Disorders Interview Schedule (ADIS) (Mother self-report) Questionnaires: 1. Spence Children's Anxiety Scale –parent/child version (SCAS-c/p) 2. Child Anxiety Impact Scale- parent/child version (CAIS-c/p) 3. Depression Anxiety Stress Scales (DASS) 4. Penn State Worry Inventory 5. Mattick Social Phobia Scale and Social Interaction Assessment Scale (SPS, SIAS) 6. Over-involvement questionnaire (POI) parent self-report 7. Social Communication Questionnaire (SCQ) 8.The Short Moods and Feelings Questionnaire-Child/Parent version (SMFQ-C/P) 9.The Strengths and Difficulties Questionnaire - Child/Parent version (SDQ-C/P)

Research assessment 1. (pre-treatment) Conducted at University of Reading	1. Laboratory assessment of mother-child interaction and associated cognitions 2. Spence Children's Anxiety Scale-teacher report (SCAS-T) 3. Teacher Report Form (TRF) 4. Teacher report- child adjustment to school 5. Health economic assessments (EQ-5D, HUI-2, diaries)
Research assessment 1b. (mid-treatment) Conducted at University of Reading/ Local CAMH service	Structured clinical interviews: 1. Anxiety disorders Interview Schedule-Child/Parent version (ADIS-C/P) 2. Anxiety Disorders Interview Schedule (ADIS) (Mother self-report) Questionnaires: 1. Spence Children's Anxiety Scale –parent/child version (SCAS-c/p) 2. Child Anxiety Impact Scale- parent/child version (CAIS-c/p) 3. Depression Anxiety Stress Scales (DASS) 4. Penn State Worry Inventory 5. Mattick (SPS, SIAS) 6. Over-involvement questionnaire (POI) parent self-report 7. The Short Moods and Feelings Questionnaire-Child/Parent version (SMFQ-C/P) 8. The Strengths and Difficulties Questionnaire - Child/Parent version (SDQ-C/P)

	9. Therapy Questionnaire 10. Health economic assessments (EQ-5D, HUI-2, diaries)
Research assessment 2 (post-treatment) Conducted at University of Reading	Structured clinical interviews: 1. Anxiety Disorders Interview Schedule-Child/Parent version (ADIS-C/P) 2. Anxiety Disorders Interview Schedule (ADIS) (Mother self-report) Questionnaires: 1. Spence Children's Anxiety Scale –parent/child version (SCAS-c/p) 2. Child Anxiety Impact Scale- parent/child version (CAIS-c/p) 3. Depression Anxiety Stress Scales (DASS) 4. Penn State Worry Inventory 5. Mattick (SPS, SIAS) 6. Over-involvement questionnaire (POI) parent self-report 7. The Short Moods and Feelings Questionnaire-Child/Parent version (SMFQ-C/P) 8. The Strengths and Difficulties Questionnaire - Child/Parent version (SDQ-C/P)

	9. Health economic assessments (EQ-5D, HUI-2, diaries) Other 1. Laboratory assessment of mother-child interaction and associated cognitions
Research assessment 3 (6 months post-treatment) Conducted at University Of Reading/ Local CAMH service	Structured clinical interviews: 1. Anxiety Disorders Interview Schedule-Child/Parent version (ADIS-C/P) Questionnaires: 1. Spence Children's Anxiety Scale –parent/child version (SCAS-c/p) 2. Child Anxiety Impact Scale- parent/child version (CAIS-c/p) 3. Depression Anxiety Stress Scales (DASS) 4. Penn State Worry Inventory 5. Mattick (SPS, SIAS) 6. Over-involvement questionnaire (POI) parent self-report 7. The Short Moods and Feelings Questionnaire-Child/Parent version (SMFQ-C/P) 8. The Strengths and Difficulties Questionnaire - Child/Parent version (SDQ-C/P) 9. Spence Children's Anxiety Scale-teacher report (SCAS-T) 10. Teacher Report Form (TRF) 11. Teacher report- child adjustment to school

	12. Health economic assessments (EQ-5D, HUI-2, diaries)
Research assessment 4 (12 months post-treatment) Conducted at University Of Reading/ Local CAMH service	Structured clinical interviews: 1. Anxiety disorders Interview Schedule-Child/Parent version (ADIS-C/P) Questionnaires: 1. Spence Children's Anxiety Scale –parent/child version (SCAS-c/p) 2. Child Anxiety Impact Scale- parent/child version (CAIS-c/p) 3. Depression Anxiety Stress Scales (DASS) 4. Penn State Worry Inventory 5. Mattick (SPS, SIAS) 6. Over-involvement questionnaire (POI) parent self-report 7. The Short Moods and Feelings Questionnaire-Child/Parent version (SMFQ-C/P) 8. The Strengths and Difficulties Questionnaire - Child/Parent version (SDQ-C/P) 9. Spence Children's Anxiety Scale-teacher report (SCAS-T) 10. Teacher Report Form (TRF) 11. Teacher report- child adjustment to school 12. Health economic assessments (EQ-5D, HUI-2, diaries)