

# Treatment of childhood anxiety disorder in the context of maternal anxiety disorder: a randomised controlled trial and economic analysis

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**Declared competing interests of authors:** Cathy Creswell was supported by a Medical Research Council Clinician Scientist Fellowship (G0601874).

Published May 2015

DOI: 10.3310/hta19380

## Scientific summary

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Health Technology Assessment 2015; Vol. 19: No. 38

DOI: 10.3310/hta19380

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# Scientific summary

## Background

Anxiety disorders are among the most common psychological disorders in childhood and are associated with adverse outcomes throughout the life course. Psychological treatments [specifically cognitive–behavioural therapy, (CBT)] have established effectiveness; however, one group who have not been found to benefit as much as others are children with anxiety disorders who have a parent who also has an anxiety disorder.

There has been limited consideration of how to improve treatment outcomes for children with anxiety disorders in the context of parental anxiety disorder. Two trials have delivered CBT for the parental disorder alongside CBT for the child; however, in both these cases the parental CBT was brief and did not significantly improve parental anxiety. It remains unclear whether or not successful treatment of parental anxiety would lead to benefits in child anxiety outcomes following CBT.

An alternative explanation for the relatively poor outcomes for children with anxiety disorders in the context of parental anxiety is that particular parenting responses (that are more common among highly anxious parents) may reinforce child anxiety disorder and, thus, militate against good treatment outcomes. Particular parental responses that have been implicated in the maintenance of child anxiety disorders include an overprotective parenting style, expressed anxiety when the child faces a challenge, and negative expectations about the child's competence and coping.

The aim of the trial was to establish the relative clinical effectiveness and cost-effectiveness of treatments of (i) maternal anxiety, and (ii) key parenting responses, for children with anxiety disorders who have a primary-caregiving mother with a current anxiety disorder.

## Objectives

This randomised controlled trial (RCT) for child anxiety disorder occurring in the context of maternal anxiety disorder, set out to address the following principal questions:

1. Is the impact of child cognitive–behavioural therapy (CCBT) enhanced by first providing CBT to the mother for her own anxiety disorder?
2. Is the impact of CCBT enhanced by the addition of therapeutic measures designed to target maternal parenting responses?

In addition the following secondary questions were addressed:

- i. Is sustained improvement in child anxiety significantly associated with a reduction in maternal anxiety?
- ii. Is sustained improvement in child anxiety significantly associated with improvements in maternal modelling, encouragement, overcontrolling/overprotective behaviour and associated cognitions?

## Methods

We carried out a RCT in which we compared CCBT with (i) CBT focused on the maternal anxiety disorder in addition to CCBT, and (ii) an intervention focused on promoting positive maternal responses to the child in addition to CCBT. The randomisation ratio was 1 : 1. The randomisation was carried out with a remote facsimile system and was minimised for child age, gender, primary anxiety disorder diagnosis, and baseline severity of the child and the mother's primary anxiety disorder.

Participants were recruited from referrals to NHS Child and Adolescent Mental Health Services across Berkshire.

The inclusion criteria for children were age (7–12 years) and primary diagnosis of a current anxiety disorder according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* (American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th edn. Washington, DC: American Psychiatric Association; 2000). The inclusion criteria for mothers were that the mother was the primary carer and had a current DSM-IV anxiety disorder. Exclusion criteria for children were significant and intellectual impairment, a current prescription of psychotropic medication that had not been at a stable dose for at least 1 month and without agreement to maintain a stable dose for the duration of the study, and previous receipt of six or more sessions of CBT. Exclusion criteria for mothers were significant intellectual impairment, a severe comorbid disorder (that would interfere with the mothers ability to participate in treatment sessions), or a current prescription of psychotropic medication that had not been at a stable dose for at least 1 month and without agreement to maintain a stable dose for the duration of the study.

The primary outcomes were the number of children who were free of their primary anxiety disorder diagnosis, and the number who were classified as 'much' or 'very much' improved on the Clinical Global Impression – Improvement scale immediately after the treatment phase. Further follow-ups were conducted 6 and 12 months after the end of treatment. Secondary outcomes were the severity of the child's primary diagnosis, the number of children who were free of all their anxiety diagnoses, child- and mother-reported child anxiety symptoms, impact and comorbid symptoms, and teacher-reported anxiety and adjustment at school.

Outcomes for the economic analyses were identified and measured using quality-adjusted life-years (QALYs), estimated on the basis of child reports on the European Quality of Life-5 Dimensions at all assessments from baseline to the 12-month follow-up. Costs associated with each treatment arm were based on patient-level resource use data, collected as an integral part of the trial data collection process on the basis of mother and therapist report.

All children received individual CBT over eight weekly sessions. Mothers randomised to the maternal cognitive-behavioural therapy (MCBT) treatment arm received eight weekly individual CBT sessions focused on their own difficulties with anxiety. Mothers in the other two arms received a non-specific intervention [non-directive counselling (NDC)] to balance for therapist contact. Mothers in the CCBT + mother-child interaction (MCI) arm received 10 therapeutic sessions (over 8 weeks; eight with the mother alone and two with the mother and child) which were designed to target potentially anxiogenic maternal parenting behaviours. Those in the other two treatment arms received a non-specific intervention to balance for therapist contact (family health; FH). All therapists followed written manuals, received regular supervision and audio-recorded treatment sessions so that adherence to treatment protocols could be evaluated.

## Results

A total of 676 potential participants were assessed for eligibility. Of these, 435 participants did not meet eligibility criteria (in the majority of cases because the mother did not have a concurrent anxiety disorder) and 30 eligible families did not give consent to participate. A total of 211 children were randomised, with 84% assessed at the post-treatment assessment, and 72% and 65% at 6- and 12-month follow-up assessments, respectively.

At baseline 69 participants were randomised to the MCBT + CCBT arm, 71 participants to MCI + CCBT and 71 participants to CCBT + non-specific interventions. The three randomised groups were comparable at baseline. Analysis of audio-recordings of treatment sessions showed that there were no significant differences in adherence to the CCBT treatment protocol across the three treatment arms. The content of the targeted and non-specific interventions were significantly different in the case of both MCBT and NDC, and MCI and FH, in both cases indicating that the content of the treatments differed as intended. There was also evidence that both the MCBT and MCI interventions were associated with some change in the variables that they were targeting. Immediately after the MCBT intervention, mothers in the CCBT + MCBT arm were 1.63 times more likely to have recovered from their primary diagnosis and 2.51 times more likely to have recovered from all their anxiety diagnoses compared with mothers in the CCBT arm. However, there were no significant differences on maternal self-report questionnaire scores. Furthermore, by the later assessment points maternal recovery rates improved for all treatment arms and differences between arms were no longer significant. In comparison to those in the CCBT arm, mothers who received CCBT + MCI showed a greater change in observed overprotection and expectations relating to how scared and in control their child would be compared with the CCBT arm. Significant differences were not found on any other measures of parenting response.

The primary analysis indicated that, for the number of children free of their primary diagnosis, although the CCBT + MCBT and CCBT + MCI arms were associated with better outcomes, these were not significantly different from the CCBT arm [CCBT + MCBT risk ratio (RR) 1.21, 95% confidence interval (CI) 0.86 to 1.71,  $p = 0.280$ ; CCBT + MCI vs. CCBT RR 1.24, 95% CI 0.88 to 1.74,  $p = 0.219$ ]. This was also the case for the number 'much' or 'very much' improved (CCBT + MCBT RR 1.24, 95% CI 0.99 to 1.57,  $p = 0.065$ ; CCBT + MCI RR 1.18, 95% CI 0.93 to 1.50,  $p = 0.179$ ). At the 6- and 12-month follow-up assessments CCBT + MCI (but not CCBT + MCBT) continued to be associated with relatively high recovery rates, but neither of the groups differed significantly from CCBT. Significantly more children (92%) in the CCBT + MCI arm, compared with the CCBT arm (73%), showed a reduction in severity of their primary diagnosis 6 months post treatment [ $\chi^2(1) = 6.19$ ;  $p = 0.013$ ]. A similar pattern was found at the 12-month follow-up; however, this was not statistically significant. No significant differences were found on child, mother or teacher between treatment arms at any assessment point.

Analysis of the secondary research questions yielded inconsistent results, both across reporters and assessment time points. There was not a consistent pattern of association between change in maternal anxiety or parenting responses and change in child outcomes, so clear conclusions about mechanisms of change cannot be drawn at this stage.

The economic evaluations suggested that from a health service perspective only, the mean health cost of the CCBT + MCBT arm was on average £233.55 (95% CI –£6.81 to £473.92) higher than the CCBT arm, whereas mean child QALY gain was 0.033 (95% CI –0.101 to 0.035) lower. Similarly, incremental health-care costs in the CCBT + MCI arm were on average £233.16 (95% CI –£6.81 to £473.92) higher than the CCBT arm, with the child QALY gain 0.028 (95% CI –0.030 to 0.086) higher. The cost-effectiveness acceptability curve (CEAC) for the CCBT + MCBT arm suggested that, given the distribution of the incremental cost-effectiveness ratios, CCBT + MCBT is highly unlikely to be cost-effective at current willingness-to-pay thresholds for an extra QALY (£20,000–30,000) with a probability lower than 0.1. The CEAC for the CCBT + MCI arm, however, revealed that the probability that CCBT + MCI is cost-effective in comparison with CCBT alone is around 75%. These results should, however, be interpreted in light of an

important limitation of the data, namely the high percentage of missing values in some of the follow-up resource use and outcome variables. This shortcoming was dealt with using appropriate data imputation techniques; however, imputation cannot account for potentially non-random reasons for missing data.

## Conclusions

### *Implications for health care*

- The novel intervention that focused on modifying maternal parenting responses was associated with some benefit to children and mothers with anxiety disorders, and is likely to be cost-effective. Incorporating effective measures to address maternal cognitions and behaviours when interacting with her child may improve health outcomes for children with anxiety disorders in the context of maternal anxiety disorder.
- We can be confident that supplementing individual CCBT with CBT to target the maternal anxiety disorder is unlikely to confer substantial health benefits and is unlikely to be cost-effective. Given the intensity of this intervention and its general lack of effectiveness we think it is unlikely that supplementing CCBT with this intervention will improve child outcomes.

### *Future research implications*

- Given that CCBT alone was sufficient for the majority of patients, it is possible that any benefits from the MCI and MCBT interventions may be enhanced in particular contexts; for example, in the context of particular maternal or child anxiety disorders or high levels of severity. Future research that directly addresses these possibilities is warranted.
- The relatively low level of association between change in maternal anxiety and responses and child anxiety, may suggest that other factors may account for the modest treatment outcomes typically found among children with anxiety disorders who have mothers with anxiety disorders (such as genetic or broader social/environmental factors). Future research is warranted to address these issues.
- The economic evaluation provides insight as to the broad range of services accessed by this client group, hence it is recommended that future economic evaluations in this area incorporate data collection on this full range of services in order to capture the full impact of new interventions for this client group.

## Trial registration

This trial is registered as ISRCTN19762288.

## Funding

This trial was funded by the Medical Research Council (MRC) and Berkshire Healthcare Foundation Trust and managed by the National Institute for Health Research (NIHR) on behalf of the MRC–NIHR partnership (09/800/17) and will be published in full in *Health Technology Assessment*; Vol. 19, No. 38.

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 5.116

*Health Technology Assessment* is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index and is assessed for inclusion in the Database of Abstracts of Reviews of Effects.

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## This report

This issue of *Health Technology Assessment* contains a project originally commissioned by the MRC but managed by the Efficacy and Mechanism Evaluation Programme. The EME programme was created as part of the National Institute for Health Research (NIHR) and the Medical Research Council (MRC) coordinated strategy for clinical trials. The EME programme is funded by the MRC and NIHR, with contributions from the CSO in Scotland and NISCHR in Wales and the HSC R&D, Public Health Agency in Northern Ireland. It is managed by the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) based at the University of Southampton.

The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from the material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the MRC, NETSCC, the HTA programme, the EME programme or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme, the EME programme or the Department of Health.

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