An explanatory randomised controlled trial testing the effects of targeting worry in patients with persistent persecutory delusions: the Worry Intervention Trial (WIT)

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Declared competing interests of authors: none

Published March 2015
DOI: 10.3310/eme02010

Scientific summary

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Efficacy and Mechanism Evaluation 2015; Vol. 2: No. 1
DOI: 10.3310/eme02010

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Background

Persecutory delusions are a key experience in psychosis, at the severe end of a paranoia continuum in the general population. They are associated with anxiety, depression, insomnia and major reductions in social functioning. Treatments require significant improvement. Our approach is to translate recent advances in understanding delusions into efficacious treatment, carefully taking one key causal factor at a time. In our research we have found worry to be an important factor in the development and maintenance of persecutory delusions. This is plausible: worry brings implausible ideas to mind, keeps them there and makes the experience distressing. Reducing worry should lead to reductions in persecutory delusions. Our pilot data supported this prediction but targeting worry had not been evaluated in a rigorous clinical trial.

Objective

The objective was to test the clinical efficacy of a brief cognitive–behavioural intervention for worry for patients with persistent persecutory delusions and determine how the treatment might reduce delusions. Also embedded within the trial were theoretical studies to improve the understanding of worry in patients with psychosis. We aimed to test the intervention in addition to standard care. A psychological intervention control group was not included in the design; instead, we aimed to show a large treatment effect, greater than would be expected by attention effects alone, and that the treatment worked specifically by reducing worry. The trial hypotheses were:

1. the worry intervention will reduce levels of worry in patients with persecutory delusions
2. the worry intervention will reduce persecutory delusions
3. the improvements will be maintained at follow-up
4. worry will be the mediator of the changes in persecutory delusions.

Methods

An explanatory randomised controlled trial – called the Worry Intervention Trial (WIT) – with patients with persecutory delusions was carried out. Patients were randomised to the worry intervention in addition to standard care or to standard care. The trial used a web-based randomisation system written by a clinical trials unit. Randomisation occurred after the baseline assessment was fully complete. A stratified randomisation procedure was used involving four strata and a randomly permuted block procedure with variable block sizes. Stratification was on the basis of centre (Oxford Health NHS Foundation Trust/Southern Health NHS Foundation Trust) and level of worry ('moderate' when $44 \leq$ worry score ≤ 62, 'high' when $63 \leq$ worry score). Assessors were graduate psychologists and their reliability for interview measures was assessed. Assessments were carried out by an assessor blind to treatment allocation at 0 weeks, 8 weeks (post treatment) and 24 weeks. The trial patients were recruited equally from Oxford Health NHS Foundation Trust and Southern Health NHS Foundation Trust.

Participants

A total of 150 patients with persistent persecutory delusions in the context of non-affective psychosis took part. The inclusion criteria were a current persecutory delusion; scoring at least 3 on the conviction scale of the Psychotic Symptom Rating Scales (PSYRATS); that the delusion has persisted for at least 3 months; a clinical diagnosis of schizophrenia, schizoaffective disorder or delusional disorder (i.e. a diagnosis of non-affective psychosis); a clinically significant level of worry, as indicated by a score of > 44 on the

Penn State Worry Questionnaire (PSWQ); age between 18 and 65 years; and, when major changes in medication are being made, entry to the study would not occur until at least a month after stabilisation of dosage. Criteria for exclusion were a primary diagnosis of alcohol or substance dependency or personality disorder; organic syndrome or a learning disability; a command of spoken English inadequate for engaging in therapy; and currently having individual cognitive–behavioural therapy (CBT). The clear majority of the patients had had persecutory delusions for several years. The most common diagnosis was schizophrenia. (It is of note for the applicability of the therapy that only eight patients with persecutory delusions who were screened for the trial were excluded for having an insufficient level of worry.) Recruitment took place from November 2011 to September 2013, with the last assessments completed in March 2014.

Intervention

The six-session, highly manualised CBT intervention aimed to reduce time worrying and did not dispute the content of delusions. It was provided by clinical psychologists who had clinical supervision once a week. Therapy competence was checked by an independent clinician rating a random selection of audiotaped sessions. Home visits were made for patients unable to attend clinics. The patient and clinician worked through the therapy based on six therapy booklets that they shared. The main techniques were psychoeducation about worry, identification and reviewing of positive and negative beliefs about worry, increasing awareness of the initiation of worry and individual triggers, use of worry periods, planning activity at times of worry and learning to 'let go' of worry. Tasks were set between sessions. Whenever patients were agreeable, telephone calls were made or texts were sent between sessions to encourage the trying out of new strategies.

Main outcome measures

The main outcome measures were of worry (PSWQ) and persecutory delusions (PSYRATS).
Secondary outcome measures were paranoia (Paranoid Thoughts Scale), overall psychiatric symptoms (Positive and Negative Syndrome Scale), psychological well-being (Warwick–Edinburgh Mental Well-being Scale), rumination (Perseverative Thoughts Questionnaire) and a patient-chosen outcome (Choice of Outcome in CBT for Psychoses).

Analysis

All main analyses were carried out at the end of the last follow-up assessment (i.e. there were no interim analyses) and were based on the intention-to-treat principle, with due consideration being given to potential biases arising from loss to follow-up. Random- or mixed-effects models were fitted to the repeated measures to estimate treatment effects for outcomes, controlling for stratum [treatment centre crossed by initial level of worry (moderate/high)] and the corresponding baseline assessment for the outcome under investigation. Secondary trial analyses to investigate putative meditational mechanisms was carried out with allowance being made for the repeated measures of both the putative mediator (worry) and the outcome (delusions). This involved the use of structural equation modelling. All statistical testing was two-tailed.

Results

In total, 73 patients were randomised to the new treatment and 77 to standard care alone. Almost 90% of those allocated to the psychological treatment received it. The therapy was assessed by an independent clinician, who showed that it was competent. In total, 95% of the patients provided primary outcome follow-up data. For the primary outcomes, compared with treatment as usual, the therapy led to highly significant reductions in both worry [PSWQ: 6.35, 95% confidence interval (CI) 3.30 to 9.40; $p < 0.001$] and the persecutory delusions (PSYRATS: 2.08, 95% CI 0.64 to 3.51; $p = 0.005$). The intervention also led to significant improvements in all of the secondary outcomes. All gains were maintained. A planned mediation analysis indicated that change in worry explained 66% of the change in the delusions. Medical notes were checked for adverse events during the trial. There were no deaths, admissions to secure units or formal complaints about therapy. There were six suicide attempts (two in the treatment group and

four in the control group). There were two serious violent incidents (one in each allocation group). None of the adverse events was related to the therapy or the assessments. We also found that (1) in a qualitative study patients without intervention report a passive relationship with worry ('natural drift'), feeling unable to do anything about it; (2) in an experimental study a bout of worry in the patient brings on depersonalisation experiences; and (3) in comparison with a non-clinical general population sample the patient group has a very low level of psychological well-being.

Conclusions

This was the first large randomised controlled trial specifically focused on the individual treatment of patients with persecutory delusions. Long-standing delusions were significantly reduced by a brief CBT intervention targeted at worry. The intervention also improved well-being, which has not been shown in this patient group before, and reduced overall levels of psychiatric problems. The key recommendation for research is that an evaluation of the intervention in routine clinical setting across multiple sites is now indicated. We recommend that the contents of the intervention booklets are developed for online and app delivery so that the intervention, with health professional support, has the possibility for greater self-management. We also recommend that the intervention is tested in younger and older age groups. Comparison of the intervention with an attention control condition would also be informative. Further, we recommend carrying out research that combines the treatment with brief interventions that target other key causes of persecutory delusions.

Trial registration

This trial is registered as ISRCTN23197625.

Funding

This project was funded by the Efficacy and Mechanism Evaluation (EME) programme, a MRC and NIHR partnership.

Efficacy and Mechanism Evaluation

ISSN 2050-4365 (Print)

ISSN 2050-4373 (Online)

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This report

The research reported in this issue of the journal was funded by the EME programme as project number 09/160/06. The contractual start date was in September 2011. The final report began editorial review in June 2014 and was accepted for publication in October 2014. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The EME editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

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