

Project Title:	The effects of reducing worry in patients with persecutory delusions: an explanatory randomised controlled trial.
Project Ref:	09/160/06
Cost:	£662,320
Lead Applicant & Institution:	Professor Daniel Freeman Oxford University
Start Date:	1 September 2011
Plain English Summary:	<p>Delusions are a key symptom of severe mental illnesses, particularly schizophrenia. Persecutory delusions are the most distressing delusion type, the most likely to be acted upon, are associated with suicide, and are a predictor of admission to psychiatric hospital. Existing treatments, pharmacological and psychological, are only partially effective; many people do not respond and many have only partial responses.</p> <p>A way to improve treatment is to target the mechanisms causing delusions to persist. Recent research carried out by our team has identified worry as a key factor in maintaining persecutory delusions. This is very plausible: worry keeps fears in mind, leads to more catastrophic content, and makes the experience more distressing.</p> <p>Therefore in a pilot randomised controlled study we targeted worry mechanisms in patients with persecutory delusions. A brief cognitive-behavioural worry intervention led to large reductions in both worry and persecutory delusions. The aim of the new research is threefold: to carry out a rigorous methodological evaluation of the efficacy of a worry intervention for patients with persecutory delusions; to establish how the treatment might work; and to further the theoretical understanding of worry in psychosis.</p> <p>Key advantages of the intervention are its popularity with patients (it does not dispute the validity of their beliefs), its brevity, and that it can be readily incorporated into clinical services. The study will be a randomised controlled trial of 150 patients with persecutory delusions. It is the additional receipt of the worry intervention to standard psychiatric treatment that will be evaluated.</p> <p>We predict that the intervention will reduce levels of worry and reduce the persecutory delusions, especially the distress that they cause an individual. We also predict improvement in quality of life for patients. Further, we predict that the intervention will work by reducing the cognitive processes that underlie worry. In addition, embedded into the assessments will be a theoretical study of worry, testing how worry exacerbates persecutory delusions.</p>

The main ethical issue is that the control group do not receive an additional intervention: we will therefore offer all control participants on completion of the trial a therapy session on worry and provide self-help reading materials.

The trial will be carried out in two centres (Oxford and Hampshire) and last 2.5 years. The staffing will be one research worker and a part-time clinical psychologist in each centre. Our team is exceptionally well-placed to carry out both the clinical and theoretical aspects of the study. We have led the theoretical studies of persecutory delusions and worry, carried out the pilot study, have previously run a number of large randomised controlled trials for psychosis, and have the statistical expertise to test the mechanisms underlying treatment. For the running of the study we will also work with a clinical trials unit.

Abstract:

BACKGROUND:
Our approach to advancing the treatment of psychosis is to focus on key single symptoms and develop interventions that target the mechanisms that maintain them. In our theoretical research we have found worry to be an important factor in persecutory delusions. Worry brings implausible ideas to mind, keeps them there, and makes the experience distressing. Therefore we aim to test the clinical efficacy of a cognitive-behavioural intervention for worry for patients with persecutory delusions, determine how the worry treatment might reduce delusions, and develop the theoretical understanding of worry in psychosis. The project will produce a brief, easily administered intervention that can be readily used in services.

RESEARCH DESIGN:
An explanatory randomised controlled trial with 150 patients with persecutory delusions will be carried out. Patients will be randomised to the worry intervention in addition to standard care or to standard care. Randomisation will be carried out independently, assessments carried out blind, and therapy competence and adherence monitored. Two theoretical studies will be built into the baseline assessment.

POPULATION:
Individuals with persecutory delusions and worry in the context of a schizophrenia spectrum diagnosis. They will not have responded adequately to previous treatment.

PLANNED INTERVENTION:
A 6 session cognitive-behavioural intervention will be presented on computer and assisted by a therapist. The control condition will be treatment as usual, which is typically antipsychotic medication and regular appointments.

PROPOSED OUTCOME MEASURES:
The principal hypotheses are that a worry intervention will reduce levels of worry and that it will also reduce the persecutory delusions. The key outcome measures will therefore be the Penn State Worry Questionnaire and the Psychotic Symptoms Rating Scale – Delusions. Quality of life and service-user led reported outcomes will also be examined.

ASSESSMENT AND FOLLOW-UP:
0 weeks (baseline), 8 weeks (post treatment) and 24 weeks (follow up).

PROPOSED SAMPLE SIZE:
The trial will run in two large NHS Trusts that cover a population of 2.4 million. In our randomised controlled pilot study the intervention led to a worry reduction of effect size 1.05 and a delusion reduction of effect size 1.35. We have conservatively powered the study to detect a lower effect size of 0.52. 150 patients are required (75 in each condition), allowing for 20% drop-out.

	<p>STATISTICAL ANALYSIS: The statistical analysis strategy will follow the intention-to-treat principle and involve the use of linear mixed models to evaluate and estimate the relevant between- and within-subjects effects (allowing for the possibility of missing data). Both traditional regression and newer instrumental variables analyses will examine mediation.</p> <p>TIMETABLES: The trial will take 2.5 years: 0-2 months, training staff and setting up recruitment; 2-22 months, recruitment, intervention and assessments; 22-28 months, final interventions and follow-ups; 28-30 months, final data checking and analysis. The publication will be submitted within six months of the trial ending. The pilot recruitment rate was equivalent to 6 patients per month per full time researcher. We have therefore planned a recruitment rate of 4 patients per month per centre, consistent with many of our other studies.</p>
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