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ORIGINAL PAPER

Depression treated by homeopaths: a study protocol for a pragmatic cohort multiple randomised controlled trial

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Background: **The most commonly recommended treatments for depression are psychological/psychotherapeutic treatments, and antidepressant drugs. However, 38 percent of patients with depression do not use these recommended treatments. Some patients seek homeopathic treatment for depression, but insufficient evidence exists to conclude as to the effectiveness, cost-effectiveness and safety of treatment by homeopaths for patients with depression. The aim of this trial is to evaluate the acceptability and comparative clinical and cost-effectiveness of the offer of adjunctive treatment provided by homeopaths for patients with self-reported depression.**

Method: **This pragmatic randomised controlled trial is embedded within the population based South Yorkshire Cohort (SYC) of whom nine percent self-report long-term depression. The SYC is designed to facilitate 'cohort multiple' randomised controlled trials (cmRCT). A self-completed questionnaire will be used to both screen and collect baseline data from potential trial participants. The primary outcome is PHQ-9. One-hundred-and-sixty-two participants will be randomly selected to the intervention group (Offer of treatment by a homeopath). The results of the Offer and the No Offer groups will be compared at 6 and 12 months using both an intention to treat (ITT) and complier average causal effect (CACE) analysis. Cost-effectiveness analysis will involve calculation of quality adjusted life year (QALY). In order to help interpret the quantitative findings a selection of up to 30 patients in the offer group will be invited to participate in qualitative interviews after the first consultation and after a minimum of 6 months. Interviews will be assessed by two researchers and results will be analysed using thematic analysis. Triangulation will be used to combine results from qualitative and quantitative methodologies at the interpretation stage, to see if results agree, offer complementary information on the same issue or contradict each other.** *Homeopathy* (2014) **103**, 147–152.

Keywords: Homeopathy; Depression; Cohort multiple randomised controlled trial; Effectiveness; Cost-effectiveness; Qualitative study; Mixed method

Background

Depression is the leading cause of burden of disease in middle- and high-income countries, with over 150 million people in the world suffering from unipolar depressive disorders.[1] Depression is also associated with considerable comorbidities.[2] In the UK, depression is the second largest contributor to disability adjusted life years.

The most commonly recommended treatments in the UK are psychological/psychotherapeutic treatment for minor to moderate depression, and antidepressant drugs for persistent and more severe depression.[3] The prescription of antidepressants in England increased by 9.1% from 2010 to 2011, with 46.7 million prescriptions issued.[4] Some systematic reviews suggest that antidepressants are

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effective, with small effect sizes[5], while others report that antidepressants have no effect in mild and moderate depression,[6] little effect on remission[3] or only borderline effectiveness,[7] or are only effective in more severe depression. Antidepressants are also known to cause significant side-effects[8]. Although antidepressant maintenance treatment has been found to be effective in many patients 17−30% still experience relapse of their depression symptoms over a 1−3 year period.[9]

Psychological and psychotherapeutic treatments such as cognitive behavioural therapy (CBT), counselling, interpersonal therapy, and psychodynamic approaches are recommended for mild to moderate depression by the National Institute for Health and Care Excellence (NICE) in the United Kingdom, but these recommendations are based on a limited number of depression trials, thus limiting the validity of their conclusions.[3] Effect sizes for such treatment modalities have also been found to be small.[10] As many as 38% of patients with depression are not using recommended treatments.[3]

Depression is one of the five most common reasons why patients use complementary and alternative therapies[11] and one of the main reasons why patients consult with homeopaths, both within the UK[12] and outside the UK[13].

Homeopathy is provided in some publicly funded healthcare systems and has been provided continuously in the UK publicly funded healthcare system, the National Health Service (NHS), since its inception in 1948. The first principle in homeopathy is treating 'like with like',[14] i.e. a substance that causes certain symptoms in healthy people may cure the same symptoms in those who are ill. The second (and more controversial) principle, is the process of serial dilution and succussion carried out to reduce risk of side effects and to maintain the medicinal properties of homeopathic medicinal products (HMPs). HMPs are European Union registered through a special simplified registration procedure.

Reviews of systematic reviews assessing the evidence base for homeopathy in any type of medical condition reach varying conclusions: no overall strong evidence in favour of homeopathy,[15] clinical evidence supporting the effectiveness and safety, but not the cost-effectiveness of homeopathy,[16] and positive (but not convincing) results in most trials.[17] Reviews of the evidence of the safety indicate that HMPs may cause mild transient side-effects, but not strong or persisting side-effects.[16]

In observational studies, fifty to eighty percent of patients receiving treatment from homeopaths for depression report at least moderate improvement.[18−23] A single double-blinded placebo-controlled randomised trial to assess the efficacy of HMPs found that individually prescribed HMPs were non-inferior to fluoxetine at 4 and 8 weeks of treatment.[24] A limitation of this trial was however high attrition rates. Two double-blinded placebo-controlled trials testing the efficacy of individually prescribed HMPs both failed to recruit sufficient numbers of participants, preventing analysis of results[25] or resulting in premature ending of the trial.[26]

No pragmatic randomised controlled trials (RCTs) of the real world effectiveness and cost-effectiveness of treatment by homeopaths for depression have been conducted. There is a need for high quality clinical trials which can inform clinical practice and commissioning, and innovative methodologies to address the challenges of recruitment. This trial does not aim to assess the efficacy of homeopathic medicines, but the effectiveness of a total 'package of care'. The trial has high external validity and thereby advances the field by providing evidence on the extent to which treatment provided by homeopaths in 'real world practice' in addition to usual care is of benefit to patients self-reporting depression compared to usual care alone.

Aims

The aim of this trial is to evaluate the acceptability and the comparative clinical and cost effectiveness of the offer of adjunctive treatment provided by homeopaths for patients with self-reported unipolar depression in addition to usual care, compared to usual care alone.

Methods and design

This study uses the 'cohort multiple' RCT (cmRCT) design[27] with participants recruited from the population based South Yorkshire Cohort (SYC) cohort, a large observational study and multiple trials facility. Over 27,000 patients have been recruited to the cohort from 41 GP practices in South Yorkshire and have provided baseline data on a range of socio-demographics, socio-economics, comorbidities (including depression), health resource use and health related quality of life (HRQoL). Over 22,000 participants have given consent to be contacted by researchers again and for their data to be used comparatively, and 89% of these participants have given consent to access their routine health records. Baseline data will facilitate the screening process, and minimise the time spent on recruitment.

Nine percent (n = 2000) of SYC participants self-report long-standing depression. These 2000 patients will be sent a screening and baseline data collection questionnaire (including the primary and secondary outcome measures). In case of insufficient response, questionnaires will also be sent to participants who reported suffering from anxiety or depression on the day of completing the questionnaire, adding up to a total of 5700 participants.

Inclusion criteria

Eligible trial group participants must be aged 18−85 and have a minimum baseline PHQ-9 score of 10 points, including scoring 2 points for either question 1 (little interest or pleasure in doing things) or question 2 (feeling down, depressed, or hopeless). A threshold of 10 suggests moderate level of depression and is considered the limit for clinically relevant depression.[28]

Exclusion criteria

These are kept to a minimum in order to maximise the external validity of the trial and include: no current or past diagnosis of bipolar disorder, Alzheimer's disease,