COCHRANE CORNER

Psychological therapies for treatment-resistant depression in adults: a Cochrane Review†

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See commentary in this issue.

Background

Antidepressants are a first-line treatment for adults with moderate to severe major depression. However, many people prescribed antidepressants for depression don't respond fully to such medication, and little evidence is available to inform the most appropriate 'next step' treatment for such patients, who may be referred to as having treatment-resistant depression (TRD). National Institute for Health and Care Excellence (NICE) guidance suggests that the 'next step' for those who do not respond to antidepressants may include a change in the dose or type of antidepressant medication, the addition of another medication, or the start of psychotherapy. Different types of psychotherapies may be used for TRD; evidence on these treatments is available but has not been collated to date.

Along with the sister review of pharmacological therapies for TRD, this review summarises available evidence for the effectiveness of psychotherapies for adults (18–74 years) with TRD with the goal of establishing the best 'next step' for this group.

Objectives

To assess the effectiveness of psychotherapies for adults with TRD.

Search methods

We searched the Cochrane Common Mental Disorders Controlled Trials Register (until May 2016), along with CENTRAL, MEDLINE, Embase, and PsycINFO via OVID (until 16 May 2017). We also searched the World Health Organization (WHO) trials portal (ICTRP) and ClinicalTrials.gov to identify unpublished and ongoing studies. There were no date or language restrictions.

Selection criteria

We included randomised controlled trials (RCTs) with participants aged 18–74 years diagnosed with unipolar depression that had not responded to minimum four weeks of antidepressant treatment at a recommended dose. We excluded studies of drug intolerance. Acceptable diagnoses of unipolar depression were based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) or earlier versions, International Classification of Diseases (ICD)-10, Feighner criteria, or Research Diagnostic Criteria. We included the following comparisons.

1 Any psychological therapy versus antidepressant treatment alone, or another psychological therapy.
2 Any psychological therapy given in addition to antidepressant medication versus antidepressant treatment alone, or a psychological therapy alone.

Primary outcomes required were change in depressive symptoms and number of dropouts from study or treatment (as a measure of acceptability).

Data collection and analysis

We extracted data, assessed risk of bias in duplicate, and resolved disagreements through discussion or consultation with a third person. We conducted random-effects meta-analyses when appropriate. We summarised continuous outcomes using mean differences (MDs) or standardised mean differences (SMDs), and dichotomous outcomes using risk ratios (RRs).

Main results

We included six trials ($n = 698$; most participants were women approximately 40 years of age). All studies evaluated psychotherapy plus usual care (with antidepressants) versus usual care (with antidepressants). Three studies addressed the addition of cognitive–behavioural therapy (CBT) to usual care ($n = 522$), and one each evaluated intensive short-term dynamic psychotherapy (ISTDP) ($n = 60$), interpersonal therapy (IPT) ($n = 34$), or group dialectical behavioural therapy (DBT) ($n = 19$) as the intervention. Most studies were small (except one trial of CBT was large), and all studies were at high risk of detection bias for the main outcome of self-reported depressive symptoms.

A random-effects meta-analysis of five trials ($n = 575$) showed that psychotherapy given in addition to usual care (vs usual care alone) produced improvement in self-reported depressive symptoms (MD –4.07 points, 95% confidence interval (CI) –7.07 to –1.07 on the Beck Depression Inventory (BDI) scale) over the short term (up to six months). Effects were similar when data from all six studies were combined for self-reported depressive symptoms (SMD –0.40, 95% CI –0.65 to –0.14; $n = 635$). The quality of this evidence was moderate. Similar moderate-quality evidence of benefit was seen on the Patient Health Questionnaire-9 Scale (PHQ-9) from two studies (MD –4.66, 95% CI 8.72 to –0.59; $n = 482$) and on the Hamilton Depression Rating Scale (HAMD) from four studies (MD –3.28, 95% CI –5.71 to –0.85; $n = 193$).

High-quality evidence shows no differential dropout (a measure of acceptability) between intervention and comparator groups over the short term (RR 0.85, 95% CI 0.58 to 1.24; six studies; $n = 698$).

Moderate-quality evidence for remission from six studies (RR 1.92, 95% CI 1.46 to 2.52; $n = 635$) and low-quality evidence for response from four studies (RR 1.80, 95% CI 1.2 to 2.7; $n = 556$) indicate that psychotherapy was beneficial as an adjunct to usual care over the short term.

With the addition of CBT, low-quality evidence suggests lower depression scores on the BDI scale over the medium term (12 months) (RR –3.40, 95% CI –7.21 to 0.40; two studies; $n = 475$) and over the long term (46 months) (RR –1.90, 95% CI –3.22 to –0.58; one study; $n = 248$). Moderate-quality evidence for adjunctive CBT suggests no difference in acceptability (dropout) over the medium term (RR 0.98, 95% CI 0.66 to 1.47; two studies; $n = 549$) and lower dropout over long term (RR 0.80, 95% CI 0.66 to 0.97; one study; $n = 248$).

Two studies reported serious adverse events (one suicide, two hospitalisations, and two exacerbations of depression) in 4.2% of the total sample, which occurred only in the usual care group (no events in the intervention group).

An economic analysis (conducted as part of an included study) from the UK healthcare perspective (National Health Service (NHS)) revealed that adjunctive CBT was cost-effective over nearly four years.

Authors' conclusions

Moderate-quality evidence shows that psychotherapy added to usual care (with antidepressants) is beneficial for depressive symptoms and for response and remission rates over the short term for patients with TRD. Medium- and long-term effects seem similarly beneficial, although most evidence was derived from a single large trial. Psychotherapy added to usual care seems as acceptable as usual care alone.

Further evidence is needed on the effectiveness of different types of psychotherapies for patients with TRD. No evidence currently shows whether switching to a psychotherapy is more beneficial for this patient group than continuing an antidepressant medication regimen. Addressing this evidence gap is an important goal for researchers.