Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy

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CRD summary

The authors concluded that pharmacotherapy and psychotherapy are both effective for treating depression in older adults and treatment decisions should be based on other factors. Due to poor reporting of review methodology, the method of evidence synthesis and the inclusion of non-randomised evidence, it is not possible to determine the reliability of these conclusions.

Authors' objectives

To compare the effects of pharmacotherapy with psychotherapy for depressed older adults.

Searching

MEDLINE, PsycINFO, PSYNDEX and the Cochrane Library were searched; the search terms were reported. The dates of the searches were not reported. No language restrictions were employed.

Study selection

Study designs of evaluations included in the review

Controlled studies were eligible for inclusion in the review. Both randomised and non-randomised trials were included.

Specific interventions included in the review

Studies that compared a psychotherapeutic or a pharmacotherapeutic intervention with a control condition (placebo or waiting list) were eligible for inclusion. Studies that assessed maintenance therapy, combination treatments or collaborative treatments were excluded.

The pharmacotherapies used in the included studies were serotonin-specific re-uptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAO-Is) and other drugs. The latter included: acetyl-L-carnitine, an analogue of adrenocorticotropic hormone, alprazolam, bupropion, medifoxamine, flovoxamine, iproniazid, L-sulpiride, methylphenidate, mianserin, minaprine, mirtazapine, nomifensine, trazodone, tryptophan, venlafaxine, viloxazine, combined dihydroergocristine and L-5-hydroxytryptophan. The studies of pharmacotherapy all employed a placebo control condition. Psychotherapy studies evaluated cognitive-behavioural therapy (CBT) and a variety of other psychotherapies, and used a variety of control conditions: drug placebo, irrelevant activity, usual care and waiting list control. A minority of the included studies directly compared pharmacotherapy, psychotherapy and control. The mean duration of all the interventions was 8.3 weeks (standard deviation 4.8); the mean was 7.3 weeks for pharmacotherapy studies and 9.4 weeks for psychotherapy studies.

Participants included in the review

Studies of patients with a mean age of at least 60 years who met the criteria for major depressive disorder, minor depressive disorder or dysthymic disorder, according to the International Classification of Diseases (ICD-10) or American Psychiatric Association's DSM criteria (DSM-III, DSM-IIIR or DSM-IV), were eligible for inclusion. Studies of patients with and without physical or cognitive co-morbidities were eligible for inclusion. Some studies included in-patients.

Outcomes assessed in the review

Studies that presented sufficient data to allow the calculation or estimation of the change in clinician-rated or self-rated severity of depression and/or remission and treatment response rates were eligible for inclusion. The included studies used several rating scales, such as the Hamilton Depression Scale, the Montgomery-Asberg Depression Scale, the Beck Depression Inventory and the Geriatric Depression Scale.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The studies were assessed for validity using the following criteria: randomisation, blinding of the assessors and use of intention-to-treat analysis. The authors did not state how many reviewers performed the validity assessment.

Data extraction
The study data were coded. Inter-rater agreement on coding was assessed for 20% of the studies. Any disagreements were resolved by consensus. Data on depression scores were extracted, and effect sizes were calculated using the difference between the post-treatment scores for the intervention and control groups using reported statistics; effect sizes were adjusted for differences in baseline values between treatment groups. Where more than one treatment was evaluated, separate effect sizes were calculated for each treatment. Where more than one outcome measure was employed, The effect size was calculated as the mean of the two measures. Odds ratios (ORs) were calculated for the proportion of patients who responded to treatment and patients who experienced remission.

Methods of synthesis
How were the studies combined?
The studies were combined using a Mantel-Haenszel random-effects meta-analysis and pooled OR with 95% confidence intervals (CIs) were calculated for dichotomous data. Weighted mean effect sizes (d) with 95% CIs were calculated for depression scores.

How were differences between studies investigated?
Statistical heterogeneity between the studies was assessed using the Q statistic for effect size and the chi-squared statistic for ORs. Studies of pharmacotherapy and psychotherapy were analysed separately. Differences between the effect sizes for pharmacotherapy and psychotherapy were assessed by examining the degree of overlap of CIs and using the binomial effect size display in which the proportion of patients in each treatment group with above-average improvement was calculated. Pharmacotherapy studies were grouped according to drug class, while psychotherapy studies were subdivided into CBT and other psychotherapies and individual and group treatments, and these subgroups were also analysed separately. Meta-regression was used to examine the influence of various variables on the results: treatment, type of medical condition, in-patient, comorbidity of all patients, treatment duration, mean age, percentage of females, random assignment, blinding of the outcome assessors and intention-to-treat analysis.

Results of the review
Eighty-nine studies (5,328 patients) were included in the review.

Seventy-nine studies were randomised controlled trials. Seventy-three studies used blinded or masked outcome assessors. Forty-eight studies used intention-to-treat analysis.

Treatment response.

The pooled OR for all studies was 2.30 (95% CI: 2.01, 2.63; 59 subgroups). The pooled OR was 2.24 (95% CI: 1.93, 2.59; 43 subgroups) for all pharmacotherapy studies and 2.63 (95% CI: 1.90, 3.64; 16 subgroups) for all psychotherapy studies. For studies using different classes of pharmacotherapy, the pooled ORs were as follows: SSRIs, 1.83 (95% CI: 1.54, 2.18; 16 subgroups); TCAs, 4.54 (95% CI: 3.06, 6.74; 14 subgroups); MAO-Is, 9.47 (95% CI: 3.44, 25.31; 2 subgroups); other, 2.46 (95% CI: 1.66, 3.66; 11 subgroups). For studies of CBT the pooled OR was 2.77 (95% CI: 1.97, 3.89; 13 subgroups), and for other forms of psychotherapy it was 1.71 (95% CI: 0.63, 4.65; 93 subgroups). No statistically significant heterogeneity was detected except in the analysis of other forms of psychotherapy.

Remission.

The pooled OR was 2.03 (95% CI: 1.67, 2.46; 22 subgroups) for all pharmacotherapy studies and 2.47 (95% CI: 1.76,

3.47; 14 subgroups) for all psychotherapy studies. No statistically significant heterogeneity was detected.

Clinician-rated depression.

The pooled effect size for all studies was -0.80 (95% CI: -0.90, -0.69; 112 subgroups). The pooled effect size was -0.69 (95% CI: -0.81, 0.57; 77 subgroups) for all pharmacotherapy studies and -1.09 (95% CI: -1.26, -0.91; 35 subgroups) for all psychotherapy studies. For studies using different classes of pharmacotherapy, the pooled effect sizes were as follows: SSRIs, 0.48 (95% CI: -0.66, -0.30; 21 subgroups); TCAs, -0.93 (95% CI: -1.21, -0.65; 22 subgroups); MAO-Is, -0.79 (95% CI: -1.07, 0.51; 6 subgroups); other, -0.72 (95% CI: -0.95, -0.48; 28 subgroups). For studies of CBT the pooled effect size was -1.22 (95% CI: -1.42, -1.03; 26 subgroups), and for other forms of psychotherapy it was -0.75 (95% CI: -1.01, -0.49; 9 subgroups). Statistically significant heterogeneity between studies was found for all analyses with the exception of CBT and other psychotherapies.

Self-rated depression.

The pooled effect size for all studies was -0.76 (95% CI: -0.87, -0.64; 80 subgroups). The pooled effect size was -0.62 (95% CI: -0.79, 0.45; 28 subgroups) for all pharmacotherapy studies and -0.83 (95% CI: -0.98, -0.69; 52 subgroups) for all psychotherapy studies. For studies using different classes of pharmacotherapy, the effect sizes were as follows: SSRIs, 0.22 (95% CI: -0.35, -0.10; 4 subgroups); TCAs, -0.83 (95% CI: -1.20, -0.46; 10 subgroups); MAO-Is, -0.80 (95% CI: -1.19, 0.40; 3 subgroups); other, -0.67 (95% CI: -0.97, -0.37; 11 subgroups). For studies of CBT the effect size was -0.88 (95% CI: -1.05, -0.71; 40 subgroups), and for other forms of psychotherapy it was -0.69 (95% CI: -0.95, -0.42; 12 subgroups). Statistically significant heterogeneity between studies was found for all analyses with the exception of SSRIs, MAO-Is and other psychotherapies.

Pooled effect sizes for studies of major depression and for those including patients with minor depression or dysthymia were also calculated.

Clinician-rated depression. Treatment significantly improved effect sizes for clinician-rated depression compared with control for all studies (d -0.80, 95% CI: -0.90, -0.69, p<0.001; 112 subgroups), for pharmacotherapy studies (d -0.69, 95% CI: -0.81, -0.57, p<0.001; 77 subgroups) and for psychotherapy studies (d -1.09, 95% CI: -1.26, -0.91, p<0.001; 35 subgroups). Psychotherapy treatment showed larger effect sizes than pharmacological interventions (non-overlapping 95% CIs and above average improvement reported in 72.4% receiving psychotherapy versus 66.3% receiving pharmacotherapy). Control groups receiving medication reported greater improvements than psychotherapy groups (d = -0.91 versus d = -0.33).

Self-rated depression. Treatment significantly improved effect sizes for self-rated depression compared with control for all studies (d -0.76, 95% CI: -0.87, -0.64, p<0.001; 80 subgroups), for pharmacotherapy studies (d -0.62, 95% CI: -0.79, -0.45, p<0.001; 28 subgroups) and for psychotherapy studies (d -0.83, 95% CI: -0.98, -0.69, p<0.001; 52 subgroups). Psychotherapy and pharmacotherapy showed similar treatment effect (above average improvement reported in 69.2% receiving psychotherapy versus 64.8% receiving pharmacotherapy). Statistically significant heterogeneity was detected for all these analyses.

Studies comparing psychotherapy, pharmacotherapy and control (5 studies).

No differences were found between pharmacotherapy and psychotherapy in clinician-rated depression (d = -0.54 versus control and d = -0.41 versus control, respectively) or self-rated depression (d = -0.27 versus control and d = -0.19 versus control, respectively) effect sizes.

Subgroup analyses.

There were no significant differences between drug groups in clinician-rated depression. CBT was associated with larger effect size for clinician-rated depression than other types of psychotherapy, SSRIs, other drugs and all drugs combined. For those studies that included patients with minor depression and/or dysthymias, psychotherapy was associated with larger treatment effects for clinician-rated depression than pharmacotherapy. Results were reported for all these subgroups.

Response and remission rates.

No significant differences were found between pharmacotherapy and psychotherapy in response or remission rates.

Authors' conclusions

Available treatments for depression are effective, with moderate to large effect sizes, but comparisons of psychotherapy and pharmacology should be interpreted with caution.

CRD commentary

The review question and the inclusion criteria were clear although broad. The authors searched a number of relevant databases and did not employ any language restrictions, thereby reducing the chance that relevant studies might have been omitted from the review. However, they did not report any attempts to identify unpublished studies, which might have increased the possibility of publication bias. The authors reported making some attempt to minimise bias and error in the extraction of data, but did not report the use of such procedures in the assessment of study validity or the selection of studies. The results of the validity assessment were used to inform the analysis only through the use of meta-regression; subgroups or separate analyses within the primary analysis may have been more informative. The use of meta-analysis to combine randomised and non-randomised studies might not have been appropriate, and the high levels of statistically significant heterogeneity found in the analyses indicate that results were inconsistent among the studies.

Various potential sources of differences between the studies were examined. The reasons for the review's focus on effect sizes, rather than perhaps the more interpretable response and remission rates, were not clear. For studies that compared pharmacotherapy and psychotherapy, data were reported for each treatment versus control rather than a direct comparison between treatments; reasons for this were also unclear. Statements on relative efficacy were based predominantly on indirect comparisons. A very specific set of circumstances needs to be met for such a comparison to be valid, and some of these circumstances (e.g. comparability of placebo response rates) did not appear to have been met here. The authors' conclusions, that comparisons between pharmacotherapy and psychotherapy should be interpreted with caution, appear appropriate in view of the absence of adequate comparisons within studies. However, given the poor reporting of some review methodology and the high levels of clinical, methodological and statistical heterogeneity, it is not possible to determine the reliability of these conclusions.

Implications of the review for practice and research

Practice: The authors stated that treatment choice should be based on factors such as contraindications, treatment access, or patient preferences.

Research: The authors stated that further randomised controlled trials and a subsequent meta-analysis comparing pharmacotherapy, psychotherapy and a control condition in older depressed patients are required. Studies should also be conducted in patients with varying severity of depression, be set in usual clinical practice settings, compare interventions with other treatments (including electroconvulsive therapy), assess long-term outcomes, and evaluate the cost-effectiveness of interventions.

Bibliographic details

Pinquart M, Duberstein P R, Lyness J M. Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. American Journal of Psychiatry 2006; 163(9): 1493-1501

PubMedID

16946172

DOI

10.1176/ajp.2006.163.9.1493

Other publications of related interest

1. Gerson S, Belin TR, Kaufman A, Mintz J, Jarvik L. Pharmacological and psychological treatments for depressed older patients: a meta-analysis and overview of recent findings. Harv Rev Psychiatry 1999;7:1-28. 2. Klawansky S. Meta-analysis on the treatment of depression in late life. In: Schneider LS, Reynolds CF, editors. Diagnosis and treatment of depression in late life. Washington (DC): American Psychiatric Press; 1997.

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Antidepressive Agents /therapeutic use; Depressive Disorder /drug therapy /psychology /therapy; Depressive Disorder, Major /psychology /therapy; Dysthymic Disorder /drug therapy /therapy; Humans; Psychotherapy /methods; Randomized Controlled Trials as Topic /statistics & numerical data; Treatment Outcome

AccessionNumber
12006004077

Date bibliographic record published
31/12/2007

Date abstract record published
31/12/2007

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.