Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression; a meta-analysis,
de Maat, S.C.M.; Dekker, J.J.M.; Schoevers, R.; de Jonghe, F.

published in
Psychotherapy Research
2006

DOI (link to publisher)
10.1080/10503300600756402

document version
Publisher's PDF, also known as Version of record

Link to publication in VU Research Portal

citation for published version (APA)

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To cite this Article De Maat, Saskia; Dekker, Jack; Schoevers, Robert and De Jonghe, Frans (2006) 'Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: A meta-analysis', Psychotherapy Research, 16: 5, 566 — 578

To link to this Article DOI: 10.1080/1050330600756402
URL: http://dx.doi.org/10.1080/1050330600756402
Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: A meta-analysis

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(Received 11 April 2006; accepted 12 April 2006)

Abstract
We investigated the efficacy of pharmacotherapy and psychotherapy for depression by searching for RCT’s. Studies were classified according to chronicity and severity and a meta-analysis was applied. Ten studies were included. Remission did not differ between psychotherapy (38%) and pharmacotherapy (35%). No differences were found in chronic, or in non-chronic depression, and in mild or in moderate depression. Both treatments performed better in mild than in moderate depression. Dropout was larger in pharmacotherapy (28%) than in psychotherapy (24%). At follow-up relapse in pharmacotherapy (57%) was higher than in psychotherapy (27%). Psychotherapy and pharmacotherapy appear equally efficacious in depression. Both treatments have larger effects in mild than in moderate depression, but similar effects in chronic and non-chronic depression and at follow-up psychotherapy outperforms pharmacotherapy.

In the past 25 years, a number of reviews and meta-analyses comparing the efficacy of psychotherapy and pharmacotherapy in depression have been conducted (e.g., Casacalenda, Perry, & Looper, 2002; DeRubeis, Gelfand, Tang, & Simons, 1999; Dobson, 1989; Gloaguen, Cottraux, Cucherat, & Blackburn, 1998; Hollon, Jarrett, et al., 2005; Hollon, Shelton, & Loosen, 1991; Hollon, Thase, & Markowitz, 2002; Jarrett, 1995; Robinson, Berman, & Neimeyer, 1990; Royal Australian and New Zealand College of Psychiatrists, 1983; Steinbrueck, Maxwell, & Howard, 1983; Weissman, Jarrett, & Rush, 1987; Wexler & Cicchetti, 1992). It has been argued that many of these reviews and meta-analyses present methodological limitations. They often do not provide intention-to-treat (ITT) analyses, present effect sizes from which obviously no remission rates can be deduced, include flawed studies (e.g., studies that did not use standardized diagnostic criteria), and present response rates instead of remission rates (Casacalenda et al., 2002). An even more important limitation may be the striking methodological and clinical heterogeneity of the studies included in most reviews and meta-analyses. Clinical heterogeneity refers to differences in patient samples, treatment protocols, and treatment settings across studies. We mention three examples. In Casacalenda et al.’s meta-analysis (2002), three trials regard primary care patients, whereas the other three trials consider psychiatric outpatients. Treatment duration varies from 10 to 34 weeks. Psychotherapy conditions include cognitive therapy and interpersonal psychotherapy as well as problem-solving therapy and social work counseling. In the meta-analysis of Gloaguen et al. (1998), settings vary even more, including hospital patients, outpatients, volunteers, students, adolescents, and geriatric patients. Treatment duration varies from 4 to 79 weeks. Not surprisingly, the authors frequently report that the hypothesis of intertrial homogeneity was rejected. The review of Hollon, Jarrett, et al. (2005) considers primary care, geriatric and adult in- and outpatients suffering from dysthymia or major depressive disorder (MDD). Although some of the reviewers (e.g., Gloaguen et al., 1998) do address the issue of heterogeneity, most of the reviews and meta-analyses mentioned previously do not include statistical analyses assessing the influence of the clinical heterogeneity on the review outcome. Clinical heterogeneity among studies included in reviews or meta-analyses makes data pooling hazardous (see Cochrane Reviewers’ Handbook 4.2.2; Cochrane Collaboration, 2004). It certainly does not allow specific conclusions regarding particular patients groups or settings. Heterogeneity may provide a partial explanation for the rather inconsistent conclusions reached by different reviews. Many of them conclude that psychotherapy...
and pharmacotherapy are equally efficacious, but some deduce that psychotherapy outperforms pharmacotherapy (Dobson, 1989; Gloaguen et al., 1998; Royal Australian and New Zealand College of Psychiatrists, 1983; Steinbrueck et al., 1983; Weissman et al., 1987). In this article, we present the results of a meta-analysis based on randomized controlled trials (RCTs) published between 1980 and 2005, comparing psychotherapy with pharmacotherapy in adult psychiatric outpatients with non-psychotic unipolar depression.

We increased clinical homogeneity among studies by applying rather strict inclusion criteria regarding patient samples, diagnoses, and treatment settings (see Appendix). Subsequently, we statistically tested the heterogeneity among the included studies to assess the extent to which we had achieved clinical homogeneity. Thus, studies were selected on the basis of clinical criteria only. Statistical heterogeneity analysis was not used as a selection criterion but as a test run afterward. The primary research question regards the relative efficacy of pharmacotherapy and psychotherapy in the acute treatment of depression assessed at treatment termination and at follow-up. The secondary question regards possible differences in dropout rates during treatment. We took into consideration two variables known to influence treatment prognosis: chronicity and severity. To that end, we differentiated among mild, moderate, and severe depression and between chronic and nonchronic depression.

**Method**

**Search Strategy**

A systematic search for RCTs was performed in MEDLINE, EMBASE, Cochrane Controlled Trials Register, Cochrane Database of Reviews and Protocols, and PsychInfo. Search headings were DEPRESSION, MAJOR DEPRESSIVE DISORDER, PSYCHOTHERAPY, PHARMACOTHERAPY, ANTIDEPRESSANTS. Limits were (randomised controlled trial[Publication Type] OR controlled clinical trial[Publication Type] OR randomised controlled trials OR random allocation OR double-blind method OR single-blind method OR clinical trial[Publication Type] OR clinical trials OR (clinical AND trial*) OR ((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*)) OR placebos OR placebo* OR random* OR research design OR comparative study OR evaluation studies OR follow up studies OR prospective studies OR control OR controlled OR prospective* OR volunteer*) NOT (Animal[MESH] NOT (Human[MESH] AND Animal[MESH])) and a time limit of 1980 (the year that Diagnostic and Statistical Manual of Mental Disorders (3rd ed. [DSM–III] was published) until 2005. Titles and abstracts were screened. References of the retrieved articles were searched. Book chapters on treatment of depression were retrieved. No special efforts were made to discover unpublished data. Figure A1 is a quorum flow diagram of the process and results of literature search.

To obtain a clinically rather homogeneous sample, several selection criteria were applied. To be included, the study should compare psychotherapy with pharmacotherapy and focus on efficacy of acute treatment (no maintenance treatment or sequential treatment). The study sample should consist of psychiatric outpatients (no primary care patients or inpatients), aged between 19 and 65 years (no geriatric patients or children), diagnosed with unipolar major depression according to DSM–III–R (American Psychiatric Association, 1980), DSM–IV–R (American Psychiatric Association, 1994), or research diagnostic criteria (Spitzer et al., 1978). Treatment protocols in the studies should apply a formal (according to behavioral, cognitive, psychodynamic, or client-centered theories and techniques), time-limited (maximum 6 months) individual psychotherapy and an adequate treatment with regular antidepressants (i.e., an adequate dose [different per antidepressant] administered during an adequate time period [at least 4 weeks] by a registered clinician). A regular antidepressant is approved as such by national authorities. Method sections were checked for the specifics of the treatment regimen, but no efforts were made to obtain additional information. The study should report remission rates and dropout rates. Methodological quality was judged according to four criteria of Cochrane Collaboration:

1. The study should have a randomized design to minimize selection bias.
2. Apart from the treatments, the two study groups must have been treated equally to minimize performance bias.
3. The study should report on selective dropout in the treatment conditions (e.g., have ITT analyses or specify differences in dropout).
4. Detection bias should be minimized by blind assessment of outcomes.

Two reviewers, who needed to agree on all criteria in order to include a study, judged all selection criteria independently. No studies were excluded because of reviewer disagreement.

The main outcome of the meta-analysis was efficacy at treatment termination, expressed in remission rates, and at follow-up, expressed in
Significant results (using was the natural approximate chi-square test; non-
the same quantity. The heterogeneity test we used
heterogeneity suggests that the studies are not estimating
different from each other than one would expect
among these studies. Statistical heterogeneity occurs
in the different studies. It is a
Statistical heterogeneity is the variability in the
treatment effects in the different studies. It is a
Statistical heterogeneity is the variability in the
remedies to treatment A to produce one recovery from
depression, which would not have occurred had they
been given treatment B. The dropout rates and
relapse rates were pooled calculating the relative risk.
Remission rates at treatment termination were
pooled in an ITT sample (i.e., a sample consisting
of all randomized patients). Relapse rates at follow-
up were pooled against all patients remitted at
treatment termination.

All data were analyzed using the Review Manager
4.2 software of the Cochrane Collaboration. Dichot-
omous data (relative risk and odds ratio) were
analyzed using the Mantel-Haenszel fixed-effects
model with 95% confidence intervals. Our analyses
included a formal test of statistical heterogeneity. Statistical heterogeneity is the variability in the
treatment effects in the different studies. It is a
consequence of clinical or methodological diversity
among these studies. Statistical heterogeneity occurs
when the observed treatment effects are more
different from each other than one would expect
based on random chance alone. Significant hetero-
geneity suggests that the studies are not estimating
the same quantity. The heterogeneity test we used
was the natural approximate chi-square test; non-
significant results (using $p = .10$ as a limit) indicate a
lack of evidence for heterogeneity in the results. The
test also describes the percentage of the variability in
effect estimates ($I^2$) resulting from heterogeneity
rather than to sampling error. An $I^2$ of more than
50% indicates notable heterogeneity (Cochrane Re-
vievers’ Handbook 8.7.2; Cochrane Collaboration,
2004).

All analyses were also performed in subsamples
regarding chronicity and severity of the depression.
First, studies regarding chronic depression (the
majority of patients were diagnosed as presenting
with depression lasting at least 2 years) were
differentiated from studies regarding nonchronic
depression. Second, using the mean baseline scores
on the 17-item Hamilton Depression Rating Scale
(HDRS; Hamilton, 1967), studies regarding mild
(12–19 points), moderate (20–24 points), and
severe (25 points or more) depression were differ-
etiated.

**Outcome of the Literature Search**

The quorum flow diagram in the Appendix shows
the process and results of the literature search.
Table I lists the studies considered suitable for our
review. As can be seen in Table I, our meta-analysis
is based on 10 studies that, taken together, include
1,233 patients (640 treated with pharmacotherapy
and 593 treated with psychotherapy). In Elkin et al.
(1989), there were two psychotherapy conditions
(cognitive–behavioral therapy [CBT] and interper-
sional therapy [IPT]). In Blackburn and Moore
(1997), there were two antidepressants groups. We
decided to combine the similar treatment groups in
these two studies. Entering two comparisons for
each study in the meta-analysis would violate the
assumption that all comparisons in a meta-analysis
should be independent (Cooper & Hedges, 1994).

**Chronic Versus Nonchronic Depression.** We found eight studies of nonchronic depression (Blackburn &
Bishop, 1981; Blackburn, Bishop, Glen, Whalley, &
Christie, 1981; Blackburn & Moore, 1997; Elkin
et al., 1989; Hautzinger, de Jong-Meyer, Treiber,
Rudolf, & Thien, 1996; Hollon et al., 1992;
Murphy, Carney, Knesevich, Wetzel, & Withworth,
1995; Murphy, Simons, Wetzel, & Lustman, 1984)
and three of chronic depression (DeRubeis et al.,
2005; Jarrett et al., 1999; Keller et al., 2000). In the
Keller study, 35% of the patients suffered from
chronic major depression, 42% from MDD plus
dysthymia, and 23% from recurrent depression
without complete remission between episodes,
which in our opinion signifies that all patients
suffered from chronic depression. In the DeRubeis
study, 90% of the patients had chronic or recurrent
depression. Mean duration of the last episode was
7.5 years in the Keller study, 46 months in the
DeRubeis study, and 73 months (in the psychother-
apy group) and 50 months (in the pharmacotherapy
group) in the Jarrett study.

**Mild Versus Moderate Depression.** Eight studies
provided 17-item HDRS mean baseline scores.
The Jarrett et al. study, however, used the 21-item
version and the Keller study the 24-item version. We
used the O’Sullivan, Fava, Agustin, Baer, and
Rosenbaum (1997) report to translate the 21- and
24-item scores into 17-item scores. The authors
found a ratio of 1.098 between the 21-item and 17-
item HDRS and a ratio of 1.25 between the 24-item
and 17-item HDRS. We calculated that the mean
baseline scores in the Jarrett et al. study, 21.1 points
(21.1/1.098) and 20.3 points (20.3/1.098) 17-item HDRS points, respectively.
Table I. Studies Included in the Meta-Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Duration/sessions</th>
<th>Pre-Tx HDRS(^a) post-Tx</th>
<th>Remission (n/N) (%)</th>
<th>Dropout (n/N) (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackburn et al. (1981)</td>
<td>Cognitive therapy (n = 17)</td>
<td>20 weeks/23</td>
<td>18.9 – 6.8</td>
<td>8/17 (47)</td>
<td>3/17 (18)</td>
<td>Combined therapy not included.</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (amitriptyline or clomipramine) (n = 16)</td>
<td>20 weeks</td>
<td>17.4 – 8.3</td>
<td>10/16 (63)</td>
<td>3/16 (19)</td>
<td>Outpatients only. Remission definition: HDRS ≤ 9, BDI ≤ 8. Relapse: At 24 months relapse is defined by physicians indicating symptoms that need treatment (Blackburn et al., 1986). Combined therapy and cognitive therapy + placebo conditions not included. Remission definition: HDRS ≤ 7. Relapse: BDI score &gt; 15 (Simons et al., 1986).</td>
</tr>
<tr>
<td>Elkin et al. (1989)</td>
<td>IP psychotherapy (n = 63)</td>
<td>16 weeks/16-20</td>
<td>19.6 – 9.8</td>
<td>26/63 (41)</td>
<td>16/63 (25)</td>
<td>Relapse: BDI score &gt; 15 separated by 1 week (Evans et al., 1992).</td>
</tr>
<tr>
<td></td>
<td>Cognitive therapy (n = 62)</td>
<td>16 weeks/16-20</td>
<td>19.6 – 10.7</td>
<td>21/62 (34)</td>
<td>25/62 (40)</td>
<td>Pharmacotherapy (nortriptyline) (n = 24)</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (imipramine) (n = 57)</td>
<td>16 weeks</td>
<td>19.5 – 9.8</td>
<td>24/63 (38)</td>
<td>26/63 (41)</td>
<td>Combined therapy not included. Remission definition: HDRS ≤ 6. Relapse: 2 DBI scores separated by 1 week (Evans et al., 1992).</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (imipramine) (n = 57)</td>
<td>12 weeks</td>
<td>23.8 – 14.2</td>
<td>19/57 (33)</td>
<td>25/57 (44)</td>
<td>Combined therapy not included. Remission definition: HDRS ≤ 6. Relapse: 2 DBI scores &gt; 15 separated by 1 week (Evans et al., 1992).</td>
</tr>
<tr>
<td>Murphy et al. (1995)</td>
<td>Cognitive therapy (n = 11)</td>
<td>16 weeks/20</td>
<td>15.7 – 2.27</td>
<td>11/11 (100)</td>
<td>0/11 (0)</td>
<td>Relapse: 2 DBI scores &gt; 15 separated by 1 week (Evans et al., 1992).</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (desipramine) (n = 12)</td>
<td>16 weeks</td>
<td>16.4 – 9.7</td>
<td>4/12 (33)</td>
<td>5/12 (42)</td>
<td>Combination therapy not included. Outpatients only. Remission definition: HDRS ≤ 6. Relapse: 2 DBI scores &gt; 15 separated by 1 week (Evans et al., 1992).</td>
</tr>
<tr>
<td>Hautzinger et al. (1996)</td>
<td>CBT (n = 40)</td>
<td>8 weeks/24</td>
<td>22.9 – 8.5 (c)</td>
<td>14/40 (35)</td>
<td>10/40 (25)</td>
<td>Only acute treatment phase included. Two pharmacotherapy groups are pooled. Remission definition: HDRS ≤ 6.</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (amitriptyline) (n = 38)</td>
<td>8 weeks</td>
<td>25.1 – 8.8 (c)</td>
<td>9/38 (24)</td>
<td>18/38 (47)</td>
<td>Pharmacotherapy (nortriptyline) (n = 24)</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (phenelzine) (n = 36)</td>
<td>10 weeks</td>
<td>20.3 – 8.6a</td>
<td>21/36 (58)</td>
<td>9/36 (25)</td>
<td>Pharmacotherapy (nortriptyline) (n = 24)</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (nefazodone) (n = 226)</td>
<td>12 weeks</td>
<td>26.8 – 14.7b</td>
<td>64/226 (28)</td>
<td>59/226 (26)</td>
<td>Pharmacotherapy (amitriptyline) (n = 38)</td>
</tr>
<tr>
<td>Hollon, DeRubeis et al. (2005)</td>
<td>Cognitive therapy (n = 60)</td>
<td>16 weeks/20-24</td>
<td>M baseline whole sample</td>
<td>24/60 (40)</td>
<td>9/60 (15)</td>
<td>Placebo condition not included. 90% of patients have chronic or recurrent depression. Remission definition: HDRS ≤ 7. Relapse: 2 weeks meeting criteria MDD or HDRS &gt; 13 (Hollon et al., 2005).</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy (paroxetine) (n = 120)</td>
<td>16 weeks</td>
<td>23.4</td>
<td>55/120 (46)</td>
<td>19/120 (16)</td>
<td>Pharmacotherapy (nortriptyline) (n = 24)</td>
</tr>
</tbody>
</table>

Note. HDRS = Hamilton Depression Rating Scale; BDI = Beck Depression Inventory; IP = interpersonal; Tx = treatment; RDC = research diagnostic criteria; MDD = major depressive disorder; CBT = cognitive–behavioral therapy; IDS = Inventory of Depressive Symptomatology.

\(^a\)21-item HDRS. \(^b\)24-item HDRS; modified intention to treat.
The mean baseline score of 27 points in the Keller study corresponds to 22 (27/1.25) 17-item HDRS points.

In all, we found five studies of (on average) mild depression (Blackburn et al., 1981; Elkin et al., 1989; Jarrett et al., 1999; Murphy et al., 1984, 1995) and five of (on average) moderate depression (Blackburn & Moore, 1997; DeRubeis et al., 2005; Hautzinger et al., 1996; Hollon et al., 1992; Keller et al., 2000). We did not find suitable studies regarding severe depression.

Follow-Up Studies. Six publications reported follow-up data. Hollon, DeRubeis, et al. (2005) add follow-up data to DeRubeis et al. (2005); Evans et al. (1992) to Hollon et al. (1992); Shea et al. (1992) to Elkin et al. (1989); Simons, Murphy, Levine, and Wetzel (1986) to Murphy et al. (1984); and Blackburn, Eunson, and Bishop (1986) to Blackburn et al. (1981). Hautzinger et al. (1996) report follow-up data in their own publication. Patients did not relapse if they (a) were remitted after acute treatment and (b) did not meet criteria for depression at follow-up. There were differences across studies in the definition of relapse (see Table I for the definitions of remission and relapse per study). In most studies, follow-up was naturalistic (i.e., there was no control for receiving treatment during follow-up). In three studies (Evans et al., 1992; Shea et al., 1992; Simons et al., 1986), the authors provided data on reentering treatment during follow-up. However, we based our analyses on the relapse data defined by cutoff scores or depression criteria and not on definitions that included “reentering treatment.” There were considerable differences between follow-up phases across studies. Follow-up durations varied from 1 year (Hautzinger et al., 1996; Hollon et al., 1992; Simons et al., 1986) to 1.5 year (Shea et al., 1992) and 2 years (Blackburn et al., 1986; Evans et al., 1992). In the Blackburn et al. study, treatment was continued for 6 months in the so-called follow-up period (anti-depressants at a normal regimen, psychotherapy at a 6-week booster session regimen). In the Shea et al. study, both pharmacotherapy and psychotherapy were gradually reduced in 4 to 6 weeks after termination. Furthermore, in this study, we combined the results of both psychotherapy conditions because entering two comparisons for each study in the meta-analysis would violate the assumption that all comparisons in a meta-analysis should be independent (Cooper & Hedges, 1994). In the follow-up data of Hautzinger et al., no differentiation was made between inpatients and outpatients. In Simons et al., medication was tapered before being discontinued at treatment termination. In Hollon et al., one medication group received a placebo after treatment termination, whereas the other group continued medication. We included only the first group in our analysis. Patients who had been treated with psychotherapy in the Hollon et al. study received three booster sessions. The Evans et al. study had a medication continuation group and a noncontinuation group. We included only the latter in our meta-analysis.

Results

Dropout Rates

The dropout rates are shown in Figure 1. As can be seen, the pooled dropout rate in pharmacotherapy (28.43%) is larger than that in psychotherapy (23.6%). The difference (4.83%) is statistically significant (RR = 1.29, p = .009). The chi-square test of heterogeneity indicates a lack of evidence for heterogeneity (p = 0.73 and I² = 0%).

<table>
<thead>
<tr>
<th>Study</th>
<th>Pharmacotherapy n/N</th>
<th>Psychotherapy n/N</th>
<th>RR (fixed)</th>
<th>Weight %</th>
<th>RR (fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackburn, 1981</td>
<td>3/16</td>
<td>3/17</td>
<td>2.17</td>
<td>1.06</td>
<td>1.06 [0.25, 4.52]</td>
</tr>
<tr>
<td>Murphy, 1984</td>
<td>8/24</td>
<td>5/24</td>
<td>3.74</td>
<td>1.60</td>
<td>1.60 [0.61, 4.19]</td>
</tr>
<tr>
<td>Elkin, 1989</td>
<td>26/63</td>
<td>41/125</td>
<td>20.54</td>
<td>2.65</td>
<td>2.65 [0.75, 9.64]</td>
</tr>
<tr>
<td>Hollon, 1992</td>
<td>25/57</td>
<td>3/25</td>
<td>9.35</td>
<td>1.22</td>
<td>1.22 [0.67, 2.22]</td>
</tr>
<tr>
<td>Murphy, 1995</td>
<td>5/12</td>
<td>0/11</td>
<td>0.39</td>
<td>10.15</td>
<td>10.15 [0.63, 164.77]</td>
</tr>
<tr>
<td>Hautzinger, 1996</td>
<td>18/38</td>
<td>10/40</td>
<td>7.28</td>
<td>1.89</td>
<td>1.89 [1.01, 3.57]</td>
</tr>
<tr>
<td>Blackburn, 1997</td>
<td>10/48</td>
<td>3/27</td>
<td>2.87</td>
<td>1.88</td>
<td>1.88 [0.56, 6.23]</td>
</tr>
<tr>
<td>Jarrett, 1999</td>
<td>5/36</td>
<td>5/36</td>
<td>3.74</td>
<td>1.80</td>
<td>1.80 [0.67, 4.85]</td>
</tr>
<tr>
<td>Keller, 2000</td>
<td>59/226</td>
<td>59/228</td>
<td>40.94</td>
<td>1.08</td>
<td>1.08 [0.79, 1.49]</td>
</tr>
<tr>
<td>DeRubeis, 2005</td>
<td>19/120</td>
<td>9/60</td>
<td>8.97</td>
<td>1.06</td>
<td>1.06 [0.51, 2.19]</td>
</tr>
</tbody>
</table>

Total (95% CI): 640/593

Test for heterogeneity: significance (p = 0.009). The chi-square test of heterogeneity indicates a lack of evidence for heterogeneity (p = 0.73 and I² = 0%).

Figure 1. Relative risk of dropout in psychotherapy versus pharmacotherapy.
Efficacy at Treatment Termination

Relative Risk of Remission. Figure 2 shows the remission rates and relative risk for remission. As can be seen, the pooled remission rate for psychotherapy (37.94%) is somewhat larger than for pharmacotherapy (34.84%), but the difference (3.1%) is not statistically significant (pooled RR = 0.91, p = .24). The chi-square test of heterogeneity indicates a lack of evidence for heterogeneity (p = .23 and I² = 23.7%).

Chronicity. Table II separately shows the relative risk for remission in the three studies of chronic depression and the eight studies of nonchronic depression. As can be seen, the pooled remission rates of psychotherapy and pharmacotherapy do not differ significantly in chronic depression (36.11% and 36.64%, respectively, p = .83) and in nonchronic depression (41.14% and 32.17%, respectively, p = .12). In both analyses, the chi-square test of heterogeneity indicates that there is no evidence for heterogeneity (nonchronic: p = 0.14/I² = 38%; chronic: p = .58/I² = 0%). It also appears that the pooled remission rates of chronic and nonchronic depression do not differ significantly for psychotherapy (36.11% and 41.14%, respectively, p = .31) and pharmacotherapy (36.64% and 32.17%, respectively, p = .25). In the last two analyses, heterogeneity was not an issue because we made only one comparison between two groups of studies.

Severity. Table III separately shows the relative risk for remission in the five studies of mild depression and the five studies of moderate depression. The pooled remission rates of psychotherapy and pharmacotherapy do not differ significantly in mild depression (46.47% and 44.37%, respectively, p = .34) and moderate depression (33.15% and 31.90%, respectively, p = .44). In the analysis of moderate depression, no evidence for heterogeneity was found (p = .55/I² = 0%), but in the analysis of mild depression the chi-square test of heterogeneity indicated moderate heterogeneity (p = .07/I² = 54.3%). This is possibly due to the outlying results of Murphy et al. (1984), which, compared with the other studies, show a larger difference in remission between psychotherapy (100%) versus pharmacotherapy (33%). The pooled remission rates of mild and moderate depression do differ significantly both for psychotherapy (46.47% and 33.15%, respectively, p = .001) and pharmacotherapy (44.37% and 31.90%, respectively, p = .003). In the last two analyses, heterogeneity was not an issue because we made only one comparison between two groups of studies.

Odds Ratio of Remission. Figure 3 shows the odds ratios for remission. The pooled OR is 0.87, and the difference between pharmacotherapy and psychotherapy is not statistically significant (p = .24). The chi-square test of heterogeneity indicates no evidence for heterogeneity (p = .30 and I² = 16%).

The odds ratios in subanalyses regarding chronicity and severity of depression do not indicate any statistically significant differences between the two treatments in chronic (p = .82) and nonchronic (p = .12) depression or in mild (p = .35) and moderate (p = .44) depression. All chi-square tests indicate a lack of evidence for heterogeneity (ps = .58, .17, .10, and .58, respectively).

Numbers Needed to Treat

Pooled data show that 32 patients would need to be treated with psychotherapy to produce one recovery from depression, which would not have occurred had they been given antidepressants (NNT = 32; 1/0.031).

![Figure 2. Relative risk of remission in psychotherapy versus pharmacotherapy.](image-url)
Efficacy at Follow-Up

Figure 4 shows the relative risk of relapse during follow-up. There is a statistically significant difference (RR = 0.46, p < .0001) between the pooled relapse rate of pharmacotherapy (56.56%) and that of psychotherapy (26.51%). The chi-square test of heterogeneity indicates that the results lack evidence of heterogeneity (p = .68, I² = 0%). Because there was considerable clinical heterogeneity in the follow-up phases across studies, we performed various analyses on subgroups of studies. First, we excluded the study of Hollon, Jarrett, et al. (2005). We consider it an outlier because the patients treated with medication received placebos throughout the follow-up period. Second, we discriminated between follow-up durations (combining the studies with 1-year follow-up and combining studies with 1.5- to 2-year follow-ups). All subanalyses showed results similar to those of the overall analysis (i.e., a significant difference in favor of psychotherapy). The homogeneity hypothesis was not rejected in any of these analyses.

Discussion

We performed a meta-analysis comparing psychotherapy and pharmacotherapy in the treatment of adult psychiatric outpatients suffering from mild to moderate major depression. In contrast to existing reviews, our meta-analysis furthered homogeneity of the included studies by applying strict clinical inclusion and exclusion criteria. We performed statistical tests a posteriori supporting our argument that the included studies were indeed sufficiently homogeneous. In addition, we took into account two potential determinants of treatment prognosis by performing subanalyses on chronicity and severity of depression.

Psychotherapy and pharmacotherapy appeared equally effective at treatment termination. This means that in the long-standing controversy regarding the relative effectiveness of both treatment modalities, our results support the “no difference” point of view.

According to clinical lore, chronicity and severity influence the relative effectiveness of the two therapeutic modalities. However, we found no differences in efficacy between both treatments in chronic and nonchronic depression and in mild and moderate depression. Understandably, but unfortunately, we found no data regarding severe depression.

Our results show that severity, in contrast to chronicity, affects the efficacy of both treatments. They have superior results in mild depression compared with moderate depression. This may indicate that monotherapies are not the first choice in moderate depression (HDRS > 20). This hypothesis is supported by the findings of Thase et al. (1997), who report a statistically significant and clinically relevant difference in favor of combined therapy over psychotherapy in more severe (HDRS > 19), but not less severe (HDRS < 20), depression. Several reviews and meta-analyses (Friedman et al., 2004; Hegerl, Plattner, & Möller, 2004; Hollon et al., 1992; Jarrett et al., 2005; Pampallona, Bollini, Tibaldi, Kupelnick, & Munizza, 2004) report superior results of combined treatment compared with medication alone, especially for more severely depressed patients.

The parity in efficacy found at treatment termination does not seem to last beyond actual treatment.

Table II. ITT Remission Rates in Studies of Chronic a and Nonchronic b Depression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Psychotherapy</th>
<th>Pharmacotherapy</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies of chronic depression</td>
<td>36.11%</td>
<td>36.64%</td>
<td>RR = 0.98, p = .83</td>
</tr>
<tr>
<td>Studies of nonchronic depression</td>
<td>41.14%</td>
<td>32.17%</td>
<td>RR = 0.83, p = .12</td>
</tr>
<tr>
<td>Significance</td>
<td>RR = 0.90, p = .31</td>
<td>RR = 1.14, p = .25</td>
<td></td>
</tr>
</tbody>
</table>

Note. ITT = intention to treat; RR = relative risk.

aJarrett et al., 1999; Keller et al., 2000; DeRubeis et al., 2005. bBlackburn et al., 1981; Murphy et al., 1984; Elkin et al., 1989; Hollon et al., 1992; Murphy et al., 1995; Hautzinger et al., 1996; Blackburn & Moore, 1997.

Table III. ITT Remission Rates in Studies of Mild a and Moderate b Depression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Psychotherapy</th>
<th>Pharmacotherapy</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies of mild depression</td>
<td>46.47%</td>
<td>44.37%</td>
<td>RR = 0.90, p = .34</td>
</tr>
<tr>
<td>Studies of moderate depression</td>
<td>33.15%</td>
<td>31.90%</td>
<td>RR = 0.92, p = .44</td>
</tr>
<tr>
<td>Significance</td>
<td>RR = 1.40, p = .001</td>
<td>RR = 1.39, p = .003</td>
<td></td>
</tr>
</tbody>
</table>

Note. ITT = intention to treat; RR = relative risk.

aBlackburn et al., 1981; Murphy et al., 1984, 1995; Elkin et al., 1989; Jarrett et al., 1999. bHollon et al., 1992; Hautzinger et al., 1996; Blackburn & Moore, 1997; Keller et al., 2000; DeRubeis et al., 2005.
Our follow-up data show that twice as many patients relapse after pharmacotherapy termination than after psychotherapy termination. According to our results, the idea that short-term therapies yield short-lived effects applies more to pharmacotherapy than to psychotherapy. The difference might even be larger than presented here, because in two of the six follow-up studies we included (Blackburn et al., 1986; Hollon et al., 1992) the study design seems to favor pharmacotherapy above psychotherapy. In the Blackburn et al. study, pharmacotherapy was continued for 6 months, whereas psychotherapy was provided only at a 6-weekly booster session regimen. In the Hollon et al. study, medication was substituted by placebo during the follow-up period, whereas patients treated with psychotherapy received only three booster sessions. Furthermore, in the Evans et al. and Simons et al. studies, more pharmacotherapy patients than psychotherapy patients sought treatment during follow-up, possibly indicating a relapse that was not accounted for in our relapse data. Our findings regarding relapse are comparable to those reported in the reviews of Hollon, Jarrett, et al. (2005) and Gloaguen et al. (1998). In addition, the follow-up studies of Hollon, DeRubeis, et al. (2005) and Evans et al. (1992) show that psychotherapy patients are no more likely to relapse than pharmacotherapy patients who keep taking medication. In our opinion, our relapse data, apart from obvious clinical implications, are highly relevant for establishing cost–benefit ratios, a topic that is not addressed in this review nor in the included RCTs.

We found that dropout rates in pharmacotherapy are significantly higher than in psychotherapy, although the difference (5%) is not impressive. As researchers and clinicians alike know, medication nonadherence is a major problem in pharmacotherapy. Still, psychotherapy too is beset with the problem of noncompliance, because 20% to 25% of patients drop out.

Our review has several limitations. First, conclusions based only on the results of RCTs have well-known limitations. An obvious one is selection bias. RCTs leave patients with serious comorbidity, such as drug dependence, suicide intentions, or severe personality disorders, out of scope. In fact, the majority of suitable patients do not end up in RCTs as a result of all inclusion and exclusion criteria that have to be met. Keitner, Posternak, and

<table>
<thead>
<tr>
<th>Study</th>
<th>Pharmacotherapy n/N</th>
<th>Psychotherapy n/N</th>
<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackburn, 1981</td>
<td>10/16</td>
<td>8/17</td>
<td>2.05 1.88 [0.54, 7.53]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murphy, 1984</td>
<td>8/24</td>
<td>12/24</td>
<td>5.64 0.50 [0.16, 1.61]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elkin, 1989</td>
<td>24/63</td>
<td>47/125</td>
<td>13.75 1.02 [0.55, 1.91]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hollon, 1992</td>
<td>19/57</td>
<td>8/25</td>
<td>5.23 1.06 [0.39, 2.90]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murphy, 1995</td>
<td>4/12</td>
<td>11/11</td>
<td>5.51 0.02 [0.00, 0.49]</td>
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<td></td>
</tr>
<tr>
<td>Hautzinger, 1996</td>
<td>9/38</td>
<td>14/40</td>
<td>7.34 0.58 [0.12, 1.55]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blackburn, 1997</td>
<td>9/48</td>
<td>8/27</td>
<td>5.87 0.55 [0.18, 1.64]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jarrett, 1999</td>
<td>21/36</td>
<td>21/36</td>
<td>6.17 1.00 [0.39, 2.55]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keller, 2000</td>
<td>64/226</td>
<td>72/228</td>
<td>36.23 0.86 [0.57, 1.28]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeRubeis, 2005</td>
<td>55/120</td>
<td>24/60</td>
<td>12.22 1.27 [0.68, 2.38]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 640 593 100.00 0.87 [0.68, 1.10]

Test for heterogeneity: Chi² = 10.72, df = 9 (P = 0.30), I² = 16.0%
Test for overall effect: Z = 1.18 (P = 0.24)

Figure 3. Odds ratio of remission rates of psychotherapy versus pharmacotherapy.

DeRubeis, et al. (2005) and Evans et al. (1992) show that psychotherapy patients are no more likely to relapse than pharmacotherapy patients who keep taking medication. In our opinion, our relapse data, apart from obvious clinical implications, are highly relevant for establishing cost–benefit ratios, a topic that is not addressed in this review nor in the included RCTs.

We found that dropout rates in pharmacotherapy are significantly higher than in psychotherapy, although the difference (5%) is not impressive. As researchers and clinicians alike know, medication nonadherence is a major problem in pharmacotherapy. Still, psychotherapy too is beset with the problem of noncompliance, because 20% to 25% of patients drop out.

Our review has several limitations. First, conclusions based only on the results of RCTs have well-known limitations. An obvious one is selection bias. RCTs leave patients with serious comorbidity, such as drug dependence, suicide intentions, or severe personality disorders, out of scope. In fact, the majority of suitable patients do not end up in RCTs as a result of all inclusion and exclusion criteria that have to be met. Keitner, Posternak, and

<table>
<thead>
<tr>
<th>Study</th>
<th>Psychotherapy n/N</th>
<th>Pharmacotherapy n/N</th>
<th>RR (fixed) 95%CI</th>
<th>Weight %</th>
<th>RR (fixed) 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shea, 1992</td>
<td>16/44</td>
<td>9/18</td>
<td>20.98 0.73 [0.40, 1.33]</td>
<td></td>
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</tr>
<tr>
<td>Evans, 1992</td>
<td>2/10</td>
<td>5/10</td>
<td>8.21 0.40 [0.10, 1.60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simons, 1986</td>
<td>2/10</td>
<td>1/9</td>
<td>2.58 0.30 [0.01, 6.62]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hautzinger, 1996</td>
<td>5/27</td>
<td>8/19</td>
<td>15.43 0.44 [0.17, 1.14]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blackburn, 1986</td>
<td>1/6</td>
<td>6/8</td>
<td>8.45 0.22 [0.04, 1.39]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hollon, 2005</td>
<td>11/35</td>
<td>27/35</td>
<td>44.35 0.41 [0.24, 0.69]</td>
<td></td>
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</table>

Total (95%CI) 132 99 100.00 0.46 [0.33, 0.65]

Test for heterogeneity: Chi² = 3.13, df = 5 (P = 0.68), I² = 0%
Test for overall effect: Z = 4.38 (P < 0.0001)

Figure 4. Relative risk of relapse rates.
Ryan (2003), for example, mention that only 14.5% of eligible depressed patients eventually took part in an RCT. Second, our meta-analysis only compares psychotherapy with pharmacotherapy, leaving comparisons with combined therapy out of scope. Third, efficacy was measured with the HDRS only. Most of the studies we found did not assess social functioning or quality of life, which are the ultimate goals of therapy. Some studies measured depression with other scales, such as the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). Because it was not our aim to compare scales, and we used the HDRS as inclusion criterion, we did not perform a meta-analysis on the BDI. However, it certainly would be interesting to perform meta-analyses based on both scales. Fourth, the methodological quality of the included studies varied. Some studies of actual treatment (Blackburn et al., 1981; Murphy et al., 1995) and all follow-up studies were characterized by small sample sizes, lacking statistical power to detect differences. Although some studies (e.g., the Keller study) controlled for medication compliance, most did not. In short, only the two more recent studies (Hegerl et al., 2004; Sackett, 1998) correspond well to actual research criteria. Fifth, allegiance effects (Gaffan, Tsaousis, & Kemp-Wheeler, 1995) cannot be excluded.

Perhaps more important than these limitations is that we based our conclusions concerning severity of depression on mean baseline scores of the studies, not on individual patient data. We are aware that this is a rather rough division of a spectrum. Nevertheless, our results do not seem to diverge from the two more recent studies (Hegerl et al., 2004; Sackett, 1998) correspond well to actual research criteria. Fifth, allegiance effects (Gaffan, Tsaousis, & Kemp-Wheeler, 1995) cannot be excluded.

We conclude that depressed patients profit equally from psychotherapy and pharmacotherapy after short-term treatment. Furthermore, it may be concluded that they seem to benefit more from psychotherapy than from pharmacotherapy during the 1- to 2-year follow-up period.

References

References marked with an asterisk indicate studies included in the meta-analysis.


Efficacy of psychotherapy and pharmacotherapy for depression


**Appendix**

Potentially relevant RCT’s identified in literature search and screened for retrieval ($n = 1,601$)

RCT’s relevant for more detailed evaluation ($n = 75$)

Second screening of publications retrieved and screened ($n = 26$)

RCT’s included in meta-analysis ($n = 10$)

RCT’s excluded based on screening of titles and abstracts ($n = 1,526$)

Publications excluded based on primary care ($n = 5$), age ($n = 5$), design ($n = 15$), therapy ($n = 12$), inpatients ($n = 6$), other ($n = 8$). Total: 49

Publications excluded based on therapy ($n = 6$), inpatients ($n = 2$), double publication ($n = 2$), methodological ($n = 6$). Total: 16

Figure A1. Quorum flow diagram.
Zusammenfassung

Die relative Effizienz von Psychotherapie und Pharmakotherapie bei der Behandlung von Depressionen: Eine Meta-Analyse


Résumé

L’efficacité respective de la psychothérapie et de la pharmacothérapie dans le traitement de la dépression : une méta-analyse

Nous avons investigué l’efficacité de la pharmacothérapie et de la psychothérapie de la dépression en récoltant des RCTs. Les études étaient classées en fonction de la chronicité et de la sévérité pour être soumises à une méta-analyse. Dix études étaient inclues. La rémission était la même entre psychothérapie (38%) et pharmacothérapie (35%). Le facteur chronicité comme la distinction entre dépression légère et moyenne n’aboutissaient pas à des différences entre les approches. Les deux traitements obtenaient de meilleurs résultats pour la dépression légère que la dépression moyenne. L’arrêt précoce était plus fréquent dans la pharmacothérapie (28%) que dans la psychothérapie (24%). A la katamnèse, la rechute était plus fréquente après la pharmacothérapie (57%) qu’après la psychothérapie (27%). La psychothérapie et la pharmacothérapie semblent avoir la même efficacité dans le traitement de la dépression. Les deux traitements sont plus efficaces dans la dépression légère, ne se distinguent pas pour ce qui concerne les dépressions chroniques et non-chroniques, et sur le plan katamnestique, la psychothérapie s’avère plus puissante que la pharmacothérapie.

Resumen

Eficacia relativa de la psicoterapia y la farmacoterapia en el tratamiento de la depresión.

Un meta-análisis

Hemos investigado la eficacia de la fármacoterapia y la psicoterapia para la depresión por medio de los RCT. Los estudios se clasificaron de acuerdo con la cronicidad y severidad de los casos y se les aplicó metaanálisis. Se incluyeron diez estudios. La remisión no difirió entre psicoterapia (38%) y fármacoterapia (35%). No se encontraron diferencias entre la depresión crónica y la no crónica ni entre la leve y la moderada. Ambos tratamientos fueron más efectivos en la depresión leve que en la moderada. El abandono fue mayor en la fármacoterapia (28%) que en la psicoterapia (24%). En el seguimiento, la recaída fue mayor en fármacoterapia (57%) que en psicoterapia (27%). La psicoterapia y la fármacoterapia aparecen como igualmente eficaces en la depresión. Ambos tratamientos tienen mayores efectos en la depresión leve que en la moderada pero efectos similares en la depresión crónica y no crónica y en el seguimiento la psicoterapia supera a la fármacoterapia.

Resumo

A eficácia relativa da psicoterapia e da farmacoterapia no tratamento da depressão: uma meta-análise

Investigámos a eficácia da farmacoterapia e da psicoterapia para a depressão procurando ensaios clínicos randomizados (ECR). Os estudos foram classificados de acordo com a cronicidade e severidade e aplicou-se uma meta-análise. Foram incluídos dez estudos. A taxa de remissão não foi diferente na psicoterapia (38%) e na farmacoterapia (35%). Não se encontraram diferenças na depressão crónica ou não crónica nem na depressão leve ou moderada. Ambos os tratamentos obtiveram melhores resultados com depressões leves do que em moderadas. Os níveis de abandono foram mais elevados na farmacoterapia (28%) que na psicoterapia (24%). No seguimento (follow-up) há mais recaídas com a farmacoterapia (57%) do que com a psicoterapia (27%). A psicoterapia e a farmacoterapia parecem ser igualmente eficazes na depressão. Ambos os tratamentos possuem maiores efeitos na depressão leve que na moderada, mas efeitos similares na depressão crónica e não-crónica, e no seguimento (follow-up) a psicoterapia é mais eficaz que a farmacoterapia.

Sommaio

Rispettiva efficacia della psicoterapia e farmacoterapia nel trattamento della depressione: una meta-analisi

Abbiamo studiato l’efficacia della farmacoterapia e della psicoterapia per la depressione cercando studi di RCT. Gli
studi erano classificati secondo la cronicità e la gravità e
un’meta-analisi.
Erano inclusi dieci studi. La remissione non ha differito
fra la psicoterapia (38%) e la farmacoterapia (35%).
Nessuna differenza è stata trovata nei cronici, o nella
depressione non cronica, lieve o moderata. Entrambi i
trattamenti hanno prestazioni migliori nella forma lieve
che nella depressione moderata. Il dropout era maggiore
nel trattamento farmacoterapico (28%) che in quello
psicoterapico (24%). Al follow-up la percentuale di
ricaduta in farmacoterapia (57%) era superiore alla
psicoterapia (27%). La psicoterapia e la farmacoterapia
sembrano ugualmente efficaci nella cura della depressione.
Entrambi i trattamenti hanno effetti più grandi nella forma
lieve che nella depressione moderata, ma nella depressione
cronica e non cronica, al follow-up, la psicoterapia fornisce
risultati migliori rispetto alla farmacoterapia.

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