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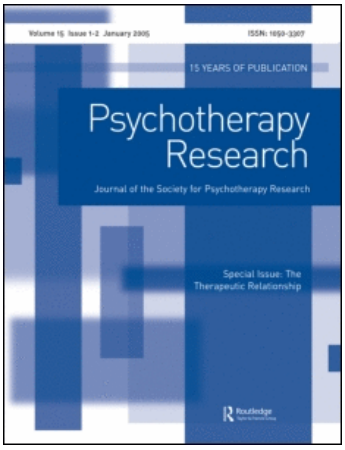

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Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: A meta-analysis

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Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: A meta-analysis

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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

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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 nonpsychotic 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

relapse rates. Remission rates were pooled calculating the relative risk (RR) and the odds ratio (OR). The relative risk is the ratio between the risks of an event (e.g., remission) in group A and in group B. The odds ratio is the ratio between two odds: the odds on an event in group A and the odds on the same event in group B. Both an odds ratio and a relative risk amounting to 1 signify that there is no difference between the two treatments. Numbers needed to treat (NNT) were calculated, indicating the number of patients who would need to be treated with 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. Dichotomous 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 heterogeneity suggests that the studies are not estimating the same quantity. The heterogeneity test we used was the natural approximate chi-square test; nonsignificant 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 Reviewers' 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 differentiated.

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 interpersonal 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 psychotherapy 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 (psychotherapy) and 20.3 points (pharmacotherapy), correspond to 19 (21.1/1.098) and 18 (20.3/1.098) 17-item HDRS points, respectively.

Table I. Studies Included in the Meta-Analysis

Study	Treatment	Duration/sessions	Pre-Tx HDRS[a] – post-Tx	Remission (*n*/*N*) (%)	Dropout (*n*/*N*) (%)	Comment
Blackburn et al. (1981)	Cognitive therapy ($n=17$)	20 weeks/23	18.9–6.8	8/17 (47)	3/17 (18)	Combined therapy not included.
	Pharmacotherapy (amitriptyline or clomipramine) ($n=16$)	20 weeks	17.4–8.3	10/16 (63)	3/16 (19)	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).
Murphy et al. (1984)	Cognitive therapy ($n=24$)	12 weeks/20	18.8–7.7	12/24 (50)	5/24 (21)	Combined therapy and cognitive therapy + placebo conditions not included. Remission definition: HDRS ≤7. Relapse: BDI score >15 (Simons et al., 1986).
	Pharmacotherapy (nortriptyline) ($n=24$)	12 weeks	20.9–10.9	8/24 (33)	8/24 (33)	
Elkin et al. (1989)	IP psychotherapy ($n=63$)	16 weeks/16–20	19.6–9.8	26/63 (41)	16/63 (25)	Placebo Tx condition not included. Remission definition: HDRS ≤6. Relapse: 2 weeks symptoms meeting RDC for MDD (Shea et al., 1992).
	Cognitive therapy ($n=62$)	16 weeks/16–20	19.6–10.7	21/62 (34)	25/62 (40)	
	Pharmacotherapy (imipramine) ($n=57$)	16 weeks	19.5–9.8	24/63 (38)	26/63 (41)	
Hollon et al. (1992)	Cognitive therapy ($n=25$)	12 weeks/20	24.1–13.3	8/25 (32)	9/25 (36)	Combined therapy not included. Remission definition: HDRS ≤6. Relapse: 2 DBI scores >15 separated by 1 week (Evans et al., 1992).
	Pharmacotherapy (imipramine) ($n=57$)	12 weeks	23.8–14.2	19/57 (33)	25/57 (44)	
Murphy et al. (1995)	Cognitive therapy ($n=11$)	16 weeks/20	15.7–2.27	11/11 (100)	0/11 (0)	Relaxation therapy condition not included. Remission definition: HDRS ≤7.
	Pharmacotherapy (desipramine) ($n=12$)	16 weeks	16.4–9.70	4/12 (33)	5/12 (42)	
Hautzinger et al. (1996)	CBT ($n=40$)	8 weeks/24	22.9–8.5 (c)	14/40 (35)	10/40 (25)	Combination therapy not included. Outpatients only. Remission definition: BDI & HDRS ≤9. Relapse: IDS score >29.
	Pharmacotherapy (amitriptyline) ($n=38$)	8 weeks	25.1–8.8 (c)	9/38 (24)	18/38 (47)	
Blackburn & Moore (1997)	Cognitive therapy ($n=27$)	16 weeks/16	19.9–10.7	8/27 (30)	3/27 (11)	Only acute treatment phase included. Two pharmacotherapy groups are pooled. Remission definition: HDRS ≤6.
	Pharmacotherapy (physician choice) ($n=48$)	16 weeks	20.2–11.4 20.8–13.3	9/48 (19)	10/48 (21)	
Jarrett et al. (1999)	Cognitive therapy ($n=36$)	10 weeks/20	21.1–10.2[a]	21/36 (58)	5/36 (14)	Placebo condition not included. Study considered atypical depression. Remission definition: HDRS ≤9.
	Pharmacotherapy (phenelzine) ($n=36$)	10 weeks	20.3–8.6[a]	21/36 (58)	9/36 (25)	
Keller et al. (2000)	Cognitive–behavioral analysis system ($n=228$)	12 weeks/16–20	26.4–15.1[b]	72/228 (32)	55/228 (24)	Combined therapy not included. Study considered chronic depression. Remission definition: HDRS ≤8.
	Pharmacotherapy (nefazodone) ($n=226$)	12 weeks	26.8–14.7[b]	64/226 (28)	59/226 (26)	
Hollon, DeRubeis et al. (2005)	Cognitive therapy ($n=60$)	16 weeks/20–24	*M* baseline whole sample: 23.4	24/60 (40)	9/60 (15)	Placebo condition not included. 90% of patients have chronic or recurrent depression. Remission definition: HDRS ≤7. Relapse: 2 weeks meeting criteria MDD or HDRS >13 (Hollon et al., 2005).
	Pharmacotherapy (paroxetine) ($n=120$)	16 weeks		55/120 (46)	19/120 (16)	

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 (antidepressants at a normal regimen, psychotherapy at a 6-weekly 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 $I^2 = 0\%$).

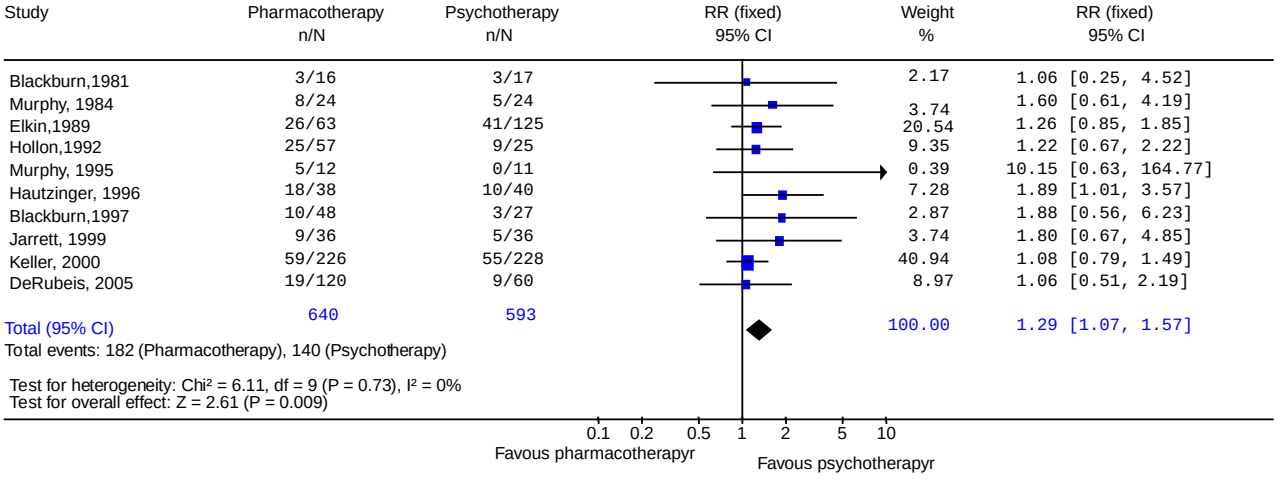

Figure 1. Relative risk of dropout in psychotherapy versus pharmacotherapy.

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 $I^2 = 23.7\%$).

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: $p = 0.14/I^2 = 38\%$; chronic: $p = .58/I^2 = 0\%$). 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 ($p = .55/I^2 = 0\%$), but in the analysis of mild depression the chi-square test of heterogeneity indicated moderate heterogeneity ($p = .07/I^2 = 54.3\%$). 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 $I^2 = 16\%$).

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).

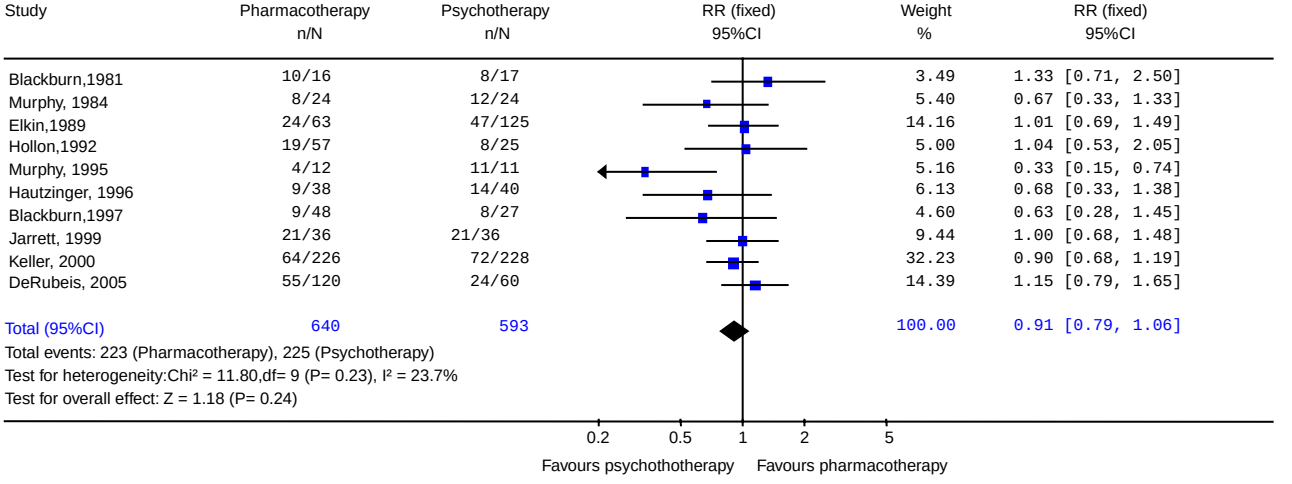

Figure 2. Relative risk of remission in psychotherapy versus pharmacotherapy.

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

Variable	Psychotherapy	Pharmacotherapy	Significance
Studies of chronic depression	36.11%	36.64%	RR = 0.98, $p = .83$
Studies of nonchronic depression	41.14%	32.17%	RR = 0.83, $p = .12$
Significance	RR = 0.90, $p = .31$	RR = 1.14, $p = .25$	

Note. ITT = intention to treat; RR = relative risk.
[a]Jarrett et al., 1999; Keller et al., 2000; DeRubeis et al., 2005. [b]Blackburn 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.

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 ($p = .68$, $I^2 = 0\%$). 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, Jarrett, et al., 2005; Pampallona, Bollini, Tibaldi, Kupelnick, & Munizza, 2004) report superior results of combined treatment compared with medication alone, especially for more severe depressed patients.

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

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

Variable	Psychotherapy	Pharmacotherapy	Significance
Studies of mild depression	46.47%	44.37%	RR = 0.90, $p = .34$
Studies of moderate depression	33.15%	31.90%	RR = 0.92, $p = .44$
Significance	RR = 1.40, $p = .001$	RR = 1.39, $p = .003$	

Note. ITT = intention to treat; RR = relative risk.
[a]Blackburn et al., 1981; Murphy et al., 1984, 1995; Elkin et al., 1989; Jarrett et al., 1999. [b]Hollon et al., 1992; Hautzinger et al., 1996; Blackburn & Moore, 1997; Keller et al., 2000; DeRubeis et al., 2005.

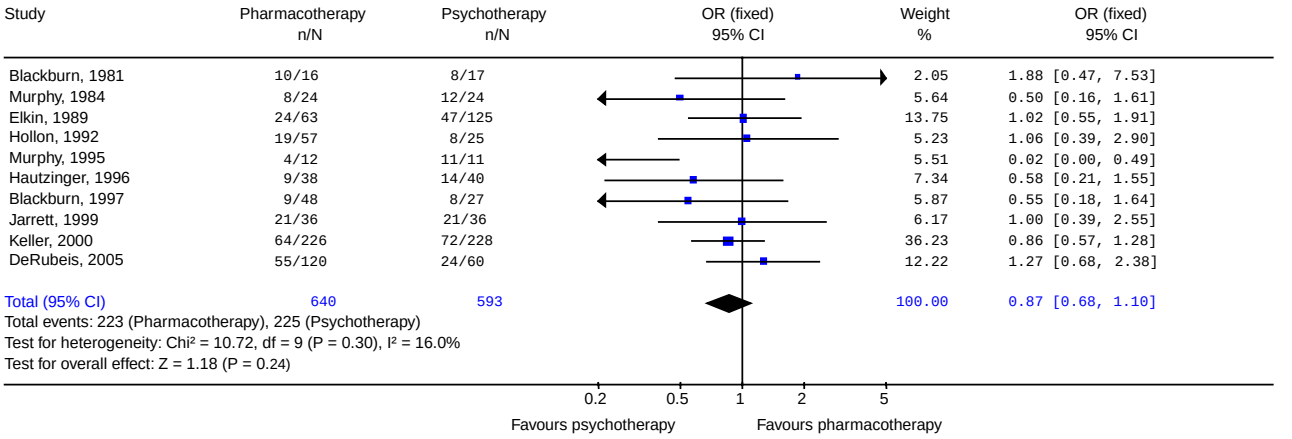

Figure 3. Odds ratio of remission rates of psychotherapy versus pharmacotherapy.

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

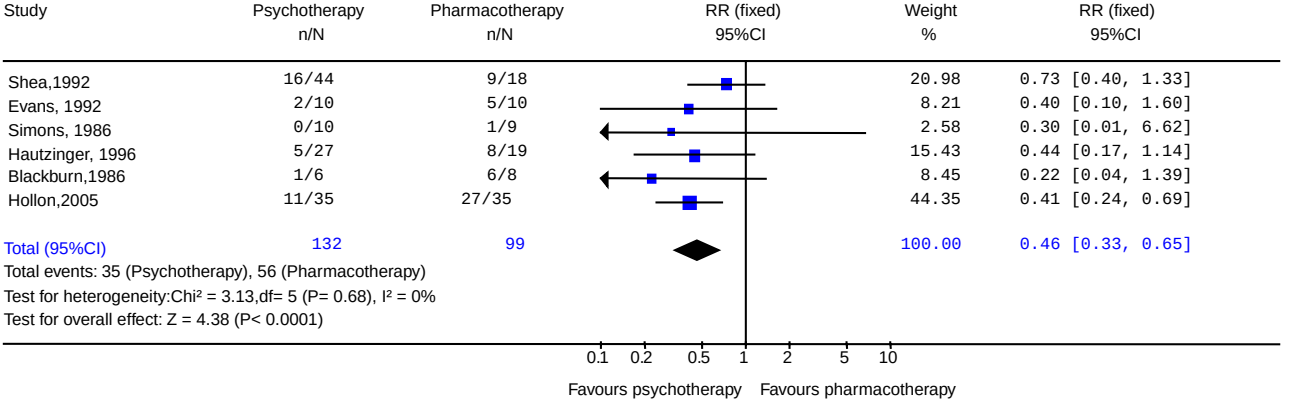

Figure 4. Relative risk of relapse rates.

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 findings based on individual patients. Blackburn and Moore (1997), Hollon et al. (1992), Hautzinger et al. (1996), and Elkin et al. (1989) performed subanalyses on severity. They too did not find significant differences between psychotherapy and pharmacotherapy in less severe (HDRS <20) and more severe (HDRS >19) depressed patients. Our HDRS cutoff scores for the distinction among mild, moderate, and severe depression are in accordance with what is mostly found in literature. Unfortunately, Hamilton did not define cutting scores for his scale. The result is that there are no generally accepted definitions of mild, moderate, and severe depression. According to clinical lore, mild depression and moderate depression range, respectively, from 12–14 to 18–20 and from 18–20 to 24–26 HDRS points (17-tem version).

Finally, although our approach explicitly aimed to further homogeneity, it cannot be denied that the included studies still present some heterogeneity. Psychotherapy includes cognitive therapy and interpersonal therapy; pharmacotherapy includes tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs). The importance of this point, however, may be limited because meta-analytic studies found no significant differences between TCAs and SSRIs (Anderson, 2000) or between psychodynamic therapy and CBT (Leichsenring, 2001) in the treatment of depressed outpatients. Only one study in our meta-analysis considered IPT; the remaining studies applied CBT. Therefore, it may be argued that our conclusions do not merit psychotherapy per se but apply mainly to cognitive therapy. Treatment durations varied, and, although the differences in psychotherapy sessions across studies are limited, the efficacy of pharmacotherapy might be somewhat weighted down by studies with relatively short treatment periods (e.g., Hautzinger et al., 1996). The definition of remission differs per study, with cutoff scores varying from 6 to 9 HDRS points. This is quite a disparity; according to Jonghe and Swinkels (2005), most researchers agree that a difference of 3 points borders on clinical significance. The follow-up studies are obviously heterogeneous in various clinical aspects, so much so that we were somewhat surprised to find all the tests in this area indicating strong homogeneity of the results. There are no generally accepted definitions of relapse. Most authors applied more or less strict HDRS or MDD criteria, but some (e.g., Evans et al., 1992; Shea et al., 1992; Simons et al., 1986) included "reentering treatment" in one of their relapse definitions. It appears that more pharmacotherapy patients than psychotherapy patients reenter treatment during follow-up. This might have underestimated the relapse rates for pharmacotherapy in our study. All in all, pooling these data is debatable, and interpretation of the relapse rates should be done cautiously. Our results, however, are corroborated by the studies of Hollon, Jarrett, et al. (2005) and Gloaguen et al. (1998), who simply listed relapse rates of individual trials, not pooling the data, and came to comparable conclusions.

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.

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Appendix

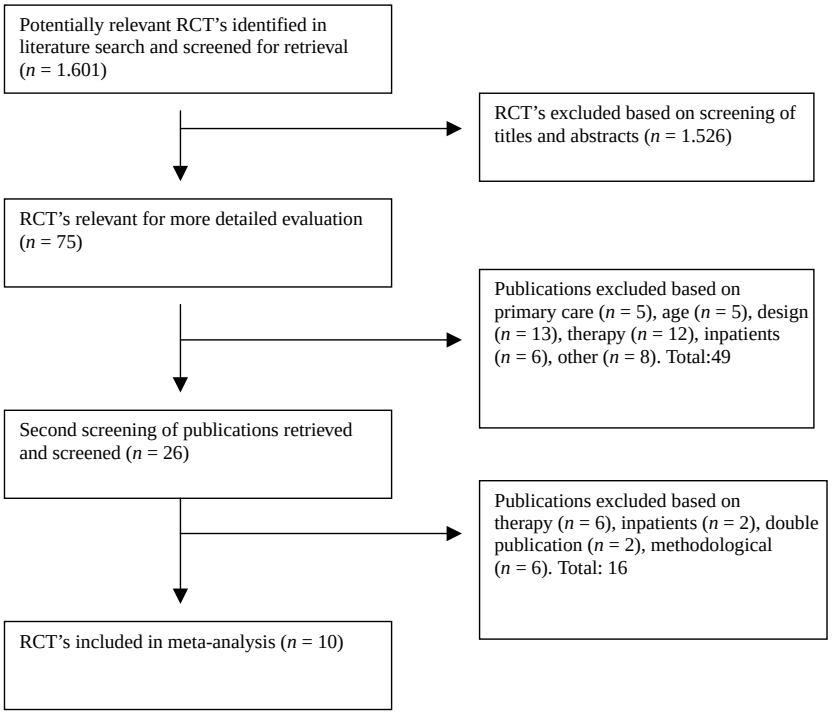

Figure A1. Quorum flow diagram.

Zusammenfassung

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

Wir haben die Effektivität von Pharmakotherapie und Psychotherapie bei Depression mit Hilfe von randomisierten kontrollierten Studien untersucht. Zur Durchführung einer Meta-Analyse wurden Untersuchungen nach Chronizität und Schweregrad von Depression klassifiziert. 10 Studien wurden berücksichtigt. Die Remissionen zeigten keinen Unterschied zwischen Psycho- (35%) und Pharmakotherapie (38%). Es gab auch keine Unterschiede bei chronischen und nichtchronischen Depressionen und im Vergleich von leichten und mittelschweren Depressionen. Beide Behandlungen waren besser bei leichten als bei mittelschweren Depressionen. Dropout war größer bei Pharmakotherapie (28%) als bei Psychotherapie (24%). Die Rezidivraten bei der Katamnese waren höher bei Pharmako- (57%) als bei Psychotherapie (27%). Psychotherapie und Pharmakotherapie erscheinen gleichermaßen effizient bei der Behandlung von Depressionen, beide Behandlungen zeigen größere Effekte bei leichter als bei mittelschwerer Depression und ähnliche Effekte bei chronischer und bei nicht-chronischer Depression. Bei katamnestischen Erhebungen ist die Psychotherapie jedoch der Pharmakotherapie überlegen.

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 catamnèse, 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 catamnestique, 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 farmacoterapia (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.

Sommario

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.

心理對藥物治療在憂鬱症的療效：一個後設分析

摘要

我們透過 RCT 法探討藥物對心理治療在憂鬱症上的治療效果。有十篇研究，按照慢性以及嚴重性的性質作分類，之後我們應用後設分析。依憂鬱減輕的程度來看，心理治療（38%）以及藥物治療（35%）之間並沒有差異，而慢性或非慢性，以及輕度或中度憂鬱之間，亦沒有差異。這兩種治療方法對輕度憂鬱來說都比中度憂鬱要好，而流失率是藥物治療（28%）高於心理治療（24%），後續復發上，藥物治療（57%）是高於心理治療（27%）。心理以及藥物治療對憂鬱症似乎都有同樣的療效，兩種治療對輕度憂鬱的治療效果都高過於中度憂鬱，但是慢性或非慢性憂鬱症則是差異不大，後續來看，心理治療的效果比藥物治療好。