Are Psychological and Pharmacologic Interventions Equally Effective in the Treatment of Adult Depressive Disorders? A Meta-Analysis of Comparative Studies

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Objective: A large number of studies suggest that both psychological and pharmacologic therapies are effective in the treatment of mild-to-moderate depressive disorders. Whether both types of intervention are equally effective has not been established definitively.

Data Sources: A database was developed through a comprehensive literature search (from 1966 to May 2007) in which 6947 abstracts in PubMed (1244 abstracts), PsycINFO (1736), EMBASE (1911), and the Cochrane Central Register of Controlled Trials (2056) were examined. Abstracts were identified by combining terms indicative of psychological treatment and depression (both MeSH terms and text words). For this database, the primary studies from 22 meta-analyses of psychological treatment for depression were also collected.

Study Selection: For the current study, the abstracts of 832 studies were examined.

Data Extraction: Thirty randomized trials were included in a meta-analysis that compared the effects of a psychological treatment for 3178 adults with a diagnosed depressive disorder (major depressive disorder, dysthymia, minor depressive disorder) with the effects of a pharmacologic treatment.

Data Synthesis: In studies of patients with dysthymia, pharmacotherapy was significantly more effective than psychotherapy (d = –0.28, 95% CI = –0.47 to –0.10). In patients with major depressive disorder, treatments with selective serotonin reuptake inhibitors (SSRIs) were significantly more effective than psychological treatments, while treatment with other antidepressants did not differ significantly. Subgroup and metaregression analyses did not show that pretest severity of depressive symptoms was associated with differential effects of psychological and pharmacologic treatments of major depressive disorder. Dropout rates were smaller in psychological interventions compared with pharmacologic treatments (odds ratio = 0.66, 95% CI = 0.47 to 0.92).

Conclusions: Pharmacologic treatments may be more effective than psychological interventions in the treatment of dysthymia. Pharmacologic treatment with SSRIs may also be more effective in the treatment of major depressive disorder, although these differences are small and probably have little meaning from a clinical point of view. We can conclude that both psychological and pharmacologic therapies are effective in the treatment of depressive disorders and that each has its own merits.

(J Clin Psychiatry 2008;69:1675–1685)

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The authors have no personal affiliations or financial relationships with any commercial interest to disclose relative to the article.

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In the past decades, hundreds of randomized trials and dozens of meta-analyses examining pharmacologic[1] and psychological treatments[2] for depression have been conducted. This huge body of literature has shown that both types of interventions can be effective in treating depressive disorders, in particular, mild-to-moderate major depression.

Although both types of intervention have been found to be effective, it is not known whether they are equally effective for all types of depression. While most studies have found that both types of treatment are equally effective, the statistical power to detect smaller differences has been too low in most studies. Meta-analyses have generally found that both types of intervention are equally effective in the treatment of mild and moderate depression.[3–5] Whether the same is true for more severe cases is less certain.[6,7]

However, most meta-analyses in this area have not focused on studies in which the 2 types of treatments have

FOR CLINICAL USE

- In patients with major depressive disorder, pharmacotherapy and psychotherapy are about equally effective, although treatment with selective serotonin reuptake inhibitors may be somewhat more effective than psychotherapy.
- In patients with dysthymia, pharmacotherapy seems to be significantly more effective than psychotherapy.
- Dropout rates seem to be smaller in psychological interventions compared with pharmacotherapy.

been compared directly to each other in one and the same trial. The majority of earlier meta-analyses concentrated on the overall effects of psychological or pharmacologic treatments compared with control conditions. The results of such meta-analyses may very well be influenced by factors that differed among the various studies, such as length of treatment, type of treatment, or initial symptom severity.[8,9] This means that possible differences between the effects of the 2 types of treatments may very well be artifacts, which do not reflect true superiority of one of the types of treatment over the other.[8] Direct comparisons of treatments, on the other hand, are better equipped to rule out the influence of study characteristics, and they certainly provide more reliable evidence about a possible superiority of 1 type of therapy over the other.[8]

The last comprehensive meta-analysis, which examined the relative impact of psychological and pharmacologic treatments, was conducted in 1990,[3] while the overwhelming majority of comparative studies have been conducted since 1990. One recent, smaller meta-analysis[5] examined comparative studies of psychological and pharmacologic treatments and also found them to be equally effective. However, this study included only one third of the currently available comparative studies and did not conduct subgroup analyses to examine whether there were differences between types of psychological treatment or types of pharmacologic treatment, nor did it conduct extensive heterogeneity analyses.[5]

We decided therefore to conduct a meta-analysis of comparative studies of psychological and pharmacologic therapies in which we focused specifically on analyses of heterogeneity.

METHOD

Identification and Selection of Studies

Studies were traced by means of several methods. First, we used a database of 832 articles on the psychological treatment of depression in general.[10–12] This database was developed through a comprehensive literature search (from 1966 to May 2007) in which we examined 6947 abstracts in PubMed (1244 abstracts), PsycINFO (1736), EMBASE (1911), and the Cochrane Central Register of Controlled Trials (2056). We identified these abstracts by combining terms indicative of psychological treatment and depression (both MeSH terms and text words). For this database, we also collected the primary studies from 22 meta-analyses of psychological treatment for depression.[2] For the current study, we examined the abstracts of these 832 studies.

We included studies in which (1) the effects of a psychological treatment (2) for adults (3) with a depressive disorder (4) were compared with the effects of a pharmacologic treatment (5) in a randomized trial. No language restrictions were applied. Only studies in which the subjects met diagnostic criteria for a depressive disorder (major depressive disorder, dysthymia, minor depressive disorder) were included. Studies aimed at subjects with elevated levels of depressive symptoms (as measured with self-report measures) but no indication of diagnosis were excluded, as were studies aimed at relapse prevention or maintenance treatments.

Quality Assessment

We assessed the validity of included studies using a number of basic criteria, as suggested in the Cochrane Handbook[13]: allocation to conditions conducted by an independent (third) party, blinding of assessors of outcomes, and completeness of follow-up data. We did not check for the fourth criterion for validity (adequacy of random allocation concealment to respondents), because it was not possible in these studies to conceal the randomization to patients.

Meta-Analyses

For each comparison between psychological and pharmacologic treatments, we calculated the effect size (Cohen's d) indicating the difference between the 2 types of treatment at posttest. We calculated the effect sizes by subtracting (at posttest) the mean score of the psychotherapy group from the mean score of the pharmacotherapy group and dividing the result by the pooled standard deviations of the 2 groups. Effect sizes of 0.8 can be assumed to be large, while effect sizes of 0.5 are moderate, and effect sizes of 0.2 are small.[14] When psychological treatments are compared with control groups, usually

effect sizes of 0.6 or larger are found.[3,12] In our meta-analysis, effect sizes of zero were assumed to indicate that there was no difference between the effects of psychotherapy and those of pharmacotherapy.

In the calculations of effect sizes, we only used those instruments that explicitly measured symptoms of depression. If more than 1 depression measure was used, the mean of the effect sizes was calculated so that each study (or contrast group) only provided 1 effect size.

We only used the effect sizes indicating the differences between psychological and pharmacologic treatments at posttest. Although some studies also reported outcomes at follow-up, most did not (18 of 30 studies). We decided not to examine the differential effects at follow-up, because the number of effect sizes was relatively low. In addition, the follow-up period differed considerably among these studies, and in several studies, treatments were continued and others discontinued.

To calculate pooled mean effect sizes, we used the computer program Comprehensive Meta-Analysis, version 2.2.021 (Biostat, Englewood, N.J.). As we did not know whether we would find heterogeneity among the studies, we decided to calculate mean effect sizes both with the random-effects model and with the fixed-effects model. In the fixed-effects model, it is assumed that all studies in the meta-analysis are drawn from the same "population" of studies and all factors that could influence the effect size are the same in all the study populations. In the random-effects model, it is assumed that the included studies are drawn from "populations" of studies that differ from each other systematically (heterogeneity). In this model, the effect sizes resulting from included studies not only differ because of the random error within studies (as in the fixed-effects model), but also because of true variation in effect size from 1 study to the next. Because the results of the random- and fixed-effects models were found to be the same or almost the same in our analyses, we only report the results of the random-effects model.

Publication bias was tested by inspecting the funnel plots of the meta-analyses and by using Duval and Tweedie's trim and fill procedure,[16] which yields an estimate of the effect size after the publication bias has been taken into account.

As indicator of homogeneity, we calculated the Q statistic. We also calculated the I^2 statistic, which is an indicator of heterogeneity in percentages. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity, with 25% as low, 50% as moderate, and 75% as high heterogeneity.[17]

Subgroup analyses were conducted according to the mixed-effects model. In this model, studies within subgroups are pooled with the random-effects model, while tests for significant differences between subgroups are conducted with the fixed-effects model.

For continuous variables, we used meta-regression analyses to test whether there was a significant relationship between the continuous variable and the effect size, as indicated with a z value and an associated p value.

Finally, we examined whether the dropout from the intervention differed between pharmacologic and psychological treatments. Because dropout is a dichotomous outcome, we calculated the odds ratio (OR) of dropout from psychotherapy compared with pharmacologic treatment (instead of a standardized effect size). Again, we conducted all meta-analyses both with the fixed-effects model and with the random-effects model using the same computer program, and we calculated the Q statistic and the I^2 statistic to estimate heterogeneity between study outcomes.

RESULTS

Characteristics of the Included Studies

Thirty studies with a total of 3178 patients were included (1612 patients in the psychotherapy conditions and 1566 in the pharmacotherapy conditions, Table 1).[7,18–46] In 7 studies,* 2 psychological treatments were compared with a pharmacologic treatment. Therefore, we could include 37 comparisons between a psychological and a pharmacologic intervention in the analyses.

Patients were recruited through clinical referrals (14 studies),† from the community (8 studies),‡ or through other methods (8 studies).§ Twenty-three studies were aimed at adults with a depressive disorder in general,‖ while the remaining 7 studies targeted more specific groups.¶ Twenty-five studies were aimed at patients with a major depressive disorder,# while the remaining studies were aimed at patients with dysthymia (2 of which also included patients with minor depressive disorder[18,46]). In 23 studies,** the 17-item Hamilton Rating Scale for Depression (HAM-D) score at pretest was presented (which ranged from 16 to 23.89), while 19 studies reported the pretest Beck Depression Inventory (BDI) score (ranging from 17.74 to 30.25).††

Fifteen comparisons examined cognitive-behavioral therapy, 7 interpersonal psychotherapy, 5 problem-solving therapy, and 12 other psychological treatments. Selective serotonin reuptake inhibitors (SSRIs) were examined in 15 comparisons, while tricyclic antidepressants (TCAs) were examined in 16 comparisons (other medications in 6 comparisons).

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* References 22, 24, 30, 34, 36, 39, 42.
† References 18–20, 24, 25, 27, 29, 37–42, 45.
‡ References 21, 26, 30, 32–34, 44, 46.
§ References 7, 22, 23, 28, 31, 35, 36, 43.
‖ References 7, 18–26, 28–32, 34, 37–42, 45.
¶ References 27, 33, 35, 36, 43, 44, 46.
# References 7, 19, 20, 22, 24–29, 31–45.
** References 7, 18, 20, 22–31, 35–44.
†† References 19, 20, 23–26, 28, 30, 31, 33, 34, 36–41, 43, 44.

Table 1. Selected Characteristics of Included Studies

Study	Population	Recruitment Method	Definition of Depression	Psychological Treatment	N	No. of Sessions	Pharmacologic Treatment	N	Measure	Country
Barrett et al, 2001[18]	Adults	Clinical	DYS or minorD + HAM-D score ≥ 10	PST	80	6	Paroxetine	80	HSCL-D, HAM-D	United States
Bedi et al, 2000[19]	Adults	Clinical	MDD (RDC)	Counseling	50	Not reported	Protocol	52	BDI	United Kingdom
Blackburn and Moore, 1997[20]	Adults	Clinical	MDD (RDC) + HAM-D score ≥ 16	CBT	27	16	Antidepressant of choice	48	HAM-D	United Kingdom
Browne et al, 2002[21]	Adults	Community	DYS (DSM-IV/UM-CIDI)	IPT	83	10	Sertraline	117	MADRS, CES-D, VAS	Canada
DeRubeis et al, 2005[7]	Adults	Combined	MDD (DSM-IV/SCID) + HAM-D score ≥ 20	CBT	60	18	Paroxetine	120	HAM-D	United States
Dimidjian et al, 2006[22]	Adults	Combined	MDD (SCID)	CBT	39	24	Paroxetine	56	HAM-D, BDI-II	United States
				Behavior therapy	36	24				
Dunner et al, 1996[23]	Adults	Not reported	DYS (DSM-III-R/SCID)	CBT	13	16	Fluoxetine	18	HAM-D, BDI	United States
Elkin et al, 1989[24]	Adults	Clinical	MDD (SADS/RDC) + HAM-D score > 14	IPT	59	16	Imipramine	57	BDI, HAM-D	United States
				CBT	59	16				
Hollon et al, 1992[25]	Adults	Clinical	MDD (RDC) + BDI score > 20 + HAM-D score > 14	CBT	22	20	Imipramine	32	HAM-D, BDI, RDS, MMPI-d	United States
Jarrett et al, 1999[26]	Adults	Community	MDD with atypical features + HAM-D 21-item score > 14	CBT	36	20	Phenelzine	36	HAM-D, BDI	United States
Keller et al, 2000[27]	Adults[a]	Clinical	MDD + DYS OR recurrent MDD (DSM-IV/SCID) + HAM-D score > 20	CBASP	228	18	Nefazodone	226	HAM-D	United States
Leff et al, 2000[28]	Adults	Combined	MDD (PSE) + HAM-D score ≥ 14	Couple therapy	40	16	Desipramine	37	HAM-D, BDI	United Kingdom
Lopez Rodriguez et al, 2004[29]	Adults	Clinical	MDD (DSM-IV)	Bellak's psychotherapy	10	Not reported	Fluoxetine	10	HAM-D	Mexico
Markowitz et al, 2005[30]	Adults	Community	DYS (SCID)	IPT	23	17	Sertraline	24	HAM-D, BDI, CDRS	United States
				Supportive therapy	26	17				
Martin et al, 2001[31]	Adults	Combined	MDD (DSM-IV/SCID) + HAM-D score ≥ 18	IPT	13	16	Venlafaxine	15	HAM-D, BDI	United Kingdom
McBride et al, 2007[32]	Adults	Community	MDD (DSM-IV/SCID)	CBT	21	16	Pharmacotherapy	21	BDI	Canada
McKnight et al, 1992[33]	Adult women	Community	MDD (DSM-III/SADS) + MMPI-d score ≥ 29 + BDI score ≥ 20	CBT	21	8	Tricyclic antidepressant	22	MMPI-d, BDI	
McLean and Hakstian, 1979[34]	Adults	Community	MDD (Feighner criteria)	Psychodynamic psychotherapy	37	10	Amitriptyline	39	BDI	Canada
				Behavior therapy	38					
Miranda et al, 2003[35]	Women[b]	Screening	MDD (PCEMD)	CBT	90	8	Paroxetine or bupropion	88	HAM-D	United States
Mohr et al, 2001[36]	MS patients	Screening	MDD (DSM-IV/SCID) + HAM-D score > 16 + BDI score > 16	CBT	20	16	Sertraline	21	BDI, HAM-D	United States
				Supportive expressive therapy	22	16				
Murphy et al, 1984[37]	Adults	Clinical	MDD (Feighner criteria) + BDI score > 20 + HAM-D score > 14	CBT	24	20	Nortriptyline	24	HAM-D, BDI	United States
Mynors-Wallis et al, 1995[38]	Adults	Clinical	MDD (RDC) + HAM-D score > 13	PST	30	6	Amitriptyline	31	HAM-D, BDI	United Kingdom
Mynors-Wallis et al, 2000[39]	Adults	Clinical	MDD + HAM-D score > 13	PST (GP)	39	6	Fluvoxamine or paroxetine	36	HAM-D, BDI	United Kingdom
				PST (nurses)	41	6				

(continued)

Table 1 (continued). Selected Characteristics of Included Studies

Study	Population	Recruitment Method	Definition of Depression	Psychological Treatment	N	No. of Sessions	Pharmacologic Treatment	N	Measure	Country
Rush et al, 1977[40]	Adults	Clinical	MDD (Feighner criteria) + BDI score ≥ 20 + HAM-D score ≥ 14	CBT	19	20	Imipramine	22	HAM-D, BDI, RDS	United States
Schulberg et al, 1996[41]	Adults	Clinical	MDD (DYS/DSM-III-R) + HAM-D score > 13	IPT	93	16	Nortriptyline	91	HAM-D	United States
Scott and Freeman, 1992[42]	Adults	Clinical	MDD (DSM-III)	CBT Counseling	29 29	16 16	Amitriptyline	31	HAM-D	United Kingdom
Sloane et al, 1985[43]	Elderly	Not reported	MDD (RDC) + HAM-D score > 17	IPT	19	16	Nortriptyline	18	HAM-D	United States
Thompson et al, 2001[44]	Elderly	Community	MDD (SADS/RDC) + HAM-D score > 14 + BDI score > 16	CBT	31	18	Desipramine	33	BDI, HAM-D	United States
Weissman et al, 1979[45]	Adults	Clinical	MDD (RDC/SADS) + RDS score ≥ 7	IPT	25	16	Amitriptyline	24	RDS	United States
Williams et al, 2000[46]	Elderly	Community	DYS or minorD + HAM-D score > 10	PST	80	6	Paroxetine	137	20-item HSCL-D	United States

[a]Adults with chronic depression.
[b]Low-income women.
Abbreviations: BDI = Beck Depression Inventory, CBASP = cognitive-behavioral analysis system of psychotherapy, CBT = cognitive-behavioral therapy, CDRS = Cornell Dysthymia Rating Scale, CES-D = Center for Epidemiological Studies-Depression scale, DYS = dysthymia, GP = general practitioner, HAM-D = Hamilton Rating Scale for Depression, HSCL-D = Hopkins Depression Scale, IPT = interpersonal psychotherapy, MADRS = Montgomery-Asberg Depression Rating Scale, MDD = major depressive disorder, minorD = minor depressive disorder, MMPI-d = Minnesota Multiphasic Personality Inventory-depression, MS = multiple sclerosis, PCEMD = Primary Care Evaluation of Mental Disorders, PSE = Present State Examination, PST = problem-solving treatment, RDC = research diagnostic criteria, RDS = Raskin Depression Scale, SADS = Schedule for Affective Disorders and Schizophrenia, SCID = Structured Clinical Interview for DSM-IV, UM-CIDI = University of Michigan Composite International Diagnostic Interview, VAS = visual analogue scale.

The quality of the included studies varied. Fourteen of the 30 studies reported that allocation to conditions was conducted by an independent party.* Blinding of assessors was reported in 17 studies,† while another 3 studies[19,32,34] only used self-report measures (in these cases, blinding of assessors was not relevant). Intention-to-treat analyses were conducted in 21 studies (the other studies were limited to completers-only analyses).‡

Differences Between Psychological and Pharmacologic Interventions: Overall Effect Sizes

The mean effect size (Cohen's d) of the 37 comparisons indicating the difference between psychological and pharmacologic interventions was –0.07 (95% CI = –0.15 to 0.01), suggesting a trend ($z = -1.66$, $p < .1$) that pharmacologic interventions may be somewhat more effective than psychological interventions (Table 2). Heterogeneity was low (Q = 45.75, not significant [NS], $I^2 = 21.31$). The effect sizes and 95% confidence intervals of the individual contrast groups are plotted in Figure 1.

When we limited the analyses to the effect sizes for the HAM-D, comparable effect sizes were found, although the difference between psychological and pharmacologic interventions was no longer significant (d = 0.02; 95% CI = –0.13 to 0.16; z = 0.23, NS; Q = 16.95, NS; $I^2 = 23.29$; N = 14). The same was true when we limited the analyses to the effect sizes found for the BDI (d = –0.04; 95% CI = –0.16 to 0.08; z = –0.72, NS; Q = 29.72, NS; $I^2 = 22.62$).

In our analyses, we included 7 studies in which 2 psychological treatments were compared to a pharmacologic treatment. This means that multiple comparisons from these 7 studies were included in the same analysis. These multiple comparisons, however, are not independent of each other, which may have resulted in an artificial reduction of heterogeneity. Therefore, we conducted another meta-analysis, in which we included only 1 comparison per study (Table 2). From the 7 studies with multiple comparisons, we included only the comparison with the largest effect size (i.e., the largest difference between the psychological and pharmacologic treatments), because this was considered the most conservative approach in estimating heterogeneity in the meta-analyses. As can be seen in Table 2, these analyses did indicate that heterogeneity increased somewhat in some analyses, although this increase was small, and the overall level of heterogeneity was still low ($I^2 = 27.55$).

* References 18, 21, 22, 24, 26–28, 30, 35, 37–39, 42, 46.
† References 17, 21–23, 25–28, 30, 37–39, 41–43, 45, 46.
‡ References 7, 18, 20, 22, 24–28, 30, 31, 35–41, 44, 46.

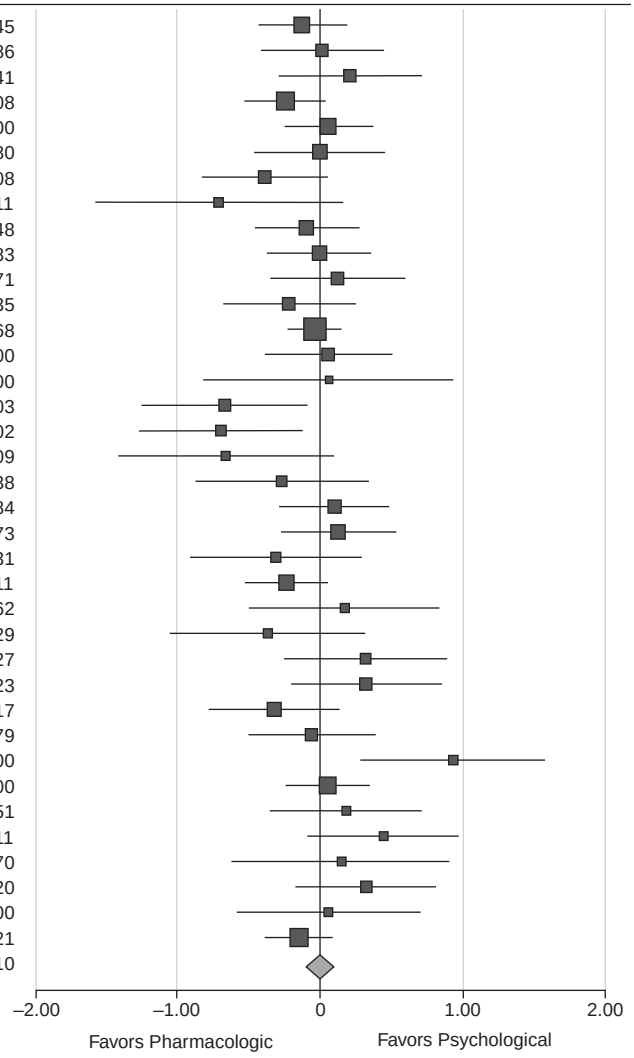
Table 2. Results of Meta-Analyses Comparing the Effects of Psychological and Pharmacologic Treatments of Depression[a]

Results	Completers (N)	d	95% CI	z	Q	I^2 (%)	p
Effect at posttest							
All studies	37	–0.07	–0.15 to 0.01	–1.66	45.75	21.31	
BDI only	24	–0.04	–0.16 to 0.08	–0.72	29.72	22.62	
HAM-D-17 only	14	0.02	–0.13 to 0.16	0.23	16.95	23.29	
All studies (multiple comparisons excluded)[b]	30	–0.07	–0.16 to 0.02	–1.50	40.03	27.55	
Subgroup analyses (all studies)							
Recruitment							
Clinical	18	0.02	–0.09 to 0.13	0.36	20.57	17.34	NS
Community	10	–0.17	–0.33 to –0.01	–2.10*	13.09	31.24	
Combined	4	–0.09	–0.29 to 0.11	–0.90	2.30	0	
Other	5	–0.21	–0.44 to 0.03	–1.74	3.61	0	
Target group							
Adults	31	–0.06	–0.16 to 0.03	–1.38	40.06	25.11	NS
Specific group	6	–0.10	–0.27 to 0.07	–1.13	5.44	8.13	
Diagnostic category							
MDD	31	–0.02	–0.10 to 0.06	–0.49	31.32	4.22	†
Dysthymia (+ minorD)	6	–0.28	–0.47 to –0.10	–3.06†	6.79	26.36	
Diagnostic category[c]							
MDD	31	–0.02	–0.10 to 0.06	–0.49	31.32	4.22	†
Dysthymia	4	–0.44	–0.70 to –0.19	–3.37†	3.44	12.70	
Analyses							
Intention to treat	27	–0.05	–0.15 to 0.05	–1.06	39.82*	34.71	NS
Completers	10	–0.11	–0.27 to 0.04	–1.47	5.56	0	
Type of psychotherapy							
CBT	15	0.03	–0.11 to 0.17	0.43	19.16	26.91	NS
IPT	7	–0.18	–0.35 to 0.00	–1.96*	6.99	14.10	
PST	5	–0.11	–0.27 to 0.04	–1.40	3.53	0	
Supportive	4	–0.15	–0.62 to 0.32	–0.62	8.80*	65.91	
Other	6	–0.07	–0.22 to 0.07	–1.01	3.35	0	
Medication							
SSRI	15	–0.20	–0.31 to –0.10	–3.90‡	12.28	0	†
TCA	16	0.09	–0.02 to 0.21	1.58	14.73	0	
Other	6	–0.07	–0.22 to 0.07	–0.98	4.44	0	
Subgroup analyses (MDD only)[d]							
Recruitment							
Clinical	17	0.04	–0.08 to 0.16	0.61	19.84	19.36	NS
Community	6	–0.02	–0.21 to 0.17	–0.22	4.37	0	
Combined	4	–0.09	–0.29 to 0.11	–0.90	2.30	0	
Other	4	–0.17	–0.41 to 0.07	–1.37	2.20	0	
Target group							
Adults	26	–0.01	–0.10 to 0.07	–0.30	25.83	3.22	NS
Specific group	5	–0.04	–0.31 to 0.23	–0.29	5.23	23.46	
Analyses							
Intention to treat	23	–0.01	–0.11 to 0.09	–0.17	29.29	24.89	NS
Completers	8	–0.03	–0.21 to 0.16	–0.30	2.03	0	
Type of psychotherapy							
CBT	14	0.04	–0.09 to 0.18	0.63	16.42	20.81	NS
IPT	5	–0.07	–0.27 to 0.13	–0.72	2.99	0	
PST	3	–0.04	–0.39 to 0.31	–0.23	3.24	38.26	
Supportive	3	0.04	–0.38 to 0.46	–0.18	3.66	45.32	
Other	6	–0.07	–0.22 to 0.07	–1.01	3.35	0	
Medication							
SSRI	9	–0.16	–0.30 to –0.01	–2.09*	4.63	0	*
TCA	16	0.09	–0.02 to 0.21	1.58	14.73	0	
Other	6	–0.07	–0.22 to 0.07	–1.01	3.35	0	
Subgroup analyses (severity)							
Pretest BDI (only MDD)							
10–29	20	–0.07	–0.19 to 0.06	–1.08	24.91	23.71	NS
≥ 30	4	0.13	–0.31 to 0.59	0.60	8.62*	65.19	
Pretest HAM-D (only MDD)							
≤ 20	9	0.06	–0.11 to 0.22	0.67	10.16	21.29	NS
> 20	13	–0.03	–0.20 to 0.13	–0.37	18.01	33.36	

[a]A positive effect size indicates a superior effect of the psychological treatment.
[b]In these analyses, 1 of the 2 comparisons in the 7 studies in which 2 psychotherapies were compared with a pharmacologic treatment was removed from the analyses (the one with the smallest effect size).
[c]In these analyses, the 2 studies in which patients with dysthymia and/or minorD were removed from the analyses.
[d]In these analyses, only studies of patients with MDD were included (the studies of patients with dysthymia or minorD were excluded).
*p < .05, †p < .01, ‡p < .001.
Abbreviations: BDI = Beck Depression Inventory, CBT = cognitive-behavioral therapy, HAM-D-17 = 17-item Hamilton Rating Scale for Depression, IPT = interpersonal psychotherapy, MDD = major depressive disorder, minorD = minor depressive disorder, NS = not significant, PST = problem-solving treatment, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

Figure 1. Standardized Effect Sizes Indicating Differences Between the Effects of Psychological and Pharmacologic Treatment of Depression at Posttest

Study	Statistic: Standard Difference in Means	Lower Limit	Upper Limit	p
Barrett et al, 2001[18]	–0.12	–0.43	0.19	0.45
Bedi et al, 2000[19]	–0.04	–0.47	0.39	0.86
Blackburn and Moore, 1997[20]	0.21	–0.29	0.71	0.41
Browne et al, 2002[21]	–0.25	–0.53	0.03	0.08
DeRubeis et al, 2005[7]	0.00	–0.31	0.31	1.00
Dimidjian et al, 2006 BA[22]	–0.06	–0.52	0.40	0.80
Dimidjian et al, 2006 CT[22]	–0.39	–0.83	0.05	0.08
Dunner et al, 1996[23]	–0.71	–1.58	0.16	0.11
Elkin et al, 1989 CBT[24]	–0.13	–0.49	0.23	0.48
Elkin et al, 1989 IPT[24]	–0.04	–0.40	0.32	0.83
Hollon et al, 1992[25]	0.09	–0.38	0.56	0.71
Jarrett et al, 1999[26]	–0.22	–0.68	0.24	0.35
Keller et al, 2000[27]	–0.04	–0.23	0.15	0.68
Leff et al, 2000[28]	0.00	–0.45	0.45	1.00
Lopez Rodriguez et al, 2004[29]	0.00	–0.88	0.88	1.00
Markowitz et al, 2005 IPT[30]	–0.67	–1.26	–0.08	0.03
Markowitz et al, 2005 SUP[30]	–0.70	–1.27	–0.13	0.02
Martin et al, 2001[31]	–0.66	–1.42	0.10	0.09
McBride et al, 2007[32]	–0.27	–0.88	0.34	0.38
McLean and Hakstian, 1979 A[34]	0.04	–0.34	0.42	0.84
McLean and Hakstian, 1979 B[34]	0.07	–0.33	0.47	0.73
McKnight et al, 1992[33]	–0.31	–0.91	0.29	0.31
Miranda et al, 2003[35]	–0.24	–0.53	0.05	0.11
Mohr et al, 2001 A[36]	0.17	–0.50	0.84	0.62
Mohr et al, 2001 B[36]	–0.37	–1.05	0.31	0.29
Murphy et al, 1984[37]	0.32	–0.25	0.89	0.27
Mynors-Wallis et al, 1995[38]	0.32	–0.21	0.85	0.23
Mynors-Wallis et al, 2000 A[39]	–0.32	–0.78	0.14	0.17
Mynors-Wallis et al, 2000 B[39]	–0.06	–0.51	0.39	0.79
Rush et al, 1977[40]	0.93	0.28	1.58	0.00
Schulberg et al, 1996[41]	0.00	–0.29	0.29	1.00
Scott and Freeman, 1992 A[42]	0.18	–0.35	0.71	0.51
Scott and Freeman, 1992 B[42]	0.44	–0.10	0.98	0.11
Sloane et al, 1985[43]	0.15	–0.62	0.92	0.70
Thompson et al, 2001[44]	0.32	–0.17	0.81	0.20
Weissman et al, 1979[45]	0.00	–0.65	0.65	1.00
Williams et al, 2000[46]	–0.15	–0.39	0.09	0.21
	–0.07	–0.15	0.01	0.10



Abbreviations: BA = behavioral activation treatment, CBT = cognitive-behavioral therapy, CT = cognitive therapy, IPT = interpersonal therapy, SUP = supportive therapy.

Neither the funnel plots nor Duval and Tweedie's trim and fill procedure pointed at a significant publication bias. The effect size indicating the difference in reduction of depressive symptomatology between psychological and pharmacologic treatments did not change significantly after adjustment for possible publication bias (the observed and adjusted effect size did not differ significantly from each other). We also found no indications of publication bias when we limited the analyses to studies on major depressive disorder (and excluded studies on dysthymia).

Subgroup and Metaregression Analyses

We conducted several subgroup analyses with the effect sizes indicating the difference between psychological and pharmacologic treatments at posttest (Table 2). The subgroups we examined included differences in recruitment method (clinical, community, combined, other), target group (adults in general, specific group), diagnostic category (major depressive disorder, dysthymia with or without minor depression), type of analyses (intention-to-treat, completers only), type of psychotherapy (cognitive-behavioral therapy, interpersonal psychotherapy, prob-

lem-solving therapy, supportive therapy, other), and type of medication (SSRI, TCA, other).

As can be seen in Table 2, the studies in which patients suffered from dysthymia differed significantly ($p < .01$) from the studies in which patients with major depressive disorder were examined. In studies of patients with dysthymia, pharmacotherapy was significantly more effective than psychotherapy (d = –0.28, 95% CI = –0.47 to –0.10, $p < .01$). In studies focusing on patients with major depressive disorder, the difference between psychological and pharmacologic treatment was not significant (d = –0.02, 95% CI = –0.10 to 0.06). In 2 studies,[18,46] both patients with dysthymia and those with minor depressive disorder were included. When these 2 studies were removed from the analyses, the difference between studies of dysthymia patients and patients with major depressive disorder remained significant ($p < .01$). And in the 4 comparisons with dysthymia patients,[21,23,30] the difference between psychological and pharmacologic treatment also remained significant (d = –0.44, 95% CI = –0.70 to –0.19, $p < .01$).

We also found that type of medication was significantly associated with differences in effects between psychological and pharmacologic treatments ($p < .01$). Treatment with SSRIs was significantly more effective than psychological treatment ($p < .001$), while treatment with TCAs or other pharmacologic treatments did not differ significantly from psychological therapies.

In most subgroup analyses, heterogeneity was low. In the analyses in which psychological treatments were compared with different types of pharmacologic treatments (SSRI, TCA, other), heterogeneity was zero.

Because we found that the effect sizes in studies with dysthymia patients differed from studies with major depressive disorder patients, we repeated all subgroup analyses for the studies in which only patients with major depressive disorder were included (Table 2). The number of studies with dysthymia patients was too small for the purpose of conducting separate subgroup analyses.

As can be seen in Table 2, the results of the subgroup analyses limited to studies of patients with major depressive disorder did not differ much from the earlier subgroup analyses. Type of medication remained significantly associated with differences in effects between psychological and pharmacologic treatments ($p < .05$), while heterogeneity remained at zero.

Severity of Depression

We examined whether the difference between psychological and pharmacologic treatments was associated with severity of depression at pretest in 2 ways. Because the level of depressive symptoms (assessed with the HAM-D and BDI) was expected to be lower in the studies of dysthymia, we limited these analyses to the studies of major depressive disorder.

First, we conducted a metaregression analysis to examine whether the effect sizes were associated with the mean scores on the HAM-D and the BDI at pretest. In 24 studies, the pretest BDI score was presented. A metaregression of these studies did not indicate that the pretest BDI score was significantly associated with the effect size (point estimate of slope = 0.002, 95% CI = –0.05 to 0.06, z = 0.08, $p = .93$). In another metaregression analysis in which we examined whether the pretest HAM-D score was significantly associated with the effect size, no indication was found that this was true (23 studies, point estimate of slope = 0.002, 95% CI = –0.04 to 0.05, z = 0.08, $p = .93$).

Second, we conducted subgroup analyses to examine whether the effect sizes were associated with pretest severity (Table 2). We made a subgroup of studies in which the patients had a mean BDI score less than 30 and another subgroup in which the mean BDI score was greater than or equal to 30 (a score ≥ 30 indicates severe depression).[47] No significant difference between these 2 subgroups was found, although the 4 studies in which the patients had a pretest BDI score greater than or equal to 30 indicated that psychotherapy was significantly more effective than pharmacotherapy.

We also analyzed a subgroup of studies* in which the mean pretest HAM-D score was less than 20 and 1 subgroup in which the mean pretest HAM-D score was greater than or equal to 20.† The effect sizes in these 2 subgroups did not differ significantly from each other.

Differences in Drop-Out Rates

We compared the drop-out rate in psychological and pharmacologic treatments in 24 studies (30 comparisons, Table 3).‡ The analyses indicated that the drop-out rate was smaller in psychological treatments compared with pharmacologic treatments with an OR of 0.66 (95% CI = 0.47 to 0.92, z = –2.42, $p < .05$). Heterogeneity was high ($Q = 94.95$, $p < .001$, $I^2 = 69.46$).

We conducted the same subgroup and metaregression analyses as we did with the effect sizes (Table 3). As can be seen in Table 3, none of the subgroup analyses indicated that there were significant differences between subgroups. Levels of heterogeneity were moderate to high in most subgroups. We also found no indication that severity of depression was associated with dropout, both from the subgroup analyses (Table 3) and the metaregression analyses (BDI: point estimate of slope = –0.038, 95% CI = –0.115 to 0.040, z = –0.96, NS; HAM-D: point estimate of slope = –0.023, 95% CI = –0.107 to 0.052, z = –0.68, NS).

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* References 23, 24, 28, 35, 37, 38, 42, 44.
† References 7, 20, 22, 25, 31, 36, 39, 40, 43.
‡ References 7, 18, 20, 22–28, 30, 33–41, 43–46.

Table 3. Results of Meta-Analyses Comparing the Drop-Out Rates of Psychological and Pharmacologic Treatments of Depression

Results	Completers (N)	Odds Ratio	95% CI	z	Q	I^2 (%)	p
Overall							
All studies	30	0.66	0.47 to 0.92	–2.42*	94.95‡	69.46	
Subgroup analyses							
Recruitment							
Clinical	13	0.85	0.65 to 1.11	–1.18	14.23	15.64	NS
Community	8	0.68	0.42 to 1.10	–1.57	9.99	29.94	
Combined	4	0.32	0.11 to 0.90	–2.15*	14.31†	79.04	
Other	5	0.50	0.08 to 3.07	–0.75	28.51‡	85.97	
Target group							
Adults	24	0.65	0.47 to 0.88	–2.75†	50.48†	54.44	NS
Specific group	6	0.60	0.17 to 2.05	–0.82	37.58‡	86.69	
Diagnostic category							
MDD	25	0.60	0.40 to 0.90	–2.50*	90.98‡	73.62	NS
Dysthymia (+ minorD)	5	0.85	0.57 to 1.28	–0.77	3.88	0	
Analyses							
Intention to treat	24	0.72	0.50 to 1.05	–1.72	83.96‡	72.61	NS
Completers	6	0.41	0.20 to 0.86	–2.36*	7.06	29.15	
Type of psychotherapy							
CBT	13	0.60	0.30 to 1.20	–1.45	53.63‡	77.62	NS
IPT	5	0.80	0.44 to 1.46	–0.73	6.64	39.73	
PST	5	0.96	0.55 to 1.67	–0.15	6.93	42.26	
Other	7	0.49	0.23 to 1.01	–1.93	24.14‡	75.15	
Medication							
SSRI	13	0.90	0.48 to 1.69	–0.34	61.01‡	80.33	NS
TCA	14	0.49	0.32 to 0.75	–3.26†	25.45*	48.92	
Other	3	0.82	0.56 to 1.21	–0.99	1.06	0	
Pretest BDI score							
10–29	18	0.60	0.40 to 0.91	–2.40*	36.65†	53.62	NS
≥ 30	3	0.64	0.20 to 2.00	–0.77	4.50	55.51	
Pretest HAM-D score							
≤ 20	7	0.84	0.34 to 2.06	–0.38	32.62‡	81.60	NS
> 20	13	0.50	0.27 to 0.91	–2.25*	43.45‡	72.38	

*p < .05.
†p < .01.
‡p < .001.
Abbreviations: BA = behavioral activation treatment, BDI = Beck Depression Inventory, CBT = cognitive-behavioral therapy, CT = cognitive therapy, HAM-D = Hamilton Rating Scale for Depression, IPT = interpersonal psychotherapy, MDD = major depressive disorder, minorD = minor depressive disorder, NS = not significant, PST = problem-solving treatment, SSRI = selective serotonin reuptake inhibitor, SUP = supportive therapy, TCA = tricyclic antidepressant.

DISCUSSION

When the results of all included studies were taken into account, we found some indications that pharmacologic treatment is somewhat more effective than psychological treatment. However, this difference was very small (d = –0.07) and probably has no meaning from a clinical perspective. When we explored what caused this difference, we found several important results.

First, we found that pharmacotherapy is more clearly superior to psychotherapy in the treatment of dysthymia. In the studies of patients with pure dysthymia, a differential effect of –0.44 was found, indicating a moderate effect. And the difference between the 2 types of treatment in dysthymia was significantly larger than the difference in patients with major depressive disorder.

The second important finding was that SSRIs were significantly more effective than psychotherapy and that the difference between the 2 types of treatment was significantly larger when SSRIs were used compared with studies in which other medications were used. Although the difference between SSRIs and psychotherapy was significant (p < .05), it was small in terms of effect sizes (d = –0.16), and it is not clear whether such a small effect is clinically relevant. This finding is remarkable, however, because most studies examining differential effects of SSRIs and TCAs find that both are equally effective.[1]

We found few indications of heterogeneity in the analyses, indicating that there were few systematic differences between the outcomes. When we differentiated between studies examining dysthymia and those studying major depressive disorder, the heterogeneity was zero. The same was true when we differentiated between studies examining TCAs, SSRIs, and other antidepressant medications. This can be seen as an indication that the heterogeneity in the overall analyses, although low at the beginning, can be explained by these 2 variables and supports the stability of our findings.

Dropout, however, was significantly lower in psychotherapy compared with pharmacologic treatment. This is probably related to the side effects of pharmacologic treatments and may be associated with the fact that most

patients prefer psychological therapies more than pharmacologic treatments.[19]

We could not find any evidence that the differential effects of psychological and pharmacologic treatments are related to the severity of the depressive disorder at pretest. Relatively few studies, however, focused on patients with very severe depression, and it can be argued that the most severe cases are unlikely to end up in a comparative trial of medication versus psychological treatment. However, in light of the current discussion on the suitability of psychological treatment for more severely depressed patients, the present findings do not strongly support the notion that psychological treatment is insufficient for more severe cases of depression.

This study has several limitations. First, the number of studies we could include was still relatively small, and the quality of several of the included studies was not optimal. Second, we did not examine the long-term effects of both treatments. It may well be possible that there are major differences between the 2 treatments in the longer term. Third, studies on pharmacologic treatments often include psychological treatment components and unrealistic monitoring such as weekly visits, which may have distorted the actual differences between psychological and pharmacologic treatments. Furthermore, we only examined the effects in the short term and have not focused on differences in the long term. Because of these limitations, the results of this meta-analysis should be considered with caution.

More research is needed to examine our findings further. It is especially important to examine the mechanisms through which both treatments work and to examine which patients may benefit more from 1 of the 2 types of treatment. It is also important to examine for which cases combined treatment is better. We can conclude that both psychological and pharmacologic therapies are effective in the treatment of depressive disorders and that each has its own merits.

Drug names: desipramine (Norpramin and others), fluoxetine (Prozac and others), imipramine (Tofranil and others), nortriptyline (Pamelor and others), paroxetine (Paxil, Pexeva, and others), phenelzine (Nardil), sertraline (Zoloft and others), venlafaxine (Effexor and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

REFERENCES

1. Anderson IM. Meta-analytic studies on new antidepressants. Br Med Bull 2001;57:161–178
2. Cuijpers P, Dekker J. Psychologische behandeling van depressie: een systematisch overzicht van meta-analyses [Psychological treatment of depression; a systematic review of meta-analyses]. Ned Tijdschr Geneesk 2005 Aug;149(34):1892–1897
3. Robinson LA, Berman JS, Neimeyer RA. Psychotherapy for the treatment of depression: a comprehensive review of controlled outcome research. Psychol Bull 1990;108:30–49
4. Dobson KS. A meta-analysis of the efficacy of cognitive therapy for depression. J Consult Clin Psychol 1989;57:414–419
5. De Maat S, Dekker J, Schoevers R, et al. Relative efficacy of psychotherapy and pharmacotherapy in the treatment of depression: a meta-analysis. Psychother Res 2006;16:566–578
6. DeRubeis RJ, Gelfand LA, Tang TZ, et al. Medication versus cognitive behavior therapy for severely depressed outpatients: mega-analysis of four randomized comparisons. Am J Psychiatry 1999;156:1007–1013
7. DeRubeis RJ, Hollon SD, Amsterdam JD, et al. Cognitive therapy vs medications in the treatment of moderate to severe depression. Arch Gen Psychiatry 2005;62:409–416
8. Spielmans GI, Pasek LF, McFall JP. What are the active ingredients in cognitive and behavioral psychotherapy for anxious and depressed children? a meta-analytic review. Clin Psychol Rev 2007 Jun;27(5):642–654
9. Shadish WR, Sweeney RB. Mediators and moderators in meta-analysis: there's a reason we don't let dodo birds tell us which psychotherapies should have prizes. J Consult Clin Psychol 1991;59:883–893
10. Cuijpers P, van Straten A, Warmerdam L. Behavioral treatment of depression: a meta-analysis of activity scheduling. Clin Psychol Rev 2007;27:318–326
11. Cuijpers P, van Straten A, Smit F. Psychological treatments of subthreshold depression: a meta-analytic review. Acta Psychiatr Scand 2007;115: 434–441
12. Cuijpers P, van Straten A, Warmerdam L, et al. Characteristics of effective psychological treatments of depression: a meta-regression analysis. Psychother Res 2008. In press
13. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 [updated May 2005]. In: The Cochrane Library, Issue 3. Chichester, UK: John Wiley & Sons, Ltd; 2005
14. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988
15. Wolf FM. Meta-Analysis: Quantitative Methods for Research Synthesis. Beverly Hills, Calif: Sage; 1986
16. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000 Jun;56(2):455–463
17. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–560
18. Barrett JE, Williams JWJ, Oxman TE, et al. Treatment of dysthymia and minor depression in primary care: a randomized trial in patients aged 18 to 59 years. J Fam Pract 2001;50:405–412
19. Bedi N, Chilvers C, Churchill R, et al. Assessing effectiveness of treatment of depression in primary care; partially randomised preference trial. Br J Psychiatry 2000;177:312–318
20. Blackburn IM, Moore RG. Controlled acute and follow-up trial of cognitive therapy and pharmacotherapy in out-patients with recurrent depression. Br J Psychiatry 1997;171:328–334
21. Browne G, Steiner M, Roberts J, et al. Sertraline and/or interpersonal psychotherapy for patients with dysthymic disorder in primary care: 6-month comparison with longitudinal 2-year follow-up of effectiveness and costs. J Affect Dis 2002;68:317–330
22. Dimidjian S, Hollon SD, Dobson KS, et al. Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. J Consult Clin Psychol 2006;74:658–670
23. Dunner DL, Schmaling KB, Hendrickson H, et al. Cognitive therapy versus fluoxetine in the treatment of dysthymic disorder. Depression 1996;4(1):34–41
24. Elkin I, Shea MT, Watkins JT, et al. Treatment of depression collaborative research program. Arch Gen Psychiatry 1989;46:971–982
25. Hollon SD, DeRubeis RJ, Evans MD, et al. Cognitive therapy and pharmacotherapy for depression: singly and in combination. Arch Gen Psychiatry 1992;49:774–781
26. Jarrett RB, Schaffer M, McIntire D, et al. Treatment of atypical depression with cognitive therapy or phenelzine: a double-blind, placebo-controlled trial. Arch Gen Psychiatry 1999;56:431–437
27. Keller MB, McCullough JP, Klein DN, et al. A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. New Engl J Med 2000;342:1462–1470
28. Leff J, Vearnals S, Brewin CR, et al. The London Depression Intervention Trial: randomised controlled trial of antidepressants v couple therapy in the treatment and maintenance of people with depression living with

a partner: clinical outcome and costs. Br J Psychiatry 2000 Aug;177: 95–100
29. Lopez Rodriguez J, Lopez Butron MA, Vargas Terrez BE, et al. Estudio doble ciego con antidepresivo, psicoterapia breve y placebo en pacientes con depresion leve a moderada [Double blind study with antidepressant, brief psychotherapy and placebo in patients with mild to moderate depression]. Salud Mental 2004;27:53–61
30. Markowitz JC, Kocsis JH, Bleiberg KL, et al. A comparative trial of psychotherapy and pharmacotherapy for "pure" dysthymic patients. J Affect Dis 2005;89:167–175
31. Martin SD, Martin E, Rai SS, et al. Brain blood flow changes in depressed patients treated with interpersonal psychotherapy or venlafaxine hydrochloride: preliminary findings. Arch Gen Psychiatry 2001;58: 641–648
32. McBride C, Segal Z, Kennedy S, et al. Changes in autobiographical memory specificity following cognitive behavior therapy and pharmacotherapy for major depression. Psychopathology 2007;40(3):147–152
33. McKnight DL, Nelson-Gray RO, Barnhill J. Dexamethasone suppression test and response to cognitive therapy and antidepressant medication. Behav Ther 1992;23:99–111
34. McLean PD, Hakstian AR. Clinical depression: comparative efficacy of outpatient treatments. J Consult Clin Psychol 1979;47:818–836
35. Miranda J, Chung JY, Green BL, et al. Treating depression in predominantly low-income young minority women: a randomized controlled trial. JAMA 2003;290:57–65
36. Mohr DC, Boudewyn AC, Goodkin DE, et al. Comparative outcomes for individual cognitive-behavior therapy, supportive-expressive group psychotherapy, and sertraline for the treatment of depression in multiple sclerosis. J Consult Clin Psychol 2001;69:942–949
37. Murphy GE, Simons AD, Wetzel RD, et al. Cognitive therapy and pharmacotherapy singly and together in the treatment of depression. Arch Gen Psychiatry 1984;41:33–41
38. Mynors-Wallis LM, Gath DH, Lloyd-Thomas AR, et al. Randomised controlled trial comparing problem solving treatment with amitriptyline and placebo for major depression in primary care. BMJ 1995;310: 441–445
39. Mynors-Wallis LM, Gath DH, Day A, et al. Randomised controlled trial of problem solving treatment, antidepressant medication, and combined treatment for major depression in primary care. BMJ 2000;320:26–30
40. Rush AJ, Beck AT, Kovacs M, et al. Comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressed outpatients. Cog Ther Res 1977;1(1):17–37
41. Schulberg HC, Block MR, Madonia MJ, et al. Treating major depression in primary care practice: eight-month clinical outcomes. Arch Gen Psychiatry 1996;53:913–919
42. Scott AI, Freeman CP. Edinburgh primary care depression study: treatment outcome, patient satisfaction, and cost after 16 weeks. BMJ 1992;304:883–887
43. Sloane RB, Staples FR, Schneider LS. Interpersonal therapy vs nortriptyline for depression in the elderly: clinical and pharmacological studies in psychiatric disorders. Biol Psychiatry New Prospects 1985:344–346
44. Thompson LW, Coon DW, Gallagher-Thompson D, et al. Comparison of desipramine and cognitive/behavioral therapy in the treatment of elderly outpatients with mild-to-moderate depression. Am J Geriatr Psychiatry 2001;9:225–240
45. Weissman MM, Prusoff BA, DiMascio A, et al. The efficacy of drugs and psychotherapy in the treatment of acute depressive episodes. Am J Psychiatry 1979;136:555–558
46. Williams JW, Barrett J, Oxman T, et al. Treatment of dysthymia and minor depression in primary care: a randomized controlled trial in older adults. JAMA 2000;284:1519–1526
47. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: 25 years of evaluation. Clin Psychol Rev 1988;8: 77–100

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