The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons

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Although psychotherapy and antidepressant medication are efficacious in the treatment of depressive and anxiety disorders, it is not known whether they are equally efficacious for all types of disorders, and whether all types of psychotherapy and antidepressants are equally efficacious for each disorder. We conducted a meta-analysis of studies in which psychotherapy and antidepressant medication were directly compared in the treatment of depressive and anxiety disorders. Systematic searches in bibliographical databases resulted in 67 randomized trials, including 5,993 patients that met inclusion criteria, 40 studies focusing on depressive disorders and 27 focusing on anxiety disorders. The overall effect size indicating the difference between psychotherapy and pharmacotherapy after treatment in all disorders was g=0.02 (95% CI: −0.07 to 0.10), which was not statistically significant. Pharmacotherapy was significantly more efficacious than psychotherapy in dysthymia (g=0.30), and psychotherapy was significantly more efficacious than pharmacotherapy in obsessive-compulsive disorder (g=0.64). Furthermore, pharmacotherapy was significantly more efficacious than non-directive counseling (g=0.33), and psychotherapy was significantly more efficacious than pharmacotherapy with tricyclic antidepressants (g=0.21). These results remained significant when we controlled for other characteristics of the studies in multivariate meta-regression analysis, except for the differential effects in dysthymia, which were no longer statistically significant.

Key words: Psychotherapy, antidepressant medication, depressive disorders, anxiety disorders, dysthymia, obsessive-compulsive disorder, meta-analysis

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Depressive and anxiety disorders are highly prevalent (1,2) and associated with high levels of service use, a considerable disease burden (3), substantial economic costs (4–6), and a significant loss of quality of life for patients and their relatives (7,8). Several efficacious treatments for depressive and anxiety disorders are available, including different forms of psychotherapy and antidepressant medication (9–11). Although both types of treatment have been found to be efficacious, it is not known whether they are equally efficacious for all types of depressive and anxiety disorders. There is evidence from meta-analyses of studies comparing psychotherapy and pharmacotherapy directly that they are about equally efficacious in depression (12) and generalized anxiety disorder (GAD) (13). It is not clear whether this is true for all depressive and anxiety disorders. For example, for obsessive-compulsive disorder (OCD) and social anxiety disorder (SAD), no meta-analyses of direct comparisons between psychotherapy and pharmacotherapy have been conducted yet, even though a considerable number of such comparative trials have been carried out.

Furthermore, it remains unclear whether all types of psychotherapy and all types of antidepressant medications have comparable effects. In one previous meta-analysis, we found that treatment with selective serotonin reuptake inhibitors (SSRIs) was somewhat more effective than treatment with psychotherapy (12), whereas tricyclic antidepressants (TCAs) and psychotherapy were equally effective. A re-analysis of those data, however, showed that there were no significant differences between psychotherapy and SSRIs after adjusting for differential drop-out from both treatments. Another meta-analysis confirmed that psychotherapy and SSRIs were equally effective, when only *bona fide* psychotherapies were included (14).

It is also possible that there are differences between different forms of psychotherapy. There are some indications from meta-analytic research that interpersonal psychotherapy (IPT) may be somewhat more efficacious than other psychotherapies in the treatment of depression (15,16), although this is not confirmed in all meta-analyses (17). There are also some indications that psychodynamic psychotherapy (18) and non-directive supportive counselling (19) may be somewhat less efficacious than other psychotherapies. Given these potential differences between psychotherapies, it is conceivable that the differential effects of psychotherapy and pharmacotherapy may depend on the type of psychotherapy. Earlier meta-analyses may have failed to detect these differential effects because of the small number of included studies and the resulting lack of statistical power.

We report here the results of an overall meta-analysis of the studies in which psychotherapy and antidepressant medication for depressive and anxiety disorders were directly compared with each other.

METHODS

Identification and selection of studies

Several strategies were used to identify relevant studies. We searched four major bibliographical databases (PubMed, PsycInfo, EMBASE and the Cochrane database of randomized trials) by combining terms indicative of each of the disorders with terms indicative of psychological treatment (both MeSH terms and text words) and randomized controlled trials. We also checked the references of 116 earlier meta-analyses of psychological treatments for the included disorders. Details of the searches and exact search strings are given in Figure 1.

We included randomized trials in which the effects of a psychological treatment were directly compared with the effects of antidepressant medication in adults with depressive disorder, panic disorder with or without agoraphobia, GAD, SAD, OCD, or post-traumatic stress disorder (PTSD). Only studies in which subjects met diagnostic criteria for the disorder according to a structured diagnostic interview – such as the Structured Clinical Interview for DSM-IV (SCID), the Composite International Diagnostic Interview (CIDI) or the Mini International Neuropsychiatric Interview (MINI) – were included. Comorbid mental or somatic disorders were not used as an exclusion criterion. Studies on inpatients, adolescents and children (below 18 years of age) were excluded. We also excluded maintenance studies, aimed at people who had already recovered or partly recovered after an earlier treatment, and studies on other types of medication, such as benzodiazepines for anxiety disorders. Studies in English, German, Spanish and Dutch were considered for inclusion.

Quality assessment and data extraction

We evaluated the quality of included studies using the Cochrane Collaboration "risk of bias" assessment tool (20). This tool assesses possible sources of bias in randomized trials, including the adequate generation of allocation sequence, the concealment of allocation to conditions, the prevention of knowledge of the allocated intervention (masking of assessors), and dealing with incomplete outcome data (this was rated as positive when intention-to-treat analyses were conducted, meaning that all randomized patients were included in the analyses). The assessment was conducted by two independent researchers, and disagreements were solved through discussion.

We also coded the participant characteristics (disorder, recruitment method, target group); the type of antidepressant which was used (SSRI, TCA, monoamine oxidase inhibitor (MAOI), other or protocolized treatment including several antidepressants); and the characteristics of the psychotherapy (format, number of sessions, and type of psychotherapy). The types of psychotherapy we identified were cognitive-behavioral therapy (CBT), IPT, problem-solving therapy, non-directive supportive counselling, psychodynamic psychotherapy, and others. Although CBTs used a mix of different techniques, we clustered them together in one group. We rated a therapy as CBT when it included cognitive restructuring or a behavioral approach (such as exposure and response prevention). When a therapy used a mix of CBT and IPT, we rated it as "other", along with other therapeutic approaches.

Meta-analyses

For each comparison between a psychotherapy and a pharmacotherapy, the effect size indicating the difference between the two groups at post-test (Hedges' g) was evaluated. Effect sizes were calculated by subtracting (at post-test) the average score of the psychotherapy group from the average score of the pharmacotherapy group, and dividing the result by the pooled standard deviation. Because some studies had relatively small sample sizes, we corrected the effect size for small sample bias (21).

In the calculations of effect sizes in studies of patients with depressive disorders, we used only those instruments that explicitly measured symptoms of depression. In studies examining anxiety disorders, we only used instruments that explicitly measured symptoms of anxiety. If more than one measure was used, the mean of the effect sizes was calculated, so that each study provided only one effect size. If means and standard deviations were not reported, we used the procedures of the Comprehensive Meta-Analysis software (version 2.2.021) to calculate the effect size using dichotomous outcomes; and if these were not available either, we used other statistics (such a t value or p value). To calculate pooled mean effect sizes, we also used the Comprehensive Meta-Analysis software. Because we expected considerable heterogeneity among the studies, we employed a random effects pooling model in all analyses.

We only examined the differential effects at post-test and did not look at the longer-term effects. The types of outcomes reported at follow-up and the follow-up periods differed widely between studies. Furthermore, some studies reported only naturalistic outcomes, while others delivered booster sessions and maintenance treatments during the whole follow-up period or part of it. Because of these large differences, we decided it was not meaningful to pool the results of these outcomes.

As a test of homogeneity of effect sizes, we calculated the I^2 statistic. A value of 0% indicates no observed heterogeneity, and higher values indicate increasing heterogeneity, with 25% as low, 50% as moderate, and 75% as high heterogeneity (22). We calculated 95% confidence intervals around I^2 (23) using the non-central chi-squared-based approach within the Heterogi module for Stata (24).

We conducted subgroup analyses according to the mixed effects model, in which studies within subgroups are pooled

	Depression	GAD	SAD	Panic	OCD/PTSD	Total
21,729 references identified by literature search						
Pubmed	3320	547	296	849	91	5103
Cochrane	2988	1309	752	1436	128	6613
PsycInfo	2710	337	246	424	32	3749
Embase	4389	372	661	764	78	6264
Total	13407	2565	1955	3473	329	21729
⇓						
After removal of duplicates						
	9860	1562	1228	2032	221	14903
⇓						
Earlier meta-analyses checked for references						
	42	7	14	26	27	116
⇓						
Full-text papers retrieved						
	1344	136	247	493	58	2278
⇓						
Reasons for exclusion						
No correct comparison	235	49	83	169	27	563
Duplicate study	306	32	24	52	5	419
No diagnosis	165	32	52	112	2	363
No control group	167	7	39	33	3	249
No psychotherapy	151	7	1	76	3	238
Other reason	280	8	41	40	10	379
Total	1304	135	240	482	50	2211
⇓						
Included in meta-analysis	40	1	7	11	OCD: 6 PTSD: 2	67

GAD – generalized anxiety disorder, SAD – social anxiety disorder, OCD – obsessive-compulsive disorder, PTSD – post-traumatic stress disorder

Figure 1 Selection and inclusion of studies

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 by a Z value and an associated p value.

We tested for publication bias by inspecting the funnel plot on primary outcome measures and by Duval and Tweedie's trim and fill procedure (25), which yields an estimate of the effect size after the publication bias has been taken into account. We also conducted Egger's test of the intercept to quantify the bias captured by the funnel plot and test whether it was significant.

Multivariate meta-regression analyses were conducted with the effect size as the dependent variable. To decide which variables should be entered as predictors in the regression model, we first defined a reference group within each category of variables. To avoid collinearity among the predictors of the regression model, we first examined whether high correlations were found among the variables that could be entered into the model. Next, we calculated the correlations between all predictors (except the reference variables). Because no correlations were higher than r=0.60, all predictors could be entered in the regression models. Multivariate regression analyses were conducted in STATA MP, version 11 for Mac.

RESULTS

Selection and inclusion of studies

After examining a total of 21,729 abstracts (14,903 after removal of duplicates), we retrieved 2,278 full-text papers for

Table 1 Selected characteristics of included studies

Study	Disorder	Psychotherapy	Medication	Quality*	Country
Bakhshani et al (26)	GAD	CBT (n=7)	TCA (n=7)	− − − +	Iran
Bakker et al (27)	PAN	CBT (n=35)	SSRI (n=32)	− − − +	Europe
			TCA (n=32)		
Barber et al (28)	MDD	DYN (n=51)	Mixed/other (n=55)	− − + +	USA
Barlow et al (29)	PAN	CBT (n=65)	TCA (n=83)	− − + +	USA
Barrett et al (30)	Mood	PST (n=80)	SSRI (n=80)	+ + + +	USA
Bedi et al (31)	MDD	Counseling (n=39)	Mixed/other (n=44)	+ + − −	Europe
Black et al (32)	PAN	CBT (n=25)	SSRI (n=25)	− − − −	USA
Blackburn & Moore (33)	MDD	CBT	Mixed/other	− − − +	Europe
Blanco et al (34)	SAD	CBT (n=32)	MAOI (n=35)	+ + + +	USA
Blomhoff et al (35)	SAD	BT (n=98)	SSRI (n=95)	+ + + +	Europe
Browne et al (36)	DYS	IPT (n=122)	SSRI (n=117)	+ + + −	Canada
Clark et al (37)	PAN	CBT (n=16)	TCA (n=16)	− − + −	Europe
Dannon et al (38)	PAN	CBT (n=23)	SSRI (n=27)	− − − −	Israel
David et al (39)	MDD	CBT (n=56)	SSRI (n=57)	− − + +	Europe
		REBT (n=57)			
Davidson et al (40)	SAD	CBT (n=42)	SSRI (n=39)	+ + + +	USA
Dekker et al (41)	MDD	DYN (n=59)	Mixed/other (n=44)	− − + −	Europe
Dunlop et al (42)	MDD	CBT (n=41)	SSRI (n=39)	+ + + +	USA
Dunner et al (43)	DYS	CBT (n=9)	SSRI (n=11)	− − + −	USA
Elkin et al (44)	MDD	IPT (n=61)	TCA (n=57)	+ + + +	USA
		CBT (n=59)			
Faramarzi et al (45)	MDD	CBT (n=29)	SSRI (n=30)	− − + −	Iran
Finkenzeller et al (46)	MDD	IPT (n=23)	SSRI (n=24)	+ − + +	Europe
Foa et al (47)	OCD	BT (n=19)	TCA (n=27)	− − + −	USA
Frank et al (48)	MDD	IPT (n=160)	SSRI (n=158)	− − + +	USA
Frommberger et al (49)	PTSD	CBT (n=10)	SSRI (n=11)	− − − −	Europe
Hegerl et al (50)	Mood	CBT (n=52)	SSRI (n=76)	+ + + +	Europe
Heimberg et al (51)	SAD	CBT (n=28)	MAOI (n=27)	− − + +	USA
		Counseling (n=26)			
Hendriks et al (52)	PAN	CBT (n=20)	SSRI (n=17)	+ + + +	Europe
Hoexter et al (53)	OCD	CBT (n=13)	SSRI (n=13)	+ − + −	Brazil
Hollon et al (54)	MDD	CBT (n=25)	TCA (n=57)	− − + +	USA
Jarrett et al (55)	MDD	CBT (n=36)	MAOI (n=36)	+ + + +	USA
Keller et al (56)	MDD	CBASP (n=226)	SNRI (n=220)	+ + + +	USA
Kolk et al (57)	PTSD	EMDR (n=24)	SSRI (n=26)	− − + +	USA
Koszycki et al (58)	PAN	CBT (n=59)	SSRI (n=62)	+ + + +	Canada
Lesperance et al (59)	MDD	IPT (n=67)	SSRI (n=75)	+ + + +	Canada
Loerch et al (60)	PAN	CBT (n=14)	MAOI (n=16)	− − + +	Europe
Markowitz et al (61)	DYS	IPT (n=23)	SSRI (n=24)	− − + +	USA
		Counseling (n=26)			
Marshall et al (62)	MDD	CBT (n=37)	Mixed/other (n=30)	− − − −	Canada
		IPT (n=35)			
Martin et al (63)	MDD	IPT (n=13)	SNRI (n=15)	− − − +	Europe

Table 1 Selected characteristics of included studies *(continued)*

Study	Disorder	Psychotherapy	Medication	Quality*	Country
McBride et al (64)	MDD	CBT (n=21)	Mixed/other (n=21)	− − − −	Canada
McKnight et al (65)	MDD	CBT	TCA	− − − −	USA
McLean & Hakstian (66)	MDD	DYN (n=44)	TCA (n=49)	− − + −	Canada
		BT (n=42)			
Miranda et al (67)	MDD	CBT (n=90)	Mixed/other (n=88)	+ + + +	USA
Mohr et al (68)	MDD	CBT (n=20)	SSRI (n=15)	− − − +	USA
		Supp Ex (n=19)			
Mörtberg et al (69)	SAD	CBT ind (n=32)	Mixed/other (n=33)	+ + + +	Europe
		CBT grp (n=35)			
Murphy et al (70)	MDD	CBT (n=22)	TCA (n=24)	+ + − +	USA
Murphy et al (71)	MDD	PST (n=29)	TCA (n=27)	+ + + +	Europe
Mynors-Wallis et al (72)	MDD	PST gp (n=39)	SSRI (n=36)	+ + + +	Europe
		PST n (n=41)			
Nakatani et al (73)	OCD	BT (n=10)	SSRI (n=10)	− − + −	Japan
Nazari et al (74)	OCD	EMDR (n=30)	SSRI (n=30)	− − + −	Iran
Oosterbaan et al (75)	SPH	CBT (n=28)	MAOI (n=27)	− − + +	Europe
Prasko et al (76)	SPH	CBT (n=22)	MAOI (n=20)	− − + −	Europe
Ravindran et al (77)	DYS	CBT (n=24)	SSRI (n=22)	+ + + −	Canada
Reynolds et al (78)	MDD	IPT (n=16)	TCA (n=25)	− − + +	USA
Rush et al (79)	MDD	CBT (n=19)	TCA (n=22)	− − + +	USA
Salminen et al (80)	MDD	DYN (n=26)	SSRI (n=25)	− − − +	Europe
Schulberg et al (81)	MDD	IPT (n=93)	TCA (n=91)	− −+ +	USA
Scott & Freeman (82)	MDD	CBT (n=29)	TCA (n=26)	+ + + +	Europe
		Counseling (n=29)			
Shamsaei et al (83)	MDD	CBT (n=40)	SSRI (n=40)	+ − + −	Iran
Shareh et al (84)	OCD	CBT (n=6)	SSRI (n=6)	− − − −	Iran
Sharp et al (85)	PAN	CBT (n=29)	SSRI (n=29)	− − − −	Europe
Sharp et al (86)	Mood	Counseling (n=112)	Mixed/other (n=106)	+ + + +	Europe
Sousa et al (87)	OCD	CBT (n=25)	SSRI (n=25)	− − + −	Brazil
Spinhoven et al (88)	PAN	CBT (n=20)	SSRI (n=19)	− − − +	Europe
Thompson et al (89)	MDD	CBT (n=36)	TCA (n=33)	− − − +	USA
Van Apeldoorn et al (90)	PAN	CBT (n=36)	Mixed/other (n=37)	+ + + +	Europe
Weissman et al (91)	MDD	IPT (n=23)	TCA (n=20)	− − + −	USA
Williams et al (92)	Mood	PST (n=113)	SSRI (n=106)	+ + + +	USA

*A positive or negative sign is given for four quality criteria: allocation sequence, concealment of allocation to conditions, blinding of assessors, and intention-to-treat analysis

GAD – generalized anxiety disorder, PAN – panic disorder with or without agoraphobia, MDD – major depressive disorder, Mood – mixed mood disorder, SAD – social anxiety disorder, DYS – dysthymic disorder, OCD – obsessive-compulsive disorder, PTSD – post-traumatic stress disorder, CBT – cognitive-behavioral therapy, DYN – psychodynamic therapy, PST – problem-solving therapy, BT – behavior therapy, IPT – interpersonal psychotherapy, REBT – rational emotive behavior therapy, CBASP – cognitive behavioral analysis system of psychotherapy, EMDR – eye movement desensitization and reprocessing, Supp Ex – supportive-expressive therapy, ind – individual format, grp – group format, gp – delivered by a general practitioner, n – delivered by a nurse, TCA – tricyclic antidepressant, SSRI – selective serotonin reuptake inhibitor, MAOI – monoamine oxidase inhibitor, SNRI – serotonin-norepinephrine reuptake inhibitor

further consideration. We excluded 2,211 of the retrieved papers. The flow chart describing the inclusion process, including the reasons for exclusion, is presented in Figure 1. A total of 67 studies met the inclusion criteria for this meta-analysis. Selected characteristics of the included studies (26–92) are reported in Table 1.

Characteristics of included studies

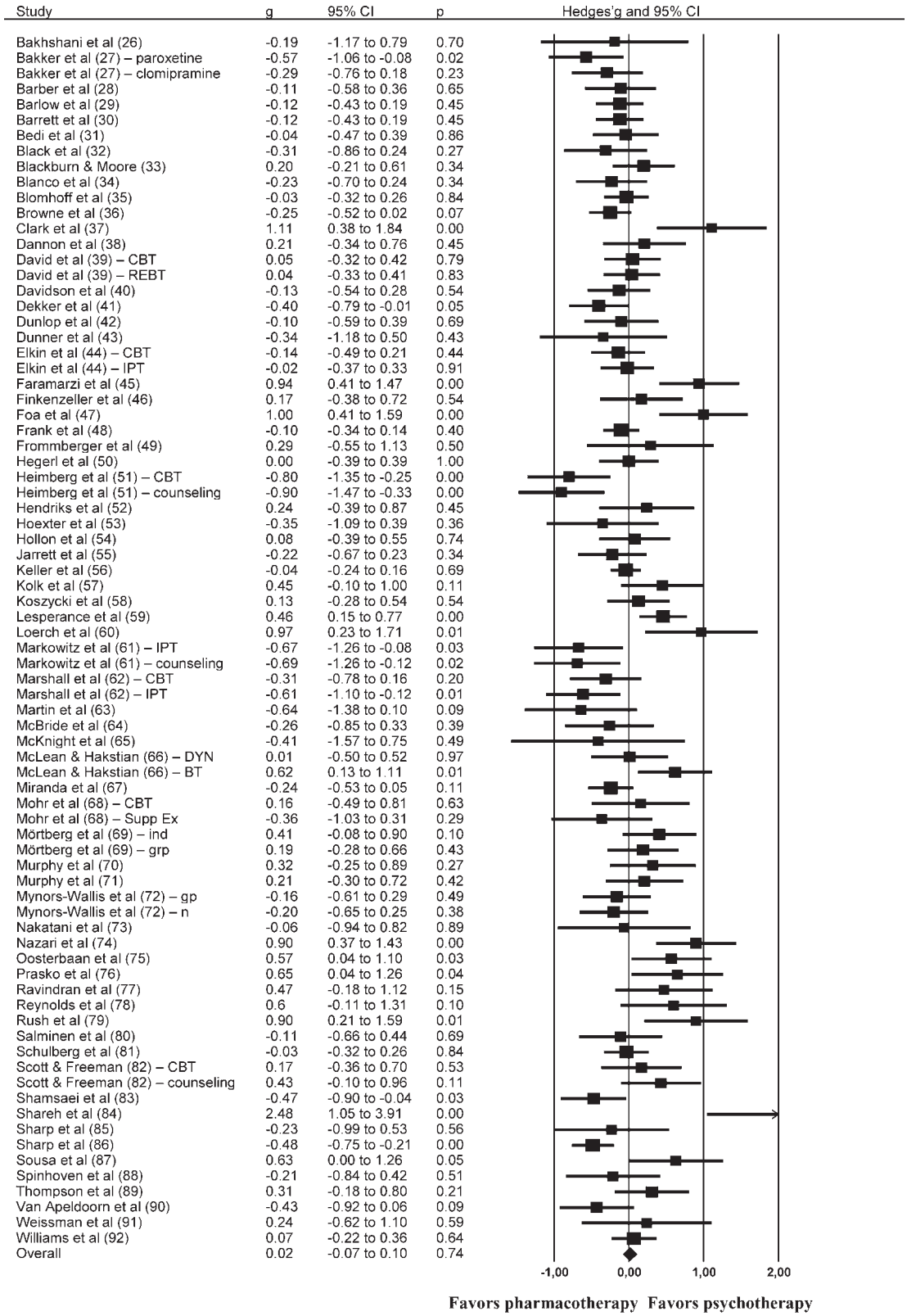
In the 67 studies, a total of 5,993 patients participated (3,142 in the psychotherapy and 2,851 in the pharmacotherapy conditions). Forty studies focused on depressive

Table 2 Comparative effects of psychotherapy and pharmacotherapy: subgroup analyses

		N	g	95% CI	I^2	95% CI	p
All studies		78	0.02	−0.07 to 0.10	62	52 to 70	
Possible outliers removed		68	−0.07	−0.14 to 0.01	41	21 to 56	
One effect size per study (highest)		67	0.06	−0.03 to 0.15	62	51 to 71	
One effect size per study (lowest)		67	0.03	−0.07 to 0.12	62	51 to 71	
Mood disorders							
	Any mood disorder	48	−0.03	−0.14 to 0.08	52	0 to 47	**0.01**
	Major depression	39	0.02	−0.10 to 0.13	46	22 to 63	
	Dysthymia	5	**−0.30**	−0.60 to −0.00	55	0 to 83	
	Mixed mood disorders	4	−0.14	−0.45 to 0.17	64	0 to 88	
Anxiety disorders							
	Any anxiety disorder	30	0.10	−0.05 to 0.25	71	59 to 80	
	Panic disorder	12	0.00	−0.28 to 0.28	62	28 to 79	
	SAD	9	−0.03	−0.34 to 0.28	74	50 to 87	
	OCD	6	**0.64**	0.20 to 1.08	72	36 to 88	
	Other	3	0.24	−0.39 to 0.86	0	0 to 90	
Psychotherapy type							
	Cognitive-behavioral therapy	49	0.09	−0.03 to 0.20	60	46 to 71	0.12
	Interpersonal psychotherapy	11	−0.09	−0.31to 0.14	65	33 to 82	
	Problem-solving therapy	5	−0.04	−0.36 to 0.27	0	0 to 79	
	Counseling	6	**−0.33**	−0.64 to −0.02	69	27 to 87	
	Other	7	0.07	−0.21 to 0.34	67	27 to 85	
Treatment format							
	Individual	62	0.02	−0.08 to 0.12	61	48 to 70	0.89
	Group	14	0.03	−0.18 to 0.25	71	50 to 83	
Pharmacotherapy							
	SSRI	37	0.01	−0.12 to 0.13	58	40 to 71	**0.02**
	TCA	20	**0.21**	0.04 to 0.39	52	19 to 71	
	MAOI	7	−0.05	−0.34 to 0.25	83	65 to 91	
	Mixed/protocol/other	14	−0.19	−0.37 to 0.00	49	5 to 72	
Recruitment							
	Only clinical samples	36	0.07	−0.06 to 0.20	55	34 to 69	0.52
	Also community recruitment	35	−0.03	−0.16 to 0.10	65	50 to 76	
	Other recruitment method	7	−0.04	−0.34 to 0.25	76	49 to 89	
Country							
	USA	31	−0.07	−0.21 to 0.07	52	28 to 68	0.17
	Europe	29	0.03	−0.11 to 0.17	56	34 to 71	
	Other	18	0.15	−0.04 to 0.34	76	62 to 85	
Quality							
	Score 0–1	31	0.10	−0.06 to 0.25	69	56 to 79	0.44
	Score 2–3	23	−0.03	−0.19 to 0.13	65	46 to 78	
	Score 4	24	−0.02	−0.17 to 0.12	38	0 to 62	

All subgroup analyses were conducted with the random effects model; a positive effect size indicates superior effects of psychotherapy; the p values indicate whether the effect sizes in the subgroups differ significantly from each other; significant values are highlighted in bold

SAD – social anxiety disorder, OCD – obsessive-compulsive disorder, SSRI – selective serotonin reuptake inhibitor, TCA – tricyclic antidepressant, MAOI – monoamine oxidase inhibitor



CBT – cognitive-behavioral therapy, REBT – rationale emotive behavior therapy, IPT – interpersonal psychotherapy, DYN – psychodynamic therapy, BT – behavior therapy, Supp Ex – supportive-expressive therapy, ind – individual format, grp – group format, gp – delivered by a general practitioner, n – delivered by a nurse

Figure 2 Differential effects of psychotherapy and pharmacotherapy (Hedges' g)

Table 3 Standardized regression coefficients of characteristics of psychotherapy and pharmacotherapy studies

		Full model			Parsimonious model		
		Coef.	95% CI	p	Coef.	95% CI	p
Disorder							
	MDD	Ref.					
	Dysthymia	−0.01	−0.46 to 0.43				
	Other mood disorder	0.02	−0.42 to 0.45				
	Panic disorder	−0.10	0.42 to 0.21				
	SAD	0.12	−0.28 to 0.53				
	OCD	0.52	0.01 to 1.03	<0.05	0.76	0.36 to 1.15	<0.001
	Other anxiety disorder	0.32	−0.30 to 0.95				
Recruitment from clinical samples only		0.05	−0.17 to 0.26				
Adults in general vs. specific target group		−0.41	−0.70 to-0.13	<0.01	−0.27	−0.50 to - 0.05	<0.05
Psychotherapy							
	CBT	Ref.					
	ITP	−0.16	−0.45 to 0.12				
	Counseling	−0.51	−0.92 to −0.19	<0.05	−0.41	−0.72 to −0.09	<0.05
	Other therapy	−0.03	−0.39 to 0.33				
Pharmacotherapy							
	SSRI	Ref.					
	TCA	0.32	0.06 to 0.58	<0.05	0.31	0.11 to 0.50	<0.01
	MAOI	0.07	−0.34 to 0.48				
	Other	−0.23	−0.51 to 0.05				
Individual psychotherapy format		0.01	−0.27 to 0.28				
Number of psychotherapy sessions		0.01	−0.02 to 0.04				
Quality of study		0.00	−0.07 to 0.08				
Country							
	USA	Ref.					
	Europe	0.26	0.03 to 0.49	<0.05	0.18	0.00 to 0.36	<0.05
	Other	−0.00	−0.31 to 0.31				
Constant		0.31	−0.29 to 0.91		0.09	−0.12 to 0.29	

MDD – major depressive disorder, SAD – social anxiety disorder, OCD – obsessive-compulsive disorder, CBT – cognitive-behavioral therapy, ITP – interpersonal psychotherapy, SSRI – selective serotonin reuptake inhibitor, TCA – tricyclic antidepressant, MAOI – monoamine oxidase inhibitor

disorders (32 on major depressive disorder, four on dysthymia, and four on mixed mood disorders) and 27 on anxiety disorders (11 on panic disorder with or without agoraphobia, six on OCD, seven on SAD, two on PTSD, and one on GAD). Many studies (n=32) recruited patients exclusively from clinical samples, and most (n=56) were aimed at adults in general instead of a more specific population (such as older adults or patients with a comorbid somatic disorder). Most psychotherapies (49 of the 78 that were examined in these studies) were characterized as CBT; 11 studies examined IPT, five problem-solving therapy, six non-directive counseling, four psychodynamic therapies, and the remaining three other therapies. Most therapies (n=62) used an individual treatment format, and the number of treatment sessions ranged from 6 to 20, with most therapies (n=45) having between 12 and 18 sessions. The antidepressants that were examined in the studies included SSRIs (n=37), TCAs (n=20), SNRIs (n=2), MAOIs (n=7), and treatment protocols with different types of antidepressant medication (n=12). Most studies were conducted in the United States (n=27) or in Europe (n=23).

Quality assessment

The quality of the studies varied. Twenty-seven studies reported an adequate sequence generation, while the other 40 did not. Twenty-four studies reported allocation to conditions by an independent (third) party. Forty-nine studies reported blinding of outcome assessors or used only self-report outcomes, whereas 18 did not report blinding. Forty-two studies conducted intention-to-treat analyses (a post-treatment score was analyzed for every patient even if the last observation

prior to attrition had to be carried forward or that score was estimated from earlier response trajectories). Twenty studies met all four quality criteria, four studies met three criteria, and the remaining 43 studies met two criteria or less.

Comparative effects of psychotherapy and pharmacotherapy

The overall mean effect size indicating the difference between psychotherapy and pharmacotherapy at post-test for all 78 comparisons was 0.02 (95% CI: −0.07 to 0.10; Table 2), in favor of psychotherapy, but not significantly different from zero. Heterogeneity was moderate to high (I^2=62; 95% CI: 52 to 70). The results of these overall analyses are presented in Figure 2.

Removing possible outliers (in which the 95% CI of the effect size did not overlap with the 95% CI of the pooled effect size) resulted in a small, non-significant effect size in favor of pharmacotherapy and somewhat lower heterogeneity (I^2=41; low to moderate).

In this meta-analysis, we included ten studies in which two psychological treatments were compared with the same pharmacotherapy group, as well as one study in which one psychological treatment was compared with two different types of antidepressant medication. This means that multiple comparisons from these studies, not independent from each other, were included in the same analysis, which may have resulted in an artificial reduction of heterogeneity and may have affected the pooled effect size. We examined the possible effects of this by conducting an analysis in which we included only one effect size per study. First, we included only the comparison with the largest effect size from these studies and then we conducted another analysis in which we included only the smallest effect size. As can be seen from Table 2, the resulting effect sizes as well as the levels of heterogeneity were comparable with the overall analyses.

We found no indications for publication bias. The effect size did not change after adjusting for publication bias according to Duval and Tweedie's trim and fill procedure, and according to this procedure no missing study had to be imputed.

Univariate moderator analyses

We examined whether there were significant differences between psychotherapy and pharmacotherapy in specific subgroups of studies. The results of these subgroup analyses are presented in Table 2. We found that the effect size was significantly associated with the type of disorder ($p<0.01$). More specifically, we found that pharmacotherapy was more efficacious than psychotherapy in dysthymia (differential effect size: g=−0.30; 95% CI: −0.60 to −0.00; I^2=55; 95% CI: 0 to 83). By contrast, psychotherapy was more efficacious than pharmacotherapy in OCD (differential effect size: g=0.64; 95% CI: 0.20 to 1.08; I^2=72; 95% CI: 36 to 88).

We also found that type of pharmacotherapy was significantly associated with the differential effect size ($p<0.05$). Treatment with a TCA was significantly less efficacious than psychotherapy (g=0.21; 95% CI: 0.04 to 0.39; I^2=52; 95% CI: 19 to 71), while there was no significant difference between other types of pharmacotherapy and psychotherapy. Furthermore, we found that treatment with non-directive supportive counseling was less efficacious than pharmacotherapy (g=−0.33; 95% CI: −0.64 to −0.02; I^2=69; 95% CI: 27 to 87).

We did not find that the effect size was associated with the treatment format in psychotherapy, recruitment method of patients, country where the study was conducted, or the quality of the study.

Multivariate meta-regression analyses

Because we found several important moderators of outcome in the univariate moderator analyses, we decided to conduct a multivariate meta-regression analysis in which we entered the relevant predictors simultaneously. The results of these analyses are presented in Table 3. The effects of psychotherapy were still significantly higher than those of pharmacotherapy in studies on OCD, even after adjusting for other characteristics of the included studies. We also found that non-directive supportive counseling was still significantly less efficacious than pharmacotherapy, and TCAs remained significantly less efficacious than psychotherapy. In dysthymia, psychotherapy and pharmacotherapy did no longer differ significantly from each other.

In the multivariate meta-regression analysis, the effects of two predictors became significant: studies in Europe had a higher pooled effect size (indicating superior effects of psychotherapy) than studies in other parts of the world, and pharmacotherapy was significantly more efficacious in studies among specific target groups (such as older adults and patients who also had a general medical disorder) than in those among adults in general.

We also conducted a (manual) back-step meta-regression analysis. In this analysis, we dropped the least significant variable in each step, until only significant predictors ($p<0.05$) were retained in the model (Table 3). In this parsimonious model, we found that the same predictors were significant as in the full meta-regression model.

DISCUSSION

In this meta-analysis, we found that the differences in effects between psychotherapy and antidepressant medication were small to non-existent for major depression, panic disorder and SAD. We also found evidence that pharmacotherapy was significantly more efficacious in dysthymia, and that psychotherapy was significantly more efficacious in OCD. Furthermore, pharmacotherapy was significantly more efficacious than non-directive counseling,

and psychotherapy was significantly more efficacious than pharmacotherapy with TCAs. These associations remained significant when we controlled for other characteristics of the studies in multivariate meta-regression analysis, except for the differential effects in dysthymia, which were no longer significant. In these multivariate meta-regression analyses, we also found that psychotherapy was more efficacious in studies from Europe compared with those from other countries, and that pharmacotherapy was significantly more efficacious in studies among specific target groups than in those among adults in general.

The present results indicate that different kinds of antidepressants and psychotherapies have varying degrees of efficacy in treating depression and anxiety disorders. TCAs and non-directive counseling seemed to be less efficacious than the other treatments, although we found in an earlier meta-analysis that the lower effects of non-directive counseling may be caused in part by researcher allegiance (93). The finding that psychotherapy is less efficacious than pharmacotherapy in dysthymia is in line with earlier meta-analytic research (94). However, the number of studies is small and the difference was no longer statistically significant after adjusting for quality and other study characteristics. As such, the finding is not very stable and more research is needed to examine this issue.

In OCD, the outcomes are rather straightforward in that psychotherapy is clearly more efficacious than antidepressants, even adjusting for quality and other characteristics of the studies. This is the first meta-analysis to show that psychotherapy is more efficacious than pharmacotherapy. This finding is also important from a clinical perspective, because OCD is often regarded as the most severe anxiety disorder.

One of the strengths of this study is the broad range of disorders and treatments we included. But the study also has some limitations. First, for several disorders insufficient numbers of studies were available. We only had a few studies examining PTSD, GAD and dysthymia. Second, the quality of many of the included studies was not optimal. Third, because of the many differences between the studies, we only examined the differential effects of psychotherapy and pharmacotherapy at post-test, and did not look at the longer-term effects. There are indications that psychotherapy may have sustained effects over the longer-term, while antidepressants do not have strong effects when the patients stop taking them (95). Fourth, we only considered the effects of treatments on the disorders they were designed to address. Finally, while it is well known that pharmacotherapies have several side effects, which are often reported in the studies, the idea that psychotherapies can have negative effects has only recently been recognized (96), and these negative effects are typically not reported in the studies. It was, therefore, not possible to compare psychotherapies and pharmacotherapies in terms of negative effects.

Despite the limitations, we can conclude that pharmacotherapy and psychotherapy have comparable effects in several depressive and anxiety disorders, but this is not true for all disorders, especially not for OCD and possibly dysthymia. Furthermore, most psychotherapies and pharmacotherapies are equally efficacious, but this again is not true for all treatments, especially for TCAs and non-directive supportive counseling. Finally, while treatments may be equal in effects, they may not be equal in terms of patient preferences and costs, which deserve further investigations across disorders.

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