Psychological treatment of depression: Results of a series of meta-analyses

4 authors:

Pim Cuijpers
VU University Amsterdam

778 PUBLICATIONS   27,657 CITATIONS

SEE PROFILE

Gerhard Andersson
Linköping University

784 PUBLICATIONS   22,219 CITATIONS

SEE PROFILE

Tara Donker
The Black Dog Institute

47 PUBLICATIONS   1,712 CITATIONS

SEE PROFILE

Annemieke van Straten
VU University Amsterdam

180 PUBLICATIONS   8,869 CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Project   Review of therapeutic and training effects View project

Project   The iSOFIE Project (https://www.iterapi.se/sites/isofie/) View project

Psychological treatment of depression: Results of a series of meta-analyses

PIM CUIJPERS, GERHARD ANDERSSON, TARA DONKER,
ANNEMIEKE VAN STRATEN

Cuijpers P, Andersson G, Donker T, van Straten A. Psychological treatment of depression: Results of a series of meta-analyses. Nord J Psychiatry 2011; Early Online, 1–11.

Background: In the past few decades, a considerable number of studies have examined the effects of psychotherapies for adult depression. *Aim:* We described the results of a series of meta-analyses examining what this large body of research has contributed to our knowledge of these treatments of depression. *Results:* We found that different types of psychotherapy are efficacious in the treatment of adult depression, including cognitive behavior therapy, interpersonal psychotherapy, problem-solving therapy, non-directive supportive therapy and behavioral activation therapy. Differences between types of psychotherapy are small. The efficacy of psychotherapy for mild to moderate depression is about the same as the efficacy of pharmacotherapy, and that combined treatment is more effective than psychotherapy alone and pharmacotherapy alone. Psychotherapy is not only effective in depressed adults in general, but also in older adults, women with postpartum depression, patients with general medical disorders, in inpatients, in primary care patients, patients with chronic depression and in subthreshold depression. *Conclusions:* We found no evidence showing that psychotherapy is less efficacious in severe depression (with mean baseline Hamilton Depression Rating Scale scores up to 31, mean Beck Depression Inventory scores up to 35.85 and mean Beck Depression Inventory-II scores up to 36.50), but effects are smaller in chronic depression. We also found that the effects of psychotherapy are probably overestimated because of publication bias and the relatively low quality of many studies in the field.

• *Depression, Major depression, Meta-analysis, Psychotherapy, Psychological treatment.*

Cuijpers, Ph.D., Professor of Clinical Psychology, Department of Clinical Psychology, VU University Amsterdam, Van der Boechorststraat 1, 1081 BT Amsterdam, The Netherlands, E-mail: p.cuijpers@psy.vu.nl; Accepted 8 June 2011.

In the past three decades, about 250 controlled and comparative studies have examined the efficacy of psychological treatments for depression in adults. These studies have clearly shown that these treatments reduce symptoms of depression and improve the quality of life of afflicted persons. Additionally, an increasing number of effectiveness trials suggest that psychological treatments can be delivered with maintained effects in clinically representative conditions (1). It is not surprising, therefore, that in clinical guidelines for the management of depressive disorders, psychotherapy is typically considered a first-line treatment (2–5).

In the past few years, we have built a comprehensive database of studies examining psychological treatments of depression. We have used this database to answer several research questions. We have not only examined which psychotherapies are effective, whether psychotherapy is as effective as pharmacotherapy, whether combined treatments are more effective than psychotherapy or pharmacotherapy

alone, but we also examined whether these therapies are effective in specific target groups, such as older adults and women with postpartum depression, whether individual treatments are more effective than group treatments, whether computerized treatments are as effective as face-to-face therapies, and whether these treatments are also effective in patients with chronic depression or dysthymia. Furthermore, we have examined whether there are indications for publication bias in studies on psychotherapy for adult depression and whether the often low quality of these studies has an impact on the effect sizes of the studies.

In this paper, we will give an overview of the meta-analyses that have been published, as well as some new data and analyses. First, we will examine what treatments are efficacious in treating adult depression. Second, we will examine other aspects of the treatment, such as delivery format (individual, group, guided self-help), the relationship between number of treatment sessions and outcome, the relation between outcome and who delivers

the treatment. Third, we will examine the association between characteristics of the depressed individual and the outcome of psychotherapy for adult depression, including the type of depressive disorder, treatment format, specific target groups and severity of depression at baseline.

Method

Searches and inclusion of studies

The methods in this series of meta-analyses have been described in an earlier paper (6). Key materials, overviews of the goals and mission and an overview of all other meta-analyses that have used this database can be downloaded from the website for this project (www. evidencebasedpsychotherapies.org).

In brief, the database was developed through a comprehensive literature search (of works dating from 1966 to January 2010; an update until January 2011 is now in progress). We searched major bibliographical databases (PsycINFO, PubMed, Embase, Cochrane Central Register of Controlled Trials, Dissertation Abstracts International) and retrieved a total of 1120 papers for further study. We included studies examining the effects of a psychological treatment on adults with a depressive disorder according to a diagnostic interview or an elevated level of depressive symptomatology (as indicated by a score above a cut-off score on a validated self-report depression scale like the Beck Depression Inventory).

Only randomized trials were included, in which at least one of the following contrasts was examined: 1) a psychological treatment was compared with a control condition (waiting list; care-as-usual; pill placebo; psychological placebo); 2) a psychological treatment was compared with pharmacotherapy for depression; 3) a psychological treatment was compared with the combination of psychological and pharmacological treatment; 4) pharmacological treatment was compared with the combination of psychological and pharmacological treatment; 5) an individual psychological treatment was compared with a group treatment. We also included: 6) studies in which one of seven major psychological treatments was compared with another psychological treatment. These seven major types of treatment were examined in five or more studies (cognitive behavior therapy; non-directive supportive therapy; behavioral activation therapy; psychodynamic therapy; problem-solving therapy; interpersonal psychotherapy; social skills training); operational definitions of these treatments are described elsewhere (7). We excluded studies on children and adolescents below 18 years of age; studies in which the psychological intervention could not be distinguished from other elements of the intervention (managed care interventions and disease management programs); studies aimed at maintenance treatments and relapse prevention; and studies which

included both participants with depression and anxiety. Comorbid general medical or psychiatric disorders were not used as an exclusion criterion. No language restrictions were applied, except for studies in Chinese.

Data extraction and quality assessment

We extracted several characteristics of the studies (year of publication; country; number of participants per condition), the study population (recruitment method; target group; definition of depression) and the interventions (type of psychotherapy; format; number of sessions). We also assessed the quality of included studies using three basic criteria from the 'Risk of bias' assessment tool, developed by the Cochrane Collaboration (8). We assessed the following criteria: whether the allocation sequence was adequately generated; whether outcome assessors were blinded (when only self-report measures were used, we assumed that this was positive) and whether incomplete outcome data were adequately handled (we assessed whether intention-to-treat analyses were conducted).

Meta-analyses

For each study, we calculated effect sizes (Cohen's d) by subtracting (at post-test) the average score of the control group (M_d) from the average score of the experimental group (M_e) and dividing the result by the pooled standard deviations of the experimental and control group (SD_{ec}). Effect sizes of 0.80 and higher are regarded as large, while effect sizes of 0.50–0.79 are moderate and lower effect sizes are small (9). In the calculations of effect sizes, only those instruments were used that explicitly measure symptoms of depression. If more than one measure was used, the mean effect size was calculated, so that each study (or contract group) resulted in only one effect size. We pooled the mean effect sizes with the computer program Comprehensive Meta-analysis (version 2.2.021; CMA), developed for support in meta-analysis, using the random effects model.

Because the effect size is difficult to interpret from a clinical perspective, we also calculated the numbers-needed-to-be-treated (NNT). The NNT is the number of persons that have to be treated in order to generate one more positive outcome than in the control group (10). We used the formulae provided by Kraemer & Kupfer (10) to calculate the NNT.

In order to examine heterogeneity, we 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. We also calculated the Q-statistic, but only report whether this was significant.

Subgroup analyses and univariate meta-regression analyses were conducted according to the procedures

implemented in CMA version 2.2.021. In the subgroup-analyses, we used mixed effects analyses that pooled studies within subgroups with the random effects model but tested for significant differences between subgroups with the fixed effects model.

Publication bias was tested by inspecting the funnel plot on primary outcome measures, and by Duval & Tweedie's trim and fill procedure (11) which yields an estimate of the effect size after the publication bias has been taken into account (as implemented in CMA, version 2.2.021).

What is reported in this paper?
In this paper, we will summarize the results of the meta-analyses that have used the database of randomized trials and have been published until now, and present some new results based on the most recent update of the database. We will not be able to describe all the details of these studies, but we will only describe the main results. Because several meta-analyses have been published one or a few years ago, recent studies that are included in the current database may not be included in the earlier meta-analyses.

Results
Overview of studies included in the database
A total of 243 studies have been included in our database of studies examining psychotherapies for adult depression (from the searches until January 2010). An overview of characteristics of these studies as well as the references can be downloaded from the website of the project (www.evidencebasedpsychotherapies.org). The majority of the 243 studies included a comparison between psychotherapy and a control group [147], with another type of psychotherapy [63], a comparison with pharmacotherapy [39] or with a combined treatment [20]. Furthermore, in 32 studies, pharmacotherapy was compared with combined treatment, 17 studies compared combined treatment with the combination of psychotherapy and placebo, and 12 studies compared individual and group psychotherapies. Separate papers have been published earlier about each of these comparisons (www.evidencebasedpsychotherapies.org).

In Fig. 1, we have presented the 243 trials over time and according to the country where the study was conducted (these data have not been published before). As can be seen, the absolute number of trials has increased considerably, especially since the second half of the 1990s. Before that, most research was conducted in the USA (73.1–88.5% of all studies during that time). Since the second half of the 1990s, the number of studies from other parts of the world has increased considerably, especially in the UK, the rest of the European Union, and in the past 5 years also in non-Western countries. In the period since 2005, only 30.6% of the research in this area was conducted in the USA.
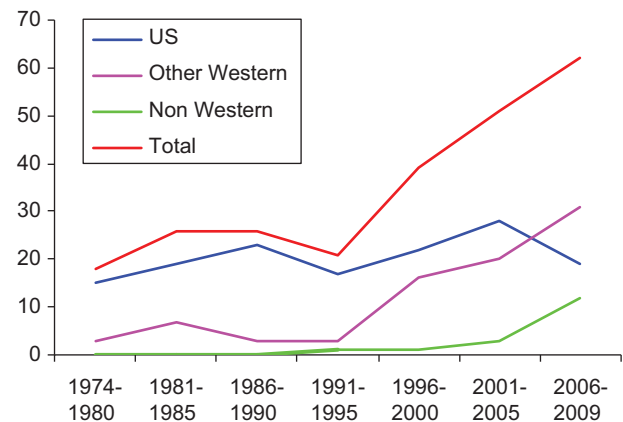

Fig. 1. Randomized studies examining psychotherapy for adult depression: Absolute number per region in periods of 5 years ($n = 243$).

Psychotherapy vs. control conditions
We found 147 studies in which psychotherapy was compared with a control condition. These 147 studies included 215 comparisons between psychotherapy and control groups. The overall effect size of these comparisons was $d = 0.66$ (95% CI 0.60–0.73; these data have not been published earlier), which corresponds with a NNT of 2.78 (Table 1). Some studies had very large effect sizes and may be regarded as outliers. After excluding studies with an effect size of $d = 1.5$ or higher, the overall mean effect size decreased to $d = 0.53$ (95% CI 0.47–0.58; NNT = 3.42). Heterogeneity was moderate to high in these analyses. Again, these data were not published in an earlier meta-analysis.

In many studies, more than one psychotherapy condition was compared with the same control group. Because these comparisons are not independent of each other, they may affect the level of heterogeneity and the mean effect size. Therefore, we conducted additional analyses with only one comparison between a psychotherapy condition and control condition per study. First, we included only the largest effect size from each study. The resulting mean effect size was $d = 0.69$ (95% CI 0.61–0.77; NNT = 2.67). Then we included only the smallest effect size of study, which resulted in a mean effect size of $d = 0.56$ (95% CI 0.49–0.63). Heterogeneity remained at a moderate to high level.

We examined the influence of major characteristics of the studies, the psychotherapies and the patients in a meta-regression analysis. The results are shown in Table 2. As can be seen only type of control condition, and the country where the study was conducted were significantly associated with the effect size. Studies in which care-as-usual control groups or other control groups (pill placebo or psychological placebo) were used, resulted in considerably smaller effect sizes than studies with waiting list control groups. Studies conducted in non-Western

Table 1. Effects of psychological treatments of depression compared with control groups: Overall effects.

	N_{comp}	d	95% CI	Z	I^2†	NNT
All psychological treatments	215	0.66	0.60–0.73	19.47***	65.02***	2.78
Outliers excluded	190	0.53	0.47–0.58	19.07***	44.65***	3.42
Multiple comparisons excluded, highest retained	147	0.69	0.61–0.77	16.63***	47.38***	2.67
Multiple comparisons excluded, lowest retained	147	0.56	0.49–0.63	15.49***	59.90***	3.25

$^oP < 0.1$; $*P < 0.05$; $**P < 0.01$; $***P < 0.001$.

†The P-values in this column indicate whether the Q-statistic is significant (the I^2 statistics does not include a test of significance).

countries usually resulted in larger effect sizes than studies conducted in Western countries.

We examined several specific types of psychotherapies in separate meta-analyses, including behavioral activation therapy (12), problem-solving therapy (13), interpersonal psychotherapy (14) and the "Coping with Depression" course, a psychoeducational version of cognitive behavior therapy (15). The main results of these meta-analyses are presented in Table 3.

Are all psychotherapies equally effective?

We found seven types of psychotherapy, which could be compared with a control group in at least five studies (Table 3): cognitive behavior therapy, behavioral activation therapy, self-control therapy, problem-solving therapy, interpersonal psychotherapy, non-directive supportive therapy and short-term psychodynamic psychotherapy (comprehensive definitions are given elsewhere) (7). As

can be seen in Table 3, all of these types of therapy are efficacious compared with a control group, with effect sizes ranging from 0.57 to 0.87. The NNTs range from 2.15 to 4.00.

These analyses make it clear that there are several types of psychotherapy that are effective in the treatment of depression, when these therapies are compared with control conditions. But are these therapies equally effective? Are there no differences between the psychotherapies in terms of effects? The best way to examine whether different types of psychotherapy are actually equally efficacious is to examine studies in which depressed persons are randomly assigned to two (or more) different types of psychotherapy. Such direct comparisons are better equipped to examine differences between types of therapy than studies in which patients are randomized to a psychotherapy or a control group, because they rule out the influence of study characteristics. Consequently, they provide more

Table 2. Regression coefficients of study characteristics in relation to the effect size of psychological therapies of depression compared with control conditions: Multivariate meta-regression analyses.

	B	95% CI	P
Year of publication	−0.01	−0.02 to 0.01	0.25
Recruitment			
Community	Ref		
Clinical	−0.12	−0.36 to 0.12	0.33
Other	0.06	−0.18 to 0.30	0.64
Target groups (adults vs. more specific group)	−0.02	−0.23 to 0.20	0.87
Diagnosed mood disorder (y/n)	0.08	−0.12 to 0.27	0.44
Type of psychotherapy (CBT vs. other types)	0.04	−0.16 to 0.24	0.70
Format			
Individual	Ref		
Group	−0.16	−0.37 to 0.05	0.14
Guided self-help	−0.12	−0.49 to 0.26	0.55
Number of sessions	−0.00	−0.03 to 0.02	0.88
Control group			
Waiting list	Ref		
Care-as-usual	−0.36	−0.61 to −0.11	*0.004*
Other	−0.34	−0.61 to −0.09	*0.008*
Country			
USA	Ref		
Other Western	−0.03	−0.23 to 0.18	0.81
Non-Western	0.41	0.08–0.74	*0.015*
Number of respondents	−0.00	−0.00 to 0.00	0.45
Meets 3 quality criteria	−0.11	−0.37 to 0.14	0.38
Constant	15.21	−9.09 to 39.52	0.22

Table 3. Effect sizes of different types of psychotherapies.

	N	D	95% CI	I^2	NNT	Ref
Different types of psychotherapy vs. control groups						
Cognitive behavior therapy	91	0.67	0.57–0.78	59.88***	2.75	48
Behavioral activation therapy	10	0.87	0.60–1.15	20.87	2.16	12
Self-control therapy	6	0.45	0.11–0.79	47.95	4.00	48
Problem-solving therapy	13	0.83	0.45–1.21	82.80***	2.26	13
Interpersonal psychotherapy	16	0.63	0.36–0.90	82.96***	2.91	14
Non-directive supportive therapy	14	0.57	0.37–0.77	36.81	3.18	48
Short-term psychodynamic psychotherapy	5	0.69	0.30–1.08	33.42	2.67	17
Direct comparisons of different types of psychotherapy						
Cognitive behavior therapy vs. all other therapies	56	0.03	− 0.04 to 0.11	0	166.67	7
Non-directive supportive therapy vs. all other therapies	30	− 0.17	− 0.32 to − 0.03	40.80*	10.42†	7
Behavioral activation therapy vs. all other therapies	21	0.14	− 0.02 to 0.30	0	12.82	7
Psychodynamic therapy vs. all other therapies	16	− 0.07	− 0.21 to 0.08	0	25.00†	7
Problem-solving therapy vs. all other therapies	7	0.40	− 0.07 to 0.88	72.78**	4.50	7
Interpersonal psychotherapy vs. all other therapies	8	0.21	0.01–0.42	21.98	8.47	7
Social skills training vs. all other therapies	7	0.05	− 0.26 to 0.36	0	35.71	7
Direct comparisons between different treatment formats						
Individual vs. group psychotherapies	19	0.20	0.05–0.35	0	8.93	18
Guided self-help vs. face-to-face therapies	9	− 0.15	− 0.41 to 0.11	2.04 ns	11.90	19
Psychotherapy vs. pharmacotherapy and combined treatments†						
Psychotherapy vs. pharmacotherapy	37	− 0.07	− 0.15 to 0.01	21.31	25.00	20, 21
Psychotherapy vs. combined treatment	19	0.35	0.24–0.45	0	5.10	22
Pharmacotherapy vs. combined treatment	22	0.30	0.17–0.43	32.63º	5.95	23
Combined vs. psychotherapy plus placebo	16	0.25	0.03–0.46	57.22**	7.14	24
Psychotherapy for specific target groups vs. control groups						
Older adults	23	0.72	0.59–0.85	80.20***	2.56	25, 26
Women with postpartum depression	19	0.61	0.37–0.85	64.84**	2.99	27
Patients with general medical disorders	18	1.00	0.57–1.44	92.5***	1.91	28
Patients in primary care	20	0.31	0.17–0.45	45.58*	5.75	29
Inpatients	15	0.29	0.13–0.44	0	6.17	30
Patients with subthreshold depression	6	0.42	0.23–0.60	0	4.27	31
Patients with chronic depression	8	0.23	0.06–0.41	0	7.69	32

º$P < 0.1$; *$P < 0.05$; **$P < 0.01$.

†In these comparisons, a positive sign indicates that the first treatment of column one is more effective than the second one.

reliable evidence about a possible superiority of one type of therapy over the other (16). In such comparative studies, effect sizes indicate the difference between two treatments at post-test, instead of the difference between a therapy and a control group.

In one recent meta-analysis (7), we examined 51 studies in which seven major types of psychotherapy are directly compared with other psychotherapies in at least five studies. For each of these seven types of psychotherapy, we conducted a separate meta-analysis. In these analyses, we calculated the mean effect sizes indicating the differences between the two therapies. The results are summarized in Table 3. As can be seen, the differences between the types of psychotherapy are small. No indications were found that cognitive behavior therapy, behavioral activation therapy, psychodynamic therapy, problem-solving therapy and social skills training differ significantly from each other. However, interpersonal psychotherapy is significantly more efficacious than other therapies, and non-directive supportive therapy is significantly less efficacious than other therapies, although the

effect sizes are small and of minor clinical relevance (more details can be found in reference 7).

Two more recent meta-analyses are relevant in this respect. In one meta-analysis, it is found that psychodynamic therapies are somewhat less effective than other psychotherapies (17). In another meta-analysis, we found that interpersonal psychotherapy is not more or less effective than other psychotherapies (14). These results indicate that all psychotherapies are more or less equally effective, and although there may be small differences, such differences can vary over different meta-analyses and are, therefore, not very stable.

Does treatment format matter?
In our searches, we found 15 studies (with 19 direct comparisons) in which individual treatments are directly compared with group treatments (18). We found that individual therapies are significantly more effective than group therapies although the effect size was small ($d = 0.20$; 95% CI 0.05–0.35; NNT = 8.93). We also found indications that drop-out rates are lower in individual interventions

compared with group treatments ($n = 12$; OR $= 0.56$; 95% CI 0.37–0.86; $P < 0.01$).

In nine studies, guided self-help is directly compared with face-to-face treatment of depression (individual or group therapy) (19). In this meta-analysis, we examined the difference between guided self-help and face-to-face therapies in patients with depression and anxiety disorders (total number of studies was 21). A small and non-significant difference is found between guided self-help and face-to-face treatment in the depression studies ($d = -0.15$; 95% CI -0.41 to 0.11). We also found no indication that the drop-out rate in guided self-help is higher than in face-to-face therapies (RR $= 1.14$; 95% CI 0.77–1.67).

In a separate meta-analysis on computerized treatments and Internet-based treatments for depression, we included 12 studies, with a total of 2446 participants (20). Nine of the 12 interventions are delivered via the Internet. The mean effect size of the 15 comparisons between Internet-based and other computerized psychological treatments vs. control groups at post-test is $d = 0.41$ (95% CI 0.29–0.54). However, this estimate is moderated by a significant difference between supported $d = 0.61$ (95% CI 0.45–0.77) and unsupported treatments $d = 0.25$ (95% CI 0.14–0.35). Overall, the finding regarding guided self-help appears to yield guided computerized treatments as well, although there are few direct comparisons between computer-based and face-to-face therapies.

Psychotherapy and pharmacotherapy

A considerable number of studies have compared the efficacy of psychotherapy with those of pharmacotherapy for depression (21, 22), psychotherapy vs. the combination of psychotherapy and pharmacotherapy (23), and pharmacotherapy vs. the combination of psychotherapy and pharmacotherapy (24). In our database, we also found a considerable number of studies in which a combined treatment of psychotherapy and pharmacotherapy is compared with the combination of psychotherapy and pill placebo (25).

In our meta-analysis of studies ($n = 30$) comparing the efficacy of psychotherapy with that of pharmacotherapy (21), we calculated the effect sizes, which indicate the difference between the two types of treatment (instead of the difference between the therapy and a control group). In this study we found a trend ($P < 0.1$) indicating that pharmacotherapy is slightly more effective than psychotherapy, but this difference is very small ($d = 0.07$; NNT $= 25.00$). However, when we differentiated between studies of patients with major depression and those with dysthymia, we found that pharmacotherapy is significantly more efficacious than psychotherapy in patients with dysthymia ($d = -0.28$; 95% CI -0.47 to -0.10; NNT $= 6.41$). We also found indications that in patients with major depression, treatments with SSRIs are significantly more

efficacious than psychotherapy. Drop-out rates are, however, smaller in psychotherapy compared with pharmacotherapy ($n = 30$; OR $= 0.66$; 95% CI 0.47–0.92).

In an additional study (22) with the same set of studies, we examined whether the higher drop-out rate in pharmacotherapy has an effect on the outcomes of the meta-analysis. We conducted these analyses with modified intention-to-treat analyses, in which patients who dropped out were assumed not to have improved during therapy. After adjusting the effect sizes (in this case we calculated the relative risk of improvement instead of Cohen's d), no significant difference between psychotherapy and pharmacotherapy is found any more ($P > 0.1$).

In our meta-analysis of studies in which psychotherapy alone is compared with the efficacy of combined psychotherapy and pharmacotherapy, we could include 18 studies (23). In this meta-analysis, we found clear indications that the combined treatment is more efficacious than psychotherapy alone ($d = 0.35$; NNT $= 5.10$). We did not examine differences in drop-out rate between psychotherapy and combined treatments.

We examined 25 studies in which pharmacotherapy is only compared with the combination of psychotherapy and pharmacotherapy (24). We found a mean effect size of $d = 0.31$ (95% CI 0.20–0.43; NNT $= 5.95$), in favor of the combined treatment. We also found that studies aimed at patients with dysthymia result in considerably smaller effect sizes than studies aimed at patients with major depression. In this study, we found that drop-out rates are significantly higher in the pharmacotherapy conditions compared with the combined therapy conditions.

In 16 studies, a combined treatment of psychotherapy and pharmacotherapy is compared with the combination of psychotherapy and pill placebo (25). These studies examine the exact contribution of active medication to the effects of combined treatments. We found an effect size of $d = 0.25$ (95% CI 0.03–0.46; NNT $= 7.14$). No significant difference is found in terms of drop-out rates.

Psychotherapy for specific target groups

Most studies of psychotherapy have included depressed adults in general. However, several more specific target groups have been examined in a considerable number of studies. In our meta-analysis, we included 23 comparisons between psychotherapy and a control group in *older adults* (26). These comparisons found strong evidence that psychotherapy is efficacious in older depressed adults ($d = 0.72$; 95% CI 0.59–0.85; NNT $= 2.56$). In a meta-regression analysis, we found no indication that the effect size for older adults differs from the effect size for younger adults, suggesting that psychotherapy in older adults is as efficacious as in younger adults (27).

Another target group that has been examined in a considerable group of studies comprises *women with postpartum depression*. In a meta-analysis of these studies (28),

we found that the mean effect size for these studies is significant ($d = 0.61$; 95% CI 0.37–0.85; NNT = 2.99), indicating that psychotherapy is also efficacious in this target group.

The third target group that has been examined in a relatively large number of studies is the group of *patients with general medical disorders*. Although this includes a broad range of different disorders, we pooled them together into one group of studies (29). The effect size of these studies is comparable with the effect size found in adults with depression in general ($d = 1.00$; 95% CI 0.57–1.44; NNT = 1.91). These results indicate that psychotherapy is also efficacious for patients with general medical disorders who also suffer from depression or an elevated level of depressive symptoms.

Another target group is *primary care patients with depression*. Most depressed patients are treated in primary care, and psychotherapy is becoming an important treatment option in that setting. The effect size found for the 15 studies examining depressed primary care patients is $d = 0.31$ (95% CI 0.17–0.45; NNT = 5.75), which is significantly smaller than the effect found in studies conducted in other settings ($d = 0.75$; 95% CI 0.65–0.84; NNT = 2.48) (30). In this meta-analysis, we also found that studies in which patients are referred by their GP for treatment have significantly higher effect sizes ($d = 0.43$; NNT = 4.20) than studies in which patients are recruited through systematic screening ($d = 0.13$, not significantly different from zero; NNT = 13.51).

We found 14 studies that examined the effects of psychotherapies for *depressed inpatients* (31). Psychological treatments were found to have a small ($d = 0.29$; 95% CI 013–0.44; NNT = 6.17), but statistically significant additional effect on depression compared with usual care and structured pharmacological treatments only.

A considerable number of studies has examined the effects of psychotherapy in specific diagnostic categories. One group of studies has focused on *patients with subthreshold depression*, in which patients do have depressive symptoms but do not meet diagnostic criteria for a depressive disorder (established with a diagnostic interview). We could include seven randomized controlled trials in a meta-analysis of these studies (32). The mean effect size found for these seven studies is $d = 0.42$ (95% CI 0.23–0.60; NNT = 4.27), indicating a moderate effect. However, because the level of depressive symptomatology is already relatively low in these subjects compared with subjects with major depression, the possibilities for improvement are limited. In this meta-analysis we also found that psychological treatment of subthreshold results in a smaller risk of developing major depression (relative risk RR = 0.70; 95% CI 0.47–1.03; $P < 0.1$).

We also found 16 studies examining psychotherapy in *patients with chronic depression or dysthymia* (33). We found that psychotherapy has a small but significant effect ($d = 0.23$; 95% CI 0.06–0.41; NNT = 7.69) on depression when compared with control groups. Psychotherapy is, however, significantly less effective than pharmacotherapy in direct comparisons ($d = -0.31$), especially SSRIs, but that this finding is wholly attributable to dysthymic patients (the studies examining dysthymia patients are the same studies that examined SSRIs). Combined treatment is more effective than pharmacotherapy alone ($d = 0.23$), but even more so with respect to psychotherapy alone ($d = 0.45$), although again this difference may have reflected the greater proportion of dysthymic samples in the latter. No significant differences are found in drop-out rates between psychotherapy and the other conditions. In this meta-analysis, we also found that the effect size of the study is significantly associated with the number of treatment sessions. At least 18 treatment sessions are needed to realize optimal effects of psychotherapy.

Measuring outcome in psychotherapy for depression

One of the problems in research on treatments of depression is that outcomes can be based on continuous outcomes (such as self-report instrument or clinician rated instruments) but also on dichotomous outcomes (such as having a diagnosis of depression, or the number of patients with clinically relevant change). Although it is possible to convert the two types of outcomes to each other, it has not been tested whether this results in systematic differences. In one meta-analysis, we calculated effect sizes using both types of outcomes, and compared the results (34). Although there are considerable differences between the two types of outcomes in individual studies, both types of outcomes result in very similar pooled effect sizes. The pooled effect size based on the continuous outcome is somewhat more conservative ($d = 0.59$; OR = 2.92) than the one based on the dichotomous outcome ($d = 0.64$; OR = 3.17).

Another question related to measuring outcome, is whether self-report measures and clinician-rated instruments for depression result in comparable outcomes in research on psychotherapy. We conducted a meta-analysis in which randomized controlled trials were included examining the effects of psychotherapy for adult depression (35). Only studies were included in which both a self-report and a clinician-rated instrument were used. We calculated the effect size (Hedges' g) based on the self-report measures, the effect size based on the clinician-rated instruments, and the difference between these two effect sizes (Δg). Hedges' g is the same as Cohen's d in terms of interpretation and calculation, except that Hedges' g is adjusted for small sample sizes in included studies. The differential effect size is $\Delta g = 0.20$ (95% CI 0.10–0.30), indicating that clinician-rated instruments resulted in a significantly higher effect size than self-report instruments from the same studies. This

meta-analysis clearly indicates that clinician-rated and self-report measures of improvement following psychotherapy for depression are not equivalent.

Is baseline severity of depression related to outcome?

It is widely believed that psychological treatment has little effect on more severely depressed patients. This belief is based, in part, on the findings of the influential Treatment of Depression Collaborative Research Program, in which cognitive behavior therapy (CBT) did not differ from placebo in more severely depressed patients whereas antidepressant medications did (36, 37). We conducted meta-regression analyses assessing whether mean pretreatment depression scores predicted psychological treatment vs. control condition post-treatment effect size and subgroup analyses summarizing the results of studies reporting within-study analyses of depression severity and psychological treatment outcome (38). In these analyses, we found no indication that pretreatment mean depression scores predict psychological treatment vs. control condition post-treatment effect size, even after adjusting for relevant study characteristics. This was true for the Beck Depression Inventory (mean baseline scores ranged from 14.11 to 35.85), the Beck Depression Inventory-II (range of baseline scores: 17.89–36.50), and the Hamilton Depression Rating Scale (range of baseline scores: 8.34–31.00). In a smaller subset of studies that report within-study severity analyses, post-treatment effect sizes are even higher for high-severity patients ($d = 0.63$; 95% CI 0.31–0.94) than for low-severity patients ($d = 0.22$; 95% CI -0.05 to 0.49). These findings suggest that when compared with control conditions, psychological treatment might be more efficacious for high-severity than for low-severity patients.

Have the effects of psychotherapy been overestimated?

Although psychotherapy has been found to have moderate to large effects on depression in most meta-analyses described until now, we also found indications that these effects may have been overestimated.

In one meta-analysis, we examined the association between study quality and effect size (39). We assessed eight quality criteria: participants met diagnostic criteria for a depressive disorder, a treatment manual was used, the therapists were trained, treatment integrity was checked, intention-to-treat analyses were used, $n \geq 50$, randomization was conducted by an independent party, and assessors of outcome were blinded. Only 11 studies (16 comparisons) met these eight quality criteria. The effect size found for the high-quality studies ($d = 0.22$; 95% CI 0.14–0.31) is significantly smaller ($P < 0.001$) than in the other studies ($d = 0.75$; 95% CI 0.66–0.84),

even after restricting the sample to the subset of other studies that used the kind of care-as-usual or non-specific controls that tend to be used in the high-quality studies. The number needed to be treated in the high-quality studies is 8.06, while it is 2.48 in the lower-quality studies.

In another meta-analysis, we examined the possibility of publication bias in studies on psychotherapy for adult depression (40). Evidence of such bias has been found in many intervention fields, including that of depression treatment (41). We examined indirect indications for publication bias based on the symmetry of the funnel plot. A funnel plot gives a measure of study size (the standard error) on the vertical axis as a function of effect size on the horizontal axis. Large studies appear at the top of the graph and tend to cluster near the mean effect size. Smaller studies appear towards the bottom of the graph. As there is more sampling variation in effect size estimates in the smaller studies, they will be dispersed across a range of values. Studies can be expected to be distributed symmetrically about the pooled effect size when publication bias is absent. In the presence of bias, it can be expected that the lower part of the plot will show a higher concentration of studies on one side of the mean than on the other. This is caused by the fact that smaller studies (appearing towards the bottom of the funnel plot) are more likely to be published if they have larger than average effects, which makes them more likely to meet the criterion for statistical significance (42). Duval & Tweedie's trim and fill procedure (11) gives the possibility of calculating an adjusted effect size after possible publication bias has been taken into account. The unadjusted effect size of 175 comparison between psychotherapy and a control group is $d = 0.67$ (95% CI 0.60–0.75), but after adjustment for publication bias this is reduced to $d = 0.42$ (95% CI 0.33–0.51; number of imputed studies was 51).

These studies point out that the effects of psychotherapy for adult depression probably have been overestimated, and that the true effects are smaller than has been assumed on the basis of earlier meta-analyses.

Discussion

In the past few decades, a considerable number of studies has examined the effects of different psychotherapies for adult depression. In this paper, we described the results of a series of meta-analyses examining what this large body of research has contributed to our knowledge of these treatments of depression. We saw that different types of psychotherapy are efficacious in the treatment of adult depression, including cognitive behavior therapy, interpersonal psychotherapy, problem-solving therapy, non-directive supportive therapy, psychodynamic therapy and behavioral activation therapy. Interpersonal psychotherapy may be somewhat more effective than other therapies,

while non-directive supportive therapy may be somewhat less efficacious. We also saw that psychotherapies can be efficaciously delivered in individual, group and guided self-help format (including computerized treatments), although group psychotherapy may be somewhat less efficacious than individual therapy and may result in somewhat higher drop-out rates. The efficacy of psychotherapy is about the same as the efficacy of pharmacotherapy, but not in patients with dysthymia. Drop-out, however, is lower in psychotherapy. Combined treatment is more efficacious than psychotherapy alone and pharmacotherapy alone. Psychotherapy is not only efficacious in depressed adults in general, but also in older adults, women with postpartum depression and patients with general medical disorders. There are no indications that psychotherapy is less efficacious in these groups. We found no evidence showing that psychotherapy is less efficacious in severe depression. Unfortunately, we also found that the effects of psychotherapy are probably overestimated because of publication bias and the relatively low quality of many studies in the field.

Based on this overview of meta-analyses on depression, there are indications that there is a therapeutic window for psychological treatments for depression. In medical treatments and pharmacotherapy in particular, the term "therapeutic window" refers to the range of doses of a drug that are actually effective in treating a particular disease. Doses below the therapeutic window are too weak to have any effect; doses above the window cause unacceptable side-effects. This reasoning also concerns diagnoses for which a particular treatment is suitable. For example, unless there is an infection, antibiotics should not be prescribed. In other words, patients may be within or outside of the therapeutic window for a treatment for various reasons. In addition the treatment may be suitable or unsuitable and might only work within a range of doses (e.g. not too much and not too little). The differential effect sizes derived from the meta-analyses reviewed above suggest that psychological treatments for depression works best when the depressive symptoms are in the mild to moderate range, and less well with chronic and more severe symptoms.

This overview has several limitations. First, we reviewed a very large number of studies and 30 published meta-analyses. Such an approach has the advantage of a helicopter view of a broad field of research, but also necessarily leaves out many of the details of these studies, which are just as vital to understanding the research field. Second, although the overall number of studies was considerable, the number of studies examining specific subgroups of studies was still small. As a result, where we found no indication for a significant difference between subgroups, it may in fact have been a lack of statistical power, which prevented us from finding such a difference. Third, meta-analyses cannot

provide an answer to the question "what treatment, by whom, works for this depressed individual", which is the most important answer to be answered by treatment outcome research (43–45). Fourth, we limited this review to the outcomes of psychotherapy in the short term. However, it is well documented that the relapse rates in depression are very high. It is estimated that up to 85% of people who recover from a major depressive episode will experience a second episode within 15 years of naturalistic follow-up, and each additional episode increases the risk of relapse by 18% (46, 47). For an answer to the question "what treatment, by whom, works for this depressed individual?", the long-term effects of psychotherapy are just as important as the short-term efficacy.

When we look at the large number of studies and meta-analyses examining the efficacy of psychotherapies for adult depression, it becomes clear that this field has made enormous progress in the last three decades. Not only do we know that psychotherapies are efficacious in the treatment of adult depression, we also know several types of psychotherapies that are efficacious, that these treatments are about equally efficacious, and we know that they are efficacious in several specific target populations. Unfortunately, we know much less about the treatments that have not been tested in controlled trials (48), and there are therefore reasons to believe that further meta-analytic summaries will be needed.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Hunsley J, Lee CM. Research-informed benchmarks for psychological treatments: Efficacy studies, effectiveness studies, and beyond. Prof Psychol Res Pract 2007;38:21–33.
2. Karasu TB, Gelenberg A, Merriam A, Wang P. Practice guideline for the treatment of patients with major depressive disorder, 2nd edition. Washington DC: American Psychiatric Association, 2000.
3. NICE, National Institute for Clinical Excellence. Depression: Management of depression in primary and secondary care. National Clinical Practice Guideline Number 23, National Collaborating Centre for Mental Health, UK, 2004.
4. Socialstyrelsen. Nationella riktlinjer för vård vid depression och ångestsyndrom 2010 – Stöd för styrning och ledning. Stockholm: Socialstyrelsen 2010.

5. Segal ZV, Whitney DK, Lam RW, CANMAT Depression Work Group. Clinical guidelines for the treatment of depressive disorders III. Psychotherapy. Can J Psychiatry 2001;46:29S–37S.

6. Cuijpers P, van Straten A, Warmerdam L, Andersson G. Psychological treatment of depression: A meta-analytic database of randomized studies. BMC Psychiatry 2008;8:36.

7. Cuijpers P, van Straten A, Andersson G, van Oppen P. Psychotherapy for depression in adults: A meta-analysis of comparative outcome studies. J Consult Clin Psychol 2008;76:909–922.

8. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions 4.2.6 [updated September 2006]. In: Cochrane Library, Issue 4, 2006. Chichester: Wiley; 2006.

9. Cohen J. Statistical power analysis for the behavioral sciences. New York: Academic Press; 1977.

10. Kraemer HC, Kupfer DJ. Size of treatment effects and their importance to clinical research and practice. Biol Psychiatry 2006;59:990–6.

11. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometr 2000;56:455–63.

12. Cuijpers P, van Straten A, Warmerdam L. Behavioral treatment of depression: A meta-analysis of activity scheduling. Clin Psychol Rev 2007;27:318–26.

13. Cuijpers P, van Straten A, Warmerdam L. Problem solving therapies for depression: A meta-analysis. Eur Psychiatry 2007;22:9–15.

14. Cuijpers P, Geraedts AS, van Oppen P, Andersson G, Markowitz JC, van Straten A. Interpersonal psychotherapy of depression: A meta-analysis. Am J Psychiatry 2011, in press.

15. Cuijpers P, Muñoz RF, Clarke GN, Lewinsohn PM. Psychoeducational treatment and prevention of depression: The "Coping with Depression" course thirty years later. Clin Psychol Rev 2009;29:449–58.

16. 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;27:642–54.

17. Driessen E, Cuijpers P, de Maat SCM, Abbass AA, de Jonghe F, Dekker JJM.. The efficacy of short-term psychodynamic psychotherapy for depression: A meta-analysis. Clin Psychol Rev 2010;30:25–36.

18. Cuijpers P, van Straten A, Warmerdam L. Are individual and group treatments equally effective in the treatment of depression in adults? A meta-analysis. Eur J Psychiatry 2008;22:38–51.

19. Cuijpers P, Donker T, van Straten A, Li J, Andersson G. Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies. Psychol Med 2010;40:1943–57.

20. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: A meta-analysis. Cogn Behav Ther 2009;38:196–205.

21. Cuijpers P, van Straten A, van Oppen P, Andersson G. Are psychological and pharmacological interventions equally effective in the treatment of adult depressive disorders? A meta-analysis of comparative studies. J Clin Psychiatry 2008;69:1675–85.

22. Cuijpers P, van Straten A, van Oppen P, Andersson G. Comparing psychotherapy and pharmacotherapy for adult depression: Adjusting for differential drop-out rates. J Clin Psychiatry 2010;71:1246.

23. Cuijpers P, van Straten A, Warmerdam L, Andersson G. Psychological treatment versus combined treatment of depression: A meta-analysis. Depress Anx 2009;26:279–88.

24. Cuijpers P, Dekker J, Hollon SD, Andersson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: A meta-analysis. J Clin Psychiatry 2009;70:1219–29.

25. Cuijpers P, van Straten A, Hollon SD, Andersson G. The contribution of active medication to combined treatments of psychotherapy and pharmacotherapy for adult depression: A meta-analysis. Acta Psychiatr Scand 2010;121:415–23.

26. Cuijpers P, van Straten A, Smit F. Psychological treatment of late-life depression: A meta-analysis of randomized controlled trials. Int J Geriatr Psychiatry 2006;21:1139–49.

27. Cuijpers P, van Straten A, Smit F, Andersson G. Is psychotherapy for depression equally effective in younger and older adults? A meta-regression analysis. Int Psychogeriatr 2009;21:16–24.

28. Cuijpers P, Brännmark JG, van Straten A. Psychological treatment of postpartum depression: A meta-analysis. J Clin Psychol 2008;64:103–18.

29. Van Straten A, Geraedts A, Verdonck-de Leeuw I, Andersson G, Cuijpers P. Psychological treatment of depressive symptoms in patients with medical disorders: A meta-analysis. J Psychosom Res 2010;69:23–32.

30. Cuijpers P, van Straten A, van Schaik A, Andersson G. Psychological treatment of depression in primary care: A meta-analysis. Br J Gen Pract 2009;59:120–27.

31. Cuijpers P, Clignet F, van Meijel B, van Straten A, Li J, Andersson G. Psychological treatment of depression in inpatients: A systematic review and meta-analysis. Clin Psychol Rev, in press.

32. Cuijpers P, van Straten A, Smit F. Psychological treatments of subthreshold depression: A meta-analytic review. Acta Psychiatr Scand 2007;115:434–41.

33. Cuijpers P, van Straten A, Schuurmans J, van Oppen P, Hollon SD, Andersson G. Psychotherapy for chronic major depression and dysthymia: A meta-analysis. Clin Psychol Rev 2010;30:51–62.

34. Cuijpers P, Smit F, Hollon SD, Andersson G. Continuous and dichotomous outcomes in studies of psychotherapy for adult depression: A meta-analytic comparison. J Affect Dis 2010;126:349–57.

35. Cuijpers P, Li J, Hofmann SG, Andersson G. Self-reported versus clinician-rated symptoms of depression as outcome measures in psychotherapy research on depression: A meta-analysis. Clin Psychol Rev 2010;30:768–78.

36. Elkin I, Gibbons RD, Shea MT, Sotsky SM, Watkins JT, Pilkonis PA, Hedeker D.. Initial severity and differential treatment outcome in the National Institute of Mental Health Treatment of Depression Collaborative Research Program. J Consult Clin Psychol 1995;63:841–7.

37. Elkin I, Shea MT, Watkins JT, Imber SD, Sotsky SM, Collins JF, Parloff MB. National Institute of Mental Health Treatment of Depression Collaborative Research Program: General effectiveness of treatments. Arch Gen Psychiatry 1989;46:971–82.

38. Driessen E, Cuijpers P, Hollon SD, Dekker JJM. Does pre-treatment severity moderate the efficacy of psychological treatment of adult outpatient depression? A meta-analysis. J Consult Clin Psychol 2010;78:668–80.

39. Cuijpers P, van Straten A, Bohlmeijer E, Hollon SD, Andersson G. The effects of psychotherapy for adult depression are overestimated: A meta-analysis of study quality and effect size. Psychol Med 2010;40:211–223.

40. Cuijpers P, Smit F, Bohlmeijer ET, Hollon SD, Andersson G. Is the efficacy of cognitive behaviour therapy and other psychological treatments for adult depression overestimated? A meta-analytic study of publication bias. B J Psychiatry 2010;196:173–8.

41. Turner EH, Matthews AA, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. N Engl J Med 2008;358:252–60.

42. Borenstein M. Software for publication bias. In: Rothstein H, Sutton AJ, Borenstein M, editors. Publication bias in metaanalysis: Prevention, assessment and adjustments. New York: Wiley; 2005. p. 391–403.

43. Paul GL. Strategy of outcome research in psychotherapy. J Consult Psychol 1967;31:109–18.

44. Stiles WB, Shapiro DA, Elliott R. Are all psychotherapies equivalent? Am Psychol 1986;41:165–80.

45. Roth A, Fonagy P. What works for whom?, 2nd edition. New York: Guilford Publications; 2004.

46. Mueller TI, Leon AC, Keller MB, Solomon DA, Endicott J, Coryell W, et al. Recurrence after recovery from major depressive disorder during 15 years of observational follow-up. Am J Psychiatry 1999;156:1000–6.

47. Vittengl JR, Clark LA, Dunn TW, Jarrett RB. Reducing relapse and recurrence in unipolar depression: A comparative meta-analysis of cognitive-behavioral therapy's effects. J Consult Clin Psychol 2007;75:475–88.

48. Barlow DH. Negative effects from psychological treatments. A perspective. Am Psychol. 2010;65:13–20.
49. Cuijpers P, van Straten A, Driessen E, van Oppen P, Bockting C, Andersson G. Depression and dysthymic disorders. In: Sturmey P, Hersen M, editors. Handbook of evidence based practice in clinical psychology. New York: Wiley, in press.

Pim Cuijpers, Department of Clinical Psychology, VU University Amsterdam, and EMGO Institute, The Netherlands.

Gerhard Andersson, Department of Behavioural Sciences and Learning, Swedish Institute for Disability Research, Linköping University, Sweden and Department of Clinical Neuroscience, Psychiatry Section, Karolinska Institute, Stockholm, Sweden.
Tara Donker, Department of Clinical Psychology, VU University Amsterdam, and EMGO Institute, The Netherlands.
Annemieke van Straten, Department of Clinical Psychology, VU University Amsterdam, and EMGO Institute, The Netherlands.

11