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A multidimensional meta-analysis of psychotherapy and pharmacotherapy for obsessive-compulsive disorder

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Abstract

A number of qualitative and meta-analytic reviews point to the efficacy of psychotherapeutic and pharmacological interventions for obsessive-compulsive disorder (OCD). In this article, we report a multidimensional meta-analysis of psychological and pharmacological treatment studies for OCD published between 1980 and 2001, examining a range of variables not previously meta-analyzed, including exclusion rates and exclusion criteria, percent of patients improved or recovered post-treatment, mean post-treatment symptomatology, and long-term outcome. These additional metrics provide a more nuanced view of the strengths and limitations of the existing data and their implications for clinical practice. Behavioral and cognitive-behavioral therapy, and a range of pharmacological interventions, lead to substantial improvement for the average patient, with individual psychotherapies and clomipramine and other Serotonin reuptake inhibitors faring best across multiple metrics. However, OCD symptoms persist at moderate levels even following adequate treatment course, and no replicable data are available on maintenance of gains for either form of treatment at 1 year or beyond. Future research should track recruitment and exclusion of study participants, include more comorbid patients, and focus on longer-term follow-up using multiple indices of outcome. More research on combined pharmacological and psychotherapeutic interventions is also indicated.

Keywords: Obsessive-compulsive; Multidimensional meta-analysis; Psychotherapy; Pharmacotherapy; Treatment; Clomipramine; SSRI; ERP; CBT; Serotonin reuptake inhibitors; Combined pharmacological and psychotherapeutic interventions

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Obsessive-compulsive disorder (OCD) is a debilitating illness with a chronic course if untreated. The Epidemiological Catchment Area study reported a point prevalence of 1.3% and a lifetime prevalence of 2.5% in the general population (Karno, Golding, Sorensen, & Burnam, 1988; Regier et al., 1993; Robins et al., 1984). Over the last two decades, researchers have made progress in identifying effective treatments, including psychotherapy, pharmacotherapy, and combined treatments. Controlled clinical trials consistently demonstrate that exposure and response prevention (ERP), cognitive-behavioral therapy (CBT), and cognitive therapy (CT) substantially reduce obsessive-compulsive symptomatology, rendering these treatments some of the most effective psychosocial interventions for any psychiatric disorder (Abramowitz, 1997; Lindsay, Crino, & Andrews, 1997; Mclean et al., 2001; van Oppen et al., 1995). Meta-analyses have revealed high effect sizes for these interventions and few substantial differences in outcome among bona fide psychotherapies (Emmelkamp & Beens, 1991; Emmelkamp, Visser, & Hoekstra, 1988; McLean et al., 2001; van Oppen et al., 1995).

Likewise, meta-analytic reviews support use of antidepressants in the treatment of OCD (Abramowitz, 1997; Flament & Bisserbe, 1997; Greist, Jefferson, Kobak, Katzelnick, & Serlin, 1995; Kobak, Greist, Jefferson, Katzelnick, & Henk, 1998; Piccinelli, Pini, Bellantuono, & Wilkinson, 1995; Stein, Spadaccini, & Hollander, 1995). Although individual comparisons have suggested that clomipramine is superior to the other Serotonin reuptake inhibitors, meta-analyses have not found these differences to be significant (Abramowitz, 1997; Cox, Swinson, Morrison, & Lee, 1993; Kobak et al., 1998; Piccinelli et al., 1995; van Balkom et al., 1994). Existing meta-analyses and reviews suggest that approximately 60–70% of patients will show some improvement following treatment (Flament & Bisserbe, 1997; Kobak et al., 1998; Rasmussen, Eisen, & Pato, 1993). In a recent meta-analytic review of combined treatments for anxiety disorders, Foa, Franklin and Moser (2002) found that medication neither enhances nor reduces the effectiveness of CBT for OCD. As with other anxiety disorders, however, research on CBT/pharmacotherapy combinations tends to be inconsistent (Cottraux et al., 1990; Foa et al., 2002).

Evidence is clear that both psychotherapeutic and psychopharmacological treatments can be very helpful for patients suffering with OCD. Nevertheless, recent research on the efficacy of empirically supported therapies (ESTs) and pharmacological treatments for other disorders suggests that dichotomous judgments about treatments (i.e., as either supported or unsupported) may not be sufficiently nuanced to capture the complexities involved in evaluating the applicability and utility of treatments for a given disorder in everyday clinical practice (Nakash-Eisikovits, Dierberger, & Westen, 2002; Thompson-Brenner, Glass, & Westen, 2003; Westen & Morrison, 2001; Westen, Novotny, & Thompson-Brenner, 2004). For disorders such as depression, generalized anxiety disorder, and bulimia nervosa, problems identified in the literature include: (1) poor reporting of screening and inclusion/exclusion criteria, which limits knowledge about generalizability; (2) high exclusion rates, particularly for patients with comorbid psychopathology; (3) exclusive focus in reviews on indices such as effect size that, while crucially important, do not yield comprehensive data on variables of clinical relevance, such as the percent of patients whose symptoms actually remit with treatment; and (4) limited data on long-term maintenance of treatment gains.

The goal of this study is to provide a *multidimensional meta-analytic review* that specifically addresses these limitations. We begin by briefly describing a range of variables that provide a more comprehensive meta-analytic account of the state of the existing literature. We then present two meta-analytic investigations, one focusing on psychotherapeutic treatments for OCD and the other on

pharmacological and combined interventions. We conclude with implications for practice and future research.

1. Multidimensional meta-analysis

A multidimensional meta-analysis presents a range of statistics bearing on clinical utility and external validity, which can be important in assessing the strengths and limitations of treatments of psychiatric disorders, whether psychotherapeutic or pharmacologic (or both). One important variable pertains to the process by which patients are selected and screened. Studies that screen out a high proportion of subjects or that implement stringent exclusion criteria before patients are even referred for potential participation may or may not be applicable to patients in the community. For example, over 30% of patients with OCD have comorbid major depression (Freeston & Ladouceur, 1998; Steketee, Henninger, & Pollard, 2000), and an additional 50% receive at least one other anxiety disorder diagnosis (Freeston & Ladouceur, 1998; Steketee et al., 2000). Thus, researchers who exclude patients for comorbid disorders such as these must either limit their conclusions to non-comorbid obsessive-compulsive patients or conduct additional studies testing their treatments on comorbid patients. Thus, we aggregate data on both criteria for inclusion/exclusion and percent of patients excluded.

Second, no single index of outcome provides a comprehensive description of the effects of a treatment; a more nuanced portrait may require presentation of multiple metrics. Effect size provides a crucial index of the effect an average patient can expect to achieve; however, it does not yield information on response variability, notably the percent of patients who recover or experience clinically significant improvement. For some disorders, improvement short of recovery is useful to report, particularly if the disorder is difficult to treat completely, such as OCD. In addition to effect size, then, two useful indices are *percent recovered* and *percent improved* (or percent improved and recovered combined).

Even if meta-analysts quantify percent improved or recovered, they may come to different conclusions depending on the denominator they choose—that is, percent improved or recovered out of what group of patients? The most liberal estimate uses the number of completers in the numerator, eliminating participants who failed to complete for whatever reasons. A more conservative estimate uses the number of patients randomized, or the number who actually began treatment (intent to treat sample). Consumers of research can draw the most accurate conclusions if researchers report both intent-to-treat and completer analyses (see Kendall, 1999). Because the intent-to-treat/completer distinction is orthogonal to the distinction between recovery and clinically significant improvement, we present four metrics: percent recovered of completers, percent recovered of the intent-to-treat sample, percent improved of completers, and percent improved of the intent-to-treat sample.

Equally important in evaluating efficacy is the *absolute magnitude* of mean symptoms at termination or follow-up. Researchers might describe a treatment as highly efficacious because it yields a strong effect size and produces improvement in a large percentage of cases, but this conclusion may be misleading to consumers if the treatment does not in fact produce recovery.

A final variable of crucial importance is *sustained efficacy* over time. A treatment that produces an *initial response*, or a response that holds for 3 to 6 months after termination, may or may not be an efficacious treatment for a disorder such as OCD that tends to be longstanding.

2. Study 1: A multidimensional meta-analysis of psychotherapies for OCD

2.1. Method

2.1.1. Selection of studies

We used a two-phase search process to identify randomized controlled trials (RCTs) of psychotherapy for OCD published between January 1980 and December 2001: (1) a search of PsycINFO and Medline, using the keywords "obsessive-compulsive" and "OCD"; and (2) a manual review of prior meta-analyses and reviews for studies not obtained using the first procedure. To be included, a study had to test the efficacy of a specific psychotherapy against a control condition, an alternative psychotherapy, a medication,[1] or some combination of these. We included both initial publications and follow-up studies, provided that the follow-up interval was 12 months or longer (an interval we chose because of its clinical meaningfulness for disorders such as OCD that tend to have a chronic course). To be included, studies also had to require that all subjects have a diagnosis of OCD, had to include valid measures of outcome for the primary symptoms, and had to be experimental in design (including randomized patient assignment, standardized treatments, and blind outcome assessment); hence, open trials, single-blind studies, and case studies were excluded. We also excluded studies that presented re-analyses of data already included, were limited to specific subtypes or subpopulations whose characteristics may be very different from the general population of patients with the disorder (e.g., OCD patients with tic disorders); were published in a language other than English; or included fewer than nine patients in each group.[2] All decisions of this sort were made a priori, before examining individual studies. Fifteen studies met inclusion criteria (marked with asterisks in the reference section). Of these, 5 included a wait-list or control condition and the remaining 10 studies included psychotherapy treatment conditions alone.

2.1.2. Procedure

Variables assessed included number of participants, percent of patients who met initial criteria who were included (screened into the study), percent of patients who completed treatment, percent of patients who dropped out, effect sizes, percent of patients who improved with treatment, percent of patients who recovered with treatment, and mean post-treatment symptomatology (e.g., mean Yale–Brown Obsessive-Compulsive Scale [YBOCS] scores following treatment).

Decisions about how to code or define variables reflected our consistent efforts to make methodological decisions prior to examining the data where possible to remain maximally blind (an issue infrequently addressed in meta-analytic work; see Westen & Morrison, 2001). With respect to specific variables that may require clarification, *number of participants* refers to the number of people who actually began treatment (i.e., the number who were randomized to any given treatment condition

[1] We included psychotherapy plus pharmacotherapy trials only if the trials included a "clean" psychotherapy group (i.e., a psychotherapy condition without either a placebo or active medication), as our focus in this first meta-analysis was psychotherapy rather than pharmacotherapy.

[2] We decided a priori to exclude studies with an N below 10 in each experimental condition both because of methodological concerns about studies that build in too little power to detect effects (Hayes, Barlow, & Nelson-Gray, 1999) and because of the problem of maintaining blindness in small-N studies. However, we decided to loosen the criterion of 10 subjects per group to 9 per group because we were able to find only 12 studies with an N >10 that met criteria for inclusion in our meta-analysis. When we changed the entry criterion to N >9, we were able to add an additional three studies.

minus those who never attended the first treatment session).[3] *Percent included* describes the percentage of patients who met inclusion criteria and were screened into the study, which typically occurred after a patient was referred or self-referred for the disorder under investigation, and often after a telephone screen or in-person assessment. *Percent completed* refers to the percent of patients who completed the treatments out of those two began.

To measure *effect size*, we used Cohen's *d* (Cohen, 1988), calculated using the following formula: (mean of group 1−mean of group 2)/[(SD1^2+SD2^2)/2]). Experimental conditions were considered controls if the authors explicitly referred to them as such. Because many studies did not include either a control group or the descriptive statistics necessary to calculate treatment vs. control effect sizes, we also calculated within-treatment, or pre vs. post, effects using the equation: (pre-test mean−post-test mean)/pooled pre- and post-test standard deviations. For analyses of effect size, we aggregated across widely used, psychometrically sound measures of OCD symptomatology, including the YBOCS, Maudsley Obsessive-Compulsive Inventory (MOCI), Padua Inventory, and Compulsive Activity Checklist.

With regard to percent of subjects who improved or recovered, definitions of improvement and recovery varied across studies and were often not reported. Three studies reported on *percent improved*, with definitions of improvement ranging from 30% to 50% improvement on obsessive-compulsive symptom measures; only three studies reported on percent recovered. For analyses of *post-treatment mean symptomatology*, we used the most common measure of OCD outcome included across studies, the YBOCS, which has become the "gold standard" for assessment of obsessive-compulsive symptoms (Feske & Chambless, 2000).

2.1.3. Results

The primary sample consisted of data from 15 clinical trials, including a total of 33 treatment groups. Treatments included 18 ERP conditions, 5 CBT conditions, and 5 CT conditions; 25 conditions were administered individually, and 5 in groups. Treatment group data are presented in Table 1. Of the 15 clinical trials, 5 included control conditions, 3 of which were wait-list controls and 2 were alternative therapy conditions (a progressive muscle relaxation condition and an anxiety management training condition). In both alternative treatment controls, patients received some form of professional attention but not the preferred form of treatment.

The total number of patients across all studies was 705 with a mean duration of illness of 10.34 years (S.D.=3.14 years). Across all treatment conditions, mean duration of treatment was 16.0 sessions (S.D.=6.93) held over 10.21 weeks (S.D.=5.14), totaling a mean of 21.60 h (S.D.=11.20). In a second set of analyses, we meta-analyzed data from follow-up studies of 1 year or longer. Although 13 of the 15 studies reported follow-up data, only two studies reported data at 1-year post-treatment or beyond.

2.1.4. Inclusion and completion rates

Table 1 summarizes inclusion and completion rates. Although numbers of potential subjects screened and excluded are important data for generalizing from any sample, they were presented for only 3 of the 15 studies. Across the three studies, 52.62% of patients were excluded from the average study (range: 34–85%). All studies required that OCD be the primary diagnosis, although the method used to

[3] This served to make our final estimate of completion rate a comparably liberal one, given that we did not factor in attrition between randomization and commencement of treatment.

Table 1
Descriptive statistics and outcome estimates across all psychosocial treatments

	Psychotherapy (aggregate)			Control		
	Mean (S.D.)	Median	N[a]	Mean (S.D.)	Median	N
Number of subjects	37.93 (23.22)	30.00	15	16.80 (9.15)	14.00	5
% Included of screened	47.38 (28.75)	49.00	4	23.50 (12.02)	23.50	2
% Completed of entered[b]	87.89 (9.02)	90.00	15	90.20 (11.86)	91.00	5
% Improved						
Of completed	64.09 (20.89)	72.68	4		–	–
Of entered	57.93 (22.27)	66.35	4	–	–	–
% Recovered						
Of completed	38.22 (10.13)	41.00	3	–	–	–
Of entered	25.03 (5.17)	22.08	3	–	–	–
Effect size						
Treatment vs. control	1.12 (.93)	1.04	3	–	–	–
Pre vs. Post	1.52 (.66)	1.19	13	0.12 (.21)	0.12	2
Post-treatment YBOCS[c]	12.69 (2.29)	12.25	8	22.00 (3.90)	22.00	3

[a] N here refers to the sampling unit, i.e., number of studies, not number of subjects.
[b] Percent of entered refers to intent-to-treat sample.
[c] YBOCS=Yale–Brown Obsessive-Compulsive Scale. Additional outcome measures were used in calculating aggregate effect size estimates.

determine this was not reported. Most studies (10/15) excluded patients for psychotic or organic disorders or concurrent psychotherapy or pharmacotherapy (9/15). Four others excluded patients for any history of psychological treatment, and an additional 3 for "major medical conditions." Although most of these represent reasonable exclusion criteria, several studies also excluded for comorbidity, including substance use disorders (7/15), major depressive disorder (3/15), suicidality (3/15), and Axis II disorders (1/15). One of the questions raised by the exclusionary criteria is whether treatment for OCD is more effective with certain types of patients than with others. One way to address this concern is to assess psychiatric comorbidity and examine its association with outcome within studies; however, this was typically not reported.

2.1.5. Effect size

With respect to effect sizes, overall initial response was high, as reported in prior meta-analyses. Few studies reported data that would allow us to assess treatment vs. control effect sizes, however. The pre- vs. post-treatment effect size for aggregate measures of OCD was impressive, as can be seen in Table 1. These high effect sizes are in contrast with the marginal pre- vs. post-treatment effect sizes for the control/wait-list conditions. When we examined specific psychosocial treatments (see Table 2), effect sizes were similar across subgroups, including ERP, CBT, and CT, although they were slightly stronger for ERP and CBT, respectively. Likewise, the pre- vs. post-treatment effect sizes were slightly higher for individual therapy (1.48, S.D.=0.77, n=26) than for group therapy (1.17, S.D.=0.35, n=2), although the number of studies limits any ability to calculate the significance of that difference.

2.1.6. Percent improved and recovered

Only 4 of the 15 studies reported improvement rates post-treatment, and only 3 reported recovery rates. Definitions of improvement at post-treatment were inconsistent, ranging from 25% to 50%

Table 2
Outcome estimates by treatment (psychotherapies)

	Exposure and response prevention			Cognitive therapy			Cognitive-behavioral therapy		
	Mean (S.D.)	Median	N^a	Mean (S.D.)	Median	N	Mean (S.D.)	Median	N
%Improved									
Of completed	68.80 (17.88)	70.00	5	56.57 (26.91)	67.00	3	–	–	–
Of entered[b]	61.72 (19.46)	63.60	5	51.60 (27.72)	63.00	3	–	–	–
%Recovered									
Of completed	38.22 (8.86)	39.00	3	49.84 (4.48)	49.84	2	–	–	–
Of entered	31.14 (10.38)	29.00	3	41.88 (2.65)	41.88	2	–	–	–
Effect size									
Treatment vs. control	1.16 (1.31)	1.16	2	–	–	–	–	–	–
Pre vs. Post	1.53 (.87)	1.32	16	1.54 (.54)	1.22	5	1.39 (.52)	1.27	4
Post-treatment YBOCS[c]	12.48 (3.11)	12.10	9	13.10 (.53)	13.30	3	14.15 (2.76)	14.15	2

[a] N here refers to the sampling unit, i.e., number of cases, not number of studies.
[b] Percent of entered refers to intent-to-treat sample.
[c] YBOCS=Yale–Brown Obsessive-Compulsive Scale. Additional outcome measures were used in calculating aggregate effect size estimates.

improvement on OCD measures, notably the YBOCS. The three studies that used YBOCS scores as an indication of recovery post-treatment implemented definitions of recovery as a YBOCS cutoff of 8 (Cottraux et al., 2001) or a YBOCS cutoff of 12 with a 6-point decrease (McLean et al., 2001; Van Oppen et al., 1995). Further, many psychopharmacology treatment studies for OCD studies have used a YBOCS Total score of >16 as an inclusion criterion for subjects, indicating that such a score represents clinically significant obsessive-compulsive symptomatology (e.g., Koran et al., 1996; The Clomipramine Collaborative Study Group, 1991; 1994; Zohar, Judge, & OCD Paroxetine Study Investigators, 1996). Thus, in the discussion below, we consider a YBOCS score below 12 as indicating that minimal obsessive-compulsive symptoms; a score between 12 and 16 indicating subclinical symptomatology, and a score of 16 or higher indicating clinically significant OCD symptoms.

As can be seen in Table 1, across all treatments, about two-thirds of the patients who *completed* treatment improved (range: 33–78%), whereas only one-third met recovery criteria (range: 27–47%). Among the intent-to-treat sample (i.e., including patients who chose not to complete), about one-half of patients improved (range: 25–74%), compared to only one-fourth who recovered (range: 22–33%). Findings were again strongest for ERP. Also, of patients who *completed* treatment, a higher percentage recovered in individual therapy (mean=44%, range: 29–53%) than in group therapy (mean=28%, range:16–39%). Of the intent-to-treat sample, 37% (range: 22–40%) of patients in individual therapy recovered, compared to 22% (range: 15–29%) of those in group therapy.

2.1.7. Post-treatment symptomatology

An index of outcome that has received little attention is post-treatment mean symptomatology. At termination, across all active treatments, the mean YBOCS score was 12.70 (S.D.=2.29, n=8), representing a substantial improvement from the pre-treatment mean of 24.85 (S.D.=2.76, n=8) but not a return to health for a large percent of subjects. As seen in Tables 1 and 2, the ERP post-treatment YBOCS score was lower than the post-treatment scores for CBT and CT. The average post-treatment

score for the wait-list/control conditions was 22.00 (S.D.=3.90, *n*=3), demonstrating negligible change from the mean pre-treatment score of 23.09 (S.D.=3.13, *n*=4).

2.1.8. Follow-up

We intended to report the above variables at 1 year of follow-up and beyond. Although 13/15 studies reported follow-up post-treatment, only two studies included follow-up at or beyond 1-year post-treatment. We could not aggregate those data in any meaningful way, however, because the investigators reported data using the last observation carried forward (LOCF) method, which does not allow readers to distinguish between data collected at 12 weeks and 12 months. LOCF is a useful method for avoiding spuriously high estimates of outcome for patients who drop out without improvement, but it renders follow-up data difficult to interpret. Thus, no replicable data are available on the maintenance of treatment gains at 1 year and beyond.

3. Study 2: meta-analysis of pharmacotherapy for OCD

3.1. Methods and materials

3.1.1. Selection of studies

To maximize the likelihood of obtaining all relevant published research reports, we used a three-phase search process. First, we performed an issue-by-issue search of 22 high quality, high-impact journals that routinely publish efficacy research, including research on OCD (e.g., *American Journal of Psychiatry*, *Archives of General Psychiatry*). Next, we conducted an exhaustive computer search of PsycINFO and Medline using the keywords "obsessive compulsive." Last, we manually reviewed prior meta-analyses and reviews for studies not obtained using the first two procedures. We included studies published between January 1980 and December 2001.

To be included, a study had to test the efficacy of a specific medication against a control condition, an alternative medication, psychotherapy, or some combination of these. We included both initial publications and follow-up studies, provided that the follow-up interval was 12 months or longer (an interval we chose because of its clinical meaningfulness for disorders such as OCD that tend to have chronic courses). In addition, studies had to be experimental in design (including randomized patient assignment, standardized treatments, and blind outcome assessment) and include valid measures of outcome. Accordingly, open trials, single-blind studies, and case studies were excluded. Similarly, studies that included only idiosyncratic measures of outcome and did not report on improvement or recovery were excluded. We also excluded reports that presented re-analyses of data already included, were limited to specific subtypes or subpopulations whose characteristics may be different from the general population of patients with the disorder (e.g., child/adolescent, geriatric OCD patients), were published in a language other than English, or included fewer than 10 patients in each group.[4] Further, we excluded studies in which pharmacotherapy was added adjunctively (e.g., in treatment-refractory OCD). All decisions of this sort were made a priori, before examining individual studies.

[4] We decided a priori to exclude studies with an N below 10 in each experimental condition both because of methodological concerns about studies that build in too little power to detect effects (Hayes et al., 1999) and because of the problem of maintaining blindness in small-N studies.

Thirty-two studies met inclusion criteria (marked with asterisks in the reference section). Four studies included a combined pharmacotherapy plus psychotherapy condition (treated separately in analyses here), and the remaining studies included a pharmacological treatment condition alone. Of these, six studies had a cross-over design (included in the primary analyses[5]).

3.1.2. Procedure

Analyses were conducted at two levels. First, we considered aggregate pharmacotherapy and control condition data. Second, we examined specific medication classes, including SRIs, tricyclics, MAOIs, and anxiolytics. In these analyses, clomipramine is presented as an SRI rather than a tricyclic because prior research has indicated that in an OCD population, it more closely resembles the selective SRIs than the other tricyclics.

Variables assessed were the same as those included in Study 1, with the addition of percent of patients who dropped out due to side effects. When available, we also present post-treatment scores for the National Institute of Mental Health Obsessive-Compulsive Scale [NIMHOCS] scores in addition to YBOCS scores. As with Study 1, vis-à-vis percent of subjects who improved, definitions of improvement varied across studies and were often not reported. In these analyses, we considered both *percent improved* with regard to OCD symptoms as well as *percent improved* in terms of general psychiatric function as measured by the Clinical Global Improvement (CGI) scale. For analyses of *post-treatment mean symptomatology*, we used the most common measures of OCD outcome included across studies, the YBOCS and the NIMHOCS.

3.1.3. Results

The primary sample included data from 32 clinical trials (6 of which had a cross-over design), including a total of 68 treatment conditions. Active treatments included 36 SRI conditions (18 clomipramine, 8 fluvoxamine, 4 sertraline, 4 fluoxetine, 1 paroxetine, and 1 citalopram); 4 tricyclic conditions (excluding clomipramine; 2 imipramine and 2 desipramine); 3 MAOI conditions (2 phenelzine and 1 clorgyline); 2 anxiolytic conditions (buspirone and clonazepam); and 2 "other" medications (clonidine and inositol). Twenty-one studies included a placebo condition. The total number of patients across these 32 studies was 3588, with a mean duration of illness of 13.45 years (S.D.=4.87). Across all treatment conditions, the mean duration of treatment was 9.56 weeks (S.D.=2.46). In secondary analyses, we meta-analyzed outcome data for combined pharmacotherapy plus psychotherapy (n=4 studies) and treatment refractory OCD (n=7 studies).

3.1.4. Inclusion and completion rates

Table 3 summarizes inclusion and completion rates. Although the number and percentage of potential subjects screened and excluded are important information for generalizing from any sample, as in the psychotherapy literature, few studies presented these data. Across the six studies that did so, the average study excluded approximately one third of patients (range: 3–50%). Most studies did, however, describe their exclusion criteria. Six required that OCD be the primary diagnosis, although how this was determined and the reliability of that determination were generally not reported. The majority (23/32)

[5] We ran analyses using cross-over design as a moderator variable and found that it was not significantly associated with outcome ($p>.05$); thus, we do not differentiate between noncross-over and cross-over studies here.

Table 3
Descriptive statistics and outcome estimates across all pharmacological treatments

	Pharmacotherapy (aggregate)			Pharmacotherapy plus psychotherapy			Placebo		
	Mean (S.D.)	Median	N[a]	Mean (S.D.)	Median	N	Mean (S.D.)	Median	N
Number of subjects	78.26 (89.16)	28.00	32	10.93 (2.15)	48.00	3	54.57 (42.63)	26.00	21
% Included of screened	69.45 (21.02)	62.80	6	–	–	–	67.75 (35.85)	67.75	2
% Completed of entered	82.56 (9.63)	85.15	32	73.57 (10.46)	79.20	3	85.78 (11.96)	89.30	21
% Improved									
Of completed	63.80 (21.29)	68.50	9	–	–	–	23.66 (19.28)	21.40	7
Of entered[b]	49.48 (14.10)	50.60	9	–	–	–	19.39 (14.07)	20.00	7
% Recovered	–	–	–	–	–	–	–	–	–
Effect size									
Treatment vs. control	0.83 (.58)	0.73	20	–	–	–	–	–	–
Pre vs. post	1.18 (.58)	1.09	27	1.72 (.90)	1.88	3	0.32 (.38)	0.22	20
Post-treatment YBOCS[c]	17.19 (2.09)	17.23	23	14.10	14.10	1	22.15 (2.69)	21.36	16

[a] N here refers to the sampling unit, i.e., number of studies, not number of subjects.
[b] Percent of entered refers to intent-to-treat sample.
[c] YBOCS=Yale–Brown Obsessive-Compulsive Scale; where reported, additional outcome measures are included in aggregate effect size estimates.

also excluded patients with significant medical conditions. Most studies (appropriately) excluded patients for psychotic/organic mental disorders (22/32) or concurrent psychotherapy/pharmacotherapy (22/32). Many studies also excluded for comorbidity, including any Axis I disorder (10/32), substance use disorders (22/32), depression (19/32), bipolar disorder (18/32), panic disorder (16/32), agoraphobia (14/32), eating disorders (14/32), suicidality (6/32), and Axis II disorders (5/32). Thus, although we could not determine the percent of patients excluded in most studies, the majority imposed substantial restrictions beyond presence of an OCD diagnosis (and substantially beyond the restrictions imposed on patients enrolled in psychotherapy samples). Likewise, to assess generalizability, it is helpful to know the psychiatric comorbidity of the studied patients, which was most often not reported.

As in the psychotherapy studies, where over 85% completed the treatment, most patients who entered treatment completed. Across medication classes, completion rates were comparable, ranging from 80% for tricyclics to 92% for MAOIs. Of the subjects who entered active treatment, an average of 8% (S.D.=6, n=28) dropped out because of side effects, compared to 2% (S.D.=2, n=17) in placebo conditions. With regard to medication class, dropout rates due to side effects ranged from 7% (S.D.=10, n=2) for MAOIs to 10% (S.D.=7, n=4) for tricyclics (excluding clomipramine).

3.1.5. Effect size

With respect to effect size, initial response rate was high (Table 3).[6] For the most widely reported outcome measures of OCD (the YBOCS and the NIMHOCS), treatment vs. control effect sizes were

[6] Although the YBOCS is generally thought to be the most sensitive to clinical change, effect sizes across outcome measures were comparable in most cases.

0.90 (S.D.=0.64, *n*=16) on the YBOCS and 0.97 (S.D.=0.65, *n*=11) on the NIMHOCS. Aggregate effect size across all OCD outcome measures for pre- vs. post-treatment averaged 1.26 (S.D.=0.61, *n*=20) on the YBOCS and 1.49 (S.D.=0.56, *n*=14) on the NIMHOCS. These high effect sizes are in contrast with the low pre- vs. post-treatment effect sizes for the placebo conditions on aggregate OCD measures (see Table 1), as well as on the YBOCS (effect size=0.38, S.D.=0.45, *n*=16). The placebo conditions produced a surprisingly large effect size of 0.49 (S.D.=0.31, *n*=11) on the NIMHOCS, although this is still quite low when compared to the active treatments.

When we examined specific medication classes (see Table 4), clear differences emerged. In terms of treatment vs. control effect sizes, SRIs had the most impressive effect size, 0.91, while those of the other medication classes were low and similar to one another. When we investigated individual medications (see Table 4), clomipramine had the largest effect size, 1.35. Effect sizes for other medications ranged from 0.35 for imipramine to 0.86 for fluvoxamine. As would be expected, pre- vs. post-treatment effects sizes were more impressive than treatment vs. control effect sizes for all medications. Clomipramine, once again, had the highest effect size of 1.55. Effect sizes for the other SRIs were also impressive, ranging from 0.81 for fluoxetine to 1.36 for sertraline. In contrast, the other tricyclics had comparably low effect sizes of 0.67 (S.D.=0.50, *n*=2) for imipramine and 0.11 (S.D.=0.22, *n*=2) for desipramine. In the only published study of citalopram, using this new medication had a pre- vs. post- effect size of 2.01 (*n*=1), which may be noteworthy given the large sample size (*n*=300).

3.1.6. Percent improved and recovered

Nine of the thirty two studies reported post-treatment improvement rates for OCD symptomatology. Definition of improvement ranged from 20% to 35% improvement on the YBOCS and/or the NIMHOCS. Although the vast majority of studies published after 1989 use a criterion of 25% or greater decrease in score, it is of note that these definitions are substantially more lax than definitions used in other literatures, such as treatment of bulimia, where 50% reduction in symptoms is the norm (Nakash-Eisikovits et al., 2002). We planned to report on *percent recovered*; however, no studies presented these

Table 4
Outcome estimates by medication class

	SRIs			Tricyclics			MAOIs			Anxiolytics		
	Mean (S.D.)	Median	*N*[a]	Mean (S.D.)	Median	*N*	Mean (S.D.)	Median	N	Mean (S.D.)	Median	*N*
%Improved												
Of completed	70.13 (21.73)	68.50	9	–	–	–	–	–	–	60.00	60.00	1
Of entered[b]	52.54 (12.84)	52.50	9	–	–	–	–	–	–	48.00	48.00	1
%Recovered	–	–	–	–	–	–	–	–	–	–	–	–
Effect size												
Treatment vs. control	0.91 (.57)	0.73	18	0.35	0.35	1	0.33	0.33	1	0.33	0.33	1
Pre vs. post	1.34 (.50)	1.30	26	0.39 (.46)	0.25	4	0.60 (.55)	0.41	3	1.06 (.09)	1.06	2
Post-treatment YBOCS[c]	16.84 (1.83)	16.90	27	25.80	25.80	1	16.30	16.30	1	17.69 (1.29)	17.69	2

[a] *N* here refers to the sampling unit, i.e., number of studies, not number of subjects.

[b] Percent of entered refers to intent-to-treat sample.

[c] YBOCS=Yale–Brown Obsessive-Compulsive Scale; additional outcome measures were used in calculating aggregate effect size estimates.

data. In terms of general improvement (beyond OCD symptoms), 11 studies reported improvement rates indicated by "much improved/very much improved" ratings on the CGI.

As can be seen from Table 3, across all treatments, almost two-thirds of patients who *completed* improved, whereas only one-half of the intent-to-treat sample improved. Approximately 20% of subjects in placebo conditions also improved. By medication class, improvement rates were only available for the SRIs and the anxiolytics; however, the rate of improvement for anxiolytics was based on only one study with a relatively small *N*, so no conclusions about the comparability of improvement rates across medication classes can be drawn (Table 4).

3.1.7. Post-treatment symptomatology

Across all active treatments, the mean decrease in YBOCS score was 7.1, resulting in a mean post-treatment score of 17.19. Mean decrease in NIMHOCS score was 2.5, resulting in a post-treatment score of 6.60. In contrast, for the placebo conditions, the mean decrease in YBOCS and NIMHOCS scores were 1.8 and .8, respectively, resulting in post-treatment means of 22.15 on the YBOCS and 8.48 on the NIMHOCS (see Table 3). As demonstrated in Table 4, mean post-treatment YBOCS and NIMHOCS scores were similar for SRIs, MAOIs, and anxiolytics, while they were substantially higher for the tricyclics.

3.1.8. Follow-up

Few studies included any type of follow-up, resulting in a lack of data regarding the long-term efficacy of pharmacological interventions. Those studies that did include a follow-up were often short in duration (e.g., 16 weeks; Montgomery et al., 1993), open extensions (e.g., Mallya, White, Waternaux, & Quay, 1992), single-blind trials (e.g., Romano et al., 2001), or presentations of last-observation-carried-forward (LOCF) data (e.g., Greist, Jefferson, Kobak, Chouinard et al., 1995).

Only one study (Katz, DeVeaugh-Geiss, & Landau, 1990) carried out a year-long double-blind extension of clomipramine without using the LOCF method. Of the 101 treatment responders who entered the active treatment extension phase, the vast majority (n=73) dropped out. For the 28 subjects who completed the extension, pre-treatment vs. post-extension effect size was slightly higher than pre vs. post-treatment effect size (1.58 vs. 1.48). Further, the mean post-extension NIMHOCS score was 4.4 (S.D.=2.3, n=28), demonstrating substantial improvement from the mean pre-treatment score of 9.8 (S.D. 1.6, n=134) and the mean post-treatment score of 6.2 (S.D.=2.8, n=120). These data indicate that the patients who remain on clomipramine experience continued treatment gains during a long-term extension phase, but that most patients cannot tolerate the medication for long periods or do not find it useful over the long run.

3.1.9. Combined pharmacotherapy and psychotherapy studies

We conducted a secondary set of analyses on combined pharmacotherapy plus psychotherapy studies (see Table 3). The sample included data from three clinical trials (and one follow-up study), including a total of four active pharmacotherapy plus psychotherapy treatment conditions. Treatments included one imipramine plus ERP and three fluvoxamine plus psychotherapy conditions. (The psychotherapies for the fluvoxamine studies included two using ERP and one using Cognitive therapy.) The total number of patients across the three studies was 225, with a mean duration of illness of 11.31 years (S.D.=2.29). Across all treatment conditions, the mean duration of treatment was 20 weeks (S.D.=5.29). Almost 80% of subjects who entered treatment completed, with 11.2% (S.D.=5.6) dropping out because of medication side effects.

With regard to treatment outcome, the average pre- vs. post-treatment effect size for OCD symptomatology for the pharmacotherapy plus psychotherapy conditions was very high, at 1.72, and higher than the effect sizes for pharmacotherapy alone. The pre- vs. post-treatment effect size for depressive symptomatology was similarly high at 1.51, and also higher than that of pharmacotherapy alone. Only one study presented post-treatment symptomatology data in the form of post-treatment YBOCS or NIMHOCS scores, and no information is available on percent improved or recovered; thus, no conclusions can be drawn regarding treatment outcome as measured by these variables.

Two of the three trials reported long-term follow-up (Cottraux et al., 1990; Foa, Kozak, Steketee, & McCarthy, 1992). Cottraux, Mollard, Bouvard, and Marks (1993) evaluated approximately half of their original sample 1-year post-treatment and reported that the vast majority of participants were no longer taking medications or receiving behavior therapy. Effect sizes were lower than they had been post-treatment, ranging from 0.48 to 0.56, but rates of improvement were higher, ranging from 70% to 75%. In contrast, Foa et al. (1992) found high effect sizes that remained at both 1- and 2-year follow-ups post-treatment discontinuation, with medication or placebo plus psychotherapy faring comparably.

4. Discussion

The data reported here replicate findings reported in other meta-analyses and reviews regarding the efficacy of psychotherapy for OCD and extend them in a number of ways. Consistent with prior meta-analyses, both psychotherapy and pharmacotherapy produce substantial decreases in OCD symptoms, reflected in (a) pre-treatment vs. post-treatment effect sizes; (b) a substantial percentage of patients who improve with treatment and (c) considerable declines in symptoms from pre- to post-treatment.

Across outcome metrics, although all psychotherapies show strong effects, the more behaviorally (as opposed to cognitively) oriented psychotherapies tended to be more efficacious, as consistent with other reviews (Abramowitz, Franklin, & Foa, in press). Among medications, effect sizes for clomipramine stand out, suggesting, as have prior reviews, that this nonspecific SRI is more effective than the selective SRIs and tricyclics in targeting obsessive-compulsive symptoms. It is worth noting, however, that the largest effect sizes for clomipramine are found in early studies and have not been as clearly replicated in more recent studies comparing it with other SRIs. However, patients receiving clomipramine were more likely to drop out because of side effects than those taking the selective SRIs, and the single study that examined long-term extension of clomipramine therapy found that only a minority of patients remained on it over the course of a year despite its very positive initial effects.

For combined therapies, we found impressive effect sizes on average, which were higher than pharmacotherapy alone (1.72 vs. 1.18). These effect sizes are also higher than those reported for psychotherapy alone, suggesting that combined pharmacotherapy and psychotherapy may be the most effective intervention for patients with OCD, although these conclusions remain tentative because of the paucity of clinical trials for combined therapies.

4.1. Inclusion/exclusion and generalizability

The extent to which researchers exclude patients who would frequently present for treatment with the disorder in clinical practice is integral to external validity. The vast majority of studies did not

report on the number of potential subjects screened, thus limiting interpretation of generalizability. In the psychotherapy literature, based on the few studies that provided adequate data to make a determination, roughly half of the patients who applied for treatment were excluded. Unfortunately, only 3 of the 15 reported relevant data on exclusion rates, rendering generalizability uncertain. For the pharmacological treatments, approximately one-third of those screened were excluded in the few studies reporting these data.

Although some exclusion criteria are obviously appropriate (e.g., psychotic disorders), it is possible that other common exclusion criteria, particularly comorbidity (e.g., major depression other anxiety disorders, or substance abuse), would impact the treatment course and thus limit generalizability. While these exclusion criteria may limit applicability of these findings to patients with comorbidity, it is worth noting that several studies (not analyzed here) have made efforts to examine treatment efficacy specifically in patients with comorbid anxiety and affective disorders (e.g., Hoehn-Saric et al., 2000; Steketee, Chambless, & Tran, 2001). One preliminary report suggests that concurrent major depression may adversely affect long-term outcome in patients with OCD (Steketee et al., 2001). Another (Gershuny, Baer, Jenike, Minichiello, & Wilhelm, 2002) finds that a co-morbid diagnosis of PTSD is a negative prognostic indicator for treatment of OCD via behavior therapy. We would recommend that researchers eliminate any exclusion criteria beyond those a reasonable clinician would apply in practice, to maximize the generalizability to everyday practice (see Westen, Novotny, & Thompson-Brenner, 2004), and routinely assess the relation between comorbid pathology and outcome.

4.2. Improvement and recovery

Large effect sizes suggest that psychotherapy, SRIs, as well their combinations can be effective in alleviating obsessive-compulsive symptoms. While these data are very promising, particularly for a disorder that is typically chronic and difficult to treat, consideration of improvement and recovery rates provides a more complete portrait. First, only a few of the psychotherapy studies reported data that allowed us to calculate treatment vs. control effect sizes (as opposed to pre- vs. post-treatment effect sizes, which are influenced by many factors other than treatment, such as passage of time), limiting our ability to assess treatment efficacy. Second, across all three types of interventions, only a few studies reported the percent of patients who improved or recovered. The available data suggest that for psychotherapy, roughly two-thirds of patients who complete treatment improve upon termination, and one-third completely recover. Of patients *entering* psychotherapy (intent-to-treat sample), about half improve, whereas only one-quarter can expect to recover completely. In the pharmacotherapy studies, the majority of patients completing treatment but only half of those who initially enter treatment experience improvement, and no data are available on recovery. These rates suggest that across both treatment approaches, a third of those who complete a course of treatment for OCD, and nearly half of those who begin but do not follow through with treatment, will not make expected gains. These conclusions should be interpreted with caution as they are based on limited data, highlighting the need for consistent criteria for improvement and recovery in the treatment of OCD, as well as the importance of future studies addressing improvement and recovery rates. However, they point to important potential caveats in the way we describe the potential effects of these treatments to consumers.

Third, despite achieving substantial improvement, most patients cannot expect to fully recover with treatment, as can be seen by examining post-treatment symptoms assessed through the YBOCS and NIMHOCS. Post-treatment YBOCS scores for all active treatments declined substantially from pre-treatment. However, post-treatment scores across all active treatments remained in what appears to be a clinically significant range. The psychotherapy studies had post-treatment YBOCS scores averaging 12.70. For pharmacotherapy, we found average post-treatment YBOCS scores of 17.19. The data indicate that that the average patient receiving treatment continues to experience mild to moderate obsessive-compulsive symptoms upon termination (Feske & Chambless, 2000). The range of outcome statistics provided here suggests that although we currently have powerful treatments for OCD, the search for additional intervention strategies should continue.

4.3. Maintaining improvement over time

In terms of *sustained efficacy* (the ability of these treatments to produce lasting symptomatic changes), the lack of useful follow-up data at 1 year and beyond makes conclusions about the stability of positive outcomes uncertain. In the psychotherapy sample, 2 of the 14 studies reported follow-up data at 1 year or beyond, but we were unable to analyze these data because they carried data forward from earlier observations (the LOCF method). Although the LOCF method is useful in reporting data at treatment termination or shortly thereafter, it presents severe limitations when dealing with follow-up data. Because follow-up data are essential to drawing conclusions about treatment efficacy, future studies should clearly include substantially longer follow-up intervals. In the pharmacotherapy sample, only one study presented 1-year follow-up data in a double-blind continuation study (Katz et al., 1990). While these studies suggested that continued gains were made when pharmacotherapy was extended beyond the acute treatment phase, more research in this area is clearly needed.

Beyond follow-up studies, a growing body of research has examined maintenance of treatment gains over time, typically through discontinuation trials. For example, several studies have found that obsessive-compulsive symptoms return within several weeks of treatment discontinuation (Maina, Albert, & Bogetto, 2001; Pato, Zohar-Kadouch, Zohar, Murphy, 1988; Pigott et al., 1990). However, one recent study suggested that treatment gains may be maintained at lower doses of pharmacotherapy than those required during the acute treatment phase (Mundo, Bareggi, Pirola, Bellodi, & Smeraldi, 1997). In a more naturalistic follow-up of combined pharmacotherapy and psychotherapy (Cottraux et al., 1993), the investigators recontacted approximately one-half of their original sample and found that the vast majority were not participating in any treatment and had relapsed. Taken together, these findings suggest that continued pharmacological intervention is needed to maintain treatment gains long-term.[7] Further research is warranted to clarify the maintenance of treatment gains over time, as well as to determine the relative efficacy of combined treatments.

[7] Contrasting this suggestion, however, is Foa et al.'s (1992) combined pharmacotherapy and psychotherapy report, in which treatment gains were maintained at one and two year follow-up. It is worth noting that in this trial the combined therapies were imipramine or placebo plus behavior therapy; due to the generally low response rate elicited by imipramine alone (e.g., Zohar & Insel, 1987), it is likely that the behavioral treatment (rather than the medication) instigated both the initial and sustained responses in this trial.

4.4. Implications

The data reported here reaffirm the prevailing wisdom that behavioral and cognitive-behavioral therapies, pharmacological therapy, and (based on initial data) their combination lead to substantial and clinically meaningful reductions in symptomatology for patients who are often quite severely impaired at the beginning of treatment and who have suffered with their symptoms for many years. A few of the treatment recommendations indicated by this review are highlighted.

(1) Psychotherapy approaches using behavioral elements either alone or in addition to cognitive elements may be more effective than those with cognitive elements alone.
(2) Individual therapy may be more effective than psychotherapy.
(3) Combined treatment approaches show promise.
(4) No clear guidelines are available regarding treatment of patients with substantial comorbidity.

Inclusion of a broad range of outcome metrics qualifies any general conclusions that can be drawn from this literature in ways that are important in evaluating the clinical utility of different forms of treatment and in designing the next generation of research. Based on these meta-analyses (and our difficulty obtaining relevant data on a number of metrics), we offer the following recommendations for future research, many of which are consistent with the recommendations CONSORT statement for improving the quality of randomized control trials (Moher, Schulz, & Altman, 2001):

(1) Reporting of clinical trials should include flowcharts that allow readers to see how many patients were screened, how many were randomized to each condition, how many completed treatment, how many dropped out because of side effects, how many recovered, how many improved, how many remained recovered or improved at follow-up, and so forth (Egger, Juni, & Bartlett, 2001).
(2) Comorbidity on both Axis I and Axis II should be routinely assessed, and tested as potential moderators of treatment outcome.
(3) Researchers should minimize exclusion criteria, including both “primary” and comorbid diagnoses, so that patients treated in clinical trials more fully resemble patients treated in the community.
(4) Clear consensual criteria for clinically meaningful reduction in OCD symptoms as well for post-treatment scores should be established.
(5) Data on percent improved, percent recovered, and levels of post-treatment symptoms for intent-to-treat and study completers should routinely be presented.
(6) Studies should routinely build in follow-up intervals of at least 2 years, so that clinicians and consumers can make informed decisions about durability of treatment effects.
(7) More research on combined interventions, including timing of interventions, is needed.

4.5. Limitations

The data presented here are not, of course, without limitations. The quality of a meta-analysis is dependent upon the quality and comprehensiveness of the data being meta-analyzed, and to the extent

that, for example, adequate follow-up data are unavailable, we can draw few conclusions about enduring treatment effects. Further, meta-analyses can overstate effect sizes if studies that yield negative results are not published and hence are not subjected to aggregation along with data from published accounts. Nevertheless, meta-analytic methods can be very useful in summarizing data across studies quantitatively, by providing comparable metrics across studies, treatments, and disorders, and by avoiding many of the limits of subjective reviews.

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