EARLY CAREER PSYCHIATRISTS META-ANALYSIS

Long-Term Outcome of Obsessive-Compulsive Disorder in Adults: A Meta-Analysis

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ABSTRACT

Objective: To study the long-term rate and predictors of remission in adults with obsessive-compulsive disorder (OCD), using meta-analysis.

Data Sources: The MEDLINE database was searched to May 2013 using the search terms *obsessive-compulsive disorder*, *prospective*, *outcome study*, *clinical course*, *remission*, *prognosis*, *follow-up*, and *long-term* and limits for language (English), species (humans), and age (adults). This was supplemented by manual bibliographic cross-referencing.

Study Selection: English-language studies from peer-reviewed journals on adults with *DSM-III-R, DSM-IV, DSM-IV-TR, ICD-9*, or *ICD-10* diagnosis of OCD followed up for \geq 1 year and treated with serotonin reuptake inhibitors and/or cognitive-behavioral therapy that reported rate of remission (Yale-Brown Obsessive Compulsive Scale [YBOCS] score < 16 at longest follow-up) were included.

Data Extraction: Data were gathered as numbers/means/ percentages/categories on sample size, study design, followup duration, age at assessment, illness duration, age at illness onset, gender, marital status, inpatient/outpatient status, family history, baseline YBOCS score, comorbidities, and remission.

Results: Seventeen studies (pooled N = 1,265) fit the selection criteria and were used for the meta-analysis. The pooled sample had a mean follow-up duration 4.91 years and was predominantly male and outpatient and had onset of illness in the second decade, illness duration more than 10 years, and moderate-to-severe OCD. Pooled remission rate was 53% (95% Cl, 42%–65%). Prospective studies showed higher pooled remission rate than retrospective studies (55% [95% Cl, 45%–65%] vs 50% [95% Cl, 27%–73%], P < .001). Indian studies showed higher pooled remission rate than others (71% [95% Cl, 59%–83%] vs 48% [95% Cl, 37%–59%], P < .001). Age at onset (t = -7.08, P = .019), illness duration (t = -8.13, P = .015), baseline YBOCS score (t = -6.81, P = .021), and male gender (t = -5.92, P = .027) had significant negative association with remission on meta-regression.

Conclusion: A high long-term remission rate found in this meta-analysis is contrary to generally held beliefs about poor outcome of individuals with OCD. Multicenter, prospective, long-term studies should systematically examine course and outcome in larger samples, emphasizing symptomatic and functional recovery.

J Clin Psychiatry 2014;75(9):1019–1027 © Copyright 2014 Physicians Postgraduate Press, Inc.

Submitted: October 18, 2013; accepted February 17, 2014 (doi:10.4088/JCP.13r08849). Corresponding author: Eesha Sharma, MD, Department of

Psychiatry, King George Medical University, Lucknow, Uttar Pradesh (226003), India (eesha.250@gmail.com). O bsessive-compulsive disorder (OCD) accounts for 2.5% of the total global Years Lost to Disability and is among the top 20 causes of illness-related disability in people aged 15–44 years.¹ It has lifetime prevalence rates of 0.5%–2%,² usually begins before the age of 25 years, and is described as a chronic illness, with a waxing and waning course and low rates of remission.^{3,4} There is lack of clarity on the long-term outcome of OCD, and rates of remission vary considerably across studies.

Longitudinal follow-up studies conducted over the last 3-4 decades show varying outcomes for patients with OCD. Goodwin et al⁵ reviewed 13 naturalistic follow-up studies of the pre-serotonin reuptake inhibitor (SRI)/cognitive-behavioral therapy (CBT) era and found a favorable prognosis for the disorder. They found waning in severity of OCD with passage of time and spontaneous remissions with recovery in about one third of the subjects. In their review, outpatients fared better, with 60%-80% of them becoming asymptomatic 1-5 years after diagnosis. In the longest prospective follow-up study, Skoog and Skoog⁶ found a lengthy duration of disorder for most patients, with almost 75% patients having OCD at follow-up after 4 decades. Improvement was observed in 83% of subjects, with partial recovery in 28% and full recovery in only 20% of the patients. These studies reported outcomes of patients before effective treatments for OCD were available. As pointed out by Rasmussen and Eisen,⁷ they had several methodological limitations-retrospective study design, small sample size, lack of standardized criteria to determine diagnosis, hospital-based samples not representative of the spectrum of the disorder found in the general population, biases in inclusion and exclusion criteria, chart review rather than personal interview, absence of structured interviews, and lack of consensus regarding the definition of relapse, remission, and recovery. Also, inclusion of lobotomized patients and highly varying duration of follow-up periods across and within individual studies add to inconclusive data.8

Among studies done on adult OCD patients in the recent past, some have found low rates of remission (12%–20%),^{8,9} others moderate rates (27%–38%),^{10,11} and some fairly high rates (76%–86%).^{12,13} Even the predictors of remission are inconsistent across studies. Lower age at onset of OCD,⁶ longer duration of illness,^{10,14} duration of untreated illness,¹⁵ greater symptom severity,^{9,10,14} poor insight,¹⁶ presence of comorbid Axis I disorders,¹² and certain personality disorders, such as schizotypal personality disorder,¹⁷ have been associated with lesser likelihood of remission. Data from recent studies need to be interpreted in light of widespread availability of effective treatments.^{18–20} While clinical trials show efficacy of these interventions over placebo or wait-list controls in the short term, the important question is whether the long-term outcome of OCD has improved. It is important to have a clearer understanding of the outcome of a disorder, both for the patient and for the clinician. The common question asked by patients and their families is what happens to their illness in the long run. For a clinician, it should be possible to offer at least a reasonably accurate prognosis.

A meta-analysis of long-term outcome of pediatric OCD,²¹ published almost a decade ago, found pooled mean persistence rates of 41% and 60% for "full OCD" and "full or subthreshold OCD," respectively, implying good prognosis for pediatric OCD. Although many naturalistic long-term follow-up studies of adult OCD patients have been published since the advent of effective treatments for OCD, to the best of our knowledge, there has been no attempt to analyze the existing data with meta-analytic approach. In this study, we aimed to study the rate of remission and predictors of remission over long-term (≥ 1 year) naturalistic follow-up in adult patients with OCD treated with SRIs or CBT or a combination of both using a meta-analytic approach.

METHOD

Eligibility

Given the inevitable methodological limitations in longterm naturalistic follow-up studies, we kept the inclusion criteria broad: (1) English language studies from peer-reviewed journals; (2) follow-up duration \geq 1 year; (3) adult sample (\geq 18 years of age); (4) *DSM-III-R*, *DSM-IV*, *DSM-IV-TR*, *ICD-9*, or *ICD-10* diagnosis of OCD; (5) treatment with any one of the SRIs or CBT or a combination of both; (6) the Yale-Brown Obsessive Compulsive Scale (YBOCS) or comparable measure like Psychiatric Status Ratings (PSRs)²² used as the measure of disease severity; and (7) availability of data on remission (YBOCS total score < 16 at longest follow-up). We excluded follow-up studies of patients with refractory OCD and those who underwent neurosurgical interventions, to avoid selection bias. Thirteen follow-up studies⁵ published prior to the advent of effective therapies were obviously excluded.

Remission, defined as a YBOCS^{23,24} rating < 16 at longest follow-up, was the primary outcome measure. Pallanti et al²⁵ have defined this measure as the "most successful" outcome that indicates symptom reduction to a minimal level, in nonepisodic course OCD. Even though it may not tell us about the degree of dysfunction or the quality of life for a given patient, reduction in symptoms in OCD often directly leads to betterment in quality of life. This is unlike schizophrenia and bipolar disorder, in which the cognitive and negative symptom dimensions are difficult to treat and lead to considerable impairment after remission of positive symptoms.^{26–28} The YBOCS rating has been found to correlate with all measures of the Quality of Life (QOL) scale,²⁹ and functioning appears to be increasingly affected at YBOCS scores greater than 20.

Search Strategy

A systematic search was carried out on the MEDLINE database to May 2013 using the search terms *obsessive*compulsive disorder, prospective, outcome study, clinical

- The long-term prognosis for obsessive-compulsive disorder (OCD) is more favorable than was previously thought; more than half of patients with OCD achieve remission over 5 years of follow-up.
- Onset in late adolescence and young adulthood, female gender, a shorter duration of illness, and a lower baseline severity are associated with better outcome.
- Treatment with a combination of psychotherapy and medications may lead to better outcomes in the long term.

course, remission, prognosis, follow-up, and *long-term*. On adding filters for species (humans), language (English), and age (adults), the online search gave 426 results. Abstracts of all of the results were screened. The online search was supplemented by a manual search of bibliographic cross-referencing. A total of 66 long-term follow-up studies of OCD in adult subjects were located. Of these, 49 studies were excluded on the basis of selection criteria, and the remaining 17 studies^{8,10–12,14,30–41} were selected for meta-analysis (Table 1). The study selection procedure is depicted in Figure 1.

Data Extraction

One of the authors (E.S.) reviewed the 17 studies in detail to confirm fitness for inclusion in the meta-analysis and data extraction. Another author (Y.C.J.R.) confirmed study inclusion and the extracted data. Discrepancies were resolved by consensus. Authors of some of the studies were contacted for clarifications when necessary. If 2 studies had overlapping samples, the study with the longer duration of follow-up was included. Four of the studies started as randomized trials and later followed up participants naturalistically. Data synthesis was done for these studies by calculation of sample size weighted means and standard deviations for all independent and dependent variables, the means of which were given separately for the comparison groups.

Statistical Analysis

Random effects model, as given by DerSimonian and Laird,⁴² was used for meta-analysis. Q test, for heterogeneity among studies, was significant. The main outcome measure, the rate of remission, was assessed as a sample size-weighted pooled proportion along with the corresponding standard error. Similarly, pooled means, pooled proportions, and standard errors were calculated for other variables. Subgroup analyses were done for study design (retrospective vs prospective) and Indian versus other studies. The latter analysis was conducted because the 4 Indian studies included in the meta-analysis had much higher remission rates than the others. Funnel plot showed 5 studies as outliers. Four of these were the Indian studies with their higher remission rates. The fifth study was one by Eisen et al¹⁴ that had a large sample size but a low rate of remission. Influence analysis was done for this study.

Table 1 Ond-Term	Eolle	ow-I In Studio	s of OCD In	uchinded in the	Meta-Analyo	ie. Study C	haracteristic	sand Racel	ne Data
	5		Follow-Up			- (Age at	
			Duration,				Age at OCD	Assessment,	
Study	Z	Patient Source	Mean (SD), v	Design	Diagnostic Criteria	Males, % (n)	Onset, Mean (SD), v	Mean (SD), y	Exclusion Criteria
Eisen et al, 1999 ⁸	66	Inpatient and outpatient	2	Prospective	DSM-III-R	45 (30)	19.9 (5)	33.7 (11.8)	Primary diagnosis other than OCD
Zitterl et al, 2000 ³⁰	70	Inpatient	1.5	Prospective	DSM-III-R	NR	NR	NR	Psychosis, epilepsy, substance use disorder, substantial medical illness, history of neurosurgery
Alonso et al, 2001 ³¹	60	Outpatient	2.5 (1.2)	Prospective	DSM-IV	66.7 (40)	17.5 (7.6)	30.2 (10)	Substance use disorder, age <18 and >65 years, severe organic or neurologic pathology except tics
van Oppen et al, 2005 ³²	102	Outpatient	5.5 (1.34)	Retrospective	DSM-III-R	43.1 (44)	NR	36.3 (10.5)	OCD with obsessions only, suicidality, organic brain disease, psychosis, substance use disorder, severe medical disorder, cognitive-behavioral therapy in last 6 months, high-dosage benzodiazepines, other psychotropics in last 4 weeks
Rufer et al, 2005 ¹¹	30	Inpatient	7.2	Retrospective	DSM-III-R	40 (12)	24 (9.3)	32.4 (9.2)	Primary affective disorder, psychosis, substance use, organic brain disorder, epilepsy, suicidality, pregnancy
Biondi and Picardi, 2005 ³³	32	NR	3.13	Prospective	DSM-III-R	65.6 (21)	NR	34.7	NR
Reddy et al, 2005^{12}	75	Outpatient	12	Retrospective	DSM-IV	75 (56)	24.5 (9.5)	30.1 (9.5)	Primary diagnosis other than OCD
Catapano et al, 2006 ¹⁰	55	NR	б	Prospective	NI-WSQ	NR	NR	NR	Significant neurologic illness except tics, substance use, serious medical illness contraindicating antiobsessional treatment, psychosis, other Axis I disorder that developed prior to OCD
Math et al, 2007^{34}	77	Inpatient and outpatient	S	Retrospective	DSM-IV	69.04 (53)	22.9 (9.66)	36.3 (11.04)	NR
Whittal et al, 2008 ³⁵ (sample 1)	41	NR	2	Prospective	DSM-IV	36.6 (15)	23.4 (13.9)	36.1 (11.4)	Active thought disorder, uncontrolled bipolar disorder, organic mental disorder, concurrent psychological treatment for Axis I or II disorder except marital therapy or supportive therapy for depression, medication changed during acute treatment
Whittal et al, 2008 ³⁵ (sample 2)	45	NR	2	Prospective	DSM-IV	51.1 (23)	22.5 (9.9)	35.4 (9.82)	Same as for Whittal, 2008 (sample 1)
Braga et al, 2010 ³⁶	42	NR	7	Prospective	NI-WSQ	38.1 (16)	14.8 (6.9)	36.8 (13.2)	Suicidality, posttraumatic brain injury OCD, severe social phobia, severe personality disorder, severe anorexia nervosa, mental retardation, YBOCS score < 16
Cabedo et al, 2010^{37}	36	Outpatient	1	Prospective	DSM-IV	NR	NR	34.16(8.61)	NR
Marcks et al, 2011^{38}	42	NR	15 = (2. 2)	Prospective	DSM-III-R	NR	NR 22 - (2 - 2)	NR	Organic brain syndrome, psychosis in last 6 months
Bloch et al, 2013^{5}	83 212	NK Outnotiont	11.7 (1.2) E	Retrospective Detrospective	NK Dem 117 Tr	NK 42 7 (02)	23.4 (7.9) 17 0 (0 E)	42 (9.9) 20 0 (17 0)	NK Ourseis montal discordar
Elsen et al, 2013 ⁴⁰ Cherian et al, 2013 ⁴⁰	c17	Outpatient Outpatient	с 1.04 (0.05)	Retrospective Prospective	DSM-IV-IK DSM-IV-TR	45.7 (51) 56.7 (51)	(c.e) e./1 (10.7 (7.01)	27.65 (8.5)	Organic mental disorder Psychosis, bipolar disorder, mental retardation, organicity
Cherian et al, 2014 ⁴¹	106	Outpatient	4.16 (0.75)	Prospective	DSM-IV-TR	66 (70)	21.1 (7.58)	28.05 (9.06)	Psychosis, bipolar disorder, mental retardation, organicity
Abbreviations: NR=nc	ot reco	orded, OCD = ob	sessive-comp	oulsive disorder,	YBOCS= Yale-]	Brown Obses	sive Compulsi	ve Scale.	



To examine predictors of remission, we used random effects multivariate meta-regression, done by using varianceweighted least squares with aggregate level data. Due to inadequacy of data reported in majority of the studies, only 8^{8,11,14,31,34,36,40,41} could be used for this analysis. On the basis of predictors of remission reported in existing literature, we examined age at onset of OCD, duration of illness, duration of follow-up, baseline YBOCS score, and proportion of males. All analyses were done using STATA version 12.1 (StataCorp 2011. Stata Statistical Software: Release 12. StataCorp LP; College Station, Texas), with user-written programs for meta-regression.⁴³

RESULTS

The earliest long-term follow-up of OCD patients treated with currently approved treatments was published by Foa et al in 1984,⁴⁴ but this study was excluded because it did not meet all the inclusion criteria. The 17 selected studies, as per eligibility criteria, gave 18 samples. The article by Whittal et al³⁵ had follow-ups of 2 separate samples. A total of 1,265 individuals were included in this meta-analysis. The included studies with baseline characteristics are summarized in Table 1.

Study Characteristics

Studies included in this meta-analysis were published in the last 15 years and had subjects with a primary diagnosis of OCD, as per DSM-III-R or ICD-9 or later versions of either classification system. Eleven^{8,10,30,31,33,35-38,40,41} of the 18 samples were prospectively followed up. A larger number of subjects in the pooled data were outpatients as seen from the 11 studies that reported this—2 studies followed up only inpatients,^{11,30} 7 only outpatients,^{12,14,31,32,37,4041} and 2 had both inpatients and outpatients.^{8,34} Subjects with organic/ neurologic disorders, psychosis, substance use, primary affective disorders, and suicidal risk were excluded in most studies. In 15 samples, patients received SRIs or CBT or both, depending on clinical need. One study¹⁰ had patients receiving only SRIs, while 2 studies^{36,37} were follow-ups of patients treated with CBT in individual and group formats. In the Indian studies, patients were treated mostly with SRIs. In 3 of them,^{12,40,41} 15%–18% of the patients received CBT in addition to SRIs, and, in the fourth study,³⁴ 40% received CBT in addition to SRIs.

Follow-up duration in these studies varied from 1 to 15 years. The sample size weighted mean follow-up duration was 4.91 years. Males made up 55% of the total number of

Study		Effect Size (95% CI)	% Weight
van Oppen et al (2005) ³²		0.43 (0.33-0.53)	5.70
Rufer et al (2005) ¹¹		0.43 (0.26-0.61)	5.20
Math et al (2007) ³⁴		0.72 (0.62-0.82)	5.69
Marcks et al (2011) ³⁸		0.42 (0.27-0.57)	5.40
Braga et al (2010) ³⁶		- 0.79 (0.66–0.91)	5.55
Biondi and Picardi (2005) ³³	.	0.34 (0.18–0.51)	5.29
Reddy et al (2005) ¹²		0.76 (0.66–0.86)	5.70
Cabedo et al (2010) ³⁷		0.67 (0.51-0.82)	5.36
Catapano et al (2006) ¹⁰	x	0.56 (0.43-0.70)	5.51
Zitterl et al (2000) ³⁰		0.31 (0.21–0.42)	5.64
Alonso et al (2001) ³¹		0.58 (0.46-0.71)	5.55
Eisen et al (1999) ⁸		0.52 (0.40-0.64)	5.58
Whittal et al sample 1 (2008) ³⁵		0.61 (0.46–0.76)	5.40
Whittal et al sample 2 (2008) ³⁵	-	0.40 (0.26-0.54)	5.44
Cherian et al (2014) ⁴¹	-	- 0.81 (0.74–0.89)	5.80
Cherain et al (2013) ⁴⁰		0.53 (0.43-0.64)	5.67
Bloch et al (2013) ³⁹		0.51 (0.40-0.61)	5.65
Eisen et al (2013) ¹⁴	*	0.16 (0.11–0.21)	5.88
Overall $(l^2 = 95.1\%, P < .001)$		0.53 (0.42–0.65)	100.00
-0.91	().91	
Veights are from random effects analysis.			

Figure 2. Individual and Sample Size Weighted Pooled Rates of Remission for All 18 Samples Included in the Meta-Analysis^a

subjects. The pooled mean age of subjects was 34.74 years (95% CI, 34.10–35.39). Mean duration of illness was 13.78 years (95% CI, 13.13–14.44), while the mean age at onset of OCD was 20.53 years (95% CI, 19.96–21.09). Mean YBOCS severity score at baseline was 24.10 (95% CI, 23.68–24.51). Four studies reported the proportion of juvenile onset OCD,^{12,32,40,41} and this gave a pooled rate of 42% (95% CI, 37%–47%). Pooled proportion of subjects with comorbidities was 52% (95% CI, 48%–56%) and for depression separately was 36% (95% CI, 31%–40%). Comorbidities other than depression reported in these studies were anxiety disorders and personality disorders. A pooled rate of 14% (95% CI, 10–17%) was found for family history of OCD from the 5 studies^{12,31,34,40,41} that reported this.

Given the naturalistic follow-up design of these studies, treatment was not controlled for and rates of treatment adherence varied. Overall, more than 60% patients, and up to 90%¹¹ in some studies, were on some form of treatment. Dropout rates were less than 30% in 14 of the samples, while 4 samples had dropout rates over 50%. Of the latter, 2 samples were follow-ups over 11 and 15 years, respectively,^{38,39} but 2 were follow-ups of only 2 years.³⁵

Predictors of remission were not reported by all studies. Age at onset of OCD, duration of illness, duration of follow-up, male gender, and baseline severity of illness (baseline YBOCS score) are the variables that have been previously studied as predictors, and we included them in our meta-regression. Some studies examined other predictors, too. For example, partial remission predicted greater likelihood of a relapse than complete remission.^{8,36} Eisen et al¹⁴ have examined symptom dimensions as predictors and reported that hoarding predicted low remission while overresponsibility for harm predicted high remission rates. Presence of comorbidities was not a significant predictor in most studies, including the study by Zitterl et al,³⁰ in which the primary aim was to see the effect of depression on outcomes in OCD.

Quantitative Analysis

Remission, defined as a YBOCS score of <16 at longest follow-up, was the primary outcome measure. The pooled rate of remission was 53% (95% CI, 42%–65%) (Figure 2). On subgroup analysis, retrospective studies had a pooled rate of 50% (95% CI, 27%–73%), while prospective studies had 55% (95% CI, 45%–65%), the difference being statistically significant (P<.001) (Figure 3). Indian studies gave a much larger (P<.001) pooled rate of remission—71% (95% CI, 59%–83%)—compared to other studies—48% (95% CI, 37%– 59%) (Figure 4). We did an influence analysis for the study by Eisen et al,¹⁴ since this study gave low rates of remission even though it had the largest sample size. Exclusion of this study increased the pooled rate of remission to 56%.

When predictors of remission were examined individually using meta-regression, none of the predictors was statistically significant. However, when examined together, using multivariate meta-regression, age at onset (t=-7.08, P=.019), duration of illness (t=-8.13, P=.015), baseline YBOCS score (t=-6.81, P=.021), and proportion of males (t=-5.92, P=.027) were significant predictors. Duration of follow-up had a positive association (t=3.34, P=.079) with remission; however, this was not statistically significant. When multiple covariates are fitted in meta-regression, the null hypothesis that the coefficients of the covariates are all zero is tested by F test (F_{5,2}=26.85, P=.036) with Knapp-Hartung adjustment. Restricted maximal likelihood estimate

Figure 3. Pooled Rates of Remission From Subgroup Analysis of Retrospective Versus Prospective Studies^a

Study		Effect Size (95% CI)	% Weight
Retrospective			
van Oppen et al (2005) ³²		0.43 (0.33-0.53)	5.70
Rufer et al (2005) ¹¹		0.43 (0.26-0.61)	5.20
Math et al (2007) ³⁴		0.72 (0.62–0.82)	5.69
Reddy et al (2005) ¹²		0.76 (0.66-0.86)	5.70
Bloch et al (2013) ³⁹		0.51 (0.40-0.61)	5.65
Eisen et al (2013) ¹⁴	*	0.16 (0.11-0.21)	5.88
Subtotal (l ² =97.3%, P < .001)		0.50 (0.27-0.73)	33.82
Prospective			
Marcks et al (2011) ³⁸		0.42 (0.27-0.57)	5.40
Braga et al $(2010)^{36}$		- 0.79 (0.66–0.91)	5.55
Biondi and Picardi (2005) ³³		0.34 (0.18-0.51)	5.29
Cabedo et al (2010) ³⁷		0.67 (0.51-0.82)	5.36
Catapano et al $(2006)^{10}$	_	0.56 (0.43-0.70)	5.51
Zitterl et al $(2000)^{30}$		0.31 (0.21-0.42)	5.64
Alonso et al $(2001)^{31}$	*	0.58 (0.46-0.71)	5.55
Fisen et al $(1999)^8$		0.52 (0.40-0.64)	5.58
Whittal et al sample 1 (2008) ³⁵		0.61 (0.46-0.76)	5.40
Whittal et al sample 2 (2008) ³⁵		0.40 (0.26-0.54)	5.44
Cherian et al $(2014)^{41}$		- 0.81 (0.74–0.89)	5.80
Cherian et al $(2013)^{40}$	_	0.53 (0.43-0.64)	5.67
Subtotal ($l^2 = 88.1\% P < 0.01$)		0.55 (0.45-0.65)	66.18
Overall $(l^2 = 95.1\% P < 0.01)$		0.53 (0.42-0.65)	100.00
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^a Weights are from random effects analysis			

Figure 4. Pooled Rates of Remission From Subgroup Analysis of Other Versus Indian Studies^a

Study		Effect Size (95% CI)	% Weight
Other			
van Oppen et al (2005) ³²		0.43 (0.33-0.53)	5.70
Rufer et al (2005) ¹¹		0.43 (0.26-0.61)	5.20
Marcks et al (2011) ³⁸		0.42 (0.27-0.57)	5.40
Braga et al (2010) ³⁶		— 0.79 (0.66–0.91)	5.55
Biondi and Picardi (2005) ³³		0.34 (0.18-0.51)	5.29
Cabedo et al (2010) ³⁷	1 .	0.67 (0.51-0.82)	5.36
Catapano et al (2006) ¹⁰		0.56 (0.43-0.70)	5.51
Zitterl et al (2000) ³⁰		0.31 (0.21-0.42)	5.64
Alonso et al (2001) ³¹	- <u> </u> .	0.58 (0.46-0.71)	5.55
Eisen et al (1999) ⁸		0.52 (0.40-0.64)	5.58
Whittal et al sample 1 (2008) ³⁵	<u> </u>	0.61 (0.46-0.76)	5.40
Whittal et al sample 2 (2008) ³⁵		0.40 (0.26-0.54)	5.44
Bloch et al (2013) ³⁹	*	0.51 (0.40-0.61)	5.65
Eisen et al (2013) ¹⁴	*	0.16 (0.11-0.21)	5.88
Subtotal (<i>I</i> ² = 92.4%, <i>P</i> < .001)	\sim	0.48 (0.37–0.59)	77.14
Indian	1		
Math et al (2007) ³⁴		0.72 (0.62-0.82)	5.69
Reddy et al (2005) ¹²		- 0.76 (0.66–0.86)	5.70
Cherian et al (2014) ⁴¹		- 0.81 (0.74-0.89)	5.80
Cherian et al (2013) ⁴⁰	-*-	0.53 (0.43-0.64)	5.67
Subtotal (<i>I</i> ² = 84.2%, <i>P</i> < .001)	\sim	0.71 (0.59–0.83)	22.86
Overall (<i>I</i> ² = 95.1%, <i>P</i> < .001)		0.53 (0.42–0.65)	100.00
-0.91	·	0.91	
Waights are from random effects analysis			

of between-study variance, given as tau2, was 0.0008; percentage residual variation due to between-study heterogeneity, given by I^2_{res} , was 30.68%; and proportion of between-study variation explained by the covariates, given by adjusted R^2 , was 98.26%.

DISCUSSION

Outcome

In this first meta-analysis of long-term outcome in adults with OCD, the main finding was the relatively high rate of remission (pooled remission rate, 53%) at a mean follow-up duration of 4.91 years. The study findings have important clinical implications. Contrary to the popular perception that OCD is a chronic illness with low rates of remission,^{3,4,8,14} this study has demonstrated that long-term prognosis of OCD is not necessarily bleak. In fact, the review by Goodwin et al in 1969,⁵ much before the advent of effective treatment options, pointed out a "certain measure of optimism" about the natural course of the disorder, particularly in outpatients. When compared to remission rates of other major psychiatric disorders that follow a chronic course, this remission rate is relatively higher. AlAqeel et al,⁴⁵ in their systematic review, reported remission rates of 35.6% and 37% in first-episode and multipleepisode schizophrenia, respectively. The Harvard/Brown Anxiety Research Project,46 the first large prospective, longitudinal study on all anxiety disorders, found lower rates of remission for other anxiety disorders: 39% and 38% for panic disorder⁴⁷ and generalized anxiety disorder,⁴⁸ respectively, at 5-year follow-up, and an even lower rate of 35% for social anxiety disorder at 10-year follow-up.49

Short-term treatment outcomes in OCD have been examined in multiple randomized controlled trials. With pharmacotherapy alone, overall 40%–60% patients do not improve.⁵⁰ Kobak et al⁵¹ conducted a quantitative analysis on the efficacy of SRIs and CBT in OCD and found an average effect size of 0.87, with no significant differences among various medications and between medication and CBT, when methodological variables were controlled. Olatunji et al,⁵² in their meta-analysis on CBT in OCD, reported large effect sizes for effectiveness, with CBT outperforming control conditions on primary (OCD symptoms) and secondary outcome measures (depression). However, data from short-term clinical trials cannot be used to reliably predict probability of remission in the long-term. That the data from long-term naturalistic follow-up studies give a measure of hope for patients with OCD is reassuring since the patients and the families can be offered a favorable prognosis. Data from naturalistic follow-up studies cannot be used to comment on the efficacy of any particular intervention since the treatment is typically uncontrolled and decided by clinical necessity. Nonetheless, most patients in the followup studies included in this meta-analysis were aggressively treated with SSRIs and/or CBT, prompting us to speculate that continued long-term treatment may have a favorable effect on the outcome. Moreover, since 15 of the 18 samples in this meta-analysis used a combination of pharmacologic and psychological intervention guided by clinical need, it is possible to speculate that combined approaches may lead to better long-term outcomes. There is evidence from shortterm clinical trials that a combination of CBT and drugs may be better than drugs alone.^{20,53} Addition of CBT as an augmenting strategy has also been demonstrated to be effective both in partial responders^{54,55} and in nonresponders to SSRIs.^{56,57} Therefore, there is a compelling clinical need to examine the efficacy of a combination therapy of CBT and SRIs over SRIs and CBT alone on the long-term outcome of OCD. Most studies reported that around 60% of individuals continued to be on some form of treatment during followup. In some studies, treatment rates reached 90%. The sum total of individuals at intake into studies was 1,691, of whom 1,265 individuals were followed up. A dropout rate of only 25.2% shows that a large majority of OCD patients persisted with treatment. In a long-term follow-up study of selective serotonin reuptake inhibitor (SSRI) nonresponders, continued efforts at treatment, particularly addition of CBT, had a favorable influence on outcome.58

This meta-analysis included 4 studies from India^{12,34,40,41} that together gave a pooled remission rate of 71%. This is much higher than in the other studies (48%). All 4 of these studies were done at the same center. These studies did not have overlapping samples. The remission rate from these studies is somewhat similar to the 86% remission reported in a 20-year-long follow-up of the community sample described by Angst et al.¹³ The high rate of remission in the Indian studies should be interpreted by keeping in mind the clinical characteristics of the samples. Patients were a largely self-referred, drug-naive, outpatient sample with a moderate severity of illness, low comorbidity rates, and shorter duration of illness. Although the samples were recruited from a tertiary university teaching hospital, a sizeable number of patients were drug-naive and never treated before (39%-72%). The hospital caters to both self-referred (walk-in) and referred patients and functions as a first-contact clinical service for a vast majority of patients from the local community (ie, the state of Karnataka in which it is situated and the adjacent districts of the other states). Mental health services in the country are still underdeveloped, and tertiary hospitals often become the only affordable first-contact services

unlike in other countries where tertiary hospitals essentially cater to severely ill, refractory, and difficult-to-treat patients. Importantly, most patients in these studies were treated with drugs alone (60%–85%) due to low therapist availability. In India, drugs are the first choice of treatment, even in disorders such as OCD and anxiety and depressive disorders, in which the efficacy of psychotherapy is well established, as there are very few trained therapists and the clinical load is unusually high. In addition, most patients who consult for treatment at this center come from faraway places and not from the city itself, making administration of CBT on a routine basis difficult and a less practical approach.

A high rate of remission reported by the Indian studies is obviously optimistic compared to the findings of other studies and are perhaps generalizable to a large majority of OCD patients who are moderately ill and seek outpatient treatment. Since the remission rate in the Indian studies was higher than in the studies from other parts of the world, it is tempting to speculate that cultural factors may have an effect on outcome. In the long-term follow-up studies of schizophrenia, outcome has been consistently favorable in developing countries⁵⁹ and the favorable outcome has been attributed to cultural factors such as integrity of family systems in the developing world and greater tolerance for mental illness. It is important to examine if similar factors have any effect on the outcome in OCD. However, it should also be kept in mind that these 4 studies are all from the same center and may not be reflective of outcomes from other centers in the country.

On subgroup analysis, prospective studies were found to have higher remission rates (55%) than retrospective studies (50%). Prospective studies are likely to have better treatment compliance, more intensive interventions, and regular therapist contact, factors that may account for their better outcome.

Predictors of Remission

Five variables were examined as predictors of remissionage at onset of OCD, duration of illness, baseline YBOCS severity, duration of follow-up, and proportion of males. We chose these 5 variables as they have been cited by multiple earlier studies as being predictive of outcome in OCD,^{5,60–62} and data on them were available in a majority of the studies included in the meta-analysis. When examined together, male gender, age at onset, duration of illness, and baseline severity of illness had significant negative association with outcome. Interestingly, none of these were significant predictors when examined individually. High degree of confounding effect among these variables may be responsible for this. Curiously, age at onset was negatively correlated with remission, implying better outcome with earlier onset of illness. Earlier onset, pediatric onset in particular, is typically associated with poor outcome.²¹ Our finding has to be interpreted with caution since the sample in this meta-analysis mostly had onset in late adolescence and early adulthood (age at onset of OCD = 20.53 years, 95% CI, 19.96-21.09) and not at a very young age (ie, pediatric or early adolescent). Therefore, the

finding suggests that those with onset in late adolescence or young adulthood may have a better outcome. Duration of follow-up had a positive association, although the finding was not statistically significant. Goodwin et al⁵ had concluded from their review that a longer duration of follow-up may see a larger number of people remitting from the illness.

Limitations

Obsessive-compulsive disorder is often comorbid with other psychiatric disorders. This meta-analysis found a 52% rate of comorbidity, the most common comorbid disorders being depression, other anxiety disorders, and personality disorders. Pooled rate of comorbid depression was 36%. Several studies have found comorbid illnesses to predict outcome in OCD⁶³; however, due to inadequate data in the studies included in this meta-analysis, we were unable to examine this. Similarly, juvenile onset of illness and family history of OCD could not be examined, as only 4 and 5 studies gave these data, respectively. In view of the fact that treatment was typically not controlled in the naturalistic prospective studies, effect of individual treatments or their combination on outcome cannot be commented upon. In the Indian studies, remission rate was high despite the fact that most patients received only SRIs, tempting us to speculate that even SRIs alone may have significant effect on outcome. Insight has been associated with outcome,¹⁶ but most of the follow-up studies do not report on insight. Finally, most studies included in the review did not provide other measures of outcome, such as quality of life, disability, and functioning. Examining these variables, besides illness severity or remission, would provide a more comprehensive account of long-term outcome.

CONCLUSION

In conclusion, in this first meta-analysis on long-term outcome in OCD in adults, we found outcome of OCD to be not all that pessimistic. More than half of the patients seem to achieve remission in the long run. Remission rate was higher in prospective studies and in studies from one center in India. The latter finding needs replication from other centers. It would be valuable to understand if cultural factors have any role in the long-term course and outcome of OCD. Onset of OCD in late adolescence or young adulthood, low baseline severity, and short duration of illness appear to be related to a better outcome, while male gender appears to be related to a poorer outcome. Finally, there is a need for multicenter, prospective follow-up studies that systematically examine the course and outcome of OCD in larger representative samples with an emphasis on not just symptomatic but also functional recovery.

Funding/supported: This work was done as part of Dr Sharma's 1-year postdoctoral fellowship program in obsessive-compulsive disorder and related disorders, at the National Institute of Mental Health and Neuro

Sciences, Bangalore, India. The authors report no other sources of financial or material support.

Acknowledgments: The authors acknowledge Dr Jagadisha Thirthalli, MD, Additional Professor, Department of Psychiatry, National Institute of Mental Health and Neuro Sciences, Bangalore, India, for reviewing the manuscript and providing valuable suggestions. Dr Thirthalli reports no potential conflict of interest relevant to the subject of this article.

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