

Predicting Course of Illness in Patients With Severe Obsessive-Compulsive Disorder

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ABSTRACT

Objective: Few data are available to inform clinical expectations about course and prognosis of severe obsessive-compulsive disorder (OCD). Such information is necessary to guide clinicians and to inform criteria for invasive interventions for severe and intractable OCD. This study sought to examine course and prospective predictors of a chronic course in patients with severe OCD over 5 years.

Method: A selected subset of adults in the Brown Longitudinal Obsessive-Compulsive Study (BLOCS) was included. Adult BLOCS participants were enrolled between 2001 and 2006. All participants in the current study (N = 113) had DSM-IV OCD diagnosis, severe OCD symptoms at baseline, and at least 1 year of follow-up data.

Results: Cox proportional hazard models were used to examine the general pattern of course in the severe OCD sample based on Longitudinal Interval Follow-Up Evaluation (LIFE) psychiatric status ratings, as well as test predictors of chronically severe course. Results indicated that approximately half of patients with severe OCD at baseline had illness drop to a moderate or lower range of severity during 5 years of follow-up (50.4%) and that marked improvement was rare after 3 years of severe illness. The only unique predictor of a more chronically severe course was patient report of ever having been housebound for a week or more due to OCD symptoms ($P < .05$).

Conclusions: Findings of this study were 3-fold: (1) half of participants with severe OCD have symptom improvement over 5 years of follow-up, (2) the majority of participants that drop out of the severe range of symptom severity do so within the first 3 years of follow-up, and (3) patient-reported history of being housebound for 1 week or more due to OCD is a significant predictor of OCD's remaining severe over the 5-year follow-up.

J Clin Psychiatry 2015;76(12):e1605–e1610
dx.doi.org/10.4088/JCP.14m09468

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Obsessive-compulsive disorder (OCD) is chronic and debilitating.^{1–3} While well-established, efficacious treatments have been identified for OCD—most notably exposure/response prevention (ERP) and serotonin reuptake inhibitors (SRIs)—there remains a minority of OCD patients who do not benefit from available approaches. Such treatment-refractory cases can be particularly challenging when combined with very severe symptoms. Unfortunately, few data are available to inform clinical expectations about course and prognosis of severe OCD.

For patients with severe and intractable OCD—those with severe OCD who do not show improvement with standard first- and second-line treatment approaches—neurosurgical interventions such as lesion procedures and deep brain stimulation are sometimes considered. Due to the highly invasive nature of these procedures and the availability of highly effective noninvasive treatments, these procedures are considered only for patients with severe and intractable OCD. While these invasive procedures have been used for severe OCD for decades, data guiding clinicians in identifying ideal candidates remain limited. This is, in part, a circular problem. Eligibility criteria are stringent in order to prevent patients who may benefit from less invasive approaches from unnecessarily assuming the risks of these invasive procedures. These criteria include minimum thresholds for symptom severity, functional impairment, chronicity, and treatment approaches tried without substantial benefit. Keeping eligibility criteria conservative, however, results in a very small pool of patients who receive such procedures, which in turn limits data available to identify ideal candidates for these interventions and refine eligibility criteria. As a result, many existing eligibility criteria are based on expert consensus and have not been empirically validated.

One such criterion for eligibility for many of these procedures is that severe OCD persist for a minimum of 5 years. While data suggest that OCD is often chronic,^{4–6} there is little information to guide clinicians in determining when a patient's severe OCD is unlikely to improve. Similarly limited are empirical data to aid clinicians in predicting which patients' OCD is likely to remain severe over time. Treatment-refractory OCD has been associated with a more chronic course, more functional impairment, greater severity, lower socioeconomic status, presence of religious/sexual obsessions, and greater family accommodation.⁷ However, to our knowledge, there are no longitudinal data to suggest which factors may predict a more severe course of the disorder for those with treatment-refractory OCD.

Studies in broader OCD samples suggest several variables that may be related to course of OCD. Greater functional impairment predicts lower probability of remission,^{6,8} earlier age at onset^{6,9} relates to more chronic course, and longer duration predicts lower probability of remission.⁴ Greater symptom severity has also been linked to lower probability of remission.^{4,9} Specific comorbidities have been associated with worse course of OCD, though number of Axis I comorbidities does not predict course.^{4,9} Comorbid major depressive disorder (MDD) has been associated with worse course^{8,10}

- Few data have been available to inform clinical expectations about course and prognosis of severe obsessive-compulsive disorder (OCD).
- In this study, half of patients with severe OCD at baseline had illness improve to a moderate, or lower, level of severity over the course of 5 years.
- Assessment of past functioning, particularly whether someone has ever been housebound for a week or more due to OCD, may be useful in determining prognosis for patients with severe OCD.

and has been found to predict poor treatment response by some,^{11–13} though not by others.^{14–16} Features of obsessive-compulsive personality disorder (OCPD) have been tied to worse outcomes,¹⁷ greater probability of relapse following remission of OCD,⁴ and poorer response to behavior therapy for OCD.¹⁸ However, others have found no impact of OCPD on outcomes.^{8,19,20} Nevertheless, it remains unclear whether any of these correlates of outcome in OCD samples with broad ranges of severity differentiate between those with severe OCD who will improve and those who will face a more refractory course of severe symptoms.

The primary goal of this study is to examine the course of severe OCD in a longitudinal sample over 5 years to inform both refinement of neurosurgical criteria as well as clinical evaluation of prognosis for severe OCD. Using Cox proportional hazard regression, we sought to answer the following questions: (1) How long must a patient's OCD remain severe before we can be reasonably certain that it will not remit? (2) Can we identify variables that will increase our ability to predict whose OCD is likely to remain severe over the 5 years? We hypothesized that measures of OCD severity, past and current functioning, cognitive-behavioral therapy (CBT) and medication use, age at OCD onset, and comorbid depression and OCPD at baseline would be meaningful predictors of OCD's remaining severe over the 5 years.

METHOD

Participants

Our sample was a selected subset of adults participating in the Brown Longitudinal Obsessive-Compulsive Study (BLOCS),⁵ primary outcomes of which have been published elsewhere.^{4,9} (For complete inclusion and exclusion criteria for the BLOCS, see Pinto et al.⁵) Briefly, all adult participants were aged 19 years or older, had a primary diagnosis of *DSM-IV* OCD (defined as the disorder that participants considered their biggest problem overall across their lifetime), and had sought treatment for OCD within the 5 years prior to study entry. The only exclusion criterion was the presence of an organic mental disorder. Participants were recruited from a range of psychiatric treatment settings in Southeastern Massachusetts and Rhode Island. The study was approved by the institutional review boards of Butler Hospital and Brown University.

For inclusion in the present analysis, all participants had OCD rated as "severe" or worse at baseline assessment and had at least 1 year of follow-up data. This represents approximately a third of the total adult BLOCS sample ($n = 113$; 34.8%). The resulting subset was 54.0% female and 95.6% white and had a mean age of 38.5 years. BLOCS participants were enrolled between 2001 and 2006.

Measures

The Longitudinal Interval Follow-Up Evaluation (LIFE) is a semistructured instrument designed to assess longitudinal course of Axis I disorders.²¹ The LIFE generates a 6-point OCD psychiatric status rating (PSR) based on OCD symptom severity, indicating whether participants meet criteria for OCD (at a moderate [PSR = 4], severe [PSR = 5], or extreme [PSR = 6] level of distress and impairment) or are in partial (PSR = 3) or full remission (PSR = 2, PSR = 1). PSRs are reliable and valid measures of symptom severity frequently used in longitudinal studies.^{22,23} Reliability and validity of the LIFE are reported elsewhere.²² The LIFE was administered at baseline and annual follow-ups to assess severity of Axis I disorders, including OCD.

The Yale-Brown Obsessive Compulsive Scale (Y-BOCS), a 10-item, gold-standard, rater-administered severity scale, was administered at baseline to assess OCD severity.^{24,25} The OCD Database, a semistructured clinical interview developed to collect detailed demographic and clinical information, was used to assess age at OCD symptom onset, treatments received, and OCD-related functioning, including whether participants were ever housebound due to OCD for 1 week or more due to OCD symptoms.²⁶ The Global Assessment of Functioning (GAF), an evaluator-rated measure, was used to assess overall functioning in the worst week over the past month.²⁷ A modified version of the Psychosocial Treatment Inventory was used to assess baseline patient report of CBT treatment received.²⁸ The Structured Clinical Interview for *DSM-IV* Axis I Disorders-Patient Edition (SCID-I) and Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (SCID-II) were administered at baseline to establish baseline Axis I and II diagnoses, respectively.^{29,30}

Procedures

Weekly OCD PSRs from the LIFE were used for each subject from study entry to 5 years (260 weeks). The dependent variable was whether a participant's OCD remained in the severe range (PSR of 5 or greater). A patient's OCD was considered to have "dropped out" of the severe range if symptoms improved to a PSR of 4 (ie, moderate) or lower for at least 8 consecutive weeks. Using Cox proportional hazard models, we first fit an unconditional model to examine the general pattern of course in the severe group. Next, we tested a model with potential predictors of chronically severe course, given severe OCD at baseline. Univariate analyses were first conducted to screen potential predictors for inclusion in the final prediction model (see Collett³¹), and all predictors with a P value of $< .20$ were included in the prediction model. Variables evaluated for

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inclusion in this model were selected based on both related literature and clinical experience, given the limited nature of literature focusing on severe OCD. Categorical predictors were evaluated using descriptive Kaplan-Meier curves and the log rank test of equality across strata. Continuous predictors were evaluated for inclusion using Cox proportional hazard regression.

RESULTS

Descriptive Analysis

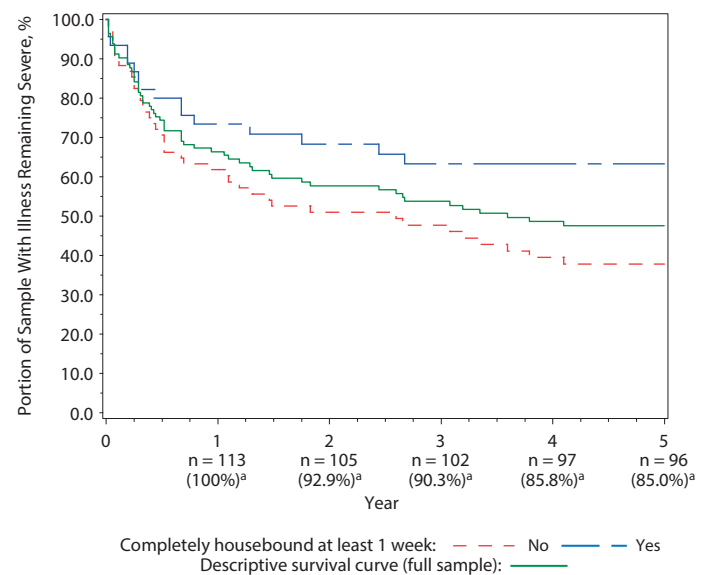
An unconditional descriptive model was used to determine the likelihood that someone with severe OCD will have their illness drop out of the severe range over the 5 years and describe the pattern of patients with severe OCD at baseline who had illness leaving the severe range over time. This study included right- but not left-censored data, and data coverage was acceptable (see Figure 1). 50.4% of the sample ($n=57$) had OCD that dropped out of the severe range for 8 weeks or more over the 5 years. Examination of the corresponding survival curve indicated that the majority of these improvements occurred within the first 2 to 3 years (82% and 89% of improvements, respectively), with a more gradual rate thereafter (Figure 1).

Prediction Model

To identify baseline predictors of whether or not a patient's OCD will drop from the severe range over 5 years, we used a Cox proportional hazard regression model. Variables considered for inclusion in the prediction model included baseline symptom severity (Y-BOCS score), age at onset of major OCD symptoms, clinician-rated baseline level of functioning (GAF score), patient report of past severe functional impairment (whether or not the patient had ever been housebound for a week or more due to OCD) prior to baseline, OCPD as assessed by the SCID-II, current MDD at baseline, patient report of lifetime number of CBT sessions at baseline, patient report of trial of weekly CBT (minimum 13 sessions offered 1 to 2 times per week in single treatment episode) prior to baseline, and total duration of psychotropic medication use at baseline (see Table 1 for descriptive statistics). Five predictors met criteria for inclusion in the prediction model: Y-BOCS ($\chi^2=4.07$, $P=.044$), GAF ($\chi^2=5.12$, $P=.024$), housebound ($\chi^2=4.99$, $P=.026$), lifetime CBT sessions ($\chi^2=1.65$, $P=.199$), and OCPD ($\chi^2=3.48$, $P=.06$). Age at onset ($\chi^2=0.19$, $P=.66$), current MDD ($\chi^2=0.95$, $P=.33$), weekly CBT trial ($\chi^2=0.32$, $P=.57$), and medication duration ($\chi^2=0.05$, $P=.82$) did not meet criteria for entry into the final model.

Results of the prediction model are presented in Table 2. This model included only 106 of the total 113 participants as 7 participants had missing baseline data on 1 or more predictors. Tests for violations of the assumption of

Figure 1. Survival Curves for Full Sample and Houseboundness



^aSample sizes and percentages at each year reflect the full sample; they do not necessarily reflect accurate values for the univariate or multivariate models. Censored data are not explicitly represented.

Table 1. Descriptive Statistics for Predictors of OCD Severity^a

Baseline Predictor	Value (N = 113)
Y-BOCS score	27.5 (3.97)
Age at onset, y	17.1 (8.76)
GAF score	41.3 (6.48)
No. of lifetime CBT sessions	19.31 (34.93)
Psychotropic medication duration, y	9.16 (8.26)
Housebound, % (n)	39.8 (45)
OCPD, % (n)	36.3 (41)
Current MDD, % (n)	30.1 (34)
Weekly CBT trial, % (n)	18.6 (21)

^aValues shown as mean (SD) unless otherwise noted.

Abbreviations: CBT=cognitive-behavioral therapy, GAF=Global Assessment of Functioning, MDD=major depressive disorder, OCD=obsessive-compulsive disorder, OCPD=obsessive-compulsive personality disorder, Y-BOCS=Yale-Brown Obsessive Compulsive Scale.

Table 2. Results of Proportional Hazards Regression Model

Baseline Predictor	B (SE)	χ^2	P Value	Hazard Ratio	95% Confidence Interval ^a
Housebound	-0.79 (0.34)	5.47	.019	0.46	0.24-0.88
OCD severity (Y-BOCS score)	-0.08 (0.04)	3.65	.056	0.93	0.86-1.00
No. of lifetime CBT sessions	-0.005 (0.005)	0.82	.366	1.00	0.99-1.01
Functioning (GAF score)	0.04 (0.03)	2.74	.098	1.05	0.99-1.10
OCPD diagnosis	-0.55 (0.31)	3.09	.079	0.58	0.31-1.07

^aWald confidence limits.

Abbreviations: CBT=cognitive-behavioral therapy, GAF=Global Assessment of Functioning, OCD=obsessive-compulsive disorder, OCPD=obsessive-compulsive personality disorder, Y-BOCS=Yale-Brown Obsessive Compulsive Scale.

proportionality were nonsignificant. Only 1 predictor in the model uniquely predicted greater relative risk of OCD's remaining in the severe range over the 5 years: patient report of whether they had ever been housebound for a week or more due to OCD ($P=.019$; Figure 1). The hazard ratio indicated that patients who reported never being housebound for a week or more due to OCD were more than twice as likely as

those who had been housebound to have illness drop out of the severe range (assuming all other variables are constant).

DISCUSSION

This study provides the first examination of predictors of 5-year course in a prospective, longitudinal investigation of severe OCD. The main findings of the study were 3-fold: (1) half of the participants with severe OCD experience noteworthy symptom improvement over 5-year follow-up, with symptoms decreasing to or below the moderate range for a minimum of 8 weeks; (2) the majority of participants that drop out of the severe range do so within the first 3 years; and (3) history of being housebound for 1 week or more due to OCD is a more relevant predictor of OCD's remaining severe than traditional measures of symptom severity, global functioning, and comorbidity. This suggests that in addition to current levels of severity and functioning, more distal factors may have important predictive utility.

Results from this study suggest that approximately half who present with severe OCD remain chronically severe over 5 years of follow-up, consistent with the chronicity and persistent significant impairment reported with this disorder.⁶ Importantly, however, 50% of our participants did have illness improve to at least the moderate range during the course of the study, with the majority (89%) of such improvements occurring during the first 3 years of evaluation. Indeed, 82% of participants that dropped out of the severe range did so within the first 2 years of observation, and another 7% between years 2 and 3. This suggests that the likelihood of improvement to a moderate symptom level is rare for individuals with OCD who have been consistently severely ill for 3 years or more. This highlights a potential need to reconsider our treatment strategies for individuals with severe OCD. Surgery criteria requiring 5 years of severe symptoms may be, on the whole, too stringent.

Although research frequently highlights the influence of comorbid disorders on OCD prognosis, neither MDD nor OCPD was a significant predictor of a chronic severe course. In contrast to our results, a 15-year naturalistic prospective study of anxiety disorders found that OCD participants with comorbid MDD were significantly less likely to remit from OCD than those without MDD.¹⁰ Differences between these studies may help reconcile the discrepancy. The impact of MDD on course may be less pronounced in the current investigation, as all participants were severely ill compared to those in the study by Marcks and colleagues,¹⁰ who had no lower bound on OCD severity. Individuals with comorbid MDD may present with more severe OCD symptoms,^{32,33} making symptom improvement less likely. Alternatively, depression may influence OCD treatment. Although early studies found that comorbid MDD had a deleterious effect on OCD treatment outcome,¹¹⁻¹³ our lack of significant finding regarding MDD is consistent with more recent treatment studies finding no relationship between depression and OCD treatment response.³⁴ The role of MDD in the treatment of OCD remains an area for future exploration.

While a connection between OCPD and OCD is well established, few studies have investigated the influence of OCPD on OCD course. Comorbid OCPD approached significance in both the univariate and final model ($P = .06$ and $P = .08$, respectively), providing measured support for future investigations into the potential impact of OCPD on severe OCD course. Notably, in our larger sample of individuals with primary OCD,⁴ while OCPD did not emerge as a significant predictor of remission, it did predict relapse. Though our sample size here did not allow for the examination of predictors of subsequent worsening following improvement in a severely ill sample, future research should clarify if OCPD also differentiates between those with severe OCD who are unable to sustain improvement and those that remain improved.

Consistent with prior research with more broadly defined samples, baseline OCD severity and global functioning were significant univariate predictors of OCD course.^{4,6} However, neither of these variables remained significant in the presence of houseboundness. Patient report of ever being housebound due to OCD for 1 week or more was the only significant predictor of OCD's leaving the severe range during the 5-year period in our prediction model. This finding, if replicated, has significant implications for both assessment and treatment of OCD. It suggests the need to consider not only current severity and overall functioning, but also the utility of assessing past or worst-ever functioning. Nearly 40% of our severe sample reported a history of being housebound for 1 week or more due to OCD symptoms, highlighting the frequency of what is arguably a marker of extreme functional impairment. The reasons a patient with OCD may become housebound should also be investigated in future work. Past houseboundness may indicate a tendency to engage in extreme avoidance strategies or high levels of illness accommodation by family members. Assessment of these factors may be informative above and beyond a history of being housebound. If our finding is confirmed in other work, asking about houseboundness due to OCD may be a useful addition to the duration criteria in refining criteria for neurosurgical interventions.

Beyond the implications for neurosurgical entry criteria, candidates for which are few,³⁵ these findings also have important implications for treatment planning for OCD patients more broadly. Clinicians who assess for a history of impairment significant enough to result in houseboundness will quickly learn a key predictor of prognosis that may allow them to plan treatment more appropriately and aggressively. For example, a clinician may wish to plan (or refer) for an intensive course of ERP, schedule more frequent medication follow-ups, and perhaps recommend case management or involve social workers in the treatment to ensure a focus not only on symptoms, but also on functioning and management of activities of daily living.

Limitations of this investigation also warrant consideration. First, participants were all treatment-seeking and predominantly white, limiting generalizability. Second,

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because of the naturalistic study design, treatments were not controlled, precluding examination of treatment effects on severe OCD course. Relatedly, while this design allowed thorough characterization of the sample during the study, we cannot say how long patients experienced severe OCD prior to enrollment. This is an important caveat and a reason these findings should be confirmed in other samples. Third, we examined only a limited number of predictors in the present study. While we included those predictors we believed to be the best candidates, additional predictors should be examined in future work (eg, family accommodation). Moreover, use of a priori power analyses in future studies will ensure adequate power, as survival analyses often require large samples to be adequately powered. It is possible that with a larger sample in the present study other predictors may have reached statistical significance. Fourth, although the LIFE is a well-validated and frequently used measure of longitudinal course,^{22,36,37} PSRs lack the precision of other symptom rating scales, making the distinction between moderate and severe OCD a broad one. A related point is that the definition of symptom improvement used here and in other BLOCS publications (ie, 8 consecutive weeks) was selected to reflect a clinically meaningful time period of symptom change, but does not formally reflect *DSM*, nor does it imply that all individuals who improved remained improved indefinitely. In this study, 50.9% of the subsample

whose OCD dropped from the severe range did have illness re-enter the severe range for at least 1 week during the remainder of the 5-year period. However, the majority of those who experienced a return of OCD to the severe range following symptom improvement did not have illness that remained “chronically” severe: This group ($n = 29$) spent an average of only 26% of their remaining weeks with OCD in the severe range (from the week of the initial drop below the severe range), and only 4 of the 29 spent more than half of their remaining weeks with illness in the severe range. Finally, data on age at onset, past functional impairment, and symptoms over the follow-up intervals were retrospective and therefore subject to memory bias. However, this study represents one of the few prospective investigations of OCD and, to our knowledge, is the first to examine course of severe OCD.

In summary, this study examined course and prospective predictors of a chronic course in severe OCD. Our results suggest that marked improvement is rare after 3 years of severe illness. Nevertheless, half of those with severe OCD do, in fact, remit to a moderate symptom level. History of being housebound for a week or more due to OCD was the single strongest predictor of OCD's remaining severe throughout the 5 years. These findings highlight the need to consider more basic markers of functional impairment and history of functional impairment.

Submitted: August 25, 2014; accepted January 9, 2015.

Potential conflicts of interest: None of the authors has any financial conflicts of interest to disclose.

Funding/support: Financial support for the project came from a grant from the National Institute of Mental Health (R01MH06021) to Dr Rasmussen.

Role of the sponsor: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Mental Health or the National Institutes of Health. The funding agency played no role in the conduct, interpretation, or reporting of study results.

Previous presentation: Portions of these data were presented at the 20th annual International Obsessive-Compulsive Disorder Foundation 2013 conference; July 19–21, 2013; Atlanta, Georgia.

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