**Schizophrenia Bulletin** vol. 39 no. 1 pp. 151–160, 2013
doi:10.1093/schbul/sbr077
Advance Access publication July 28, 2011

# The 5-Year Course of Obsessive-Compulsive Symptoms and Obsessive-Compulsive Disorder in First-Episode Schizophrenia and Related Disorders



**Lieuwe de Haan*, Bouke Sterk, Luuk Wouters, and Don H. Linszen**

Department of Psychiatry, Early Psychosis Section, Academic Medical Center, University of Amsterdam, Meibergdreef 5, 105 AZ Amsterdam, The Netherlands

*To whom correspondence should be addressed; tel: 00-31-208913574, fax: 00-31-808913536, e-mail: l.dehaan@amc.uva.nl

***Objective*: To determine the course of obsessive-compulsive symptoms (OCS) and obsessive-compulsive disorder (OCD) in first-episode schizophrenia and related disorders and their relationship with clinical characteristics. *Methods*: Consecutively, admitted patients with a first-episode of schizophrenia, schizophreniform disorder, or schizoaffective disorder were screened for OCS, and these were measured with the Yale-Brown Obsessive-Compulsive Scale. Positive and Negative Syndrome Scale and Montgomery Åsberg Depression Rating Scale were used to assess severity of other symptoms. The course of 3- and 5-year symptoms, psychotic relapse, substance use, remission, full recovery, suicide, and social functioning were assessed. *Results*: One hundred and eighty-six consecutively admitted and consenting patients were included. Five years after admission, OCS could be assessed in 172 patients. Ninety-one patients (48.9%) reported no OCS symptoms on any of the assessments. OCS restricted to the first assessments occured in 15.1%, 13.4% had persistent OCS, 7.0% had no OCS at first assessment but developed OCS subsequently, and 15.6% had intermittent OCS. The proportion of patients with comorbid OCD varied between 7.3% and 11.8% during follow-up. OCD was associated with more severe depressive symptoms and poorer premorbid functioning and social functioning at follow-up. *Conclusions*: The 5-year course of OCS/OCD in patients with first-episode schizophrenia or related disorders is variable. OCS/OCD comorbidity was not associated with a more severe course of psychotic symptoms and relapse. Comorbid OCD was associated with more severe depressive symptoms, social dysfunction and worse premorbid functioning. Specific treatment options for schizophrenia patients with comorbid OCD are needed.**

*Key words:* psychosis/longitudinal/outcome/OCD/schizophrenia/OCS

Schizophrenia is a heterogeneous disorder. Differences between patients and changes within patients are substantial.[1] Obsessive-compulsive symptoms (OCS) or obsessive-compulsive disorder (OCD) occur frequently in schizophrenia patients.[2–5] Although earlier studies reported relatively low comorbidity rates of OCS/OCD,[6,7] recent studies have revealed much higher comorbidity rates: for OCS varying from 10% to 64%[1,3,8] and for OCD from 7.8% to 31.7%.[1,9,10] The prevalence of OCD in the general community is clearly lower (2%–3%).[11] The occurrence of de novo OCD during treatment with atypical antipsychotic drugs,[12,13] raise the possibility that a part of the reported association of OCS/OCD in schizophrenia patients may be medication-induced.[14,15]

OCS can emerge before, concurrent with, or after onset of psychotic symptoms.[16] It is proposed earlier that this probably reflects to different etiologies and clinical course of OCS in schizophrenia.[17] A difference in etiology, nature, and course of OCS may have therapeutic implications.[17,18]

There are conflicting findings concerning the impact of OCS/OCD on clinical characteristics. An earlier hypothesis proposed that schizophrenia patients develop OCS in an attempt to reduce psychotic symptoms and thus, the presence of OCS could be an indicator of good prognosis.[19] Subsequent research on the relationship of OCS/OCD with positive, negative, and global symptoms yielded contradictory results. In a recent systematic review and meta-analysis, Cunill and colleagues[20] found more severe global, positive, and negative symptoms if OCS were present. And when there is comorbid OCD, current evidence shows that schizophrenia patients often display a worse clinical course, poor treatment response, worse long-term outcome, and greater prefrontal cortex functional impairments.[18] Neurobiological studies comparing schizophrenia with and without comorbid OCD are sparse and findings are merely inconclusive. Neurobiological studies comparing schizophrenia and OCD do

demonstrate clear differences, suggesting that they constitute 2 distinct disorders.[18]

An important challenge facing clinicians and researchers is differentiating obsessions from delusions. The *Diagnostic and Statistical Manual of Mental Disorders, fourth edition*, (DSM-IV)[21] allows the diagnosis of OCD with the specifier "with poor insight". This raises difficulty in differentiating an obsession with poor insight from a delusion, particularly because OCD has traditionally been distinguished from psychotic disorders on the basis of individuals recognizing compulsions or obsessions as ego-dystonic, implying the presence of insight. The scholarly administration of standardized diagnostic scales, such as the Structured Clinical Interview (SCI) for DSM-IV axis I psychiatric disorders (SCID-I)[22] and scales to assess severity of psychopathology, such as the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS),[23] increase the interrater reliability but do not solve the problem of disentangling delusions form obsessions. Here, we will use the conservative definition of OCS according to the SCID-patient edition[24] (see methods section).

There are methodological concerns with most studies on comorbid OCS/OCD in the course of schizophrenia and related disorders. Several studies included patients in later phases of the disorder, and most studies have a cross-sectional design.[3,20,25] These methodological concerns may partly explain the inconclusive findings so far. Changes in time within patients may be substantial; however, we lack specific knowledge on the course and the prognostic validity of comorbid OCS in schizophrenia patients. We therefore conducted a prospective study with consecutively admitted first-episode patients with schizophrenia, schizophreniform, or schizoaffective disorder. The goal of the present study is to assess: (1) The 5-year course of OCS/OCD. (2) The relationship between OCS/OCD and demographic and clinical characteristics. (3) The predictive validity of OCS/OCD presence at first admission for the 5-year course.

## Methods

### *Participants*

Patients aged 15–28 years of age were eligible for this prospective 5-year follow-up study. They had to meet DSM-IV-Revised criteria for schizophrenia, schizophreniform, or schizoaffective disorder and were suffering from a first episode. All patients were admitted to the specialized Early Psychosis Department of the Academic Psychiatric Center of the Academic Medical Center of the University of Amsterdam between 1996 and 2000. This department has inpatient and outpatient facilities. All mental health services in Amsterdam intended to refer all first-episode patients. The study was approved by the local ethical review board. After a complete description of the study, written informed consent was obtained from all subjects. When a subject was younger than 18 years, we also obtained informed consent from the parents. All patients fulfilling the inclusion criteria were included, there were no exclusion criteria. Patients were assessed at admission (t1), 6 weeks (t2), 3 years (t3), and 5 years (t4) after admission.

### *Diagnosis*

DSM-IV diagnosis was based on the SCID-I and with the use of all available information (a 2-hour interview with the patient and a separate 2-hour interview with involved family members). OCS were defined according to the SCID-P as persistent, repetitive, intrusive, and distressful thoughts (obsessions) not related to the patient's delusions, or repetitive goal-directed rituals (compulsions) clinically distinguishable from schizophrenic mannerisms or posturing. Consequently, patients whose obsessional thoughts or compulsions were related to psychotic content of thoughts were not diagnosed with comorbid OCS or OCD. Diagnosis was discussed with all involved clinicians and researchers. All patients were asked whether OCS had been present most of the time since the previous assessment. Diagnosis of comorbid OCD was assessed according to DSM-IV criteria.

### *Demographic and Other Characteristics*

At admission, the following characteristics were assessed: gender, age at onset of first psychotic symptom, type of onset (acute, insidious), duration of untreated psychosis, premorbid functioning as assessed with the Premorbid Adjustment Scale (PAS).[26] Prognostic factors were assessed with the prognostic scale.[27]

### *Severity of Psychopathology*

Severity of psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS)[28] based on information collected in a semistructured interview (SCI-PANSS). The severity of depression was assessed with the Montgomery Åsberg Depression Rating Scale (MADRS).[29] PANSS and MADRS were administered at admission, 6 weeks and 3 years after admission. Severity of OCS were assessed with the Y-BOCS[23] at all assessments. The Y-BOCS has shown good internal consistency and interrater reliability in patients with schizophrenia and related disorders.[30,31] The intraclass correlation coefficient for the PANSS positive, negative, and general psychopathology subscales were 0.91, 0.84, and 0.76, respectively. Interrater agreement for MADRS total score and Y-BOCS total score was good (weighted $\kappa = 0.78$ and 0.73).

### *Outcome, Psychotic Relapse*

The Life Chart Schedule (LCS)[32] was used to assess course of symptoms, treatment, substance use, residence,

and social functioning at 3 and 5 years after admission. The LCS yields reliable ratings of the long-term course of schizophrenia when assessed by trained raters.[32] Psychotic relapse was rated as present when both of the following criteria were met: (1) recurrence or exacerbation of psychotic symptoms with a duration of $\geq$1 week and (2) an increase of prescribed antipsychotic medication.[8]

*Definition of Symptomatic Remission*

Remission of psychopathology was assessed according to the criteria of Andreasen and collegueas.[33]

*Definition of Social Functioning*

Social functioning was assessed for the last year of follow-up to be either good or poor: good social functioning being characterized by nonresidential living and following a study or having a regular job (paid or voluntarily) and poor social functioning being characterized by residential living or not following a study nor having a regular job.

*Definition of Full Recovery*

Patients with symptomatic remission and good social functioning from year 4 to year 5 after admission were considered fully recovered.

*Statistical Analyses*

Categorization of subject groups, depending on research question, is shown in table 1. Repeated-measures ANOVA was used to assess changes in OCS over time, and ANOVA was used to test differences among groups in follow-up outcomes. Cox-regressions were done to assess psychotic relapse, both with and without possible confounding by gender, ethnicity, education, duration of untreated psychosis, early onset, type of onset, prognostic scale score, premorbid adjustment score, PANSS scores at admission, lack of insight, medication noncompliance, and substance abuse. There was no need to exclude confounders to avoid multicollinearity. All analyses were performed with SPSS (version 15.01, 2006).

**Table 1.** Categorization of Subjects According OCS/OCD Status, Depending on Research Question

I. To describe occurrence and persistence of OCS/OCD during 5-y follow-up, subjects were categorized in:
  a. For each assessment
    1. No OCS
    2. OCS but without OCD
    3. OCD
  b. Summary of all assessments
    1. No occurrence of OCS during the study period (never met criteria for obsessions or compulsions on any assessment)
    2. Only initial OCS (OCS only present at admission or at admission and after 6 wk)
    3. Persistent OCS (OCS at all assessments, and in between assessments, during the first 3 y)
    4. OCS de novo (no OCS at admission but OCS at 2 or more consecutive assessments thereafter)
    5. Intermittent OCS (no OCS at admission and intermittent OCS on one or more assessments thereafter)

II. To analyze the relationship between OCS/OCD and demographic and clinical characteristics, subjects were categorized based on persistent absence or presence of OCS or OCD in contrast groups:
  1. No occurrence of OCS during study period
  2. OCS during study period (OCS on one or more of the assessments and never a diagnosis of OCD)
  3. OCD during study period (met criteria for DSM-IV OCD at any of the assessments and had OCS on all assessments)[a]

III. To study whether initial presence of OCS/OCD is a predictor of the first 5-y course, subjects were categorized in:
  1. Initial no OCS (without OCS at admission and 6 wk after admission)
  2. Initial OCS/no OCD (OCS both at admission and 6 wk after admission, but no diagnosis of OCD)
  3. Initial OCD (with OCD both at admission and 6 wk after admission)

*Note*: OCS, obsessive-compulsive symptoms; OCD, obsessive-compulsive disorder; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.
[a]Based on this definition, patients, who met criteria for DSM-IV OCD at any of the assessments and had no OCS on all assessments, were not categorized and left out of analysis.

## Results

*Characteristics of Study Sample*

Two hundred and sixty-four consecutively admitted patients were assessed for eligibility. One hundred and eighty-nine patients met all inclusion criteria and gave written informed consent. During the study period, 3 of these were rediagnosed and were excluded from further analysis (1 with a drug induced psychosis and 2 with a bipolar disorder). Of these 186, 153 were male (82%) and the mean age at admission was 21.1 years (SD 3.0). DSM-IV diagnoses at admission were schizophrenia ($n$ = 108, 58%), schizoaffective disorders ($n$ = 42, 23%), and schizophreniform disorder ($n$ = 36, 19%). After 5-year follow-up, we were able to assess the DSM-IV diagnoses in 172 patients. The DSM-IV diagnoses after 5-year follow-up were schizophrenia ($n$ = 142, 83%), schizoaffective disorders ($n$ = 21, 12%), and schizophreniform disorder ($n$ = 9, 5%). Seventeen patients with an initial diagnosis of schizoaffective disorder and 23 patients with an initial diagnosis of schizophreniform disorder were reclassified into schizophrenia after 5 years. We found no significant differences in dropout from the study between diagnostic categories. OCS status was assessed at admission and 6 weeks after admission in all 186 patients, after 3 years in 177, and after 5 years in 172. Complete data on clinical status were obtained from 177 (95%) at 3 years and from 152 (82%) at 5 years. From 27 patients for whom

**Table 2.** Occurrence (%) of Different Type of Obsessions and Compulsions in all Assessments During 5-y Follow-Up in OCD or OCS Subjects

| | OCD (69 Assessments) (%) | OCS (131 Assessments) (%) |
|---|---|---|
| Obsessions | | |
| Aggressive | 42 | 34 |
| Somatic | 27 | 15 |
| Symmetry, exactness | 39 | 45 |
| Sexual | 30 | 24 |
| Religious | 25 | 20 |
| Compulsions | | |
| Checking | 53 | 62 |
| Washing | 35 | 15 |
| Ordering | 33 | 28 |
| Counting | 39 | 31 |
| Hoarding | 6 | 0 |

*Note*: OCS, obsessive-compulsive symptoms; OCD, obsessive-compulsive disorder.

not all clinical data were available at 5-year follow-up, we were able to contact an involved professional caregiver or family member. Therefore, 179 patients were available for full recovery analysis.

*I. Five-Year Course of OCS/OCD.*

At admission, 58 patients of 186 (31.2%) reported OCS. Of these, 22 (11.8%) also fulfilled DSM-IV criteria for OCD. Six weeks after admission, 57 (30.6%) reported OCS, including 22 (11.8%) with OCD. Three years after admission, 51 patients of 177 (28.7%) reported OCS, including 13 (7.3%) with OCD. Five years after admission, 41 of 172 patients (22.4%) reported OCS, including 14 (8.1%) with OCD. We found no significant differences between diagnostic categories in mean Y-BOCS total scores at admission (schizophrenia: 3.4, SD 6.7, schizophreniform disorder: 3.0, SD 5.9, and schizoaffective disorder: 3.5, SD 6.5) nor after 5 year (2.4, SD = 5.8; 0.9, SD 2.7; 2.8, SD 4.5, respectively).

*Presence and Continuity of OCS (Including Those Fulfilling DSM-IV Criteria for OCD)*

*1. No OCS During Study Period*

Ninety-one patients (48.9%) had no OCS on any of the assessments and reported no OCS between assessments.

*2. Only Initial OCS*

Twenty-eight patients (15.1%) had OCS only at admission or at admission and after 6 weeks. Of these 28, 11 patients only had OCS at admission (mean Y-BOCS total score t1 8.30, SD 6.38), 17 patients had OCS at admission and after 6 weeks (mean Y-BOCS total score at t1: 11.00, SD 4.29, t2: 9.29, SD 4.76).

*3. Persistent OCS*

Twenty-five patients (13.4%) had persistent OCS. Twenty-three patients had OCS at all assessments (mean Y-BOCS total score at t1: 15.35, SD 9.32, t2: 14.26, SD 8.75, t3: 13.52, SD 9.22, and t4: 13.96, SD 7.89). Two patients had OCS during the first 3 years but not after 5 years (mean Y-BOCS total score at t1: 12.50, SD 2.12, t2: 13.00, SD 1.41, t3: 12.00, SD 0.00).

*4. OCS De Novo*

Thirteen patients (7.0%) had OCS de novo. One patient had no OCS at admission and OCS on all following assessments (Y-BOCS total score at t2: 8, t3: 11, t4: 8). Twelve patients had OCS at 3 and 5 years (mean Y-BOCS total score at t3: 10.75, SD 4.22, t4: 9.00, SD 4.51). Seven of patients with OCS de novo were using olanzapine, 2 were using risperidone, and 4 did not use antipsychotic medication at the moment of OCS onset.

*5. Intermittent OCS*

Twenty-nine patients (15.6%) had intermittent OCS of whom 21 had no OCS at admission and OCS only at 1 of the 3 following assessments (11 only at t2, 7 only at t3, and 3 only at t4). Three patients had no OCS at admission, but OCS 6 weeks and 3 years after admission. Two patients reported OCS at admission and 5 years after admission, 3 patients reported OCS at admission and after 3 years.

*Time Trend Severity OCS.* To assess whether mean OCS score changed during follow-up, a one-way repeated measures ANOVA was conducted to compare total Y-BOCS scores at all assessments. The means and SDs were: t1: 3.81, SD 7.06; t2: 3.34, SD 6.57; t3: 3.13, SD 6.38; and t4: 2.63, SD 5.97. Although mean Y-BOCS score decreased, there was no significant effect for time (Wilks' lambda = 9.6, $F_{(3, 172)} = 2.18$, $P = .09$, multivariate partial eta squared = 0.04).

*Occurrence of Different Type of Obsessions or Compulsions.* In almost all patients, type of occurrence was stable (see table 2).

*II. Relationship between OCS/OCD and Demographic and Clinical Characteristics*

*Demographic Characteristics and Premorbid Adjustment* One-way between group ANOVAs were conducted to explore the relationship between categories based on OCS/OCD status and demographic and preclinical factors. We found no significant differences between groups based on OCS/OCD status in gender, ethnicity, prognostic scale score, age at onset of psychosis, type of onset (acute, subacute, and insidious) nor duration of untreated psychosis. There was a significant difference in PAS scores for the 3 OCS/OCD contrast groups

**Table 3.** Demographic and Premorbid Characteristics by Comorbid OCS/OCD Group

| | No OCS ($n$ = 91) | OCS ($n$ = 69) | OCD ($n$ = 16) | Tests Statistics[a] | $P$ Value |
|---|---|---|---|---|---|
| Gender (male/female) | 80/11 | 57/12 | 14/2 | 2.62 | .62 |
| Premorbid adjustment scale, mean total (SD) | 15.0 (6.2) | 14.2 (6.4) | 11.0 (3.9) | $F_{2,185}$ = 4.08 | .019 |
| Prognostic scale score, mean total (SD) | 39.1 (10.3) | 40.6 (11.3) | 39.9 (11.0) | $F_{2,186}$ = 0.42 | .66 |
| Age at onset of psychosis in years (SD) | 18.9 (3.1) | 19.0 (2.6) | 18.9 (2.0) | $F_{2,186}$ = 0.43 | .65 |
| Age of onset before 18 y (%) | 31 (34) | 22 (32) | 4 (25) | .86 | .65 |
| Type of onset | | | | | |
| Acute (%) | 9 (10) | 9 (13) | 1 (6) | | |
| Subacute (%) | 33 (36) | 26 (38) | 4 (25) | 3.21 | .53 |
| Insidious (%) | 49 (54) | 34 (49) | 11 (69) | | |

*Note*: OCS, obsessive-compulsive symptoms; OCD, obsessive-compulsive disorder; No OCS Group, No OCS during study period (patients who never met criteria for obsessions or compulsions on all assessments); OCS Group, OCS during study period (never a diagnosis of OCD and OCS on one or more of the assessments); OCD Group, OCD during study period (Patients who met criteria for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* OCD at any of the assessments and had OCS on all assessments).
[a]ANOVA for continuous variables, chi-square test for categorical variables.

($F_{2,185}$ = 4.08, $P$ = .019). Post hoc comparisons using the Tukey honestly significant difference (HSD) test indicated that the mean PAS score for OCD patients ($M$ = 10.95, SD 3.88) was significantly different from no OCS patients ($M$ = 15.00, SD 6.24) (see table 3).

*OCS/OCD and Severity of Other Symptoms* One-way between group ANOVAs was conducted to explore whether categories based on OCS/OCD status were associated with differences in psychopathology severity. We found no statistically significant differences in mean total scores of PANSS nor in the positive, negative, and general subscales at any of the assessments (see table 4). Cross-sectional analyses of the relationship between OCS severity and psychotic severity (PANSS positive score) showed no association: ie, at admission (Spearman rho = −.079, $P$ = .298), 6 weeks (Spearman rho = −.004, $P$ = .966) nor 3 years after admission (Spearman rho = .006, $P$ = .946).

We did find a statistically significant difference between categories based on OCS/OCD status in mean total MADRS score: t1 ($F_{2,169}$ = 3.6, $P$ = 0.028); t2 ($F_{2,156}$ = 4.2, $P$ = 0.017); and t3 ($F_{2,136}$ = 3.5, $P$ = .033). The effect size calculated using eta squared was, respectively, 0.04, 0.05, and 0.05. In Cohen's terms, this would be considered a medium effect.[34] Post hoc comparisons using the Tukey HSD test indicated that the mean MADRS score for OCD subjects, 6 weeks after admission, was significantly higher than the mean MADRS score of no OCS subjects, $P$ = .022. At other assessments, post hoc Tukey HSD testing revealed no significant differences. Cross-sectional correlation between OCS severity and MADRS were at admission (Spearman rho = .197, $P$ = .009), 6 weeks after admission (Spearman rho = .088, $P$ = .272), and 3 years after admission (Spearman rho = .189, $P$ = .031).

Chi-square tests were done to explore whether the following categorical variables were significantly differently distributed between groups with persistent absence of OCS, presence of OCS at any assessment, or OCD at any assessment (see table 1, section II): 1 or 2 and more psychotic relapses during 5-year follow-up; continuously psychotic; symptomatic remission, at least during one period of 6 months, during 5-year follow-up; full recovery at end of follow-up; suicide; severe aggressive behavior directed at others; good social functioning at end of follow-up; nicotine use; cannabis abuse or dependence; other drug abuse or dependence; alcohol use. We found only significant differences in good social functioning at end of follow-up ($P$ = .033) and in nicotine use ($P$ = .004) between groups (see table 5).

*Nicotine Use* Only 121 patients, whose status on smoking was the same at all assessments, were considered relevant for this analysis. Of these 121, 81 were smokers and 40 were nonsmokers. Change over time in Y-BOCS scores in both groups was not significant nor were any of the pair wise comparisons. Therefore, we compared mean Y-BOCS scores averaged over time. Mean Y-BOCS score of nonsmokers was significantly higher than for smokers (6.12, SD 7.23 vs 2.58, SD 5.16): $t$ = 2,771; $df$ = 59,266; 2-sided $P$ = .007).

*Suicide Attempts and Suicide* We found no significant differences in suicide attempts and suicide between patients with or without OCS or OCD. Fifteen patients made a suicide attempt during follow-up. Three of them reported OCS during follow-up. Seven patients committed suicide during 5-year follow-up. One of them was diagnosed with OCD at admission (14.3%). Six reported no OCS at admission.

### *III. Is Initial Presence of OCS/OCD a Predictor of the First 5-Year Course?*

Out of 122 initial OCS-negative patients, 3 had insufficiently reliable relapse data and 13 continued to have

**Table 4.** Severity of Psychopathology in Patients by Comorbid OCS/OCD

| | At Admission | | | 6 wk After Admission | | | 3 y After Admission | | |
|---|---|---|---|---|---|---|---|---|---|
| | No OCS ($n$ = 91) | OCS ($n$ = 69) | OCD ($n$ = 16) | No OCS ($n$ = 91) | OCS ($n$ = 69) | OCD ($n$ = 16) | No OCS ($n$ = 91) | OCS ($n$ = 69) | OCD ($n$ = 16) |
| PANSS, total score (SD) | 84.0 (22.1) | 80.4 (19.0) | 86.7 (20.0) | 69.9 (18.0) | 70.9 (17.0) | 72.5 (24.0) | 59.0 (19.0) | 64.4 (18.5) | 65.6 (15.2) |
| Positive subscale (SD) | 20.8 (8.1) | 20.2 (7.0) | 20.4 (7.2) | 17.0 (6.0) | 16.5 (4.9) | 14.3 (5.3) | 13.0 (5.0) | 14.2 (6.1) | 12.4 (3.5) |
| Negative subscale (SD) | 22.0 (6.8) | 20.0 (6.8) | 22.5 (7.8) | 18.3 (6.0) | 18.0 (6.2) | 19.2 (9.0) | 16.0 (6.8) | 17.8 (6.5) | 18.9 (6.3) |
| General subscale (SD) | 41.2 (11.5) | 40.2 (9.7) | 43.8 (9.0) | 34.6 (9.4) | 36.1 (9.0) | 39.0 (11.3) | 29.9 (9.6) | 32.4 (9.1) | 34.3 (9.8) |
| MADRS, total score (SD) | 17.4 (8.5) | 20.5 (10.7) | 23.3 (9.3)[a] | 14.1 (8.4) | 16.9 (10.4) | 21.4 (12.2)[b] | 11.1 (9.7) | 14.9 (10.9) | 17.5 (9.0)[c] |
| Y-BOCS, total score (SD) | 0 (0) | 5.9 (7.1) | 17.7 (9.1) | 0 (0) | 5.4 (6.9) | 16.1 (8.1) | 0 (0) | 4.4 (5.5) | 15.4 (9.3) |
| Obsessions subscale (SD) | 0 (0) | 3.3 (5.0) | 9.9 (7.0) | 0 (0) | 2.8 (4.2) | 9.3 (7.0) | 0 (0) | 2.6 (3.2) | 7.9 (6.7) |
| Compulsions subscale (SD) | 0 (0) | 2.6 (4.2) | 7.7 (6.2) | 0 (0) | 2.7 (4.2) | 6.8 (6.0) | 0 (0) | 1.8 (3.7) | 7.5 (6.6) |

*Note*: OCS, obsessive-compulsive symptoms; OCD, obsessive-compulsive disorder; No OCS, No OCS during study period (patients who never met criteria for obsessions or compulsions on all assessments); OCS, OCS during study period (never a diagnosis of OCD and OCS on one or more of the assessments); OCD, OCD during study period (patients who met criteria for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* OCD at any of the assessments and had OCS on all assessments); PANSS, Positive and Negative Syndrome Scale; MADRS, Montgomery Åsberg Depression Rating Scale; Y-BOCS, Yale-Brown Obsessive-Compulsive Scale.
[a]$F_{2,169} = 3.6$, $P = .028$.
[b]$F_{2,156} = 4.2$, $P = .017$.
[c]$F_{2,136} = 3.5$, $P = .033$.

chronic psychotic symptoms. Out of 22 initial OCS-positive but OCD-negative patients, 3 continued to have chronic psychotic symptoms. Thirteen patients (7.0%) had OCD both at t1 and t2. They all had sufficiently reliable relapse data and none continued to have chronic psychotic symptoms. Twenty-two patients (11.8%) had a different OCS or OCD status on t1 and t2 and were therefore not included in the full recovery and relapse analyses (see table 1, section III).

*Relapse: Comparing 106 Initial OCS-Negative, 19 Initial OCS/no OCD and 13 Initial OCD Patients.*

During 5-year follow-up, 36 initial OCS-negative patients (33%), 3 initial OCS/no OCD patients (16%), and 2 initial OCD patients (15%) relapsed once. Twenty OCS-negative patients (18%), 3 initial OCS/no OCD patients (16%), and 5 initial OCD patients (38%) relapsed more than once. There was no significant difference in relapse status between groups (chi-square test: 8.6, $P = .20$). Survival analyses comparing initial OCS-negative with initial OCS-positive and initial OCD patients neither revealed any significant effect of initial OCS/OCD status on time to relapse (respective $P$-values: .477 and .570 without correction; .898 and .619 with correction for confounding).

*Symptomatic Remission and Full Recovery: Comparing 122 Initial OCS-Negative, 22 Initial OCS/no OCD and 13 Initial OCD Patients.*

Data on full recovery was available for all patients alive 5 years after admission. After 5-year follow-up, 45 initial OCS-negative patients (37%), 10 initial OCS/no OCD patients (45%), and 4 initial OCD patients (31%) reached symptomatic remission. Eighteen initial OCS-negative patients (15%), 5 initial OCS/no OCD patients (23%), and 1 initial OCD patients (8%) reached full recovery. There was no significant difference in symptomatic recovery and full recovery between groups (chi-square tests, respectively: 2.4, $P = .66$ and .7, $P = .67$).

## Discussion

To the best of our knowledge, this is the first prospective study of the 5-year course of comorbid OCS and OCD in a relatively large cohort of young patients with first-episode schizophrenia, schizophreniform, or schizoaffective disorder. This study yields 6 main findings. The first finding concerns the prevalence and persistence of OCS and OCD: about half of patients reported OCS at least once during 5-year follow-up. A minority (13.4%) had persistent OCS. Prevalence of OCS and OCD at different assessments varied between 22.7%–30.6% and 7.3%–11.8%, respectively. A recent meta-analysis estimated a mean OCD prevalence in patients with a psychotic disorder of 12.1% (95% CI 7.0%–17.1%).[35] The goal of the diagnostic procedure and definition of OCS, we used, has been to avoid inclusion of obsessive thoughts and compulsive behavior that is directly related to psychosis. Therefore, we expect that our procedure is more specific but may be less sensitive than diagnostic procedures and definitions used from 1970 to 1990, when OCS without insight were included in the comorbid OCD group. This may have contributed to the relatively low prevalence figures of comorbid OCS and OCD we found. Craig

**Table 5.** Five-y Follow-Up Outcomes in Patients by Comorbid OCS/OCD Group

| | No OCS ($n$ = 91) (%) | OCS ($n$ = 69) (%) | OCD ($n$ = 16) (%) | Test[a] | $P$ Value |
|---|---|---|---|---|---|
| Psychotic relapse during 5 y | | | | | |
| One psychotic relapse (%) | 30 (33) | 15 (22) | 3 (19) | | |
| Two or more psychotic relapses | 16 (18) | 8 (12) | 4 (25) | 9.54 | .15 |
| Continuously psychotic | 20 (22) | 11 (16) | 3 (19) | | |
| Symptomatic remission during follow-up | 34 (37) | 34 (49) | 5 (31) | 5.39 | .25 |
| Full recovery at 5-y follow-up | 15 (16) | 13 (19) | 2 (13) | .84 | .66 |
| Suicide | 6 (7) | 0 (0) | 1(6.) | | |
| Severe aggressive behavior | 9 (10) | 6 (8.7) | 1(6) | | |
| Good social functioning at 5-y follow-up | 49 (54) | 45 (65) | 5 (31) | 6.83 | .033 |
| Substance (ab)use | | | | | |
| Nicotine use | 53 (58) | 28 (41) | 6 (38) | 10.87 | .004 |
| Cannabis abuse or dependence | 25 (28) | 15 (22) | 3 (19) | .19 | .39 |
| Hard drugs abuse or dependence | 8 (9) | 6 (9) | 1 (6) | .46 | .80 |
| Alcohol use | 49 (54) | 35 (51) | 8 (44) | 2.90 | .23 |

*Note*: OCS, obsessive-compulsive symptoms; OCD, obsessive-compulsive disorder; No OCS, No OCS during study period (patients who never met criteria for obsessions or compulsions on all assessments); OCS, OCS during study period (never a diagnosis of OCD and OCS on one or more of the assessments); OCD Group, OCD during study period (patients who met criteria for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* OCD at any of the assessments and had OCS on all assessments).
[a]Chi-square test for categorical variables.

and colleagues[8] also showed relatively low prevalence rates and large fluctuation in first admission patients. De novo occurrence of OCS was found in 8% of patients. Some of these de novo OCS could be induced by treatment with antipsychotic medication.

Second, we found that comorbid OCD status was associated with more severe depressive symptoms. Other researchers also found associations between OCS and depressive symptoms or related factors. Schizophrenia patients with OCS were found to be more likely to experience greater levels of hopelessness, prefer avoidant focused coping strategies, and show more depressive symptoms.[36,37] OCD was found to be an independent risk factor for suicidal ideation and suicide attempts in patients with schizophrenia.[38] We did not find an association between OCS/OCD and severity of positive, negative, nor disorganization symptoms. Others found comparable and different findings.[4,39] Taken together, our results support the earlier found association between comorbid OCD and depressive symptoms. Our results also support the tentative conclusion that there is no robust association between OCS/OCD status and severity of other symptoms in schizophrenia or related disorders.

Third, we found that comorbid OCD was associated with poorer premorbid functioning. Poor premorbid functioning is a very relevant prognostic factor in schizophrenia.[40] To the best of our knowledge, there are no reports on the association between premorbid functioning and OCD comorbidity in schizophrenia.

Fourth, nicotine users had lower mean OCS scores. It is well known that the rate of smoking is high among patients with schizophrenia and related disorders. In contrast, patients with OCD tend to smoke less than the general population.[41] No differences in smoking habits of schizophrenia patients with or without comorbid OCS were found in earlier studies.[42,43] However, these studies were cross-sectional and relatively small. An explanation for our finding might be that patients with schizophrenia and OCS have a lower propensity to use nicotine, alternatively smoking may diminish OCS. However, before further possible explanations are warranted, the found association needs replication first.

Fifth, OCS/OCD during admission did not predict time to psychotic relapse and was not related with remission or full recovery. A priori we thought that several characteristics of our methods would enable us to show an effect of initial OCS/OCD comorbidity on psychotic relapse and remission. We chose to compare groups with maximal contrast concerning OCD/OCS status. Moreover, we succeeded in assessing a detailed report of psychotic relapse in a prospective 5-year design with acceptable dropout figures. Nevertheless, we did not find an association with psychotic relapse nor with remission. Contrary to our findings, 2 studies report an association between OCD and readmission to a psychiatric hospital. In 102 patients with chronic schizophrenia, the presence of OCS was associated with a higher median number of days in hospital (54 vs 24) in the previous 5 years.[44] In a study of 54 adolescent schizophrenia patients, those with comorbid OCD required (although nonsignificant) more often rehospitalization (54% vs 38%) than patients without comorbid OCD.[4] It is important to recognize that we studied the predictive effect of initial OCD/OCS on psychotic relapse and

not OCD at endpoint with a retrospective assessment of previous hospitalization.

Sixth, OCD comorbidity was associated with poor social functioning at the end of follow-up. Only one-third of patients with comorbid OCD who had OCS during all assessments, reached good social functioning after 5-year follow-up compared with patients with OCS, but without OCD (65% good social functioning) and patients without OCS (54% good social functioning). Social functioning is impaired in both schizophrenia and in OCD. OCD patients report multiple daily life problems, poor work status, and tense social networks[45] and have worse quality of life than any other patient group, except patients with schizophrenia.[46] In concordance with our findings, others found that patients with schizophrenia and comorbid OCD had greater disability in work and social life.[9] The finding that both schizophrenia patients without OCS and schizophrenia patients with comorbid OCD appear to have worse social functioning than patients with OCS is intriguing. One might speculate that mild OCS may protect against worse social functioning but that syndromal OCD may worsen social functioning or that OCD comorbidity develops in subjects with already compromised social functioning. This result is in concordance with the finding of an earlier study of our group in which mild OCS was associated with less severe negative symptoms than no OCS comorbidity or OCD comorbidity.[25] This line of thought is in concordance with the earlier hypothesis that OCS may be a sign of a healthy response against the overwhelming psychotic decompensation. However, this explanation remains speculative.

### *Strengths and Limitations*

We consider the inclusion of a relatively large consecutively admitted first-episode sample as a strength of our study. The prospective design and detailed evaluation during 5-year follow-up, together with the relatively low dropout rate is another strength. We acknowledge several methodological limitations of our study. First, although all mental health centers in Amsterdam collaborate with our department and intended to refer all first-episode patients, we have missed cases. We were not able to include patients who refuse treatment and/or are so disturbed that persistent treatment in a closed ward or forensic institute is needed. Therefore, generalization of our findings to all patients with schizophrenia or related disorders may not be justified. However, we are confident that our findings apply for patients with a first episode of schizophrenia or related disorders who are willing to collaborate with professional caregivers. Second, the reliability and validity of assessment of OCS and severity of OCS in patients with schizophrenia or related disorders is still under debate. However, several recent publications support the reliability and validity of the assessment of OCS with the Y-BOCS in these patients.[30,31] Third, although we assessed OCS 4 times during 5-year follow-up and asked patients about persistence of OCS between assessments, we have not directly assessed OCS status or severity between assessments. Therefore, we can not rule out the possibility that we may have missed transient OCS or substantial remission of OCS.

### *Clinical Implications*

During the first 5-year course of schizophrenia or related disorders, substantial fluctuation occurs in reported OCS between and within patients and only a minority of patients have persistent OCS. Therefore, a longitudinal research perspective is needed to disentangle the nature of the relationship between OCS and schizophrenia. We might speculate that in some schizophrenia patients, OCS emerges only during stressful periods, while others develop enduring and debilitating OCD. This raises the question whether comorbid OCS needs always specific treatment in patients with schizophrenia or related disorders. We propose that the natural course of comorbid OCS can be awaited when OCS is not severe. However, treatment of enduring OCD is warranted because OCD causes substantial suffering.

Initial OCS/OCD seems not to be associated with a more severe course of psychotic symptoms, however, comorbid OCD probably worsen the overall prognosis. We replicated the repeatedly found association between comorbid OCD, worse social functioning, and depression symptoms. Thus, comorbid OCD may affect outcome. Although reversed causality cannot be excluded, ie, patients with worse social functioning or depressive symptoms may be more prone to develop OCD. Comorbid OCD appears to be a persistent disorder in 1 of 10 patients with schizophrenia or related disorders. In case of comorbid OCD, some patients might benefit from adjunctive medication (ie, selective serotonin reuptake inhibitors)[18] in order to reduce the severity of both obsessive-compulsive and depressive symptoms.

## Funding

Dutch Health Research and Development Council (ZonMw) (28-1241-2).

## Acknowledgments

We want to thank all patients and their parents for their contribution. We thank Annick Fransen for her help concerning references. ZonMw had no further role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. The authors have declared that there are no conflicts of interest in relation to the subject of this study.

## References


1. Buckley PF, Miller BJ, Lehrer DS, Castle DJ. Psychiatric comorbidities and schizophrenia. *Schizophr Bull*. 2009;35: 383–402.
2. Bermanzohn PC, Porto L, Arlow PB, Pollack S, Stronger R, Siris SG. Hierarchical diagnosis in chronic schizophrenia: a clinical study of co-occurring syndromes. *Schizophr Bull*. 2000;26:517–525.
3. Fabisch K, Fabisch H, Langs G, Huber HP, Zapotoczky HG. Incidence of obsessive-compulsive phenomena in the course of acute schizophrenia and schizoaffective disorder. *Eur Psychiatry*. 2001;16:336–341.
4. Nechmad A, Ratzoni G, Poyurovsky M, et al. Obsessive-compulsive disorder in adolescent schizophrenia patients. *Am J Psychiatry*. 2003;160:1002–1004.
5. Poyurovsky M, Fuchs C, Weizman A. Obsessive-compulsive disorder in patients with first-episode schizophrenia. *Am J Psychiatry*. 1999;156:1998–2000.
6. Jahrreiss W. Uber Zwangsvorstellungen im Verlauf der Schizophrenie. *Arch Psychiatr Nervenkr*. 1926;77:740–788.
7. Harrowes WM. The significance of a neurotic reaction as a precursor of schizophrenias. *J Ment Sci*. 1931;77:375–407.
8. Craig T, Hwang MY, Bromet EJ. Obsessive-compulsive and panic symptoms in patients with first-admission psychosis. *Am J Psychiatry*. 2002;159:592–598.
9. Braga RJ, Mendlowicz MV, Marrocos RP, Figueira IL. Anxiety disorders in outpatients with schizophrenia: prevalence and impact on the subjective quality of life. *J Psychiatr Res*. 2005;39:409–414.
10. Katerndahl DA, Realini JP. Lifetime prevalence of panic states. *Am J Psychiatry*. 1993;150:246–249.
11. Fullana MA, Mataix-Cols D, Caspi A, et al. Obsessions and compulsions in the community: prevalence, interference, help-seeking, developmental stability, and co-occurring psychiatric conditions. *Am J Psychiatry*. 2009;166:329–336.
12. de Haan L, Linszen DH, Gorsira R. Clozapine and obsessions in patients with recent-onset schizophrenia and other psychotic disorder. *J Clin Psychiatry*. 1999;60:364–365.
13. Tranulis C, Potvin S, Gourgue M, Leblanc G, Mancini-Marie A, Stip E. The paradox of quetiapine in obsessive-compulsive disorder. *CNS Spectr*. 2005;10:356–361.
14. Ghaemi SN, Zarate CA Jr, Popli AP, Pillay SS, Cole JO. Is there a relationship between clozapine and obsessive-compulsive disorder?: a retrospective chart review. *Compr Psychiatry*. 1995;36:267–270.
15. Lykouras L, Alevizos B, Michalopoulou P, Rabavilas A. Obsessive-compulsive symptoms induced by atypical antipsychotics. a review of the reported cases. *Prog Neuropsychopharmacol Biol Psychiatry*. 2003;27:333–346.
16. Sterk B, Lankreijer K, Linszen DH, De Haan L. Obsessive compulsive symptoms in first episode psychosis and in subjects at ultra high risk for developing psychosis; onset and relationship to psychotic symptoms. *Aust N Z J Psychiatry*. 2011;45:400–406.
17. Hwang MY, Opler LA. Management of schizophrenia with obsessive-compulsive disorder. *Psychiat Ann*. 2000;30:23–28.
18. Hwang MY, Kim SW, Yum SY, Opler LA. Management of schizophrenia with obsessive-compulsive features. *Psychiatr Clin North Am*. 2009;32:835–851.
19. Stengel E. A study of some clinical aspects of the relationship between obsessional neurosis and psychotic reaction types. *J Ment Sci*. 1945;91:166–187.
20. Cunill R, Castells X, Simeon D. Relationships between obsessive-compulsive symptomatology and severity of psychosis in schizophrenia: a systematic review and meta-analysis. *J Clin Psychiatry*. 2009;70:70–82.
21. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders 4th ed Washington, DC: The Association; 1994.*
22. Cassano GB, Pini S, Saettoni M, Rucci P, Dell'Osso L. Occurrence and clinical correlates of psychiatric comorbidity in patients with psychotic disorders. *J Clin Psychiatry*. 1998;59:60–68.
23. Goodman WK, Price LH, Rasmussen SA, et al. The yale-brown obsessive compulsive scale: I. development, use, and reliability. *Arch Gen Psychiatry*. 1989;46:1006–1011.
24. Spitzer RL, Williams JBW, Gibbon M, First MB. *Structured Clinical Interview for DSM-III-R (SCID)—Patient Edition.* Washington, DC: American Psychiatric Press; 1990.
25. Haan De L, Hoogenboom B, Beuk N, Amelsvoort van T, Linszen D. Obsessive-compulsive symptoms and positive, negative, and depressive symptoms in patients with recent-onset schizophrenic disorders. *Can J Psychiatry*. 2005;50:519–524.
26. Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. *Schizophr Bull*. 1982;8:470–484.
27. Strauss JS, Carpenter WT. The prediction of outcome in schizophrenia. II. Relationship between predictor and outcome variables; a report from the WHO International Pilot Study of Schizophrenia. *Arch Gen Psychiatry*. 1974;31:37–42.
28. Ciapparelli A, Paggini R, Marazziti D, et al. Comorbidity with axis I anxiety disorders in remitted psychotic patients 1 year after hospitalization. *CNS Spectr*. 2007;12:913–919.
29. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. 1979;134:382–389.
30. de Haan L, Hoogeboom B, Beuk N, Wouters L, Dingemans PM, Linszen DH. Reliability and validity of the Yale-Brown Obsessive-Compulsive Scale in schizophrenia patients. *Psychopharmacol Bull*. 2006;39:25–30.
31. Boyette L, Swets M, Meijer C, Wouters L. GROUP Authors. Factor structure of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) in a large sample of patients with schizophrenia or related disorders and comorbid obsessive-compulsive symptoms. *Psychiatry Res*. 2011;186:409–413.
32. Susser E, Finnerty M, Mojtabai R, et al. Reliability of the life chart schedule for assessment of the long-term course of schizophrenia. *Schizophr Res*. 2000;42:67–77.
33. Andreasen NC, Carpenter WT, Jr., Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry*. 2005;162:441–449.
34. Cohen J. *Statistical Power Analysis for the Behavioral Sciences.* 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
35. Achim AM, Maziade M, Raymond É, Olivier D, Mérette C, Roy M-A. How prevalent are anxiety disorders in schizophrenia? a meta-analysis and critical review on a significant association [published online ahead of print December 03, 2009]. *Schizophr Bull*. 2009. doi: 10.1093/schbul/sbp148.
36. Lysaker PH, Marks KA, PIicone JB, et al. Obsessive and compulsive symptoms in schizophrenia: clinical and neurocognitive correlates. *J Nerv Ment Dis*. 2000;18878–83.

37. Lysaker PH, Whitney KA, Davis LW. Obsessive-compulsive and negative symptoms in schizophrenia: associations with coping preference and hope. *Psychiatry Res*. 2006;141:253–259.
38. Sevincok L, Akoglu A, Kokcu F. Suicidality in schizophrenic patients with and without obsessive-compulsive disorder. *Schizophr Res*. 2007;90:198–202.
39. Rajkumar RP, Reddy YCJ, Kandavel T. Clinical profile of "schizo-obsessive" disorder: a comparative study. *Compr Psychiatry*. 2005;49:262–268.
40. McGlashan TH. Premorbid adjustment, onset types, and prognostic scaling: still informative? *Schizophr Bull*. 2008;34:801–805.
41. Bejerot S, Humble M. Low prevalence of smoking among patients with obsessive-compulsive disorder. *Compr Psychiatry*. 2007;40:268–272.
42. Fawzi MH, Fawzi MM, Khedr HH, Fawzi MM. Tobacco smoking in Egyptian schizophrenia patients with and without obsessive-compulsive symptoms. *Schizophr Res*. 2007;95:236–246.
43. Dome P, Teleki Z, Gonda X, Gaszner G, Mandl P, Rihmer Z. Relationship between obsessive-compulsive symptoms and smoking habits amongst schizophrenic patients. *Psychiatry Res*. 2006;144:227–231.
44. Berman I, Kalinowski A, Berman SM, Lengua J, Green AI. Obsessive and compulsive symptoms in chronic schizophrenia. *Compr Psychiatry*. 1995;36:6–10.
45. Moritz S. A review on quality of life and depression in obsessive-compulsive disorder. *CNS Spectr*. 2008;13(9 suppl 14):16–22.
46. Bobes J, Gonzalez MP, Bascaran MT, Arango C, Saiz PA, Bousono M. Quality of life and disability in patients with obsessive-compulsive disorder. *Eur Psychiatry*. 2001;16:239–245.