Acta Psychiatr Scand 2011: 123: 136–146

DOI: 10.1111/j.1600-0447.2010.01609.x

ACTA PSYCHIATRICA SCANDINAVICA

Can obsessions drive you mad? Longitudinal evidence that obsessive-compulsive symptoms worsen the outcome of early psychotic experiences

Van Dael F, van Os J, de Graaf R, ten Have M, Krabbendam L, Myin-Germeys I. Can obsessions drive you mad? Longitudinal evidence that obsessive-compulsive symptoms worsen the outcome of early psychotic experiences.

Objective: Although there is substantial comorbidity between psychotic disorder and obsessive-compulsive disorder (OCD), little is known about how these clinical phenotypes, and their subclinical extended phenotypes, covary and impact on each other over time. This study examined cross-sectional and longitudinal associations between both (extended) phenotypes in the general population.
Method: Data were obtained from the three waves of the NEMESIS-study. A representative population sample of 7076 participants were assessed using the composite international diagnostic interview (CIDI) at baseline (T_0), 1 year later at T_1 and again 2 years later at T_2.
Results: At T_0, a lifetime diagnosis of psychotic disorder was present in 1.5% of the entire sample, in 11.5% of the people with any OC symptom and in 23.0% of individuals diagnosed with OCD. OC symptoms at T_0 predicted incident psychotic symptoms at T_2. Similarly, T_0 psychotic symptoms predicted T_2 OC symptoms. The likelihood of persistence of psychotic symptoms or transition to psychotic disorder was higher if early psychosis was accompanied by co-occurring OC symptoms, but not the other way around.
Conclusion: OCD and the psychosis phenotype cluster together and predict each other at (sub)clinical level. The co-occurrence of subclinical OC and psychosis may facilitate the formation of a more 'toxic' form of persistent psychosis.

F. Van Dael[1], J. van Os[1,2], R. de Graaf[3], M. ten Have[3], L. Krabbendam[4], I. Myin-Germeys[1]

[1]Department of Neuropsychiatry and Psychology, South Limburg Mental Health Research and Teaching Network, EURON, Maastricht University, Maastricht, the Netherlands, [2]King's College London, King's Health Partners, Department of Psychosis Studies, Institute of Psychiatry, Denmark Hill, London, UK, [3]Netherlands Institute of Mental Health and Addiction (Trimbos Institute), Utrecht and [4]Centre Brain and Learning, Department of Psychology and Education, VU University, Amsterdam, the Netherlands

Key words: psychosis; obsessive-compulsive disorder; comorbidity; prevention

Inez Myin-Germeys, Department of Psychiatry and Neuropsychology, Maastricht, University, PO Box 616 (VIJV), 6200 MD Maastricht, the Netherlands.
E-mail: i.germeys@sp.unimaas.nl

Accepted for publication August 31, 2010

Significant outcomes

- The obsessive-compulsive disorder and psychosis phenotype cluster together and predict each other at clinical and subclinical level.
- When psychotic symptoms are accompanied by obsessive-compulsive symptoms, the risk for transition to psychotic disorder with need for care is increased.
- This knowledge may be helpful for clinicians in decision-making for early interventions and follow-up.

Limitations

- Despite the large sample, numbers are quite low in some of the longitudinal and more complex interaction models.
- Obsessive-compulsive (OC) symptoms may be underreported with the used questionnaire composite international diagnostic interview (CIDI).
- Information is lacking on the role of specific psychotic symptom dimensions (positive, negative disorganizational symptoms) on comorbdity with OC symptoms.
- The 3- year longitudinal follow-up is relatively short.

Introduction

Although the co-occurrence of obsessive-compulsive disorder (OCD) and schizophrenia has been reported consistently for more than a century (1), reports are less consistent with regard to the extent of this comorbidity (2). Reported rates of schizophrenia in OCD patients vary from 4.0% to 12.2% (3–5), and the reported prevalence of OCD in subjects with schizophrenia ranges from 1.1% to 59.2% (6, 7). Many factors may contribute to heterogeneity in reported results. In clinical studies, diagnoses were based mostly on diagnostic hierarchy as defined in DSM, thus excluding, for example, obsessions that in content were related to any other Axis 1 disorder. Two studies, assessing lifetime occurrence of OCD and schizophrenia in a general population sample without hierarchical exclusions, yielded considerably higher comorbidity rates (59.2% OCD in schizophrenia, compared to 1.1–46.6% in reports applying hierarchical exclusions and 12.2% schizophrenia in OCD compared to 4.0% respectively) (3, 5, 7, 8). Other factors influencing heterogeneity of study findings include sample selection, diagnostic criteria, type of prevalence assessment (retrospective, cross-sectional, longitudinal) and type of symptom assessment (therapist report, short or more extensive assessment tools), applied to two heterogeneous disorders that have been shown to display a broad range of symptoms (3, 5, 7–9). In addition, both psychotic disorder and OCD have subthreshold extended phenotypes that can be measured in general population samples (10, 11); comorbidities may vary depending on whether analysis is carried out at the level of clinical or extended phenotype.

Therefore, to fully understand the level of covariation between psychosis and OCD, the broad distribution of symptomatic expression at both clinical level and subclinical level should be included. To our knowledge, no previous studies have included the issue of comorbidity across the spectrum of expression.

It has been suggested that OCD and psychosis may not only cluster cross-sectionally, but also influence each other longitudinally, in terms of onset and prognosis. Studies investigating this issue have reported contradictory results (2, 12, 13), OCD impacting positively, negatively or not at all on aspects of course and outcome of schizophrenia (2, 8, 13–18). In addition, it is unclear whether OCD is impacting on psychosis or whether there is a reciprocal relationship with psychosis moderating risk for OCD.

The current study is a cross-sectional and prospective longitudinal investigation in the general population focusing on clinical and subclinical OC and psychotic symptoms.

Aims of the study

The aim of this study was to examine i) the cross-sectional association between obsessive-compulsive disorder (OCD) and psychosis, at clinical and subclinical levels of phenotypic expression, ii) whether baseline OCD predicts follow-up incidence of psychosis and, *vice versa*, whether baseline psychosis predicts follow-up OCD, and iii) whether the co-occurrence of obsessive-compulsive (OC) and psychotic symptoms predicts persistence of psychosis or OC symptoms respectively.

Material and methods

Sample

The study is part of the Netherlands Mental Health Survey and Incidence Study (NEMESIS), a longitudinal study of the prevalence, incidence, course and consequences of psychiatric disorders in the Dutch general population. Subjects were contacted at three points over a period of 3 years: at baseline (T_0 – lifetime assessments), 1 year thereafter (T_1 – assessing the period between T_0 and T_1) and again 2 years after T_1 (T_2 – assessing the period between T_1 and T_2) (19). A multistage, stratified, random sampling procedure was used to first select 90 municipalities, then a sample of private households, and finally a Dutch-speaking individual aged 18–64 years within each household. Individuals living in institutions, including individuals residing in psychiatric hospitals, were not included in the sampling frame. All subjects were sent an introductory letter from the Minister of Health, inviting them to participate. A total of 7076 subjects were enlisted at T_0. The response rate was 69.7%. Nearly 44% of non-responders agreed to fill in a postal questionnaire, including a General Health Questionnaire (20), and were found to have the same mean GHQ score (responders: 1.19; non-responders: 1.16). At T_1, 5618 subjects participated for the second time (response: 79.4%); at T_2, 4848 subjects participated (response of T_1 participants: 86.3%). The sample was found to be representative of the Dutch population in terms of sex, marital status, and level of urbanization (19), with the exception of a slight underrepresentation of individuals in the age group 18–24 years.

Presence of psychiatric disorder at T_0, demographic variables held constant, only slightly increased the probability of loss to follow-up between T_0 and T_1, as well as between T_1 and T_2 (21).

Instruments

CIDI. Subjects were interviewed at home with the (CIDI; http://www3.who.int/cidi/), version 1.1 (22) which measures DSM-III-R diagnoses. The CIDI is a fully structured interview that yields DSM-III-R and ICD-10 diagnoses. It is designed for use by trained interviewers who are not clinicians and has satisfactory inter-rater reliability (23) and test–retest reliability (24). Ninety interviewers experienced in systematic data collection administered the interview, having received a 3-day training course in recruiting and interviewing, followed by a 4-day course at the World Health Organization-CIDI training centre in Amsterdam, the Netherlands.

Camberwell assessment of Need (CAN). Need for care was assessed using the CAN (25). The CAN includes 22 items (e.g. daytime activities, psychological distress, household skills). All CAN items can be scored 0 (no problem), 1 (there was a problem, but the problem is met), 2 (unmet need).

CIDI psychosis rating

Ratings from the 17 items of the CIDI core psychosis sections, assessed at T_0, T_1 and T_2 on delusions (13 items) and hallucinations (four items) were used (items G1–G13, G15, G16, G20, G21). These concern classic psychotic symptoms involving, for example, thought interference and passivity phenomena (i.e. first-rank delusions), persecution and auditory hallucinations. All these items can be rated in six ways: '1' – no symptom; '2' – symptom present but not clinically relevant (not bothered by it and not seeking help for it); '3' – symptom result of ingestion of drugs; '4' – symptom result of somatic disease; '5' – clinical psychotic symptom (presence of distress and help-seeking); '6' – symptom may not really be a symptom because there appears to be some plausible explanation for it.

At all three time points, clinical re-interview or clinical consultation procedures were in place to reduce false-positive ratings (26).

For the purpose of the analyses, subclinical psychotic experiences were broadly defined as any CIDI rating of 2, 3, 4, or 6 on any of the 17 psychosis items. The justification for these broad ratings was derived from a previous study, where it was shown that the different ratings on the CIDI psychosis items were strongly associated with each other (27). In addition, the different ratings independently showed a similar pattern of associations with known risk factors for psychosis (27).

Psychosis ratings at T_0 and T_1

Three increasing levels of psychosis were defined: (i) any T_0 subclinical psychotic experience (any CIDI rating of 2, 3, 4, or 6 on any of the 17 psychosis items; hereafter referred to as T_0 psychotic experience), (ii) any T_0 clinical psychotic symptom (a CIDI rating of 5 on any of the 17 CIDI core psychosis items; hereafter referred to as T_0 psychotic symptom) and (iii) T_0 diagnosis of psychotic disorder (any DSM-III-R affective or non-affective psychotic disorder; hereafter referred to as T_0 psychotic disorder). Similar levels were defined for the T_1 assessment.

Psychosis outcomes at T_2

To assess T_2 psychotic experiences in terms of clinical relevance, psychosis at T_2 was specified at two levels, one involving the presence of positive psychotic symptoms assessed with the brief psychiatric rating scale (BPRS) and one using additional clinical judgment of need for care (28).

T_2 outcome of BPRS psychotic symptoms. At T_2, two items of the BPRS (29), 'unusual thought content' and 'hallucinations' were assessed by a clinician in a telephone re-interview with anybody with a rating of 2, 5, or 6 on any of the CIDI psychosis items at T_2. The clinical re-interview rate was 74.4% (163 of 220 individuals). The BPRS ratings were discussed in a consensus meeting attended by two psychologists and two psychiatrists after each telephone re-interview. All four clinicians had received training in the BPRS and used this instrument routinely in clinical practice. They were blind to the information from the CIDI at T_0 and T_1, as well as to the hypotheses of this study. The range of scores for each BPRS symptom was from 1 (absent) to 7 (very severe) (30). The BPRS was used to define a psychosis outcome, defined as any rating >1 on either of the two BPRS items (hereafter: T_2 BPRS psychotic symptoms).

T_2 outcome of Needs-based diagnosis of psychotic disorder. As the most widely used system of classification of psychiatric disorders, the DSM-IV (31) allocates 'patient status' on the basis of disability and distress rather than clinical need, a procedure was applied that yielded a needs-based diagnosis to identify incident cases of psychosis at T_2. This definition of the psychosis outcome allowed us to not only use classical criteria for allocation of patient status on the basis of severity and functional impairment (as, for example, in

DSM) but additionally use a clinical judgement of need for care, as recommended for case identification in the general population (32). Need for care in relation to psychotic symptoms and psychological distress was assessed in the consensus meeting by four clinicians, after information was gathered in the areas of need as defined by the CAN (33).

Information on need for care, thus collected was combined with the BPRS to define a more stringent T_2 clinical outcome (hereafter: T_2 needs-based diagnosis of psychotic disorder), defined as the combination of (i) BPRS pathology-level psychotic symptom (any rating >3 on either of the two BPRS positive psychosis items) and (ii) clinician consensus on probable/definite need for care.

CIDI rating of OC symptoms and disorder

OC symptoms were examined using 5 from the 19 items of the CIDI OCD-sections. For two obsession items (K1, K1a), two ratings were provided: '1', no symptom and '5', true psychiatric symptom. The three compulsion items (K9, K10, K11) were rated similarly, and in addition, a third rating was added of '2', indicating that the symptom was present but not clinically relevant (not bothered by it and not seeking help for it).

OC symptoms were defined both at T_0 and T_2 at two levels: (i) any obsession or compulsion, defined as a rating of 2 or 5 on any of the obsession/compulsion items mentioned earlier (hereafter: OC symptom) and (ii) presence of OCD, defined as a CIDI-generated DSM-III-R diagnosis of OCD.

Analysis

All analyses were carried out using the software package STATA, version 11 (34).

Cross-sectional association between OCD and psychosis. Associations between T_0 OCD (clinical disorder and subclinical OC symptoms) and the three T_0 psychosis variables (psychotic experience, psychotic symptom and psychotic disorder) were assessed using logistic regression analyses. Associations were adjusted for the *a priori* demographical confounders of age, sex, level of education, marital status (living alone or not), urbanicity, and use of alcohol and drugs.

Associations have been reported between psychosis and affective symptom dimensions (35–37), between OCD and mood disorders (38–40), and between psychosis and anxiety disorders (41, 42). Therefore, to assess whether any association between psychosis and OCD was independent from the overlap between psychosis and anxiety and mood disorders in general, all associations were additionally adjusted, in a second step, for lifetime presence of other anxiety disorders (panic disorder, agoraphobia, social phobia, simple phobia, generalized anxiety disorder) and mood disorders (major depression, bipolar disorder, dysthymia).

Longitudinal associations between T_0 OCD and T_2 psychosis. For those without a T_0 or T_1 diagnosis of psychotic disorder, the risk of T_2 BPRS psychotic symptoms and of incident T_2 needs-based diagnosis of psychotic disorder was calculated as a function of the presence of a T_0 OCD. To ensure that the associations were not because of any missed diagnosis of psychotic disorder at baseline and were additionally adjusted for the variable T_0 psychotic experience.

Associations were adjusted for the same demographical confounders as well as presence of mood and non-OCD anxiety disorders; the latter adjustment is also necessary for reason of reports that psychotic disorder may be expressed initially as non-psychotic diagnoses (43–45).

To assess whether the association between T_0 OCD and T_2 psychosis outcomes reflects a predictive function rather than passive comorbidity, the fit of the reverse model was tested, that is, whether T_0 psychosis variables increased the risk for T_2 OCD.

Association between co-occurrence of subclinical OC and psychotic symptoms and later clinical psychosis. To test the hypothesis that individuals with clustering of the OCD extended phenotype and the psychosis extended phenotype would display greater risk of developing T_2 needs-based diagnosis of psychotic disorder compared to individuals with either extended phenotypes in isolation, an interaction was fitted between T_1 OC symptoms and T_1 psychotic symptoms as independent variables in the model with T_2 BPRS psychotic symptoms and T_2 needs-based diagnosis of psychotic disorder as the dependent variable. For the latter analyses, T_1 rather than T_0 measures were used as the independent variables, given that T_0 measures reflect lifetime exposure so that symptoms of OC and psychosis, rated as present at T_0, may well have occurred at entirely different periods in time, i.e. they may not reflect true co-occurrence. As the T_1 measure reflected the brief interval of 1 year, actual co-occurrence is much more likely if both OC and psychosis symptoms were rated as present at T_1.

The inverse interaction model was also tested: whether the co-occurrence of OCD and psychosis extended phenotypes at T_1 was associated with

increased risk of developing a diagnosis of OCD or OC symptoms at T_2.

In line with recent advances in the conceptualization of interaction, we calculated the statistical additive interaction rather than the multiplicative interaction, as the former is more likely to yield information on the degree of synergism between causes, that is the extent to which both causes depend on each other or coparticipate in disease causation (46). To calculate the statistical interaction under an additive model, the BINREG procedure in the STATA statistical programme (34), which fits generalized linear models for the binomial family estimating risk differences, was used. Interactions were assessed by Wald test.

Risk set 1. For the T_0 cross-sectional analyses, the risk set consisted of all individuals who participated in the T_0 CIDI interview (n = 7076).

Risk set 2. For the longitudinal analyses, the sample was restricted to individuals who i) had participated in the T_0 CIDI interview with the exception of the individuals with a lifetime diagnosis of psychotic disorder (n = 107), ii) had post-T_0 CIDI interviews at T_1 (n = 5536), with the exception of the individuals with an incident diagnosis of psychotic disorder at that time (n = 11), and iii) had not missed T_2 CIDI interview and re-interview by clinicians about the presence of psychotic symptoms if they had been eligible for this clinical re-interview. Applying these combined criteria yielded a risk set for the longitudinal analyses of 4673 individuals. (Fig. 1)

Risk set 3. For the analysis of the inverse model (association between T_0 psychosis and T_2 OCD), the sample was restricted to all individuals who i) had participated in the T_0 CIDI interview with the exception of the individuals with a lifetime diagnosis of OCD (n = 61), ii) had post-T_0 CIDI interviews at T_1 (n = 5567), with the exception of the individuals with an incident diagnosis of OCD at that time (n = 13), and iii) had not missed T_2 CIDI interview. Applying these combined criteria, the risk set for this analysis consisted of 4746 individuals.

Results

Descriptives

Data on demographics and OCD and psychosis variables at T_0, T_1, and T_2 are shown in Table 1 for risk sets 1, 2, and 3. The distribution of demographic variables was comparable across risk sets.

Cross-sectional association between OCD & psychosis

T_0 OCD was present in 0.5% (28/5838) of the people without any psychotic experience, in 1.2% (11/930) of the people with a T_0 psychotic experience (without disorder nor symptom), in 3.9% (8/203) of the people with a T_0 psychotic symptom (without the disorder), and in 13.1% (14/107) of those with a T_0 psychotic disorder.

Associations between T_0 OC symptoms and the psychosis phenotype became progressively stronger when increasingly more stringent definitions were used along the psychosis and OCD extended phenotypes respectively (Table 2).

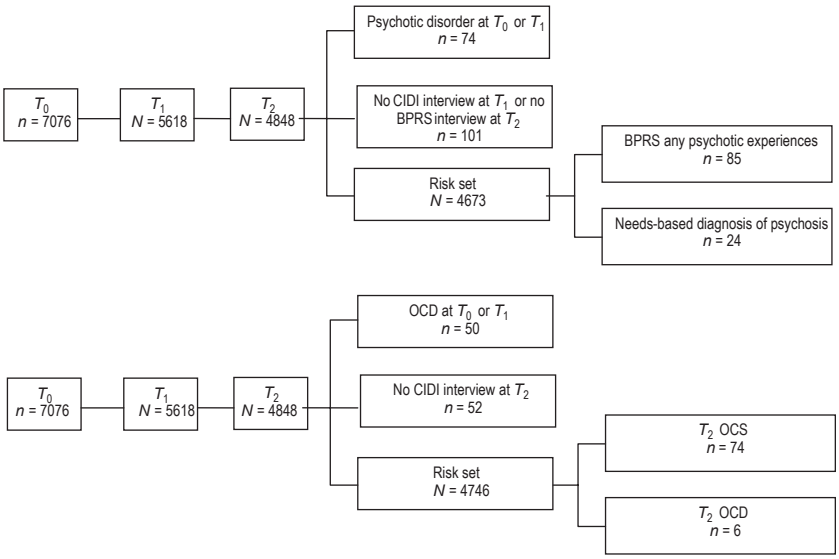

Fig. 1. Flowchart for risk set 1 and 2.

Table 1. Demographics, OCD, and psychosis variables at T_0, T_1, and T_2 for risk sets 1, 2, and 3

	Risk set 1 (whole sample)	Risk set 2 (longitudinal)	Risk set 3 (inverse)
N (%)	7076 (100)	4673 (100)	4746 (100)
T_0 Psychotic experience (%)	1237 (17.5)	676 (14.5)	742 (15.6)
T_0 Psychotic symptom (%)	295 (4.2)	102 (2.2)	152 (3.2)
T_0 Psychotic disorder* (%)	107 (1.5)	0	52 (1.1)
T_0 OC symptom (%)	409 (5.8)	237 (5.1)	229 (4.8)
T_0 obsession (%)	372 (5.3)	219 (4.7)	213 (1.5)
T_0 compulsion (%)	83 (1.2)	39 (0.83)	34 (0.7)
T_0 OC disorder (%)	61 (0.86)	29 (0.62)	0 (0)
T_1 psychotic symptom (%)	72 (1.3)	28 (0.6)	
T_1 OC symptom (%)	117 (2.1)	81 (1.7)	
T_2 BPRS psychotic symptom (%)	104 (2.2)	85 (1.8)	97 (2.1)
T_2 needs-based diagnosis of psychotic disorder (%)	33 (0.69)	24 (0.5)	30 (0.6)
Mean age (SD)	41.2 (12.2)	41.2 (11.9)	41.3 (11.9)
Gender (% male)	46.6	46.8	46.6
Level of education (%)			
Lowest	28.0	24.3	24.6
Low	36.3	36.6	36.5
High	7.4	7.6	7.6
Highest	27.0	30.4	30.0

*Affective and non-affective.
OCD, obsessive-compulsive disorder; OC, obsessive-compulsive; BPRS, brief psychiatric rating scale.

Table 2. Unadjusted cross-sectional associations between T_0 OC symptoms/OCD and T_0 psychotic symptom/T_0 psychotic disorder (disorder excluded from symptoms excluded from experiences)

	T_0 Psychosis		
	T_0 psychotic experience 13.8% (930/6765)	T_0 psychotic symptom 2.9% (203/6968)	T_0 psychotic disorder 1.5% (107/7075)
T_0 OC			
T_0 OC symptom 4.9% (348/7016)			
% (n/N)	11.6% (107/919)	16.4% (32/195)	35.5% (33/93)
OR (95% CI)	4.2 (3.3–5.4) $P < 0.0005$	4.5 (3.0–6.6) $P < 0.0005$	11.5 (7.4–17.9) $P < 0.0005$
T_0 OCD 0.9% (61/7076)			
% (n/N)	1.2% (11/930)	3.9% (8/203)	13.1% (14/107)
OR (95% CI)	2.5 (1.2–5.0) $P < 0.011$	7.1 (3.3–15.3) $P < 0.0005$	22.2 (11.8–41.7) $P < 0.0005$

Total sample: $n = 7076$; OR = odds ratio (95% confidence interval).
OCD, obsessive-compulsive disorder; OC, obsessive-compulsive.

The associations changed only marginally after adjustment for the confounders age, sex, level of education, marital status, urbanicity, and use of alcohol and drugs both at the level of symptom (OR: 3.7, $P < 0.0005$, 95% CI: 2.5–5.6) as at the level of disorder (OR: 15.9, $P < 0.000$, 95% CI: 8.1–31.3). When additionally adjusted for other anxiety disorders and mood disorders, the association between presence of OCD and psychosis was reduced but remained significant both at the level of disorder (OR: 2.7, $P < 0.017$, 95% CI: 1.2–6.0), at the level of symptoms (OR: 2.4, $P < 0.0005$, 95% CI: 1.5–3.7) and even at the lowest measured levels of expression of the phenotype (OR: 2.7, $P < 0.0005$, 95% CI: 2.1–3.6).

Table 3. Association [OR (95% CI)] between T_0 OC symptoms/OCD and T_2 psychosis outcomes (= T_2 BPRS psychotic symptoms and T_2 needs-based diagnosis of psychotic disorder respectively)

	T_2 Psychosis	
	T_2 BPRS psychotic symptom 1.8% (85/4673)	T_2 needs-based diagnosis of psychotic disorder 0.5% (24/4673)
T_0 OC		
T_0 OC symptom, not adjusted 5.1% (237/4673)	4.2 (2.4–7.5) $P < 0.0005$	6.4 (2.5–16.2) $P < 0.0005$
T_0 OC symptom, adjusted for T_0 psychotic symptoms	3.0 (1.6–5.6) $P < 0.001$	3.5 (1.3–9.7) $P < 0.015$
Adjusted for T_0 psychotic symptoms and other confounders*	3.0 (1.5–5.9) $P < 0.001$	3.8 (1.2–12.2) $P < 0.021$
T_0 OCD, not adjusted 0.6% (29/4673)	6.4 (1.9 – 21.6) $P < 0.003$	15.6 (3.5 – 69.5) $P < 0.0005$
T_0 OCD Adjusted for T_0 psychotic symptoms	4.3 (1.1 – 16.7) $P < 0.037$	8.6 (1.5 – 48.8) $P < 0.015$
Adjusted for T_0 psychotic symptoms, and other confounders	3.8 (0.9–16.1) $P < 0.074$	9.4 (1.1–79.6) $P < 0.040$

*Age, sex, level of education, marital status (living alone or not), urbanicity, use of alcohol and drugs, other anxiety disorders, mood disorders.
OCD, obsessive-compulsive disorder; OC, obsessive-compulsive; BPRS, brief psychiatric rating scale.

Association between T_0 OCD and subsequent psychosis

The T_0 OCD phenotype, at symptom level as well as at disorder level, was significantly associated with an increased risk of i) T_2 BPRS psychotic symptoms and ii) a T_2 needs-based diagnosis of psychotic disorder (Table 3). These associations remained significant when adjusted for any T_0 psychotic symptom or experience.

When adjusted not only for any T_0 psychotic symptom, but additionally for non-OCD anxiety disorders and mood disorders at T_0 and for the confounders age, sex, level of education, marital status, use of alcohol and drugs, and urbanicity, associations for T_0 OC symptoms remained significant, whereas for T_0 OCD, they remained significant in the model with the T_2 needs-based psychosis outcome, but were just short of conventional alpha in the model of the T_2 BPRS psychotic symptoms (Table 3).

In risk set 3, T_0 psychotic disorder was significantly associated with T_2 OC symptoms, also after adjustment for T_0 OC symptoms, other anxiety and mood disorders and the other confounders mentioned earlier. None of the subjects with T_0

Table 4. Association [OR (95% CI)] between T_0 psychotic symptoms/disorder and T_2 OC symptoms/OCD

	T_2 OCD	
	T_2 OC symptoms 1.6% (74/4746)	T_2 OCD 0.13% (6/4746)
T_0 Psychosis		
T_0 psychotic symptoms 3.2% (152/4746)	6.9 (3.7–12.9) $P < 0.0005$	15.3 (2.8–84.2) $P < 0.002$
Adjusted for T_0 OC symptoms	3.3 (1.7–6.7) $P < 0.001$	6.9 (1.1–43.6) $P < 0.04$
Adjusted for T_0 OC symptoms and other confounders	2.9 (1.4–6.2) $P < 0.004$	9.0 (1.2–70.4) $P < 0.04$
T_0 diagnosis psychosis 1.1% (52/4746)	7.7 (3.2–18.4) $P < 0.0005$	(No T_2 OCD)
Adjusted for T_0 OC symptoms	2.8 (1.1–7.6) $P < 0.04$	(No T_2 OCD)
Adjusted for T_0 OC symptoms and other confounders*	2.3 (0.8–7.3) $P < 0.14$	(No T_2 OCD)

*Age, sex, level of education, marital status (living alone or not), urbanicity, use of alcohol and drugs, other anxiety disorders, mood disorders.
OR = odds ratio (95% confidence interval).
OCD, obsessive-compulsive disorder; OC, obsessive-compulsive.

psychotic disorder developed full T_2 OCD. Having T_0 psychotic symptoms without a T_0 psychotic disorder was significantly associated with both T_2 OCD and T_2 OC symptoms, also after adjustment for T_0 OC symptoms (Table 4).

Early OCD-psychosis co-occurrence and later clinical outcome

The presence of T_1 psychotic symptoms significantly increased the risk of T_2 needs-based diagnosis of psychotic disorder, as reported previously (47). For those with co-occurring T_1 OC symptoms, this risk-increasing effect was higher compared to those without co-occurring T_1 OC symptoms. The difference in risk increase on the additive scale between the groups with and without T_1 OC symptoms was i) 47.2% for T_2 BPRS psychotic symptoms outcome and ii) 40.4% for a T_2 needs-based diagnosis of psychotic disorder outcome (Table 5). These interactions remained significant when adjusted for the presence of T_0 psychotic symptoms (Risk difference: i) 42.4%; $\chi^2 = 5.51$; $P = 0.018$ and ii) Risk difference: 38.9%; $\chi^2 = 4.3$; $P = 0.038$)). In the inverse model, there was no significant interaction between present T_1 OC symptoms and T_1 psychotic symptoms in predicting T_2 OCD or T_2 OC symptoms (Table 5; Fig. 2a,b).

Discussion

The results of this population-based study showed a cross-sectional association between subclinical and clinical OCD and subclinical and clinical psychosis, independent of other anxiety and mood disorders and demographic confounders. In the longitudinal analyses, it was shown that the T_0 OCD (extended) phenotype was associated with the development of future subclinical and clinical psychosis, and conversely, that the T_0 (extended) psychosis phenotype was associated with future OCD. These findings could still be attributed to the

Table 5. Interactions between T_1 psychotic symptoms and T_1 OC symptoms in predicting psychosis and OCD respectively. Additive scale (risk differences)

	No T_1 psychotic symptom	T_1 psychotic symptom	Increase in risk by T_1 psychotic symptom
Risk for T_2 BPRS psychotic symptoms (n = 85)			
No T_1 OCS (%)	1.6	10.0	8.4
T_1 OCS (%)	6.8	62.5	55.6
Difference in risk increase			47.2% (10.8–83.7)
Additive interaction			$\chi^2 = 6.44$, df = 1, $P = 0.011$
Risk for T_2 needs-based diagnosis of psychotic disorder (n = 24)			
No T_1 OCS (%)	0.4	10.0	9.6
T_1 OCS (%)	0	50	50
Difference in risk increase			40.4% (3.3–77.5)
Additive interaction			$\chi^2 = 4.56$, df = 1, $P = 0.033$
	No T_1 OCS	T_1 OCS	Increase in risk by T_1 OCS
Risk for T_2 OCS			
No T_1 psychotic symptom (%)	1.1	20.6	19.5
T_1 psychotic symptom (%)	10.5	50	39.5
Difference in risk increase (%)			20.0
Additive interaction			$\chi^2 = 1.11$, df = 1, $P = 0.29$
Risk for T_2 OCD			
No T_1 psychotic symptom (%)	0.1	0	−0.1
T_1 psychotic symptom (%)	0	12.5	12.5
Difference in risk increase (%)			12.6
Additive interaction			$\chi^2 = 1.16$, df = 1, $P = 0.28$

OCD, obsessive-compulsive disorder; OC, obsessive-compulsive; BPRS, brief psychiatric rating scale.

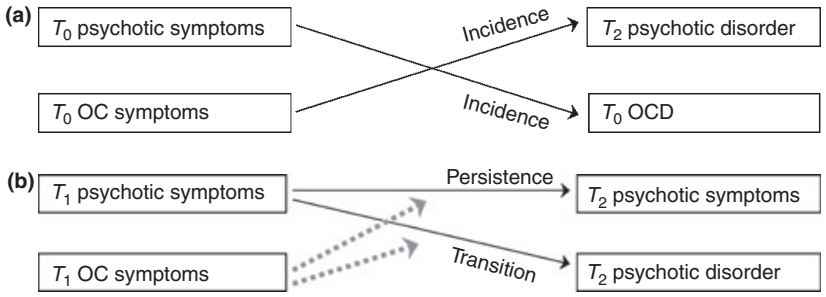

Fig. 2. (a) The obsessive-compulsive disorder extended phenotype (disorder and symptoms without disorder) at T_0 predicted incident psychosis (disorder and symptoms) at T_2. Similarly, T_0 psychotic symptoms predicted T_2 obsessive-compulsive (OC) symptoms. (b) Given the early presence of psychotic symptoms, the likelihood of persistence of psychosis symptoms or transition to psychotic disorder was higher if early psychosis was accompanied by co-occurrence of OC symptoms (dotted grey arrows).

high rates of comorbidity, without a specific impact of OC symptoms on the course of psychotic symptoms. However, in the interaction models, the risk-increasing effect of 'comorbid' OC and psychotic symptoms on a future psychosis (clinical) outcome was considerably stronger then the risk-increasing effect of comorbid OC and psychotic symptoms on a future OCD outcome. This suggests a specific impact of OC symptoms on psychotic symptoms in increasing the risk for transition to psychosis.

Comorbidity

The analyses revealed a much greater than chance comorbidity. The prevalence of OCD in psychosis was 13.1%, somewhat at the lower end of the reported range from 1% up to 59% in previous studies (6, 7). The rather low estimation in this study is in line with comorbidity findings based on short screening questionnaires like the diagnostic interview schedule or its successor the CIDI (8–14%) compared to studies using more extensive questionnaires like PANSS and YBOCS (23–47%) (8). It is possible that the CIDI may lead to underreporting of OC symptoms as it includes only two questions regarding obsessions and three regarding compulsions. The lifetime prevalence of OCD of 0.86% in this study indeed was lower than the 2–3% reported in most other studies (42, 48). Thus, the estimates in the current study can be considered conservative.

Comorbidity may arise from a number of sources. The comorbidity between OCD and psychosis may be because of shared etiological influences. Environmental risk factors like pre- and perinatal stressful events, childhood trauma and negative life events, being part of an ethnic minority and use of cannabis and other drugs tend to be associated with both OCD and psychosis (49–53). An increased vulnerability in late adolescence and a tendency for males to get affected earlier than females are also common correlates of both OCD and psychosis (7, 54). Both disorders are associated with a number of alterations in neuropsychological performance (impaired attention and error monitoring, impaired inhibition, and impaired visuospatial skills) (8) as well as neuroanatomical and neurobiological changes (volume changes in basal ganglia and prefrontal cortex; alterations in dopaminergic neurotransmission) (55, 56).

Overlapping diagnostic criteria may also contribute to the apparent comorbidity. Obsessions and delusions, core symptoms of OCD and psychosis, respectively, share some features in their conceptualization: both concern persistent thoughts or ideas that become overvalued and go together with elevated preoccupation, distress, anxiety and, frequently, impact on behaviour (31, 57, 58). However, there remains a distinct conceptual difference between these symptoms. Delusions typically are defined as false beliefs that are held with high conviction, not amenable to reason, and ego-syntonic by their holder, who is lacking insight and does not unfold any resistance. Obsessions are defined as recurrent and persistent thoughts, impulses or images, that are experienced as intrusive and inappropriate (i.e. ego-dystonic), and typically accompanied by insight: they are recognized as a product of one's own mind and elicit resistance (31).

Another possible source of comorbidity is confounding or population stratification, which occurs when two disorders have non-overlapping sets of risk factors, but these risk factors both tend to be more common in certain strata of the population (59). The association between (subclinical) OC and psychosis, however, was shown to be independent of confounding by other anxiety and mood disorders as well as a number of non-shared risk factors and demographic variables.

Finally, Berkson's bias may affect the results, when subjects with more than one disorder are more likely to be part of a clinical sample (60, 61). However, our findings were derived from a non-clinical, general population sample, suggesting that the overlap cannot be explained by the effect of any referral bias. Summarizing, there is some evidence for shared etiological factors contributing to the observed comorbidity, although the role of overlapping diagnostic criteria cannot be ruled out.

OC symptoms predict clinical psychosis

A second important finding in the longitudinal part of the study is that T_0 (subclinical) OCD predisposes for incident psychosis and for transition of psychotic experiences to clinical psychosis with need for care. This finding strengthens previous reports of a risk-increasing effect of OCD on the development of psychosis (62, 63), although this was not replicated in some studies (64, 65). Although we also found a reverse association of psychotic symptoms predisposing for incident OCD, only OC symptoms appeared to have a specific interaction with psychotic symptoms in augmenting the risk for later psychotic disorder with need for care; the reverse was not found. Thus, OC symptoms may have a deleterious influence on the course and outcome of psychosis.

The precise nature of this ''toxic'' effect remains unclear. In studies on psychological models of OCD, persons prone to OCD show a cognitive style characterized by unsuccessful thought suppression and the tendency to make negative interpretations that involve the idea that the person's choice can result in harm, which needs to be neutralized. Consequent to this cognitive style, occasional intrusive thoughts tend to re-occur, cause distress and become a symptom (66). In severe cases of OCD, insight can become tenuous as obsessions progress to overvalued ideas. At some point, an obsessional concern may be regarded as justified and beyond reasonable question, thereby corresponding to the definition of a delusion. It is attractive to speculate that the development of a delusional appraisal or belief of an intrusive thought, particularly in presence of this obsession-prone cognitive style, may also predispose for psychosis, which is in line with current psychological models of psychosis (67).

Limitations

Despite the large sample, numbers were quite low in some of the longitudinal analyses. For example, only three subjects with T_0 OCD developed a T_2 needs-based diagnosis of psychotic disorder, and in the interaction models of T_1 comorbid psychotic and OC symptoms, controlled for T_0 psychotic symptoms, there were no subjects with OC symptoms, but without psychotic symptoms, developing psychosis with need for care.

This study does not provide information on the difference in nature of symptoms between schizophrenia with OC symptoms and schizophrenia without OC symptoms. For this purpose, the CIDI does not cover sufficiently the negative and cognitive symptoms and qualitative differences between different kinds of obsessions and compulsions. As mentioned earlier, the CIDI may lack sensitivity compared to more extensive questionnaires, particularly for OC symptoms. Finally, the duration of the follow-up period of 3 years is relatively short.

To our knowledge, this is the first study on the association between clinical and subclinical OCD and psychosis in a general population sample using a longitudinal design. Increased comorbidity rates between OCD and psychosis were found, suggesting an etiological relationship with a partially shared or similar etiological pathway.

The finding that OC symptoms predict psychotic disorder with need for care is important for identifying subjects at risk for psychosis. For clinicians, it can be helpful in follow-up and treatment planning to account for the apparent deleterious effect of OC symptoms on psychosis. However, although there is some evidence for an etiological relationship, the mechanism of the mutual impact of OC and psychotic symptoms is still poorly understood and requires further research.

References

1. Westphal K. Ueber Zwangvorstellungen. Arch Psychiatr Nervenkr 1878;**8**:734–750.
2. Byerly M, Goodman W, Acholonu W, Bugno R, Rush AJ. Obsessive compulsive symptoms in schizophrenia: frequency and clinical features. Schizophr Res 2005;**76**:309–316.
3. Karno M, Golding JM, Sorenson SB, Burnam MA. The epidemiology of obsessive-compulsive disorder in five US communities. Arch Gen Psychiatry 1988;**45**:1094–1099.
4. Kolada JL, Bland RC, Newman SC. Epidemiology of psychiatric disorders in Edmonton. Obsessive-compulsive disorder. Acta Psychiatr Scand Suppl 1994;**376**:24–35.
5. Eisen JL, Rasmussen SA. Obsessive compulsive disorder with psychotic features. J Clin Psychiatry 1993;**54**:373–379.
6. Jahrreis W. Uber Zwangvorstellungen im Verlauf der Schizophrenie. Arch Psychiatr Nervenkr 1926;**77**:740–788.
7. Bland RC, Newman SC, Orn H. Schizophrenia: lifetime co-morbidity in a community sample. Acta Psychiatr Scand 1987;**75**:383–391.
8. Berman I, Merson A, Viegner B, Losonczy MF, Pappas D, Green AI. Obsessions and compulsions as a distinct cluster

of symptoms in schizophrenia: a neuropsychological study. J Nerv Ment Dis 1998;**186**:150–156.
9. Reay R, Mitford E, Mccabe K, Paxton R, Turkington D. Incidence and diagnostic diversity in first-episode psychosis. Acta Psychiatr Scand 2010;**121**:315–319.
10. Scott J, Welham J, Martin G et al. Demographic correlates of psychotic-like experiences in young Australian adults. Acta Psychiatr Scand 2008;**118**:230–237.
11. De Bruijn C, Beun S, De Graaf R, Ten Have M, Denys D. Subthreshold symptoms and obsessive-compulsive disorder: evaluating the diagnostic threshold. Psychol Med 2010;**40**:989–997.
12. Poyurovsky M, Weizman A, Weizman R. Obsessive-compulsive disorder in schizophrenia: clinical characteristics and treatment. CNS Drugs 2004;**18**:989–1010.
13. Lysaker PH, Lancaster RS, Nees MA, Davis LW. Patterns of obsessive-compulsive symptoms and social function in schizophrenia. Psychiatry Res 2004;**125**:139–146.
14. Nechmad A, Ratzoni G, Poyurovsky M et al. Obsessive-compulsive disorder in adolescent schizophrenia patients. Am J Psychiatry 2003;**160**:1002–1004.
15. Ongur D, Goff DC. Obsessive-compulsive symptoms in schizophrenia: associated clinical features, cognitive function and medication status. Schizophr Res 2005;**75**: 349–362.
16. 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.
17. Eisen JL, Beer DA, Pato MT, Venditto TA, Rasmussen SA. Obsessive-compulsive disorder in patients with schizophrenia or schizoaffective disorder. Am J Psychiatry 1997;**154**:271–273.
18. Poyurovsky M, Hramenkov S, Isakov V et al. Obsessive-compulsive disorder in hospitalized patients with chronic schizophrenia. Psychiatry Res 2001;**102**:49–57.
19. Bijl RV, Van Zessen G, Ravelli A, De Rijk C, Langendoen Y. The Netherlands Mental Health Survey and Incidence Study (NEMESIS): objectives and design. Soc Psychiatry Psychiatr Epidemiol 1998;**33**:581–586.
20. Goldberg D, Williams P. User's guide to the GHQ. Windsor: NFER-Nelson, 1988.
21. De Graaf R, Bijl RV, Smit F, Ravelli A, Vollebergh WA. Psychiatric and sociodemographic predictors of attrition in a longitudinal study: The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Am J Epidemiol 2000;**152**:1039–1047.
22. Robins LN, Wing J, Wittchen HU et al. The Composite International Diagnostic Interview. An epidemiologic Instrument suitable for use in conjunction with different diagnostic systems and in different cultures. Arch Gen Psychiatry 1988;**45**:1069–1077.
23. Cottler LB, Robins LN, Grant BF et al. The CIDI-core substance abuse and dependence questions: cross-cultural and nosological issues. The WHO/ADAMHA Field Trial. Br J Psychiatry 1991;**159**:653–658.
24. Wittchen HU. Reliability and validity studies of the WHO – Composite International Diagnostic Interview (CIDI): a critical review. J Psychiatr Res 1994;**28**:57–84.
25. Phelan M, Slade M, Thornicroft G et al. The Camberwell Assessment of Need: the validity and reliability of an instrument to assess the needs of people with severe mental illness. Br J Psychiatry 1995;**167**:589–595.
26. Van Os J, Hanssen M, Bijl RV, Ravelli A. Strauss (1969) revisited: a psychosis continuum in the general population? Schizophr Res 2000;**45**:11–20.
27. Van Os J, Hanssen M, Bijl RV, Vollebergh W. Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. Arch Gen Psychiatry 2001;**58**:663–668.
28. Johns LC, Van Os J. The continuity of psychotic experiences in the general population. Clin Psychol Rev 2001;**21**:1125–1141.
29. Overall J, Gorham D. The Brief Psychiatric Rating Scale (BPRS): recent developments in ascertainment and scaling. Psychopharmacol Bull 1988;**24**:97–99.
30. Lukoff D, Ventura J. Manual for the expanded brief psychiatric rating scale. Schizophr Bull 1986;**12**:594–602.
31. Association AP. Diagnostic and statistic manual of mental disorders, 4th edn. Washington, DC: American Psychiatric Press, 1994.
32. Spitzer RL. Diagnosis and need for treatment are not the same. Arch Gen Psychiatry 1998;**55**:120.
33. Slade M, Phelan M, Thornicroft G, Parkman S. The Camberwell Assessment of Need (CAN): comparison of assessments by staff and patients of the needs of the severely mentally ill. Soc Psychiatry Psychiatr Epidemiol 1996;**31**:109–113.
34. StataCorporation. STATA Statistical Software: Release 11.0. Texas: College Station, 1984–2009.
35. Krabbendam L, Myin-Germeys I, De Graaf R et al. Dimensions of depression, mania and psychosis in the general population. Psychol Med 2004;**34**:1177–1186.
36. Kaymaz N, van Os J. Murray et al. (2004) revisited: is bipolar disorder identical to schizophrenia without developmental impairment? Acta Psychiatr Scand 2009;**120**: 249–252.
37. Bora E, Yucel M, Fornito A, Berk M, Pantelis C. Major psychoses with mixed psychotic and mood symptoms: are mixed psychoses associated with different neurobiological markers? Acta Psychiatr Scand 2008;**118**:172–187.
38. Denys D, Tenney N, Van Megen HJ, De Geus F, Westenberg HG. Axis I and II comorbidity in a large sample of patients with obsessive-compulsive disorder. J Affect Disord 2004;**80**:155–162.
39. Spinella M. Mood in relation to subclinical obsessive-compulsive symptoms. Int J Neurosci 2005;**115**:433–443.
40. Mancebo MC, Garcia AM, Pinto A et al. Juvenile-onset OCD: clinical features in children, adolescents and adults. Acta Psychiatr Scand 2008;**118**:149–159.
41. Braga RJ, Petrides G, Figueira I. Anxiety disorders in schizophrenia. Compr Psychiatry 2004;**45**:460–468.
42. Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Mol Psychiatry 2010;**15**: 53–63.
43. Svirskis T, Korkeila J, Heinimaa M. Axis-I disorders and vulnerability to psychosis. Schizophr Res 2005;**75**:439–446.
44. Lewis G, David AS, Malmberg A, Allebeck P. Non-psychotic psychiatric disorder and subsequent risk of schizophrenia. Cohort study. Br J Psychiatry 2000;**177**:416–420.
45. Weiser M, Reichenberg A, Rabinowitz J et al. Association between nonpsychotic psychiatric diagnoses in adolescent males and subsequent onset of schizophrenia. Arch Gen Psychiatry 2001;**58**:959–964.
46. Darroch J. Biologic synergism and parallelism. Am J Epidemiol 1997;**145**:661–668.
47. Hanssen M, Bak M, Bijl R, Vollebergh W, Van Os J. The incidence and outcome of subclinical psychotic experiences in the general population. Br J Clin Psychol 2005;**44**(Pt 2):181–191.

48. Weissman MM, Bland RC, Canino GJ et al. The cross national epidemiology of obsessive compulsive disorder. The Cross National Collaborative Group. J Clin Psychiatry 1994;**55**(Suppl):5–10.
49. Cromer KR, Schmidt NB, Murphy DL. An investigation of traumatic life events and obsessive-compulsive disorder. Behav Res Ther 2007;**45**:1683–1691.
50. Read J, Van Os J, Morrison AP, Ross CA. Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. Acta Psychiatr Scand 2005;**112**:330–350.
51. Hultman CM, Sparen P, Takei N, Murray RM, Cnattingius S. Prenatal and perinatal risk factors for schizophrenia, affective psychosis, and reactive psychosis of early onset: case–control study. BMJ (Clinical Research Ed.) 1999;**318**:421–426.
52. Vasconcelos MS, Sampaio AS, Hounie AG et al. Prenatal, perinatal, and postnatal risk factors in obsessive-compulsive disorder. Biol Psychiatry 2007;**61**:301–307.
53. Crum RM, Anthony JC. Cocaine use and other suspected risk factors for obsessive-compulsive disorder: a prospective study with data from the Epidemiologic Catchment Area surveys. Drug Alcohol Depend 1993;**31**:281–295.
54. Zohar AH, Ratzoni G, Pauls DL et al. An epidemiological study of obsessive-compulsive disorder and related disorders in Israeli adolescents. J Am Acad Child Adolesc Psychiatry 1992;**31**:1057–1061.
55. Stein DJ. Neurobiology of the obsessive-compulsive spectrum disorders. Biol Psychiatry 2000;**47**:296–304.
56. Gross-Isseroff R, Hermesh H, Zohar J, Weizman A. Neuroimaging communality between schizophrenia and obsessive compulsive disorder: a putative basis for schizo-obsessive disorder? World J Biol Psychiatry 2003;**4**:129–134.
57. Freeman D, Garety PA, Kuipers E, Fowler D, Bebbington PE. A cognitive model of persecutory delusions. Br J Clin Psychol 2002;**41**(Pt 4):331–347.
58. Jenike MA. Clinical practice. Obsessive-compulsive disorder. N Engl J Med 2004;**350**:259–265.
59. Klein DN, Riso LP. Psychiatric disorders: problems of boundaries and comorbidity. In: Costello CG, ed. Basic issues in psychopathology. New York: Guilford Press, 1993:19–66.
60. Regeer EJ, Krabbendam L, De Graaf R, Have MT, Nolen WA, Van Os J. Berkson's bias and the mood dimensions of bipolar disorder. Int J Methods Psychiatr Res 2009;**18**:279–286.
61. Maric N, Myin-Germeys I, Delespaul P, De Graaf R, Vollebergh W, Van Os J. Is our concept of schizophrenia influenced by Berkson's bias? Soc Psychiatry Psychiatr Epidemiol 2004;**39**:600–605.
62. Niendam TA, Berzak J, Cannon TD, Bearden CE. Obsessive compulsive symptoms in the psychosis prodrome: correlates of clinical and functional outcome. Schizophr Res 2009;**108**:170–175.
63. Tien AY, Eaton WW. Psychopathologic precursors and sociodemographic risk factors for the schizophrenia syndrome. Arch Gen Psychiatry 1992;**49**:37–46.
64. Goodwin DW, Guze SB, Robins E. Follow-up studies in obsessional neurosis. Arch Gen Psychiatry 1969; **20**:182–187.
65. Poyurovsky M, Koran LM. Obsessive-compulsive disorder (OCD) with schizotypy vs. schizophrenia with OCD: diagnostic dilemmas and therapeutic implications. J Psychiatr Res 2005;**39**:399–408.
66. Salkovskis PM. Understanding and treating obsessive-compulsive disorder. Behav Res Ther 1999;**37**(Suppl 1):S29–S52.
67. Maher BA. Anomalous experience and delusional thinking: the logic of explanations. In: Maher BA, Oltmanns TF, eds. Delusional beliefs. Oxford, England: John Wiley & Sons, 1988:15–33.