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Clinical Aspects of Schizo-Obsessive Disorder – A Systematic Review

Aspetos Clínicos da Perturbação Esquizo-Obsessiva – Revisão Sistemática

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Clinical Aspects of Schizo-Obsessive Disorder – A Systematic Review

ORIENTADOR

Professor Doutor Manuel Fernandez Esteves

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Faculdade de Medicina da Universidade do Porto, 31 / 03 / 2021

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Dedicatória

Aos meus pais, responsáveis por mais um sucesso – os meus heróis.

Aos meus avós, que vivem este e todos os outros como se fossem deles – e são.

Ao Hugo, por me mostrar possibilidades onde só vejo dificuldades, a minha maior companhia.

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Clinical Aspects of Schizo-Obsessive Disorder – A Systematic Review

Running title: Aspects of Schizo-Obsessive Disorder – Review

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Clinical Aspects of Schizo-Obsessive Disorder – A Systematic Review

Mariana Nobre and Manuel Esteves

Abstract

Objective

The occurrence of OCS or OCD in the context of schizophrenia has been observed since the early 20th century. This comorbidity was proposed as a nosological entity in 1997 and has been a matter of scientific interest since then. This work aims to review clinical data available on the Schizo-Obsessive Disorder and to clarify its psychopathological importance in clinical practice using a systematic approach.

Methods

Research was carried out according to PRISMA guidelines in three databases – MEDLINE, Scopus and Web of Science. The references obtained were then screened and scanned for eligibility by two investigators. Risk of bias was assessed for each study with NIH tools.

Results and discussion

265 references were obtained and 46 studies were included. The found prevalence of OCS and OCD in schizophrenia was 30.7% and 12.1-12.3%, respectively. Other epidemiological and clinical data were reviewed, including differential diagnosis between delusions and obsessions and the several contexts in which OCS or OCD occur in relation to schizophrenia.

Conclusion

Schizo-obsessive disorder is considered a clinical spectrum. OCS in schizophrenia are similar to those observed in OCD. Evidence on schizophrenia symptoms in this context is conflicting. This dimension of schizophrenia and OCS comorbidity remains controversial.

Keywords: Schizophrenia; Obsessive-Compulsive Disorder; Psychopathology; Comorbidity

Introduction

The association between obsessions and schizophrenia has long been observed, as early as a century ago. Eugen Bleuler, considered one of the fathers of modern psychiatry, suggested in 1911 that patients with chronic obsessions might be schizophrenic. Decades later, this relationship justified a literary review by Erwin Stengel in 1945.[1] In 1997, Zohar brought attention to the importance of the research on this disorder and questioned if this was a new nosological category.[2] Today, this schizo-obsessive entity is well recognized and has been the subject of investigation. Whether this entity is a pure comorbidity, a subtype of schizophrenia or a distinct psychopathological condition remains in question. This review aims to summarize clinical evidence available on the schizo-obsessive disorder in a systematic approach, to present its known characteristics and hopefully provide a tool for psychiatrists in the recognition of this association.

Methods

This systematic review was conducted following the PRISMA statement[3] guidelines.

Research

The data in this study were retrieved from three databases – MEDLINE, Scopus and Web of Science. The date of the last search was 28-12-2020. The query used in all databases was “schizo obsessive disorder”. No filters or limits were used.

Eligibility criteria and study selection

The references obtained were firstly screened independently by two investigators (MN + ME) based on their title and abstract. Narrative reviews, observational studies, and systematic reviews with or without meta-analysis were eligible for screening if the title or abstract mentioned a) schizo-obsessive disorder, b) schizophrenia with obsessive-compulsive symptoms or c) comorbidity between obsessive-compulsive disorder and schizophrenia. All these records were screened regardless of publication date. Case reports, opinion articles and letters were excluded. Discrepancies in selected references were resolved by consensus between both investigators.

Studies were then included in the review if epidemiological, etiological, pathophysiological, clinical or prognostic aspects were discussed. Additional references were obtained by scrutinizing the bibliography of relevant articles.

Data collection process and items

Data were collected by both investigators (MN+ME) using a Word form (title of publication, author, year of publication, study type, country of study, setting, number of participants, diagnostic criteria for schizophrenia and OCD, scores used for assessing psychotic symptoms, scores used for assessing OCS and study conclusions).

Quality of included studies

Regarding quality of the included studies, risk of bias was assessed independently by both investigators for each study at study level using the Quality Assessment Tools from the National Institutes of Health according to the type of study.[4,5] Risk of bias of narrative reviews was not assessed.

Results

The database search yielded 250 references – 81 in MEDLINE, 89 in Scopus and 80 in Web of Science. 131 were duplicated and were removed. 119 were screened of which 74 were excluded. The remaining 45 were sought for retrieval and 43 were assessed for eligibility. All were eligible and included. 3 articles identified by citation search were also included. The total number of studies included was 46. The PRISMA flow-chart of this process is represented in Fig. **1**.

Study characteristics

14 narrative reviews, 24 observational studies, 7 systematic reviews and 1 book chapter were included.

Table **1** lists the included narrative reviews and their most relevant characteristics.

All observational studies had a cross-sectional design, except one with a prospective design, and included inpatients or outpatients. Consecutive sampling was used for patients with schizophrenia with obsessive-compulsive symptoms (OCS) or obsessive-compulsive disorder (OCD) and consecutive or matched sampling was used for the control groups [patients with “pure” schizophrenia (SZ), patients with “pure” obsessive-compulsive disorder (OCD) or healthy subjects (HS)]. The Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition (SCID-I/P) was used for schizophrenia and OCD diagnosis. The Scale for the Assessment of Positive Symptoms (SAPS), the Scale for the Assessment of Negative Symptoms (SANS) and the Positive and Negative Syndrome Scale (PANSS) were used to assess schizophrenia positive and negative symptoms severity. Yale–Brown Obsessive Compulsive Scale (Y-

BOCS), Brown Assessment of Beliefs Scale (BABS) and Modified Maudsley Obsessive-Compulsive Inventory (MMOCI) were used to assess obsessions and compulsions severity. The Scale to Assess Unawareness in Mental Disorder (SUMD) was used to assess disorder insight. Other scales and scores were used depending on the variable studied in each article.

Table **2** lists the included observational studies and their characteristics.

Of the seven systematic reviews, four have meta-analysis and were rated as good quality studies. The other three do not have meta-analysis and were found to have fair quality. Table **3** lists the included systematic reviews and their most relevant characteristics.

Discussion

General aspects

The term schizo-obsessive disorder (SOD) refers to a clinical spectrum of disorders with schizophrenia characteristics and OCD characteristics. Poyurovsky and colleagues have proposed diagnostic criteria for this disorder.[6] In this work, we review the clinical aspects of patients with schizophrenia and OCS or OCD. According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V), schizophrenia is characterized by delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior – positive symptoms – and negative symptoms (e.g., diminished emotional expression or avolition). OCD is characterized by obsessions and/or delusions.[7]

Epidemiology

In a meta-analysis, the prevalence of OCS in schizophrenia was estimated in 30.7%.[8] The prevalence of OCD in two different meta-analyses was estimated in 12.1% (95% CI 7.0-17.1%) and 12.3% (95% CI 9.7%-15.4%).[8,9] This is considerably higher than the lifetime risk in general population (1.9%).[10]

Schizophrenia and OCD aggregate strongly in families similarly to other psychopathologies. In a cross-sectional study, the authors hypothesize that the OC component of schizo-obsessive disorder translates in an occurrence of OCD-related disorders in first-degree relatives higher than the observed in “pure” schizophrenia patients, similarly to what happens in first-degree relatives of OCD patients. The morbid risk for OCD-spectrum disorders in relatives of schizo-obsessive patients was 6.63%, four times the observed risk in “pure” schizophrenia patients and in general population. Additionally, this study found that the risk

of SOD in first-degree relatives of SOD patients was 2.2% compared to 0% in relatives of pure SZ patients. This finding supports the hypothesis that schizo-obsessive disorder has familial aggregation.[11]

Clinical aspects

Both schizophrenia and OCD are chronic psychopathologies with episodes of symptoms exacerbation.[12] The clinical differentiation between schizophrenia delusions and OCD obsessions is nuclear in the approach of schizo-obsessive disorder. [12-16]

Differentiation between obsessions and delusions

In this section of the work, we will first present the DSM-5 definitions of delusions and obsessions and then proceed to expose their differential characteristics.

Delusions and obsessions are disturbances of thought. According to the DSM-5, delusions are false beliefs that result from an incorrect inference of reality and so are disturbances of the content of thought. They persist even when confronted with conflicting evidence. Depending on the content of the delusion, it may be a cause of anxiety and distress.[7] Obsessions are recurrent and persistent thoughts, impulses or images experienced as intrusive and unwanted that cause considering anxiety or suffering. Therefore, they are disturbances of the possession of thought. This means that delusions are beliefs recognized as truthful and entertained by the patient while obsessions are intruding, typically not recognized as truthful and opposed by the patient. [7,15]

A delusional patient may react with a repetitive behavior or mental act thematically related to the content of the delusion in an attempt to reduce the anxiety caused by it, e.g., a patient with persecutory delusion may check repeatedly if his/her persecutor is watching him/her. Compulsions are repetitive behaviors or mental acts with the intent of neutralizing the obsession, but they do not have a realistic connection to what they are aiming to neutralize or are clearly excessive.[7,15]

It has been suggested that obsessions and delusions may be differentiated by their content (e.g. contamination *vs* persecution), insight into the nature of the thought, idea or image (ego-dystonic obsession *vs* ego-syntonic delusion), anxiety source (sense of invasion of obsessions *vs* content associated anxiety in delusions) and associated rituals previously described.[12] In everyday clinical practice, this categorization is not always achievable because these characteristics are not maintained in same cases (e.g. in OCD with

poor insight[17]). Although this differential diagnosis remains a challenge and may not be always possible[16,18], clinicians must be aware of the clinical and possibly prognostic value of it.

OCS/OCD in psychotic disorders prodrome

The occurrence of OCS and OCD in psychotic disorders prodrome was studied in a population of ultra-high risk of psychosis (UHRP) adolescents (aged 12-22).[19] 20% of the participants were found to have OCD, a considerably higher prevalence than the observed in general population. The most common obsession in this population is aggression and the most common compulsions are checking and hoarding.[20] This subset of patients did not differ from UHRP patients without OCD in schizophrenia symptoms severity and the OCD diagnosis did not correlate to progression to psychosis. However, these OCS were responsible for higher distress and suicidal ideation in the OCD+ population.[19,21] It is suggested that the DSM-5 categorical diagnosis of OCD might dilute the effect of OCS in schizophrenia symptoms severity.[22]
Another study suggests that OCD might be a useful marker in UHRP for later progression to schizophrenia.[23]

OCS/OCD during the course of schizophrenia

In a study including 133 schizo-obsessive patients, OCS onset occurred a mean of 3 years earlier than psychotic symptoms onset. In this and other studies, OCS preceded psychotic symptoms in half the patients. Psychotic symptoms preceded OCS in a quarter of patients and the disorders had a simultaneous onset in the remaining sample.[12,23-25] In comparison with 113 patients with "pure" schizophrenia, the SOD group had an earlier schizophrenia onset. [23,26-28] This was also found in the adolescent population.[24] In a systematic review, OCD diagnosis was associated with a three-fold higher risk of a later schizophrenia diagnosis compared to "pure" schizophrenia patients.[20,29]

Obsessive-compulsive symptoms

The majority of schizo-obsessive patients have both obsessions and compulsions.[12,24,27,28,30-33] OCS in schizophrenia are mostly assessed using the Y-BOCS score. The most prevalent obsessions in SOD were found to be contamination and aggression/harming, although other types were documented.[20,24,25,30,32-35] The most prevalent compulsions are washing, doubting and checking.[24,30,32,34,36] Regarding severity, the

majority of patients had moderate to severe OCS, associated with Y-BOCS scores between 15 and 28.[24,32,34,37]

Regarding insight, most SOD patients had good or fair insight into OCS.[12,30] This proportion is compatible to that observed in "pure" OCD. Awareness of schizophrenia was not modifiable by the present of OCS.[30] These findings overlap with those found in adolescents with schizophrenia.[31]

The referred characteristics of OCS in the context of schizophrenia do not differ from OCS in OCD.[21,33]

Psychotic symptoms

The effect of OCS on the schizophrenia psychotic symptoms has been widely studied and the results remain inconclusive. Psychotic symptoms are commonly assessed with SAPS, SANS and PANSS scores.

It has been suggested that OCD has a protective effect only in early stages of schizophrenia illness.[12,25,38]

In some studies, higher scores of negative symptomatology were observed in chronic schizophrenia patients with OCD. [12,34] In other studies, positive symptoms were correlated with moderate and severe OCS.[26,39,40]

Another study found that SOD had lesser disability and a better prognosis then "pure" schizophrenia.[38]

In many studies, OCS were found to be independent from psychotic symptoms.[12,33,41,42]

The previously mentioned categorical diagnosis of OCD instead of a dimension interpretation of OCS might account for these disparities.[22]

Comorbidities and functional impairments

Regarding other psychopathology, SOD was associated with a higher rate of anxiety and personality disorders[28,32,38] as well as with higher depression scores[38]. Adolescent schizo-obsessive patients were found to have a higher rate of OCD disorders, particularly tic disorders, compared to "pure" schizophrenia patients[24]. In their adult counterparts, higher rates of body dysmorphia and tic disorders were found.[43]

A meta-analysis that studied cognitive functioning found no differences between schizophrenic patients with or without OCD.[44] Another study corroborated this finding.[45] The only variable associated with worse cognitive functioning was advanced age. Considering that an older age correlates with longer duration of disease, this is in line with other studies that found a negative effect of OCS in schizophrenic chronic illness.[44] Additionally, 23.5% (*vs* 12.1% in all schizo-obsessive patients) of patients from a chronic hospitalized population had concomitant OCD. [32]

Other studies found schizo-obsessive patients were more cognitively impaired, namely had more neurological soft signs (markers of neurological disability)[33], a more impaired abstract thinking[40], more

eye-tracking disfunction[46] and a higher attention deficit[47] than their "pure" schizophrenic counterparts. These findings support the double jeopardy hypothesis which proposes that schizo-obsessive patients are more disabled than "pure" schizophrenic and "pure" OCD patients because of the overlap between pathologies.[40]

Clinical outcomes

Schizo-obsessive patients had a higher number of hospitalizations, more psychiatric emergencies and more previous suicide attempts compared to OCD patients.[41,48] In some studies, schizo-obsessive patients were found to have a poorer quality of life than their schizophrenia counterparts.[12,25,34,40,49-51]

In a population of clozapine-treated schizo-obsessive patients, 13.8% had at least one suicide attempt.[48]

Antipsychotics-induced or exacerbated OCS/OCD

The induction or exacerbation of OCS or OCD in schizophrenia in the context of antipsychotic treatment has been described.[12,20,29,35,52] Clozapine, an atypical antipsychotic, is the most frequently associated with this phenomenon.[20] In a population of 65 clozapine-treated schizophrenia patients, 29.2% had *de novo* OCS and 13.8% had *de novo* OCD.[48] A predominant anti-serotonergic profile combined with low anti-dopaminergic potency might explain this pro-obsessive feature of clozapine.[39] This effect is expected to be duration and dose-dependent.[14,48]

Strengths, limitations and future directions

In this review, we carried out a systematic research on the clinical aspects of schizo-obsessive disorder and successfully summarized up-to-date evidence while complying to PRISMA guidelines.

This systematic review has several limitations that reflect the limitations of the gathered research. Not all studies included were deemed of "good quality" and therefore risk of bias was not negligible. Regarding the methods of the cited works, there is not a standardized assessment of OCS. While some studies consider only DSM-IV OCD diagnosis, others consider Y-BOCS evaluated OCS, in some cases as a singular phenomenon (with or without OCS) and in others as a severity-categorized one (mild, moderate or severe). For these reasons, large prospective studies are still lacking, particularly in UHRP populations, as well as

clinical trials focused on the association between antipsychotic treatment and onset or exacerbation of OCS in schizophrenia.

Conclusion

Schizo-obsessive disorder is a clinical spectrum characterized by positive and negative schizophrenia symptoms co-existing with OCS similar to those observed in OCD. Evidence on the relationship between OCS and schizophrenia symptoms severity is conflicting. However, many authors have found that this disorder is associated with a poorer quality of life. Atypical antipsychotics, particularly clozapine, appear to have a role in inducing or exacerbating OCS. For these reasons, it is a clinical entity with which psychiatrists should be familiarized.

In light of the evidence reviewed in this work, schizo-obsessive disorder can be considered a subtype of schizophrenia and not a distinct clinical entity, but the controversy remains.

We hope this study might aid clinicians in the identification of this dimension of schizophrenia psychopathology and in patient management.

Disclosure

The authors declare that they have no conflict of interest. No funding was received for this work.

References

1. Rosen I. The clinical significance of obsessions in schizophrenia. J Ment Sci 1957;103(433):773-85. (In eng). DOI: 10.1192/bjp.103.433.773.
2. Zohar J. Is There Room for a New Diagnostic Subtype—The Schizo-obsessive Subtype? CNS Spectrums 1997;2(3):49-50. DOI: 10.1017/S1092852900004612.
3. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Systematic Reviews 2021;10(1):89. DOI: 10.1186/s13643-021-01626-4.
4. Health NIo. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools).
5. Health NIo. Quality Assessment of Systematic Reviews and Meta-Analyses. (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools).
6. Poyurovsky M, Zohar J, Glick I, Koran LM, Weizman R, Tandon R, et al. Obsessive-compulsive symptoms in schizophrenia: implications for future psychiatric classifications. Comprehensive Psychiatry 2012;53(5):480-483. (Article) (In English). DOI: 10.1016/j.comppsych.2011.08.009.
7. Association AP. Diagnostic and statistical manual of mental disorders: DSM-5™, 5th ed. Arlington, VA, US: American Psychiatric Publishing, Inc., 2013.
8. Swets M, Dekker J, van Emmerik-van Oortmerssen K, Smid GE, Smit F, de Haan L, et al. The obsessive compulsive spectrum in schizophrenia, a meta-analysis and meta-regression exploring prevalence rates. Schizophr Res 2014;152(2-3):458-68. (In eng). DOI: 10.1016/j.schres.2013.10.033.

9. Achim AM, Maziade M, Raymond E, Olivier D, Mérette C, Roy MA. How prevalent are anxiety disorders in schizophrenia? A meta-analysis and critical review on a significant association. Schizophr Bull 2011;37(4):811-21. (In eng). DOI: 10.1093/schbul/sbp148.
10. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62(6):593-602. (In eng). DOI: 10.1001/archpsyc.62.6.593.
11. Poyurovsky M, Kriss V, Weisman G, Faragian S, Schneidman M, Fuchs C, et al. Familial aggregation of schizophrenia-spectrum disorders and obsessive-compulsive associated disorders in schizophrenia probands with and without OCD. Am J Med Genet B Neuropsychiatr Genet 2005;133b(1):31-6. (In eng). DOI: 10.1002/ajmg.b.30148.
12. Poyurovsky M, Weizman A, Weizman R. Obsessive-compulsive disorder in schizophrenia - Clinical characteristics and treatment. Cns Drugs 2004;18(14):989-1010. (Book Chapter) (In English). DOI: 10.2165/00023210-200418140-00004.
13. Bottas A, Cooke RG, Richter MA. Comorbidity and pathophysiology of obsessive-compulsive disorder in schizophrenia: Is there evidence for a schizo-obsessive subtype of schizophrenia? Journal of Psychiatry & Neuroscience 2005;30(3):187-193. (Review) (In English) (<Go to ISI>://WOS:000229154300004).
14. Passos R, Ferreira MD, Morgado P. Comorbidity between Schizophrenia and Obsessive-Compulsive Disorder: A Literature Review. Psilogos 2014;12(2):77-85. (Review) (In Portuguese) (<Go to ISI>://WOS:000216830800007).
15. Oulis P, Konstantakopoulos G, Lykouras L, Michalopoulou PG. Differential diagnosis of obsessive-compulsive symptoms from delusions in schizophrenia: A phenomenological approach. World J Psychiatry 2013;3(3):50-6. (In eng). DOI: 10.5498/wjp.v3.i3.50.
16. Zhou TH, Baytunca B, Yu X, Öngür D. Schizo-Obsessive Disorder: the Epidemiology, Diagnosis, and Treatment of Comorbid Schizophrenia and OCD. Current Treatment Options in Psychiatry 2016;3(3):235-245. (Review). DOI: 10.1007/s40501-016-0085-6.
17. Hollander E, Rosen J, Black D, Carrasco JL, Cottraux J, DeCaria C, et al. OC spectrum disorders: The impulsive and schizo-obsessive clusters. CNS Spectrums 1999;4(5 SUPPL. 3):16-21. (Review). DOI: 10.1017/s1092852900007379.
18. Attademo L, Bernardini F, Quartesan R. Schizo-Obsessive Disorder: A Brief Report of Neuroimaging Findings. Psychopathology 2016;49(1):1-4. (In eng). DOI: 10.1159/000443837.
19. 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(1-3):170-5. (In eng). DOI: 10.1016/j.schres.2008.11.023.
20. Sharma LP, Reddy YCJ. Obsessive-compulsive disorder comorbid with schizophrenia and bipolar disorder. Indian J Psychiatry 2019;61(Suppl 1):S140-s148. (In eng). DOI: 10.4103/psychiatry.IndianJPsychiatry_527_18.
21. Frias-Ibanez A, Palma-Sevillano C, Farriols-Hernando N. Comorbidity between obsessive-compulsive disorder and schizophrenia: Prevalence, explanatory theories, and nosological status. Actas Espanolas De Psiquiatria 2014;42(1):28-38. (Review) (In English) (<Go to ISI>://WOS:000333138700004).
22. Cunill R, Castells X. Schizo-Obsessive Disorder. In: Ritsner MS, ed. Handbook of Schizophrenia Spectrum Disorders, Vol II: Phenotypic and Endophenotypic Presentations. Berlin: Springer-Verlag Berlin; 2011:403-448.
23. Faragian S, Fuchs C, Pashinian A, Weizman R, Weizman A, Poyurovsky M. Age-of-onset of schizophrenic and obsessive-compulsive symptoms in patients with schizo-obsessive disorder. Psychiatry Research 2012;197(1-2):19-22. (Article) (In English). DOI: 10.1016/j.psychres.2012.02.024.
24. Poyurovsky M, Faragian S, Shabeta A, Kosov A. Comparison of clinical characteristics, co-morbidity and pharmacotherapy in adolescent schizophrenia patients with and without obsessive-compulsive disorder. Psychiatry Research 2008;159(1-2):133-139. (Article) (In English). DOI: 10.1016/j.psychres.2007.06.010.
25. de Haan L, Sterk B, Wouters L, Linszen DH. The 5-year course of obsessive-compulsive symptoms and obsessive-compulsive disorder in first-episode schizophrenia and related disorders. Schizophr Bull 2013;39(1):151-60. (In eng). DOI: 10.1093/schbul/sbr077.
26. Owashi T, Ota A, Otsubo T, Susa Y, Kamijima K. Obsessive-compulsive disorder and obsessive-compulsive symptoms in Japanese inpatients with chronic schizophrenia - a possible schizophrenic subtype. Psychiatry Res 2010;179(3):241-6. (In eng). DOI: 10.1016/j.psychres.2009.08.003.

27. Devi S, Rao NP, Badamath S, Chandrashekhar CR, Janardhan Reddy YC. Prevalence and clinical correlates of obsessive-compulsive disorder in schizophrenia. Compr Psychiatry 2015;56:141-8. (In eng). DOI: 10.1016/j.comppsych.2014.09.015.
28. Üçok A, Ceylan ME, Tihan AK, Lapçin S, Ger C, Tükel R. Obsessive compulsive disorder and symptoms may have different effects on schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2011;35(2):429-33. (In eng). DOI: 10.1016/j.pnpbp.2010.08.021.
29. du Montcel CT, Pelissolo A, Schurhoff F, Pignon B. Obsessive-Compulsive Symptoms in Schizophrenia: an Up-To-Date Review of Literature. Current Psychiatry Reports 2019;21(8):8. (Review) (In English). DOI: 10.1007/s11920-019-1051-y.
30. Poyurovsky M, Faragian S, Kleinman-Balush V, Pashinian A, Kurs R, Fuchs C. Awareness of illness and insight into obsessive-compulsive symptoms in schizophrenia patients with obsessive-compulsive disorder. Journal of Nervous and Mental Disease 2007;195(9):765-768. (Article) (In English). DOI: 10.1097/NMD.0b013e318142ce67.
31. Faragian S, Kurs R, Poyurovsky M. Insight into obsessive-compulsive symptoms and awareness of illness in adolescent schizophrenia patients with and without OCD. Child Psychiatry Hum Dev 2008;39(1):39-48. (In eng). DOI: 10.1007/s10578-007-0069-2.
32. Poyurovsky M, Hramenkov S, Isakov V, Rauchverger B, Modai I, Schneidman M, et al. Obsessive-compulsive disorder in hospitalized patients with chronic schizophrenia. Psychiatry Research 2001;102(1):49-57. (Article) (In English). DOI: 10.1016/s0165-1781(01)00238-4.
33. Sevincok L, Akoglu A, Arslantas H. Schizo-obsessive and obsessive-compulsive disorder: Comparison of clinical characteristics and neurological soft signs. Psychiatry Research 2006;145(2-3):241-248. (Article) (In English). DOI: 10.1016/j.psychres.2005.11.010.
34. Grover S, Sahoo S, Surendran I. Obsessive-compulsive symptoms in schizophrenia: a review. Acta Neuropsychiatr 2018:1-11. (In eng). DOI: 10.1017/neu.2018.27.
35. Toro Martínez E. [Schizophrenia with obsessive-compulsive symptoms or the group of schizo-obsessive schizophrenias: clinical characteristics and prognosis]. Vertex 2008;19(79):114-22. (In spa).
36. Doyle M, Chorcorain AN, Griffith E, Trimble T, O'Callaghan E. Obsessive compulsive symptoms in patients with Schizophrenia on Clozapine and with Obsessive Compulsive disorder: a comparison study. Compr Psychiatry 2014;55(1):130-6. (In eng). DOI: 10.1016/j.comppsych.2013.09.001.
37. Menculini G, Balducci PM, Attademo L, Bernardini F, Lucarini E, Moretti P, et al. Obsessive-compulsive symptoms and schizophrenia spectrum disorders: the impact on clinical and psychopathological features. A descriptive study on acute inpatients. Journal of Psychopathology 2019;25(2):58-62. (Article) (In English) (<Go to ISI>://WOS:000474388400003).
38. Rajkumara RP, Reddy YCJ, Kandavel T. Clinical profile of "schizo-obsessive" disorder: a comparative study. Comprehensive Psychiatry 2008;49(3):262-268. (Article) (In English). DOI: 10.1016/j.comppsych.2007.09.006.
39. Kumar M, Sharma P, Goel N. Impact of Obsessive Compulsive Symptoms in Schizophrenia: A Clinical Study. International Journal of Scientific Study 2015;2(12):80-83. (Article) (In English). DOI: 10.17354/ijss/2015/110.
40. Cunill R, Huerta-Ramos E, Castells X. The effect of obsessive-compulsive symptomatology on executive functions in schizophrenia: a systematic review and meta-analysis. Psychiatry Res 2013;210(1):21-8. (In eng). DOI: 10.1016/j.psychres.2013.05.029.
41. Frías A, Palma C, Farriols N, Salvador A, Bonet J, Bernáldez I. Psychopathology and quality of life among patients with comorbidity between schizophrenia spectrum disorder and obsessive-compulsive disorder: no evidence for a "schizo-obsessive" subtype. Compr Psychiatry 2014;55(5):1165-73. (In eng). DOI: 10.1016/j.comppsych.2014.03.016.
42. Tonna M, Ottoni R, Paglia F, Monici A, Ossola P, C DEP, et al. Obsessive-Compulsive Symptoms in Schizophrenia and in Obsessive-Compulsive Disorder: Differences and Similarities. J Psychiatr Pract 2016;22(2):111-6. (In eng). DOI: 10.1097/pra.0000000000000131.
43. Poyurovsky M, Fuchs C, Faragian S, Kriss V, Weisman G, Pashinian A, et al. Preferential aggregation of obsessive-compulsive spectrum disorders in schizophrenia patients with obsessive-compulsive disorder. Canadian Journal of Psychiatry-Revue Canadienne De Psychiatrie 2006;51(12):746-754. (Article) (In English). DOI: 10.1177/070674370605101204.
44. Dijkstra L, Vermeulen J, de Haan L, Schirmbeck F. Meta-analysis of cognitive functioning in patients with psychotic disorders and obsessive-compulsive symptoms. Eur Arch Psychiatry Clin Neurosci 2020 (In eng). DOI: 10.1007/s00406-020-01174-3.
45. Meijer JH, Swets M, Keeman S, Nieman DH, Meijer CJ. Is a schizo-obsessive subtype associated with cognitive impairment? Results from a large cross-sectional study in patients with

psychosis and their unaffected relatives. J Nerv Ment Dis 2013;201(1):30-5. (In eng). DOI: 10.1097/NMD.0b013e31827ab2b2.
46. Docherty AR, Coleman MJ, Deutsch CK, Levy DL. COMPARISON OF PUTATIVE ENDOPHENOTYPES IN SCHIZOPHRENIA PATIENTS WITH AND WITHOUT OBSESSIVE-COMPULSIVE DISORDER: IS THERE EVIDENCE FOR A SCHIZO-OBSESSIVE SUBTYPE? Schizophrenia Bulletin 2011;37:3-3. (Meeting Abstract) (In English) (<Go to ISI>://WOS:000287746000010).
47. Gershoni A, Hermesh H, Fineberg NA, Eilam D. Spatial behavior reflects the mental disorder in OCD patients with and without comorbid schizophrenia. CNS Spectr 2014;19(1):90-103. (In eng). DOI: 10.1017/s1092852913000424.
48. Szmulewicz AG, Smith JM, Valerio MP. Suicidality in clozapine-treated patients with schizophrenia: role of obsessive-compulsive symptoms. Psychiatry Res 2015;230(1):50-5. (In eng). DOI: 10.1016/j.psychres.2015.07.089.
49. Lysaker PH, Whitney KA. Obsessive-compulsive symptoms in schizophrenia: prevalence, correlates and treatment. Expert Rev Neurother 2009;9(1):99-107. (In eng). DOI: 10.1586/14737175.9.1.99.
50. Dominguez RA, Backman KE, Lugo SC. Demographics, Prevalence, and Clinical Features of the Schizo-obsessive Subtype of Schizophrenia. CNS Spectr 1999;4(12):50-6. (In eng). DOI: 10.1017/s1092852900006829.
51. Loyzaga C, Nicolini H, Apiquian R, Fresan A. An approach to schizo-obssesive phenomena. Salud Mental 2002;25(3):12-18. (Article) (In Spanish) (<Go to ISI>://WOS:000177264100002).
52. Scotti-Muzzi E, Saide OL. Schizo-obsessive spectrum disorders: an update. Cns Spectrums 2017;22(3):258-272. (Review) (In English). DOI: 10.1017/s1092852916000390.

Figures and tables

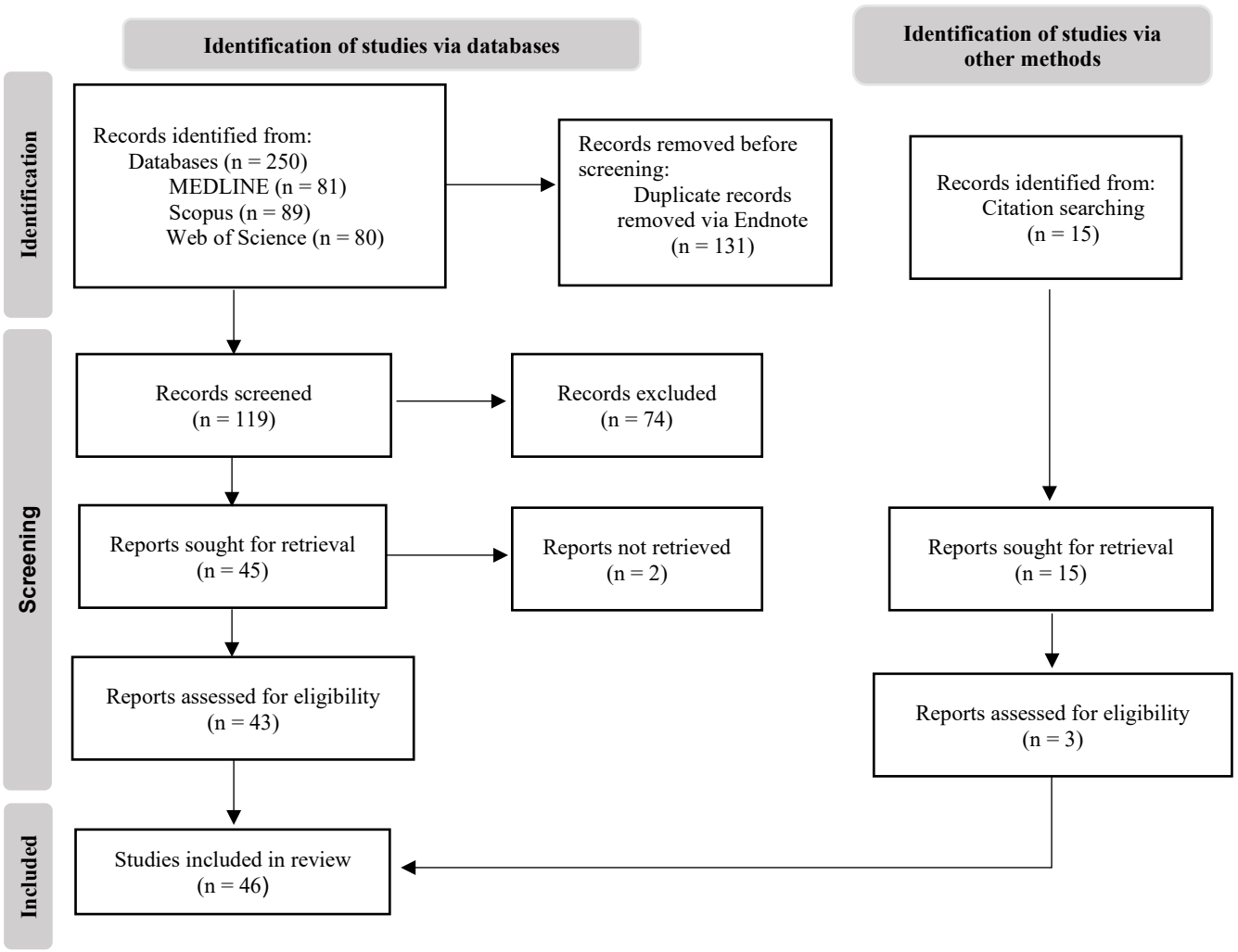

Fig. 1 PRISMA[3] flow diagram for search and screening

Table 1 Narrative reviews characteristics

Reference	Study type	Main findings and conclusions
Zohar, J. (1997)[2]	Narrative review	- Suggests that schizo-obsessive disorder has poor prognosis and specific response to antipsychotics.
Poyurovsky, M. *et al.* (2012)[6]	Narrative review	- Proposes diagnostic criteria for an obsessive-compulsive symptom subgroup of schizophrenia.
Poyurovsky, M. *et al.* (2004)[12]	Narrative review	- Supports the hypothesis that OCS and OCD can have a protective effect in early schizophrenia but contribute to a worse prognosis in chronic illness.
Bottas, A. *et al.* (2005)[13]	Narrative review	- Presents the hypothesis that the effect of OCS in schizophrenia depends on the stage of illness.
Passos, R. *et al.* (2014)[14]	Narrative review	- Distinguishes schizo-obsessive patients in three groups regarding temporal relation between OCS and schizophrenia.
Oulis, P. *et al.* (2013)[15]	Narrative review	- Suggests that the differential diagnosis between obsessions and delusions should be based on the thought source (internal *vs* external).
Zhou, T. H. *et al.* (2016)[16]	Narrative review	- Suggests that there is a continuum between obsessions and delusions and that clinical differentiation might not be possible.
Hollander, E. *et al.* (1999)[17]	Narrative review	- Highlights the clinical importance of differentiating OCD with poor insight from schizophrenia with OCS.
Attademo, L *et al.* (2012)[18]	Narrative review	- States that schizo-obsessive disorder diagnosis is a clinical challenge.
du Montcel, C. T., et al. (2019)[29]	Narrative review	- Concludes that OCS could be considered a severity marker in SZ.
Grover, S. *et al.* (2008)[34]	Narrative review	- Presents that, in a nosology sense, the DSM-5 contemplates co-morbid diagnosis of the two disorders simultaneously.
Toro Martínez E. (2008)[35]	Narrative review	- Highlights the heterogenicity of this subset of schizophrenia disorders.
Lysaker, P.H. *et al.* (2009)[50]	Narrative review	- Concludes that OCS in the context of SZ translate in a worse prognosis.
Loyzaga C., *et al* (2002)[52]	Narrative review.	- Presents that that patients who present the SOD have more severe symptom and worst prognosis.

Table 2 Observational studies characteristics

Reference	Study type	Setting	N of participants	Scores used	Risk of bias	Main findings and conclusions
Poyurovsky, M. *et al.* (2005)[11]	Cross-sectional	Inpatients	57 SZ+OCD 60 SZ 50 healthy subjects	SCID-I/P for SZ and OCD diagnosis Y-BOCS	Quality rating: Good Criteria: - Yes #1-5 - No #5 and #14 - NA #6-13	- Relatives of SZ+OCD patients have a higher risk for SZ+OCS, OCD and OCD spectrum disorders compared to relatives of "pure" SZ patients. - The assessed risk for schizophrenia in relatives of schizophrenia patients is 7.5-9.4%. - These findings support the hypothesis that schizo-obsessive disorder is a distinct clinical entity.
Niendam, T., *et al.* (2009)[19]	Prospective.	UHRP subjects (aged 12-22)	64 UHRP subjects 26 non-prodromal comparison (NPC) subjects	SIPS	Quality rating: Good - Yes #1-4, 6, 9 and 11 - No #5, 7, 10 and 12-14 - NA #8	- 20% had OCS or an OCD diagnosis. - Presents OCS as a prodrome in schizophrenia but does not correlate OCS with a poorer outcome.
Faragian, S. *et al.* (2012)[23]	Cross-sectional	Inpatients	133 SZ+OCD 113 SZ	SCID-I/P for SZ and OCD diagnosis SAPS and SANS Y-BOCS CGI	Quality rating: Good Criteria: - Yes #1-4, #7, #9 and #11 - No #5, #10 and #14 - NA #6, #8 and #13	- In SZ+OCD patients, OCS onset occurs a mean of 3 years earlier than psychotic symptoms. - OCS preceded psychotic symptoms in half the patients, OCS and psychotic symptoms emerged simultaneously in a quarter of patients and psychotic symptoms preceded OCS in the other quarter of patients. - SZ+OCD patients have an earlier onset of SZ compared to non-OCD SZ patients.
Poyurovsky, M., *et al.* (2008)[24]	Cross-sectional	Inpatients	22 SZ+OCD (aged 13–18 years) 22 SZ (aged 13-18 years)	SCID-I/P for SZ and OCD diagnosis SAPS and SANS Y-BOCS CGI	Quality rating: Good Criteria: - Yes #1-4 - No #2 and #14 - NA #6-13	- The clinical characteristics of adolescent SZ+OCD patients are comparable to those observed in their adult counterparts. - Adolescent SZ+OCD patients have an earlier onset of schizophrenia symptoms, a higher prevalence of OCD spectrum disorders but do not have more severe schizophrenic symptoms than "pure" SZ patients.

SCID-I/P Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition | Y-BOCS Yale–Brown Obsessive Compulsive Scale
SIPS Structured Interview for Prodromal Syndromes | BABS Brown Assessment of Beliefs Scale | PANSS Positive and Negative Syndrome Scale
SUMD Scale to Assess Unawareness in Mental Disorder | SAPS Scale for the Assessment of Positive Symptoms | SANS Scale for the Assessment of Negative Symptoms
CGI Clinical Global Impression | SUMD Scale to Assess Unawareness in Mental Disorder

Table 2 (continued)

Reference	Study type	Setting	N of patients	Scores used	Risk of bias	Main findings and conclusions
de Haan *et. al* (2013)[25]	Prospective (5-year follow-up)	First episode psychosis	186 SZ	SCID-I/P for SZ and OCS diagnosis PANSS Y-BOCS MADRS	Quality rating: Good Criteria: - Yes #1-13 - No #14	- Half the patients had OCS at least once during the follow-up period. - OCD was associated with more depression symptoms and worse functioning.
Owashi *et. al* (2010)[26]	Cross-sectional	Inpatients	92 SZ	SCID-I/P for SZ diagnosis MINI for OCD diagnosis Y-BOCS	Quality rating: Good Criteria: - Yes #1-5 and 14 - No #5 and #14 - NA #6-13	- 14.1% were diagnosed with OCD. - SZ+OCS patients had an earlier onset of schizophrenia and more positive symptoms. Y-BOCS had a positive correlation with positive symptom score, but not with negative symptom score. OCS were associated with more severe schizophrenic symptoms.
Devi *et. al* (2015)[27]	Cross-sectional	Inpatients	200 SZ	SCID-I/P for SZ diagnosis PANSS Y-BOCS	Quality rating: Good Criteria: - Yes #1-5 and 14 - No #5 and #14 - NA #6-13	- The majority of patients had both obsessions and compulsions. - SZ+OCS had an earlier onset of schizophrenia.
Üçok *et. al* (2011)[28]	Cross-sectional	Outpatients	184 SZ	SCID for SZ PANSS Y-BOCS	Quality rating: Good Criteria: - Yes #1-5 and 14 - No #5 and #14 - NA #6-13	- SZ+OCD patients had an earlier age of onset and more psychiatric comorbidities- - No relationship was found between PANSS and OCS.

SCID-I/P Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition | PANSS Positive and Negative Syndrome Scale
Y-BOCS Yale–Brown Obsessive Compulsive Scale | MADRS Montgomery Asberg Depression Rating Scale | MINI Mini-International Neuropsychiatric Interview

Table 2 (continued)

Reference	Study type	Setting	N of patients	Scores used	Risk of bias	Main findings and conclusions
Poyurovsky, M. *et al.* (2007)[30]	Cross-sectional	Inpatients	57 SZ+OCD 80 SZ	SCID-I/P for SZ and OCD diagnosis SAPS and SANS Y-BOCS and BABS CGI and SUMD	Quality rating: Good Criteria: - Yes #1-4 - No #5 and #14 - NA #6-13	- Roughly 85% of SZ+OCD patients have a good or fair insight into OCS. The remaining 15% with poor insight are within the 10-36% proportion of patients with "pure" OCD that present poor insight. - Supports the notion that OCS in schizophrenia are independent of core schizophrenia symptoms. - Concludes that the awareness of schizophrenia in SZ+OCS patients is not modifiable by OCS.
Faragian, S. *et al.* (2008)[31]	Cross-sectional	Inpatients (acute psychosis)	22 adolescents with SZ+OCD 22 adolescents with SZ	SCID-I/P for SZ and OCD diagnosis SAPS and SANS Y-BOCS and BABS CGI and SUMD	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- Roughly 85% of adolescent SZ+OCD patients exhibit good or fair insight into OCD. 13.7% have poor insight, a similar proportion to that found in adult subjects. - Roughly 1/3 of these subjects have lack of insight of schizophrenia and efficacy of treatment. - OCD does not modify schizophrenia insight which is compatible with findings in adult subjects.
Poyurovsky, M. *et al.* (2001)[32]	Cross-sectional	Inpatients	35 SZ (chronic hospitalized patients) 14 SZ+OCD	SCID-I/P for SZ and OCD diagnosis SAPS and SANS Y-BOCS CGI	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- 23.5% of this chronic hospitalized patient population had concomitant OCD. - The SZ+OCD patients were 1.7-fold more impaired in social behavior (P=0.032) and had higher levels of anxiety than "pure" SZ and having higher scores in hostility (P=0.002), panic attacks and phobias (P=0.02) and behaviors not otherwise specified (P=0.02). - Supports the hypothesis that OCS and OCD can have a protective effect in early schizophrenia but contribute to a worse prognosis in chronic illness.
Sevincok, L. *et al.* (2006)[33]	Cross-sectional	Outpatients	16 SZ+OCD 23 OCD 23 healthy controls	SCID-I/P for SZ and schizoaffective disorder diagnosis SAPS and SANS Y-BOCS CGI, NES	Quality rating: Good Criteria: - Yes #1-5 and 14 - NA #6-13	- NSS are reportedly more frequently present in schizophrenic patients and they may be present before illness onset. Total NES scores were higher in SZ+OCD patients (P=0.001).

SCID-I/P Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition
SAPS Scale for the Assessment of Positive Symptoms | SANS Scale for the Assessment of Negative Symptoms | PANSS Positive and Negative Syndrome Scale
Y-BOCS Yale–Brown Obsessive Compulsive Scale | BABS Brown Assessment of Beliefs Scale | BABS Brown Assessment of Beliefs Scale
CGI Clinical Global Impression | SUMD Scale to Assess Unawareness in Mental Disorder
NES Neurological Evaluation Scale

Table 2 (continued)

Reference	Study type	Setting	N of participants	Scores used	Risk of bias	Main findings and conclusions
Doyle, M. *et al.* (2014)[36]	Cross-sectional	Outpatients	62 SZ patients treated with clozapine 35 OCD	SCID-I/P for SZ and OCD diagnosis MMOCI BPRS	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- OCD patients had more behavioral symptoms with more distress and SZ-OCS had more cognitive symptoms and less distress. - It suggests that treatment with clozapine may precipitate new OCS with different characteristics than those occurring in the context of OCD.
Menculini, G. *et al.* (2019)[37]	Cross-sectional	Inpatients	76 SZ or schizoaffective disorder patients	SCID-I/P for SZ and schizoaffective disorder diagnosis PANSS Y-BOCS	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- 44.7% patients presented moderate to severe OCS. - SZ+OCS patients had more negative symptoms ($p = 0.003$) and a higher PANSS total score ($p = 0.007$), which includes domains for anxiety and depression. This higher prevalence of negative symptoms is linked to lower functioning and worse quality of life.
Rajkumara, R. P. *et al.* (2008)[38]	Cross-sectional	Outpatients	55 SZ+OCD 50 SZ	SCID-I/P for SZ and OCD diagnosis PANSS Y-BOCS CGI	Quality rating: Good Criteria: - Yes #1-4 - No #5 and #14 - NA #6-13	- SZ+OCD patients were more likely to have first rank symptoms and were less likely to have been hospitalized. - SZ+OCD patients have a higher prevalence of anxiety and personality disorders. This group also has significantly higher depression scores.
Kumar, M., *et al.* (2015)[39]	Cross-sectional	Outpatients	100 SZ categorized in 3 groups according to Y-BOCS score	SCID-I/P for SZ and OCD diagnosis PANSS Y-BOCS	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- 38% of patients have clinically significant OCS and 14% have moderate OCS. - There was a correlation between positive schizophrenia symptoms and OCS in the moderate and severe OCS groups ($P = 0.026$ and 0.037, respectively).
Frías, A. *et al.* (2014)[41]	Cross-sectional	Parcially-hospitalized and outpatients	30 SZ+OCD 37 SZ 30 OCD	SCID-I/P for SZ and schizoaffective disorder diagnosis PANSS Y-BOCS SUMD	Quality rating: Good Criteria: - Yes #1-5 and 14 - NA #6-13	- SZ+OCD patients displayed a poorer insight than their "pure" SZ counterparts ($P = 0.004$). - OCD patients had higher functioning than both psychotic groups. - SZ+OCD patients had a higher number of hospitalizations ($P<0.001$), more psychiatric emergencies ($P = 0.003$), as well as more suicide attempts compared to OCD patients.
Tonna *et. al* (2016)[42]	Cross-sectional	Outpatiens	35 SZ 31 OCD	SCID for SZ and OCD diagnosis PANSS Y-BOCS	Quality rating: Good Criteria: - Yes #1-4 - No #5 and #14 - NA #6-13	- No relationship between Y-BOCS and PANSS was found.

SCID-I/P Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition | GAF Global Assessment of Functioning
MMOCI Modified Maudsley Obsessive-Compulsive Inventory | BPRS Brief Psychiatric Rating Scale
PANSS Positive and Negative Syndrome | Y-BOCS Yale–Brown Obsessive Compulsive
TDI Thought Disorder Index | PANSS Positive and Negative Syndrome Scale
CGI Clinical Global Impression | SUMD Scale to Assess Unawareness in Mental Disorder

Table 2 (continued)

Reference	Study type	Setting	N of participantes	Scores used	Risk of bias	Main findings and conclusions
Poyurovsky, M. *et al* (2006)[43]	Cross-sectional	Inpatients (acute exacerbation)	100 SZ+OCD 100 SZ 35 OCD	SCID-I/P for SZ and OCD diagnosis PANSS Y-BOCS	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- The presence of OCD in schizophrenia patients appears to have an effect on clinical outcomes of schizophrenia, including preferential aggregation of OCD spectrum disorders.
Meijer, J. H. *et al.* (2013)[45]	Cross-sectional	Inpatients and outpatients	984 SZ 1824 first-degree relatives 573 healthy subjects	SCID-I/P for SZ and OCD diagnosis PANSS Y-BOCS CAPE	Quality rating: Good Criteria: - Yes #1-4 - No #5 and 14 - NA #6-13	- This study did not find an association between OCS and cognitive performance. - These results do not support the existence of a schizo-obsessive distinct entity.
Docherty, A. R. *et al.* (2011)[47]	Cross-sectional	Outpatients	15 SZ+OCD 174 SZ 147 healthy subjects	SCID-I/P for SZ and OCD diagnosis BPRS and GAF TDI	Quality rating: Fair Criteria: - Yes #1-2 - No #5 - NR #3-4 - NA #6-13	- SZ and SZ+OCD have similar clinical characteristics except for a higher rate of eye-tracking dysfunction in SZ+OCD.
Gershoni, A. *et al.* (2014)[48]	Cross-sectional	Not specified	6 SZ+OCD 10 OCD Healthy controls	SCID-I/P for SZ diagnosis Y-BOCS	Quality rating: Fair Criteria: - Yes #1-2 - No #3-5 and 14 - NA #6-13	- Patients and respective controls were videotaped in their homes performing motor tasks related to their compulsions. - This study suggests that SZ+OCD patients combine the repetitive acts related to OCD with the ritualistic movements across the room related to attention deficit. On the other hand, OCD is associated with high attention and dysfunction of impulse control while executing compulsions.
Szmulewicz, A. G., *et al.* (2015)[49]	Cross-sectional	Patients treated with clozapine	65 SZ	SCID-I/P for SZ and schizoaffective disorder diagnosis Y-BOCS	Quality rating: Good - Yes #1-5 and 14 - NA #6-13	- Prevalence of OCS was 29.2% and prevalence of OCD was 13.8%. - Y-BOCS was a significant independent predictor of suicide attempts (p=0.04).
Dominguez, R. A. *et al.* (1999)[51]	Cross-sectional	Outpatients	17 SZ+OCD 35 SZ	SCID-I/P for SZ and OCD diagnosis MMOCI	Quality rating: Good Criteria: - Yes #1-4 - No #5 and #14 - NA #6-13	- In the sample of this Miami-based study, 70% of SZ+OCD patients were Hispanic. - The majority of SZ+OCS patients have a satisfactory response to antipsychotic treatment.

SCID-I/P Structured Clinical Interview for DSM-IV Axis I Disorders Patient Edition | PANSS Positive and Negative Syndrome Scale
Y-BOCS Yale–Brown Obsessive Compulsive Scale | CAPE Community Assessment of Psychic Experiences
BPRS Brief Psychiatric Rating Scale | GAF Global Assessment of Functioning | TDI Thought Disorder Index
MMOCI Modified Maudsley Obsessive-Compulsive Inventory

Table 3 Systematic reviews characteristics

Reference	Study type	Risk of bias	Main conclusions
Swets, M. *et. al* (2014)[8]	Systematic review with meta-analysis	Quality rating: Good Criteria - Yes #1-8	- The prevalence of OCS in schizophrenia is 30.7% (95% CI = 23.0%–39.6%). The prevalence of OCD in schizophrenia is 12.3% (95% CI = 9.7%–15.4%).
Achim, A. M. *et al.* (2011)[9]	Systematic review with meta-analysis	Quality rating: Good Criteria - Yes #1-8	- 52 studies were included. The total number of participants was 4032. High prevalence rates of every anxiety disorder were revealed in schizophrenia patients. - Prevalence rates of OCD in schizophrenia patients is 12.1% (7-17.1%).
Sharma, L. P. and Y. C. J. Reddy (2019)[20]	Systematic review	Quality rating: Fair Criteria - Yes #1-4 - No #5-7 - NA #8	- Patients with OCD have a 3-fold higher risk of developing schizophrenia than those without OCD. - Patients whose parents have OCD have an IRR of 4.31 of having schizophrenia.
Frias-Ibanez, A. *et al.* (2014)[21]	Systematic review	Quality rating: Fair Criteria - Yes #1 and #3 - No #2 and #4-7 - NA #8	- Prevalence of OCD comorbidity and schizophrenia is 12-15% of schizophrenia patients, a six-fold prevalence compared to the expected in general population.

IRR Incident risk ratio

Table 3 (continued)

Reference	Study type	Risk of bias	Main conclusions
Cunill, R. *et al.* (2013)[40]	Systematic review with meta-analysis	Quality rating: Good Criteria: - Yes #1-8	- 11 studies were included. The total number of participants was 571, most with a diagnosis of schizophrenia (93.5%). Mean Y-BOCS total score in SZ+OCD patients was 18.5. - This review showed that SZ+OCD patients are more impaired in abstract thinking than schizophrenia patients.
Dijkstra, L *et al.* (2020)[45]	Systematic review with meta-analysis	Quality rating: Good Criteria: - Yes #1-8	- A total of 2738 patients were included. - The study did not find significant differences in cognitive domains between schizophrenic patients with and without OCS.
Scotti-Muzzi, E. and O. L. Saide (2017)[53]	Systematic review	Quality rating: Fair Criteria: - Yes #1 and 3 - No #2, 4-7 - NA #8	- The spectrum of schizo-obsessive disorders comprises OCD, OCD with poor insight, OCD with schizotypal personality disorder, schizophrenia with OCS, schizophrenia with OCD and finally schizophrenia. The DSM-5 allows this spectral view.

Y-BOCS Yale–Brown Obsessive Compulsive Scale

Anexos

1. Normas “Brazilian Journal of Psychiatry”
2. Reporting guidelines PRISMA

Brazilian Journal of Psychiatry
bjp
Revista Brasileira de Psiquiatria
Brazilian Psychiatric Association

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First choose the type of manuscript you wish to submit. You may choose between Original Article, Brief Communication, Review Article, Special Article, Editorial or Letter to the Editors. Manuscripts must be written in English. The table below shows the maximum number of words, references and tables/figures for each manuscript type.

Manuscript type	Main text words	Abstract words	References	Tables + figures
Original Articles	5000	Structured, 200	40	6
Review Articles	6000	Structured, 200	Unlimited	6
Brief Communications	1500	Structured, 200	15	2
Special Articles	6000	Unstructured, 200	Unlimited	6
Letters to the Editors	500	No abstract	5	1
Editorials	900	No abstract	5	1

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- **Review articles:** These should be systematic reviews and should include critical assessments of literature and data sources, critically reviewing and evaluating existing knowledge on a designated topic, in addition to commenting on studies by other authors. The search strategy and selection process should be described in detail, according to PRISMA or other appropriate guidelines.
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Title page: Page 1 should contain full title, authors' names, their departments and institutions, including the city and country of origin. Please also include a running title with a maximum of 50 characters (letters and spaces). The full name, telephone number, fax number, e-mail address and full postal address of the corresponding author should be stated.

Abstract: Page 2 should present a structured abstract (not exceeding 200 words) with the following sections: Objective, Methods, Results, and Conclusion (check table with abstract requirements for each manuscript type, above). Please indicate three to five keywords in strict accordance with Medical Subject Headings. Do not include an abstract in Portuguese or any language other than English. If applicable, inform the clinical trial registration number at the end of the abstract (see below).

Clinical Trial Registration: The *Brazilian Journal of Psychiatry* supports the clinical trial registration policies of the World Health Organization (WHO) and the ICMJE, recognizing the importance of such initiatives for the registration and disclosure of trial results to the international community through open access. According to this recommendation and to the BIREME/OPAS/OMS guidelines for journals indexed in the LILACS and SciELO databases, the *Brazilian Journal of Psychiatry* will only accept for publication clinical trials that have been registered in Clinical Trials Registries that meet the WHO and ICMJE requirements.

Main text: The manuscript file (main text) must be written in English, double-spaced throughout, and should contain the following items in this order: title page, abstract, manuscript text, acknowledgment section, references, figure legends, and tables. Use 10-, 11-, or 12-point font size. All terms or abbreviations should be spelled out at first mention in the text and also in table/figure legends. All units should be metric. Avoid Roman numerals.

The Methods section should include information on ethics committee approval and informed consent procedures, as well as compliance with institutional and national standards for the care and use of laboratory animals, where applicable.

Reference list: Authors are responsible for the accuracy and completeness of their references and for correct in-text citation. Number references in the order they appear in the text; do not alphabetize. In text, tables, and legends, identify references with superscript Arabic numerals. References cited only in tables or figure legends should be numbered in accordance with the first citation of the table/figure in the text.

Please observe the style of the examples below. To include manuscripts accepted, but not published, inform the abbreviated title of the journal followed by "Forthcoming" and the expected year of publication. Information from manuscripts not yet accepted should be cited only in the text as personal communication. Reference accuracy is the responsibility of the authors. Journal titles should be abbreviated in accordance with Index Medicus.

Examples:

- **Journal article:** Coelho FM, Pinheiro RT, Silva RA, Quevedo LA, Souza LD, Castelli RD, et al. Major depressive disorder during teenage pregnancy: socio-demographic, obstetric and psychosocial correlates. Braz J Psychiatry. 2013;35:51-6.
  List all authors when six or fewer. When there are seven or more, list only the first six authors and add "et al."
- **Book:** Gabbard GO. Gabbard's treatment of psychiatric disorders. 4th ed. Arlington: American Psychiatric Publishing; 2007.
- **Book chapter:** Kennedy SH, Rizvi SJ, Giacobbe P. The nature and treatment of therapy-resistant depression. In: Cryan JF, Leonard BE, editors. Depression: from psychopathology to pharmacotherapy. Basel: Karger; 2010. p. 243-53.
- **Theses and dissertations:** Trigeiro A. Central nervous system corticotropin releasing factor (CRF) systems contribute to increased anxiety-like behavior during opioid withdrawal: an analysis of neuroanatomical substrates [dissertation]. San Diego: University of California; 2011.

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page and paragraph/ table #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both. **- MANDATÓRIO**	Title
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. **– SEGUIR RECOMENDAÇÕES DA REVISTA**	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. **– MANDATÓRIO** ***O rationale corresponde à justificação da importância da revisão sistemática***	Page 1, "introduction" section, 1st paragraph
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). **- MANDATÓRIO**	Page 1, "introduction" section, 1st paragraph
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. **– FACULTATIVO**	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. **– MANDATÓRIO** ***É altamente recomendado, de acordo com as boas práticas da Cochrane, que não sejam aplicados critérios de exclusão baseados na língua e/ou data de publicação dos estudos.***	Page 1, "eligibility criteria and study selection" subsection, 1st and 2nd paragraph
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. **– MANDATÓRIO** ***Em consonância com as boas práticas da Cochrane, é mandatório que se verifique pesquisa em pelo menos duas bases de pesquisa bibliográfica (idealmente, deverão ser pesquisadas duas bases generalistas e uma específica da área). No caso de revisões sistemáticas de estudos experimentais/ensaios clínicos aleatorizados, é altamente recomendado que uma das bases pesquisadas corresponda à CENTRAL ou a bases de ensaios clínicos como a ClinicalTrials.gov.*** ***Estudos de revisão da literatura em que a pesquisa decorra numa única base de dados não serão***	Page 1, "research" section, 1st paragraph

		classificados como revisões sistemáticas.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. **– MANDATÓRIO** ***A query de pesquisa deve ser obrigatoriamente disponibilizada. A utilização de filtros de pesquisa da InterTASC é altamente recomendada (https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home)***	Page 1, "research" section, 1st paragraph
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). **– MANDATÓRIO** ***As fases de selecção dos estudos primários devem ser descritas. Em consonância com as boas práticas da Cochrane, é mandatório que o processo de selecção envolva duas fases (fase de rastreio, em que os registos são seleccionados por título e abstract, e fase de inclusão, na qual se procede à leitura integral dos full texts). Em cada uma destas fases, o processo de selecção deve mandatoriamente envolver dois investigadores actuando de forma independente.***	Page 1, "eligibility criteria and study selection" subsection, 1st and 2nd paragraphs + page 12, fig. 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. **– MANDATÓRIO** ***Trata-se de descrever de que forma se procedeu à extracção de dados dos estudos primários. Em consonância com as boas práticas da Cochrane, tal processo deverá envolver dois investigadores de forma independente.***	Page 2, "data collection process and items" subsection, 1st paragraph
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. **– MANDATÓRIO** ***Trata-se de descrever as variáveis para as quais foi obtida informação.***	Page 2, "data collection process and items" subsection, 1st paragraph
Risk of bias in individual studies / Risk of bias across studies	12/ 15	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. **– MANDATÓRIO** ***Em todas as revisões sistemáticas, deverá existir um processo de avaliação da qualidade dos estudos primários. No caso de revisões sistemáticas de estudos experimentais/ensaios clínicos aleatorizados, a aplicação dos critérios de risco de viés (Risk of Bias) da Cochrane é altamente recomendada. No caso de revisões sistemáticas de estudos observacionais, poderão ser seguidos os critérios ROBINS ou os critérios dos National Institutes of Health (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools).***	Page 2, "quality of included studies" subsection, 1st paragraph, and pages 13-20, tables 1-3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). **– FACULTATIVO. APENAS NECESSÁRIO SE FOR FEITA META-ANÁLISE**	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. **– FACULTATIVO. APENAS NECESSÁRIO SE FOR FEITA META-ANÁLISE**	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. **– FACULTATIVO. APLICÁVEL APENAS SE FOR FEITA META-ANÁLISE**	NA

PRISMA 2009 Checklist

RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. **– MANDATÓRIO**	Page 2, "results" section, 1st paragraph, and page 12, fig.1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. **– MANDATÓRIO**	Page 2, "data collection process and items" subsection, 1st paragraph, and pages 13-20, tables 1-3
Risk of bias within and across studies	19/ 22	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). **– MANDATÓRIO**	Page 2, "data collection process and items" subsection, 1st paragraph, and pages 13-20, tables 1-3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. **– FACULTATIVO. APLICÁVEL APENAS SE FOR FEITA META-ANÁLISE**	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency. **– FACULTATIVO. MANDATÓRIO APENAS SE FOR FEITA META-ANÁLISE**	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). **– FACULTATIVO. APLICÁVEL APENAS SE FOR FEITA META-ANÁLISE**	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). **– MANDATÓRIO**	Pages 3-8, "discussion" section and pages 13-20, tables 1-3
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). **– MANDATÓRIO**	Pages 7-8, "strengths, limitations and future directions" subsection, 1st

			and 2nd paragraph
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research. – **MANDATÓRIO**	Page 7, "conclusion" section, 1st paragraph and pages 7-8, "strengths, limitations and future directions" subsection, 3rd paragraph
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. – **SEGUIR RECOMENDAÇÕES DA REVISTA**	Page 8, "disclosure" section, 1st paragraph

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