CNS Spectrums

www.cambridge.org/cns

Lessons from a multicenter, international, large sample size analysis of patients with obsessive–compulsive disorders: an overview of the ICOCS Snapshot studies

Matteo Vismara[1], Beatrice Benatti[1,2], Naomi A. Fineberg[3,4,5], Eric Hollander[6], Michael Van Ameringen[7], Jose M. Menchon[8], Joseph Zohar[9] and Bernardo Dell'Osso[1,2,10]

[1]University of Milan, Department of Mental Health, Department of Biomedical and Clinical Sciences Luigi Sacco, Milan, Italy, [2]"Aldo Ravelli" Center for Neurotechnology and Brain Therapeutic, University of Milan, Milan, Italy, [3]School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK, [4]Hertfordshire Partnership University NHS Foundation Trust, Welwyn Garden City, UK, [5]University of Cambridge School of Clinical Medicine, Cambridge, UK, [6]Department of Psychiatry and Behavioral Sciences, Albert Einstein College of Medicine, Montefiore Medical Center, New York, USA, [7]Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada, [8]Psychiatry Unit at the Hospital Universitari de Bellvitge-IDIBELL, University of Barcelona, Ciber-sam, Barcelona, Spain, [9]Post-Trauma Center, Research Foundation by the Sheba Medical Center, Tel Aviv University, Sackler School of Medicine, Israel and [10]Department of Psychiatry and Behavioral Sciences, Bipolar Disorders Clinic, Stanford University, CA, USA

Review

Cite this article: Vismara M, Benatti B, Fineberg NA, Hollander E, Van Ameringen M, Menchon JM, Zohar J, and Dell'Osso B (2024). Lessons from a multicenter, international, large sample size analysis of patients with obsessive–compulsive disorders: an overview of the ICOCS Snapshot studies. *CNS Spectrums* **29**(1), 40–48.
https://doi.org/10.1017/S1092852923002432

Received: 05 July 2023
Accepted: 06 September 2023

Keywords:
Obsessive–compulsive disorder; international database; gender; suicide; pharmacotherapy; geographical differences

Corresponding author:
Matteo Vismara;
Email: matteo.vismara@unimi.it

Abstract

Obsessive–compulsive disorder (OCD) is a prevalent and highly disabling condition, characterized by a range of phenotypic expressions, potentially associated with geo-cultural differences. This article aims to provide an overview of the published studies by the International College of Obsessive-Compulsive Spectrum Disorders, in relation to the Snapshot database which has, over the past 10 years, gathered clinical naturalistic data from over 500 patients with OCD attending various research centers/clinics worldwide. This collaborative effort has provided a multi-cultural worldwide perspective of different socio-demographic and clinical features of patients with OCD. Data on age, gender, smoking habits, age at onset, duration of illness, comorbidity, suicidal behaviors, and pharmacological treatment strategies are presented here, showing peculiar differences across countries.

Introduction

Obsessive–compulsive disorder (OCD) is a prevalent and highly disabling mental health condition, characterized by a range of phenotypic expressions.[1] Recent updates in the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) and in the International Classification of Diseases 11th Revision emphasized the growing significance of OCD, indicating it as the archetypal example of a new spectrum of obsessive–compulsive and related disorders. These changes are expected to provide new impetus in the understanding of the pathophysiology, phenomenology, and therapeutic interventions of OCD and related conditions.

The "Snapshot project" conducted by the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS), in collaboration with the European College of Neuropsychopharmacology-Obsessive Compulsive Research Network (ECNP-OCRN), has, over the past decade, gathered clinical naturalistic data from research sites across the globe—that is, North America (Canada, the United States, and Mexico), Africa (South Africa), Europe (Spain, Italy, Turkey, and Bulgaria), and the Middle East (Israel)—creating a large database of consecutive outpatients affected by OCD. Detailed information about participating centers and assessment procedures have been documented elsewhere.[2] Briefly, patients had to be diagnosed as affected by OCD through the administration of the Mini-International Neuropsychiatric Interview[3] and the main socio-demographic and clinical variables were collected by clinicians during assessment or through revision of clinical charts. Data were there incorporated in a common web-database. All centers participating to the ICOCS initiative have a well-established expertise in diagnosing and treating OCD, typically operating as academic or tertiary clinics. A rigorous methodology and consistency were maintained during data collection and diagnostic procedure to minimize potential inter-institutional differences in sampling. In its final version, the database encompassed a total of 504 patients, although the specific subset of patients analyzed in each study might have varied (see Table 1 for details), considering data were elaborated from the database at different times or because of missing data. The present short review of the pooled

Table 1. Overall Results from the ICOCS Snapshot Database Studies

Article	Sample size*	Main aim of the study	Most relevant findings
Benatti et al., 2022[4]	491	Explore demographic, geographical and clinical differences between male and female pts with OCD.	Female pts compared to male pts showed: - more frequent adult onset (>18 years old; 67% vs. 33%, $p < 0.005$); - older age at illness onset (20.9 ± 10.8 vs. 17.7 ± 9.0 years, $p < 0.005$); - lower years of education (13.1 ± 4.0 vs. 14.0 ± 3.9 years; $p < 0.05$); - higher rate of being married (50.8% vs. 33.5%; $p < 0.001$); - higher rate of living with a partner (47.5% vs. 37.6%; $p < 0.001$). Geographical differences: - Americas (Canada, the United States, and Mexico) showed higher rates of female OCD patients compared to male (78.3% vs. 21.7%; $p < 0.001$).
Benatti et al., 2021[5]	409	Investigate prevalence and correlates of current suicide risk (assessed by Item C of the MINI).	Current suicidal risk prevalence: 15.9%, with no differences after covarying for sociodemographic variables. Most represented countries on current suicidal risk prevalence: Italy (30.8%), South Africa (16.9%), Israel (9.2%), Canada (7.7%), and the United Kingdom (6.2%). Higher current suicide risk was associated with higher rates of major depression and generalized anxiety disorder, higher severity of OCD, depressive symptoms, and higher levels of disability.
Dell'Osso et al., 2020[6]	401	Investigate prevalence and clinical characteristics of comorbidity with BD in pts with OC.	Prevalence of comorbid BD: 6.2%. Pts with comorbid BD compared to pts without showed: - more frequent previous psychiatric hospitalization (48.2% vs. 20.6%, $p < 0.001$); - more frequent augmentation therapies (77.3% vs. 48.5%, $p < 0.001$); - greater severity of OCD (Y-BOCS mean score 25.7 vs. 22.5, $p < 0.001$).
Dell'Osso et al., 2018[7]	425	Assess prevalence and clinical characteristics of previous SA in pts with OCD.	Prevalence of previous SA: 14.6%. Pts with previous SA compared to pts without SA showed higher rates of: - comorbid psychiatric disorders (60% vs. 17%, $p < 0.001$); - comorbid medical disorders (51% vs. 15%, $p < 0.001$); - previous psychiatric hospitalization (62% vs. 11%, $p < 0.001$); - past/current CBT (66% vs. 38%, $p < 0.001$). Geographical differences: - higher rates of previous SA in European (40%) and South African (39%) vs. North American (13%) and Middle Eastern (8%) patients ($p < 0.001$).
Dell'Osso et al., 2017[8]	416	Assess prevalence and clinical characteristics of geriatric patients with OCD (G-OCD ≥ 65 years).	Prevalence of G-OCD: 6%. G-OCD pts compared to younger (<65 years) pts showed: - later age at onset (29.4 ± 15.1 vs. 18.7 ± 9.2 years, $p < 0.001$); - more frequent adult onset (≥18 years, 75% vs. 41.1%, $p < 0.001$); - less frequent use of CBT (20.8% vs. 41.8%, $p < 0.05$); - higher rate of females (75% vs 56.4%, $p = 0.07$).
Dell'Osso et al., 2016[9]	431	Assess prevalence and clinical features of different AAO in pts with OCD.	Prevalence: - childhood onset (≤12 years): 21%; - adolescent onset (13–17): 36%; - adult onset (≥18): 43%. Differences among the three subgroups: - higher female rate in pts with adult onset (66.8% vs. 33.2%, $p < 0.05$), but not in the other subgroups (childhood onset: 52.2% vs. 47.8%; adolescent onset: 50.3% vs. 49.7%); - higher rate of patients on CBT only in the childhood- and adolescent-onset groups (3.2% and 2.6%, respectively) compared to the adult-onset group (1.2%, $p < 0.001$); - higher rate of patients on CBT in augmentation to pharmacological treatment in pts with childhood- (51.6%) and adolescent-onset (47%) vs. adult-onset (32.6%, $p < 0.05$). Differences between pre-adult (<18 years) compared to adult onset pts: - higher female rate in pts with adult onset (66.8% vs. 33.2%, $p < 0.001$); - higher rate of patients on CBT in the pre-adult-onset subgroup (5.8% vs. 1.2%, $p < 0.001$); - higher rate of patients on CBT in addition to pharmacological treatment in the pre-adult onset subgroup (48.8% vs. 32.6%, $p < 0.001$).

Table 1. *Continued*

Article	Sample size*	Main aim of the study	Most relevant findings
Dell'Osso et al., 2015[10]	483	Investigate prevalence and clinical correlates of cigarette smoking in pts with OCD.	Prevalence: - current smoking pts (CSPs): 24.4%; - former smoking pts (FSPs): 19.9%; - pts who had never smoked (NSPs): 55.7%. Gender differences: - females were overrepresented, compared to males, in CSPs (17% vs. 7.4%, $p < 0.001$) and NSPs (35.6% vs. 20.1%, $p < 0.001$); - more males in the FSPs subgroup (12.4% vs. 7.4%, $p < 0.001$). Comorbidity rate: - higher psychiatric comorbidities rate in NSPs (10.1%) when compared to FSPs (5.1%) and to CSPs (2.8%, $p < 0.05$); - among pts with comorbid Tourette's syndrome and tic disorder, CSPs were significantly more represented than FSPs and NSPs ($p < 0.05$)**; - higher medical comorbidities in NSPs (9.1%) when compared to FSPs (6.2%) and to CSPs (2.6%, $p < 0.001$); - higher previous suicide attempts in FSPs (5.7%) when compared to NSPs (4.7%) and to CSPs (2.7%, $p < 005$). Treatments: - higher rate of pts on psychotropic medications in NSPs (39%) when compared to FSPs (12.4%) and to CSPs (13.6%, $p < 0.05$); - higher rate of patients on CBT (alone or in augmentation) in NSPs (21.2%) when compared to FSPs (5.7%) and to CSPs (11.6%, $p < 0.001$). Geographical differences: - the highest number of NSPs in the Italian sample and the highest number of CSPs in the South African sample ($p < 0.001$).
Lochner et al., 2014[11]	457	Investigate comorbidity with OCSDs and other—previously classified—DSM-Axis I disorders in pts with OCD.	Comorbidity with OCSDs: - highest comorbidity rates (>5%): tic disorder (12.5%), body dysmorphic disorder (8.71%), self-injurious behaviors (7.43%), compulsive shopping (6.97), intermittent explosive disorder (5.33%), and trichotillomania (5.31%). Comorbidity with non-OCSDs Axis-I disorders: - highest comorbidity rates (>10%): major depressive disorder (15.42%), social anxiety disorder (14.37%), generalized anxiety disorder (13.35%), dysthymic disorder (13.13%), and panic disorder with/out agoraphobia (11.69%); - positive correlation with OCD symptom severity (Y-BOCS) and number of comorbid mood and anxiety disorders ($p < 0.01$). Geographical differences across sites in comorbidity rates emerged for major depressive disorder ($p < 0.001$), dysthymic disorder ($p < 0.001$), social anxiety disorder ($p < 0.001$), generalized anxiety disorder ($p < 0.05$), panic disorder ($p < 0.05$), tic disorder ($p < 0.001$), body dysmorphic disorder ($p < 0.001$), self-injurious behaviors ($p < 0.001$), anorexia nervosa ($p = 0.002$), bulimia nervosa ($p < 0.001$), binge-eating disorder ($p < 0.05$), trichotillomania ($p < 0.001$), and compulsive shopping ($p = 0.001$); South African sample had significantly larger number of comorbid Axis I when compared to Spain ($p = 0.007$).
Van Ameringen, 2014[12]	361	Investigate different pharmacological treatment strategies in patients with OCD.	Pts on current psychotropic medication: 87.8%. Primary drug treatments: - SSRIs (77.6%), TCAs (14.5%), SNRIs (6.0%), and others (1.9%); - no significant differences on clinical improvement (CGI-I) between different SSRIs agents. Monotherapy: - 44% pts; - type of medications: SSRIs (85%), TCAs (8.8%), SNRIs (5.0%), antipsychotic (0.6%), benzodiazepine (0.6%); - no significant differences in clinical improvement (CGI-I) or symptom severity (Y-BOCS) between monotherapy agents. Augmentative strategies: - 49.5% pts, mean number of augmentation strategies used per patient: 1.53 ± 0.7; - one agent (59%), two agents (29%), 3–5 agents (12%); - type of medications: antipsychotics (30.3%), benzodiazepines (24.9%), antidepressants (21.9%);

Table 1. *Continued*

Article	Sample size*	Main aim of the study	Most relevant findings
			- pts in the augmentation group compared to those treated with monotherapy showed higher functional impairment (SDS, 18.9 ± 7.7 vs. 16.9 ± 7.7, $p < 0.05$), but no differences in clinical improvement (CGI-I) or symptom severity (Y-BOCS and CGI-S); - pts augmented with mood stabilizers compared to those augmented with other agents showed higher symptom severity (Y-BOCS, 25.8 ± 7.2 vs. 22.2 ± 7.3, $p < 0.05$). Geographical differences: - higher rates of monotherapy in South Africa (85.3%) when compared to Canada (34.4%) and Europe (43.2%, $p < 0.001$); - higher rates of augmentation with "other" medication classes in Canada (35.7%) when compared to Europe (5.7%) and South Africa (20.0%, $p < 0.001$); - YBOCS scores higher in Europe (23.8 ± 7.6) when compared to Canada (20 ± 7.4, $p = 0.001$); - SDS scores higher in Europe (18.6 ± 7.8) when compared to South Africa (14.76.7, $p = 0.032$); - CGI-S scores higher in Europe (4.6 ± 1.2) when compared to Canada (4.2 ± 1.3, $p = 0.037$).
Dell'Osso et al., 2013[2]	376	Assess the influence of AAO and DOI on long-term outcomes in pts with OCD	AAO: - earlier AAO predictive of CBT in augmentation to pharmacological treatment (OR = 0.94, $p < 0.001$); - later AAO predictive of panic disorder comorbidity (OR = 1.05, $p = 0.02$); - inverse relationship between AAO and social disability (SDS, social life domains, $r = -0.12$, $p = 0.048$). DOI: - longer DOI predictive of psychiatric hospitalization (OR = 1.03, $p = 0.01$) - shorter DOI predictive of panic disorder comorbidity (OR = 0.93, $p = 0.02$) - direct relationship between DOI and family, work, and social disability (SDS, family ($r = 0.14$, $p = 0.017$), work ($r = 0.13$, $p = 0.035$), and social life domains ($r = 0.14$, $p = 0.02$)).

Abbreviations: AAO, age at onset; BD, bipolar disorders; CBT, cognitive-behavioral therapy; CGI-I: Clinical Global Impression, I: Improvement Scale, S: Severity Scale; DOI, duration of illness; DSM, Diagnostic and Statistical Manual of Mental Disorders; MINI, Mini-International Neuropsychiatric Interview; OCSDs, obsessive–compulsive spectrum disorders; OR, odds ratio; SA, suicide attempts; SDS, Sheehan Disability Scale; SNRIs, serotonin norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants; Y-BOCS, Yale-Brown Obsessive–Compulsive Scale.
*Differences in sample size depend on missing data for the specific variable investigated in each paper.
**No mean/percentage data available in the original paper.

study data aims to provide an overview of the most relevant findings emerging from the various constituent studies making up the Snapshot database.

Findings from the ICOCS database studies

The ICOCS studies have explored the influence of the following variables: age, gender, smoking habits, age at onset, duration of illness, comorbidity, suicidal behaviors, and pharmacological treatment strategies. Published studies and summarized results are outlined in Table 1.

Socio-demographic characteristics

One of the most recent studies from the Snapshot database investigated the influence of gender on OCD.[4] In line with prior published findings,[13,14] the study revealed that male OCD patients showed a significantly earlier age of onset of symptoms when compared to female counterparts. However, no significant differences in the severity of OCD symptoms were observed between the genders. Additionally, the study noted that females were more likely to be married, living with a partner, and had a lower education level, which could be linked to the later age at OCD onset in this subgroup. Moreover, females were more prominently represented in the group of patients with adult-onset (occurring at or after 18 years of age), while the gender distribution was similar in the childhood (≤13 years) and adolescent-onset (between 13 and 17 years) subgroups.[9] This lack of male predominance in the early-onset subgroups contradicts previous literature, which typically shows a higher male rate in such cases.[14] Although the exact mechanisms underlying this phenomenon remain unclear, several lines of evidence suggest that androgens may play a critical role in the onset and exacerbation of certain cases of OCD. In this study, which collected patients from various institutions, it is possible that cultural differences—that need to be further investigated—might have influenced the onset of the illness and mitigated differences between genders.

Mindful of the limitations in knowledge about OCD among the elderly, another study aimed to characterize the clinical presentation of older patients with OCD (≥65 years old), that represented a significant minority (6%) of the overall sample in the ICOCS database. These elderly patients with OCD were more frequently female and exhibited a distinct pattern of illness compared with their younger counterparts, in terms of a later age at onset of OCD and a less frequent use of cognitive behavioral therapy (CBT).[8] Previous findings regarding geriatric OCD patients are scarce and restricted to a few studies. For instance, a single-center study comparing 32 OCD geriatric patients (≥60 years old) to 601 non-geriatric patients revealed a similar prevalence of elderly patients (5.3%) and, similarly, this subset of patients was also characterized by a later age at onset. Moreover, the elderly patients exhibited fewer concerns related to symmetry, need to know, and counting rituals, while handwashing and fear of sinning were more common.[15] As in the ICOCS Snapshot dataset, no difference in severity of illness was found across age subgroups.[15] Conversely, another cross-sectional investigation on 227 subjects with OCD found a negative correlation ($r = -0.386$, $p < 0.001$) between age and Yale-Brown Obsessive–Compulsive Scale (YBOCS) score.[16]

The attitude OCD patients have toward cigarette smoking was another area of investigation in the ICOCS database, revealing that nearly one out of four OCD patients were current smokers (24%, with significant differences across countries). Among this group, females were more prominently represented.[10] Although this prevalence is relatively low when compared to patients with other psychiatric disorders (50%–80% of smokers),[17] it is higher when compared to other OCD studies (5.5%–20%).[18,19] Moreover, current smokers were over represented in patients with comorbid Tourette's syndrome or tic disorder (compared with former smokers or subjects who never smoked), suggesting a shared impulsive behavior mechanism between pathological behaviors and nicotine use. Interestingly, a higher comorbidity rate with psychiatric and medical conditions emerged in non-smokers when compared to smokers. However, this result cannot be thoroughly explained due to factors such as: i) the specific psychiatric or medical comorbidity should be considered, ii) the small sample size of each subgroup (in the original paper, only the minority of patients—less than 20%—showed a comorbidity), and iii) the inability to establish a causal relationship between smoking and comorbid psychiatric/medical conditions in cross-sectional studies.

Clinical characteristics

Results from the international database analysis investigating age at onset confirmed the well-known early-onset of OCD. Specifically, 21% of patients reported childhood-onset, 36% experienced adolescent-onset, and the minority (43%) had adult-onset OCD.[9] Taken as a whole, this study highlighted that the majority of OCD patients experienced symptoms before adulthood (ie, before the age of 18). In addition, childhood- and adolescent-onset patients had been more frequently treated with CBT, compared with adult-onset patients,[9] suggesting that CBT is an suitable first-line treatment in mild-to-moderate cases of young OCD patients.[20]

Another study conducted by the ICOCS group indicated that an early onset and longer duration of illness were negative predictors of long-term overall outcomes in OCD patients.[2] In detail, a longer duration of illness was predictive of lifetime psychiatric hospitalizations and was directly correlated with higher disability in work, social, and family life, as measured through the Sheehan Disability Scale (SDS).[21] An early age at illness onset was associated with the need for treatment augmentation of CBT and was inversely correlated with higher social disability. Conversely, panic disorder comorbidity (occurring after the onset of OCD) was correlated with a later age at onset and a shorter duration of illness [2], suggesting that this comorbidity is associated with an greater readiness to seek treatment.[22]

A recently published study from Brakoulias and colleagues collected data from more than 3,700 participants across seven countries (Australia, Brazil, India, Italy, Japan, South Africa, and Spain) representing the largest international database of OCD in the literature.[23] While this paper benefited from a large sample of patients from diverse backgrounds, it had limitations due to data being derived from studies with varying objectives and recruitment methods, resulting in heterogeneous samples. Among the clinical data analyzed in this paper, mean age of onset of OCD was 16.9 years (SD = 4.5, measured in four nations, n = 2,022) with no significant differences across countries. This mean age at onset was lower compared to the mean age at onset reported in the ICOCS database (20.6 years, SD = 10.9, as noted in the paper, Dell'Osso et al., 2013[2]). This finding underscores once more the typical early onset of OCD and, consequently, the importance of targeting interventions toward childhood age groups.[24]

https://doi.org/10.1017/S1092852923002432 Published online by Cambridge University Press

Comorbidity

Individuals with OCD frequently experience additional psychiatric disorders either concomitantly or at some point during their lifetime. This comorbidity is responsible for negative outcomes such as a higher burden of the disease and reduced responsiveness to treatment.[25]

Two reports from the ICOCS have focused on comorbidity rates in OCD.[6,11] The first study reported high cross-sectional co-occurring rates for disorders within the OCD spectrum, including tic disorder (12.5%), body dysmorphic disorder (8.7%), and compulsive self-injurious behaviors (7.4%). This supports the idea of including these conditions in the same spectrum of OC-related disorders, as well as the introduction of the new "tic-related" specifier for OCD in the DSM-5. Among other previously classified DSM-IV-Text Revised Axis I disorders, major depressive disorder, social anxiety disorder, generalized anxiety disorder, and dysthymic disorder were the most prevalent (ranging between 15% and 13%) and the number of comorbid anxiety and mood disorders strongly correlated with the severity of OCD.[11] However, it is important to note that these data may underestimate the rate of comorbid conditions in OCD. In contrast, the international database from Brakoulias, reported higher rates of comorbid conditions: major depressive disorder (50.5%), social phobia (26.4%), specific phobia (25.5%), generalized anxiety disorder (24.0%), hypomanic episode (23.7%), and dysthymia (22.5%).[23] The lower rates of psychiatric comorbidity observed in the ICOCS Snapshot database, also compared to previous single-center studies,[26] may reflect that most of the patients included in the Snapshot study were already receiving effective treatment before seeking care at an OCD specialized center. Alternatively, it could be attributed to recall bias due to the single interview method used in the Snapshot study.

A subsequent study from the ICOCS study specifically investigated the lifetime comorbidity of bipolar disorders in patients with primary OCD, showing a 6.2% rate in the ICOCS Snapshot database.[6] Subjects with comorbid bipolar disorders showed greater severity of OCD, as measured by the YBOCS, and were more likely to have lifetime psychiatric hospitalizations and augmentation pharmacotherapies, which could be related to the greater severity of their illness.

Overall, these comorbidity studies have provided new findings into the rates and patterns of specific comorbidities in OCD patients, highlighting the burden of comorbid conditions as well as the need for targeted therapeutic interventions in specific situations (eg, prescribing high doses of serotonergic antidepressants, which could induce mood elevation episodes in patients with comorbid bipolar disorders).

Suicide

Although OCD has traditionally been associated with a low suicide risk, emerging literature data disconfirmed this assumption, revealing a higher suicide risk for OCD patients compared to the general population.[27] Snapshot investigations confirmed this perspective, with 15.9% of patients reporting current suicide risk (as assessed with the suicide module [C] of the M.I.N.I.),[5] and a similar rate (14.6%) reporting suicide attempts at least once during lifetime.[7] Notably, several risk factors for suicide risk have emerged, suggesting the importance of addressing these factors during clinical interviews. These factors include a higher severity of OCD and related disability, the presence of comorbid medical or psychiatric disorders (especially, major depression and generalized anxiety disorder), and previous psychiatric hospitalizations.[5,7] When compared to the paper by Brakoulias, it was found that suicidal ideation within the last month was reported by a average of 6.4% of patients, whereas 9.0% reported having attempted suicide in their lifetime.[23]

Pharmacological treatment

The cross-sectional evaluation conducted by the ICOCS provided insights into the pharmacological treatment strategies employed in various tertiary care settings.[12] The results were in alignment with evidence-based treatment guidelines,[20] showing that 77.6% of patients were prescribed a selective serotonin reuptake inhibitor (SSRI) and 50% were utilizing at least one augmentation strategy. Among the augmentation strategies, antipsychotics were most frequently prescribed (30.3%), followed by benzodiazepines (24.9%), and antidepressants other than SSRI (21.9%). Notably, no significant differences were found in mean YBOCS scores or clinical improvement (as measured on the Clinical Global Impression, Improvement [CGI-I]) between specific monotherapy agents and, similarly, between individuals treated with at least one augmentation strategy and those treated with monotherapy. However, those in the augmentation group reported significantly higher SDS scores, indicating that augmentation was associated with a greater degree of functional impairment.[12] These results might suggest that augmentation strategies may provide limited therapeutic benefit for individuals who do not respond to first-line treatments for OCD, which challenges the robust evidence from the literature.[28] However, it is important to consider that these results are based on a cross-sectional analysis, and potential confounding factors should be attentioned. First, patients might be at different stages of treatment—with those on augmentation possibly having more treatment-resistant OCD than those on monotherapy. The lack of difference in symptoms severity might suggest that both groups improved to an equal extent, despite facing a more treatment resistant form of the illness. The lack of improvement between patients on monotherapy compared to those on augmentation could also be influenced by specific characteristics of the study's patient population, in particular the duration of illness, the number of previous treatment trials, and the increased severity of OCD in this sample—that is, patients recruited from tertiary care settings often have more severe and treatment-resistant forms of OCD, making them less likely to respond to augmentative strategies. Alternatively, the results may point to a "plateau effect" where only a limited degree of improvement can be achieved in individuals who require a next-step treatment.

Geographical/transcultural differences

The ICOCS database analysis provided a valuable trans-cultural worldwide perspective on various socio-demographic and clinical OCD features. This geographic heterogeneity in the sample had several advantages. First, it minimized the risk of possible socio-cultural bias and other confounding factors related to a single catchment area, providing an objective characterization of the phenomena under investigation. Second, it offered an opportunity to explore how cultural variations and specific local factors, especially related to the healthcare system, might influence the clinical course of OCD. Indeed, several sociodemographic differences across countries emerged from the analysis. For instance, female gender was overrepresented only in patients from the Americas (Canada, the United States, and Mexico), whereas other countries showed a more balanced gender distribution.[4] Of note, the highest

https://doi.org/10.1017/S1092852923002432 Published online by Cambridge University Press

number of non-smoking patients was observed in Italy, whereas South Africa showed the highest number of current smoking patients.[10] South African patients also exhibited a larger number of comorbid Axis I when compared to those in Spain,[11] and they were more frequently prescribed monotherapy when compared to patients in Europe or Canada.[12] With respect to suicidal behaviors, Italy, South Africa, Israel, Canada, and the United Kingdom had the highest current suicidal risk prevalence,[5] a phenomenon that partially reflects the highest rate of previous suicide attempts observed in European and South African patients.[7] Regarding disease burden, patients from Europe showed a higher severity of illness (higher scores on the YBOCS and on the CGI-severity scales) when compared to subjects from Canada; similarly, subjects from Europe showed a higher disability when compared with ones from South Africa (as measured with the SDS).[12]

Unrevealing the causal relationships responsible of these differences is complex, as several confounding factors might exist and comparative studies on OCD manifestations between countries remain limited. Moreover, ethnic minorities with OCD are often underrepresented in research, as most of the investigations focused on European or American population. Increasing our understanding of geographical and transcultural factors and their impact on the clinical presentation of OCD is, therefore, essential.

While the impact of pathophysiological mechanisms on OCD is well-determined, with core features likely relatively independent of cultural variations, some data suggest that the content of the obsessions may be an exception to this rule.[29,30] Indeed, religious believes and religiosity seem to affect the type of obsessions and severity of their manifestations, whereas certain "taboo obsessions," such as those related to sexual orientation, might be culture-bound as these have mainly been observed in Western cultures and has not been reported in the literature outside of the United States[31] or in Middle Eastern countries where religious themes are prevalent. In Brazil, a predominance of aggressive obsessions has been described.[32] Geographical differences have also been identified in previous studies that compared the clinical manifestation of OCD between countries. For example, a higher rate of comorbid generalized anxiety disorder and post-traumatic stress disorder were reported in Brazilians meanwhile Americans were more likely to endorse substance abuse disorders.[33] Rates of comorbid lifetime major depressive disorder ranged from around 30% in India and Japan to around 60% in Australia and South Africa, likely reflecting different access to treatment for these comorbid conditions.[23] Moreover, the incidence of OCD was lower in Taiwan, and there was a larger proportion of individuals with only obsessions the United States, Canada, Puerto Rico, and New Zealand, compared to Korea, where the proportion of subjects presenting only compulsions was higher than in the other cultural backgrounds.[34] Recent suicidal ideation was most prevalent in the Australian sample (up to 33.2%), while a lifetime history of a suicide attempt was highest in the South African sample (15.9%).[23]

Access to health care and treatments significantly impacts the clinical presentation of OCD. Geographical differences in treatment approaches were evident in the ICOCS Snapshot sample. A previous paper reported geographical variations in the percentage of subjects not being pharmacologically treated, with 44% OCD patients untreated in Brazil and 38% untreated in Australia. In contrast, countries like Italy, Japan, and Spain showed nearly 100% of patients on pharmacological treatment.[35] Although no country in the Snapshot database came from a low-income economy, variations in healthcare system, including public versus private options, and public policies regarding access to treatments or subsidies for drug and interventions, likely played a role in the clinical presentation of OCD. Limited access to care can impact disease severity by prolonging the duration of untreated illness. Efforts to favor access to treatment, such as reducing stigma associated with OCD and mental illness in general and increasing investments in mental health, are crucial. Recent literature data have highlighted that minorities with OCD, including Asian/Pacific Islander, Hispanic, Latino, Black, and Multiracial individuals, were often under-treated and underserved in terms of both psychological and psychiatric services compared to non-minorities.[36] Although a clear trend in this direction has not been observed in the Snapshot database (ie, no clear difference between treatment strategies in subjects from South Africa, Mexico, and Israel versus the other countries), this could be attributed to the fact that patients were included from a tertiary-care setting, where access to care is more filtered to selected individuals. Increasing education on mental health disorders and reducing stigma remain of high importance for improving access to effective care in each country. Lastly, geographical variables might be influenced by genetic differences and epigenetic mechanisms (eg, effect of food, environmental exposures), which contribute to different presentation of the disorder.[37] Therefore, a thorough evaluation of education background, cultural aspects, access to health services, and the genetic structure of populations, is crucial and should be always taken into account in clinical studies.

Discussion and future perspectives

The ICOCS Snapshot database has the unprecedented privilege to gain a global perspective on the socio-demographic and clinical features of individuals with OCD. The findings from the analysis of this database not only confirm previous literature research but also shed new light on various clinical aspects of OCD. One significant finding is the confirmation that OCD most commonly begins in pre-adult age. This emphasizes the importance of developing specific diagnostic and therapeutic pathways between child and adolescent psychiatrists, in light of the poorer prognosis associated with early-onset OCD.

Gender-related differences emerged in OCD presentation has also been highlighted, underscoring the need to further investigate how gender affects the clinical presentation of the illness and its underlying causes, such as potential influence of sex hormones.

Regarding comorbidity, while the rates of psychiatric comorbidity appeared lower when compared to previous studies, OCD was nonetheless associated with notable culture-specific rates of tobacco smoking and suicide risk. These findings emphasize the importance of addressing these comorbidities in the management of OCD. In terms of treatment, despite evidence from academic clinical trials suggesting augmentative treatments may be effective in OCD, analysis from the Snapshot database challenged this strength of evidence, suggesting that augmentation strategies may have limited therapeutic benefit for those who do not respond to first-line treatments. However, in the clinical practice, combination strategies remain the most preferred treatments in OCD and in other many psychiatric disorders, as the academic clinical trials might not reflect the real-world treatment modalities and effectiveness of medications—because of strict exclusion criteria—and the cross-sectional studies/naturalistic studies might not reflect the real therapeutic effects of medications—because of confounding factors.

https://doi.org/10.1017/S1092852923002432 Published online by Cambridge University Press

For a correct interpretation of these data, potential limitation intrinsic to the selected studies should be considered. First, the studies in the ICOCS Snapshot project were naturalistic and cross-sectional, potentially introducing recall-bias. Moreover, patients were at different stages of illness and were recruited from academic tertiary clinics (where rates of treatment-seeking subjects might be higher, as well as the rate of comorbidities and the severity of illness), therefore they might do not fully reflect the standard of care usually observed elsewhere, and such population may not adequately represent the broader population of individuals with OCD. Lastly, the varying prevalence of co-occurring conditions observed between different countries (eg, cigarette smoking, suicide, and comorbidity) might reflect a difference among those countries independently from OCD.

Of note, the collaborative network of researchers and clinicians involved in the ICOCS project have led to several position papers, including one study on the advances in the treatment of OCD,[1] on functional interventions as augmentation strategies[38] and a clinician's guide to face OCD amid the COVID-19 pandemic.[39] Overall, we believe that the past and future collaborative efforts of the ICOCS network will improve the knowledge on OCD, benefiting patients, related caregivers, and treating clinicians.

Future research should investigate the role of additional variables, such as cognitive functions or neurodevelopmental disorders (eg, autism spectrum disorders or attention deficit hyperactivity disorder) which are frequently observed alongside OCD. Transitioning to a longitudinal valuation of the sample could help to establish causal relationship among variables. Additionally, the geographical/transcultural peculiarities highlighted in the ICOCS database analysis underline the need for specific diagnostic and therapeutic strategies tailored to different populations, considering both biological and environmental factors.

Acknowledgments. The authors wish to acknowledge the International College of Obsessive-Compulsive Disorders (www. ICOCS.org) and the European College of Neuropsychopharmacology (ECNP) Obsessive-Compulsive and Related Disorders Research Network (OCRN), who have contributed to the development of this article through network opportunities.

Author contribution. Conceptualization: M.V., B.D.; Supervision: B.D.; Writing—original draft: M.V., B.B.; Writing—review and editing: M.V., B.B., N.A.F., E.H., M.V.A., J.M.M., J.Z., B.D. All authors agreed to the publication of the manuscript in its final version.

Financial support. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interest. N.A.F. declares that in the past 3 years, she has accepted research or networking grants from the UK NIHR, COST Action, Orchard; travel and/or hospitality expenses from the BAP, ECNP, RCPsych, CINP, International Forum of Mood and Anxiety Disorders, World Psychiatric Association, Indian Association for Biological Psychiatry; payment from Elsevier for editorial duties. Previously, she has accepted paid speaking engagements in various industry supported symposia and has recruited patients for various industry-sponsored studies in the field of OCD treatment. She leads an NHS treatment service for OCD. She holds board membership for various registered charities linked to OCD. She gives expert advice on psychopharmacology to the UK MHRA. B.D. has received grant/research support from LivaNova, Inc., Angelini and Lundbeck and Lecture Honoraria from Angelini, Janssen, Otzuka, and Lundbeck. M.V. has been on the advisory board of Allergan, Almatica, Brainsway, Lundbeck, Myriad Neuroscience, Otsuka, and Purdue Pharma. He has received research support from Janssen-Ortho Inc., Purdue Pharma (Canada), the Canadian Foundation for Innovation, and Hamilton Academic Health Sciences Organization (HAHSO). E.H. has received research grants from Department of Defense, Orphan Products Division of Food and Drug Administration, Roche, and GW Pharma. He has consulted from Roche and GW Pharma and he receives editorial fees from Elsevier. J.M.M. has received research or networking funding from the Spanish official research agencies CIBERSAM-ISCIII and AGAUR, has received consultation fees from Janssen, lecture fees from AbBiotics, Exeltis, and research funding from Janssen, AbBiotics, Novartis, and Medtronic in the last 36 months. J.Z. has received grant/research support from Lundbeck, Servier, Brainsway & Pfizer, NIH, and DoD. He has received honoraria or consultation fees from Servier, Pfizer, Abbott, Lilly, Actelion, AstraZeneca, SunPharma, Roche, and Brainsway, and participated in companies sponsored by Lundbeck, Roche, Lilly, Servier, and Pfizer. J.Z. was also invited to participate as a speaker's bureau in Abbott, SunPharma, and Brainsway. M.V. and B.B. report no financial relationships with commercial interests.

References

1. Fineberg NA, Hollander E, Pallanti S, et al. Clinical advances in obsessive-compulsive disorder: a position statement by the International College of Obsessive-Compulsive Spectrum Disorders. *Int Clin Psychopharmacol.* 2020;**35**(4):173–193. doi:10.1097/YIC.0000000000000314
2. Dell'Osso B, Benatti B, Buoli M, et al. The influence of age at onset and duration of illness on long-term outcome in patients with obsessive-compulsive disorder: a report from the International College of Obsessive Compulsive Spectrum Disorders (ICOCS). *Eur Neuropsychopharmacol.* 2013;**23**(8):865–871. doi:10.1016/J.EURONEURO.2013.05.004
3. Sheehan D V, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry.* 1998;**59**(Suppl 20):22–33;quiz 34–57.
4. Benatti B, Girone N, Celebre L, et al. The role of gender in a large international OCD sample: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) network. *Compr Psychiatry.* 2022;**116**:152315. doi:10.1016/J.COMPPSYCH.2022.152315
5. Benatti B, Dell'Osso B, Shen H, et al. Prevalence and correlates of current suicide risk in an international sample of OCD adults: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) network and Obsessive Compulsive and Related Disorders Network (OCRN) of the European College of Neuropsychopharmacology. *J Psychiatr Res.* 2021;**140**:357–363. doi:10.1016/J.JPSYCHIRES.2021.05.054
6. Dell'osso B, Vismara M, Benatti B, et al. Lifetime bipolar disorder comorbidity and related clinical characteristics in patients with primary obsessive compulsive disorder: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). *CNS Spectr.* 2020;**25**(3):419–425. doi:10.1017/S1092852919001068
7. Dell'Osso B, Benatti B, Arici C, et al. Prevalence of suicide attempt and clinical characteristics of suicide attempters with obsessive-compulsive disorder: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). *CNS Spectr.* 2018;**23**(1):59–66. doi:10.1017/S1092852917000177
8. Dell'Osso B, Benatti B, Rodriguez CI, et al. Obsessive-compulsive disorder in the elderly: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). *European Psychiatry.* 2017;**45**:36–40. doi:10.1016/j.eurpsy.2017.06.008
9. Dell'Osso B, Benatti B, Hollander E, et al. Childhood, adolescent and adult age at onset and related clinical correlates in obsessive-compulsive disorder: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). *Int J Psychiatry Clin Pract.* 2016;**20**(4):210–217. doi:10.1080/13651501.2016.1207087
10. Dell'Osso B, Nicolini H, Lanzagorta N, et al. Cigarette smoking in patients with obsessive compulsive disorder: a report from the International College of Obsessive Compulsive Spectrum Disorders (ICOCS). *CNS Spectr.* 2015;**20**(5):469–473. doi:10.1017/S1092852915000565
11. Lochner C, Fineberg NA, Zohar J, et al. Comorbidity in obsessive–compulsive disorder (OCD): a report from the International College of Obsessive–Compulsive Spectrum Disorders (ICOCS). *Compr Psychiatry.* 2014;**55**(7):1513–1519. doi:10.1016/j.comppsych.2014.05.020
12. Van Ameringen M, Simpson W, Patterson B, et al. Pharmacological treatment strategies in obsessive compulsive disorder: a cross-sectional

view in nine international OCD centers. *J Psychopharmacol.* 2014;**28**(6): 596–602. doi:10.1177/0269881113517955
13. Benatti B, Celebre L, Girone N, et al. Clinical characteristics and comorbidity associated with female gender in obsessive-compulsive disorder. *J Psychiatr Res.* 2020;**131**:209–214. doi:10.1016/J.JPSYCHIRES.2020.09.019
14. Fontenelle LF, Mendlowicz MV, Marques C, et al. Early- and late-onset obsessive-compulsive disorder in adult patients: an exploratory clinical and therapeutic study. *J Psychiatr Res.* 2003;**37**(2):127–133. doi:10.1016/S0022-3956(02)00087-0
15. Kohn R, Westlake RJ, Rasmussen SA, et al. Clinical features of obsessive-compulsive disorder in elderly patients. *Am J Geriatr Psychiatry.* 1997;**5**(3): 211–215. doi:10.1097/00019442-199700530-00004
16. Brakoulias V, Rehn S. Does the severity of obsessive-compulsive symptoms reduce with age? *J Affect Disord.* 2017;**213**:178–179. doi:10.1016/J.JAD.2017.02.024
17. Rüther T, Bobes J, De Hert M, et al. EPA guidance on tobacco dependence and strategies for smoking cessation in people with mental illness. *Eur Psychiatry.* 2014;**29**(2):65–82. doi:10.1016/J.EURPSY.2013.11.002
18. Abramovitch A, Pizzagalli DA, Geller DA, et al. Cigarette smoking in obsessive-compulsive disorder and unaffected parents of OCD patients. *Eur Psychiatry.* 2015;**30**(1):137–144. doi:10.1016/J.EURPSY.2013.12.003
19. Sharma P, Gale TM, Fineberg NA. Clinical correlates of tobacco smoking in OCD: a UK, case-controlled, exploratory analysis. *J Behav Addict.* 2012;**1** (4):180–185. doi:10.1556/JBA.1.2012.008
20. National Institute for Health and Care Excellence. Obsessive-compulsive disorder and body dysmorphic disorder: treatment. [NICE]. Published 2005. Accessed October 26, 2020. https://www.nice.org.uk/guidance/cg31.
21. Sheehan DV. *The Anxiety Disease*. New York: Charles Scribners Sons; 1983.
22. Goodwin R, Koenen KC, Hellman F, et al. Helpseeking and access to mental health treatment for obsessive-compulsive disorder. *Acta Psychiatr Scand.* 2002;**106**(2):143–149. doi:10.1034/J.1600-0447.2002.01221.X
23. Brakoulias V, Starcevic V, Belloch A, et al. Comorbidity, age of onset and suicidality in obsessive–compulsive disorder (OCD): an international collaboration. *Compr Psychiatry.* 2017;**76**:79–86. doi:10.1016/j.comppsych.2017.04.002
24. Fontenelle LF, Nicolini H, Brakoulias V. Early intervention in obsessive-compulsive disorder: from theory to practice. *Compr Psychiatry.* 2022;**119**: 152353 doi:10.1016/J.COMPPSYCH.2022.152353
25. Pallanti S, Grassi G, Sarrecchia ED, et al. Obsessive-compulsive disorder comorbidity: clinical assessment and therapeutic implications. *Front Psychiatry.* 2011;**2**:70. doi:10.3389/FPSYT.2011.00070
26. Stein DJ, Costa DLC, Lochner C, et al. Obsessive-compulsive disorder. *Nat Rev Dis Primers.* 2019;**5**(1):52. doi:10.1038/S41572-019-0102-3
27. Pellegrini L, Maietti E, Rucci P, et al. Suicide attempts and suicidal ideation in patients with obsessive-compulsive disorder: a systematic review and meta-analysis. *J Affect Disord.* 2020;**276**:1001–1021. doi:10.1016/J.JAD.2020.07.115
28. Albert U, Marazziti D, Di Salvo G, et al. A systematic review of evidence-based treatment strategies for obsessive-compulsive disorder resistant to first-line pharmacotherapy. *Curr Med Chem.* 2018;**25**(41):5647–5661. doi: 10.2174/0929867325666171222163645
29. Fontenelle LF, Mendlowicz MV, Marques C, et al. Trans-cultural aspects of obsessive-compulsive disorder: a description of a Brazilian sample and a systematic review of international clinical studies. *J Psychiatr Res.* 2004;**38** (4):403–411. doi:10.1016/j.jpsychires.2003.12.004
30. Nicolini H, Salin-Pascual R, Cabrera B, et al. Influence of culture in obsessive-compulsive disorder and its treatment. *Curr Psychiatry Rev.* 2017;**13**(4):285. doi:10.2174/2211556007666180115105935
31. Williams MT, Chapman LK, Simms J V., et al. Cross-cultural phenomenology of obsessive-compulsive disorder. In Abramowitz JS, McKay D, Storch EA (eds), *The Wiley Handbook of Obsessive Compulsive Disorders*. Hoboken, NJ: Wiley Blackwell; 2017, pp. 56–74. doi:10.1002/9781118890233.CH4
32. Petribú K, Bastos O. Comorbidade em trastorno obsessivo-compulsivo 3ª parte: objetivos, metodologia, resultados e discussão. *J bras psiquiatr.* 1997; **46**(8):417–425.
33. Medeiros GC, Torres AR, Boisseau CL, et al. A cross-cultural clinical comparison between subjects with obsessive-compulsive disorder from the United States and Brazil. *Psychiatry Res.* 2017;**254**:104–111. doi: 10.1016/J.PSYCHRES.2017.04.024
34. Horwath E, Weissman MM. The epidemiology and cross-national presentation of obsessive-compulsive disorder. *Psychiatr Clin North Am.* 2000;**23** (3):493–507. doi:10.1016/S0193-953X(05)70176-3
35. Kirmayer LJ, Fung K, Rousseau C, et al. Guidelines for training in cultural psychiatry. *Can J Psychiatry.* 2021;**66**(2):195–246. doi:10.1177/0706743720907505
36. Katz JA, Rufino KA, Werner C, et al. OCD in ethnic minorities. *Clin Exp Psychol.* 2020;**6**(1):01–06.
37. Zai G, Barta C, Cath D, et al. New insights and perspectives on the genetics of obsessive-compulsive disorder. *Psychiatr Genet.* 2019;**29**(5):142–151. doi:10.1097/YPG.0000000000000230
38. Varinelli A, Caricasole V, Pellegrini L, et al. Functional interventions as augmentation strategies for obsessive-compulsive disorder (OCD): scoping review and expert survey from the international college of obsessive-compulsive spectrum disorders (ICOCS). *Int J Psychiatry Clin Pract.* 2022;**26**(1):92–107. doi:10.1080/13651501.2021.1872646
39. Fineberg NA, Van Ameringen M, Drummond L, et al. How to manage obsessive-compulsive disorder (OCD) under COVID-19: a clinician's guide from the International College of Obsessive Compulsive Spectrum Disorders (ICOCS) and the Obsessive-Compulsive and Related Disorders Research Network (OCRN) of the European College of Neuropsychopharmacology. *Compr Psychiatry.* 2020;**100**:152174. doi:10.1016/j.comppsych.2020.152174