

1 **Lifetime Bipolar Disorder comorbidity and related clinical characteristics in**
2 **patients with primary Obsessive Compulsive Disorder: a report from the**
3 **International College of Obsessive-Compulsive Spectrum Disorders (ICOCS)**

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48 **Abstract**

49 **Introduction:** Bipolar Disorder (BD) and Obsessive Compulsive Disorder (OCD) are prevalent,
50 comorbid and disabling conditions, often characterized by early onset and chronic course. When
51 comorbid, OCD and BD can determine a more pernicious course of illness, posing therapeutic
52 challenges for clinicians. Available reports on prevalence and clinical characteristics of comorbidity
53 between BD and OCD showed mixed results, likely depending on the primary diagnosis of
54 analyzed samples.

55 **Methods:** We assessed prevalence and clinical characteristics of BD comorbidity in a large
56 International sample of patients with primary OCD (n=401), through the International College of
57 Obsessive Compulsive Spectrum Disorders (ICOCS) snapshot database, by comparing OCD
58 subjects with vs without BD comorbidity.

59 **Results:** Amongst primary OCD patients, 6.2% showed comorbidity with BD. OCD patients with
60 vs without BD comorbidity more frequently had a previous hospitalization ($p<.001$) and current
61 augmentation therapies ($p<.001$). They also showed greater severity of OCD ($p<.001$), as measured
62 by the Y-BOCS.

63 **Conclusion:** These findings from a large International sample indicate that approximately 1 out of
64 16 patients with primary OCD may additionally have BD comorbidity along with other specific
65 clinical characteristics, including more frequent previous hospitalizations, more complex
66 therapeutic regimens and a greater severity of OCD. Prospective international studies are needed to
67 confirm our findings.

68 **Keywords:** Bipolar Disorder, Obsessive Compulsive Disorder, comorbidity, prevalence.

69 **Introduction**

70 Obsessive Compulsive Disorder (OCD) and Bipolar Disorder (BD) are prevalent and chronic
71 conditions, frequently comorbid, difficult-to-treat and highly disabling^{1,2}. Of note, both conditions
72 have been separated into autonomous chapters by the DSM-5, respectively from anxiety disorders
73 and depressive disorders, with other spectrum conditions included within the new chapters³.

74 While comorbidity in BD represents the rule rather than the exception, OCD seems to show lower -
75 yet appreciable - rates of comorbidity, while mutual comorbidity (OCD+BD) prevalence was found
76 to differ according to patients' primary diagnosis⁴. In a recent systematic review, patients with a
77 primary OCD diagnosis showed rates of BD comorbidity ranging from 6 to 10%, while patients
78 with primary BD were found to have comorbid OCD in 11 to 21% of the cases⁴. However, given
79 the traditionally early onset of both OCD and BDs, it is often difficult to assess which condition
80 appeared first, family history being helpful - when positive - to help unraveling primary diagnosis
81 along with subsequent longitudinal evaluations.

82 Indeed, the presence of comorbidity between OCD and BD can determine a different course of
83 illness, according to the primary diagnosis. For instance, in case of primary BD, OCD comorbidity
84 was found to be associated with a more episodic course of OC symptoms, characterized by
85 symptoms' worsening during depression, symptoms' improvement during mania/hypomania, and a
86 higher mean number of depressive episodes^{4,5}. On the other hand, in patients with primary OCD,
87 the prescription of high doses of serotonergic antidepressants could induce mood elevation
88 episodes, confounding in both cases situations of real vs spurious comorbidity⁴⁻⁶. Comorbidity
89 rates, moreover, may vary according to local (e.g., when detected in general psychiatric services vs
90 tertiary clinics), clinical (severity of illness) and cultural variables (e.g., attitudes including stigma,
91 secretiveness, access to treatment)².

92 In the available literature, different studies addressed this topic, trying to better characterize this
93 phenomenon and mutual influence of these disorders. Indeed, when primary BD is comorbid with
94 OCD, the overall clinical condition may determine a more severe form of illness. In this respect,

95 comorbid patients have been differently associated with relevant disease-related variables, like an
96 earlier age at onset ^{7,8}, higher frequency of residual symptoms ⁹, poorer functioning and poorer
97 quality of life in different domains (i.e., lower GAF scale score ¹⁰, lower rate of employment in BDI
98 patients ¹¹), a higher rate of suicidal behavior ^{8,12,13}. Moreover, additional comorbidity seemed to be
99 higher in the comorbid group especially with anxiety disorders ^{7,9,11}, alcohol ¹² and substance abuse
100 ¹⁴, and with impulse control, eating, and tic disorders in BD female patients ⁹.

101 Other studies specifically assessed the clinical characteristics of primary OCD patients with vs
102 without BD comorbidity, reporting that comorbid patients present a worse clinical prognosis
103 compared to non-comorbid patients, being associated with a higher suicidal risk ¹⁵, more frequent
104 hospitalizations ^{16,17}, more severe obsessive-compulsive symptoms according to Yale-Brown
105 Obsessive Compulsive Scale (YBOCS) score ¹⁷, and a poorer response to treatments in a youth
106 OCD sample ¹⁸. Moreover, an additional comorbid disease has been reported more frequently in
107 these patients, in particular with alcohol ¹⁹ and substance abuse ¹⁷, and anxiety disorders ^{17,19}.

108 In light of the above, the aim of the present study was to assess rates and clinical correlates of BD
109 comorbidity in a large, international sample of primary OCD patients, recruited in centers affiliated
110 with the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). In
111 particular, we hypothesized that BD comorbidity rates in the ICOCS sample could parallel
112 previously reported rates in available studies of primary OCD patients, although the geographical
113 diversity of the sample might also show distinct peculiarities in terms of epidemiology and clinical
114 features. Moreover, based on the existing literature, we hypothesized that BD comorbid vs non
115 comorbid OCD patients could show a higher burden of the disease, presenting specific clinical
116 characteristics associated with a less favorable outcome like higher severity and related
117 hospitalizations, a more frequent suicidal behavior, more complex therapeutic regimens, and a
118 higher impact on social adaptation.

119

120 **Methods**

121 Among the whole ICOCS sample of 504 OCD outpatients, we selected and analyzed individuals
122 having available information on bipolar comorbidity. The resulting sample of the present analysis
123 consisted of 401 outpatients of either gender and any age, attending different OCD clinics
124 worldwide, participating in the ICOCS network. Diagnoses were obtained using the Structured
125 Clinical Interview for DSM-IV-TR Axis I disorders (SCID I) ²⁰. After obtaining patients' written
126 informed consent and approval from local Ethic Committees/Institutional Review Boards for using
127 patients' information for research purposes, socio-demographic and clinical variables were
128 collected and included in a common web database. Additional details about sample assessment have
129 been published elsewhere ²¹. Suicidal behavior was assessed with Mini-International
130 Neuropsychiatric Interview ²².

131 In a previous ICOCS publication on comorbidity with OC-related and other psychiatric conditions
132 in a slightly different sample (due to additional patients being recruited and the exclusion of other
133 patients with missing data and incomplete information), BD comorbidity had not been evaluated,
134 being set aside for separate subsequent analysis and publication ¹.

135 For the purpose of the present study, patients were categorized into two subgroups based on the
136 presence (OCD-wBD) or absence (OCD-w/oBD) of comorbidity with BD. The two subgroups were
137 compared with respect to a series of socio-demographic and clinical variables specified in Table 1.
138 Statistical analyses were performed with Pearson's chi-squared test for categorical variables and *t*-
139 test for continuous ones. For all the analyses, the level of statistical significance was set at .05.

140

141 **Results**

142 Within the overall sample, 6.2% (n=32) of OCD patients had comorbidity with BD. Socio-
143 demographic and clinical variables of the two subgroups of OCD patients with vs without BD
144 comorbidity are reported in Table 1.

145 Figure 1 shows socio-demographic and clinical variables that were found to differ between the two
146 subgroups. OCD patients with versus without BD comorbidity showed a higher rate of previous

147 psychiatric hospitalization (48.2% vs 20.6%, $p < .001$) and a higher prevalence of augmentation
148 therapies vs monotherapies (77.3% vs 48.5%, $p < .001$), being augmentation therapies those
149 compounds used as add-on for treatment resistant OCD patients. More in detail, on both OCD
150 subgroups, the most frequently prescribed augmentation therapies were antipsychotics (OCD-wBD
151 66.7% and OCD-w/oBD 34.6%), being risperidone the most represented (OCD-wBD 42.2% and
152 OCD-w/oBD 75%); given a high rate of missing data for these specific variables, both analyses did
153 not reach a statistically significant threshold.

154 Additionally, significantly higher severity of OCD emerged in OCD patients with vs without BD
155 comorbidity, as measured through the YBOCS²³ total scores (25.7 vs 22.5, $p < .001$), with no
156 statistically significant differences in obsession (12.5 vs 11.5) and compulsion (12.1 vs 10.9)
157 subscales.

158 While differences in terms of suicide attempts between the two groups were not observed, current
159 suicide risk showed as twice the rate in OCD patients with vs without BD comorbidity (31.3% vs
160 14.6%), without reaching the statistically significant threshold. Lastly, OCD patients with vs
161 without BD comorbidity were more frequently found to live alone (25% vs 13.8%), to be divorced
162 (10.3% vs 5.9%), and to be unemployed (15.6% vs 8.7%), although not a statistically significant
163 level.

164

165 **Discussion**

166 In this ICOCS report, we focused on prevalence and clinical correlates of BD comorbidity in
167 primary OCD patients. Our observed lifetime prevalence of BD comorbidity (6.2%) can be
168 positioned at the lower range in relation to the available studies in the field⁴. This is likely due to
169 the composition of the ICOCS sample, constituted by primary OCD patients attending tertiary OCD
170 clinics worldwide, and to the fact that patients with a comorbid BD diagnosis are more frequently
171 referred to community psychiatric centers or BD specialized centers. Additionally, this result might
172 derive from the limited overall comorbidity rate (35%) characterizing our sample. BD comorbidity,

173 therefore, appears to be less frequent in primary OCD patients than is OCD comorbidity in primary
174 BD patients. In this respect, previous International reports showed a higher rate of other comorbid
175 DSM-IV-TR Axis I disorders, compared to BD, with major depressive disorder and
176 anxiety disorders being the most common comorbid conditions in primary OCD patients ^{1,24}.

177 The higher rate of previous hospitalization in the comorbid cases seems to be consistent with
178 previous reports ^{4,17,19,25,26} and may likely be determined by the co-occurrence of BD episodes,
179 causing more frequent admission to hospital (following severe manic or depressive episodes), even
180 though it may also be related to OCD worsening due to a higher severity of OCD in comorbid
181 patients (as suggested by the greater severity of illness confirmed by the Y-BOCS in these
182 individuals).

183 The more complex psychopharmacological regimen observed in OCD with vs without BD
184 comorbidity, reflecting a higher rate of augmentation treatments vs monotherapies in the former
185 group, may also be interpreted as a characteristic of greater severity of OCD and overall illness,
186 making it necessary to frequently add an antipsychotic to the serotonergic reuptake inhibitor (SRI),
187 due to the severe nature of OC symptoms and in order to prevent manic switches ²⁷. The same result
188 was reported in a study with young OCD subjects, where comorbid OCD+BD patients showed a
189 more frequently poly-therapy compared to a SRI only therapy, with second generation
190 antipsychotics, including risperidone, most prevalently used in the comorbid group ²⁸. Literature
191 data support Risperidone efficacy as augmentative therapy over SRI alone in OCD resistant patients
192 ^{29,30} particularly in those patients with a history of mood instability ³¹, emphasizing Risperidone
193 potential pharmacological effect on mood stabilization. Nonetheless, OCD comorbid patients could
194 have received more frequently augmentation therapies just for the occurrence of two diagnoses,
195 each one requiring a different therapeutic regimen. Of note, no significant differences emerged with
196 respect to cognitive behavioral therapy or other psychotherapeutic treatments.

197 Arguably, another clinically relevant finding was the greater OCD severity in patients with vs
198 without BD comorbidity. Previous analyses showed mixed results in this respect ^{17,32}. As the Y-

199 BOCS focuses exclusively on obsessions and compulsions, it is not likely that the higher scores
200 would have been confounded by the presence of comorbid BD symptomatology *per se*. In fact,
201 while obsessions might possibly determine higher scores due to concomitant depressive ruminations
202 (though the two groups did not differ on depression scores) or flights of ideas, compulsions are
203 relatively pathognomonic for OCD and OC related disorders. In our analysis, both the obsessive and
204 the compulsive subscale scores, as well as the total score, were higher in the comorbid group, thus
205 indicating a more severe OCD phenotype. Nonetheless, it must be borne in mind that OCD
206 symptomatology is strongly influenced by mood phases ^{4,5}, and consequently the latter might have
207 determined an impact on YBOCS scores assessed in the present sample.

208 Lastly, even though other statistically significant differences between OCD patients with vs without
209 comorbid BD were not found, it is noteworthy to mention that current suicidal risk was almost
210 twice as high in comorbid subjects. OCD is *per se* associated with a higher suicidal ideation and
211 lifetime suicide attempts compared to the general population ^{33,34} and the comorbidity with BD
212 might increase this phenomenon. Nonetheless, in our sample, the rates of previous suicide attempt
213 were similar between the two subgroups, differing from a previous report showing a higher rate in
214 comorbid OCD patients ¹⁵ and encouraging additional investigation on suicidal behaviors and risk
215 in these patients. However, in this study, it needs to be noted that OCD patients without BD
216 comorbidity could have a range of other comorbid disorders contributing to higher suicide attempt
217 rates.

218 Finally, focusing on a sociodemographic perspective, despite not reaching the statistically
219 significant threshold, a divorced status, living alone, and being unemployed were observed at rates
220 twice as higher in OCD patients with vs without comorbid BD. These findings also deserve further
221 investigation, as they may converge in delineating a more disadvantaged sociodemographic
222 condition of OCD patients when comorbid BD is present.

223 The findings reported in the present study should be interpreted in light of some limitations. First,
224 our study did not characterize BD phases at the assessment nor other issues related to BD polarity

225 (i.e., polarity at onset or prevalent polarity) and subtype. These variables could have made our
226 results easier to interpret, likely having a major impact on several clinical characteristics, including
227 number of hospitalizations, pharmacological treatments, and YBOCS score. Additionally, OCD
228 phenotype was not assessed in the total sample nor in the two subgroups and sample collection
229 (mainly tertiary centers specialized in OCD) might have affected the results and influence their
230 generalizations. Lastly, given the International nature of the study, specific variables were recorded
231 only in a limited number of centers and consequently not analyzed due to the presence of missing
232 data that did not allowed us to compare and contrast all variables. At the same time, the
233 international sample assessed in the present study can be considered one of the strengths of this
234 report.

235 In conclusion, our results indicate that when OCD was comorbid with BD (6.2% of the cases),
236 patients were found to show an overall higher severity of illness, as documented by a higher rate of
237 hospitalization, a more complex pharmacological regimen, as well as a higher Y-BOCS score.
238 Further studies are needed to verify the impact of BD comorbidity on OCD and to clarify the
239 longitudinal relationship between these two disorders and their respective evolution.

240

241 **Conflicts of interest:**

242 Bernardo Dell'Osso reports: Angelini, speaker's bureau, speaker's fee; Lundbeck, speaker's bureau,
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264

265 **References**

266

- 267 1. Lochner C, Fineberg NA, Zohar J, et al. Comorbidity in obsessive–compulsive disorder
268 (OCD): A report from the International College of Obsessive–Compulsive Spectrum
269 Disorders (ICOCS). *Compr Psychiatry*. 2014;55(7):1513-1519.
270 doi:10.1016/j.comppsy.2014.05.020
- 271 2. Amerio A, Stubbs B, Odone A, Tonna M, Marchesi C, Ghaemi SN. The prevalence and
272 predictors of comorbid bipolar disorder and obsessive–compulsive disorder: A systematic
273 review and meta-analysis. *J Affect Disord*. 2015;186:99-109. doi:10.1016/j.jad.2015.06.005
- 274 3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*
275 *(5th Ed.)*. Arlington, VA: American Psychiatric Publishing; 2013.
- 276 4. Amerio A, Odone A, Liapis CC, Ghaemi SN. Diagnostic validity of comorbid bipolar
277 disorder and obsessive-compulsive disorder: a systematic review. *Acta Psychiatr Scand*.
278 2014;129(5):343-358. doi:10.1111/acps.12250
- 279 5. Mucci F, Toni C, Favaretto E, Vannucchi G, Marazziti D, Perugi G. Obsessive-compulsive
280 disorder with comorbid bipolar disorders: clinical features and treatment implications. *Curr*
281 *Med Chem*. November 2017. doi:10.2174/0929867324666171108145127
- 282 6. Amerio A, Tonna M, Odone A, Stubbs B, Ghaemi SN. Course of illness in comorbid bipolar
283 disorder and obsessive–compulsive disorder patients. *Asian J Psychiatr*. 2016;20:12-14.
284 doi:10.1016/j.ajp.2016.01.009
- 285 7. Jeon S, Baek JH, Yang SY, et al. Exploration of comorbid obsessive-compulsive disorder in
286 patients with bipolar disorder: The clinic-based prevalence rate, symptoms nature and clinical
287 correlates. *J Affect Disord*. 2018;225:227-233. doi:10.1016/j.jad.2017.08.012
- 288 8. Ozdemiroglu F, Sevincok L, Sen G, et al. Comorbid obsessive-compulsive disorder with
289 bipolar disorder: A distinct form. *Psychiatry Res*. 2015;230(3):800-805.
290 doi:10.1016/j.psychres.2015.11.002

- 291 9. Issler CK, Monkul ES, Amaral JA de MS, et al. Bipolar disorder and comorbid obsessive-
292 compulsive disorder is associated with higher rates of anxiety and impulse control disorders.
293 *Acta Neuropsychiatr.* 2010;22(2):81-86. doi:10.1111/j.1601-5215.2010.00457.x
- 294 10. Joshi G, Wozniak J, Petty C, et al. Clinical characteristics of comorbid obsessive-compulsive
295 disorder and bipolar disorder in children and adolescents. *Bipolar Disord.* 2010;12(2):185-
296 195. doi:10.1111/j.1399-5618.2010.00795.x
- 297 11. Shashidhara M, Sushma BR, Viswanath B, Math SB, Janardhan Reddy Y. Comorbid
298 obsessive compulsive disorder in patients with bipolar-I disorder. *J Affect Disord.*
299 2015;174:367-371. doi:10.1016/j.jad.2014.12.019
- 300 12. Magalhães PVS, Kapczinski NS, Kapczinski F. Correlates and impact of obsessive-
301 compulsive comorbidity in bipolar disorder. *Compr Psychiatry.* 2010;51(4):353-356.
302 doi:10.1016/j.comppsy.2009.11.001
- 303 13. Krüger S, Bräunig P, Cooke RG. Comorbidity of obsessive-compulsive disorder in recovered
304 inpatients with bipolar disorder. *Bipolar Disord.* 2000;2(1):71-74.
- 305 14. Angst J, Gamma A, Endrass J, et al. Obsessive-compulsive syndromes and disorders. *Eur*
306 *Arch Psychiatry Clin Neurosci.* 2005;255(1):65-71. doi:10.1007/s00406-005-0576-8
- 307 15. Saraf G, Paul I, Viswanath B, Narayanaswamy JC, Math SB, Reddy YCJ. Bipolar disorder
308 comorbidity in patients with a primary diagnosis of OCD. *Int J Psychiatry Clin Pract.*
309 2017;21(1):70-74. doi:10.1080/13651501.2016.1233344
- 310 16. Mahasuar R, Janardhan Reddy YC, Math SB. Obsessive-compulsive disorder with and
311 without bipolar disorder. *Psychiatry Clin Neurosci.* 2011;65(5):423-433. doi:10.1111/j.1440-
312 1819.2011.02247.x
- 313 17. Timpano KR, Rubenstein LM, Murphy DL. Phenomenological features and clinical impact
314 of affective disorders in OCD: a focus on the bipolar disorder and OCD connection. *Depress*
315 *Anxiety.* 2012;29(3):226-233. doi:10.1002/da.20908
- 316 18. Masi G, Berloffia S, Mucci M, et al. A NATURALISTIC EXPLORATORY STUDY OF

- 317 OBSESSIVE-COMPULSIVE BIPOLAR COMORBIDITY IN YOUTH. *J Affect Disord.*
318 2018;231:21-26. doi:10.1016/j.jad.2018.01.020
- 319 19. Perugi G, Toni C, Frare F, Traverso MC, Hantouche E, Akiskal HS. Obsessive-compulsive-
320 bipolar comorbidity: a systematic exploration of clinical features and treatment outcome. *J*
321 *Clin Psychiatry.* 2002;63(12):1129-1134.
- 322 20. First M, Spitzer R, Gibbon M, Williams J. *Structured Clinical Interview for DSM-IV-TR*
323 *Axis I Disorders, Research Version, Patient Edition (SCID-I/P).* New York: Biometrics
324 Research, New York State Psychiatric Institute; 2002.
- 325 21. Dell’Osso B, Benatti B, Buoli M, et al. The influence of age at onset and duration of illness
326 on long-term outcome in patients with obsessive-compulsive disorder: a report from the
327 International College of Obsessive Compulsive Spectrum Disorders (ICOCS). *Eur*
328 *Neuropsychopharmacol.* 2013;23(8):865-871. doi:10.1016/j.euroneuro.2013.05.004
- 329 22. Sheehan D V, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric
330 Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric
331 interview for DSM-IV and ICD-10. *J Clin Psychiatry.* 1998;59 Suppl 20:22-33;quiz 34-57.
- 332 23. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive
333 Scale. I. Development, use, and reliability. *Arch Gen Psychiatry.* 1989;46(11):1006-1011.
- 334 24. Brakoulias V, Starcevic V, Belloch A, et al. Comorbidity, age of onset and suicidality in
335 obsessive-compulsive disorder (OCD): An international collaboration. *Compr Psychiatry.*
336 2017;76:79-86. doi:10.1016/j.comppsy.2017.04.002
- 337 25. Kazhungil F, Mohandas E. Management of obsessive-compulsive disorder comorbid with
338 bipolar disorder. *Indian J Psychiatry.* 2016;58(3):259. doi:10.4103/0019-5545.192001
- 339 26. Kazhungil F, Cholakotttil A, Kattukulathil S, Kottelassal A, Vazhakalayil R. Clinical and
340 familial profile of bipolar disorder with and without obsessive-compulsive disorder: an
341 Indian study. *Trends psychiatry Psychother.* 2017;39(4):270-275. doi:10.1590/2237-6089-
342 2017-0061

- 343 27. Koran LM, Hanna GL, Hollander E, Nestadt G, Simpson HB, American Psychiatric
344 Association. Practice guideline for the treatment of patients with obsessive-compulsive
345 disorder. *Am J Psychiatry*. 2007;164(7 Suppl):5-53.
- 346 28. Masi G, Millepiedi S, Perugi G, et al. Pharmacotherapy in paediatric obsessive-compulsive
347 disorder: a naturalistic, retrospective study. *CNS Drugs*. 2009;23(3):241-252.
348 doi:10.2165/00023210-200923030-00005
- 349 29. Bloch MH, Landeros-Weisenberger A, Kelmendi B, Coric V, Bracken MB, Leckman JF. A
350 systematic review: antipsychotic augmentation with treatment refractory obsessive-
351 compulsive disorder. *Mol Psychiatry*. 2006;11(7):622-632. doi:10.1038/sj.mp.4001823
- 352 30. Dold M, Aigner M, Lanzenberger R, Kasper S. Antipsychotic Augmentation of Serotonin
353 Reuptake Inhibitors in Treatment-Resistant Obsessive-Compulsive Disorder: An Update
354 Meta-Analysis of Double-Blind, Randomized, Placebo-Controlled Trials. *Int J*
355 *Neuropsychopharmacol*. 2015;18(9):pyv047. doi:10.1093/ijnp/pyv047
- 356 31. Pfanner C, Marazziti D, Dell’Osso L, et al. Risperidone augmentation in refractory
357 obsessive-compulsive disorder: an open-label study. *Int Clin Psychopharmacol*.
358 2000;15(5):297-301.
- 359 32. Zutshi A, Reddy YCJ, Thennarasu K, Chandrashekhar CR. Comorbidity of anxiety disorders
360 in patients with remitted bipolar disorder. *Eur Arch Psychiatry Clin Neurosci*.
361 2006;256(7):428-436. doi:10.1007/s00406-006-0658-2
- 362 33. Dell’Osso B, Benatti B, Arici C, et al. Prevalence of suicide attempt and clinical
363 characteristics of suicide attempters with obsessive-compulsive disorder: a report from the
364 International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). *CNS Spectr*.
365 2018;23(01):59-66. doi:10.1017/S1092852917000177
- 366 34. Albert U, De Ronchi D, Maina G, Pompili M. Suicide risk in Obsessive-Compulsive
367 Disorder and exploration of risk factors: a systematic review. *Curr Neuropharmacol*.
368 2018;16. doi:10.2174/1570159X16666180620155941