Suicide Risk in Obsessive-Compulsive Disorder and Exploration of Risk Factors: A Systematic Review

Umberto Albert[1,*], Diana De Ronchi[1], Giuseppe Maina[2] and Maurizio Pompili[3]

[1]*Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy;* [2]*Rita Levi Montalcini Department of Neuroscience, University of Torino, Torino, Italy;* [3]*Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy*

Abstract: ***Background*:** Historically, OCD has been considered to be associated with a relatively low risk of suicide. Recent studies, on the contrary, revealed a significant association between OCD and suicide attempts and ideation. A huge variation in prevalence rates, however, is reported.

***Objective*:** To estimate prevalence rates of suicide attempts and suicidal ideation in individuals with OCD, and to identify predictors of suicide risk among subjects with OCD.

***Methods*:** We systematically reviewed the literature on suicide risk (ideation and/or attempts) and OCD. We included studies with appropriate definition of OCD, cross-sectional or prospective design, separating clinical samples from epidemiological studies, that employed a quantitative measure of suicidality and/or reported an outcome measure of the association between suicidality and OCD or examined factors associated with suicidality.

***Results*:** In clinical samples, the mean rate of lifetime suicide attempts is 14.2% (31 studies: range 6- 51.7%). Suicidal ideation is referred by 26.3-73.5% of individuals (17 studies, mean 44.1%); current suicidal ideation rate ranges between 6.4 and 75% (13 studies, mean 25.9). Epidemiological studies found that OCD increases significantly the odds of having a lifetime suicidal ideation as compared to the general population (OR: 1.9-10.3) and a history of lifetime suicide attempts (OR: 1.6- 9.9). Predictors of greater suicide risk are severity of OCD, the symptom dimension of unacceptable thoughts, comorbid Axis I disorders, severity of comorbid depressive and anxiety symptoms, past history of suicidality and some emotion-cognitive factors such as alexithymia and hopelessness.

***Conclusion*:** Overall, suicidality appears a relevant phenomenon in OCD.

ARTICLE HISTORY

Received: January 28, 2018
Revised: May 16, 2018
Accepted: June 20, 2018

DOI:
10.2174/1570159X16666180620155941

Keywords: Obsessive-compulsive disorder, suicidal ideation, suicide attempts, deaths by suicide, prevalence rates, predictors, risk factors.

1. INTRODUCTION

Historically, Obsessive-Compulsive Disorder (OCD) has been considered to be associated with a relatively low risk of suicide [1-3].

However, recent systematic reviews and meta-analyses have questioned this historical prejudice; Harris and colleagues [4] estimated, for example, that suicide risk in OCD is 10 times higher than expected in the general population, although this estimate was based on only two single studies. A subsequent meta-analysis [5] of suicide risk among patients with different anxiety disorders found in OCD a crude death rate due to suicide of 0.08% among 9776 individuals with OCD, with an estimated incidence of suicide attempts of 4%; these relatively low rates are however derived from the FDA database of patients participating in clinical trials evaluating the efficacy of antidepressants, and we may argue that severe patients could not have been enrolled in these trials due to exclusion criteria (the presence of suicide risk was often an exclusion criterion). Another meta-analysis on the association between anxiety disorders and suicidal behaviors found that the increase in the risk of suicide was demonstrated for each subtype of anxiety disorders except OCD [6]; again, results concerning the risk of suicidality in OCD were based on only 4 cohorts, thus raising doubts about the validity of these results.

More recently, Angelakis and colleagues [7] analyzed results of 48 studies on the association between suicidality and OCD (although they included and not differentiated studies performed in samples of patients with disorders other than OCD but with OC symptoms); the estimated pooled

*Address correspondence to this author at the Department of Biomedical and Neuromotor Science, Section of Psychiatry, University of Bologna, Viale C. Pepoli 5 – 40123, Bologna, Italy; Tel: +39-(0)51-2083058; Fax: +39- (0)51-521030; E-mail: umberto.albert@unibo.it

effect size revealed a moderate to high, significant association between OCD and two different types of suicidality (suicide attempts and suicidal ideation). This result is of highly clinical relevance, as clinicians could underestimate the risk of suicide in individuals with OCD based on previous historical prejudices, leading to underdiagnosing and undertreating of this disorder.

This systematic review, however, has some limitations: it did not differentiate between studies performed in clinical, presumably more severe, samples from those performed in the general population (epidemiological studies), mixing together results. Moreover, it didn't restrict the inclusion to subjects with a primary diagnosis of OCD; thus, it included samples of schizophrenic or bipolar patients where the authors analyzed the contribution of comorbid obsessive-compulsive symptoms to suicide risk of the primary non-OCD diagnosis. This could have inflated the estimate of suicide risk. Moreover, several other papers have since then been published, some of them including huge numbers of subjects diagnosed with OCD.

In addition, the exploration of which factors could contribute to suicide risk among OCD individuals is of particular relevance, since clinicians need to have potential indicators to screen and identify those patients who could benefit from specific interventions. Since the general opinion of psychiatrists is that OCD is not at risk for suicide, and since some meta-analyses on the topic supported this opinion [5, 6], another systematic review on this topic is, to our opinion, a valid contribution to both research and the clinical practice.

In providing the present paper we also want to stress that a phenomenological approach should guide clinicians in the assessment of suicide risk [8, 9]. The focus should be on what patients feel rather than on how they can be categorized. Maltsberger [10] reported that, "intense desperation is a mental emergency….Many unfortunate patients may quickly take their lives because they cannot wait for relief. Most desperate patients, enraged patients or intensely anxious patients show what they feel on their faces, body movements and demeanor". We therefore prefer the view that psychiatric disorders are contributor factors to suicide risk rather than explaining such risk in a given individual.

The aims of the present systematic review were: 1. to estimate prevalence rates of suicide attempts and suicidal ideation in individuals with a principal diagnosis of OCD; 2. to identify predictors of suicide risk among subjects with OCD. We clearly differentiated studies performed in clinical settings from epidemiological studies performed in the general population or prospective, cohort studies on nationwide registers. We also aimed at examining whether specific interventions were developed for treating individuals with OCD at higher risk for suicide (specific interventions aimed at reducing suicide risk or treating suicidality in OCD).

2. METHODS

2.1. Search Strategy

The systematic review was conducted using the PRISMA guidelines [11, 12] by searching PubMed from the date of the first available article to January 8, 2018. The search terms [suicide] OR [suicidality] OR [suicide attempts] OR [suicidal ideation] OR [suicidal thoughts] were combined with [OCD] OR [obsessive*compulsive disorder] OR [obsessive*compulsive symptoms].

2.2. Article Selection and Review Strategy

Articles were identified and assessed for eligibility by two independent reviewers (UA and GM), who independently decided which identified articles to include according to clinical importance and eligibility criteria. In case of disagreement, a third author (MP) was consulted to mediate consensual decisions. Duplicate studies were excluded. Cross-references from the articles identified were also examined. Unpublished studies, conference abstracts or poster presentations were not included. The database search was restricted to English language papers.

2.3. Eligibility Criteria

The inclusion criteria for the studies were the following: 1) studies with appropriate definition of OCD (diagnosis made through specific structured interviews and/or established international criteria); 2) adolescents and/or adults; 3) cross-sectional or prospective designs; 4) performed in clinical samples or in the general population (epidemiological studies); 5) employed a quantitative measure of suicidality in order to derive prevalence rates of current/lifetime suicide attempts, suicidal ideation and/or family history of suicide attempts/completed suicide; and/or 6) reported an outcome measure of the association between suicidality and OCD (*e.g*. odds ratios) or examined factors associated with suicidality. We deliberately excluded studies performed in samples other than OCD patients (*e.g*. individuals with Bipolar Disorder or Schizophrenia) even when they assessed the impact of obsessive-compulsive symptoms on suicidality in these patients.

3. RESULTS

3.1. Search Results

The flowchart of studies selected and included in the systematic review is provided in Fig. (**1**). In total, sixty-three studies were included in the qualitative synthesis.

For the analysis of results of the studies, we separately examined studies performed in clinical samples from epidemiological ones.

3.2. Suicide Risk in OCD: Studies in Clinical Samples

Table **1** reports results of the individual studies performed in order to assess suicide risk in clinical samples [13-48].

Thirty-six studies contributed to the analysis of prevalence rates of suicide attempts and suicidal ideation in individuals with a primary diagnosis of OCD. The vast majority of them employed a cross-sectional design and used the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Yale-Brown Obsessive-Compulsive Scale (YBOCS) to confirm the diagnosis and assess the severity of OCD. Although a wide variability exists in sample sizes, several studies enrolled several hundred patients.

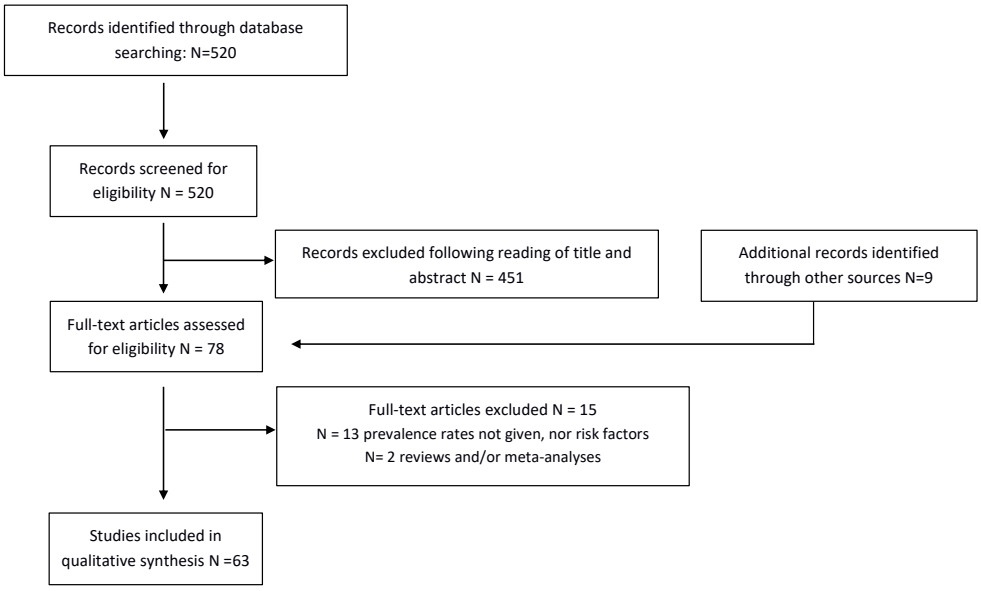

Fig. (1). Flow chart showing the selection of studies.

Nine studies reported family history rates for suicide attempts/completed suicides; across the studies, the overall rates of suicide attempts range between 11.5% to 27.1% (mean 17.9%, median 18.2%). Family history rates of completed suicide are reported by three studies only, ranging from 8.9% to 16.1%.

Prevalence rates of lifetime suicide attempts in individuals with OCD are reported by 31 studies, and range between 6% and 51.7%, with a mean of 14.2% (median 10.8%). Lifetime suicidal ideation is referred by 26.3-to-73.5% of individuals with OCD, as from 17 studies (mean 44.1%; median 36.4%); current suicidal ideation rate is reported by 13 studies, ranging from 6.4% to 75%, with a mean of 25.9% and a median of 15.6%.

Overall, suicidality appears a relevant phenomenon in OCD, as from our analysis of studies performed in clinical samples. It is possible, however, that this result of abnormally high prevalence rates of suicidality (attempts and ideation) is biased by the fact that clinical studies may have enrolled severe patients referring to specialized, tertiary centers for the treatment of resistant patients. We then examined whether epidemiological studies, enrolling all patients with a diagnosis of OCD independently from the severity of the disorder and regardless of them being treated or not, confirmed that OCD is at greater risk for suicide than the general population.

3.3. Suicide Risk in OCD: Epidemiological Studies

Table **2** presents results of epidemiological studies [49-62]. Fourteen studies provided data on the association in the general population between a baseline diagnosis of OCD (whether or not comorbid with other disorders) and suicidality (suicide attempts and/or suicidal ideation); two studies [59, 60] have been performed on National Registers (Danish Registers and Swedish National Patient Register, respectively), recruiting a huge sample of subjects diagnosed with OCD (10155 and 36788 individual affected by OCD, respectively) and providing data on the longitudinal association between OCD and death by suicide and lifetime suicide attempts over a follow-up of 9.7 and 44 years, respectively.

All studies which examined the issue found that OCD increases significantly the odds of having a lifetime suicidal ideation as compared to the general population (OR ranging between 1.9 and 10.3); the increased risk remains significant even after controlling for demographic variables and comorbid disorders (Adjusted Odds Ratio ranging from 3.8 to 5.58).

Concerning the association between OCD and lifetime suicide attempts in the general population, results are more controversial; the majority of studies found that the odds of having a history of lifetime suicide attempts is significantly higher in individuals with OCD (OR ranging from 1.6 to 9.9) [49, 51, 54, 55, 57, 58, 61]. However, controversy exists about the influence of psychiatric comorbidities on such risk: while two studies confirmed that this risk is significantly higher even in pure OCD subjects (without lifetime comorbidities) [55, 60], two other epidemiological studies were negative (no increased risk in pure OCD versus controls) [52, 58]. Moreover, the NEMESIS study [53, 56] found that the AOR for first ever incidence of suicide attempts in individuals with a baseline diagnosis of OCD was not significantly higher than that of comparison subjects over the 3-year follow-up period.

The odds ratio of dying by suicide in the two prospective studies performed in Denmark and Sweden is significantly higher (3.02-9.83) than expected, and remained significant even in pure OCD (13.18) [59, 60].

3.4. Factors Associated with Increased Suicide Risk in OCD

Given that individuals with OCD seem more at risk of suicidal ideation and (to a lesser degree) suicide attempts

Table 1. Suicidality in OCD: studies in clinical samples.

Authors	Country	Design	OCD Diagnosis	Screening for Suicidality	Mode of Suicidality	Sample N Mean Age % Males	Suicidality (%) Suicide Attempts	 Suicidal Ideation	Family History
Chia 1996 [13]	Singapore	Cross-sectional	DSM-III criteria	n/r	Lifetime suicide attempts & committed suicide	283 n/r 58%	6 (committed suicide: 1)	-	-
Apter *et al*. 2003 [14]	Israel	Cross-sectional	K-SADS	CSPS	6-Month suicide attempts	40 16.4±2.1 71%	10.3 (6-month)	-	-
Hantouche *et al*. 2003 [15]	France	Cross-sectional	Self-assessment questionnaire	n/r	Lifetime suicide ideation & attempts	574 n/r 43.9%	16.2	73.5	Suicide attempts: 22.1
Maina *et al*. 2006 [16]	Italy	Cross-sectional	SCID-I YBOCS	HDRS item 3	Current suicidal ideation	167 35.512.1 48.5%	-	26.3	-
Kamath *et al*. 2007 [17]	India	Cross-sectional	SCID-I YBOCS	SSI	Lifetime suicide attempts & current and lifetime suicidal ideation	100 27.3±9.9 59%	27	28 (current) 59 (life-time)	-
Maina *et al*. 2007 [18]	Italy	Cross-sectional	SCID-I YBOCS	HDRS item 3	Lifetime suicide attempts & current suicidal ideation	58 pure OCD* 31.8±11.9 56.9%	8.6	13.8 (current)	-
						58 OCD+MDD 38.1±14.6 48.3%	6.9	50.0	
Phillips *et al*. 2007 [19]	USA	Cross-sectional	SCID-I YBOCS	Specific questionnaire	Lifetime suicide ideation & attempts	210 39.8±12.6 41.4%	15.9	54.8 (due to OCD: 44.3)	-
Gentil *et al*. 2009[2] [20]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	BDI, BAI	Lifetime suicide ideation & attempts	630 n/r 43.7%	10.2	33.3	-
Alonso *et al*. 2010 [21]	Spain	Prospective	SCID-I YBOCS	HDRS item 3 Beck SIS	Lifetime suicide ideation & attempts	218 31.3±10.8 57.3%	8.2	34.4	-
Balci & Sevincok 2010 [22]	Turkey	Cross-sectional	SCID-I YBOCS	SSI	Lifetime suicide attempts current suicidal ideation	44 33.7±11.5 22.7%	22.7	52.7 (current)	Suicide attempts: 18.2
Hung *et al*. 2010 [23]	Taiwan	Cross-sectional	YBOCS	BSS	Current suicidal ideation	70 30.6±10.8 67.1%	-	35.7	-
Sallet *et al*. 2010[2] [24]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	BDI, BAI	Lifetime suicide attempts	815 n/r 41.7%	10.3	-	-
Mahasuar *et al*. 2011 [25]	India	Cross-sectional	SCID-I YBOCS	SSI	Lifetime suicide attempts	91 n/r 72.5%	15.4	-	Suicide attempts: 18.7

(Table 1) contd….

Authors	Country	Design	OCD Diagnosis	Screening for Suicidality	Mode of Suicidality	Sample N	Suicidality (%)		Family History
						Mean Age % Males	Suicide Attempts	Suicidal Ideation	
Torres *et al*. 2011[2] [26]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	Specifically designed questionnaire	Lifetime suicide ideation & attempts	582 34.7±10.5 43.6%	11.0	10.0 (current) 36.1 (lifetime) (20.1 suicidal plans)	Suicide attempts: 19.1 completed: 16.1
Chakraborty *et al*. 2012 [27]	India	Cross-sectional	MINI YBOCS	n/r	Lifetime suicide attempts	200 n/r 53%	7	-	-
Fontenelle *et al*. 2012 [28]	Brazil	Cross-sectional	SCID-I YBOCS D-YBOCS	BDI, BAI, BABS	Lifetime suicide attempts & current and lifetime suicidal ideation	957 n/r 43.1%	10.6	10.0 (current) 34.3 (lifetime)	Suicide attempts: 17.7 completed: 15.9
Tavares *et al*. 2012 [29]	Brazil	Cross-sectional	MINI	MINI	Lifetime suicide risk (suicidal ideation or attempts)	48 post-partum women n/r 0%	39.6		-
Viswanath *et al*. 2012 [30]	India	Cross-sectional	MINI YBOCS	n/r	Lifetime suicide attempts & current suicidal ideation	545 29.3±10.6 61%	6.2	15.6 (current)	-
Dell'Osso *et al*. 2013[1] [31]	multi-national ICOCS	Cross-sectional	YBOCS	n/r	Lifetime suicide attempts	376 42.7±12.8 39.9%	7.7	-	-
Moreira *et al*. 2013[2] [32]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	item from the BDI	Lifetime suicide ideation & attempts	455 n/r 0%	13.2	35.6	Suicide attempts: 15.4%
Torres *et al*. 2013[2] [33]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	specifically designed questionnaire	Lifetime suicide ideation & attempts	955 35.8±12.4 41.9%	10.6	10.9 (current) 36.4 (lifetime) (20.6 suicidal plans)	-
Torresan *et al*. 2013[2] [34]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	specifically designed questionnaire	Lifetime suicide ideation & attempts	858 35.4±12.1 41.3%	11.0	37.8 (lifetime) (21.6 suicidal plans)	-
De Berardis *et al*. 2014[3] [35]	Italy	Cross-sectional	SCID-I YBOCS	SSI	Lifetime suicide attempts	79 28.7±8.0 54.4%	6.3	-	Completed suicide: 8.9
Gupta *et al*. 2014 [36]	India	Cross-sectional	SCID-I YBOCS	SSI C-SSRS	Lifetime suicide attempts & current and lifetime suicidal ideation	130 31.6±9.4 53.8%	7.7	46.1 (current) 62.3 (lifetime)	-
De Berardis *et al*. 2015[3] [37]	Italy	Cross-sectional	SCID-I YBOCS	SSI	Lifetime suicide attempts current suicidal ideation	104 32.1±8.0 50%	8.7	28.8 (current)	Suicide: 11.5
Dell'Osso *et al*. 2015[1] [38]	multi-national ICOCS	Cross-sectional	YBOCS	n/r	Lifetime suicide attempts	504 43.3±13.1 40%	13.2	-	-

(Table 1) contd….

Authors	Country	Design	OCD Diagnosis	Screening for Suicidality	Mode of Suicidality	Sample N Mean Age % Males	Suicidality (%) Suicide Attempts	 Suicidal Ideation	Family History
Storch *et al*. 2015 [39]	USA	Cross-sectional	K-SADS	SIQ-JR	Current suicidal ideation	54 11.9±3.2 61.1%	-	13 (current)	-
Chandhary *et al*. 2016 [40]	India	Cross-sectional	YBOCS	C-SSRS	Lifetime suicide ideation & attempts suicidal behavior	50 n/r 60%	18.0 24.0 suicidal behavior	52	-
Kim *et al*. 2016 [41]	South Korea	Cross-sectional	SCID-I YBOCS D-YBOCS	SSI	Lifetime suicide attempts current suicidal ideation	81 28.9±7.9 62%	37.0	26.8 (current)	-
Velloso *et al*. 2016[2] [42]	Brazil C-TOC	Cross-sectional	SCID-I YBOCS D-YBOCS	specifically designed questionnaire	Lifetime suicide ideation & attempts	548 34.3±11.3 46%	19.4	61 (made suicidal plans: 32)	Suicide attempts: 27.1%
Aguglia *et al*. 2017 [43]	Italy	Cross-sectional	SCID-I YBOCS	open question	Lifetime suicide attempts	104 35.9±14.0 59.6%	8.7	-	-
Brakoulias *et al*. 2017 [44]	multi-national	Cross-sectional	SCID-I or MINI or ADIS YBOCS	open question	Suicidal ideation in the past month lifetime suicidal attempts	3711 35.2±11.9 49.2%	9	6.4 (past month)	-
Dell'Osso *et al*. 2017[1] [45]	multi-national ICOCS	Cross-sectional	YBOCS	n/r	Lifetime suicide attempts	425 42.9±12.6 42%	14.6	-	-
Khosravani *et al*. 2017 [46]	Iran	Cross-sectional	SCID-I YBOCS D-YBOCS	SSI	Lifetime suicide attempts current suicidal ideation	60 33.9±12.7 48.3%	51.7	75 (current)	Suicide attempts: 11.7
Saraf *et al*. 2017 [47]	India	Cross-sectional	MINI YBOCS	open question	Lifetime suicide attempts	171 28.9±9.5 67%	15.8	-	-
Dhyani *et al*. 2018 [48]	India	Cross-sectional	SCID-I YBOCS	SSI	Lifetime suicide attempts current suicidal ideation	52 n/r 65.4%	19.2	26.9	-

Abbreviations: n/r: not reported; * pure OCD: no lifetime comorbidities allowed. [1]partially overlapping samples; [2]partially overlapping samples from the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders; [3]partially overlapping samples. ICOCS: International College of Obsessive-Compulsive Spectrum Disorders; C-TOC: Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders. SCID-I: Structured Clinical Interview for DSM-IV Axis I Disorders; MINI: Mini International Neuropsychiatry Interview YBOCS: Yale-Brown Obsessive-Compulsive Scale; D-YBOCS: Dimensional YBOCS; ADIS: Anxiety Disorders Interview Schedule; K-SADS: Schedule for Affective Disorders and Schizophrenia for School-Age Children. CSPS: Childhood Suicide Potential Scale; HDRS: Hamilton Depression Rating Scale; SSI: Scale for Suicidal Ideation; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BABS: Brown Assessment of Beliefs Scale; BSS: Beck Scale for Suicidal Ideation; Beck SIS: Beck Suicide Intent Scale; C-SSRS: Columbia Suicide Severity Rating Scale; SIQ-JR: Suicidal Ideation Questionnaire Junior.

over their lifetimes, it is crucial to determine which patients should be considered at higher risk than others. Preventive strategies, in fact, consist primarily in identifying predictors of suicidality and intervening on modifiable risk factors. At the moment, the only pharmacological effective agents used to treat suicidality appear to be lithium in affective disorders and clozapine in schizophrenia [63-65]. No other pharmacological compound seems to have anti-suicidal properties beyond the specific effect on the psychiatric disorder for which it has an indication, that is no other drug seems to possess independent anti-suicidal effect. Early recognition and diagnosis of OCD and effective pharmacological and psychological treatments of the disorder remain then essential for the prevention of suicidality.

We then reviewed all studies which examined factors associated with suicide risk in OCD to tentatively identify predictors of suicidality. Results are presented in Table **3** [66-70]. Thirty-two studies provided data on the association between suicidality and socio-demographic and clinical variables. The most significant predictors of greater suicidality (those confirmed by several Authors) are the severity of OCD (as from the total score of the YBOCS), the symptom dimension of unacceptable thoughts (aggressive, sexual, religious obsessions), the presence of comorbid Axis I

Table 2. Suicidality in OCD: Studies in the general population.

Authors	Country	Design	OCD Diagnosis	Screening for Suicidality	Mode of Suicidality	OCD Sample§ N= Mean Age % Males	Suicidality (%) Suicide Attempts	Suicidal Ideation
Hollander *et al*. 1996-97 [49]	USA ECA Study	Cross-sectional	DIS (DSM-III criteria)	Open question	Self-reported lifetime suicide attempts	140 OCD w/t comorbidities n/r 32.9%	3.6 *vs*. 0.9 (no disorders) OR: 3.2 (CI: 1.3-8.1)	-
						266 with comorbidities n/r 38.2%	15 *vs*. 7.0 (other disorders) OR: 2.2 (CI: 1.5-3.2)	-
Goodwin *et al*. 2002 [50]	USA	Cross-sectional	Screening questionnaire	n/r	Past-month suicidal ideation	3069 range 21-55+ 31%	-	27.8% (past month)
Angst *et al*. 2004 [51]	Switzerland Zurich Study	Prospective	SPIKE	Open question	Lifetime suicide attempts	30 OCD 81 OCS mean: 20 36.7%	OCD: 26.7 OCS: 13.6 Risk ratio (OCD+OCS *vs*. no OCD/OCS): 1.6 (CI: 1.0-2.6)	-
Angst *et al*. 2005 [52]	Switzerland Zurich Study	Prospective	SPIKE	Open question	Lifetime suicide attempts	32 pure OCS* mean: 20 75%	3.1 *vs*. 2.3 controls no difference	-
Sareen *et al*. 2005 [53]	Netherlands NEMESIS	Prospective (follow-up: 3 yrs)	CIDI	CIDI	Lifetime suicide attempts & ideation	61 n/r n/r	21.3	55.7
					First ever incidence of suicidal ideation & attempts	61 n/r n/r	AOR: 1.57 (CI: 0.15-16.33) n.s.	AOR: 6.33 (CI: 1.11-35.96)
Torres *et al*. 2006 [54]	UK British National Psychiatric Morbidity Survey	Cross-sectional	CIS	n/r	Self-reported lifetime suicide ideation & attempts	114 range 16-74 39.71%	25.7 *vs*. 2.3 controls significant difference	63.5 *vs*. 10.0 controls significant difference
Nock *et al*. 2009 [55]	WHO World Mental Health Survey	Cross-sectional	CIDI	CIDI	Subsequent lifetime suicide ideation & attempts	n/r	OR: 3.4 (CI: 2.0-6.1) pure OCD OR: 2.3 (CI: 1.3-4.2)	OR 1.9 (CI: 1.3-2.8)
ten Have *et al*. 2009 [56]	Netherlands NEMESIS	Prospective (follow-up: 3 yrs)	CIDI	CIDI	First ever incidence of suicide attempts	n/r	0.4 (3-yrs) AOR 4.98 (CI: 0.64-38.53) n.s.	-
Jaisoorya *et al*. 2015 [57]	India	Cross-sectional	CIS-R CIDI	Open questions	Lifetime suicide ideation & attempts	61 15.5±1.5 70.5%	24.6 *vs*. 3.8 controls AOR: 3.9 (CI:2.6-5.7)	59 *vs*. 16.3 controls AOR: 3.8 (CI:2.8-5.1)
Cho *et al*. 2016 [58]	South Korea	Cross-sectional	CIDI	Open questions	Lifetime suicide ideation & attempts	40 n/r n/r	20 OR: 9.9 (CI: 4.5-21.8) AOR°: 2.36 (CI: 0.79-7.04), n.s.	65 OR: 10.3 (CI: 5.37-19.8) AOR°: 5.58 (CI: 2.70-11.6)

(Table 2) contd….

Authors	Country	Design	OCD Diagnosis	Screening for Suicidality	Mode of Suicidality	OCD Sample§ N= Mean Age % Males	Suicidality (%) Suicide Attempts	Suicidality (%) Suicidal Ideation
Meier *et al*. 2016 [59]	Denmark Danish Registers	Prospective (mean follow-up: 9.7 yrs)	ICD	Death by suicide	Death by suicide	10155 29.1±11.3 41.5%	Death by suicides AOR: 3.02 (CI: 1.85-4.63)	-
Fernandez de la Cruz *et al*. 2017 [60]	Sweden Swedish National Patient Register	Matched case-cohort design (44 yrs)	ICD	Death by suicide (through the Cause of Death Register) lifetime suicide attempts (hospital admissions or outpatient consultations due to suicide attempts)	Death by suicide lifetime suicide attempts	36788 n/r 43.5%	Attempts: 11.68 OR: 5.45 (CI: 5.24-5.67) death by suicide: 1.48 OR: 9.83 (CI: 8.72-11.08)	-
						10155 pure OCD (no lifetime comorbidities)	attempts: OR: 1.59 (CI: 1.36-1.87) death by suicide: OR: 13.18 (CI: 10.76-16.16),	-
Jaisoorya *et al*. 2018 [61]	India	Cross-sectional	CIS-R	Open question	Lifetime suicide attempts and ideation	164 n/r (students) 37.2%	9.8 *vs*. 3.4 (no OCD) p<.001	45.7 *vs*. 19.1 (no OCD) p<.001
Veisani *et al*. 2018 [62]	Iran	Cross-sectional	GHQ-28 SCID-I	open question	Current suicidal ideation	93 n/r n/r	-	OR in males *vs*. general population: 5.13 (CI: 2.02-16.25) OR in females *vs*. general population: 6.02 (CI: 2.08-20.0)

Abbreviations: §N of OCD patients from the general population; *pure OCS: obsessive-compulsive syndrome (including OCD) without lifetime comorbidities. °Adjusted Odds Ratio for psychiatric comorbidities and demographic variables; n/r: not reported. DIS: Diagnostic Interview Schedule; SIPKE: Structured Psychopathological Interview, Rating of the Social Consequences for Epidemiology; CIDI: Composite International Diagnostic Interview; CIS: Clinical Interview Schedule; NEMESIS: Netherland Mental Health Survey and Incidence Study; GHQ-28: 28-item General Health Questionnaire; SCID-I: Structured Clinical Interview for DSM-IV Axis I Disorders.

disorders, mainly depressive and/or bipolar disorders but also substance use disorders, the severity of comorbid depressive and anxiety symptoms (as from the Beck Depression Inventory and the Beck Anxiety Inventory or other rating scales), a past history of suicidality (previous suicide attempts, previous or current suicidal ideation), and some emotion-cognitive factors such as alexithymia and hopelessness.

Few studies examined the relative weight of each risk factor in contributing to suicidality; results from the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders [42] found with logistic regression analyses that the most important contributor to suicidality risk is a family history for suicidality, that increases that risk by 78% (as compared to an increase of 6.7% for each point in the BDI score, for example). The other significant risk factor is a previous suicide attempt; in the Swedish study that used a matched case-cohort design with a follow-up of 44 years, a previous suicide attempt resulted to be the most influential risk factor for death by suicide in OCD: it increased the risk by 4.7 times (32.8% of those OCD subjects who died by suicide had a record of a previous suicide attempt) [60]. The third major contributor to suicidality is comorbid depression: in the study by Torres and colleagues [26] comorbid MDD increased by 28.75 times the risk of suicide attempt.

3.5. Methods of Suicidal Behaviour

Fernandez de la Cruz *et al*. [60] examined the specific methods used in those who died by suicide over a period of 44 years and compared the odds of using that method relative to the general population (those who died by suicide and were not diagnosed with OCD): individual with OCD who died by suicide used more frequently poisoning (OR 4.00 vs. the general population; 46.1%) and less frequently self-injury (*e.g*. hanging, strangulation, suffocation) (OR 0.25 *vs*. the general population). The same result is evident when examining those who attempted suicide: self-poisoning was significantly associated with OCD (OR 2.33 *vs*. the general population) while self-injury was not (OR 0.78) [60].

4. DISCUSSION

4.1. Suicide Risk in OCD

The first aim of our study was to systematically review literature data on suicidality in OCD in order to tentatively

Table 3. Predictors of suicidality in OCD.

Predictors	-	Current/Lifetime Suicidal Ideation	Lifetime Suicide Attempts	Death by Suicide
Socio-demographic variables or personal factors	Male gender	Maina *et al*. 2006 [16]		Fernandez de la Cruz *et al*. 2017 [60]
	Female gender		Fernandez de la Cruz *et al*. 2017 [60]	
	Older age	Maina *et al*. 2006 [16]		
	Marital status: single	Torres *et al*. 2011 [26]	Alonso *et al* 2010 [21]	
	No children	Torres *et al*. 2011 [26]		
	Poor educational level lower social class	Maina *et al*. 2006 [16] Torres *et al*. 2011 [26]		
	Childhood trauma (childhood sexual abuse)	Ay & Erbay 2018 [66]	Khosravani *et al*. 2017 [46]	
Disorder-specific (OCD-related) variables	Severity of OCD: YBOCS total scores	Maina *et al*. 2006 [16] Balci & Sevincok 2010 [22] Hung *et al*. 2010 [23] Gupta *et al*. 2014 [36]	Velloso *et al*. 2016 [42] Dhyani *et al*. 2018 [48]	
	Contamination/washing dimension	Gupta *et al*. 2014 [36]		
	Symmetry/ordering dimension	De Berardis *et al*. 2014 [35] Gupta *et al*. 2014 [36]	Alonso *et al*. 2010 [21]	
	Unacceptable thoughts (aggressive/sexual/religious obsessions)	Balci & Sevincok 2010 [22] Torres *et al*. 2011 [26] Kim *et al*. 2016 [41] Velloso *et al*. 2016 [42] Khosravani *et al*. 2017 [46]	Velloso *et al*. 2016 [42] Khosravani *et al*. 2017 [46]	
	Hoarding dimension		Chakraborty *et al*. 2012 [27]	
	Poor insight	Gupta *et al*. 2014 [36] De Berardis *et al*. 2015 [37]		
	Premenstrual worsening of OC symptoms	Moreira *et al*. 2013 [32]	Moreira *et al*. 2013 [32]	
Comorbidities	Current/lifetime comorbid psychiatric disorders	Torres *et al*. 2013 [33]	Torres *et al*. 2013 [33] Velloso *et al*. 2016 [42] Dell'Osso *et al*. 2017 [45] Fernandez de la Cruz *et al*. 2017 [60]	
	Comorbid Bipolar Disorder	Fineberg *et al*. 2013 [68]	Fineberg *et al*. 2013 [68] Ozdemiroglu *et al*. 2015 [69] Saraf *et al*. 2017 [47]	
	Comorbid mood disorders/ comorbid Major Depressive Disorder	Maina *et al*. 2006 [16] Kamath *et al*. 2007 [17] Maina *et al*. 2007 [18] Balci & Sevincok 2010 [22] Torres *et al*. 2011 [26] Viswanath *et al*. 2012 [30]	Kamath *et al*. 2007 [17] Alonso *et al*. 2010 [21] Torres *et al*. 2011 [26] Viswanath *et al*. 2012 [30]	
	Severity of comorbid depressive symptoms	Maina *et al*. 2006 [16] Kamath *et al*. 2007 [17] Balci & Sevincok 2010 [22] Hung *et al*. 2010 [23] Torres *et al*. 2011 [26] Gupta *et al*. 2014 [36] Kim *et al*. 2016 [41] Khosravani *et al*. 2017 [46]	Kamath *et al*. 2007 [17] Alonso *et al*. 2010 [21] Velloso *et al*. 2016 [42]	

(Table 3) contd….

Predictors	-	Current/Lifetime Suicidal Ideation	Lifetime Suicide Attempts	Death by Suicide
Comorbidities	Comorbid PTSD/GAD (and other anxiety disorders)	Torres *et al*. 2011 [26] Fontenelle *et al*. 2012 [28]	Torres *et al*. 2011 [26] Fontenelle *et al*. 2012 [28]	Fernandez de la Cruz *et al*. 2017 [60]
	Severity of comorbid anxiety symptoms	Maina *et al*. 2006 [16] Balci & Sevincok 2010 [22] Hung *et al*. 2010 [23] Torres *et al*. 2011 [26] Gupta *et al*. 2014 [36] Weingarden *et al*. 2016 [70]	Torres *et al*. 2011 [26] Velloso *et al*. 2016 [42] Weingarden *et al*. 2016 [70]	
	Substance/alcohol use disorders	Gentil *et al*. 2009 [20] Torres *et al*. 2011 [26] Fineberg *et al*. 2013 [68]	Gentil *et al*. 2009 [20] Fineberg *et al*. 2013 [68] Fernandez de la Cruz *et al*. 2017 [60]	Fernandez de la Cruz *et al*. 2017 [60]
	Cigarette smoking (former)		Dell'Osso *et al*. 2015 [38]	
	Comorbid eating disorders		Sallet *et al*. 2010 [24]	
	Personality disorders		Fernandez de la Cruz *et al*. 2017 [60]	Fernandez de la Cruz *et al*. 2017 [60]
	Lifetime psychiatric hospitalizations		Dell'Osso *et al*. 2017 [45]	
	Suicidal ideation		Kamath *et al*. 2007 [17] Dhyani *et al*. 2018 [48]	
	Previous suicide attempts	Kamath *et al*. 2007 [17]	Kamath *et al*. 2007 [17] Alonso *et al*. 2010 [21]	Fernandez de la Cruz *et al*. 2017 [60]
	Family history for suicide attempts	Velloso *et al*. 2016 [42]	Velloso *et al*. 2016 [42]	
	Medical comorbidities		Dell'Osso *et al*. 2017	
Emotion-cognitive factors	Inflated responsibility	De Berardis *et al*. 2015 [37]		
	Ego-dystonic perfectionism	Kim *et al*. 2016 [41]	Kim *et al*. 2016 [41]	
	Alexithymia	Kim *et al*. 2016 [41] De Berardis *et al*. 2014 [35] De Berardis *et al*. 2015 [37]	Kim *et al*. 2016 [41]	
	Shame	Weingarden *et al*. 2016 [70]		
	Hopelessness	Kamath *et al*. 2007 [17] Balci & Sevincok 2010 [22] Gupta *et al*. 2014 [36]	Dhyani *et al*. 2018 [48]	
	Hostility	Gupta *et al*. 2014 [36]		
	Early maladaptive (mistrust/abuse) schemas	Khosravani *et al*. 2017 [67]	Khosravani *et al*. 2017 [67]	
Biological variables	Lower HDL-C levels, high triglycerides	De Berardis *et al*. 2014 [35]	Aguglia *et al*. 2017 [43]	

estimate prevalence rates of suicidal ideation and suicide attempts in individuals with OCD.

Our results confirm recent findings of a greater risk of suicidality in OCD as compared to the general population [7]. Each mode of suicidality seems to be more prevalent among patients with OCD referring for treatment: the mean rate of lifetime suicide attempts in individuals with OCD is 14.2% (median 10.8%); the mean rates of current and lifetime suicidal ideation are 25.9% (median 15.6%) and 44.1% (median 36.4%), respectively. These rates are higher than expected in the general population: for example, in the World Health Organization (WHO) World Mental Health (WMH) Survey, in which 108705 adults from 21 countries were interviewed, 12-month prevalence estimates of suicide ideation, plans, and attempts are 2.0%, 0.6%, and 0.3%, respectively, for developed countries and 2.1%, 0.7%, and 0.4%, respectively, for developing countries [71]. Our estimates of suicidality among help-seeking individuals with OCD referring to specialized centers worldwide are consistent with previous estimates of a recent meta-analysis [7], which however mixed results from clinical and epidemiological samples, included samples of individuals with disorders other than OCD (*e.g*. schizophrenic patients with OC symptoms, where suicidality risk might be more related to

schizophrenia than to comorbid OC symptoms): median rates of suicidal ideation found in their meta-analysis is 27.9% (*vs*. 36.4% in our study which included several recent papers published since the publication of their study), median rates of suicide attempts is 10.3% (*vs*. 10.8% in our study).

The evidence to date, then, is that suicidality is a relevant phenomenon in individuals with OCD; clinicians should then actively inquire about suicidality when interviewing a patient with OCD, keeping in mind that early recognition/diagnosis of the disorder and immediate setting of an appropriate treatment plan are essential elements for the prevention of suicidality. The direct inquire should include all aspects of suicidality, including suicidal ideation, plans, personal history of previous suicide attempts and family history of suicidality, since it is possible that most patients with OCD (as well as most patients with other psychiatric disorders) may not spontaneously report suicidality.

The analysis of data coming from epidemiological studies and from the two prospective cohort studies on nationwide registers confirms in the general population that individuals with OCD are at greater risk of dying by suicide (that risk is tripled over a period of 10 years of follow-up and x9.8 over 44 years of follow-up) [59, 60], having a lifetime suicidal ideation (up to 10 times that of the general population) and attempting suicide during their lifetime (up to 10 times more).

The risk of having lifetime suicidal ideation remains significantly higher even when adjusting for socio-demographic variables and for comorbidities (*in primis* MDD): this implies that OCD in its own right is associated with significant risk of suicidal ideation, probably expression of the disability associated with this disorder. The clinical implication of this finding is again that clinicians should actively inquire about past or present suicidal ideation, independently from the presence of current MDD; as a past history of suicidality (previous suicide attempts, but also previous or current suicidal ideation) [17, 48, 60] as well as a family history for suicidality (increased risk by 78%) [42] are both predictors of suicidality, the proper identification of subjects at greater risk will result in the prevention of some deaths. More controversy exists about the association between pure OCD (without lifetime comorbid disorders) and suicide attempts: some [55, 60] but not all studies [52, 53, 56, 58] found an increased risk among individuals with OCD drawn from the general population. More studies may be needed in order to clarify this issue; however, clinicians should, in our opinion, assume an attitude of prudence and consider anyway OCD at risk of attempting suicide and then constantly monitor suicidality during the follow-up of their patients.

4.2. Implications for the Treatment: Risk Identification

Risk identification remains a crucial factor for the establishment of preventive strategies: identifying predictors of suicidality and intervening on modifiable risk factors could result in the reduction of suicidality rates.

As previously stated, the only pharmacological effective agents used to treat suicidality appear to be lithium in affective disorders and clozapine in schizophrenia [63-65]. No other pharmacological compound seems to have anti-suicidal properties beyond the specific effect on the psychiatric disorder for which it has an indication, that is no other drug seems to possess independent anti-suicidal effect. Several psychotherapies appear also effective in reducing suicidality, including cognitive-behavioural therapy, dialectical behavioural therapy and problem-solving therapy, in different patient populations (but mainly they were tested in borderline personality disorder or in people referring to emergency departments for suicide attempts independently of the primary diagnosis) [72].

Early recognition and diagnosis of OCD and effective pharmacological and psychological treatments of the disorder remain then essential for the prevention of suicidality, as for all mental disorders [73-75]. For OCD, it should be highlighted that effective pharmacological treatment encompasses serotonergic drugs (SSRIs and clomipramine) with the following specificities: the use of moderate-to-high doses [76] and the need to wait several weeks (usually 12 weeks is the time required) in order to have a response (which is defined as a reduction of 25-35% of baseline symptoms) [77]. Then, other strategies, including the augmentation with CBT or some (but not all) atypical antipsychotics could be used for resistant patients [78, 79]. It is essential, then, for psychiatrists to remember these guidelines and appropriately (and aggressively) treat their patients affected by OCD.

Moreover, early and aggressive treatment of patients with any single phenomenon within the suicidality continuum may result in the prevention of deaths; a study found that suicidal ideators and suicidal attempters do not differ in any clinical characteristics and that there is a strong correlation between all suicidal phenomena (specifically, suicide risk increases significantly even when a patient wishes to be dead) [42]. Moreover, our review of risk factors found that the same variables predicted both suicidal ideation and suicide attempts.

From our review of the literature it emerges that some predictors may be identified and modified; comorbid disorders (and, specifically, comorbid depression – both in major depressive disorder but also in bipolar disorder) should be aggressively treated, and this is clinically feasible and quite easy to do.

It is very important for clinicians to keep in mind the possibility that comorbid bipolar disorder is present when, under pharmacological treatment, an individual with OCD develops aggressive behaviors and suicidal thoughts; these features of mood switching under anti-OCD drugs were reported, for example, by a significant proportion of members of the French OCD Association [80]. Moreover, a huge literature confirms that OCD is often comorbid with bipolar disorder, and that when subjects with bipolar disorder have current or lifetime OCD (or other current or lifetime anxiety disorders) the risk of suicidal behaviors increases significantly [81-86]. Given that bipolar depression is associated with significantly higher rates of suicide risk than unipolar depression [81-86], clinicians should always inquire longitudinally history of bipolar disorder when dealing with an individual with OCD who is also with depression.

The severity of comorbid anxiety symptoms (including insomnia) is also a predictor of suicide risk in subjects with OCD, and this confirms previous studies suggesting that this is a general risk factor in several psychiatric disorders [87].

Hopelessness and personality traits such as alexithymia, ego-dystonic perfectionism should also be considered when planning interventions. Regretfully, it is not common in clinical practice to screen for the presence of cognitive-emotional factors, such as hopelessness or alexithymia among others, in individuals with OCD, nor is it routine clinical practice to distinguish between ego-dystonic perfectionism from OCD symptoms. Some clinicians with a cognitive-behavioral background may assess cognitive constructs such as inflated responsibility and evaluate its impact on the severity of the disorder (including suicide risk); however, our opinion is again that it is not so common in clinical practice. Given that suicide risk is higher in people with these cognitive-emotional risk factors, we strongly suggest adding their evaluation in the baseline assessment of individuals presenting with severe OCD. We could not find studies investigating in OCD whether aggressive and specific treatment of these emotion-cognitive factors could result in a reduction of suicidality, although specific psychological interventions focused at reducing hopelessness or other cognitive distortions have been studied. We found only one specific intervention in OCD addressing anxiety sensitivity cognitive concerns as a way of reducing suicidality [88]; anxiety sensitivity reflects the fear of the autonomic arousal due to the belief that there will be adverse physical, cognitive and/or social consequences associated with this arousal. Anxiety sensitivity, in particular the cognitive domain, has been associated with suicidality in non-OCD samples; thus, reducing anxiety sensitivity could be beneficial also in individuals with OCD reducing their risk of suicide. This randomized clinical trial found that a one-session anxiety sensitivity cognitive concerns intervention produced significantly greater reduction in anxiety sensitivity and that changes in anxiety sensitivity cognitive concerns mediated the changes in suicidality at one-month follow-up [88].

This study can be considered as an example of future trials investigating specifically among individuals with OCD whether specific interventions aimed at reducing risk factors for suicidality (*e.g*. comorbid major depression, comorbid SUD, hopelessness, alexithymia, *etc*.) could really be beneficial for patients with higher suicidal risk. Unfortunately, we don't have yet any direct evidence from longitudinal studies showing that successful pharmacotherapy of pure OCD or successful pharmacotherapy of OCD comorbid with depression reduces suicide risk. We can only speculate that addressing risk factors and appropriately treating them (*e.g*. comorbid depression, whether unipolar or bipolar) would probably result in a reduction of suicide risk among individuals with OCD.

Another potential modifiable risk factor for suicidality in OCD is cigarette smoking [38]; it has been found to be an independent risk factor for suicide in patients suffering from several disorders other than OCD and it may be that the influence of nicotine exposure with suicidality is mediated by impulsive features. Interventions aimed at smoking cessation could then also reduce suicidality in OCD patients.

One interesting and clinically useful result that emerges from our systematic review is that childhood trauma/early adversities are risk factors for suicidality in OCD as they are for suicide in general [75] specifically, childhood sexual abuse was associated with suicidal ideation and attempts among individual with OCD [46, 66]. Moreover, early maladaptive schemas (mistrust/abuse schema) were associated with suicidality; as interpreted by the Authors, mistrust/abuse schema refers to an attitude recognized by avoidance of relationships with others for fear of being betrayed or misled, which in turn may be related to having suffered from physical and/or sexual abuse experiences, severe punishments or living in an emotionally or physically unsafe environment [67]. Finally, comorbid PTSD with OCD onset after PTSD (named post-traumatic OCD) was also associated with a greater risk for suicidality [28]; since the mean age of the traumatic event was 14.7 years, greater suicidality rates may represent general effects of early trauma, confirming results of the other two studies. It may be, then, that addressing adverse childhood experiences in these patients at higher risk for suicide because of having suffered a childhood trauma could result in reducing suicides.

Finally, unacceptable thoughts (aggressive, sexual or religious obsessions) are associated with suicidality [22, 26, 41, 42, 67] this may have a therapeutic implication, since the use of specific cognitive-behavior techniques such as exposure and response prevention or acceptance and commitment therapy rather than suppressing of these thoughts may prevent suicide [89].

4.3. Limitations

Our systematic review suffers from several limitations, intrinsic in the way the studies included in this review were conducted. First of all, different instruments were used to assess suicidality (from open questions, to the generic use of item 3 of the HAM-D, to specific scales such as the SSI or even better the C-SSRS) and most studies assessed suicidality cross-sectionally only; suicidality is a dynamic and dimensional phenomenon that requires active inquiring through specific instruments/rating scales specifically designed to evaluate all aspects of suicidality (from generic ideas that life is not worth living, to suicidal ideation with or without an intent to act, specific plans, to actual, interrupted and aborted previous attempts; intensity of the ideation, lethality of prior attempts and protective factors should also be assessed and registered). Studies included, moreover, are heterogeneous in terms of characteristics of samples included (*e.g*. in terms of percentage of subjects with comorbid disorders, gender distribution or mean age); these sociodemographic and clinical characteristics could influence our estimates of the true risk associated with OCD, but are more influential when trying to identify predictors of suicidality. The vast majority of studies did not use adequate statistical analyses (*e.g*. logistic regression analyses) when investigating predictors/factors associated with suicidality, so that we cannot evaluate the independent contribution of each postulated predictor of suicidality. Another source of heterogeneity is that each study compared a set of clinical and demographic variables different from other studies; the result is that for some variables (*e.g*. comorbid MDD, severity of

OCD as from YBOCS total score, severity of depressive symptoms) we have enough information to tentatively conclude that these are actually contributing to the increased risk, while for others (*e.g*. emotion-cognitive factors, for example) data are scant. Another limitation is that we included in the present review several papers from the same group of researchers, which included partially overlapping samples (*e.g*. studies from the International College of Obsessive-Compulsive Spectrum Disorders or the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders).

Being aware of these limitations, we clearly separated results of studies performed in clinical settings from those of epidemiological ones, and we clearly reported in our tables the instruments used to assess OCD, suicidality, the mode of suicidality inquires in each study, together with the principal characteristics (when available) of the samples included. We also marked all studies which included overlapping samples. When possible, finally, we included among predictors only those emerging from adequate statistical analyses.

CONCLUSION

A history-based bias, based on psychoanalytical models likely to confound obsessive-compulsive personality disorder and obsessive character traits with obsessive-compulsive disorder, may have prompted clinicians to consider people with OCD not at risk of committing suicide. This bias possibly led to underestimate this risk in clinical practice.

Our systematic review clearly showed that OCD is at a greater suicide risk, compared to the general population. Hence, clinicians should actively inquire about suicidal thoughts and attempts when interviewing a patient with OCD, keeping in mind that risk identification remains a crucial factor for establishing preventive strategies. The recognition that specific risk factors, such as content of obsessions, former Axis I comorbidity and other clinical features, are associated with suicidal ideation and attempts among individuals with OCD, could potentially lead to saving lives in the future.

CONSENT FOR PUBLICATION

Not applicable.

STANDARD OF REPORTING

PRISMA guidelines and methodology were followed.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Coryell, W. Obsessive-compulsive disorder and primary unipolar depression. Comparisons of background, family history, course, and mortality. *J. Nerv. Ment. Dis.,* **1981**, *169*(4), 220-224. [http://dx.doi.org/10.1097/00005053-198104000-00003] [PMID: 7217927]

[2] Goodwin, D.W.; Guze, S.B.; Robins, E. Follow-up studies in obsessional neurosis. *Arch. Gen. Psychiatry,* **1969**, *20*(2), 182-187. [http://dx.doi.org/10.1001/archpsyc.1969.01740140054006] [PMID: 5763526]

[3] Kringlen, E. Obsessional neurotics: A long-term follow-up. *Br. J. Psychiatry,* **1965**, *111*, 709-722. [http://dx.doi.org/10.1192/bjp.111.477.709] [PMID: 14337420]

[4] Harris, E.C.; Barraclough, B. Suicide as an outcome for mental disorders. A meta-analysis. *Br. J. Psychiatry,* **1997**, *170*, 205-228. [http://dx.doi.org/10.1192/bjp.170.3.205] [PMID: 9229027]

[5] Khan, A.; Leventhal, R.M.; Khan, S.; Brown, W.A. Suicide risk in patients with anxiety disorders: A meta-analysis of the FDA database. *J. Affect. Disord.,* **2002**, *68*(2-3), 183-190. [http://dx.doi.org/10.1016/S0165-0327(01)00354-8] [PMID: 12063146]

[6] Kanwar, A.; Malik, S.; Prokop, L.J.; Sim, L.A.; Feldstein, D.; Wang, Z.; Murad, M.H. The association between anxiety disorders and suicidal behaviors: A systematic review and meta-analysis. *Depress. Anxiety,* **2013**, *30*(10), 917-929. [PMID: 23408488]

[7] Angelakis, I.; Gooding, P.; Tarrier, N.; Panagioti, M. Suicidality in obsessive compulsive disorder (OCD): a systematic review and meta-analysis. *Clin. Psychol. Rev.,* **2015**, *39*, 1-15. [http://dx.doi.org/10.1016/j.cpr.2015.03.002] [PMID: 25875222]

[8] Pompili, M. *Phenomenology of suicide: unlocking the suicidal mind*; Pompili, M., Ed.; Springer, US, **2018**. [http://dx.doi.org/10.1007/978-3-319-47976-7]

[9] Pompili, M. Exploring the phenomenology of suicide. *Suicide Life Threat. Behav.,* **2010**, *40*(3), 234-244. [http://dx.doi.org/10.1521/suli.2010.40.3.234] [PMID: 20560745]

[10] Maltsberger, J.T. The descent into suicide. *Int. J. Psychoanal.,* **2004**, *85*(Pt 3), 653-667. [http://dx.doi.org/10.1516/3C96-URET-TLWX-6LWU] [PMID: 15228702]

[11] Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.,* **2009**, *6*(7), e1000097. [http://dx.doi.org/10.1371/journal.pmed.1000097] [PMID: 19621072]

[12] Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Int. J. Surg.,* **2010**, *8*(5), 336-341. [http://dx.doi.org/10.1016/j.ijsu.2010.02.007] [PMID: 20171303]

[13] Chia, B.H. A Singapore study of obsessive compulsive disorder. *Singapore Med. J.,* **1996**, *37*(4), 402-406. [PMID: 8993143]

[14] Apter, A.; Horesh, N.; Gothelf, D.; Zalsman, G.; Erlich, Z.; Soreni, N.; Weizman, A. Depression and suicidal behavior in adolescent inpatients with obsessive compulsive disorder. *J. Affect. Disord.,* **2003**, *75*(2), 181-189. [http://dx.doi.org/10.1016/S0165-0327(02)00038-1] [PMID: 12798258]

[15] Hantouche, E.G.; Angst, J.; Demonfaucon, C.; Perugi, G.; Lancrenon, S.; Akiskal, H.S. Cyclothymic OCD: A distinct form? *J. Affect. Disord.,* **2003**, *75*(1), 1-10. [http://dx.doi.org/10.1016/S0165-0327(02)00461-5] [PMID: 12781344]

[16] Maina, G.; Albert, U.; Rigardetto, S.; Tiezzi, M.N.; Bogetto, F. Suicidio e disturbo ossessivo-compulsivo. *Giornale Italiano di Psicopatologia,* **2006**, *12*, 31-37.

[17] Kamath, P.; Reddy, Y.C.; Kandavel, T. Suicidal behavior in obsessive-compulsive disorder. *J. Clin. Psychiatry,* **2007**, *68*(11), 1741-1750. [http://dx.doi.org/10.4088/JCP.v68n1114] [PMID: 18052568]

[18] Maina, G.; Salvi, V.; Tiezzi, M.N.; Albert, U.; Bogetto, F. Is OCD at risk for suicide? A case-control study. *Clin. Neuropsychiatry,* **2007**, *4*(3), 117-121.

[19] Phillips, K.A.; Pinto, A.; Menard, W.; Eisen, J.L.; Mancebo, M.; Rasmussen, S.A. Obsessive-compulsive disorder versus body dysmorphic disorder: A comparison study of two possibly related disorders. *Depress. Anxiety,* **2007**, *24*(6), 399-409. [http://dx.doi.org/10.1002/da.20232] [PMID: 17041935]

[20] Gentil, A.F.; de Mathis, M.A.; Torresan, R.C.; Diniz, J.B.; Alvarenga, P.; do Rosário, M.C.; Cordioli, A.V.; Torres, A.R.; Miguel, E.C. Alcohol use disorders in patients with obsessive-compulsive disorder: the importance of appropriate dual-diagnosis. *Drug Alcohol Depend.,* **2009**, *100*(1-2), 173-177. [http://dx.doi.org/10.1016/j.drugalcdep.2008.09.010] [PMID: 19004577]

[21] Alonso, P.; Segalàs, C.; Real, E.; Pertusa, A.; Labad, J.; Jiménez-Murcia, S.; Jaurrieta, N.; Bueno, B.; Vallejo, J.; Menchón, J.M. Suicide in patients treated for obsessive-compulsive disorder: A

prospective follow-up study. *J. Affect. Disord.,* **2010**, *124*(3), 300-308. [http://dx.doi.org/10.1016/j.jad.2009.12.001] [PMID: 20060171]

[22] Balci, V.; Sevincok, L. Suicidal ideation in patients with obsessive-compulsive disorder. *Psychiatry Res.,* **2010**, *175*(1-2), 104-108. [http://dx.doi.org/10.1016/j.psychres.2009.03.012] [PMID: 19923009]

[23] Hung, T.C.; Tang, H.S.; Chiu, C.H.; Chen, Y.Y.; Chou, K.R.; Chiou, H.C.; Chang, H.J. Anxiety, depressive symptom and suicidal ideation of outpatients with obsessive compulsive disorders in Taiwan. *J. Clin. Nurs.,* **2010**, *19*(21-22), 3092-3101. [http://dx.doi.org/10.1111/j.1365-2702.2010.03378.x] [PMID: 21040015]

[24] Sallet, P.C.; de Alvarenga, P.G.; Ferrão, Y.; de Mathis, M.A.; Torres, A.R.; Marques, A.; Hounie, A.G.; Fossaluza, V.; do Rosario, M.C.; Fontenelle, L.F.; Petribu, K.; Fleitlich-Bilyk, B. Eating disorders in patients with obsessive-compulsive disorder: prevalence and clinical correlates. *Int. J. Eat. Disord.,* **2010**, *43*(4), 315-325. [PMID: 19424977]

[25] Mahasuar, R.; Janardhan Reddy, Y.C.; Math, S.B. Obsessive-compulsive disorder with and without bipolar disorder. *Psychiatry Clin. Neurosci.,* **2011**, *65*(5), 423-433. [http://dx.doi.org/10.1111/j.1440-1819.2011.02247.x] [PMID: 21851451]

[26] Torres, A.R.; Ramos-Cerqueira, A.T.; Ferrão, Y.A.; Fontenelle, L.F.; do Rosário, M.C.; Miguel, E.C. Suicidality in obsessive-compulsive disorder: Prevalence and relation to symptom dimensions and comorbid conditions. *J. Clin. Psychiatry,* **2011**, *72*(1), 17-26. [http://dx.doi.org/10.4088/JCP.09m05651blu] [PMID: 21272513]

[27] Chakraborty, V.; Cherian, A.V.; Math, S.B.; Venkatasubramanian, G.; Thennarasu, K.; Mataix-Cols, D.; Reddy, Y.C. Clinically significant hoarding in obsessive-compulsive disorder: results from an Indian study. *Compr. Psychiatry,* **2012**, *53*(8), 1153-1160. [http://dx.doi.org/10.1016/j.comppsych.2012.05.006] [PMID: 22796017]

[28] Fontenelle, L.F.; Cocchi, L.; Harrison, B.J.; Shavitt, R.G.; do Rosário, M.C.; Ferrão, Y.A.; de Mathis, M.A.; Cordioli, A.V.; Yücel, M.; Pantelis, C.; Mari, Jde.J.; Miguel, E.C.; Torres, A.R. Towards a post-traumatic subtype of obsessive-compulsive disorder. *J. Anxiety Disord.,* **2012**, *26*(2), 377-383. [http://dx.doi.org/10.1016/j.janxdis.2011.12.001] [PMID: 22230220]

[29] Tavares, D.; Quevedo, L.; Jansen, K.; Souza, L.; Pinheiro, R.; Silva, R. Prevalence of suicide risk and comorbidities in postpartum women in Pelotas. *Rev. Bras. Psiquiatr.,* **2012**, *34*(3), 270-276. [http://dx.doi.org/10.1016/j.rbp.2011.12.001] [PMID: 23429772]

[30] Viswanath, B.; Narayanaswamy, J.C.; Rajkumar, R.P.; Cherian, A.V.; Kandavel, T.; Math, S.B.; Reddy, Y.C. Impact of depressive and anxiety disorder comorbidity on the clinical expression of obsessive-compulsive disorder. *Compr. Psychiatry,* **2012**, *53*(6), 775-782. [http://dx.doi.org/10.1016/j.comppsych.2011.10.008] [PMID: 22136738]

[31] Dell'Osso, B.; Benatti, B.; Buoli, M.; Altamura, A.C.; Marazziti, D.; Hollander, E.; Fineberg, N.; Stein, D.J.; Pallanti, S.; Nicolini, H.; Van Ameringen, M.; Lochner, C.; Hranov, G.; Karamustafalioglu, O.; Hranov, L.; Menchon, J.M.; Zohar, J. 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. [http://dx.doi.org/10.1016/j.euroneuro.2013.05.004] [PMID: 23791074]

[32] Moreira, L.; Bins, H.; Toressan, R.; Ferro, C.; Harttmann, T.; Petribú, K.; Juruena, M.F.; do Rosário, M.C.; Ferrão, Y.A. An exploratory dimensional approach to premenstrual manifestation of obsessive-compulsive disorder symptoms: A multicentre study. *J. Psychosom. Res.,* **2013**, *74*(4), 313-319. [http://dx.doi.org/10.1016/j.jpsychores.2012.12.004] [PMID: 23497833]

[33] Torres, A.R.; Shavitt, R.G.; Torresan, R.C.; Ferrão, Y.A.; Miguel, E.C.; Fontenelle, L.F. Clinical features of pure obsessive-compulsive disorder. *Compr. Psychiatry,* **2013**, *54*(7), 1042-1052. [http://dx.doi.org/10.1016/j.comppsych.2013.04.013] [PMID: 23746710]

[34] Torresan, R.C.; Ramos-Cerqueira, A.T.; Shavitt, R.G.; do Rosário, M.C.; de Mathis, M.A.; Miguel, E.C.; Torres, A.R. Symptom dimensions, clinical course and comorbidity in men and women with obsessive-compulsive disorder. *Psychiatry Res.,* **2013**, *209*(2), 186-195. [http://dx.doi.org/10.1016/j.psychres.2012.12.006] [PMID: 23298952]

[35] De Berardis, D.; Serroni, N.; Marini, S.; Rapini, G.; Carano, A.; Valchera, A.; Iasevoli, F.; Mazza, M.; Signorelli, M.; Aguglia, E.; Perna, G.; Martinotti, G.; Varasano, P.A.; Pressanti, G.L.; Di Giannantonio, M. Alexithymia, suicidal ideation, and serum lipid levels among drug-naïve outpatients with obsessive-compulsive disorder. *Rev. Bras. Psiquiatr.,* **2014**, *36*(2), 125-130. [http://dx.doi.org/10.1590/1516-4446-2013-1189] [PMID: 24554275]

[36] Gupta, G.; Avasthi, A.; Grover, S.; Singh, S.M. Factors associated with suicidal ideations and suicidal attempts in patients with obsessive compulsive disorder. *Asian J. Psychiatr.,* **2014**, *12*, 140-146. [http://dx.doi.org/10.1016/j.ajp.2014.09.004] [PMID: 25446904]

[37] De Berardis, D.; Serroni, N.; Campanella, D.; Rapini, G.; Olivieri, L.; Feliziani, B.; Carano, A.; Valchera, A.; Iasevoli, F.; Tomasetti, C.; Mazza, M.; Fornaro, M.; Perna, G.; Di Nicola, M.; Martinotti, G.; Di Giannantonio, M. Alexithymia, responsibility attitudes and suicide ideation among outpatients with obsessive-compulsive disorder: an exploratory study. *Compr. Psychiatry,* **2015**, *58*, 82-87. [http://dx.doi.org/10.1016/j.comppsych.2014.12.016] [PMID: 25591904]

[38] Dell'Osso, B.; Nicolini, H.; Lanzagorta, N.; Benatti, B.; Spagnolin, G.; Palazzo, M.C.; Marazziti, D.; Hollander, E.; Fineberg, N.; Stein, D.J.; Pallanti, S.; Van Ameringen, M.; Lochner, C.; Hranov, G.; Karamustafalioglu, O.; Hranov, L.; Zohar, J.; Denys, D.; Altamura, A.C.; Menchon, J.M. 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. [http://dx.doi.org/10.1017/S1092852915000565] [PMID: 26349811]

[39] Storch, E.A.; Bussing, R.; Jacob, M.L.; Nadeau, J.M.; Crawford, E.; Mutch, P.J.; Mason, D.; Lewin, A.B.; Murphy, T.K. Frequency and correlates of suicidal ideation in pediatric obsessive-compulsive disorder. *Child Psychiatry Hum. Dev.,* **2015**, *46*(1), 75-83. [http://dx.doi.org/10.1007/s10578-014-0453-7] [PMID: 24682580]

[40] Chaudhary, R.K.; Kumar, P.; Mishra, B.P. Depression and risk of suicide in patients with obsessive-compulsive disorder: A hospital-based study. *Ind. Psychiatry J.,* **2016**, *25*(2), 166-170. [http://dx.doi.org/10.4103/ipj.ipj_63_16] [PMID: 28659695]

[41] Kim, H.; Seo, J.; Namkoong, K.; Hwang, E.H.; Sohn, S.Y.; Kim, S.J.; Kang, J.I. Alexithymia and perfectionism traits are associated with suicidal risk in patients with obsessive-compulsive disorder. *J. Affect. Disord.,* **2016**, *192*, 50-55. [http://dx.doi.org/10.1016/j.jad.2015.12.018] [PMID: 26707347]

[42] Velloso, P.; Piccinato, C.; Ferrão, Y.; Aliende Perin, E.; Cesar, R.; Fontenelle, L.; Hounie, A.G.; do Rosário, M.C. The suicidality continuum in a large sample of obsessive-compulsive disorder (OCD) patients. *Eur. Psychiatry,* **2016**, *38*, 1-7. [http://dx.doi.org/10.1016/j.eurpsy.2016.05.003] [PMID: 27606439]

[43] Aguglia, A.; Albert, U.; Maina, G. Serum lipids and lifetime suicide attempts in patients with obsessive-compulsive disorder. *J. Obsessive Compuls. Relat. Disord.,* **2017**, *15*, 1-6. [http://dx.doi.org/10.1016/j.jocrd.2017.07.003]

[44] Brakoulias, V.; Starcevic, V.; Belloch, A.; Brown, C.; Ferrao, Y.A.; Fontenelle, L.F.; Lochner, C.; Marazziti, D.; Matsunaga, H.; Miguel, E.C.; Reddy, Y.C.J.; do Rosario, M.C.; Shavitt, R.G.; Shyam Sundar, A.; Stein, D.J.; Torres, A.R.; Viswasam, K. Comorbidity, age of onset and suicidality in obsessive-compulsive disorder (OCD): An international collaboration. *Compr. Psychiatry,* **2017**, *76*, 79-86. [http://dx.doi.org/10.1016/j.comppsych.2017.04.002] [PMID: 28433854]

[45] Dell'Osso, B.; Benatti, B.; Arici, C.; Palazzo, C.; Altamura, A.C.; Hollander, E.; Fineberg, N.; Stein, D.J.; Nicolini, H.; Lanzagorta, N.; Marazziti, D.; Pallanti, S.; van Ameringen, M.; Lochner, C.; Karamustafalioglu, O.; Hranov, L.; Figee, M.; Drummond, L.; Rodriguez, C.I.; Grant, J.; Denys, D.; Menchon, J.M.; Zohar, J. 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.,* **2017**, 1-8. [PMID: 28300008]

[46] Khosravani, V.; Kamali, Z.; Jamaati, A.R.; Samimi, A.M. The relation of childhood trauma to suicide ideation in patients suffering from obsessive-compulsive disorder with lifetime suicide attempts. *Psychiatry Res.,* **2017**, *255*, 139-145. [http://dx.doi.org/10.1016/j.psychres.2017.05.032] [PMID: 28549337]

[47] Saraf, G.; Paul, I.; Viswanath, B.; Narayanaswamy, J.C.; Math, S.B.; Reddy, Y.C. Bipolar disorder comorbidity in patients with a primary diagnosis of OCD. *Int. J. Psychiatry Clin. Pract.,* **2017**, *21*(1), 70-74. [http://dx.doi.org/10.1080/13651501.2016.1233344] [PMID: 27646489]

[48] Dhyani, M.; Trivedi, J.K.; Nischal, A.; Sinha, P.K.; Verma, S. Suicidal behaviour of Indian patients with obsessive compulsive disorder. *Indian J. Psychiatry,* **2013**, *55*(2), 161-166. [http://dx.doi.org/10.4103/0019-5545.111455] [PMID: 23825851]

[49] Hollander, E.; Greenwald, S.; Neville, D.; Johnson, J.; Hornig, C.D.; Weissman, M.M. Uncomplicated and comorbid obsessive-compulsive disorder in an epidemiologic sample. *Depress. Anxiety,* **1996-1997**, *4*(3), 111-119. [http://dx.doi.org/10.1002/(SICI)1520-6394(1996)4:3<111::AID-DA3>3.0.CO;2-J] [PMID: 9166639]

[50] Goodwin, R.; Koenen, K.C.; Hellman, F.; Guardino, M.; Struening, E. Helpseeking and access to mental health treatment for obsessive-compulsive disorder. *Acta Psychiatr. Scand.,* **2002**, *106*(2), 143-149. [http://dx.doi.org/10.1034/j.1600-0447.2002.01221.x] [PMID: 12121213]

[51] Angst, J.; Gamma, A.; Endrass, J.; Goodwin, R.; Ajdacic, V.; Eich, D.; Rössler, W. Obsessive-compulsive severity spectrum in the community: prevalence, comorbidity, and course. *Eur. Arch. Psychiatry Clin. Neurosci.,* **2004**, *254*(3), 156-164. [http://dx.doi.org/10.1007/s00406-004-0459-4] [PMID: 15205969]

[52] Angst, J.; Gamma, A.; Endrass, J.; Hantouche, E.; Goodwin, R.; Ajdacic, V.; Eich, D.; Rössler, W. Obsessive-compulsive syndromes and disorders: Significance of comorbidity with bipolar and anxiety syndromes. *Eur. Arch. Psychiatry Clin. Neurosci.,* **2005**, *255*(1), 65-71. [http://dx.doi.org/10.1007/s00406-005-0576-8] [PMID: 15711895]

[53] Sareen, J.; Cox, B.J.; Afifi, T.O.; de Graaf, R.; Asmundson, G.J.; ten Have, M.; Stein, M.B. Anxiety disorders and risk for suicidal ideation and suicide attempts: A population-based longitudinal study of adults. *Arch. Gen. Psychiatry,* **2005**, *62*(11), 1249-1257. [http://dx.doi.org/10.1001/archpsyc.62.11.1249] [PMID: 16275812]

[54] Torres, A.R.; Prince, M.J.; Bebbington, P.E.; Bhugra, D.; Brugha, T.S.; Farrell, M.; Jenkins, R.; Lewis, G.; Meltzer, H.; Singleton, N. Obsessive-compulsive disorder: prevalence, comorbidity, impact, and help-seeking in the British National Psychiatric Morbidity Survey of 2000. *Am. J. Psychiatry,* **2006**, *163*(11), 1978-1985. [http://dx.doi.org/10.1176/ajp.2006.163.11.1978] [PMID: 17074950]

[55] Nock, M.K.; Hwang, I.; Sampson, N.; Kessler, R.C.; Angermeyer, M.; Beautrais, A.; Borges, G.; Bromet, E.; Bruffaerts, R.; de Girolamo, G.; de Graaf, R.; Florescu, S.; Gureje, O.; Haro, J.M.; Hu, C.; Huang, Y.; Karam, E.G.; Kawakami, N.; Kovess, V.; Levinson, D.; Posada-Villa, J.; Sagar, R.; Tomov, T.; Viana, M.C.; Williams, D.R. Cross-national analysis of the associations among mental disorders and suicidal behavior: Findings from the WHO World Mental Health Surveys. *PLoS Med.,* **2009**, *6*(8), e1000123. [http://dx.doi.org/10.1371/journal.pmed.1000123] [PMID: 19668361]

[56] ten Have, M.; de Graaf, R.; van Dorsselaer, S.; Verdurmen, J.; van 't Land, H.; Vollebergh, W.; Beekman, A. Incidence and course of suicidal ideation and suicide attempts in the general population. *Can. J. Psychiatry,* **2009**, *54*(12), 824-833. [http://dx.doi.org/10.1177/070674370905401205] [PMID: 20047721]

[57] Jaisoorya, T.S.; Janardhan, R.Y.C.; Thennarasu, K.; Beena, K.V.; Beena, M.; Jose, D.C. An epidemological study of obsessive compulsive disorder in adolescents from India. *Compr. Psychiatry,* **2015**, *61*, 106-114. [http://dx.doi.org/10.1016/j.comppsych.2015.05.003] [PMID: 26038283]

[58] Cho, S.J.; Hong, J.P.; Lee, J.Y.; Im, J.S.; Na, K.S.; Park, J.E.; Cho, M.J. Association between DSM-IV anxiety disorders and suicidal behaviors in a community sample of south korean adults. *Psychiatry Investig.,* **2016**, *13*(6), 595-600. [http://dx.doi.org/10.4306/pi.2016.13.6.595] [PMID: 27909449]

[59] Meier, S.M.; Mattheisen, M.; Mors, O.; Schendel, D.E.; Mortensen, P.B.; Plessen, K.J. Mortality among persons with obsessive-compulsive disorder in denmark. *JAMA Psychiatry,* **2016**, *73*(3), 268-274. [http://dx.doi.org/10.1001/jamapsychiatry.2015.3105] [PMID: 26818216]

[60] Fernández de la Cruz, L.; Rydell, M.; Runeson, B.; D'Onofrio, B.M.; Brander, G.; Rück, C.; Lichtenstein, P.; Larsson, H.; Mataix-Cols, D. Suicide in obsessive-compulsive disorder: A population-based study of 36 788 Swedish patients. *Mol. Psychiatry,* **2017**, *22*(11), 1626-1632. [http://dx.doi.org/10.1038/mp.2016.115] [PMID: 27431293]

[61] Jaisoorya, T.S.; Janardhan Reddy, Y.C.; Nair, B.S.; Rani, A.; Menon, P.G.; Revamma, M.; Jeevan, C.R.; Radhakrishnan, K.S.; Jose, V.; Thennarasu, K. Prevalence and correlates of obsessive-compulsive disorder and subthreshold obsessive-compulsive disorder among college students in Kerala, India. *Indian J. Psychiatry,* **2017**, *59*(1), 56-62. [http://dx.doi.org/10.4103/0019-5545.204438] [PMID: 28529361]

[62] Veisani, Y.; Mohamadian, F.; Delpisheh, A. Prevalence and comorbidity of common mental disorders and associations with suicidal ideation in the adult population. *Epidemiol. Health,* **2017**, *39*, e2017031. [http://dx.doi.org/10.4178/epih.e2017031] [PMID: 28774163]

[63] Frogley, C.; Taylor, D.; Dickens, G.; Picchioni, M. A systematic review of the evidence of clozapine's anti-aggressive effects. *Int. J. Neuropsychopharmacol.,* **2012**, *15*(9), 1351-1371. [http://dx.doi.org/10.1017/S1461145711002017X] [PMID: 22339930]

[64] Zalsman, G.; Hawton, K.; Wasserman, D.; van Heeringen, K.; Arensman, E.; Sarchiapone, M.; Carli, V.; Höschl, C.; Barzilay, R.; Balazs, J.; Purebl, G.; Kahn, J.P.; Sáiz, P.A.; Lipsicas, C.B.; Bobes, J.; Cozman, D.; Hegerl, U.; Zohar, J. Suicide prevention strategies revisited: 10-year systematic review. *Lancet Psychiatry,* **2016**, *3*(7), 646-659. [http://dx.doi.org/10.1016/S2215-0366(16)30030-X] [PMID: 27289303]

[65] Smith, K.A.; Cipriani, A. Lithium and suicide in mood disorders: Updated meta-review of the scientific literature. *Bipolar Disord.,* **2017**, *19*(7), 575-586. [http://dx.doi.org/10.1111/bdi.12543] [PMID: 28895269]

[66] Ay, R.; Erbay, L.G. Relationship between childhood trauma and suicide probability in obsessive-compulsive disorder. *Psychiatry Res.,* **2018**, *261*, 132-136. [http://dx.doi.org/10.1016/j.psychres.2017.12.054] [PMID: 29304426]

[67] Khosravani, V.; Sharifi, B.F.; Samimi, A.M.; Jamaati, A.R. Early maladaptive schemas and suicidal risk in an Iranian sample of patients with obsessive-compulsive disorder. *Psychiatry Res.,* **2017**, *255*, 441-448. [http://dx.doi.org/10.1016/j.psychres.2017.06.080] [PMID: 28686949]

[68] Fineberg, N.A.; Hengartner, M.P.; Bergbaum, C.; Gale, T.; Rössler, W.; Angst, J. Lifetime comorbidity of obsessive-compulsive disorder and sub-threshold obsessive-compulsive symptomatology in the community: Impact, prevalence, socio-demographic and clinical characteristics. *Int. J. Psychiatry Clin. Pract.,* **2013**, *17*(3), 188-196. [http://dx.doi.org/10.3109/13651501.2013.777745] [PMID: 23428236]

[69] Ozdemiroglu, F.; Sevincok, L.; Sen, G.; Mersin, S.; Kocabas, O.; Karakus, K.; Vahapoglu, F. Comorbid obsessive-compulsive disorder with bipolar disorder: A distinct form? *Psychiatry Res.,* **2015**, *230*(3), 800-805. [http://dx.doi.org/10.1016/j.psychres.2015.11.002] [PMID: 26561371]

[70] Weingarden, H.; Renshaw, K.D.; Wilhelm, S.; Tangney, J.P.; DiMauro, J. Anxiety and shame as risk factors for depression, suicidality, and functional impairment in body dysmorphic disorder and obsessive compulsive disorder. *J. Nerv. Ment. Dis.,* **2016**, *204*(11), 832-839. [http://dx.doi.org/10.1097/NMD.0000000000000498] [PMID: 26998694]

[71] Borges, G.; Nock, M.K.; Haro, A.J.M.; Hwang, I.; Sampson, N.A.; Alonso, J.; Andrade, L.H.; Angermeyer, M.C.; Beautrais, A.; Bromet, E.; Bruffaerts, R.; de Girolamo, G.; Florescu, S.; Gureje, O.; Hu, C.; Karam, E.G.; Kovess-Masfety, V.; Lee, S.; Levinson, D.; Medina-Mora, M.E.; Ormel, J.; Posada-Villa, J.; Sagar, R.; Tomov, T.; Uda, H.; Williams, D.R.; Kessler, R.C. Twelve-month prevalence of and risk factors for suicide attempts in the World Health Organization World Mental Health Surveys. *J. Clin. Psychiatry,* **2010**, *71*(12), 1617-1628. [http://dx.doi.org/10.4088/JCP.08m04967blu] [PMID: 20816034]

[72] Brown, G.K.; Jager-Hyman, S. Evidence-based psychotherapies for suicide prevention: future directions. *Am. J. Prev. Med.,* **2014**, *47*(3)(Suppl. 2), S186-S194. [http://dx.doi.org/10.1016/j.amepre.2014.06.008] [PMID: 25145738]

[73] While, D.; Bickley, H.; Roscoe, A.; Windfuhr, K.; Rahman, S.; Shaw, J.; Appleby, L.; Kapur, N. Implementation of mental health service recommendations in England and Wales and suicide rates, 1997-2006: A cross-sectional and before-and-after observational study. *Lancet,* **2012**, *379*(9820), 1005-1012. [http://dx.doi.org/10.1016/S0140-6736(11)61712-1] [PMID: 22305767]

[74] Bolton, J.M.; Gunnell, D.; Turecki, G. Suicide risk assessment and intervention in people with mental illness. *BMJ,* **2015**, *351*, h4978. [http://dx.doi.org/10.1136/bmj.h4978] [PMID: 26552947]

[75] Turecki, G.; Brent, D.A. Suicide and suicidal behaviour. *Lancet,* **2016**, *387*(10024), 1227-1239. [http://dx.doi.org/10.1016/S0140-6736(15)00234-2] [PMID: 26385066]

[76] Bloch, M.H.; McGuire, J.; Landeros-Weisenberger, A.; Leckman, J.F.; Pittenger, C. Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. *Mol. Psychiatry,* **2010**, *15*(8), 850-855. [http://dx.doi.org/10.1038/mp.2009.50] [PMID: 19468281]

[77] Albert, U.; Marazziti, D.; Di Salvo, G.; Solia, F.; Rosso, G.; Maina, G. A systematic review of evidence-based treatment strategies for obsessive-compulsive disorder resistant to first-line pharmacotherapy. *Curr. Med. Chem.,* **2017**. [http://dx.doi.org/10.2174/0929867325666171222163645] [PMID: 29278206]

[78] Albert, U.; Carmassi, C.; Cosci, F.; De Cori, D.; Di Nicola, M.; Ferrari, S.; Poloni, N.; Tarricone, I.; Fiorillo, A. Role and clinical implications of atypical antipsychotics in anxiety disorders, obsessive-compulsive disorder, trauma-related, and somatic symptom disorders: a systematized review. *Int. Clin. Psychopharmacol.,* **2016**, *31*(5), 249-258. [http://dx.doi.org/10.1097/YIC.0000000000000127] [PMID: 26974213]

[79] Albert, U.; Salvo, G.D.; Solia, F.; Rosso, G.; Maina, G. Combining drug and psychological treatments for Obsessive-Compulsive Disorder: what is the evidence, when and for whom. *Curr. Med. Chem.,* **2018**, *25*(41), 5632-5646. [http://dx.doi.org/10.2174/0929867324666170712114445] [PMID: 28707590]

[80] Hantouche, E.G.; Kochman, F.; Demonfaucon, C.; Barrot, I.; Millet, B.; Lancrenon, S.; Akiskal, H.S. Bipolar obsessive-compulsive disorder: Confirmation of results of the "ABC-OCD" survey in 2 populations of patient members versus non-members of an association. *Encephale,* **2002**, *28*(1), 21-28. [PMID: 11963340]

[81] D'Ambrosio, V.; Albert, U.; Bogetto, F.; Maina, G. Obsessive-compulsive disorder and cyclothymic temperament: An exploration of clinical features. *J. Affect. Disord.,* **2010**, *127*(1-3), 295-299. [http://dx.doi.org/10.1016/j.jad.2010.06.007] [PMID: 20591494]

[82] Maina, G.; Albert, U.; Pessina, E.; Bogetto, F. Bipolar obsessive-compulsive disorder and personality disorders. *Bipolar Disord.,* **2007**, *9*(7), 722-729. [http://dx.doi.org/10.1111/j.1399-5618.2007.00508.x] [PMID: 17988362]

[83] Mucci, F.; Toni, C.; Favaretto, E.; Vannucchi, G.; Marazziti, D.; Perugi, G. Obsessive-compulsive disorder with comorbid bipolar disorders: clinical features and treatment implications. *Curr. Med. Chem.,* **2018**, *25*(41), 5722-5730. [http://dx.doi.org/10.2174/0929867324666171108145127] [PMID: 29119914]

[84] Perugi, G.; Toni, C.; Frare, F.; Travierso, M.C.; Hantouche, E.; Akiskal, H.S. Obsessive-compulsive-bipolar comorbidity: A systematic exploration of clinical features and treatment outcome. *J. Clin. Psychiatry,* **2002**, *63*(12), 1129-1134. [http://dx.doi.org/10.4088/JCP.v63n1207] [PMID: 12523872]

[85] Timpano, K.R.; Rubenstein, L.M.; Murphy, D.L. Phenomenological features and clinical impact of affective disorders in OCD: a focus on the bipolar disorder and OCD connection. *Depress. Anxiety,* **2012**, *29*(3), 226-233. [http://dx.doi.org/10.1002/da.20908] [PMID: 22109969]

[86] Simon, N.M.; Otto, M.W.; Wisniewski, S.R.; Fossey, M.; Sagduyu, K.; Frank, E.; Sachs, G.S.; Nierenberg, A.A.; Thase, M.E.; Pollack, M.H. Anxiety disorder comorbidity in bipolar disorder patients: data from the first 500 participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Am. J. Psychiatry,* **2004**, *161*(12), 2222-2229. [http://dx.doi.org/10.1176/appi.ajp.161.12.2222] [PMID: 15569893]

[87] Fawcett, J.; Scheftner, W.A.; Fogg, L.; Clark, D.C.; Young, M.A.; Hedeker, D.; Gibbons, R. Time-related predictors of suicide in major affective disorder. *Am. J. Psychiatry,* **1990**, *147*(9), 1189-1194. [http://dx.doi.org/10.1176/ajp.147.9.1189] [PMID: 2104515]

[88] Raines, A.M.; Short, N.; Allan, N.P.; Oglesby, M.E.; Schmidt, N.B. Examination of a brief anxiety sensitivity cognitive concerns intervention on suicidality among individuals with obsessive-compulsive symptoms. *Contemp. Clin. Trials,* **2015**, *45*(Pt B), 191-195. [http://dx.doi.org/10.1016/j.cct.2015.09.006]

[89] Abramowitz, J.S.; Taylor, S.; McKay, D. Potentials and limitations of cognitive treatments for obsessive-compulsive disorder. *Cogn. Behav. Ther.,* **2005**, *34*(3), 140-147. [http://dx.doi.org/10.1080/16506070510041202] [PMID: 16195053]