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# Psychiatric comorbidities of obsessive-compulsive disorder: A series of systematic reviews and meta-analyses

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#### Abstract

**Objective:** Although there is a growing number of studies on psychiatric comorbidities of obsessive-compulsive disorder (OCD), controversy remains about the strength of associations between some disorders. We present a series of systematic reviews and meta-analyses examining four psychiatric disorders frequently associated with OCD– depression, bipolar disorder, substance abuse disorder and psychosis.

**Methods:** Three electronic databases were searched up to May 2017; PsycINFO, Medline, and Web of Science. Meta-analyses using random effects models were conducted. **Results:** The meta-analyses found strong associations between all comorbidities and OCD, particularly for depression. In addition, a series of systematic reviews were conducted giving information about the characteristics of these psychiatric associations.

**Conclusion:** It is probable that these disorders share common etiological factors, and thus trans-diagnostic processes must be addressed when offering treatment. Clinical implications of these findings are discussed with suggestions for further research in the area.

#### KEYWORDS

meta-analysis, obsessive-compulsive disorder, psychiatric comorbidities, systematic review

#### 1 | INTRODUCTION

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Torres et al. (2006) found that around 62% of individuals with OCD had a psychiatric comorbidity, a large percentage given that the prevalence is just 10% in other anxiety disorders. An Australian study (Crino et al., 2005) gave an even higher figure—79.7%. Thus, it appears that comorbidity is the norm and not the exception when it comes to OCD.

Many disorders seem to be comorbid with OCD; in this line, major depression is considered the most common comorbidity of OCD. Evidence shows that comorbidity can affect treatment outcome in OCD (Overbeek et al., 2002). It is, therefore, essential to properly quantify the overlap between disorders to better inform treatment. Emerging literature shows that bipolar disorder has been suggested as a comorbidity to OCD and that OCD can have a detrimental effect on the course of bipolar disorder (Simon et al., 2004), but this deserves to be studied further. After affective disorders, psychotic disorders are usually discussed in terms of differential diagnosis. There is evidence that comorbid psychosis is related to worse treatment outcome and greater neuropsychological impairment. Thus, it is necessary to understand the strength of association between the two disorders (Eisen & Rasmussen, 1993).

Studies have shown significant comorbidity in individuals with OCD, yet the prevalence of these psychiatric disorders is heterogeneous, with different articles producing variable results. Therefore, it is important to study these correlations from both a qualitative (systematic review) and a quantitative (meta-analysis) perspective. Two main objectives drive this current paper:

- (i) appreciating the strength of the link between four psychiatric comorbidities of OCD through a series of meta-analyses
- (ii) better understanding the reciprocal effects on one another and looking at how this might need to be considered in treatment through a succession of systematic reviews

The four psychiatric comorbidities chosen for this study are major depressive disorder, bipolar disorder, psychosis and substance abuse disorder. In addition, affective disorders, specifically unipolar depression and bipolar disorder, as well as severe mental illness in the form of psychosis and the comorbidity of substance abuse disorder, were considered to be of clinical interest.

#### 2 | METHOD

#### 2.1 | Eligibility criteria

We included studies which: (1) were conducted on adult populations, defined as aged 16 or over; (2) included a measure of OCD; (3) gave the prevalence of the comorbidity studied in an OCD population; (4) were written in English, French or German; (5) were published in a peer-reviewed journal; (6) were published between May 1980 and May 2017.

#### 2.2 | Data sources and search strategy

Three electronic bibliographic databases were used—PsycInfo, MEDLINE and Web of Science. Search terms were entered successively. For bipolar disorder, cyclothymia was considered a separate disorder. The term psychosis covers schizophrenia and closely related disorders such as schizo-affective disorder.

2.3

## Study selection

Study selection was undertaken in a three-step process. At the first screening, abstracts were reviewed for information leading to exclusion (too old, letters, comments and languages other than English, German and French). Second, papers with data that could be used in a meta-analysis (following the inclusion criteria previously presented) were retained as well as duplicates. Finally, in a third wave, all articles that were not chosen for the meta-analysis but were useful for the systematic review were selected.

A total of 45 studies were collected for the meta-analyses with a sum of 54,209 participants.

#### 2.4 Data extraction

The effect size used for this project was relative risk (RR). The distinction among the various measures of RR (e.g., odds ratio, rate ratio and risk ratio) was ignored, assuming that OCD is a rare disease with a prevalence of 1.2% at 1 year (Ruscio et al., 2010).

RR was determined using raw data, mainly percentages, in the current study. Different articles using the same dataset were only included if they concerned data on different comorbid correlates to avoid duplicating data.

An electronic data extraction form was developed and piloted. The following descriptive information was extracted: the authors, the type of comorbidity studied, the number of participants, the risk ratio, the prevalence of the comorbidity in the OCD sample, the country where the study was conducted in and the diagnostic tool used to diagnose the comorbidity.

#### 2.5 | Data analyses

Four separate random-effects meta-analyses were conducted. Percentage outcomes were converted to Risk Ratios and pooled using R, in particular the packages meta and metafor.

In the absence of control groups, the prevalence of associated disorders was estimated in each case to be homogenous across studies. The prevalence of depression was taken as 8% (Kessler & Bromet, 2013), bipolar disorder at 1% (Moreira et al., 2017), psychosis at 0.87% (Perälä et al., 2007), and substance abuse disorder at 1.5% (Broman et al., 2008).

Heterogeneity was measured using the  $l^2$  statistic. Higher values of  $l^2$  represent more heterogeneity. Publication bias was determined using visually determined funnel plot symmetry.

#### 3 | RESULTS

#### 3.1 | Meta-analyses

Table 1 summarizes the characteristics of the 45 studies retained for meta-analysis.

The most used tool to diagnose OCD is the Yale-Brown Obsessive Compulsive Scale or Y-BOCS (Goodman et al., 1989) in 43.6% of cases, followed by the SCID or Structural Clinical Interview for DSM-III/DSM-IV (First, 1997) in 28.2% of cases.

The most widely used tool to diagnose psychiatric comorbidities of OCD was the SCID (First, 1997) (53.8%) followed by the MINI, the Mini International Neuropsychological Interview at 12.8% (Sheehan et al., 1998). In the case of bipolar disorder, major depressive disorder, substance abuse disorder and psychosis, we used a random effects model as the diagnostic tools were not consistent across the studies.

The sample size of these studies ranges from 25 to 1078, with an average of 345.26 participants.

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TABLE 1 Characteristics of	Characteristics of studies used in the meta-analyses	eta-analyse	S				
AuthoDate	Comorbidity	z	RR	Prevalence in OCD sample (%)	Country	Diagnostic tool of OCD	Diagnostic tool of psychiatric comorbidity
LaSalle et al. (2004)	Depression	339	8.11	65.90%	US	SCID	SCID
Lochner et al., (2014)	Depression	149	1.93	15.42%	International	MINI	MINI
Rickelt et al., (2016)	Depression	419	7.07	56.60%	Netherlands	Y-BOCS	SCID-I/P
Klein Hofmeijer-Sevink et al., (2013)	Depression	382	7.07	56.50%	Netherlands	Y-BOCS	SCID-I/P
Pinto et al., (2006)	Depression	293	8.40	67.20%	US	Y-BOCS	НАМD
Quarantini et al., (2011)	Depression	818	8.40	67.50%	Brazil	Y-BOCS	BDI
Viswanath et al., (2012)	Depression	545	3.78	30%	India	Y-BOCS	MINI
Altintas et al. (2015)	Depression	140	5.63	45%	Turkey	Y-BOCS	SCID
Prabhu et al., (2013)	Depression	161	2.80	22.40%	India	Y-BOCS	MINI
Torresan et al., (2009)	Depression	858	8.55	68.40%	Brazil	Y-BOCS	SCID
Mohammadi et al., (2007)	Depression	444	1.75	14%	Iran	SADS	SADS
Torresan et al., (2013)	Depression	330	7.42	59.40%	Brazil	Y-BOCS	SCID
Denys et al. (2004)	Depression	420	2.59	20.70%	The Netherlands	MINI	MINI
Tükel et al., (2002)	Depression	147	9.44	39.45%	Turkey	Y-BOCS	Semi-structured interviews
Bhattacharyya et al., (2005)	Depression	218	2.06	16.50%	India	SCID	SCID
Sun et al., (2015)	Depression	278	3.10	24.82%	China	SCID	SCID
Ruscio et al., (2010)	Depression	78	4.81	40.70%	US	SCID and CIDI	CIDI
Fireman et al. (2001)	Bipolar Disorder	1078	6.03	6%	NS	Case reports	Case reports
Hantouche et al. (2002)	Bipolar Disorder	628	10.99	11%	France	Case reports	DSM-IV
Maina et al., (2007)	Bipolar Disorder	204	10.29	10.30%	Italy	Y-BOCS	SCID-I

AuthoDate	Comorbidity	z	RR	Prevalence in OCD sample (%)	Country	Diagnostic tool of OCD	Diagnostic tool of psychiatric comorbidity
Marazziti et al., (2002)	Bipolar Disorder	117	20.51	20.50%	Italy	Y-BOCS	Semi-structured interviews
Perugi et al. (1997, 1998, 2002)	Bipolar Disorder	315	17.14	15.70%	Italy	III-MSD	Specially constructed OCD questionnaire
Perugi et al. (1997, 1998, 2002)	Bipolar Disorder	135	19.26	35.10%	Italy	DSM-III	Specially constructed OCD questionnaire
Timpano et al., (2012)	Bipolar Disorder	605	13.06	13.10%	US	SCID-P	SCID-P
Ruscio et al., (2010)	Bipolar Disorder	73	23.29	23.40%	US	SCID	SCID
de Haan et al., (2009)	Psychosis	757	1.97	1.70%	The Netherlands	SCID	SCID
Stanley et al., (1990)	Psychosis	25	32.18	8%	US	ADIS-R	SCID
Eisen et al. (1993)	Psychosis	475	15.73	13.68%	US	SCID	SCID
Klein Hofmeijer-Sevink et al., (2013)	Psychosis	382	5.42	4.70%	The Netherlands	Y-BOCS	sciD
Torres et al., (2006)	Psychosis	114	3.02	12.70%	Great Britain	CIS-R	CISR
Yaryura-Tobias et al., (2000)	Psychosis	132	12.19	10.60%	US	SCID	SCID
Klein Hofmeijer-Sevink et al., (2013)	Substance Abuse Disorder	382	9.08	13.60%	The Netherlands Y-BOCS	Y-BOCS	SCID
Pinto et al., (2006)	Substance Abuse Disorder	293	17.06	25.60%	US	Y-BOCS	sciD
Viswanath et al., (2012)	Substance Abuse Disorder	545	2.08	17%	India	Y-BOCS	MINI
Ruscio et al., (2010)	Substance Abuse Disorder	71	26.29	38.60%	N	SCID and CIDI	CIDI
Yaryura Tobias et al. (2000)		132	6.57	9.80%	US	SCID	SCID
							(Continues)

TABLE 1 (Continued)

TABLE 1 (Continued)							
AuthoDate	Comorbidity	z	RR	Prevalence in OCD sample (%)	Country	Diagnostic tool of OCD	Diagnostic tool of psychiatric comorbidity
	Substance Abuse Disorder						
Adam et al., (2012)	Substance Abuse Disorder	30	20.00	30%	Germany	M-CIDI	DIA-X/M-CIDI
Mancebo et al., (2009)	Substance Abuse Disorder	323	17.96	27%	US	Butler Hospital OCD Database,	SCID
Gentil et al. (2009)	Substance Abuse Disorder	630	4.97	7.50%	Brazil	Y-BOCS	SCID

#### 3.1.1 | Major depressive disorder

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Twelve studies were retained with a total of 6019 participants. The result of the meta-analysis shows a RR = 4.77 (3.58; 6.35). This indicates that individuals with OCD are more likely to have major depressive disorder than the general population. The results can be found in Figure 1. The  $I^2$  is 66% which represents a moderate level of heterogeneity.

#### 3.1.2 | Bipolar disorder

Twelve studies were retained with a total of 22,495 participants. The result of the meta-analysis shows a RR = 13.88 (6.90; 27.90). This indicates that individuals with OCD are more likely to have bipolar disorder than the general population. The results are given in Figure 2. The  $I^2$  is equal to 0%, indicating either an extremely low level of heterogeneity or a bias based on the small sample size (Higgins et al., 2003).

#### 3.1.3 | Psychosis

Eight studies were retained for meta-analysis with a total of 22,839 participants. The result of the meta-analysis shows a RR = 7.86 (3.23; 19.14). This indicates that individuals with OCD are more likely to have psychosis than the general population, as seen in Figure 3. The  $I^2$  is at 0%, which can mean extremely low heterogeneity but may be explained by the small sample size (Higgins et al., 2003).

#### 3.1.4 | Substance abuse disorder

Eight studies were retained with a total of 2406 participants. The result of the meta-analysis shows a RR = 10.07 (5.44; 18.33). This indicates that individuals with OCD are more likely to have substance abuse disorder than the

	Experim	ental	C	ontrol				Weight	Weight
Study			Events		Risk Ratio	RR	95%-CI		(random)
La Salle et al.	220	339	8	100	÷ =	8 1 1	[4.15; 15.84]	6.2%	6.0%
Lochner et al.	23	149	8	100			[0.90; 4.14]	4.8%	5.5%
Rickelt et al.	237	419	8	100			[3.62; 13.82]	6.5%	6.0%
Klein Hofmeijer-Sevink et al.		382	8	100			[3.62; 13.82]	6.4%	6.0%
Pinto et al.	197	293	8	100			[4.30; 16.42]	6.0%	6.0%
Quarantini et al.	550	818	8	100			[4.32; 16.37]	7.2%	6.0%
Viswanath et al.	165	545	8	100			[1.92; 7.45]	6.8%	6.0%
Altintas et al.	63	140	8	100			[2.82; 11.21]	4.7%	5.9%
Prabhu et al.	36	161	8	100		2.80	[1.35; 5.77]	5.0%	5.7%
Torresan et al.	587	858	8	100		8.55	[4.39; 16.65]	7.2%	6.0%
Mohammadi et al.	62	444	8	100	- <u></u>		[0.86; 3.53]	6.6%	5.8%
Torresan et al.	196	330	8	100		7.42	[3.80; 14.52]	6.2%	6.0%
Denys et al.	87	420	8	100		2.59	[1.30; 5.16]	6.5%	5.9%
TŸkel et al.	111	147	8	100		- 9.44	[4.83; 18.46]	4.8%	6.0%
Bhattacharyya et al.	36	218	8	100		2.06	[1.00; 4.28]	5.5%	5.7%
Sun et al.	69	278	8	100		3.10	[1.55; 6.22]	5.9%	5.9%
Ruscio et al.	30	78	8	100	- <u></u>	4.81	[2.34; 9.89]	3.5%	5.7%
Fixed effect model		6019		1700	¢ (	5.57	[4.71; 6.58]	100.0%	
Random effects model					<b></b>	4.77	[3.58; 6.35]		100.0%
Heterogeneity: $I^2 = 66\%$ , $\tau^2 = 10\%$	0.2403, p ·	< 0.01			1 1 1 1				
					0.1 0.5 1 2 10				

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Study	Experime Events			ontrol Total	Risk Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
Fireman et al.	65 1	1078	1	100		- 6.03	[0.85; 42.99]	16.3%	12.6%
Hantouche et al.	69	628	1	100		- 10.99	[1.54; 78.22]	15.4%	12.7%
Maina et al.	21	204	1	100		- 10.29	[1.40; 75.44]	12.0%	12.3%
Marazziti et al.	24	117	1	100		20.51	[2.83; 148.94]	9.6%	12.4%
Perugi et al.	54	315	1	100		17.14	[2.40; 122.34]	13.6%	12.6%
Perugi et al.	26	135	1	100		— 19.26	[2.66; 139.56]	10.3%	12.4%
Timpano et al.	79	605	1	100		- 13.06	[1.84; 92.79]	15.3%	12.7%
Ruscio et al.	17	73	1	100		23.29	[3.17; 171.06]	7.5%	12.3%
Fixed effect model		3155		800	🔶		[6.98; 27.84]	100.0%	
Random effects mode					<b>◇</b>	13.88	[6.90; 27.90]		100.0%
Heterogeneity: $I^2 = 0\%$ , $\tau^2$	r = 0, p = 0.9	99				1			
				(	.01 0.1 1 10	100			

#### FIGURE 2 Forest plot for bipolar disorder

Stanley, Turner & Borden 7 25 0.87 100 3 3 ± 32.18 [3.62; 286.00] 5.3%	Study	ht n)
Stanley, Turner & Borden 7 25 0.87 100 - 3 - 3 - 3 - 3 - 3 - 3 - 3 - 3 - 3 -	de Haan, Dudek-Hodge, Verhoeven & Denv	%
Figon & Desmussion 65 475 0.97 100 - 15 72 [1.02: 120.00] 21 79		%
Eisen & Rasinussen 05 475 0.07 100 15.73 [1.92, 129.00] 21.7%	Eisen & Rasmussen	%
Klein Hofmeijer-Sevink, et al. 18 382 0.87 100 5.42 [0.64; 46.04] 20.8%	Klein Hofmeijer-Sevink, et al.	%
Torres et al. 3 114 0.87 100 3.02 [0.28; 32.40] 14.0%	Torres et al.	%
Yaryura-Tobias et al. 14 132 0.87 100 12.19 [1.42; 104.65] 15.0%	Yaryura-Tobias et al.	%
Fixed effect model 1885 600 $\frac{5}{2}$ 8.94 [3.72; 21.50] 100.0%   Random effects model 7.86 [3.23; 19.14]  1   Heterogeneity: $l^2 = 0\%$ , $\tau^2 = 0, p = 0.47$ 0.01 0.1 1 10 100	Random effects model	 %

#### FIGURE 3 Forest plot for psychosis

general population. Therefore, substance abuse disorder appears to be a correlate of OCD, as seen in Figure 4. The  $I^2$  is equal to 7%, which represents a very small amount of heterogeneity.

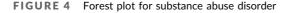
#### 3.2 | Examining the links between disorders: systematic reviews

#### 3.2.1 | Major depressive disorder

First we examined the temporal precedence of the disorders, followed by an investigation of possible mediating variables such as sex. Finally, we looked at the clinical characteristics of comorbid depression and OCD.

There is a strong correlation between OCD and depression (Crino et al., 2005), but the temporal precedence of either disorder remains a subject of debate. In an early study by Karno et al. (1988), patients with both OCD and depression declared that their OCD preceded the depression. A subsequent paper (Kessler et al., 2005) found that the age of the appearance of OCD was significantly younger than the onset of depression. Conversely, Crum and Anthony (1993) showed that patients with depression were more likely to develop OCD. In a study by Grabe et al. (2001), there was a higher prevalence of depression amongst individuals with OCD in both sexes, but the apparition of depression was a mix of before, at the same time, or after the OCD. LaSalle et al. (2004) propose that depression is secondary to the disabling effects of OCD and the demoralization when faced with the disorder. They also look at the practical side of treatment, suggesting that when depression and OCD co-exist, depression should be treated first. Rickelt et al. (2016) found that OCD and depression are strongly correlated regardless of temporal precedence.

Study	Experime Events T			ontrol Total	Ris	Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
Klein Hofmeijer-Sevink, et al	52	382	1.5	100			9.08	[1.82; 45.32]	15.2%	12.8%
Pinto et al.	75	293	1.5	100			- 17.06		14.3%	12.9%
Viswanath et al.	17	545	1.5	100	-		2.08	[0.40; 10.89]	16.2%	12.1%
Ruscio et al.	28	71	1.5	100			- 26.29	[5.23; 132.08]	7.9%	12.7%
Yaryura Tobias et al.	13	132	1.5	100			6.57	[1.24; 34.88]	10.9%	11.9%
Adam et al.	9	30	1.5	100		<u> </u>	- 20.00	[3.73; 107.28]	4.4%	11.8%
Mancebo et al.	87	323	1.5	100			- 17.96	[3.63; 88.80]	14.6%	12.9%
Gentil et al.	47	630	1.5	100			4.97	[0.99; 24.93]	16.5%	12.7%
Fixed effect model Random effects model	2	2406		800				[6.38; 19.96] [5.54; 18.33]	100.0%	 100.0%
Heterogeneity: $I^2 = 7\%$ , $\tau^2 = 0$ .	0549, p = 0.	.37				+		[0.04, 10.00]		100.0%
				0	01 0.1	1 10	100			



Altintaş and Taşkintuna (2015) found that when comparing a group of patients with OCD and those with OCD and depression, there was no difference in the ages, sex ratio, marital status, the presence of family history of OCD or the period of latency between the appearance of OCD and the start of treatment. That being said, Torresan et al. (2009) looked to find a difference between sexes. In his study, females had higher scores on depression scales. However, patients with OCD and depression showed more avoidance, less insight and less stability. Viswanath et al. (2012) showed that in patients with both illnesses, the more severe the depression becomes, the more there are obsessions (in particular religious obsessions) and compulsions (above all, the need to touch items or to confess). A further study conducted by Torresan et al. (2013) similarly showed a link between depression and sexual and religious obsessions.

Pinto et al. (2006) attempted to see whether there was a difference in levels of comorbid depression between those who developed OCD at an early age and those whose OCD appeared later in life. They found no difference in levels of prevalence of depression. A typological analysis (Sun et al., 2015) showed that the severity of OCD was linked to the severity of comorbid depression and anxiety, along with feelings of powerlessness.

We can, therefore, assume that depression could be a risk factor or a consequence of obsessive-compulsive disorder and that it is probable that the two illnesses share common etiological factors.

#### 3.2.2 | Bipolar disorder

Initially, we looked at the prevalence of OCD in bipolar disorder and the reverse, followed by the risk of misdiagnosis and the clinical characteristics of the OCD-bipolar comorbidity.

A prospective study in the United States (Crum & Anthony, 1993) showed an elevated risk of developing OCD in subjects with existing bipolar disorder. Likewise, a survey from Germany (Grabe et al., 2001) found a higher prevalence of OCD in women with bipolar disorder. Amerio et al. (2015) carried out a meta-analysis in both directions; in patients with OCD, the prevalence of bipolar disorder was 18.35%, and the prevalence of OCD in patients with bipolar disorder was 17.0%. This comorbidity seems to have a strong correlation.

A longitudinal project (Angst et al., 2004) showed that the prevalence of OCD and obsessive-compulsive symptoms was raised when a disorder on the bipolar spectrum (Bipolar I, Bipolar II, cyclothymia) was also present. The authors suggested that diagnostic errors may lead to patients with OCD being misdiagnosed with unipolar depression when, in reality, it is bipolar disorder.

Perugi et al. (1997) found that patients with comorbid bipolar disorder and OCD display significantly more sexual and religious obsessions and fewer checking compulsions. In his study, it also became apparent that in participants with this comorbidity, the onset of symptoms is less acute. A further study (Maina et al., 2007) similarly

found that in those with both disorders, there is a preponderance of males with more sexual obsessions and hoarding disorder. They also found that participants presented with higher rates of personality disorders. Perugi et al. (1997) showed that patients with comorbid bipolar disorder showed fewer rituals (such as checking) and more sexual and religious obsessions.

Perugi et al. (1998) showed that this comorbidity led to episodic OCD rather than the chronic course usually seen in patients who do not present bipolar symptoms. Marazziti et al. (2002) remarked that patients presenting with both psychiatric disorders had worse insight than those with only OCD. Patients with bipolar disorder also showed more frequent abuse of alcohol, sedatives, stimulants and caffeine (Perugi et al., 1997).

We can, therefore, assume that bipolar disorder could be a risk factor or a consequence of obsessivecompulsive disorder and that it is probable that the two illnesses share common etiological factors.

#### 3.2.3 | Psychosis

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The prevalence of comorbid OCD and psychosis shows significant variation in the few studies available for analysis, from 1.7% (de Haan et al., 2009) to 14% (Eisen & Rasmussen, 1993).

de Haan et al. (2009) found no difference between the clinical characteristics of subjects with psychosis with and without comorbid OCD. However, patients with OCD and psychosis consumed more illicit substances and were more often male. Stanley et al. (1990) remarked that patients with this comorbidity showed more delusions and visual hallucinations than auditory hallucinations, mental automatisms or negative symptoms such as alogia and apathy.

Insel and Akiskal (1986) suggested that the delusions that occur in some cases of OCD do not signify a schizophrenic diagnosis but are transient reactive affective or paranoid psychoses. They found that patients at the severe end of the OCD spectrum were more likely to present what they qualify as obsessive-compulsive psychosis.

In summary, early studies showed that patients with OCD showed no greater risk of developing schizophrenia, but later studies have shown there to be a link. It was thus important to conduct a meta-analysis and to get a clearer picture of the risk ratio.

#### 3.2.4 | Substance abuse disorder

Adam et al. (2012) found an extremely high prevalence of substance abuse disorders in patients with OCD–39.3%. One must remain vigilant in interpreting this figure as it was a "small N" study with just 30 participants in the OCD group. However, other studies from Ruscio et al. (2010), Mancebo et al. (2009) and (Viswanath et al., 2012) all also found a high level of comorbidity. In contrast, Yaryura-Tobias et al. (2000) and Gentil et al. (2009) found more moderate results. Mancebo et al. (2009) showed that the early development of OCD, as well as a comorbidity with borderline personality disorder, were risk factors in developing substance abuse disorder.

Fals-Stewart and Schafer (1992) found that patients with comorbid OCD and substance abuse that received treatment for both conditions stayed in treatment longer, showed greater reductions in OCD symptom severity and had higher abstinence rates at 12 months. Gentil et al. (2009) present the hypothesis that the appearance of OCD precedes the development of substance abuse disorder. Following the results of his study, patients with a comorbidity of OCD and substance abuse disorder are more often male, have benefitted more from treatment programs and have more suicidal ideation. A high percentage of participants with substance abuse disorder reported that psychoactive substances improved their OCD. They hypothesize that the anxiolytic characteristics of these substances intensify the risk of maintaining the concomitant substance abuse when suffering from OCD.

We can, therefore, assume that SUD could be a risk factor or a consequence of obsessive-compulsive disorder and that it is probable that the two illnesses come hand in hand regularly.

#### 4 | DISCUSSION

#### 4.1 | Clinical implications

Our series of systematic reviews and meta-analyses allow us to answer many questions emerging from recent articles concerning obsessive-compulsive disorder. All comorbidities were linked with OCD, which is essential when proposing a holistic treatment of patients presenting with this disorder. Screening for other psychiatric correlates is an important step in the treatment of both OCD and other mental illnesses.

It is not surprising to find a link between major depression and OCD which is such a disabling illness. What needs to be examined is whether this is reactional depression or a clinical major depressive disorder that was present before or after the onset of OCD. It would be interesting to introduce a longitudinal study to look at the temporal precedence of the two disorders using participants with risk factors for either or both disorders (i.e., family history). It is important to ensure the concomitant treatment of OCD and depression to avoid the demotivation that occurs with a depressive illness, thus negating the effect of the cognitive behavioural therapy used to treat OCD. In fact, Overbeek et al. (2002) found that in patients with comorbid depression and OCD, patients with only an OCD diagnosis made more improvement than the comorbid group.

It is also probable that depression and OCD share common etiologies, whether neurobiological (e.g., the anterior cingulate cortex; Graybiel & Rauch, 2000) or psychological (e.g., perfectionism; Sassaroli et al., 2008). This shows the importance of screening for depression in OCD samples and addressing trans-diagnostic processes when offering treatment. Many therapists propose to work on depression before OCD when the two are comorbid, yet it would be more relevant to take a holistic approach and address common trans-diagnostic factors.

Bipolar disorder and OCD are strongly linked (R = 13.88), with both disorders impacting one another. In addition to this, Perugi et al. (2002) found that the bipolar-OCD comorbidity is associated with the presence of other illnesses such as agoraphobia or panic disorder, making it essential to treat both illnesses as early as possible to avoid the development of other comorbidities. However, one must exercise caution in the pharmacological treatment, as the SSRIs used commonly to treat OCD are known to induce mania in a small section of patients with bipolar disorder (Bottlender et al., 1998). This comorbidity is remarkably high, and research should be conducted into common etiologies, be they neurobiological, psychological or both.

The risk ratio for developing psychosis in people with OCD is notably elevated. It is extremely important to look at the role of insight. Traditionally, awareness of the ego-dystonic characteristic of the obsessions is seen as a diagnostic criterion for OCD, and lack of insight is seen as a hallmark of psychosis and delusional thinking. However, lack of insight or reduced insight is experienced in a significant number of OCD sufferers (up to one-third; Lelliott et al., 1988). It is, therefore, debatable as to the point at which lack of insight becomes delusional. It is, therefore, possible to imagine a spectrum of OCD with schizo-typal symptoms and psychosis, with the two occurring along a continuum of insight (Insel & Akiskal, 1986) with patients at the extreme end of the spectrum displaying what can be defined as obsessive-compulsive psychosis.

OCD and substance abuse disorder are highly comorbid. This self-medication hypothesis is interesting as it acknowledges that the start of the anxiety disorder, in this case, OCD, precedes the onset of substance abuse (Robinson et al., 2009). This would allow us to hypothesize that OCD is a risk factor for substance abuse disorder. It has also been shown that those with comorbid substance abuse who received treatment for both conditions had better results and benefit more from treatment programs (Gentil et al., 2009) than those who received treatment for just one of the conditions (Fals-Stewart & Schafer, 1992). This shows the huge importance of screening for comorbidities in substance use disorder.

#### 4.2 | Limitations

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A serious limitation in the literature is a deficit of longitudinal studies. This prevents us from ascertaining the temporal precedence of the disorders studied. If we can define which disorders are a cause or a consequence of OCD, we can allow earlier intervention and prevent suffering and disability. Despite the lack of longitudinal studies, it is nevertheless technically possible to model trajectories from data collected by cross-sectional design through the use of advanced statistics. For example, De Mathis et al. (2013) show that the primary diagnosis (OCD, separation anxiety, ADHD or TIC) can predict the probability of the mean age of diagnosis of OCD and associated comorbidities using Bayesian analysis.

Despite the limitations imposed by the heterogeneity of the studies in sampling, design, measurement, statistical analysis, and resulting effects, we did find strong associations. In addition, heterogeneity was either high (depression), low (substance abuse disorder), or null—psychosis and bipolar disorder—(probably an error caused by small sample size). Larger sample sizes and looking at grey literature (literature that has not been published) would be preferable. In addition, the way that OCD is conceptualized has changed in the recent DSM-5, and the papers included in our study used the DSM-IV or DSM-III definitions of OCD to diagnose the disorder.

With the data available, we were unable to study sex differences in psychiatric comorbidities and the moderating effect of sex on the risk ratios. It is well documented that more men present psychosis (Maric et al., 2003) and substance abuse disorder is not gender-specific (Brady & Randall, 1999). Depression has emerged as an important area of focus, as epidemiologic data have consistently shown that depression is twice as common in women as in men (Kornstein, 1997). Still, studies report an almost equal gender ratio in the prevalence of bipolar disorder (Diflorio & Jones, 2010). It would be pertinent to see whether these epidemiological patterns follow the same course when comorbid with OCD. It would also be pertinent to investigate comorbidity associated with OCD subtype and age of onset and study how different OCD dimensions present some specific associations with comorbid disorders, which may be indicative of different underlying pathogenic mechanisms as suggested by Torres et al. (2016).

#### 5 | CONCLUSION

In conclusion, we found strong associations between OCD and four comorbidities—major depressive disorder, bipolar disorder, psychosis and substance use disorder. By better understanding these links, clinical applications can be developed, and early intervention can be implemented. Further research, especially longitudinal, is warranted to better understand the reciprocity of the disorders studied.

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#### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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