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Symptom improvement and remission in untreated adults seeking treatment for obsessive-compulsive disorder: A systematic review and meta-analysis

Maral Melkonian [a], Sarah McDonald [a], Amelia Scott [b], Eyal Karin [b], Blake F. Dear [b], Bethany M. Wootton [a,b,*]

[a] Discipline of Clinical Psychology, Graduate School of Health, University of Technology, Sydney, NSW, Australia
[b] Department of Psychology, Faculty of Medicine, Health and Human Sciences, Macquarie University, North Ryde, NSW, Australia

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ABSTRACT

Obsessive-compulsive disorder (OCD) is a common psychiatric condition that results in significant distress and impairment, and high societal costs. OCD is widely considered to be a chronic condition, however, our understanding of the chronicity of the disorder, and the incidence of spontaneous remission, has largely relied on longitudinal studies of individuals who have received treatment. The aim of the current study is to examine symptom improvement and rate of spontaneous remission in individuals with OCD who were assigned to a no-treatment control group within a randomized controlled trial using a meta-analytic approach. Twelve studies (n = 282; mean age = 35.52; 60.03 % female) were included in the meta-analysis. The pooled within-group effect size was negligible (g = −0.14; 95 % CI [−0.25, −0.04]) and only 4 % of participants demonstrated spontaneous remission across an average of 10.92 weeks (event rate = 0.04; [95 % CI: 0.01, 0.11]). Sample size and duration of OCD symptoms significantly moderated the effect size for symptom change. No moderators were found for symptom remission. The findings add to the small body of literature demonstrating that OCD has a chronic and unremitting course without treatment.

1. Introduction

Obsessive-compulsive disorder (OCD) is characterized by the experience of recurrent and intrusive obsessive thoughts, ideas, images, and urges, and repetitive and time-consuming compulsive behaviors (American Psychiatric Association, 2013). It is a common psychiatric disorder, with a lifetime prevalence rate of approximately 2–3 % (Australian Bureau of Statistics, 2007; Kessler et al., 2012). The disorder results in significant distress and impairment across various domains of functioning (Olatunji et al., 2007), as well as considerable societal burden due to reduced number of workdays, early retirement, and hospitalization (Andlin-Sobocki and Wittchen, 2005; Koran, 2000).

Obsessive-compulsive disorder is widely recognized to be a chronic condition (Bloch et al., 2013; Visser et al., 2014). Many individuals with OCD develop their symptoms in childhood and adolescence (Dell'Osso et al., 2016) and it is not uncommon for individuals to live with their symptoms for years or decades before seeking treatment, with duration of untreated OCD ranging between 3 and 17 years (García-Soriano et al., 2014; Perris et al., 2021). Although pediatric OCD is generally considered to have a more episodic course and higher rates of symptom remission than OCD in adults (Geller et al., 2021), to date, findings of previous studies that have examined the course of OCD in adults are mixed and have significant methodological limitations. Additionally, to date no studies have explicitly examined symptom improvement and remission in untreated OCD.

In an early study, which was conducted prior to the widespread use of effective treatments, such as CBT and pharmacotherapy, Skoog and Skoog (1999) followed 144 inpatients with OCD between 1954 and 1993 to examine the course of the disorder. They found that approximately 20 % of individuals achieved long-term symptom remission at 40-year follow-up; as defined by the absence of clinical and subclinical OCD symptoms for at least 5 years, while the remainder continued to experience clinical and subclinical symptoms. Although this study demonstrates that OCD likely follows a chronic course, many of the participants

* Corresponding author at: Discipline of Psychology, Graduate School of Health, University of Technology Sydney, PO Box 123, Broadway, Ultimo, NSW 2007, Australia.
E-mail address: bethany.wootton@uts.edu.au (B.M. Wootton).

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received some kind of treatment during the period of investigation. Additionally, the definition of OCD that was utilized throughout the study does not correspond to contemporary conceptualizations of the disorder. Thus, it is unclear if the remission status could be a result of the treatment individuals received or the way in which OCD was conceptualized.

Fineberg et al. (2013a, 2013b) conducted a naturalistic outcome study which followed 591 individuals in the general population between 1978 and 2008, and found that approximately 60 % of those with OCD met symptom remission at 30-year follow-up; as defined by the absence of clinically-relevant OCD symptoms for at least 3 years without later relapse. The higher rate of symptom remission demonstrated in this study compared with Skoog and Skoog (1999) may have been a result of utilizing a sample from the general population, in whom symptom severity is typically lower compared to those who are seeking treatment (Jónsson et al., 2011; Matthews et al., 2017). A further and significant limitation of this study is that only 30 out of the 591 participants (approximately 5 %) actually originally met diagnostic criteria for OCD, and of those, 40 % received treatment throughout the follow-up period (Fineberg et al., 2013a, 2013b). Additionally, the participants in this study had several psychiatric diagnoses, and it is unknown whether OCD was the primary condition.

Finally, in another naturalistic study, 117 outpatients with a diagnosis of OCD were generally found to retain their symptoms across a 2-year follow-up period (Mataix-Cols et al., 2002). The remission rate was examined in a subset of the total participants ($n = 66$) and a remission rate of 12 % was found; as defined by the absence of obsessions and compulsions over eight or more weeks (Eisen et al., 1999). While significant qualitative changes were observed within some symptom dimensions at 6-month follow-up (i.e., focus of contamination concerns shifted), no significant changes were observed for the remainder of the follow-up period, and qualitative changes between symptom dimensions were small and rarely observed (Mataix-Cols et al., 2002). This suggests that OCD symptoms appear to remain fairly stable across time, with some symptoms waxing and waning within OCD dimensions. However, consistent with the previous prospective studies, approximately 68 % and 18 % of the participants in this study received an adequate trial of pharmacological treatment and ERP, respectively.

In summary, due to several methodological limitations important questions remain about the natural course of OCD symptoms and whether spontaneous remission occurs. These limitations include that first, not all participants in these studies were formally diagnosed with OCD, and of those who were, many had been diagnosed using different diagnostic criteria. Second, the operational definitions of remission varied between studies. Third, standardized rating scales of symptom improvement and remission were not consistently used across the studies. Finally, and most importantly, these prospective studies included individuals who received some form of treatment during the period of analysis which subsequently limits our ability to understand the course and rates of spontaneous remission in untreated individuals.

In a recent systematic review and meta-analysis, Ferentinos et al. (2020) pooled OCD prevalence rates from epidemiological studies and found the cross-sectional (1 year) and lifetime prevalence rates of OCD in the general population was 1.6 % and 2.5 %, respectively. Although the cross-sectional rate was approximately two-thirds of the lifetime prevalence rate, suggesting some degree of remission in individuals with OCD over the long-term, the findings demonstrate that OCD symptoms remain largely chronic in nature. While these findings are consistent with the abovementioned naturalistic studies (Eisen et al., 1999; Skoog and Skoog, 1999), they were based on a total of three studies, and included individuals who had received treatment.

It is common practice in early-stage clinical trials (e.g., Phase I and II clinical trials) to compare an active treatment with a waitlist control group (Mohr et al., 2009). The goal of this approach is to control for time and other trial related procedures (e.g., symptom measurement) and examine whether symptom improvements are greater in active treatment arm(s) compared to the control arm. However, these designs also provide an opportunity to examine symptom course and spontaneous remission in an untreated group of individuals with a mental health diagnosis (Whiteford et al., 2013). Symptom improvement, as well as remission, have been observed in individuals with a variety of mental health conditions allocated to no-treatment or waitlist control groups (Furukawa et al., 2014). For instance, a systematic review and meta-analysis of 19 studies which examined spontaneous remission in untreated major depression found that approximately 20 % of individuals achieved symptom remission at 20-week follow-up (Posternak and Miller, 2001). In a similar systematic review and meta-analysis of 30 studies which examined spontaneous remission in untreated social anxiety disorder, approximately 7 % of individuals achieved symptom remission at 26-week follow-up (Steinert et al., 2017).

To date, no studies have examined symptom improvement and rate of remission in individuals with a diagnosis of OCD who do not receive treatment. To address this important gap in the literature, the aim of the current study was to examine the short-term (i.e., <6 months) symptom improvement and rate of remission of treatment-seeking individuals with OCD who were assigned to waitlist or no-treatment control groups within randomized controlled trials (RCTs), using a meta-analytic approach. The current study examined the following research questions: 1) What is the magnitude of symptom change in individuals with untreated OCD? 2) What proportion of individuals with untreated OCD achieve remission? 3) What clinical and methodological factors moderate symptom improvement and remission in untreated OCD? The results of this study will further our understanding of the course of OCD symptoms and the likelihood of symptom remission in this population.

2. Method

2.1. Registration

The current systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Page et al., 2021) statement. The protocol was registered with PROSPERO, the international prospective register of systematic reviews, on 22 January 2021 (CRD42021231642).

2.2. Search procedure

Electronic databases of PsycINFO, Medline, Embase, Cochrane Library, Scopus, and CINAHL were systematically searched to identify relevant articles from their inception years to 17 November 2021. The search terms used in the electronic database search included terminology related to OCD ('obsessive compulsive disorder' OR 'OCD'), treatment ('psychotherapy' OR 'treatment' OR 'therap*' OR 'counselling' OR 'exposure*' OR 'ERP' OR 'cognitive* therap*' OR 'CBT' OR 'behavi* therapy' OR 'serotonin' OR 'SSRI', OR 'pharmac*') and randomized controlled trial methodology ('random*' OR 'control* trial' OR 'RCT' OR 'waitlist'). The search terms utilized Boolean operators of 'AND' and were searched as keywords, title, abstract, and medical subject headings. No limitations were placed on the search results. The references of retrieved studies, as well as references of previously completed systematic reviews and meta-analyses on the treatment of OCD (Eddy et al., 2004; Olatunji et al., 2013; Öst et al., 2015; Rosa-Alcázar et al., 2008; Wootton, 2016), were screened against the database search to retrieve any additional studies that may fulfill eligibility criteria.

2.3. Eligibility criteria

To be included in the meta-analysis, individual studies were required to:

1. Include participants with a diagnosis of OCD, diagnosed using a structured diagnostic interview based on current or previous

diagnostic criteria, i.e., any version of the Diagnostic and Statistical Manual of Mental Disorders or International Classification of Disease.
2. Be a randomized controlled trial that included an untreated control group, i.e., no-treatment control or waitlist control groups. No-treatment control groups are control conditions that are not exposed to any treatments and have no expectation to receive treatment after the study has been completed, whereas waitlist control groups are provided the same treatment as the active treatment arm; however, only after the active treatment arm has completed the experimental treatment (Mohr et al., 2009). Therefore, studies which included participants who were receiving treatment for OCD outside of the study or who were not on a stable dose of pharmacological treatment were excluded.
3. Include adult participants aged 18 and over.
4. Utilize either the self-report or clinician-administered Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989) as an outcome measure with complete outcome data available. The Y-BOCS was selected as it is considered the gold-standard outcome measure for OCD, and as it is widely used in OCD research, focusing on the Y-BOCS would reduce the heterogeneity in the results. The Y-BOCS is comprised of two subscales with five items each that measure the severity of obsessions and compulsions. Total scores range from 0 to 40, and a cut-off score of 16 is considered to be clinically relevant (Baer et al., 1993; Steketee et al., 1996). The clinician-administered and self-report Y-BOCS were used as there is a moderate to high correlation on the responses between the two versions (Federici et al., 2010; Steketee et al., 1996), and they both demonstrate good internal consistency and good divergent validity (Anholt et al., 2010; Ólafsson et al., 2010).
5. Focus on the treatment of OCD symptoms as primary in the active treatment arm. Therefore, studies with an alternative primary outcome, i.e., depression and anxiety, were not included.
6. Randomize participants to active treatments and control groups at baseline. Randomized controlled trials which did not specify randomly allocating participants to active treatment and control groups were excluded.
7. Consist of original data, published in English in a peer-reviewed journal.

2.4. Study selection

Following the systematic search, duplicate titles across the databases were identified and removed by the first author. Titles and abstracts of all identified records were reviewed according to the eligibility criteria by the first author (MM), and 10 % of randomly selected records were double-screened by the second author (SM) to ensure agreement and consistency. Following the title and abstract review, 100 % of full-text articles were reviewed by the first author, and 10 % of randomly selected records were double-screened by a second author to determine final eligibility. Any disagreements at the full-text stage were resolved via consensus in conjunction with a third author.

2.5. Data extraction

Data were extracted and entered into a pre-defined and pre-piloted Microsoft Excel spreadsheet. Data were extracted by the first author and the accuracy of all data was checked by a second author. The data extraction spreadsheet included the following extraction fields where available: 1) trial characteristics (year of publication, authors, number of treatment arms, country where trial was conducted); 2) sample characteristics (mean age, proportion of females, baseline duration of disorder, baseline severity of disorder, presence of comorbidity, type of comorbidity, specific comorbidity, rate of drop-out); 3) active treatment details (treatment class, type of treatment, treatment duration, number of treatment visits); 4) control condition details (type of control, duration of control treatment in weeks); 5) outcome assessment details (type of administration, time-points of administration, baseline mean and standard deviation, post-control mean and standard deviation, author definition of remission, number of responders, total number in sample, proportion who still met criteria for OCD). The most conservative outcomes from each study were extracted, that is, intention-to-treat data were used over completer data, where available.

2.6. Risk of bias

Risk of bias (RoB) within the included studies was assessed using Version 2 of the Cochrane Risk of Bias (Sterne et al., 2019) tool. Five domains of bias which have typically been found in the results of RCTs were rated. These correspond to bias due to: 1) the randomization process, 2) deviation from intended interventions, 3) missing outcome data, 4) measurement of outcome, and 5) selective outcome reporting. Based on the information available in each RCT, RoB judgements for each domain were made according to one of three ratings, that is, low risk, high risk, and some concerns. Risk of bias ratings were completed by the first author and second author.

2.7. Data analysis

Effect size data were analyzed using Comprehensive Meta-Analysis Version 3 (Borenstein et al., 2013). Symptom change was calculated on the Y-BOCS (Goodman et al., 1989). Within-group effect sizes were computed to determine the magnitude of symptom improvement in the untreated control group using Cohen's d formula: $\frac{\overline{X}_1-\overline{X}_2}{SD_{diff}}$, where $\overline{X}_1$ is the mean at the start of the control period, $\overline{X}_2$ is the mean at the end of the control period, and SD_{diff} is the standard deviation (SD) of the difference. The SD_{diff} was computed using the following formula: $\frac{\sqrt{SD_1^2+SD_2^2-2\times r\times SD_1\times SD_2}}{\sqrt{2\ (1-r)}}$ where SD_1 is the SD at the start of the control period, SD_2 is the SD at the end of the control period, and r is the correlation between the pair of scores (Borenstein, 2009). As correlations between the pairs of scores were unavailable, a conservative estimate of $r = 0.70$ was used, consistent with previous meta-analyses (Glombiewski et al., 2010; Winkler et al., 2013; Wootton, 2016). To generate an unbiased estimate of the standardized mean difference, Cohen's d was converted to Hedges' g by multiplying it by correction factor J: $1-\frac{3}{4\ df-1}$ (Borenstein, 2009). Summary measures were reported with 95 % confidence intervals. Hedges' g was interpreted using Cohen's d conventions of small (0.2), medium (0.5), and large (0.8) effect sizes (Cohen, 1992). The pooled remission rate was calculated by examining the event rate across studies and was reported with 95 % confidence intervals. All analyses were conducted using random effects models as the true effect size/event rate varies across studies due to differences within participants, interventions, and methodology of the RCTs.

Homogeneity of effect sizes and event rates were assessed using the I^2 statistic (Higgins and Thompson, 2002) which describes the percentage of variance across studies that is due to heterogeneity rather than chance. An I^2 value of 25 % is typically considered low heterogeneity across studies, 50 % as moderate, and 75 % as high (Higgins et al., 2003). Publication bias was assessed through Duval and Tweedie's Trim and Fill method (Duval and Tweedie, 2000) which omits the most extreme small positive studies from the analysis and replaces a mirror image of the studies to produce an unbiased estimate of the effect size (Borenstein, 2009).

Subgroup analyses were conducted for symptom change and remission rate to determine the moderating effects of categorical moderators. This includes type of control arm (waitlist control vs. no-treatment control), method of outcome assessment (self-report vs. clinician-administered), severity of symptoms based on Y-BOCS severity categories, blinding of outcome assessor (yes vs. no), and RoB (high risk vs. low risk vs. some concerns). Meta-regression analyses were conducted to

determine the moderating effects of continuous moderators. This includes, sample size, baseline severity, participant age, proportion of females in sample, duration of OCD symptoms in years, year of study, percentage of participants with comorbid depressive disorders, control group length (in weeks), and rate of drop-out in the untreated control group.

3. Results

3.1. Study selection

Fig. 1 outlines the study selection process according to the PRISMA guidelines (Page et al., 2021). The database search and hand-search yielded 10,861 articles. Prior to the screening process, 5632 duplicate studies were removed. The titles and abstracts of 5229 studies were reviewed and 5163 were excluded, resulting in 66 studies. The full-text

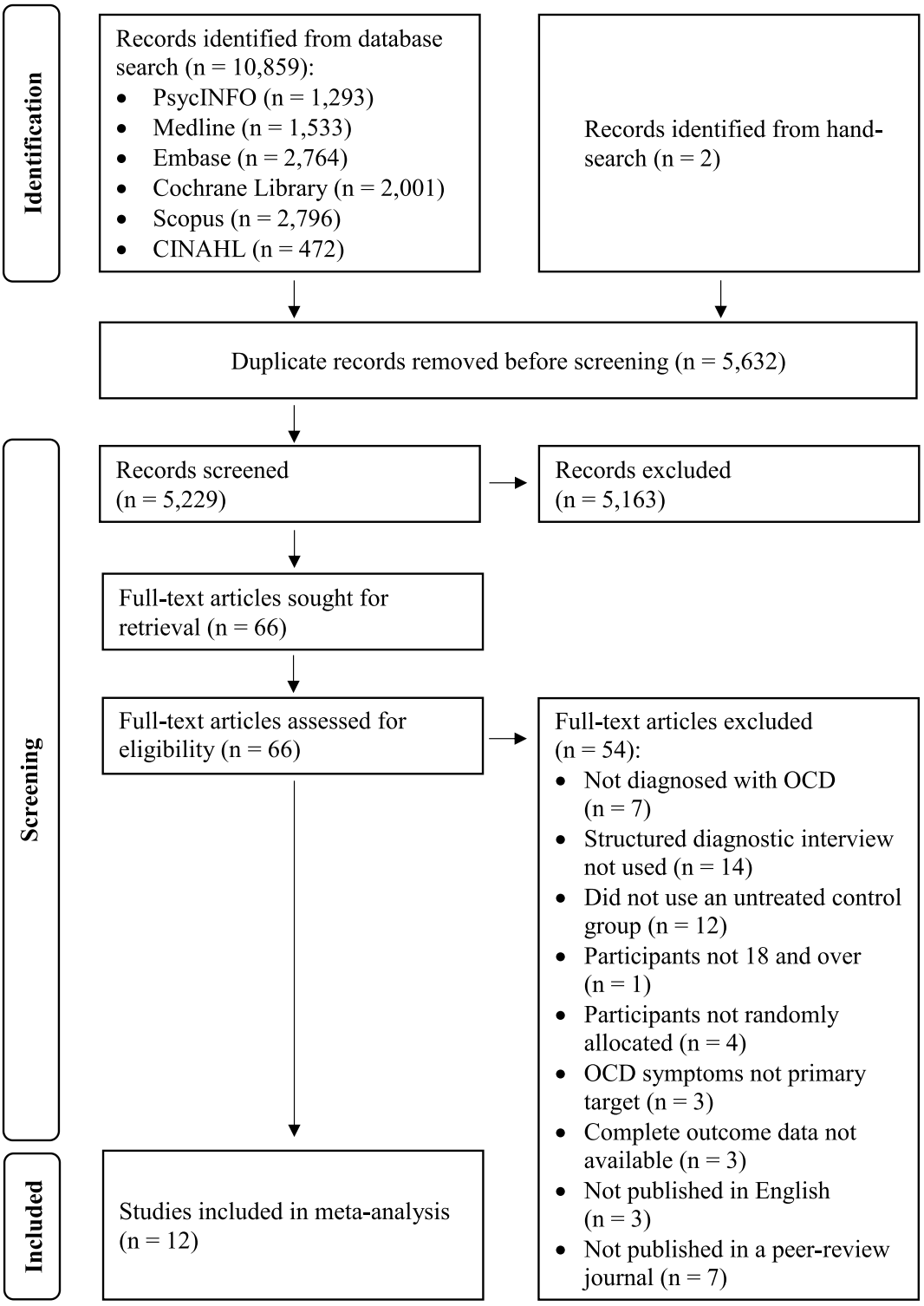

Fig. 1. PRISMA Flowchart of the Study Selection Process.

of these 66 studies were reviewed against the eligibility criteria and 54 studies were excluded, resulting in 12 studies being included in the meta-analysis. The inter-rater agreement was 100 % at the title and abstract screening stage as well as the full-text screening stage.

3.2. Study characteristics

Table 1 provides an overview of the study characteristics. A total of 351 individuals were randomized to the untreated control groups at baseline; however, 282 individuals across 12 studies were included in the analysis as 69 individuals dropped out. The mean age of the included participants ranged between 23.30 and 46.06 years, and the percentage of female participants ranged from 26.67 % to 73.80 %. Three of the 12 studies (25 %) were conducted in Brazil, three (25 %) in Canada, two (17 %) in Australia, two (17 %) in Norway, one (8 %) in Spain, and one (8 %) in Korea. The length of the untreated control groups ranged from 5 weeks to 4 months, with a mean length of 10.92 weeks.

Five of the 12 studies provided information on the duration of OCD symptoms, which ranged from 10.03 to 27.50 years. Nine of the 12 studies provided information on the rate of drop-out in the untreated control groups, which ranged from 0 % to 44 % (M = 16.70 %). The mean Y-BOCS score at baseline ranged between 17.54 and 26.88, indicating moderate to severe symptoms. Five of the 12 studies provided information on the remission status of participants, which was operationalized in several ways across the studies. Three studies employed the Jacobson and Truax (1991) criteria for reliable change index, as defined by a 10-point reduction on the Y-BOCS at the end of the control period, combined with criteria for clinically significant change, as defined by a Y-BOCS score ≤ 14 (Anderson and Rees, 2007; Vogel et al., 2014) or ≤ 12 (Wootton et al., 2013) at the end of the control period. One study employed a reduction of ≥35 % on the Y-BOCS at the end of the control period (Cordioli et al., 2003) while another study combined this with criteria for clinically significant change, as defined by a Y-BOCS score of ≤12 at the end of the control period (Launes et al., 2019).

3.3. Risk of bias

Table 1 includes the RoB for each study and Fig. 2 outlines the outcomes from the RoB assessment. Of the 12 included studies, 0 studies (0 %) were deemed to have a low RoB, 3 studies (25 %) were deemed to have some concerns about bias, and 9 studies (75 %) were deemed to have a high RoB. In 42 % of the studies, some concerns emerged about the randomization process, often due to the absence of detail provided in the published studies regarding allocation concealment practices. In 100 % of the studies, some concerns emerged about the selection of reported results, often due to the RCTs being unregistered or if registered, failing to include details of the planned analyses.

Table 1
Characteristics of Included Studies.

Study	Country	Type of control group	Control group duration (weeks)	n	Mean age (years)	% Female	Duration of OCD symptoms (years)	Percent with comorbid depressive disorder	Mean baseline Y-BOCS score	Rate of drop-out (%)	Remitted (%)	Risk of bias
Anderson and Rees (2007)	Australia	WC	10	14	34.40	64.30	13.60	–	24.10 [b,e]	17.65	0.00 [f]	High
Braga et al. (2016)	Brazil	WC	12	42	41.40	73.80	27.50	59.50	26.00 [e]	44.00		High
Cordioli et al. (2003)	Brazil	WC	12	24	–	–	–	–	24.70 [b,d]	4.20	4.20 [g]	Some concerns
Gomes et al. (2016)	Brazil	WC	12	46	37.10	67.40	25.20	26.70	26.40 [b,e]	15.20		High
Jaurrieta et al. (2008)	Spain	WC	16 [a]	19	23.30	–	–	–	24.80 [b,e]	0.00		Some concerns
Key et al. (2017)	Canada	WC	8	18	46.06	44.40	–	–	25.35 [c,e]	16.70		High
Launes et al. (2019)	Norway	WC	12	16	30.06	69.00	16.90	–	26.88 [b,d]	6.25	0.00 [h]	Some concerns
McLean et al. (2001)	Canada	WC	12	33	–	–	–	–	23.24 [b,e]	–		High
Park et al. (2006)	Korea	NTC	5	15	28.07	26.67	10.03	6.67	18.67	–		High
Vogel et al. (2014)	Norway	WC	12	1s0	40.70	70.00	–	40.00	23.40 [b,d]	20.00	0.00 [f]	High
Whittal et al. (2010)	Canada	WC	12	28	–	–	–	–	17.54 [b,d]	–		High
Wootton et al. (2013)	Australia	WC	8	17	38.58	64.70	–	47.10	21.06 [b,e]	26.32	0.00 [i]	High

Note. n = number of participants in the control group used to obtain outcome data; WC = waitlist control; NTC = no-treatment control; – = not reported.
[a] The duration of the waitlist control group of 4 months was converted to weeks for the analyses.
[b] Clinician administered Y-BOCS used as outcome method.
[c] Self-report Y-BOCS used as outcome method.
[d] Blind assessors used.
[e] Blind assessors not used.
[f] Y-BOCS score of ≤14 at the end of the control period and a 10-point reduction on the Y-BOCS from the start of the control period to the end of the control period.
[g] Reduction of ≥35 % on the Y-BOCS at the end of the control period.
[h] Reduction of ≥35 % on the Y-BOCS at the end of the control period and a Y-BOCS score of ≤12 at the end of the control period.
[i] Y-BOCS score of ≤12 at the end of the control period and a 10-point reduction on the Y-BOCS from the start of the control period to the end of the control period.

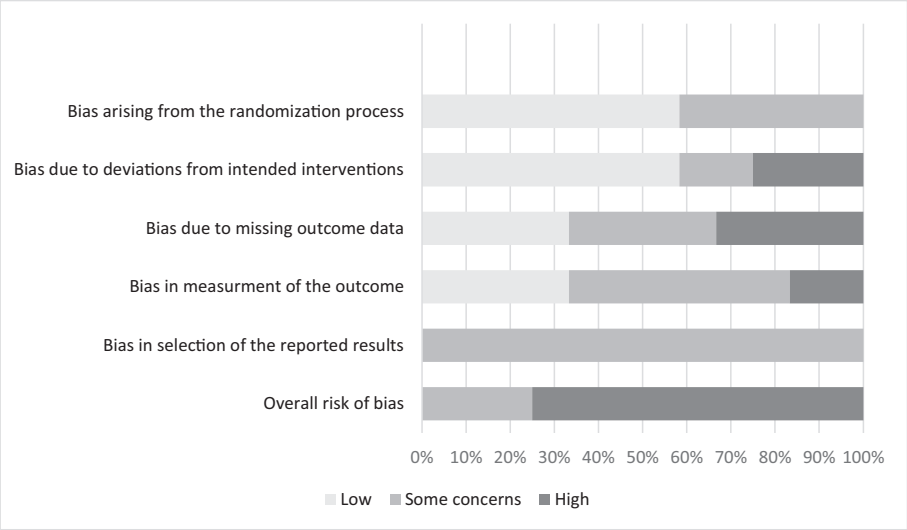

Fig. 2. Risk of Bias Bar Chart.

3.4. Symptom change

Table 2 outlines the within-group effect sizes for each of the included studies. The pooled within-group mean effect size was negligible across all untreated control groups from the start of the control period to the end of the control period ($k = 12$; $g = -0.14$; 95 % CI [−0.25, −0.04]). Heterogeneity was low ($I^2 = 21.18$). Visual inspection of the funnel plot revealed asymmetry, with a higher number of small studies falling to the right of the mean effect than to the left (see Fig. 3). The statistical examination of the funnel plot using the Trim and Fill method indicated the presence of publication bias, with 5 studies missing, resulting in a small effect size (adjusted $g = -0.23$; 95 % CI [−0.34, −0.12]).

Table 2
Within-Group Effect Sizes from the Start of the Control Period to the End of the Control Period.

Study	Type of control group	n	Start of control period to end of control period		Weight of included study
			g	95 % CI	
Anderson and Rees (2007)	WC	14	−0.09	[−0.48, 0.29]	5.95
Braga et al. (2016)	WC	42	−0.42	[−0.66, −0.18]	12.29
Cordioli et al. (2003)	WC	24	−0.27	[−0.58, 0.03]	8.61
Gomes et al. (2016)	WC	46	−0.30	[−0.52, −0.07]	13.42
Jaurrieta et al. (2008)	WC	19	−0.02	[−0.36, 0.31]	7.48
Key et al. (2017)	WC	18	0.19	[−0.16, 0.53]	7.07
Launes et al. (2019)	WC	16	0.10	[−0.26, 0.46]	6.56
McLean et al. (2001)	WC	33	−0.15	[−0.40, 0.11]	11.01
Park et al. (2006)	NTC	15	−0.06	[−0.43, 0.31]	6.27
Vogel et al. (2014)	WC	10	0.00	[−0.44, 0.44]	4.69
Whittal et al. (2010)	WC	28	−0.16	[−0.45, 0.12]	9.80
Wootton et al. (2013)	WC	17	−0.11	[−0.46, 0.25]	6.85
Overall			−0.14	[−0.25, −0.04]	

Note. WC = waitlist control; NTC = no-treatment control; n = number of participants in the control group used to obtain outcome data; CI = confidence interval.

3.5. Remission rate

Table 3 outlines the event rate (remission rate) for each of the five studies that provided information on remission status in the untreated control groups. The mean event rate was 0.04 [95 % CI: 0.01, 0.11] indicating that 4 % of individuals remitted from OCD from the start of the control period to the end of the control period. Heterogeneity was not observed ($I^2 = 0.00$). Visual inspection of the funnel plot revealed symmetry (see Fig. 4). The Trim and Fill method indicated the absence of publication bias and resulted in an unchanged event rate (adjusted event rate = 0.04; 95 % CI [0.01, 0.11]).

3.6. Moderators

3.6.1. Symptom change

Table 4 outlines the subgroup analyses of the overall effect size from the start of the control period to the end of the control period. Sub-group analyses indicated that type of control arm (waitlist control vs. no-treatment control), method of outcome (self-report vs. clinician-administered), severity of symptoms based on Y-BOCS severity categories, blinding of outcome assessor (yes vs. no), and RoB (some concerns vs. high risk) did not significantly influence the effect size. Table 5 outlines the meta-regression analyses of the overall effect size from the start of the control period to the end of the control period. Sample size was a significant moderator ($k = 12$; $Q = 8.86$; $df = 1$; $p = .00$), with increasing sample size associated with decreasing effect sizes ($z = -2.98$; 95 % CI [−0.02, −0.00]). Duration of OCD symptoms (in years) was also a significant moderator ($k = 5$; $Q = 5.23$; $df = 1$; $p = .02$), with increasing symptom duration associated with smaller effect sizes ($z = -2.29$; 95 % CI [−0.04, −0.00]). Baseline severity, participant age, proportion of females, year of study, percentage of participants with comorbid depressive disorders, control group length (in weeks; see Supplement 1), and rate of drop-out in the untreated control group did not significantly influence the effect size.

3.6.2. Remission rate

Table 6 outlines the subgroup analyses of the overall rate of remission from the start of the control period to the end of the control period. Subgroup analyses indicated that blinding of outcome assessor (yes vs. no), severity of symptoms based on Y-BOCS severity categories, and RoB

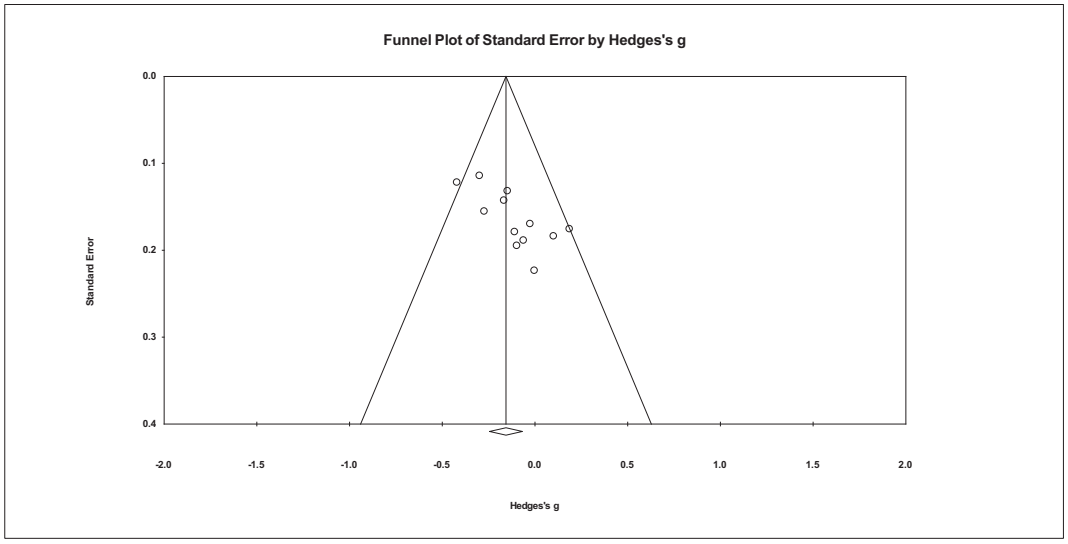

Fig. 3. Funnel Plot of Meta-Analysis.

Table 3
Rates of Remission from the Start of the Control Period to the End of the Control Period.

Study	Type of control group	Remission criteria	n	Start of control period to end of control period		Weight of included study
				Event rate	95 % CI	
Anderson and Rees (2007)	WC	Y-BOCS ≤14 + 10-point reduction	14	0.03	[0.00, 0.37]	16.72
Cordioli et al. (2003)	WC	Y-BOCS ≤35 %	24	0.04	[0.01, 0.24]	33.16
Launes et al. (2019)	WC	Y-BOCS ≤12 + ≤35 %	16	0.03	[0.00, 0.34]	16.79
Vogel et al. (2014)	WC	Y-BOCS ≤14 + 10-point reduction	10	0.05	[0.00, 0.45]	16.51
Wootton et al. (2013)	WC	Y-BOCS ≤12 + 10-point reduction	17	0.03	[0.00, 0.32]	16.82
Overall				0.04	[0.01, 0.11]	

Note. WC = waitlist control; n = number of participants in the control group used to obtain outcome data.

(some concerns vs. high risk) did not significantly influence the remission rate. Table 7 outlines the meta-regression analyses of the rate of remission from the start of the control period to the end of the control period. Sample size, baseline severity, participant age, proportion of females, year of study, control group length (in weeks; see Supplement 2), and rate of drop-out in the untreated control group did not significantly influence the remission rate.

4. Discussion

The aim of this study was to examine the incidence of spontaneous remission in individuals with OCD using a meta-analytic approach. Overall, the results indicated that OCD symptoms do not change over time without treatment, with negligible to small within-group effect sizes observed when all control groups are pooled together. While this is the first study to synthesize symptom improvement in patients with OCD who are in a no-treatment or waitlist control arm, these results are broadly consistent with Skoog and Skoog (1999) and Eisen et al. (1999) who demonstrated that most individuals with OCD continue to experience clinical and subclinical symptoms. However, these previous naturalistic studies included both treatment-seeking/receiving individuals, and non-treatment seeking/receiving individuals, making estimates of remission difficult to interpret. Thus, by including only those who were seeking treatment but randomized to control conditions, our findings are novel and provide valuable information about spontaneous remission among people seeking treatment.

The results of the current study also indicated that OCD rarely remits spontaneously, with an overall remission rate of 4 % when untreated control groups are pooled together. While these results should be considered preliminary, as they are based on only five studies, this remission rate is at least a third of the estimate found in previous naturalistic studies that included both treatment seeking and non-treatment seeking individuals (Eisen et al., 1999; Fineberg et al., 2013a, 2013b; Skoog and Skoog, 1999). It is important to point out however that the previous naturalistic studies were longitudinal in nature and participants were followed up for a much longer time period than the current study (the average length of the untreated control groups in this study was 10.92 weeks). Thus, higher remission rates may have been observed if participants were followed over a longer period. Nevertheless, compared to the previous naturalistic studies, the shorter follow-up period in the current study would have allowed more rapid fluctuations in symptoms to have been detected. Overall, the remission rate in this study is comparable to the 7 % found in untreated social anxiety disorder (Steinert et al., 2017) and lower than the 20 % found in untreated major depression (Posternak and Miller, 2001). This indicates that remission rates vary across disorders and OCD has a lower likelihood of natural remission than other mental health conditions, which supports the current conceptualization of the disorder as chronic (Visser et al., 2014).

Although a low level of heterogeneity was demonstrated for symptom change, indicating findings are generally robust across studies, two variables emerged as moderators. Firstly, studies with smaller sample sizes were associated with larger effect sizes, which is commonly observed in meta-analytic research (Schäfer and Schwarz, 2019). Secondly, studies with longer mean duration of OCD symptoms were associated with smaller effect sizes. This is consistent with a previous naturalistic study which found that a longer duration of OCD increased the risk of the disorder remaining chronic (van Oudheusden et al.,

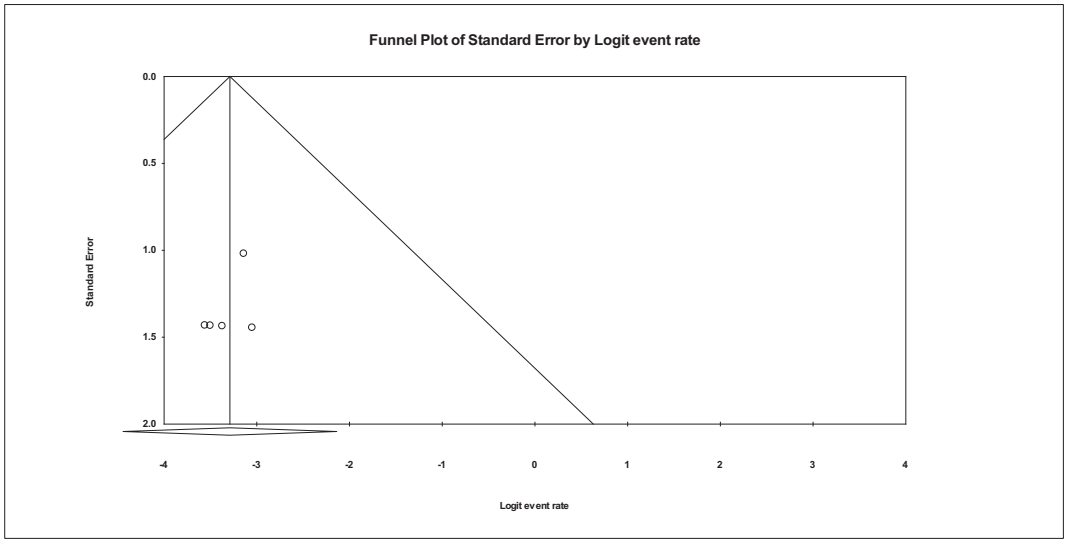

Fig. 4. Funnel Plot of Remission Rate.

Table 4
Subgroup Analyses of the Overall Effect Size from the Start of the Control Period to the End of the Control Period.

Variable	Start of control period to end of control period				
	k	*g*	95 % CI	*Q-value*	*p-Value*
Type of control arm				0.20	0.65
Waitlist control	11	−0.15	[−0.26, −0.04]		
No-treatment control	1	−0.06	[−0.43, 0.31]		
Method of outcome assessment				3.34	0.07
Self-report	1	0.19	[−0.16, 0.53]		
Clinician-administered	9	−0.15	[−0.25, −0.04]		
Blinding of outcome assessor				0.14	0.71
Yes	4	−0.12	[−0.28, 0.05]		
No	7	−0.16	[−0.31, −0.01]		
Risk of bias				0.42	0.52
Some concerns	3	−0.08	[−0.30, 0.14]		
High risk	9	−0.16	[−0.28, −0.04]		

Note. k = number of studies; CI = confidence interval.

Table 5
Meta-Regression Analyses of the Overall Effect Size from the Start of the Control Period to the End of the Control period.

Variable	Start of control period to end of control period					
	k	*β*	*Q-value*	95 % CI	*z-value*	*p-value*
Sample size	12	−0.01	8.86	[−0.02, −0.00]	−2.98	0.00
Baseline severity	12	−0.01	0.15	[−0.04, 0.03]	−0.39	0.70
Participant age	9	−0.00	0.19	[−0.03, 0.02]	−0.43	0.67
Proportion of females	8	−0.01	1.87	[−0.02, 0.00]	−1.37	0.17
Duration of OCD symptoms in years	5	−0.02	5.23	[−0.04, −0.00]	−2.29	0.02
Year of study	12	0.00	0.05	[−0.02, 0.02]	0.22	0.83
Percentage with comorbid depressive disorders	5	−0.00	1.17	[−0.01, 0.00]	−1.08	0.28
Control group length	12	−0.02	0.77	[−0.06, 0.02]	−0.88	0.38
Rate of drop-out in the untreated control group	9	−0.01	2.37	[−0.02, 0.00]	−1.54	0.12

Note. k = number of studies; β = regression co-efficient; CI = confidence interval; Comorbid depressive disorders = major depressive disorder and dysthymia.

2018); highlighting the potential importance of early intervention. No other clinical or methodological factors moderated symptom change or remission.

Several limitations of this study should be acknowledged. First, all the RCTs required individuals to be on a stable dose of pharmacological treatment, indicating some patients were not completely untreated. Nevertheless, participants still fulfilled diagnostic criteria for OCD to be included in the study, and with the exception of two studies (Launes et al., 2019; Wootton et al., 2013), where participants were on a stable dose of pharmacotherapy for 4 weeks, participants had surpassed the period required for clinical improvements to be seen from a stable and adequate course of pharmacological treatment (i.e., ≥ 12 weeks; Stein et al., 2019). Sensitivity analyses were conducted and the results were not markedly different when these two studies were omitted from the analyses (i.e., pooled within-group effect size was $g = -0.17$; 95 % CI [−0.28, −0.06]) and the mean pooled event rate was 0.04 [95 % CI: 0.01, 0.15]), thus these two studies were retained in the primary analysis. Additionally, some participants may have received treatment outside of the study and not informed study investigators. Only two of the included studies reported excluding participants from their analysis who engaged in treatment outside of the study (Braga et al., 2016; Wootton et al., 2013). Second, remission criteria varied across the included studies, raising the possibility that the remission rate found in this study may have been overestimated. Third, the RCTs in this study were of limited quality as defined by the RoB, precluding the ability to examine study quality as a potential moderator of symptom improvement and remission. As previous research has found that lower quality studies produce larger effect sizes (Cuijpers et al., 2013), the present findings may have been overestimated or underestimated. Fourth, there were a limited number of available RCTs, and the sample sizes included in these studies were relatively small. As a result, there was limited variance to investigate key moderator variables, such as control group length. As a result, the moderator analyses need to be interpreted with significant caution and be considered preliminary. Fifth, pediatric OCD studies were not included in the present study, and it is possible that the

Table 6
Subgroup Analyses of the Rate of Remission from the Start of the Control Period to the End of the Control Period.

Variable	Start of control period to end of control period				
	k	Event rate	95 % CI	*Q-value*	*p-value*
Blinding of outcome assessor				0.04	0.84
Yes	3	0.04	[0.01, 0.14]		
No	2	0.03	[0.00, 0.19]		
Risk of bias				0.00	0.95
Some concerns	2	0.04	[0.01, 0.16]		
High risk	3	0.03	[0.01, 0.16]		

Note. k = number of studies; CI = confidence interval.

Table 7
Meta-Regression Analyses of the Rate of Remission from the Start of the Control Period to the End of the Control Period.

Variable	Start of control period to end of control period					
	k	*β*	*Q-value*	95 % CI	*z-value*	*p-value*
Sample size	5	0.01	0.00	[−0.22, 0.23]	0.05	0.96
Baseline severity	5	0.01	0.00	[−0.65, 0.67]	0.04	0.97
Participant age	4	0.03	0.02	[−0.32, 0.37]	0.15	0.88
Proportion of females	4	0.04	0.02	[−0.51, 0.60]	0.16	0.88
Year of study	5	−0.02	0.03	[−0.21, 0.18]	−0.17	0.86
Control group length	5	0.09	0.05	[−0.67, 0.84]	0.23	0.82
Rate of drop-out in the untreated control group	5	−0.01	0.01	[−0.14, 0.13]	−0.12	0.91

Note. k = number of studies; β = regression co-efficient; CI = confidence interval.

inclusion of pediatric literature could change the findings. Finally, the follow-up period was on average 11 weeks and while the findings suggest that remission is uncommon over the short-term, further research is required to understand the rates of remission in the long-term.

In conclusion, the finding of the present study confirms previous reports indicating that OCD is a chronic condition that rarely remits without treatment over the short term. The findings highlight the importance of a timely diagnosis and early intervention for individuals with OCD in order to prevent long-term distress and impairment. The findings from this study can be used as a benchmark for those conducting Phase I and feasibility trials of individuals with OCD in the future and may potentially reduce the need to include untreated control groups in RCTs for OCD.

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Contributors

Blake Dear conceptualized the research idea. Bethany Wootton designed the study and supervised Maral Melkonian while working on the project. Amelia Scott and Eyal Karin contributed to the development of the study protocol. Maral Melkonian conducted the search (and Sarah McDonald acted as the secondary coder). The results were analyzed by Maral Melkonian and Bethany Wootton and assistance was provided by Eyal Karin, who is a statistician. Maral Melkonian and Bethany Wootton wrote the first draft of the manuscript. All authors contributed to and approved the final manuscript.

Declaration of competing interest

All authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2022.08.037.

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