



International Journal of Psychiatry in Clinical Practice

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ijpc20

Effects of exercise on obsessive-compulsive disorder symptoms: a systematic review and meta-analysis

Lindsay Bottoms, Montserrat Prat Pons, Naomi A. Fineberg, Luca Pellegrini, Oliver Fox, David Wellsted, Lynne M. Drummond, Jemma Reid, David S. Baldwin, Ruihua Hou, Samuel Chamberlain, Nick Sireau, Dominique Grohmann & Keith R. Laws

To cite this article: Lindsay Bottoms, Montserrat Prat Pons, Naomi A. Fineberg, Luca Pellegrini, Oliver Fox, David Wellsted, Lynne M. Drummond, Jemma Reid, David S. Baldwin, Ruihua Hou, Samuel Chamberlain, Nick Sireau, Dominique Grohmann & Keith R. Laws (2022): Effects of exercise on obsessive-compulsive disorder symptoms: a systematic review and meta-analysis, International Journal of Psychiatry in Clinical Practice, DOI: 10.1080/13651501.2022.2151474

To link to this article: https://doi.org/10.1080/13651501.2022.2151474

6

© 2022 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.



Published online: 21 Dec 2022.



🖉 Submit your article to this journal 🗷

🔾 View related articles 🗹



View Crossmark data 🗹

ORIGINAL ARTICLE

OPEN ACCESS

Effects of exercise on obsessive-compulsive disorder symptoms: a systematic review and meta-analysis

Lindsay Bottoms^a (**b**), Montserrat Prat Pons^{a,b}, Naomi A. Fineberg^{a,b} (**b**), Luca Pellegrini^{a,b} (**b**), Oliver Fox^{a,c}, David Wellsted^a (**b**), Lynne M. Drummond^{a,d} (**b**), Jemma Reid^{a,e}, David S. Baldwin^{f,g} (**b**), Ruihua Hou^f (**b**), Samuel Chamberlain^f (**b**), Nick Sireau^h, Dominique Grohmann^a (**b**) and Keith R. Laws^a (**b**)

^aSchool of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK; ^bHertfordshire Partnership University NHS Foundation Trust, Hatfield, UK; ^cQueen Square Institute of Neurology, University College London, London, UK; ^dSouth West London and St George's NHS Trust and School of Life and Medical Science, London, UK; ^eCornwall Partnership NHS Foundation Trust, Cornwall, UK; ^fClinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, UK; ^gDepartment of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa; ^hORCHARD, Cambridge, UK

ABSTRACT

Objective: This systematic review and meta-analysis assessed the efficacy of exercise in reducing OCD symptoms.

Methods: We searched PubMed, Cochrane Central Register of Controlled Trials, MEDLINE, Scopus and grey literature until March 2022. The study was preregistered at Prospero (CRD42021283931). We included randomised controlled and pre-post trials assessing physical activity as an intervention for OCD. Risk of bias was assessed using the Cochrane ROBINS-I tool and the RoB2 tool.

Results: The analysis included 6 trials (N = 92); 2 were RCTS and 4 were pre-post design studies. A random-effects meta-analysis of pre-post data identified a large reduction of OCD symptoms following exercise (g = 1.33 [95%Cl 1.06–1.61]; k = 6). Exercise was also associated with significant pre-post reductions in anxiety (g = 0.71 [95%Cl 0.37–1.05; k = 4) and depression (g = 0.57 [95%Cl 0.26–0.89]; k = 2). Risk of bias was moderate-high in uncontrolled trials on the ROBINS-I and RCTs showed 'some concerns' on the RoB2. **Conclusion:** Exercise was associated with a large pre-post reduction of OCD symptoms; however, few trials were of robust quality and all were at risk of bias. Further well-powered and better quality RCTs are required to assess the role of exercise as an intervention for OCD.

KEY POINTS

- Studies exploring exercise as an adjunct therapy for OCD have small participant numbers, therefore a systematic review and meta-analysis is needed to estimate potential efficacy.
- Pre-post analysis shows that exercise was associated with a large reduction of OCD symptoms
- The current systematic review and meta-analysis points to the potential for exercise to be beneficial for the treatment for OCD symptoms. However, more well-powered and better controlled RCTs are required to fully assess the benefit of exercise for the treatment of OCD symptoms.

Introduction

Obsessive-compulsive disorder (OCD) is a common and disabling neuropsychiatric condition which has a substantial effect on the quality of life, well-being and global functioning of affected individuals and their family members (Albert et al., 2017). Obsessivecompulsive disorder is ranked among the top 10 leading causes of global disability (WHO, 1999). It is common with lifetime prevalence being 1.3–2.3% and affects all cultures and ethnicities, follows a chronic course, causes distress and disability, disrupts functioning and places considerable burden on families (Albert et al., 2017; Pallanti et al., 2002; Veale & Roberts, 2014). With a mean age of onset of 20 years, OCD affects the most productive period in an individual's life. The costs and burden accrue with time (NICE, 2005). Disability from OCD is comparable to that of schizophrenia (Bobes et al., 2001) accounting for 2.2% of all years lost to disability, 6 and 18% of the cost of all mental and anxiety disorders, respectively (WHO, 1999; Hollander et al., 2016) and an estimated 7.9 disability adjusted life years lost per 10,000 people (Wittchen et al., 2011). Lost productivity is profound (Hollander et al., 2016) with high rates of long-term sickness absence and unemployment (Veale & Roberts, 2014).

Until recent decades, OCD was deemed untreatable. However, there is now a large evidence base for the use of cognitive behavioural therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) as first-line treatment (Fineberg et al., 2020). Whilst most patients with OCD treated with one or both these therapies will experience an improvement in their symptoms, up to 60% (Pallanti et al., 2002) will continue to have residual symptoms with ongoing disability (Eisen et al., 2013). To address this, there is growing interest in the use of augmentation strategies. Adjunctive use of dopamine-antagonists or other strategies help some initial treatment of non-responders but the effect is typically

CONTACT Lindsay Bottoms 🖾 I.bottoms@herts.ac.uk 🖃 School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK

© 2022 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

ARTICLE HISTORY

Received 5 July 2022 Revised 11 October 2022 Accepted 8 November 2022

KEYWORDS

OCD; obsessive-compulsive disorder; exercise; exercise therapy; physical activity; meta-analysis



small and most fail to respond (Fineberg et al., 2020). This has so far included the addition of alternative medications such as antipsychotics and other anti-depressants, repetitive transcranial magnetic stimulation, neurosurgical techniques including stereotactic ablation surgery and deep-brain stimulation and other types of functional interventions (Varinelli et al., 2022). There is urgent need for an alternative or adjuvant treatment that is effective, low-cost, safe and universally accessible. Exercise is a candidate intervention.

Physical exercise elevates mood, promotes wellbeing, reduces anxiety, improves cognition and is efficacious in certain mental disorders (di Liegro et al., 2019; Kandola et al., 2019; Larun et al., 2006). As response to current treatments for OCD is limited, exercise could be used as a cost effective and widely available low risk alternative or adjunctive treatment. The beneficial effect of exercise in disorders such as depression (NICE, 2009) and anxiety (Ramos-Sanchez et al., 2021) cannot simply be extrapolated to OCD, as this disorder typically responds to only a very limited range of treatments. Moreover, exercise may even have a counter-therapeutic effect by exacerbating particular obsessive-compulsive symptoms such as contamination related fears e.g., through the generation of sweat and bodily contact. There are, however, compelling reasons to support its investigation in OCD.

Exercise is likely beneficial to physical and psychiatric health through multiple mechanisms. The relationship is complex and incompletely understood, but aside from reducing body fat and improving cardiorespiratory fitness, moderate physical activity has systemic anti-inflammatory effects (Gleeson et al., 2011) with the potential to impact neuroinflammation (Małkiewicz et al., 2019). This anti-inflammatory effect appears to be dependent on the exercise intensity with a greater effect occurring at higher exercise intensities (Antunes et al., 2019). Of interest is the emerging evidence of the ability of exercise to attenuate inflammation in the central nervous system (CNS). Although the blood-brain-barrier acts to protect the CNS from the peripheral environment, there is in fact bi-directional communication of the immune system through cytokines, the vagus nerve, the sympathetic and parasympathetic nervous system, and the hypothalamic-pituitaryadrenal axis. Hence, pro-inflammatory cytokines circulating in the periphery can activate microglia (Block et al., 2007; the primary immune cell of the CNS) in the brain, affect behaviour and precipitate symptoms of depression (McCusker & Kelley, 2013). In the same way, it is thought exercise can have an inhibitory effect on microglial activation by increasing anti-inflammatory and downregulating pro-inflammatory factors (Mee-Inta et al., 2019). Different lines of evidence implicate low-grade inflammation (innate or adaptive) in the pathophysiology of OCD (Gerentes et al., 2019). A strong link exists between some infections and subsequent onset of OCD e.g., paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) (Swedo et al., 2014) or paediatric acute-onset neuropsychiatric syndromes (PANS) (Fineberg et al., 2020). Autoantibodies directed at neuronal components of cortico-striatal-thalamo-cortical (CSTC) brain circuits are identified in some children & adults with OCD (Fineberg et al., 2020).

There has been growing interest in research examining the effect of exercise for OCD. A recent review by Freedman and Richter (2021) outlines research in OCD and exercise suggesting a potential benefit of exercise, however they conclude there is a need for further research. A meta-analysis enables us to collect-ively explore in more depth the efficacy of exercise on OCD symptoms using the gold standard methods of the Yale- Brown Obsessive-Compulsive Scale (Y-BOCS) (Goodman et al., 1989), of

value for determining the magnitude of the effect size to enable future interventional research, as the number of published clinical trials remains small (Freedman & Richter, 2021). It also enables us to start to understand the potential mechanisms by including other outcome variables such as inflammation in the analysis.

There is a need to review current evidence and offer guidance for future research. Our aim was therefore to conduct a systematic review and meta-analysis examining the effectiveness of exercise on improving OCD symptom severity as well as associated mental health (including changes in depression and anxiety) and physical health symptoms. In addition, we sought to examine the acceptability and tolerability of exercise in this patient population.

Methods

The systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline (Moher et al., 2009). The protocol was registered at PROSPERO https://www.crd.york.ac. uk/PROSPERO/display_record.php?RecordID=283931 (PROSPERO, 2021) CRD42021283931.

Search strategy

Relevant English-language publications were identified by systematically searching PubMed, Cochrane Central Register of Controlled Trials, Ovid MEDLINE and Scopus. In addition, reference lists of included studies and previous reviews were searched for further research. We sought publications from the earliest date point until March 2022.

The following search terms were used:

Exercise OR physical activity OR sport AND obsessive-compulsive disorder OR OCD OR symptoms of OCD

Two independent reviewers (L.B. and M.P.) completed the initial screening process using predefined inclusion criteria (below) and Rayyan QCRI Software (Ouzzani et al., 2016). Articles were included for further review if they were original studies with primary data, human participants, and related to the topic of interest. Search results were independently reviewed and compared for discrepancies. A third reviewer (K.L.) was involved when any discrepancy between the two reviewers occurred.

Inclusion criteria

Studies were included in this meta-analysis if they met the following criteria: randomised clinical trials or pre-post studies without a control group, where the intervention was physical activity (studies were not limited by the type of physical activity, e.g., studies with yoga were included as yoga is included in the compendium of physical activity (Ainsworth et al., 2011) and improves strength and flexibility); the participants had a formal structured diagnosis of OCD in a clinical setting; the outcome of interest was OCD symptom severity evaluated using the Y-BOCS; included means and standard deviations or sufficient other data used for analyses.

Data extraction and quality assessment

For each eligible study, detailed information was extracted by two of the authors (L.B. and M.P.). Such data included: first author; publication year; total number of participants, number of controls; study design. In addition, the following data were extracted: type of physical activity intervention, total duration, session duration and intensity and frequency; adherence to exercise and adverse events; OCD symptom severity using total Y-BOCS; and any depression or anxiety measure. Other measures including global symptomatology and functional disability; health related quality of life; body mass index; change in inflammatory markers; change in cholesterol levels were planned to be recorded however there was no data reported. We also intended to include cardiorespiratory fitness as a moderator, but insufficient studies provided relevant data.

Risk of bias assessment

The quality of the included articles was assessed independently by two investigators (DG and KL). The Cochrane Risk of Bias 2 tool (Sterne et al., 2019) was used to assess risk of bias in RCTs on the following domains: selection bias, performance bias, detection bias, attrition bias. The ROBINS-I tool (Sterne et al., 2019) for non-RCTs was used to assess risk of bias due to: confounding factors, selection of participants, classification of interventions, deviations from intended intervention, missing data, measurement of outcomes, and selection of the reported results.

Statistical analysis

Random effects meta-analyses were conducted using Comprehensive Meta-Analysis Version 3.0 for Windows (Borenstein et al. 2013). We calculated Hedge's g effect sizes (and 95% confidence intervals) for pre-post as most studies failed to include a control sample. In the latter case, we assumed a correlation of .5 between pre and post conditions (we conducted a sensitivity analysis comparing the use of 0.7 and 0.5 correlations and this made little difference to the analyses). When data were unavailable in papers, we contacted corresponding authors. One study failed to provide a post-intervention and since we could not derive a response from the authors (Ranjbar et al., 2013), we carried forward the baseline SD (see Weir et al., 2018).

Effect sizes were classified as small (0.2), medium (0.5) or large (\geq 0.8) according to Cohen's rule of thumb (Cohen, 1998). Heterogeneity was assessed using the I² statistic, and for interpretation we followed Cochrane guidance (Higgins et al., 2019) where I² values were identified: 0–40% as might not be important; 30–60% as may represent moderate heterogeneity; 50–90% may represent substantial heterogeneity; 75–100% representing considerable heterogeneity.

Results

Summary of literature search

Figure 1 provides a PRISMA flowchart of the literature search and studies included for further analysis. The initial search identified 370 publications. Among these, 87 were excluded because they were duplicates and 1 because it was not in English. Then, 282 abstracts were reviewed. Among these, 271 were excluded as they did not meet the predefined inclusion criteria. Five studies were excluded after reviewing the full texts. One did not have a relevant physical activity intervention (Torous, 2021), one did not have clinically diagnosed OCD (Lancer et al., 2007), two did not use the Y-BOCS as a measure of OCD symptom severity (Abrantes et al., 2009, 2019) and one did not have the relevant population (LeBouthillier & Asmundson, 2017). Six studies were therefore included in our analyses and are detailed in Table 1 (Abrantes et al., 2017; Bhat et al., 2016; Brown et al., 2007; Packer-Hopke and Motta, 2014; Ranjbar et al., 2013; Rector et al., 2015).

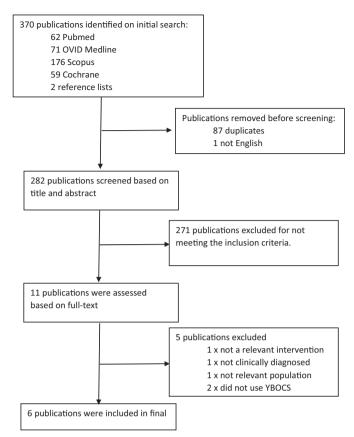


Figure 1. Flow chart of study selection.

Primary outcome

Using a random effects model, we calculated the pre-post effect size change for OCD patients who had received an exercise intervention. We assumed a correlation of .5 between pre and post conditions. This analysis revealed a large pre-post effect size reduction in Y-BOCS symptoms with a Hedges g = 1.33 (95%Cl 1.06–1.60; Figure 2). Heterogeneity was low (l^2 =9.79%) suggesting little variability in outcomes.

We also assessed the impact of small studies and possible publication bias by inspecting funnel plots and Trim and Fill analysis (Figure 3). Visual inspection of the funnel plot suggested some asymmetry and Trim and Fill analysis pointed to three possibly missing trials, that reduced the effect size g = 1.15 (0.84–1.47).

Secondary outcomes

As secondary-outcome analyses, we planned to assess the impact of exercise on depression (Figure 4) and anxiety (Figure 5). An analysis of pre-post depression scores showed that exercise was associated with significantly reduced depression (g = 0.58 [95%Cl 0.27-0.89]; k = 2) with low heterogeneity ($l^2 = 0\%$). An analysis of the pre-post change in anxiety also revealed a significant reduction of anxiety (g = 0.69 [95%Cl 0.36-1.03; k = 4), with heterogeneity being moderate ($l^2 = 43.54\%$). No other secondary outcomes were suitable for analysis because of too few reports for global symptomatology and functional disability, health related quality of life, body mass index, change in inflammatory markers and change in cholesterol levels.

Risk of bias for included studies

RCTS were rated using the Cochrane Risk of Bias 2 tool (Sterne et al., 2019; Figure 6), while non-RCTs were assessed using the

Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results
Abrantes et al, 2017 USA	<pre>N = 56 (aged 38.8 ± 13.0 year) were randomised to: exercise (intervention) (N = 28) and health education (control) (N = 28). RCT.</pre>	Had a DSM-IV diagnosis of OCD and clinical significant symptoms of OCD (Y-BOC5 ≥ 16). Either stable pharmacotherapy or CBT for more than 12 weeks. Physically inactive (<60 min of aerobic exercise a week) for past 3 months.	The exercise group attended 12 weekly aerobic exercise (AE) sessions supervised by an exercise physiologist. They were asked to exercise on their own for 2 days increasing to 4 days. Aim to attain 150 min/wk of moderate intensity aerobic exercise. Also received a monetary incentive (\$5) for each supervised session attended. Health education (HE) group received 12 weekly hour-long psychoeducation sessions on topics such as nutrition, sleep hygiene and smoking.	OCD symptoms (Y-BOCS) Depression (BDI-II) Exercise quantity questions CRF – 1 mile Rockport walking test	None	AE group attended 9.7 \pm 2.6 sessions and HE attended 9.96 \pm 2.7 sessions. No statistical difference for Y-BOCS between groups. No significant effect on depression. No significant difference in CRF.
Bhat et al., 2016 India	 N = 10 (aged 28.1 ± 8.91 years). All 28.1 ± 8.91 years). All completed exercise intervention. No control group. Prepost design. 	Confirmed OCD diagnosis by psychiatrist and scored 16 or more on the Y-BOCS.	The exercise was a specific yoga module. They completed 10 sessions of yoga over 2 weeks with each session 50 min in duration. Outcome measures measured at baseline (BL), 1 week and 2 weeks.	OCD symptoms (Y-BOCS) Clinical global impressions (CGI) Patient subjective improvement (VAS)	None	Y-BOCS significantly decreased from BL to week 1 ($p = 0.007$) and week 2 ($p = 0.002$), but no differences between weeks 1 and 2 ($p = 0.22$). CGI decreased from BL to weeks 1 and 2. VAS decreased from BL to weeks 1 and 2.
Brown et al., 2007. USA	N = 15 (aged 44.4 years). All completed the exercise intervention. No control group. Pre-post design.	Had a DSM-IV diagnosis of OCD and clinical significant symptoms of OCD (Y-BOCS > 16) for at least 3 months. Sedentary (<60 min of aerobic exercise a week) for past 6 months.	The intervention was a 12 week moderate intensity aerobic intervention with 3 components (1) aerobic exercise, (2) cognitive behavioural training and (3) an incentive system. For the exercise, they attended group exercise physiologist. Duration increased from 20 min to 40 min per session at 55–69% of age predicted HRmax. Asked to exercise 2–3 times a week in their own environment. Also received a weekly CBT for 20-30 mins prior to the exercise to increase overall fitness through behaviour change in their daily lives. Each session had a specific topic such as benefits of exercise. Finally participants received 55 for attending each group exercise session.	CRF (graded treadmill test) Body composition (BMI, BF96, hip to waist ratio) OCD Symptoms (Y-BOCS) QOL (Quality of Life Enjoyment and Satisfaction Questionnaire)	3 Weeks 6 Months	Y-BOCS significantly decreased in 69% post intervention ($\rho < 0.01$) and 50% still decreased after 6 months ($\rho < 0.05$). QOL significantly improved post intervention ($\rho < 0.01$) and had a tendency to remain improved at 6 months follow up ($\rho = 0.08$).
Packer-Hopke and Motta, 2014 USA	N=5 (aged 9-13 years). All completed the exercise intervention. No control group. Pre-post design.	Formal diagnosis of OCD and Tourette Syndome. 4 of 5 were on medication for TS but stable for 3 months. Not receiving any psychotherapy or behaviour theratov.	6-week aerobic exercise intervention following a DVD on kickboxing and dance aerobics. Completed twice a week for 30 mins. Exercised at 60- 80% of their predicted heart rate max.	Tourette symptoms OCD symptoms (Y-BOCS) Anxiety (BAI-Y)	None	Large reductions in TS, OCD and anxiety symptoms.

Table 1. Continued.						
Study	Population	Clinical info	Intervention	Outcomes	Follow-up	Results
Ranjbar et al. (2013)	N = 40 women were	Met criteria for DSM-IV	The intervention group received a 6-	OCD symptoms (Y-BOCS)	None	Significant decrease in OCD
lran	randomised in to	diagnosis of OCD	week intervention of Hatha Yoga	Anxiety (BAI)		(p < 0.05) and anxiety
	either yoga group	(interview by a	(standard yoga) twice a week (12			symptoms ($p < 0.05$).
	(N = 20,	psychiatrist), able to	sessions in total).			
	31.5 ± 7.1 years) or	contribute to Yoga	The control group watched TV twice a			
	control group ($N = 20$,	practice, no other major	week for 6 weeks.			
	33.4 ± 8.8 years).	mental health illness.				
	An RCT.					
Rector et al., 2015.	<i>N</i> = 11 (18-55 years). All	Met DSM-5 criteria for OCD,	The intervention included structured	OCD symptoms (Y-BOCS)	None	Significant decrease in OCD
Canada	completed the	had a clinician-rated Y-	group CBT for 15 weeks with a	Obsessional beliefs		symptoms with Y-BOCS
	exercise intervention.	BOCS score > 16 and	12 week customised exercise	questionnaire-44		(p < 0.01) and OBQ-44
	No control group. A	stable medication for at	programme, 3 times a week.	Depression (BDI-II)		(p < 0.01). Significant
	pre-post design.	least 12 weeks.	Gradually increasing from intensity	Anxiety (BAI)		decreases in depression
			and duration from 15-45 min.			(BDI-II, $p < 0.05$) but not
						anxiety (BAI).
RCT: randomised contro	RCT: randomised controlled trial; OCD: obsessive-compulsive disorder; DSM-IV	ulsive disorder; DSM-IV -and DSM	-and DSM-5: diagnostic and statistical manual; Y-BOCS: Yale-Brown Obsessive Compulsive Scale; BAI: Becks Anxiety Index; BDI-II: Becks	5: Yale-Brown Obsessive Compul	sive Scale; BAI:	Becks Anxiety Index; BDI-II: Becks
Depression Index II; AE:	aerobic exercise; HE: health edu	<pre>scation; OBQ-44; Obsessions Questi</pre>	Depression Index II; AE: aerobic exercise; HE: health education; OBQ-44; Obsessions Questionnaire-44; TS; Tourette syndrome; QOL: quality of life; CRF: cardiorespiratory fitness; Hrmax: maximum heart rate.	ity of life; CRF: cardiorespiratory	fitness; Hrmax: r	naximum heart rate.

ROBINS-I tool (Sterne et al., 2019; Figure 7). On the Cochrane RoB2 tool, two studies (Abrantes et al., 2017; Ranjbar et al., 2013) showed overall 'some concerns'. On the ROBINS-I, three studies showed moderate risk of bias (Brown et al., 2007; Packer-Hopke and Motta, 2014; Rector et al., 2015) while one was at serious risk of bias (Bhat et al., 2016). This suggests that three of the four non-RCTs provide sound evidence for a non-randomised study but cannot be considered comparable to a well performed randomised trial; while the fourth displays 'important problems' (Sterne et al., 2019).

A key area of weakness in non-RCTS was bias in measurement of outcomes – this largely reflects the fact that exercise intervention outcome assessments were conducted non-blind.

Discussion

As far as we are aware, the current preregistered systematic review and meta-analysis is the first to examine the efficacy of exercise in reducing OCD symptom severity. Our systematic review identified 370 publications; however, only six trials (N = 92) met inclusion criteria: four employing a pre-post design and two RCTs. A random-effects meta-analysis of pre-post changes scores revealed a large reduction in OCD symptoms (g = 1.33 (95%CI 1.06–1.61); as well as significant medium-to-large reductions in the secondary outcomes of depression (g = 0.58 [95%CI 0.27–0.89]; k = 2) and anxiety (g = 0.69 [95%CI 0.36–1.03; k = 4) following exercise. Three of four non RCTs were rated as at overall moderate risk of bias on the ROBINS-I; and both RCTs were rated as having 'some concerns' on the RoB2 tool.

The current analyses shows that various forms of exercise (e.g., aerobic exercise, yoga) may act as an effective intervention to improve the symptoms of OCD as well as the secondary outcomes of both anxiety and depression. While the effect size for OCD symptom reduction was large, analysis of the funnel plot and Trim and Fill analysis indicated some evidence of small-sample bias, with three potentially missing studies that reduced the effect size (g = 1.15 [95%CI [0.85–1.47]). Exercise was also associated with significant reductions of depression and anxiety symptoms though to a lesser degree than the reduction of OCD symptoms. With so few studies, we were unable to examine whether depression and/or anxiety reductions mediated the reduction in OCD symptomatology.

Finally, in addition, we assessed the tolerability and acceptability of exercise by looking at figures relating to the ascertainment ratio (ratio of eligible patients to those consenting to participate) and drop out and adverse events. Only 2 of the 6 studies stated how many participants were screened and then entered the study. None said how many potentially suitable people they approached. As ascertainment ratios were rarely reported and only two RCTs were identified, analysis of relative acceptability of exercise as an intervention was not feasible. Indeed, only one of the RCTs (Abrantes et al., 2017) provided data on drop-out with 5 dropping out in the exercise arm (18%) and 2 in the control arm (7%). Nonetheless, the drop-out rate when reported in the exercise condition across the 6 trials was low, with the vast majority of those starting the intervention (83 of 92: 90%) completing exercise. Accurate assessment of ascertainment and drop-out rates is still needed, however, to help to gauge feasibility of recruitment and power future full scale trials.

OCD is a disorder with a low placebo response (Sugarman et al., 2017) and given that exercise may have non-specific effects, it is important to compare the exercise arm with a control arm. As noted, 4 of the 6 studies did not have a control arm (Bhat

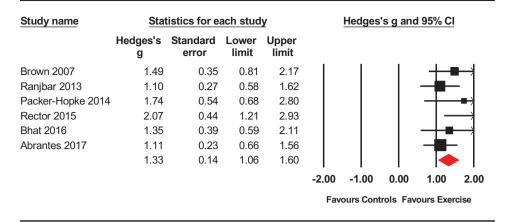


Figure 2. Effect of exercise on OCD symptoms (YBOCS).

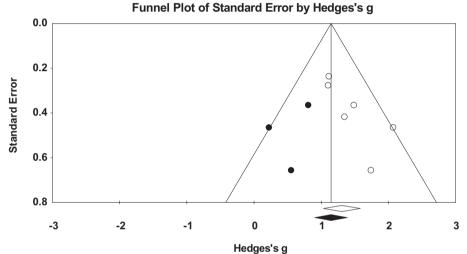


Figure 3. Funnel plot of standard error by Hedge's g.

Study name	Statistics for each study				Hedges's g and 95% Cl				
	Hedges's g	Standard error	Lower limit	Upper limit					
Rector 2015	0.71	0.27	0.18	1.24			-	■┼	
Abrantes 2017	0.51	0.19	0.14	0.88			-		
	0.58	0.16	0.27	0.88					
					-2.00	-1.00	0.00	1.00	2.00
					Favours Controls Favours Exercise				

Figure 4. Effect of exercise on depression.

et al., 2016; Brown et al., 2007; Packer-Hopke and Motta, 2014; Rector et al., 2015); and so, we cannot exclude the possibility that the attention given by the person delivering the exercise could cause an improvement in symptoms. Future trials therefore need to include control groups to unpick the specific effect of exercise beyond general effects resulting from attention or social contact and other potential benefits. Further research is needed to understand whether it is the exercise itself having an improvement on symptoms or the process of the research. In addition, we need to understand better the type of exercise, the duration and the intensity to be able to prescribe exercise as an adjunct therapy for OCD.

Limitations

The main limitations of the current study largely reflect limitations of the original studies. These limitations mainly centre on the fact that we identified only two RCTs (and 4 non-RCTs) assessing exercise as an intervention for OCD; and that the quality of research to date has been at moderate or high risk of bias. The reliance

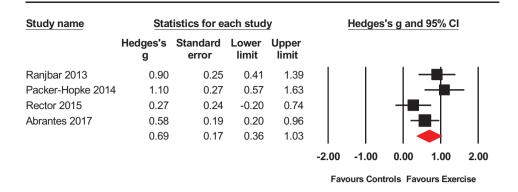
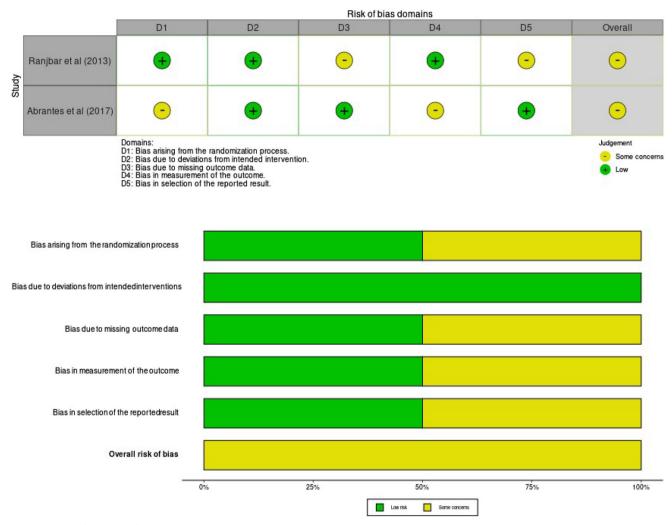


Figure 5. Effect of exercise on anxiety.





upon pre-post effect is likely to inflate effect size estimations because of their lack of a control comparison (Cuijpers et al., 2017). Pre-post analyses do not allow us to differentiate between the effects, we cannot be sure changes are attributable to the treatment itself and natural processes that may occur e.g., spontaneous remission. As already noted, baseline and post-test scores are not independent of each other and the value of the correlation is required to calculate the effect size; however, the actual correlation is unknown and had to be estimated. While we conducted a sensitivity analysis and this showed no difference, pre-post effect sizes can be less reliable in terms of estimating intervention effects (Cuijpers et al., 2017) as opposed to non-specific effects.

When performing the literature search, we excluded 5 studies that failed to meet our inclusion criteria. Two studies were excluded as they used a self-rating scale for obsessions and



Figure 7. ROBINS-I risk of bias ratings for individual non-RCTs and overall.

compulsions rather than the Y-BOCS (Abrantes et al., 2009, 2019). One study was excluded as the participants were not clinically diagnosed with OCD (Lancer et al., 2007). It is important to ensure that data are only reported from a clinical population as often people self-report to have OCD symptoms when in fact they would not meet criteria for clinical diagnosis.

Aside from there being few studies, the investigations themselves also included very small numbers of participants (median number =12.5). This undoubtedly means that existing trials have been underpowered and again, is likely to inflate the effect size and the levels of heterogeneity (see Inthout et al., 2015). The main way to assess heterogeneity is through moderator analyses; however, the small number of trials meeting our inclusion criteria meant that our pre-registered intention to assess various moderator variables was not feasible. Although no definitive minimum number of studies is required for meta-regression, we followed the general recommendations of at least 10 studies for a continuous variable, and for a categorical subgroup variable, a minimum of 4 studies per group is needed (Fu et al., 2011; Higgins et al., 2019). In conclusion, this is the first systematic review and meta-analysis exploring the effect of exercise on OCD symptoms. Our prepost effect sizes were associated with a large reduction of OCD symptoms following exercise. Nonetheless, only six small, largely uncontrolled trials were assessed and these were at moderate to high risk of bias. Therefore, it is difficult to draw conclusions on the acceptability, tolerability and effect size of exercise as a therapeutic intervention in this patient group. There is still a need for a well-designed randomised controlled pilot study to assess the promise of exercise as an intervention for OCD.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

RC's involvement in his research was funded in whole, or in part, by Wellcome [Grant number 110049/Z/15/Z and 110049/Z/15/A]. For the purpose of open access, the author has applied a CC BY public copyright licence to any Author Accepted Manuscript version arising from this submission. SRC receives honoraria from Elsevier for editorial work. NF receives honoraria from Elsevier for editorial work, from the Global Mental Health Academy for giving lectures and from the Medicines and Healthcare Products Regulatory Agency for consultation. She has received payment to her institution for research by the NIHR, COST Action and Orchard-Advancing Research in OCD, personal royalties from Oxford University Press and payment to attend scientific meetings from the British Association for Psychopharmacology, European College for Neuropsychopharmacology (ECNP), Royal College of Psychiatrists, International College for Neuropsychopharmacology, COST Action, World Psychiatric Association, International Forum for Mood and Anxiety Disorders, American College for Neuropsychopharmacology.

ORCID

Lindsay Bottoms () http://orcid.org/0000-0003-4632-3764 Naomi A. Fineberg () http://orcid.org/0000-0003-1158-6900 Luca Pellegrini () http://orcid.org/0000-0002-2855-2865 David Wellsted () http://orcid.org/0000-0002-2895-7838 Lynne M. Drummond () http://orcid.org/0000-0002-4316-6129 David S. Baldwin () http://orcid.org/0000-0003-3343-0907 Ruihua Hou () http://orcid.org/0000-0001-6127-1478 Samuel Chamberlain () http://orcid.org/0000-0001-7014-8121 Dominique Grohmann () http://orcid.org/0000-0002-9690-6733 Keith R. Laws () http://orcid.org/0000-0002-5065-0867

References

- Abrantes, A. M., Brown, R. A., Strong, D. R., McLaughlin, N., Garnaat, S. L., Mancebo, M., Riebe, D., Desaulniers, J., Yip, A. G., Rasmussen, S., & Greenberg, B. D. (2017). A pilot randomized controlled trial of aerobic exercise as an adjunct to OCD treatment. *General Hospital Psychiatry*, 49, 51–55. doi:10.1016/j.genhosppsych.2017.06.010
- Abrantes, A. M., Farris, S. G., Brown, R. A., Greenberg, B. D., Strong, D. R., McLaughlin, N. C., & Riebe, D. (2019). Acute effects of aerobic exercise on negative affect and obsessions and compulsions in individuals with obsessive-compulsive disorder. *Journal* of Affective Disorders, 245, 991–997. doi:10.1016/J.JAD.2018.11. 074
- Abrantes, A. M., Strong, D. R., Cohn, A., Cameron, A. Y., Greenberg, B. D., Mancebo, M. C., & Brown, R. A. (2009). Acute changes in obsessions and compulsions following moderate-intensity aerobic exercise among patients with obsessive-compulsive disorder. *Journal of Anxiety Disorders*, 23(7), 923–927. doi:10.1016/j. janxdis.2009.06.008
- Ainsworth, B. E., Haskell, W. L., Herrmann, S. D., Meckes, N., Bassett, D. R., Tudor-Locke, C., Greer, J. L., Vezina, J., Whitt-Glover, M. C., & Leon, A. S. (2011). 2011 compendium of physical activities: A second update of codes and MET values. *Medicine and Science in Sports and Exercise*, 43(8), 1575–1581. doi:10.1249/MSS.0B013E31821ECE12
- Albert, U., Baffa, A., & Maina, G. (2017). Family accommodation in adult obsessive–compulsive disorder: Clinical perspectives. *Psychology Research and Behavior Management*, 10, 293–304. Volume doi:10.2147/PRBM.S124359
- Antunes, B. M., Campos, E. Z., dos Santos, R. V. T., Rosa-Neto, J. C., Franchini, E., Bishop, N. C., & Lira, F. S. (2019). Anti-inflammatory response to acute exercise is related with intensity and physical

fitness. Journal of Cellular Biochemistry, 120(4), 5333-5342. doi: 10.1002/jcb.27810

- Bhat, S., Varambally, S., Karmani, S., Govindaraj, R., & Gangadhar, B. N. (2016). Designing and validation of a yoga-based intervention for obsessive compulsive disorder. *International Review of Psychiatry*, 28(3), 327–333. doi:10.3109/09540261.2016.1170001
- Block, M. L., Zecca, L., & Hong, J. S. (2007). Microglia-mediated neurotoxicity: Uncovering the molecular mechanisms. *Nature Reviews. Neuroscience*, 8(1), 57–69. doi:10.1038/nrn2038
- Bobes, J., González, M. P., Bascarán, M. T., Arango, C., Sáiz, P. A., & Bousoño, M. (2001). Quality of life and disability in patients with obsessive compulsive disorder. *European Psychiatry*, 16(4), 239–245. doi:10.1016/S0924-9338(01)00571-5.
- Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2013). *Comprehensive meta-analysis version* 3. Englewood, NJ: Biostat.
- Brown, R. A., Abrantes, A. M., Strong, D. R., Mancebo, M. C., Menard, J., Rasmussen, S. A., & Greenberg, B. D. (2007). A pilot study of moderate-intensity aerobic exercise for obsessive compulsive disorder. *The Journal of Nervous and Mental Disease*, 195(6), 514–520. doi:10.1097/01.nmd.0000253730.31610.6c
- Cohen, J. (1998). *Statistical power analysis for behavioural sciences*. Lawrence Earlbaum Associates.
- Cuijpers, P., Weitz, E., Cristea, I. A., & Twisk, J. (2017). Pre-post effect sizes should be avoided in meta-analyses. *Epidemiology* and Psychiatric Sciences, 26(4), 364–368. doi:10.1017/ S2045796016000809
- di Liegro, C. M., Schiera, G., Proia, P., & di Liegro, I. (2019). Physical activity and brain health. *Genes*, 10(9), 720. doi:10.3390/ genes10090720
- Eisen, J. L., Sibrava, N. J., Boisseau, C. L., Mancebo, M. C., Stout, R. L., Pinto, A., & Rasmussen, S. A. (2013). Five-year course of obsessive-compulsive disorder: Predictors of remission and relapse. *The Journal of Clinical Psychiatry*, 74(03), 233–239. doi: 10.4088/JCP.12M07657
- Fineberg, N. A., Hollander, E., Pallanti, S., Walitza, S., Grünblatt, E., Dell'Osso, B. M., Albert, U., Geller, D. A., Brakoulias, V., Janardhan Reddy, Y. C., Arumugham, S. S., Shavitt, R. G., Drummond, L., Grancini, B., De Carlo, V., Cinosi, E., Chamberlain, S. R., Ioannidis, K., Rodriguez, C. I., ... Menchon, J. M. (2020). Clinical advances in obsessive-compulsive disorder: A position statement by the International College of Obsessive-Compulsive Spectrum Disorders. International Clinical Psychopharmacology, 35(4), 173-193. doi:10.1097/YIC. 00000000000314
- Freedman, D. E., & Richter, M. A. (2021). A narrative review of exercise and obsessive-compulsive disorder. *General Hospital Psychiatry*, 71, 1–10. doi:10.1016/J.GENHOSPPSYCH.2021.03.014
- Fu, R., Gartlehner, G., Grant, M., Shamliyan, T., Sedrakyan, A., Wilt, T. J., Griffith, L., Oremus, M., Raina, P., Ismaila, A., Santaguida, P., Lau, J., & Trikalinos, T. A. (2011). Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. *Journal of Clinical Epidemiology*, 64(11), 1187–1197. doi:10.1016/J.JCLINEPI.2010.08.010
- Gerentes, M., Pelissolo, A., Rajagopal, K., Tamouza, R., & Hamdani, N. (2019). Obsessive-compulsive disorder: Autoimmunity and neuroinflammation. *Current Psychiatry Reports*, 21(8), 1. doi:10. 1007/s11920-019-1062-8
- Gleeson, M., Bishop, N. C., Stensel, D. J., Lindley, M. R., Mastana, S. S., & Nimmo, M. A. (2011). The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. *Nature Reviews. Immunology*, 11(9), 607–615. doi:10.1038/nri3041

- Goodman, W. K., Price, L. H., Rasmussen, S. A., Mazure, C., Delgado, P., Heninger, G. R., & Charney, D. S. (1989). The Yale-Brown Obsessive Compulsive Scale. II. Validity. *Archives of General Psychiatry*, 46(11), 1012–1016. doi:10.1001/ARCHPSYC. 1989.01810110054008
- Higgins, J. P. T., López-López, J. A., Becker, B. J., Davies, S. R., Dawson, S., Grimshaw, J. M., McGuinness, L. A., Moore, T. H. M., Rehfuess, E. A., Thomas, J., Caldwell, D. M. (2019). Synthesising quantitative evidence in systematic reviews of complex health interventions. *BMJ Global Health*, 4(Suppl 1), e000858. doi:10. 1136/BMJGH-2018-000858
- Hollander, E., Doernberg, E., Shavitt, R., Waterman, R. J., Soreni, N., Veltman, D. J., Sahakian, B. J., & Fineberg, N. A. (2016). The cost and impact of compulsivity: A research perspective. *European Neuropsychopharmacology*, 26(5), 800–809. doi:10.1016/J. EURONEURO.2016.02.006
- Inthout, J., Ioannidis, J. P. A., Borm, G. F., & Goeman, J. J. (2015). Small studies are more heterogeneous than large ones: A meta-meta-analysis. *Journal of Clinical Epidemiology*, 68(8), 860–869. doi:10.1016/J.JCLINEPI.2015.03.017
- Kandola, A., Ashdown-Franks, G., Hendrikse, J., Sabiston, C. M., & Stubbs, B. (2019). Physical activity and depression: Towards understanding the antidepressant mechanisms of physical activity. *Neuroscience and Biobehavioral Reviews*, 107, 525–539. doi:10.1016/J.NEUBIOREV.2019.09.040
- Lancer, R., Motta, R., & Lancer, D. (2007). The effect of aerobic exercise on obsessive-compulsive disorder, anxiety, and depression: A preliminary investigation. *The Behavior Therapist*, *30*(3), 57–62.
- Larun, L., Nordheim, L. v., Ekeland, E., Hagen, K. B., & Heian, F. (2006). Exercise in prevention and treatment of anxiety and depression among children and young people. *Cochrane Database of Systematic Reviews*, *3*, Art. No.: CD004691. doi:10. 1002/14651858.CD004691.pub2
- LeBouthillier, D. M., & Asmundson, G. J. G. (2017). The efficacy of aerobic exercise and resistance training as transdiagnostic interventions for anxiety-related disorders and constructs: A randomized controlled trial. *Journal of Anxiety Disorders*, *52*, 43–52. doi:10.1016/j.janxdis.2017.09.005
- Małkiewicz, M. A., Szarmach, A., Sabisz, A., Cubała, W. J., Szurowska, E., & Winklewski, P. J. (2019). Blood-brain barrier permeability and physical exercise. *Journal of Neuroinflammation*, *16*(1), 1–16. doi:10.1186/s12974-019-1403-x
- McCusker, R. H., & Kelley, K. W. (2013). Immune-neural connections: how the immune system's response to infectious agents influences behavior. *Journal of Experimental Biology*, 216(1), 84–98. doi:10.1242/jeb.073411
- Mee-Inta, O., Zhao, Z, W., Kuo, Y. M. (2019). Physical exercise inhibits inflammation and microglial activation. *Cells*, *8*(7), 691. doi:10.3390/cells8070691
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Altman, D., Antes, G., Atkins, D., Barbour, V., Barrowman, N., Berlin, J. A., Clark, J., Clarke, M., Cook, D., D'Amico, R., Deeks, J. J., Devereaux, P. J., Dickersin, K., Egger, M., Ernst, E., & Tugwell, P, PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine*, 151(4), 264–269, W64. doi:10.7326/0003-4819-151-4-200908180-00135
- NICE. (2005). Treatments for mild to moderate depression | Information for the public | Depression in adults: recognition and management | Guidance | NICE. Retrieved March 29, 2022, from https://www.nice.org.uk/guidance/cg90/ifp/chapter/Treatmentsfor-mild-to-moderate-depression

- NICE. (2009). Guidance|obsessive-compulsive disorder and body dysmorphic disorder: Treatment|Guidance. Retrieved March 29, 2022, from https://www.nice.org.uk/guidance/cg31/chapter/1-Guidance
- Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—a web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1), 210. doi:10.1186/S13643-016-0384-4
- Packer-Hople, L., & Motta, W. (2014). A preliminary investigation of the effects of aerobic exercise on childhood Tourette's Syndrome and OCD. *The Behavioural Therapist*, 37(7), 188–192.
- Pallanti, S., Hollander, E., Bienstock, C., Koran, L., Leckman, J., Marazziti, D., Pato, M., Stein, D., & Zohar, J, International Treatment Refractory OCD Consortium. (2002). Treatment nonresponse in OCD: Methodological issues and operational definitions. *The International Journal of Neuropsychopharmacology*, 5(2), 181–191. doi:10.1017/S1461145702002900
- PROSPERO. (2021). Effect of exercise on obsessive-compulsive disorder: A systematic review and meta-analysis. Retrieved March 25, 2022, from https://www.crd.york.ac.uk/prospero/display_ record.php?RecordID=283931
- Ramos-Sanchez, C. P., Schuch, F. B., Seedat, S., Louw, Q. A., Stubbs, B., Rosenbaum, S., Firth, J., van Winkel, R., & Vancampfort, D. (2021). The anxiolytic effects of exercise for people with anxiety and related disorders: An update of the available meta-analytic evidence. *Psychiatry Research*, 302, 114046. doi:10.1016/J.PSYCHRES.2021.114046
- Ranjbar, F., Broomand, M., & Akbarzadeh, A. (2013). The effect of yoga on anxiety symptoms in women with obsessive compulsive disorder. *Life Science Journal*, 10(4), 565–568. https://www. scopus.com/inward/record.uri?eid=2-s2.0-84886245878& partnerID=40&md5=d03bfdf6c0cb26e20e947aaf5582d2fd
- Rector, N. A., Richter, M. A., Lerman, B., & Regev, R. (2015). A Pilot Test of the Additive Benefits of Physical Exercise to CBT for OCD. *Cognitive Behaviour Therapy*, 44(4), 328–340. doi:10.1080/ 16506073.2015.1016448
- Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H.-Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., ... Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *British Medical Journal*, 366, 14898. doi:10.1136/BMJ.L4898
- Sugarman, M. A., Kirsch, I., & Huppert, J. D. (2017). Obsessive-compulsive disorder has a reduced placebo (and antidepressant) response compared to other anxiety disorders: A meta-analysis. *Journal of Affective Disorders*, *218*, 217–226. doi:10.1016/J.JAD. 2017.04.068
- Swedo, S., Williams, K., Buckley, A., Hommer, R., D'Souza, P., & Leckman, J. (2014). New evidence that pandas (acute-onset OCD) is a form of autoimmune encephalitis (AE). *Neuropsychopharmacology*, *39*, S287. doi:10.1038/npp.2014. 280
- Torous, J. (2021). Digital interventions for adults with symptoms of depression and children and adolescents with symptoms of obsessive-compulsive disorder. *Journal of American Medical Association*, 325(18), 1839–1840. doi:10.1001/jama. 2021.5047
- Varinelli, A., Caricasole, V., Pellegrini, L., Hall, N., Garg, K., Mpavaenda, D., Dell'Osso, B., Albert, U., & Fineberg, N. A, The International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) Expert Survey Workgroup. (2022). Functional interventions as augmentation strategies for obsessive-compulsive disorder (OCD): Scoping review and expert survey from the

international college of obsessive-compulsive spectrum disorders (ICOCS). *International Journal of Psychiatry in Clinical Practice*, 26(1), 92–107. doi:10.1080/13651501.2021.1872646.]

- Veale, D., & Roberts, A. (2014). Obsessive-compulsive disorder. British Medical Journal, 348, g2183. doi:10.1136/bmj. g2183
- Weir, C. J., Butcher, I., Assi, V., Lewis, S. C., Murray, G. D., Langhorne, P., & Brady, M. C. (2018). Dealing with missing standard deviation and mean values in meta-analysis of continuous outcomes: A systematic review. BMC Medical Research

Methodology, *18*(1), 1–14. doi:10.1186/S12874-018-0483-0/ TABLES/3

Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., Olesen, J., Allgulander, C., Alonso, J., Faravelli, C., Fratiglioni, L., Jennum, P., Lieb, R., Maercker, A., van Os, J., Preisig, M., Salvador-Carulla, L., Simon, R., & Steinhausen, H. C. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. European Neuropsychopharmacology, 21(9), 655–679. doi:10.1016/j.euroneuro.2011.07.018