



Long- term remission status in pediatric obsessive-compulsive disorder: Evaluating the predictive value of symptom severity after treatment

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ABSTRACT

It is unknown if long-term remission for pediatric obsessive-compulsive disorder (OCD) patients is associated with post-treatment OCD symptom severity. The aim of the present study was to evaluate if post-treatment symptom severity cut-offs can discriminate remitters from non-remitters in pediatric OCD patients during three years of follow-up. All participants ($N = 269$) from the Nordic Long-term OCD Treatment Study (NordLOTS) undergoing stepped-care treatment were included. Patients were rated with the Clinical Global Impression – Severity Scale (CGI-S) one ($n = 186$), two ($n = 167$), and three years ($n = 166$) after first-line cognitive-behavioral therapy. Post-treatment symptom severity scores as well as percentage reductions during treatment evaluated with the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) were analyzed using receiver operating characteristics according to the CGI-S remission scores (< 2) at follow-up. Post-treatment CY-BOCS severity scores acceptably discriminated remitters from non-remitters at one-year follow-up, but poorly for the two- and three-year follow-up. Severity percentage reduction during treatment did not discriminate remission status acceptably at any follow-up point. Post-treatment OCD symptom severity status seems to have little discriminative value for long-term remission status in pediatric patients. Further research is warranted to detect post-treatment factors of prognostic value.

1. Introduction

Obsessive-compulsive disorder (OCD) affects around 0.5–3% of children and adolescents (Heyman et al., 2001; Zohar, 1999) and often has a substantial impact on the patients' functional levels (Piacentini et al., 2007b) and quality of life (Weidle et al., 2014). Cognitive-behavioral therapy (CBT) is the first-line treatment for pediatric OCD patients (Geller and March 2012) with a meta-analysis of randomized controlled trials showing an overall response rate of 70% and a remission rate of 53% (Öst et al., 2016).

Traditionally, OCD was considered a chronic disorder with low

recovery rates (Skoog and Skoog, 1999; Stewart et al., 2004), yet a recent meta-analysis of the long-term outcome of children and adolescents with OCD shows remission rates of 62% (Liu et al., 2021). In line with suggestions for other disorders (e.g. depression, see Stahl, 1999), increasing consensus has been reached to regard remission as the ultimate goal of treatment for OCD patients (Hollander and Zohar, 2004). There are, however, inconsistencies across studies of both immediate and long-term outcomes (e.g. remission criteria). An international expert panel has agreed to define remission for OCD (across age groups) as a state where the patient no longer meets syndromal criteria for OCD or presents with a total score of 12 or less on the Children's Yale-Brown

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Obsessive-Compulsive Scale (CY-BOCS; Scahill et al., 1997) and "normal, not at all ill" or "borderline mentally ill" on the CGI-S for at least one week (Mataix-Cols et al., 2016).

CY-BOCS is considered the golden standard for evaluating pediatric OCD symptoms in the clinic and for evaluation of treatment effects in clinical trials (Lewin and Piacentini, 2010). Signal detection analyses have been conducted in order to find optimal cut-offs of CY-BOCS post-treatment symptom severity corresponding to CGI-S remission status. These studies found total symptom severity CY-BOCS cut-offs of 11 (Skarphedinsson et al., 2017) and 14 (Storch et al., 2010a), and percentage reductions of 55% (Skarphedinsson et al., 2017) and 45–50% (Storch et al., 2010a) corresponding to post-treatment remission according to the CGI-S.

The long-term outcome after treatment is an important consideration for disorders such as OCD due to its chronic and fluctuating nature (Poyraz et al., 2015). It is unknown to what extent the specific level of symptom severity after treatment raises the chances of remission status in the years after treatment. A recent study has suggested that some pediatric OCD patients may be at risk of unfortunate long-term outcomes (remaining OCD symptoms and diminished quality of life) despite apparently adequate response to immediate treatment (Jensen et al., 2020a, 2021). From the adult literature, there are indications that post-treatment *partial* remission is more indicative of future relapse than full remission (Eisen et al., 2013). Therefore, it would be valuable to detect a symptom severity threshold and/or level of symptom reduction after treatment that raises the chances of long-term remission. To the best of our knowledge, no signal detection analysis on post-treatment symptom severity status predicting long-term outcome in a pediatric OCD sample has been performed previously.

The overall objective of the present study was to evaluate the predictive value of post-treatment OCD symptom severity for long-term remission status in pediatric OCD patients. Specifically, the first aim was to evaluate how well the post-treatment symptom severity total scores and the percentage of symptom severity reduction from baseline (evaluated with the CY-BOCS during stepped-care treatment) performed with regard to discriminating between remitters and non-remitters, 1, 2 and 3 years after treatment. The second aim was to evaluate optimal cut-off total scores and percentage reductions.

2. Methods

2.1. Participants

The study included participants from the Nordic Long-term OCD Treatment Study (NordLOTS; $N = 269$) who completed CY-BOCS assessment at the end of treatment as well as CGI-S assessment at 1-year ($n = 186$), 2-year ($n = 167$), and 3-year ($n = 166$) follow-up. The participants from the NordLOTS were children and adolescents from Denmark, Norway, and Sweden in the age span of 7 to 17 years at the time of inclusion. Main inclusion criteria were a primary diagnosis of OCD according to the DSM-IV as well as severity total scores of 16 and above on the CY-BOCS. Diagnosis of OCD and comorbid diagnoses were based on K-SADS-PL (Kaufman et al., 1997). Comorbidity was allowed if it was not considered of higher treatment priority. Gender distribution was equal (51% females), and 97% of the sample was of Scandinavian origin. Further information on the NordLOTS sample can be found in Torp et al. (2015).

2.2. Procedures

Treatment was scheduled as a stepped-care design (Thomsen et al., 2013). All patients entered Step 1 which consisted of 14 sessions of manualized CBT including exposure and response prevention (Thomsen and Weidle, 2015) based on the unpublished manual by March et al. (2000). The manual was modified adding family involvement (Piacentini et al., 2007a) as a central part of the treatment. Further

information about treatment procedures can be found in Torp et al. (2015). A total of 243 patients completed Step 1. Of these patients, 177 (72.8%) were considered treatment responders according to a pre-defined CY-BOCS cut-off total score of ≤ 15 (Højgaard et al., 2017; Torp et al., 2015b). These patients terminated treatment after the 14 sessions. In all, 121 patients were considered remitters (CY-BOCS total score of ≤ 10) after Step 1.

Non-responders to Step 1 were randomized to Step 2 for either 10 weekly sessions of CBT ($n = 28$) or medication in the form of selective serotonin reuptake inhibitors (SSRI) for 16 weeks ($n = 22$) (Skarphedinsson et al., 2015b). The response rate (CYBOCS total score ≤ 15) for continued CBT was 50.0% and 45.4% for SSRI treatment (Skarphedinsson et al., 2015b). Non-responders to Step 2 CBT were offered SSRI (Skarphedinsson et al., 2015a). During the first year after the end of Step 1, the patients could receive up to four booster sessions upon request. CY-BOCS assessment was administered by independent evaluators at pre-treatment, week seven during Step 1, the end of Step 1, and 6, 12, 24, and 36 months after end of Step 1 for all patients regardless of responder status. Patients entering Step 2 were assessed with the CY-BOCS at weeks 1, 8, and 16 after Step 1 during 16 weeks of Step 2 CBT or SSRI. Intent-to-treat analyses showed that 73% of the sample were considered remitters three years after Step 1 according to a CY-BOCS score of ≤ 10 (Melin et al., 2020). The two- and three-year follow-ups were performed naturalistically with no specified procedures for further treatment. Records of treatment during this follow-up period were incomplete.

The National Ethical Committees and data authorities in Denmark, Norway, and Sweden approved the study, and written informed consent was obtained from parents. Trial registry: Nordic Long-term Obsessive-Compulsive Disorder (OCD) Treatment Study; www.controlled-trials.com; ISRCTN66385119.

2.3. Instruments

2.3.1. Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)

The Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) is considered the golden standard for the assessment of OCD symptoms severity in pediatric patients (Scahill et al., 1997). The semistructured interview is administered by a clinician and covers questions regarding the various obsessions and compulsions that patients usually present with. Further, the instrument assesses symptom severity based on time pre-occupied with, disruption by, discomfort by, resistance to, and control over obsessions and compulsions. These features are added to a total sum severity score ranging from 0 to 40. The scale has shown good internal consistency and reasonable reliability and validity (Storch et al., 2004). The interrater agreement of the intra-class correlation coefficients in the NordLOTS sample was 0.92 (95% CI = 0.78–0.97) for the total score (Torp et al., 2015b).

2.3.2. Clinical Global Impression-Severity (CGI-S)

The Clinical Global Impression-Severity (CGI-S) is an overall evaluation of psychopathology severity rated by the clinician on a Likert scale from normal (0) to extreme (6) (Guy, 1976). The scale is widely used across diagnoses and ages. In the present study, the CGI-S assessed overall OCD symptom severity.

2.3.3. Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL)

The Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL) assesses the presence of a wide range of DSM-IV pediatric mental disorders in a clinical semi-structured interview (Kaufman et al., 1997). For the present study, internalizing diagnosis was identified as any anxiety or depressive diagnosis. Likewise, externalizing diagnosis was identified as any ADHD, conduct disorder, or oppositional defiant disorder.

2.4. Statistical analyses

For all patients, the latest conducted CY-BOCS assessment during active treatment was included in the analyses as a post-treatment symptom severity score. For the majority of the sample terminating treatment after Step 1, the post-treatment assessment was conducted at the end of 14 weeks of CBT. For patients entering Step 2, the latest conducted CY-BOCS assessment during this treatment was included in the analyses instead of the post-Step 1 assessment ($n = 37$). Differences in duration from treatment termination to follow-up assessment (up to 16 weeks) between Step 1 and Step 2 patients were disregarded as it was considered more important for the analyses to include as many patients as possible. In addition, 'post-treatment assessment' would not be an accurate designation if only the post-Step 1 assessment was included.

CGI-S scores for the 1-, 2-, and 3-year follow-up were dichotomized according to the definitions for remission as suggested by e.g. Mataix-Cols et al. (2016) and Tolin et al. (2005): Scores of 0 (normal, not at all ill) and 1 (borderline mentally ill) were collapsed to represent patients showing remission during follow-up, while the other scores were collapsed to represent patients not in remission. In line with previous studies, pre- to post-treatment CY-BOCS symptom severity percentage reductions were divided into 5% interval cutoffs.

According to the first aim of the study, Receiver Operating Characteristic (ROC) analysis (Swets and Pickett, 1982) was conducted in order to evaluate the overall discriminative value of 1) post-treatment CY-BOCS total scores and 2) percentage reductions for non-remission according to the CGI-S at each follow-up time point. The area under the ROC curve (AUC) indicates the discriminative value of the classification instrument ranging from 0.5 to 1. An AUC of 0.5 indicates that the variable has no discriminative value (Hosmer and Lemeshow, 2000; Mandrekar, 2010). Values between 0.7 and 0.8 are considered acceptable, whereas the interval 0.8–0.9 is excellent and above 0.9 outstanding (Hosmer and Lemeshow, 2000; Mandrekar, 2010). Furthermore, relevant parameters (sensitivity, specificity, positive and negative predictive value, accuracy, Cohen's kappa, and the Youden Index) were provided in order to evaluate post-treatment total score and percentage reduction cut-offs in predicting long-term remissions status. In the analyses in the present study, *non-remission* was defined as the outcome for reasons of convenience. In consequence, sensitivity refers to the proportion of patients classified as non-remitters during follow-up, who were also captured as such by the post-treatment assessment. Likewise, specificity refers to the proportion of follow-up remitters that is also classified as such by the post-treatment assessment. Positive and negative predictive values refer to the rate of false positive non-remitters and false negative non-remitters. Cohen's kappa assesses chance-corrected agreement between post-treatment CY-BOCS score and CGI-S remission status during follow-up (Cohen, 1960). The Youden Index maximizes the sum of sensitivity and specificity and is a valid and widely used measure in the detection of optimal cut-offs (Hajian-Tilaki, 2018; Youden, 1950).

Post hoc logistic regression analyses were performed in order to examine whether the association between post-treatment symptom severity status and long-term remission status was influenced by the following variables: age, gender, comorbid internalizing disorder (K-SADS), comorbid externalizing disorder (K-SADS), tic disorder, and treatment step (a) Step 1 CBT only, b) Step 2 CBT, or c) Step 2 SSRI). Both main effects and interaction effects were tested.

Statistical analyses were performed using STATA/MP 17.0 (Stata-Corp, 2021).

2.5. Attrition

Patients with missing and non-missing assessments at the specific follow-up points were compared on a range of pre-treatment characteristics (Jensen et al., 2020a). It was found that patients with a missing assessment at the 1-year follow-up were associated with the following pre-treatment characteristics: older age, higher CY-BOCS symptom

Table 1
Sample characteristics.

	One year	Two year	Three year	Baseline
Number of observations	186	167	166	269
Baseline CY-BOCS total score, mean/SD	24.1/4.8	24.0/4.9	24.0/5.1	24.6/5.1
Age at baseline, mean/SD	12.5/2.8	12.3/2.7	12.3/2.7	12.8/2.7
Gender, females,%	49.5%	47.9%	48.8	138/131
Comorbidity baseline (K-SADS-PL)				
% Anxiety disorders	18.8%	18.6%	20.5%	19.3%
Depressive disorders	2.7%	2.4%	1.2%	3.7%
ADHD	10.8%	11.4%	10.2%	8.9%
ODD/CD	4.3%	3.4%	3.6%	3.7%
Tic disorder	18.3%	19.8%	19.3%	18.6%
CGI-S remitters/nonremitters, n	137/49	124/43	129/37	–
Mean CY-BOCS total score, mean/SD	6.4/6.5	6.2/6.4	5.3/6.2	–

SD=standard deviation. CY-BOCS=Children's Yale-Brown Obsessive-Compulsive Scale.

CGI-S= Clinical Global Impression - Severity.

K-SADS=Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime Version.

severity, lower global functioning, and higher levels of child-rated OCD-related functional impairment (at a $p < .05$ level; Jensen et al., 2020a). Patients with missing assessments at the 2-year and 3-year follow-up were further characterized by older age of OCD symptom onset, higher levels of harm/sexual symptom dimension factor scores, higher levels of parent-rated OCD-related functional impairment and externalizing symptoms. Patients with missing 3-year follow-up assessment also had higher levels of pre-treatment internalizing symptoms. Lastly, participants who were not assessed during follow-up were more likely to be non-responders to Step 1 CBT.

3. Results

3.1. Sample characteristics as well as CY-BOCS scores and remitter status at the follow-up points

Pre-treatment sample characteristics for available participants at each follow-up point ($n = 186$, $n = 167$, $n = 166$) as well as for the total sample ($N = 269$) can be found in Table 1. Table 1 further provides an overview of the number of remitters according to CGI-S at the three follow-up points as well as the mean CY-BOCS symptom severity total scores. The mean CY-BOCS total score at the latest available assessment during treatment (after Step 1 or after/during Step 2) was 10.28 (standard deviation (SD)=7.00) across 243 participants.

3.2. Discriminative value of post-treatment CY-BOCS total scores and percentage reductions for remission status during follow-up: area under the ROC curves

The following AUCs indicate the ability of the CY-BOCS total score and percentage symptom reductions at post-treatment to discriminate between remitters and non-remitters according to CGI-S during follow-up. For the CY-BOCS total scores, the AUC was 0.698, confidence interval (CI) = 0.607–0.790 for the 1-year follow-up point. This means that CY-BOCS total scores at post-treatment have a 70% chance to correctly discriminate remitters from non-remitters at 1-year follow-up (Mandrekar, 2010). For the 2-year and 3-year follow-up, the AUC was 0.654, CI = 0.562–0.746 and 0.607, CI = 0.506–0.708. For the percentage symptom reduction scores, the AUCs were 0.665, CI = 0.576–0.754 for the 1-year follow-up, 0.620, CI = 0.529–0.711 for the

Tables 2

a-c. Signal detection analyses of long-term non-remission status prediction: post-treatment CY-BOCS total scores.

Table 2a. 1 year follow-up						
Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Cohen's kappa
≤0	100.00%	0.00%	4.08%	100.00%	26.34%	0.00%
≤1	95.92%	13.14%	8.16%	86.87%	34.95%	5.13%
≤2	91.84%	18.25%	8.16%	81.76%	37.63%	5.90%
≤3	91.84%	22.63%	8.16%	77.38%	40.86%	8.67%
≤4	91.84%	23.36%	12.24%	76.65%	41.40%	9.14%
≤5	87.76%	29.93%	18.36%	70.08%	45.16%	11.12%
≤6	81.63%	35.04%	24.48%	64.97%	47.31%	10.94%
≤7	75.51%	37.96%	24.48%	62.05%	47.85%	9.11%
≤8	75.51%	40.88%	32.64%	59.13%	50.00%	11.28%
≤9	67.35%	48.91%	32.64%	51.10%	53.76%	12.00%
≤10	67.35%	62.77%	36.72%	37.23%	63.98%	24.50%
≤11	63.27%	71.53%	42.84%	28.47%	69.35%	30.59%
≤12	57.14%	76.64%	55.08%	23.36%	71.51%	31.51%
≤13	44.90%	84.67%	61.20%	15.33%	74.19%	30.78%
≤14	38.78%	90.51%	71.40%	9.49%	76.88%	32.96%
≤15	28.57%	95.62%	85.69%	4.38%	77.96%	29.87%
≤18	14.29%	97.81%	87.73%	2.19%	75.81%	16.25%
≤19	12.24%	98.54%	89.77%	1.46%	75.81%	14.75%
≤20	10.20%	98.54%	95.89%	1.46%	75.27%	12.07%
≤21	4.08%	99.27%	97.93%	0.73%	74.19%	4.80%
≤22	2.04%	99.27%	99.97%	0.73%	73.66%	1.89%
>22	0.00%	100.00%	100.00%	0.00%	73.66%	0.00%

Table 2b. 2 year follow-up.						
Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Cohen's kappa
≤0	100.00%	0.00%	2.33%	100.00%	25.75%	0.00%
≤1	97.67%	14.52%	6.98%	85.49%	35.93%	6.78%
≤2	93.02%	18.55%	6.98%	81.46%	37.72%	6.63%
≤3	93.02%	24.19%	6.98%	75.81%	41.92%	10.18%
≤4	93.02%	25.00%	11.63%	75.00%	42.51%	10.71%
≤5	88.37%	30.65%	18.61%	69.35%	45.51%	11.77%
≤6	81.40%	35.48%	20.94%	64.51%	47.31%	10.91%
≤7	79.07%	40.32%	20.94%	59.67%	50.30%	12.98%
≤8	79.07%	42.74%	30.24%	57.25%	52.10%	14.83%
≤9	69.77%	50.00%	39.54%	49.99%	55.09%	14.41%
≤10	60.47%	58.87%	41.87%	41.12%	59.28%	15.37%
≤11	58.14%	66.94%	46.52%	33.06%	64.67%	21.35%
≤12	53.49%	73.39%	62.80%	26.61%	68.26%	24.46%
≤13	37.21%	79.84%	74.43%	20.16%	68.86%	17.31%
≤14	25.58%	83.87%	81.41%	16.13%	68.86%	10.40%
≤15	18.60%	90.32%	88.39%	9.68%	71.86%	10.82%
≤18	11.63%	95.16%	90.72%	4.84%	73.65%	8.97%
≤19	9.30%	95.97%	90.72%	4.03%	73.65%	7.10%
≤20	9.30%	96.77%	97.70%	3.22%	74.25%	8.28%
≤21	2.33%	98.39%	100.00%	1.61%	73.65%	1.02%
≤22	0.00%	98.39%	100.00%	1.61%	73.05%	<0.00%
>22	0.00%	100.00%	100.00%	0.00%	74.25%	0.00%

Table 2c. 3 year follow-up.						
Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Cohen's kappa
≤0	100.00%	0.00%	8.11%	100.00%	22.29%	0.00%
≤1	91.89%	13.18%	8.11%	86.86%	30.72%	2.47%
≤2	91.89%	19.38%	10.81%	80.66%	35.54%	5.71%
≤3	89.19%	23.26%	10.81%	76.78%	37.95%	6.50%
≤4	89.19%	24.03%	10.81%	76.00%	38.55%	6.94%
≤5	89.19%	30.23%	18.92%	69.80%	43.37%	10.62%
≤6	81.08%	34.88%	21.62%	65.15%	45.18%	9.16%
≤7	78.38%	38.76%	27.03%	61.27%	47.59%	10.18%
≤8	72.97%	39.53%	32.44%	60.49%	46.99%	7.56%
≤9	67.57%	47.29%	40.55%	52.74%	51.81%	9.65%
≤10	59.46%	55.81%	48.66%	44.21%	56.63%	10.87%
≤11	51.35%	63.57%	54.07%	36.46%	60.84%	11.66%
≤12	45.95%	69.77%	62.18%	30.26%	64.46%	13.28%
≤13	37.84%	78.29%	70.29%	21.73%	69.28%	15.39%
≤14	29.73%	83.72%	89.21%	16.30%	71.69%	14.13%
≤15	10.81%	87.60%	94.62%	12.42%	70.48%	<0.00%
≤18	5.41%	93.02%	97.32%	6.99%	73.49%	<0.00%
≤19	2.70%	93.80%	97.32%	6.21%	73.49%	<0.00%
≤20	2.70%	94.57%	97.32%	5.43%	74.10%	<0.00%
≤21	2.70%	98.45%	100.00%	1.55%	77.11%	1.71%
≤22	0.00%	98.45%	100.00%	1.55%	76.51%	<0.00%
>22	0.00%	100.00%	100.00%	0.00%	77.71%	0.00%

Sensitivity is the proportion of patients classified as non-remitters (according to a CGI-S score of <2) during follow-up which is captured as such by the post-treatment assessment (above the specific cut-off score).

Specificity is the proportion of follow-up remitters (CGI-S <2) classified as such by the post-treatment assessment (above the specific cut-off score).

Positive and negative predictive values refer to the rate of false positive non-remitters and false negative non-remitters.

Accuracy refers to the proportion of correctly classified participants.

Cohen's kappa is the chance-corrected agreement.

2-year follow-up, and 0.585, $CI = 0.488-0.682$ for the 3-year follow-up.

3.3. Optimal cut-offs for predicting remission status during follow-up

Cut-off scores for CY-BOCS total scores and symptom severity percentage reductions corresponding to CGI-S non-remission status at 1-year, 2-year, and 3-year follow-up are provided in Tables 2 and 3. Sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and accuracy are listed for each cut-off at the different time points.

According to the Youden Index, the optimal post-treatment CY-BOCS total score cutoffs for the 1-year follow-up were: 11 with a PPV of 0.43 and an NPV of 0.28. For the 2-year follow-up, the optimal cutoff was estimated to be 12 with a PPV of 0.63 and an NPV of 0.27. The optimal cut-off for the 3-year follow-up was 5, corresponding to a PPV of 0.19 and an NPV of 0.70.

For percentage reduction during treatment, the optimal post-treatment cut-off according to the Youden Index for the 1-year follow-up was $\geq 50\%$ with a PPV of 0.67 and an NPV of 0.23. For the 2-year follow-up point, the optimal post-treatment cut-off was $\geq 80\%$ with a PPV of 0.19 and an NPV of 0.69. Finally, the 3-year follow-up optimal post-treatment cut-off was suggested to be $\geq 70\%$ with a PPV of 0.32 and an NPV of 0.57.

3.4. Post hoc analyses: the influence of potential predictors of non-remission

For the one-year follow-up, logistic regression showed an interaction effect between age and post-treatment severity reflecting a higher risk of non-remission at follow-up in cases of higher severity for older patients. However, this interaction was not significant when child age was analyzed as a binary variable reflecting age groups 7–11 and 12–17 years. No significant main or interaction effects were found for the variables: gender, comorbid internalizing disorder, comorbid externalizing disorder, tic disorder, and treatment step (a) Step 1 CBT, (b) Step 2 CBT, or (c) Step 2 SSRI). For the two- and three-year follow-up, there were no main or interaction effects of the variables.

4. Discussion

The present study evaluated the predictive value of post-treatment symptom severity for long-term remission status in pediatric OCD patients. It was found that the overall discriminative ability of both the CY-BOCS total score and percentage symptom reductions was modest. Not surprisingly, the best classification ability was found for the one-year follow-up. Specifically, the results suggested a 70% chance of predicting true remission status at the one-year follow-up with the post-treatment CY-BOCS total score; however, this chance decreased to 65% and 61% for the two- and three-year follow-ups, respectively. The discriminative value of symptom severity reductions during treatment was even lower, and the AUC for the three-year follow-up was not significantly different from a 50/50 chance of prediction. The stronger predictive value of post-treatment status for the one-year follow-up compared to the three-year follow-up could partly be explained by the fact that the last assessment for many Step 2 patients was closer in time than one year to the one-year follow-up assessment. Further, the offering of booster sessions during the first year after treatment may have had a stabilizing effect on some patients (Højgaard et al., 2017).

It cannot be ruled out that post-treatment status is of prognostic

value for some patients. The mean symptom severity/reduction for a whole sample is covering different kinds of participants. Thus an unknown number of patients may show symptom reductions by chance during the time period they are undergoing treatment. Such patients may or may not be at risk of relapse. On the other hand, some patients may present with clinical symptom severity levels after treatment, but get rid of their symptoms over time, with or without the use of therapeutic techniques/medicine.

Apparently, after two or three years, other factors than post-treatment symptom severity are more relevant for remission status. It should be investigated which indicators, or group of indicators, are more reliable in a long-term perspective. From the present study, it seems that gender, pre-treatment comorbidity, and treatment step did not predict non-remission and did not affect the association between post-treatment severity and long-term remission. However, for the one-year follow-up specifically, the analyses suggest that higher post-treatment symptom severity is a higher risk factor for non-remission at follow-up with for older patients. This is in line with previous treatment results showing that younger age predicted a better treatment outcome after Step 1 (Torp et al., 2015a). It may be that younger patients with OCD symptoms are more amenable to change, also after end of treatment than older patients. Yet, as this was not true for the two- and three-year follow-up, the finding should be interpreted with caution. Based on clinical experience and previous research, relevant factors to investigate further could be load and type of comorbidity (Allegrini et al., 2020; Rosa-Alcázar et al., 2021), the patient's level of social support (Palardy et al., 2018), compliance with homework exercises (Anand et al., 2011), ability to expand experiences to other areas than those addressed during treatment (Craske et al., 2014), insight (Catapano et al., 2010; Selles et al., 2018), family dynamics (Rosa-Alcázar et al., 2021), parental psychopathology (Wadkins and Gordon, 2019) etc. Some of these indicators may be difficult to quantify and may be better obtained by clinical judgement. Additionally, qualitative research investigating which factors patients find most important for their long-term outcome could guide clinical decision-making and larger-scale studies.

It is also a possibility that OCD symptom severity is highly important for long-term OCD remission, but that the clinical CY-BOCS symptom severity ratings do not capture all the relevant features regarding estimation of severity. It has been suggested to include avoidance in OCD severity ratings as symptom severity may be artificially low in patients with high levels of avoidance (Storch et al., 2010b). This has been supported by studies suggesting avoidance to be associated with symptom severity, treatment response and long-term outcome (Jensen et al., 2020b; Nissen and Parner, 2018; Selles et al., 2020; Wheaton et al., 2018). Further, avoidance has been included in severity ratings in the revised version of Y-BOCS (Storch et al., 2010b) as well as in patient-rated severity ratings such as the Dimensional Obsessive-Compulsive Scale (DOCS-SF) (Abramowitz et al., 2010). Resistance to obsessions and compulsions has also been put forward as a factor which may not reflect symptom severity (Storch et al., 2010b; Woody et al., 1995). Conceptually, resistance may show resemblance to insight in the sense that it reflects the patient's recognition of their symptoms as being OCD. However, it could also reflect a deeply troubled patient who is undesirably attentive toward the obsessions. This has been put forward as one of the core features of OCD (Frost and Steketee, 2002).

Another explanation for the modest ability of post-treatment CY-BOCS symptom severity in discriminating remission and non-remission during follow-up is the fact that OCD has been described as a waxing and

Tables 3

a-c. Signal detection analyses of long-term non-remission status prediction: Post-treatment symptom severity percentage reduction.

Table 3a. 1 year follow-up.						
Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Cohen's kappa
100%	100.00%	0.00%	8.16%	100.00%	26.34%	0.00%
≥95%	91.84%	16.06%	8.16%	83.95%	36.02%	4.57%
≥90%	91.84%	23.36%	10.20%	76.65%	41.40%	9.14%
≥85%	89.80%	26.28%	14.28%	73.73%	43.01%	9.87%
≥80%	85.71%	29.93%	14.28%	70.08%	44.62%	9.88%
≥75%	85.71%	35.04%	20.40%	64.97%	48.39%	13.50%
≥70%	79.59%	43.80%	30.60%	56.21%	53.23%	16.25%
≥65%	69.39%	49.64%	34.68%	50.37%	54.84%	14.05%
≥60%	65.31%	59.12%	38.76%	40.88%	60.75%	19.46%
≥55%	61.22%	70.80%	51.00%	29.20%	68.28%	28.15%
≥50%	48.98%	76.64%	67.33%	23.36%	69.35%	24.50%
≥45%	32.65%	81.02%	73.45%	18.98%	68.28%	14.33%
≥40%	26.53%	87.59%	79.57%	12.41%	71.51%	16.13%
≥35%	20.41%	90.51%	83.65%	9.49%	72.04%	13.16%
≥30%	16.33%	95.62%	87.73%	4.38%	74.73%	15.50%
≥25%	12.24%	96.35%	93.85%	3.65%	74.19%	11.45%
≥20%	6.12%	97.08%	97.93%	2.92%	73.12%	4.42%
≥15%	2.04%	97.81%	99.97%	2.19%	72.58%	<0.00%
≥10%	0.00%	98.54%	99.97%	1.46%	72.58%	<0.00%
≥5%	0.00%	99.27%	99.97%	0.73%	73.12%	<0.00%
<5%	0.00%	100.00%	100.00%	0.00%	73.66%	0.00%

Table 3b. 2 year follow-up.						
Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Cohen's kappa
100%	100.00%	0.00%	4.65%	100.00%	25.75%	0.00%
≥95%	95.35%	16.94%	6.98%	83.08%	37.13%	6.95%
≥90%	93.02%	25.00%	6.98%	75.02%	42.51%	10.71%
≥85%	93.02%	28.23%	13.96%	71.79%	44.91%	12.85%
≥80%	86.05%	31.45%	18.61%	68.56%	45.51%	10.94%
≥75%	81.40%	33.87%	23.26%	66.14%	46.11%	9.77%
≥70%	76.74%	43.55%	32.56%	56.46%	52.10%	13.94%
≥65%	67.44%	50.00%	34.89%	50.01%	54.49%	12.78%
≥60%	65.12%	56.45%	48.84%	43.56%	58.68%	16.64%
≥55%	51.16%	64.52%	55.82%	35.50%	61.08%	13.35%
≥50%	44.19%	71.77%	69.77%	28.24%	64.67%	14.73%
≥45%	30.23%	77.42%	76.75%	22.59%	65.27%	7.77%
≥40%	23.26%	86.29%	88.38%	13.72%	70.06%	10.87%
≥35%	11.63%	87.10%	95.36%	12.91%	67.66%	<0.00%
≥30%	4.65%	91.94%	95.36%	8.07%	69.46%	<0.00%
≥25%	4.65%	93.55%	97.69%	6.46%	70.66%	<0.00%
≥20%	2.33%	95.97%	97.69%	4.04%	71.86%	<0.00%
≥15%	2.33%	97.58%	100.00%	2.43%	73.05%	<0.00%
≥10%	0.00%	98.39%	100.00%	1.62%	73.05%	<0.00%
≥5%	0.00%	99.19%	100.00%	0.81%	73.65%	<0.00%
<5%	0.00%	100.00%	100.00%	0.00%	74.25%	0.00%

Table 3c. 3 year follow-up.						
Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Cohen's kappa
100%	100.00%	0.00%	8.11%	100.00%	22.29%	0.00%
≥95%	91.89%	17.05%	10.81%	82.98%	33.73%	4.47%
≥90%	89.19%	24.03%	10.81%	76.00%	38.55%	6.94%
≥85%	89.19%	27.13%	13.51%	72.90%	40.96%	8.74%
≥80%	86.49%	31.01%	16.21%	69.02%	43.37%	9.67%
≥75%	83.78%	34.11%	21.62%	65.92%	45.18%	10.16%
≥70%	78.38%	42.64%	32.43%	57.39%	50.60%	12.84%
≥65%	67.57%	48.06%	37.84%	51.96%	52.41%	10.21%
≥60%	62.16%	51.94%	54.06%	48.08%	54.22%	9.64%
≥55%	45.95%	59.69%	62.17%	40.33%	56.63%	4.31%
≥50%	37.84%	68.22%	70.28%	31.80%	61.45%	5.16%
≥45%	29.73%	75.97%	81.09%	24.05%	65.66%	5.44%
≥40%	18.92%	82.95%	86.50%	17.07%	68.67%	2.02%
≥35%	13.51%	86.82%	89.20%	13.19%	70.48%	0.39%
≥30%	10.81%	93.02%	94.61%	6.99%	74.70%	4.99%
≥25%	5.41%	93.80%	97.31%	6.21%	74.10%	<0.00%
≥20%	2.70%	95.35%	100.00%	4.66%	74.70%	<0.00%
≥15%	0.00%	96.90%	100.00%	3.11%	75.30%	<0.00%
≥10%	0.00%	98.45%	100.00%	1.56%	76.51%	<0.00%
≥5%	0.00%	99.22%	100.00%	0.78%	77.11%	<0.00%
<5%	0.00%	100.00%	100.00%	0.00%	77.71%	0.00%

Sensitivity is the proportion of patients classified as non-remitters (according to a CGI-S score of <2) during follow-up which is captured as such by the post-treatment assessment (above the specific cut-off score).

Specificity is the proportion of follow-up remitters (CGI-S <2) classified as such by the post-treatment assessment (above the specific cut-off score).

Positive and negative predictive values refer to the rate of false positive non-remitters and false negative non-remitters. Accuracy refers to the proportion of correctly classified participants. Cohen's kappa is the chance-corrected agreement.

waning disorder by nature with fluctuations in symptom severity over time (Højgaard et al., 2017; Poyraz et al., 2015). In the present sample, it has been shown how patients (who initially responded well to Step 1 CBT) transition between responder status, remission status, and relapse even during the first year of follow-up (Højgaard et al., 2017). Such fluctuations could explain the limited discriminative value of post-treatment symptom severity for long-term remission for some patients. Further, a consequence of this could be that the follow-up assessments, theoretically, may have a random touch to them. If the instructions for the CY-BOCS/CGI-S have been followed strictly, only the symptom severity during the last week is reported (Scahill et al., 1997). It is probably too ambitious to include several ratings per follow-up assessments; however, it could be explicitly stated in the instructions for raters doing follow-up assessments that they should rate the severity for the last month or two rather than for the last week. This has also been suggested by Farhat et al. (2021), even for the post-treatment assessment.

As regards the reported 'optimal cut-offs', they should be interpreted with caution, especially having concluded that the overall predictive value is low. It is, however, worth a note that the optimal cut-off for one-year remission status (CY-BOCS total score <11), which had acceptable predictive value, is close to the cut-offs corresponding to remission at post-treatment (CY-BOCS total score <11 and <12) (Skarphedinsson et al., 2017; Storch et al., 2010a). It is more a clinical decision than a statistical decision which parameters are most important when evaluating an optimal cut-off. Lewin et al. (2011) have suggested that the cost of false positives and false negatives is often weighted differently in clinical practice and in clinical trials. They state that when determining remission status in clinical practice, it is often considered more costly to the system and to the patient if too many patients are classified as false positives (Lewin et al., 2011). Yet, politicians and hospital managers may have the opposite opinion.

Accuracy is often highlighted as an important factor in the determination of optimal cut-off scores and is also provided in the present study in Tables 2 and 3. However, in cases like ours this factor can be somewhat misleading as there are far more remitters during follow-up than non-remitters. This means that a fairly high rate of accuracy could be obtained by simply (erroneously) classifying all patients as remitters as that would correctly classify all the true remitters. Yet, that would be at the expense of ignoring the false positives.

These findings have implications for both research and daily clinical practice. Implications for daily clinical practice could be monitoring of patients for a longer duration after treatment to capture patients at risk of relapse and/or remaining symptoms. Patient-rated quality of life could also be an easy-to-administer post-treatment indicator of patients in need of further treatment and/or other initiatives (Jensen et al., 2021). A study on the current sample has suggested that limited long-term treatment responders showed lower levels of quality of life during and after treatment compared to patients with better long-term treatment results and a norm group (Jensen et al., 2021). This is in line with other research suggesting quality of life as a good indicator of need for further treatment (Hertenstein et al., 2013; Norberg et al., 2008).

In evaluations of clinical trials, the post-treatment levels of symptom severity and/or levels of symptom reductions are still often the main outcome criteria in the evaluation of treatment effect. Even though this may demonstrate the treatment's immediate effect, this outcome does not offer evidence of long-lasting effects. The inclusion of long-term assessments of patients, which is increasingly provided in treatment studies (e.g. Barrett et al., 2005; Mancebo et al., 2014; Thomsen et al., 2013) is an upgrade from only providing post-treatment results.

4.1. Strengths and limitations

The main strengths of this study include a relatively large sample size as well as the stepped-care design of the study. The inclusion of post-treatment assessment during stepped-care treatment ensured a more accurate classification estimation than if we had only included assessment scores after Step 1 for all patients. Consequently, there was a time difference among the patients from post-treatment to the follow-up points which could have increased the classification quality artificially for at least the one-year follow-up point. One of the main limitations of the study is attrition. Since there was a high rate of Step 1 non-responders among the dropouts during follow-up, it is likely that post-treatment assessment would have displayed more variation if it was possible to include the dropouts. Participants with missing data during follow-up were associated with higher pre-treatment strains. This could indicate that more patients could be classified as non-remitters during follow-up if dropouts were included in the analyses and perhaps strengthen the classification value and accuracy of post-treatment assessment. Further, it is a limitation that we have incomplete records of treatment received during the second and third year of follow-up. Finally, it could be discussed to what extent CGI-S reflects the 'true' remitter status of a patient.

4.2. Conclusion

Post-treatment OCD symptom severity assessment of pediatric patients has limited discriminative value for the long-term remission status at follow-up, and the discriminative ability seems to fade over time. This indicates that it is not possible to infer much about the long-term effect of treatment based on post-treatment symptom severity status in pediatric OCD patients. Clinical trials should include long-term assessments to evaluate the possible prolonged effect of the treatment as well as assessment of factors other than symptom severity. Further research on critical post-treatment factors of long-term prognostic value for the patient is warranted.

Declaration of Competing Interest

All authors declare that they have no conflicts of interests.

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References

- Abramowitz, J.S., Deacon, B.J., Olatunji, B.O., Wheaton, M.G., Berman, N.C., Losardo, D., Hale, L.R., 2010. Assessment of obsessive-compulsive symptom dimensions: development and evaluation of the dimensional obsessive-compulsive scale. *Psychol. Assess.* 22 (1), 180–198. <https://doi.org/10.1037/a0018260>.
- Allegrini, A.G., Cheesman, R., Rimfeld, K., Selzam, S., Pingault, J.B., Eley, T.C., Plomin, R., 2020. The p factor: genetic analyses support a general dimension of psychopathology in childhood and adolescence. *J. Child Psychol. Psychiatry* 61 (1), 30–39. <https://doi.org/10.1111/jcpp.13113>.
- Anand, N., Sudhir, P.M., Math, S.B., Thennarasu, K., Janardhan Reddy, Y.C., 2011. Cognitive behavior therapy in medication non-responders with obsessive-compulsive disorder: a prospective 1-year follow-up study. *J. Anxiety Disord.* 25 (7), 939–945. <https://doi.org/10.1016/j.janxdis.2011.05.007>.

- Barrett, P., Farrell, L., Dadds, M., Boulter, N., 2005. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: long-term follow-up and predictors of outcome. *J. Am. Acad. Child Adolesc. Psychiatry* 44 (10), 1005–1014. <https://doi.org/10.1097/01.chi.0000172555.26349.94>.
- Catapano, F., Perris, F., Fabrazzo, M., Cioffi, V., Giacco, D., De Santis, V., Maj, M., 2010. Obsessive-compulsive disorder with poor insight: a three-year prospective study. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 34 (2), 323–330. <https://doi.org/10.1016/j.pnpbp.2009.12.007>.
- Cohen, J., 1960. A coefficient of agreement for nominal scales. *Educ. Psychol. Meas* 20 (1), 37–46. <https://doi.org/10.1177/001316446002000104>.
- Craske, M.G., Treanor, M., Conway, C.C., Zbozinek, T., Vervliet, B., 2014. Maximizing exposure therapy: an inhibitory learning approach. *Behav. Res. Ther.* 58, 10–23. <https://doi.org/10.1016/j.brat.2014.04.006>.
- 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. *J. Clin. Psychiatry* 74 (03), 233–239. <https://doi.org/10.4088/JCP.12m07657>.
- Farhat, L.C., Vattimo, E.F.Q., Ramakrishnan, D., Levine, J.L.S., Johnson, J.A., Artukoglu, B.B., Bloch, M.H., 2021. Systematic review and meta-analysis: an empirical approach to defining treatment response and remission in pediatric obsessive-compulsive disorder. *J. Am. Acad. Child Adolesc. Psychiatry*. <https://doi.org/10.1016/j.jaac.2021.05.027>.
- Frost, R.O., Steketee, G., 2002. *Cognitive Approaches to Obsessions and Compulsions: theory, assessment, and Treatment*. Pergamon.
- Geller, D.A., March, J., 2012. Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 51 (1), 98–113. <https://doi.org/10.1016/j.jaac.2011.09.019>.
- Guy, W., 1976. *Clinical global impressions*. In: Guy, W. (Ed.), *ECDEU Assessment Manual For Psychopharmacology*. National Institute of Mental Health, Rockville, MD, pp. 218–222.
- Hajian-Tilaki, K., 2018. The choice of methods in determining the optimal cut-off value for quantitative diagnostic test evaluation. *Stat. Methods Med. Res.* 27 (8), 2374–2383. <https://doi.org/10.1177/0962280216680383>.
- Hertenstein, E., Thiel, N., Herbst, N., Freyer, T., Nissen, C., Külz, A.K., Voderholzer, U., 2013. Quality of life changes following inpatient and outpatient treatment in obsessive-compulsive disorder: a study with 12 months follow-up. *Ann Gen Psychiatry* 12 (1), 4. <https://doi.org/10.1186/1744-859X-12-4>.
- Heyman, I., Fombonne, E., Simmons, H., Ford, T., Meltzer, H., Goodman, R., 2001. Prevalence of obsessive-compulsive disorder in the British nationwide survey of child mental health. *Br. J. Psychiatry* 179 (4), 324–329. <https://doi.org/10.1192/bjp.179.4.324>.
- Højgaard, D.R.M.A., Hybel, K.A., Ivarsson, T., Skarphedinsson, G., Becker Nissen, J., Weidle, B., Thomsen, P.H., 2017. One-Year Outcome for Responders of Cognitive-Behavioral Therapy for Pediatric Obsessive-Compulsive Disorder. *Journal of the American Academy of Child & Adolescent Psychiatry* 56 (11), 940–948. <https://doi.org/10.1016/j.jaac.2017.09.002>.
- Hollander, E., Zohar, J., 2004. Beyond refractory obsessions and anxiety states: toward remission. *J. Clin. Psychiatry* 65 (Suppl 1), 3–5. Retrieved from. <http://www.ncbi.nlm.nih.gov/pubmed/15554781>.
- Hosmer, D.W., Lemeshow, S., 2000. *Applied Logistic Regression*, 2nd Ed. <https://doi.org/10.1002/0471722146>.
- Jensen, S., Højgaard, D.R.M.A., Hybel, K.A., Mortensen, E.L., Skarphedinsson, G., Melin, K., Thomsen, P.H., 2020a. Distinct trajectories of long-term symptom severity in pediatric obsessive-compulsive disorder during and after stepped-care treatment. *J. Child Psychol. Psychiatry* 61 (9), 969–978. <https://doi.org/10.1111/jcpp.13155>.
- Jensen, S., Hybel, K.A., Højgaard, D.R.M.A., Nissen, J.B., Skarphedinsson, G., Torp, N.C., Thomsen, P.H., 2020b. The children's yale-brown obsessive-compulsive scale's auxiliary items: long-term outcome. *J. Obsessive-Compuls. Related Disord.* 27, 100589. <https://doi.org/10.1016/j.jocrd.2020.100589>.
- Jensen, S., Hybel, K.A., Højgaard, D.R.M.A., Nissen, J.B., Weidle, B., Ivarsson, T., Thomsen, P.H., 2021. Quality of life in pediatric patients with obsessive-compulsive disorder during and 3 years after stepped-care treatment. *Eur. Child Adolesc. Psychiatry* 1, 3. <https://doi.org/10.1007/s00787-021-01775-w>.
- Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Ryan, N., 1997. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *J. Am. Acad. Child Adolesc. Psychiatry* 36 (7), 980–988. <https://doi.org/10.1097/00004583-199707000-00021>.
- Lewin, A.B., De Nadai, A.S., Park, J., Goodman, W.K., Murphy, T.K., Storch, E.A., 2011. Refining clinical judgment of treatment outcome in obsessive-compulsive disorder. *Psychiatry Res.* 185 (3), 394–401. <https://doi.org/10.1016/j.psychres.2010.08.021>.
- Lewin, A.B., Piacentini, J., 2010. Evidence-based assessment of child obsessive compulsive disorder: recommendations for clinical practice and treatment research. *Child Youth Care Forum* 39 (2), 73–89. <https://doi.org/10.1007/s10566-009-9092-8>.
- Liu, J., Cui, Y., Yu, L., Wen, F., Wang, F., Yan, J., Li, Y., 2021. Long-term outcome of pediatric obsessive-compulsive disorder: a meta-analysis. *J. Child Adolesc. Psychopharmacol.* 31 (2), 95–101. <https://doi.org/10.1089/cap.2020.0051>.
- Mancebo, M.C., Boisseau, C.L., Garnaat, S.L., Eisen, J.L., Greenberg, B.D., Sibrava, N.J., Rasmussen, S.A., 2014. Long-term course of pediatric obsessive-compulsive disorder: 3 years of prospective follow-up. *Compr. Psychiatry* 55, 1498–1504. <https://doi.org/10.1016/j.comppsy.2014.04.010>.
- Mandrekar, J.N., 2010. Receiver operating characteristic curve in diagnostic test assessment. *J. Thorac. Oncol.* 5 (9), 1315–1316. <https://doi.org/10.1097/JTO.0b013e3181ec173d>.
- March, J.S., Mulle, K., Foa, E.B., and Kozak, M.J. (2000). *Treatment of pediatric obsessive-compulsive disorder cognitive behavior therapy treatment manual*. *Unpublished Manuscript*.
- Mataix-Cols, D., de la Cruz, L.F., Nordstletten, A.E., Lenhard, F., Isomura, K., Simpson, H. B., 2016. Towards an international expert consensus for defining treatment response, remission, recovery and relapse in obsessive-compulsive disorder. *World Psychiatry* 15 (1), 80–81. <https://doi.org/10.1002/wps.20299>.
- Melin, K., Skarphedinsson, G., Thomsen, P.H., Weidle, B., Torp, N.C., Valderhaug, R., Ivarsson, T., 2020. Treatment gains are sustainable in pediatric obsessive-compulsive disorder: three-year follow-up from the NordLOTS. *J. Am. Acad. Child Adolesc. Psychiatry* 59 (2), 244–253. <https://doi.org/10.1016/j.jaac.2019.01.010>.
- Nissen, J.B., Parner, E., 2018. The importance of insight, avoidance behavior, not-just-right perception and personality traits in pediatric obsessive-compulsive disorder (OCD): a naturalistic clinical study. *Nord. J. Psychiatry* 72 (7), 489–496. <https://doi.org/10.1080/08039488.2018.1486454>.
- Norberg, M.M., Calamari, J.E., Cohen, R.J., Riemann, B.C., 2008. Quality of life in obsessive-compulsive disorder: an evaluation of impairment and a preliminary analysis of the ameliorating effects of treatment. *Depress. Anxiety* 25 (3), 248–259. <https://doi.org/10.1002/da.20298>.
- Öst, L.-G., Riise, E.N., Wergeland, G.J., Hansen, B., Kvale, G., 2016. Cognitive behavioral and pharmacological treatments of OCD in children: a systematic review and meta-analysis. *J. Anxiety Disord.* 43, 58–69. <https://doi.org/10.1016/j.janxdis.2016.08.003>.
- Palardy, V., El-Baalbaki, G., Fredette, C., Rizkallah, E., Guay, S., 2018. Social support and symptom severity among patients with obsessive-compulsive disorder or panic disorder with agoraphobia: a systematic review. *Eur. J. Psychol.* 14 (1), 254–286. <https://doi.org/10.5964/ejop.v14i1.1252>.
- Piacentini, J., Langley, A., and Roblek, T. (2007a). *It's Only a False Alarm*. <https://doi.org/10.1093/med/psych/9780195310528.001.0001>.
- Piacentini, J., Peris, T.S., Bergman, R.L., Chang, S., Jaffer, M., 2007b. BRIEF REPORT: functional impairment in Childhood OCD: development and Psychometrics Properties of the Child Obsessive-Compulsive Impact Scale-Revised (COIS-R). *J. Clin. Child Adolesc. Psychol.* 36 (4), 645–653. <https://doi.org/10.1080/15374410701662790>.
- Poyraz, C.A., Turan, Ş., Sağlam, N.G.U., Batun, G.Ç., Yassa, A., Duran, A., 2015. Factors associated with the duration of untreated illness among patients with obsessive compulsive disorder. *Compr. Psychiatry* 58, 88–93. <https://doi.org/10.1016/j.comppsy.2014.12.019>.
- Rosa-Alcázar, Á., Rosa-Alcázar, A.I., Parada-Navas, J.L., Olivares-Olivares, P.J., Rosa-Alcázar, E., 2021. Predictors of parental accommodation and response treatment in young children with obsessive-compulsive disorder. *Front. Psychiatry* 12. <https://doi.org/10.3389/fpsy.2021.737062>.
- Scahill, L., Riddle, M.A., McSwiggan-Hardin, M., Ort, S.I., King, R.A., Goodman, W.K., Leckman, J.F., 1997. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *J. Am. Acad. Child Adolesc. Psychiatry* 36 (6), 844–852. <https://doi.org/10.1097/00004583-199706000-00023>.
- Selles, R.R., Højgaard, D.R.M.A., Ivarsson, T., Thomsen, P.H., McBride, N.M., Storch, E. A., Stewart, S.E., 2020. Avoidance, insight, impairment recognition concordance, and cognitive-behavioral therapy outcomes in pediatric obsessive-compulsive disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 59 (5), 650–659. <https://doi.org/10.1016/j.jaac.2019.05.030> e2.
- Selles, R.R., Højgaard, D.R.M.A., Ivarsson, T., Thomsen, P.H., McBride, N., Storch, E.A., Stewart, S.E., 2018. Symptom insight in pediatric obsessive-compulsive disorder: outcomes of an international aggregated cross-sectional sample. *J. Am. Acad. Child Adolesc. Psychiatry* 57 (8), 615–619. <https://doi.org/10.1016/j.jaac.2018.04.012> e5.
- Skarphedinsson, G., De Nadai, A.S., Storch, E.A., Lewin, A.B., Ivarsson, T., 2017. Defining cognitive-behavior therapy response and remission in pediatric OCD: a signal detection analysis of the Children's Yale-Brown Obsessive Compulsive Scale. *Eur. Child Adolesc. Psychiatry* 26 (1), 47–55. <https://doi.org/10.1007/s00787-016-0863-0>.
- Skarphedinsson, G., Weidle, B., Ivarsson, T., 2015a. Sertraline treatment of nonresponders to extended cognitive-behavior therapy in pediatric obsessive-compulsive disorder. *J. Child Adolesc. Psychopharmacol.* 25 (7), 574–579. <https://doi.org/10.1089/cap.2015.0041>.
- Skarphedinsson, G., Weidle, B., Thomsen, P.H., Dahl, K., Torp, N.C., Nissen, J.B., Ivarsson, T., 2015b. Continued cognitive-behavior therapy versus sertraline for children and adolescents with obsessive-compulsive disorder that were non-responders to cognitive-behavior therapy: a randomized controlled trial. *Eur. Child Adolesc. Psychiatry* 24 (5), 591–602. <https://doi.org/10.1007/s00787-014-0613-0>.
- Skoog, G., Skoog, I., 1999. A 40-year follow-up of patients with obsessive-compulsive disorder. *Arch. Gen. Psychiatry* 56 (2), 121–127. <https://doi.org/10.1001/archpsyc.56.2.121>.
- Stahl, S.M., 1999. *Why Settle for Silver, When You Can Go for Gold? Response vs. Recovery as the Goal of Antidepressant Therapy*. In *J. Clin. Psychiatry* 60.
- StataCorp, 2021. *Stata Statistical Software: Release 17*. StataCorp LLC, College Station, TX.
- Stewart, S.E., Geller, D.A., Jenike, M., Pauls, D., Shaw, D., Mullin, B., Faraone, S.V., 2004. Long-term outcome of pediatric obsessive-compulsive disorder: a meta-analysis and qualitative review of the literature. *Acta Psychiatr. Scand.* 110 (1), 4–13. <https://doi.org/10.1111/j.1600-0447.2004.00302.x>.
- Storch, E.A., Lewin, A.B., De Nadai, A.S., Murphy, T.K., 2010a. Defining treatment response and remission in obsessive-compulsive disorder: a signal detection analysis of the children's yale-brown obsessive compulsive scale. *J. Am. Acad. Child Adolesc. Psychiatry* 49 (7), 708–717. <https://doi.org/10.1016/j.jaac.2010.04.005>.

- Storch, E.A., Murphy, T.K., Geffken, G.R., Soto, O., Sajid, M., Allen, P., Goodman, W.K., 2004. Psychometric evaluation of the Children's Yale-Brown Obsessive-Compulsive Scale. *Psychiatry Res.* 129 (1), 91–98. <https://doi.org/10.1016/j.psychres.2004.06.009>.
- Storch, E.A., Rasmussen, S.A., Price, L.H., Larson, M.J., Murphy, T.K., Goodman, W.K., 2010b. Development and psychometric evaluation of the Yale-Brown Obsessive-Compulsive Scale—Second Edition. *Psychol. Assess.* 22 (2), 223–232. <https://doi.org/10.1037/a0018492>.
- Swets, J., Pickett, R., 1982. *Evaluation of Diagnostic Systems: Methods from Signal Detection Theory*. Academic Press, New York.
- Thomsen, P.H., Torp, N.C., Dahl, K., Christensen, K., Englyst, I., Melin, K.H., Ivarsson, T., 2013. The Nordic long-term OCD treatment study (NordLOTS): rationale, design, and methods. *Child Adolesc. Psychiatry Ment. Health* 7 (1), 41. <https://doi.org/10.1186/1753-2000-7-41>.
- Thomsen, P.H., Weidle, B., 2015. *Behandling Af Børn Og Unge Med OCD: En Praksismanual*. Retrieved from. <https://hansreitzel.dk/products/behandling-af-born-og-unge-med-ocd-bog-38922-9788741261294>.
- Tolin, D.F., Abramowitz, J.S., Diefenbach, G.J., 2005. Defining response in clinical trials for obsessive-compulsive disorder: a signal detection analysis of the Yale-Brown Obsessive Compulsive Scale. *J. Clin. Psychiatry* 66 (12), 1549–1557. <https://doi.org/10.4088/JCP.v66n1209>.
- Torp, N.C., Dahl, K., Skarphedinnsson, G., Compton, S., Thomsen, P.H., Weidle, B., Ivarsson, T., 2015a. Predictors associated with improved cognitive-behavioral therapy outcome in pediatric obsessive-compulsive disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 54 (3), 200–207. <https://doi.org/10.1016/j.jaac.2014.12.007> e1.
- Torp, N.C., Dahl, K., Skarphedinnsson, G., Thomsen, P.H., Valderhaug, R., Weidle, B., Ivarsson, T., 2015b. Effectiveness of cognitive behavior treatment for pediatric obsessive-compulsive disorder: acute outcomes from the Nordic Long-term OCD Treatment Study (NordLOTS). *Behav. Res. Ther.* 64, 15–23. <https://doi.org/10.1016/j.brat.2014.11.005>.
- Wadkins, M.J., Gordon, E., 2019. Comorbidity, parental psychopathology, and accommodation in the treatment of pediatric obsessive-compulsive disorder: a case study. *J. Cogn. Psychother* 33 (3), 242–255. <https://doi.org/10.1891/0889-8391.33.3.242>.
- Weidle, B., Jozefiak, T., Ivarsson, T., Thomsen, P.H., 2014. Quality of life in children with OCD with and without comorbidity. *Health Qual. Life Outcomes* 12 (1), 152. <https://doi.org/10.1186/s12955-014-0152-x>.
- Wheaton, M.G., Gershkovich, M., Gallagher, T., Foa, E.B., Simpson, H.B., 2018. Behavioral avoidance predicts treatment outcome with exposure and response prevention for obsessive-compulsive disorder. *Depress. Anxiety* 35 (3), 256–263. <https://doi.org/10.1002/da.22720>.
- Woody, S.R., Steketee, G., Chambless, D.L., 1995. Reliability and validity of the yale-brown obsessive-compulsive scale. *Behav. Res. Ther.* 33 (5), 597–605. [https://doi.org/10.1016/0005-7967\(94\)00076-V](https://doi.org/10.1016/0005-7967(94)00076-V).
- Youden, W.J., 1950. Index for rating diagnostic tests. *Cancer* 3 (1), 32–35. [https://doi.org/10.1002/1097-0142\(1950\)3:1<32::AID-CNCR2820030106>3.0.CO;2-3](https://doi.org/10.1002/1097-0142(1950)3:1<32::AID-CNCR2820030106>3.0.CO;2-3).
- Zohar, A.H., 1999. The epidemiology of obsessive-compulsive disorder in children and adolescents. *Child Adolesc. Psychiatr. Clin. N. Am.* 8 (3), 445–460. Retrieved from. <http://www.ncbi.nlm.nih.gov/pubmed/10442225>.