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Promoting OCD WEllness and resilience (POWER) study: Rationale, design, and methods

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Abstract

Obsessive-compulsive disorder (OCD) affects 1–2% of children and is associated with functional impairment and diminished quality of life. Several treatments are efficacious: cognitive behavioral therapy (CBT) with exposure and response prevention, serotonin reuptake inhibitor (SRI) monotherapy, and combined treatment (SRI + CBT). Expert clinician-informed practice parameters suggest that youth with mild to moderate OCD should be treated initially with CBT yet SRIs are frequently employed as the first-line intervention or in combination with psychotherapy in applied practice. Empirical data to guide SRI discontinuation in pediatric OCD are very limited. This study, Promoting OCD Wellness and Resiliency (POWER), aims to address this gap through a two phase, double-blinded, placebo-controlled, randomized controlled non-inferiority trial with the purpose of evaluating whether youth with OCD on an SRI can discontinue their medication after successful CBT augmentation and maintain wellness for a period of 24 weeks during which they receive maintenance CBT that models standard-of-care. In this paper we describe the rationale and methodological design of the POWER study.

Keywords

Obsessive-compulsive disorder; Serotonin reuptake inhibitors; Cognitive behavioral therapy; Randomized controlled trial; Children; Youth; Pediatric

1. Introduction

Obsessive-compulsive disorder (OCD) is a public health problem among children and adolescents and is relatively common, distressing, and interfering (Piacentini et al., 2007). Over 50% of adults with OCD had symptom onset in childhood (Karno et al., 1988; Keeley et al., 2007). First-line treatments for OCD are cognitive behavioral therapy (CBT) with exposure and response prevention (EX/RP), serotonin reuptake inhibitors (SRIs), or the combination (CBT + SRIs) (Alaghband-Rad and Hakimshooshtary, 2009; Bandelow et al., 2008; Geller et al., 2003; Zohar, 2008). Approximately 75–80% of youth respond to CBT, with 40–50% achieving remission (McGuire et al., 2015). Response rates to SRIs are 50–60%, with about 20–35% of youth achieving remission (Pediatric, O.C.D.T.S.T., 2004).

Practice guidelines recommend CBT alone as the first-line treatment for mild to moderate OCD and combined with pharmacotherapy for more severe cases (Geller et al., 2012). Despite the efficacy of CBT and practice guidelines, dissemination lags and many youth are started on SRIs either alone or with non-CBT treatments (e.g., supportive therapy). Potential reasons for this include limited EX/RP dissemination, lack of awareness among providers regarding the efficacy of EX/RP, and upfront costs of EX/RP, to name a few.

Although efficacious, generally safe and well tolerated, SRI medications are not without concern. First, transitory or minor side effects of these medications are relatively common (Cascade et al., 2009; Jane Garland et al., 2016) and include weight gain, sleep disturbances, headaches, dizziness, gastrointestinal issues, and sexual dysfunction (Strawn et al., 2018). Clomipramine can cause more severe side effects such as cardiac toxicity and QTc prolongation (Hamill Skoch et al., 2021; Leonard et al., 1995). Rare side effects of SRIs include syndrome of inappropriate antidiuretic hormone secretion and lowered seizure threshold (Gordon and Melvin, 2013). Collecively, these adverse effects lead to medication nonadherence and impact quality of life. Second, one of the more concerning adverse effects of SRIs is induction of behavioral activation symptoms such as irritability, restlessness, and emotional lability (Goodman et al., 2007). Third, parent and child preference data suggest that each may prefer to have either no exposure or more time-limited exposure to SRIs (Lewin et al., 2014). Parent preference is important in treatment decisions and is linked to improved outcomes and adherence in youth with OCD (Lewin et al., 2011b, 2014). Finally, given the potential for partial- or non-response to SRIs, providers may turn to antipsychotics and benzodiazepines for augmentation despite a lack of (benzodiazepine) or limited (antipsychotic) supporting efficacy data in youth with OCD (Koran and Simpson, 2013).

After a patient is started on SRIs, regardless of whether it is in combination with CBT, it remains unclear the length of time a patient should remain on SRIs. Criteria to determine who should remain on SRIs are unclear and do not contain guidance regarding withdrawal schedules. Guidelines currently suggest that pediatric patients should be kept on their medications for at least one year and then consider withdrawal if symptoms are minimal in severity (Bloch and Storch, 2015). However, empirical data informing this approach are limited. A meta-analysis evaluating SRI discontinuation studies found that adults who discontinued their SRIs were twice as likely to have a relapse in OCD symptoms than those who continued on their SRIs (Fineberg et al., 2007a). Time to relapse in OCD symptoms with discontinuation of escitalopram compared to placebo was statistically significant (Fineberg et al., 2007b). Of note, these studies did not provide CBT and therefore the patients did not learn additional skills to combat their OCD before SRI discontinuation.

There are several studies in adults to suggest that CBT augmentation can be helpful in SRI discontinuation. Most recently, Foa et al. completed a NIH-funded, first of its kind, SRI discontinuation trial in 137 adults with OCD for ≥1 year with moderate symptoms (defined by Yale-Brown Obsessive Compulsive Scale score [Y-BOCS] ≥ 18). Patients who were taking an adequate dose of SRI, who received up to 25 sessions of EX/RP and achieved wellness (YBOCS ≤14) following EX/RP were eligible for the study. Participants were randomized into the SRI continuation or SRI discontinuation groups (Foa et al., 2022). This study found that SRI discontinuation was noninferior to SRI continuation in terms of OCD symptom recurrence (Foa et al., 2022). However, there were increased rates of clinical worsening in 45% of adults in the SRI discontinuation arm compared to 24% of adults in the SRI maintenance arm. Several other studies are relevant. Cottraux et al. found that patients with an average age of 35 years (±8.7) who received CBT in addition to fluvoxamine (n = 20) were able to discontinue their medication after one year (Cottraux et al., 1990). Kordon et al. treated in-patients (n = 74) with a mean age of 35 years (±10.6) with OCD with either

CBT + SRI or CBT alone and at two-year follow up found that those in the combined treatment group who discontinued their SRI did not have significantly different relapse rates than those who received CBT monotherapy (Kordon et al., 2005). However, knowledge of youth discontinuing SRIs to date is limited to case studies. Goldstein et al. reported successful sertraline discontinuation in an 8.5-year-old male patient with treatment resistant OCD after a course of CBT that was maintained over a 7-month period (Goldstein et al., 2009). Sallinen et al. reported the successful discontinuation of fluoxetine and clomipramine after CBT augmentation for a four-month period in an 11-year-old female with OCD (Sallinen et al., 2004).

In addition to establishing evidence-based approaches for SRI discontinuation in pediatric patients with CBT augmentation, data are necessary to identify which patients are best suited for SRI discontinuation. While there are no clear predictors of whom may be more or less appropriate for SRI discontinuation, some data may be gleaned from prior studies. Previous studies have shown that comorbid disorders such as depressive disorders, chronic tic disorders, attention-deficit/hyperactivity disorder (ADHD), and disruptive behavior disorders are moderators of treatment and are associated with worse outcomes (Freeman et al., 2018; Storch et al., 2008a; Turner et al., 2018). Other moderators include early-onset OCD, familial OCD, insight, and SRI half-life. Children with early-onset OCD tend to have greater symptom severity and worse CBT response (Selles et al., 2014). Familial OCD suggests greater genetic loading and penetrance and is associated with lower CBT response (Torp et al., 2015). Poor insight has been correlated with attenuated CBT response (Garcia et al., 2010; Storch et al., 2008b). It is possible that these variables may be associated with differential outcome (i.e., worsening of symptoms for those with presence of poor insight, early onset/familial OCD, etc.) in those who are randomized to discontinue their SRI relative to those who continue their SRI.

Hypothesized mediators of SRI discontinuation outcome include family accommodation and CBT adherence. These variables will be analyzed as time-varying covariates of symptom change across all patients to understand if changes in obsessive-compulsive symptom severity is associated with either mediator. When family members provide reassurance or facilitate avoidance behaviors, this counteracts exposure skills being learned in CBT and negatively reinforces maladaptive coping (Pediatric, O.C.D.T.S.T., 2004; Turner et al., 2018). Adherence to skills learned in CBT is correlated with improved outcomes and remission during SRI discontinuation (Simpson et al., 2012), and as such, we expect that this variable will explain maintenance of gains over the discontinuation interval. Understanding patient attributes that are linked to improved outcomes from SRI discontinuation and their success with CBT could provide insights for future clinical management, such as decision-making regarding the timing and initiation of SRI discontinuation.

In this paper we describe the rationale and methodological design of the Promoting OCD Wellness and Resilience (POWER) study, which is a two phase, double-blinded, placebo-controlled, randomized controlled non-inferiority trial with the purpose of evaluating whether youth with OCD on an SRI can discontinue their medication after successful CBT augmentation and maintain wellness for a period of 24 weeks during which they receive maintenance CBT that models standard-of-care. In addition, this study will be sufficiently

powered to explore mediators to treatment such as, family accommodation, CBT adherence, and inhibitory control, as well as moderators to treatment such as comorbidity, age of onset, insight, familial OCD, and SRI half-life.

1.1. Specific aims and hypothesis

Aim 1: To determine whether children with OCD on SRIs who achieve wellness using CBT augmentation can successfully discontinue their SRI and maintain their response over 24 weeks when paired with CBT booster sessions. *Hypothesis*: Relative to those maintained on their SRI, patients switched to placebo will have non-inferior outcomes for OCD severity. Patients in the adult SRI discontinuation study performed by Foa et al. were found to have noninferior symptom worsening in the SRI discontinuation arm compared to the SRI continuation arm (Foa et al., 2022).

Aim 2: To examine theoretically relevant outcome moderators (comorbidity, age of onset, insight, familial OCD, SRI half-life, age at treatment initiation) of OCD symptom change during SRI discontinuation. *Hypothesis:* Patients with higher comorbidity, worse insight, familial OCD, younger age of onset, or on an SRI with a shorter half-life will show poorer response to SRI discontinuation (Freeman et al., 2018; Garcia et al., 2010; Pediatric, O.C.D.T.S.T., 2004; Selles et al., 2014; Storch et al., 2008a; Storch et al., 2008b).

Aim 3: To examine mediators (family accommodation, CBT adherence, inhibition) of OCD symptom change during SRI discontinuation. *Hypothesis:* Patients with more family accommodation, decreased CBT adherence, and decreased inhibition will show a poorer response to SRI discontinuation.

Aim 4: To explore rates of side effects and adverse events between patients maintained on their SRI compared to those switched to placebo.

2. Design of the POWER study

2.1. Overview

Using a two-phase randomized controlled non-inferiority trial, the POWER study evaluates medication discontinuation in pediatric patients with OCD who achieve significant improvement following flexibly dosed CBT. We will recruit 141 youth with clinically significant OCD (Children's Yale-Brown Obsessive Compulsive Scale [CY-BOCS ≥16]) despite having received and currently taking an adequate trial of an SRI. In Phase I, youth will receive 14–20 sessions of in-person or telehealth CBT (family choice). Those who achieve wellness (CY-BOCS ≤12) and maintain it over three consecutive weeks following CBT will be randomized in a double-blind fashion to Phase II. In Phase II, youth will be randomized to either SRI continuation or SRI discontinuation arms and followed for 24 weeks.

2.2. Defining wellness

A CY-BOCS score of ≤12 has been shown to be an optimal cutoff score for remission (Farhat et al., 2022; Lewin et al., 2011a; Mataix-Cols et al., 2016; Skarphedinsson et al., 2017) and will be used as the eligibility criteria to enter Phase II. Percent change was not

used as this may result in youth who achieve a certain threshold still be symptomatic, or by making it more challenging for youth with modest baseline symptoms that still meet entry criteria (e.g., CY-BOCS ~16) to qualify for Phase II.

2.3. Recruitment and initial assessment

Patients will be recruited from multiple sources including OCD clinics, community providers, and social media advertising. After initial identification of eligible participants, families will undergo a screening assessment to determine eligibility. In step A, the participant and their guardian will be contacted via a 20-min semi-scripted phone call to determine whether the patient is likely to meet the inclusion and exclusion criteria. If the participant meets criteria in step A, they will then enter step B. Here, both the parent-proxy and youth will have an in-person assessment that will include informed consent and assent, clinician-rated assessments, patient and parent-proxy self-administered questionnaires, baseline CBT assessment, physical exam, and appropriate laboratory tests including blood draws, urine toxicology, and pregnancy test (if indicated). Patients will be evaluated by a psychiatrist to ensure the patient has been placed on an appropriate dose of SRI.

2.4. Assessment timeline

Participants who are determined to be eligible during the screening and baseline assessment (step B), will begin CBT seven days later. The participant will then receive 14 to 20 CBT sessions. At every session the participant will undergo a CY-BOCS assessment completed by the therapist to mimic clinical practice, given strong convergence between ratings by therapists and independent evaluators (Lewin et al., 2011b). Independent evaluators will complete assessments at baseline, Post-Phase I, and throughout Phase II. Moderator variables will be assessed at baseline assessment and mediator variables assessed throughout Phase II. Patients who achieve wellness during Phase I and maintain it for three consecutive weeks will be assessed and then randomized in a double-blind fashion to either the SRI continuation or SRI discontinuation group in Phase II. During Phase II, participants will be assessed every two weeks by a blinded independent evaluator. Patients who do not achieve wellness after Phase I will be withdrawn from the study and offered clinical recommendations. See Fig. 1 for the study flow.

2.5. Inclusion/exclusion criteria

A total of 141 participants will be enrolled in order to have a power of 80% across all aims. Statistical power for Aims 1, 2, and 3 is based on noninferiority, moderation, and mediation respectively. Based on response rates in prior CBT studies, we expect 106 to enter the Phase II SRI discontinuation phase, and of those, 90 will complete it (Franklin et al., 2011; Storch et al., 2010).

Refer to Table 1 for inclusion and exclusion criteria and the associated rationale. Inclusion criteria include: a) Children and adolescents between the ages of 7–17 with a primary OCD diagnosis defined by the Kiddie Schedule for Affective Disorders and Schizophrenia Lifetime Version for DSM-5 (KSADS-PL) for >6 months duration. (Kaufman et al., 1997). Patients can have other psychiatric diagnoses; however, OCD needs to be the primary

diagnosis. b) CY-BOCS ≥16, which correlates with clinically significant symptom severity (Scahill et al., 1997). c) Taking one of the following non-liquid formulation SRIs at a maximum dose tolerated by the patient for at least a 12-week period (at a stable dose for the last 4 weeks): clomipramine, fluoxetine, fluvoxamine, sertraline, citalopram, and escitalopram. d) Both parent and child are verbally fluent in English.

Exclusion criteria include: a) Taking paroxetine given risk of SRI discontinuation syndrome (Hosenbocus and Chahal, 2011). b) Taking another psychotropic medication including antipsychotics or benzodiazepines. Stable ADHD medications are acceptable. c) Enrolled in concurrent OCD-focused psychotherapy. Families can choose to discontinue current psychotherapy. d) Past non-responder to a complete trial of CBT (≥9 EX/RP sessions over 14 weeks) for OCD specifically. e) Patients who have active suicidality or the following diagnoses: conduct disorder, bipolar disorder, psychotic spectrum disorder, or substance use disorder in the past six months. f) Have primary or co-primary major depression given the recommendations to remain on SRIs for six to 12 months. g) Pregnant or females engaging in unprotected sexual intercourse. h) Weight of <22.5 kg. i) Unable to swallow capsules. j) Significant intellectual disability or learning disorder that would affect their ability to engage with CBT.

2.6. Phase I: open trial CBT augmentation

2.6.1. Overview—Participants will receive 14–20 open trial in-person or telehealth (family choice) CBT sessions over 12–18 weeks. Those who achieve a meaningful response as defined below after 14 sessions or more and maintain it for three weeks will be eligible to be randomized into Phase II.

2.6.2. Open trial CBT—During Phase I, patients will receive the evidence-based CBT protocol used in the Pediatric Obsessive Compulsive Treatment Study (POTS) over 12–18 weeks with a minimum of 14 and no more than 20 telehealth or in-person (family choice) CBT sessions (Franklin et al., 2003), modified to include more substantial parental involvement, consistent with our prior work (Storch et al., 2016). It was determined to provide a full course of CBT prospectively to standardize the treatment and ensure all patients received a standard course of CBT. In addition, this will allow us to assess factors that contribute to CBT success. For the first two weeks, participants will receive twice-weekly CBT sessions and once a week thereafter to mimic standard practice and minimize family burden and impact on school and activities. During the first three sessions, patients will receive psychoeducation and cognitive training, and engage in exposure hierarchy development. The remaining sessions will focus on EX/RP specific to each youth and the last two sessions will focus on relapse prevention. After patients have completed open label CBT in Phase I where they maintained symptom remission for the last three consecutive weeks, the patient will undergo a Post-Phase I assessment to determine if they have achieved a CY-BOCS score ≤12. The three-week period starts when the participant reached CY-BOCS 12. This could mean at session ≤12 (with conclusion at session 14) at the earliest. If the patient does not achieve these parameters, they will be referred for appropriate care or continue CBT (if fewer than 20 sessions have been held).

2.6.3. Number of CBT sessions—We are allowing up to 20 sessions to increase the pool of youth that could respond to treatment and mimic clinical practice where youth often need more CBT sessions to achieve symptom remission. Previous studies have shown that between 50 and 60% of youth who received 10–14 CBT sessions achieved wellness (Pediatric, O.C.D.T.S.T., 2004; Storch et al., 2011). In addition, a study looking at non-responders to two or more medication trials showed that 66% of these youth achieved CY-BOCS ≤14 after 14 sessions of CBT (Storch et al., 2010).

2.6.4. SRI medication management—During Phase I, patients will remain stable on their SRI and complete medication logs to ensure compliance. Every four weeks (weeks 4, 8, 12, 14, and 18) patients will meet with a psychiatrist for a medical evaluation.

2.7. Phase II

2.7.1. Overview—Participants who achieve wellness in Phase I will be randomized in a 1:1 fashion into either SRI continuation or SRI discontinuation titration group and followed for up to 24 weeks. All patients will meet with a psychiatrist every two weeks during this period. Youth will receive their medication in special over-capsulized pills to ensure patients and providers remain blinded. Both groups will continue to receive maintenance CBT once every two weeks for the first four weeks and then once every four weeks thereafter for the remainder of the 24 weeks. Those who did not achieve wellness in Phase I will be directed toward appropriate treatments.

2.7.2. Randomization—Patients who achieve wellness in Phase I will begin the double-blinded Phase II. Patients will be randomized to one of two groups: 1) continued SRI or 2) SRI discontinuation titration to placebo. Participants will remain with their CBT therapist from Phase I.

2.7.3. Medication management—All patients will meet with a study psychiatrist every two weeks before every titration step down. Four-week intervals were considered however, two weeks was deemed more appropriate to monitor symptoms, ensure safety, and reduce attrition.

2.7.4. Medication withdrawal approach—For those in the SRI discontinuation titration to placebo group, their medication will be decreased every two weeks via standard titration. Each medication will be decreased at its own rate determined by the drug's half-life and the dose of the medication the patient is currently taking. Fluvoxamine, clomipramine, sertraline will be decreased by 50 mg/day/2 weeks until a dose of 50 mg/day is achieved and then decreased by 25 mg/day/2 weeks thereafter. Fluoxetine will be reduced by 20 mg/day/2 weeks due to its prolonged half-life. Citalopram will be reduced by 20 mg/day/2weeks until a dose of 20 mg/day is achieved and then it will be decreased by 10 mg/day/2weeks. Escitalopram will be reduced by 10 mg/day/2weeks until a dose of 10 mg/day is achieved and then it will be reduced by 5 mg/day/2 weeks. Patients taking paroxetine will not be included given the increased prevalence of SRI discontinuation syndrome. Participants will be given a variable number of special over-capsulized pills in the smallest denominator dose for each medication (clomipramine 25 mg, fluoxetine 10 mg, fluvoxamine 25 mg, sertraline

25 mg, citalopram 10 mg, escitalopram 5 mg). The number of capsules will not change throughout Phase II. Rather, capsules will be replaced with placebo based on the withdrawal schedule. Most patients in the SRI discontinuation group will be weaned off of medication between 6 and 8 weeks, although those on fluvoxamine could take up to 12 weeks. However, a slow taper is optimal as it limits the chance of SRI discontinuation syndrome which could mimic relapse. If at any visit the patient demonstrates an increase of 3–4 points on the CY-BOCS or is rated as "minimally worse" on the Clinical Global Impressions-Improvement (CGI-I) scale, the patient's decrease in medication will be postponed for two weeks until the following assessment.

2.7.5. Defining relapse—Relapse is defined by one of the following: 1) ≥ 50% increase on CY-BOCS score from start of Phase II plus CY-BOCS score of ≥20.2) CGI-I rating of "much" or "very much" worse at any visit during Phase II. Patients who meet this definition will be discontinued from the study and offered alternative evidence-based treatments.

2.7.6. Rescue treatment—During the weekly assessments, participants will undergo the CY-BOCS and CGI scales. If they score "minimally" worse on the CGI-I or have an increase of 3–4 points on the CY-BOCS, the next downward trend of medication will be postponed till the next assessment two weeks later. If the patient shows a relapse (≥50% increase on CY-BOCS score since the start of Phase II plus CY-BOCS score of ≥20 or a CGI-I rating of much/very much worse) at two consecutive visits, the patient will be referred for rescue treatment and the double-blinded protocol will be broken to ensure the patient receives the most appropriate treatment at that time. However, at any time during the study if the study team feels the participant warrants immediate change in treatment, the participant will be removed from the study immediately without waiting for four weeks.

2.7.7. Assessment schedule—Independent evaluator (IE) assessments, as outlined by Table 2, will be done every four weeks (weeks 4, 8, 12, 16, 20, 24). CY-BOCS will be administered every two weeks during Phase II. More comprehensive mechanistic variables will be assessed every four weeks.

2.7.8. Maintenance CBT sessions—During Phase II, patients will continue with maintenance CBT. This will include supportive therapy, in-session EX/RP as needed, and maintenance EX/RP planning between sessions. For the first four weeks, the patient will be seen bi-monthly and for weeks 5–24 of Phase II, the patient will be seen every four weeks.

2.8. Safety monitoring

At screening, Post-Phase I, and Post-Phase II, a laboratory test and a physical exam will be completed. Vital signs will be taken at every visit. At each psychiatrist visit, adverse effects will be reviewed (Coates et al., 2018). The blind will be broken in the event of serious adverse effects and a psychiatrist will meet with the patient if serious adverse effects occur in between the two-week visits.

2.9. Rater training

All assessments will be done by IEs who are blinded to treatment allocation at all time points (baseline, post-Phase I, Phase II, post-treatment, 12-month follow-up). IEs will be trained and supervised by a licensed clinical psychologist. Therapists will be graduate or post-graduate level, supervised by a licensed clinical psychologist. In order to be trained, IEs will rate and score multiple videotaped KSADS, CY-BOCS and CGI-I vignettes. Their ratings will need to be within 15% of the gold standard and within 15% of the mean of the group for KSADS and CY-BOCS. IEs will also need to be within 1 point on the CGI-I. Interviews will be audiotaped and 10–15% of them will undergo a blind review to account for inter-rater reliability and rater drift.

2.10. Masking

Great effort will be taken to ensure that the IEs remain blinded including: a) reminding participants and their parent-proxy to not provide treatment identifying information, b) IEs will focus solely on outcome measures and avoid treatment discussions, c) and all participants in Phase II will have matching SRI medication or placebo. SRI treatment will be blinded to the research staff, patient, and their parent-proxy. Capsules will be identical in appearance.

2.11. Assessments

The following scales will be used throughout enrollment, Phase I, and Phase II to track symptom improvement and to identify mediators that would affect the success of SRI discontinuation. Of note, during Phase I, CY-BOCS and CGI-S are administered by therapists to mimic routine clinical practice. See Table 2, which outlines at which point in the study each evaluation measure is used.

2.11.1. Clinician-rated measures—KSADS-PL is a structured diagnostic instrument administered at time of screening to both guardian and child, to identify current and past Diagnostic and Statistical Manual of Mental Disorders V (DSM-V) psychiatric history (Kaufman et al., 1997). The CY-BOCS is a clinician-rated instrument to assess the presence and severity of OCD symptoms in children and adolescents (Storch et al., 2019). The CGI-S is a clinician-rated 7-point rating of clinical severity. The CGI-I is a clinician-rated 7-point rating of treatment response (Busner and Targum, 2007; Guy, 1976). The Brown Assessment of Beliefs Scale-Modified for Children (BABS-C) is a five-item scale designed to assess insight into the participant's symptoms (Eisen et al., 1998). The Patient EX-RP Adherence Scale (PEAS) is a three-item assessment, given at the start of every exposure session, that assesses the patient's between-session adherence (Simpson et al., 2010). In addition to adherence, this assessment looks at the quantity and quality of exposures performed outside of the therapy sessions. The Family Accommodation Scale for Anxiety (FASA) assesses family accommodation of the child's OCD symptoms (Calvocoressi et al., 1999).

2.11.2. Parent and child measures—The Children's Florida Obsessive Compulsive Inventory (C-FOCI-II) is a self-reported measure of obsessions, compulsions, and the severity of each (Storch et al., 2009). The Sheehan Disability Scale (SDS-P/C) measures impairment in functioning in multiple domains (Sheehan et al., 1996). The Revised

Children's Anxiety and Depression Scale Child/Parent version (RCADS-C/P) is a youth and parent self-report questionnaire of anxiety and depressive symptoms (Chorpita et al., 2000). The Obsessive-Compulsive Inventory-Children's Version 5 (OCI CV-5) is a short screening tool for pediatric OCD (Chorpita et al., 2000). The Child Obsessive Compulsive Impact Scale (COIS) is a child and parent-report assessment that evaluates functional impairment experienced by the child due to OCD (Piacentini et al., 2003). The Pediatric Quality of Life Inventory (PedsQL) scale is a child- and parent-report assessment of perceived quality of life of the child (Varni et al., 1999). The Dimensional Obsessive-Compulsive Scale Child (DOCS) assesses the dimensions of obsessive-compulsive symptoms (harm, contamination, symmetry, taboo thoughts) and the Obsessive-Compulsive Trait Core Dimensions Questionnaire (OCTCDQ) assesses motivators of compulsive behavior (harm avoidance and incompleteness) ((Summerfeldt, 2019; Abramowitz et al., 2010; Summerfeldt et al., 2014). Both of these measures were adapted for this study in order to make the wording more youth friendly. The Child Avoidance Measure-Self-report (CAMS) and the Child Avoidance Measure-Parent-Report (CAMP) both measure the child's avoidance of anxiety provoking behaviors (Whiteside et al., 2013). The Child Anxiety Sensitivity Index measures the child's fear of anxiety symptoms (Silverman et al., 1999). The Child Negative Cognitive Error Questionnaire assesses four types of cognitive errors in youth (Leitenberg et al., 1986). The Children's Emotion Management Scales (for ages 8–12) and the Difficulties in Emotion Regulation Scale-18 (for ages 12+) assess emotion regulation in youth (Ogbaselase et al., 2022; Victor and Klonsky, 2016). Familial OCD will be assessed through open-ended interview. Inhibitory control will be assessed by the Barratt Impulsiveness Scale (BIS), which is a 30-item questionnaire used to assess personality and behavioral impulsivity (Patton et al., 1995).

2.11.3. Safety measures—

The Ask Suicide-Screening Questions (ASQ) is a four-question brief screening tool to assess the suicide risk of a patient (Horowitz et al., 2012).

2.12. Outcome measures

For hypothesis I, CY-BOCS total score during Phase II will be the main outcome measure. The CGI-I will be a key secondary outcome to determine symptom worsening. RCADS-C/P (anxiety/depressive symptoms), PedsQL (quality of life) and COIS-C/P (OCD-related impairment) will be examined as secondary outcomes.

2.13. Design considerations

During the development of the study protocol, several alternative designs were taken into consideration. First, we considered enrolling treatment naïve patients and prospectively treating with SRIs. Given the cost, practice protocols suggesting patients with mild to moderate OCD should begin CBT rather than SRIs first, parent preference for CBT, and limited external validity, this was decided against. Second, patients who are taking non-FDA approved SRIs (es)citalopram for OCD will be enrolled in this study. This was done given the safety and efficacy of these medications, to promote the generalizability of this study's findings, and to enhance recruitment. Third, as stated previously, mood disorders could negatively impact OCD. Patients with primary or co-primary major depressive disorder will be excluded given the recommendation for youth to remain on SRIs for a period of

6–12 months. However, children with secondary depression will be included in the study given the high rate of comorbidity with OCD. Including secondary depression will increase generalizability and allow us to examine secondary depression as a variable that could affect CBT response. We will also evaluate SRI treatment length as a variable to CBT response. Fourth, patients in this study can have varying SRI treatment lengths as long as they have been on SRIs for at least 12 weeks. SRI treatment length can affect CBT response. However, it was decided to not impose a limit on SRI treatment length in order to better reflect clinical practice. Fifth, given the different half-lives of medications, we considered blood draws to obtain blood levels of SRIs to confirm the date of when medication was no longer present. However, we decided against this given it would require blood draws above safety draws. Finally, given that participants can be enrolled in the study on one of six different medications, percentage dose reductions were taken into consideration. However, this does not reflect clinical practice so was decided against.

3. Conclusions and future directions

POWER sets out to provide an evidence-based guideline for whether SRI medication discontinuation is feasible in children and adolescents with OCD who achieved remission following EX/RP. Furthermore, this study will examine the following: 1) what factors influence whether a child with OCD will maintain wellness after medication discontinuation, and 2) the mediators that help ‘explain’ successful SRI discontinuation. Understanding these factors will address key questions of parents of youth with OCD, namely, “How long should my child remain on this medication?” and “Will my child still feel better if they stop taking this medication?” Furthermore, this study will inform more personalized approaches to treatment that provide more precisely targeted treatments as a function of the child’s need. Finally, this study will serve as a model for randomized controlled trials examining CBT treatment and SRI discontinuation in other pediatric psychiatric illness (e.g., anxiety).

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References

Abramowitz JS, Deacon BJ, Olatunji BO, Wheaton MG, Berman NC, Losardo D, Timpano KR, McGrath PB, Riemann BC, Adams T, Bjorgvinsson T, Storch EA, Hale LR, 2010. Assessment of obsessive-compulsive symptom dimensions: development and evaluation of the Dimensional Obsessive-Compulsive Scale. Psychol. Assess. 22 (1), 180–198. [PubMed: 20230164]

Alaghband-Rad J, Hakimshooshtary M, 2009. A randomized controlled clinical trial of citalopram versus fluoxetine in children and adolescents with obsessive-compulsive disorder (OCD). Eur. Child Adolesc. Psychiatr. 18 (3), 131–135.

Bandelow B, Zohar J, Hollander E, Kasper S, Moller HJ, , Wfsbp Task Force on Treatment Guidelines for Anxiety, O.-C., Post-Traumatic Stress, D, Zohar J, Hollander E, Kasper S, Moller HJ, Bandelow B, Allgulander C, AyusoGutierrez J, Baldwin DS, Buenvicius R, Cassano G, Fineberg N, Gabriels L, Hindmarch I, Kaiya H, Klein DF, Lader M, Lecrubier Y, Lepine JP, Liebowitz MR, Lopez-Ibor JJ, Marazziti D, Miguel EC, Oh KS, Preter M, Rupprecht R, Sato M, Starcevic V, Stein DJ, van Ameringen M, Vega J, 2008. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders - first revision. World J. Biol. Psychiatr. 9 (4), 248–312.

Bloch MH, Storch EA, 2015. Assessment and management of treatment-refractory obsessive-compulsive disorder in children. J. Am. Acad. Child Adolesc. Psychiatry 54 (4), 251–262. [PubMed: 25791142]

Busner J, Targum SD, 2007. The clinical global impressions scale: applying a research tool in clinical practice. Psychiatry 4 (7), 28–37.

Calvocoressi L, Mazure CM, Kasl SV, Skolnick J, Fisk D, Vegso SJ, Van Noppen BL, Price LH, 1999. Family accommodation of obsessive-compulsive symptoms: instrument development and assessment of family behavior. J. Nerv. Ment. Dis. 187 (10), 636–642. [PubMed: 10535658]

Cascade E, Kalali AH, Kennedy SH, 2009. Real-world data on SSRI antidepressant side effects. Psychiatry 6 (2), 16–18.

Chorpita BF, Yim L, Moffitt C, Umemoto LA, Francis SE, 2000. Assessment of symptoms of DSM-IV anxiety and depression in children: a revised child anxiety and depression scale. Behav. Res. Ther. 38 (8), 835–855. [PubMed: 10937431]

Coates M, Spanos M, Parmar P, Chandrasekhar T, Sikich L, 2018. A review of methods for monitoring adverse events in pediatric psychopharmacology clinical trials. Drug Saf. 41 (5), 465–471. [PubMed: 29318515]

Cottraux J, Mollard E, Bouvard M, Marks I, Sluys M, Nury AM, Douge R, Cialdella P, 1990. A controlled study of fluvoxamine and exposure in obsessive-compulsive disorder. Int. Clin. Psychopharmacol. 5 (1), 17–30. [PubMed: 2110206]

Eisen JL, Phillips KA, Baer L, Beer DA, Atala KD, Rasmussen SA, 1998. The Brown assessment of Beliefs scale: reliability and validity. Am. J. Psychiatr. 155 (1), 102–108. [PubMed: 9433346]

Farhat LC, Vattimo EFQ, Ramakrishnan D, Levine JLS, Johnson JA, Artukoglu BB, Landeros-Weisenberger A, Asbahr FR, Cepeda SL, Comer JS, Fatori D, Franklin ME, Freeman JB, Geller DA, Grant PJ, Goodman WK, Heyman I, Ivarsson T, Lenhard F, Lewin AB, Li F, Merlo LJ, Mohsenabadi H, Peris TS, Piacentini J, Rosa-Alcazar AI, Rosa-Alcazar A, Rozenman M, Sapyta JJ, Serlachius E, Shabani MJ, Shavitt RG, Small BJ, Skarphedinsson G, Swedo SE, Thomsen PH, Turner C, Weidle B, Miguel EC, Storch EA, Mataix-Cols D, Bloch MH, 2022. 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 61 (4), 495–507. [PubMed: 34597773]

Fineberg NA, Pampaloni I, Pallanti S, Ipser J, Stein DJ, 2007a. Sustained response versus relapse: the pharmacotherapeutic goal for obsessive-compulsive disorder. Int. Clin. Psychopharmacol. 22 (6), 313–322. [PubMed: 17917549]

Fineberg NA, Tonnoir B, Lemming O, Stein DJ, 2007b. Escitalopram prevents relapse of obsessive-compulsive disorder. Eur. Neuropsychopharmacol 17 (6–7), 430–439. [PubMed: 17240120]

Foa EB, Simpson HB, Gallagher T, Wheaton MG, Gershkovich M, Schmidt AB, Huppert JD, Imms P, Campeas RB, Cahill S, DiChiara C, Tsao SD, Puliafico A, Chazin D, Asnaani A, Moore K, Tyler J, Steinman SA, Sanches-LaCay A, Capaldi S, Snorrason I, Turk-Karan E, Vermes D, Kalanthroff E, Pinto A, Hamlett GE, Middleton R, Hahn CG, Xu B, Van Meter PE, Katechis M, Rosenfield D, 2022. Maintenance of wellness in patients with obsessive-compulsive disorder who discontinue medication after exposure/response prevention augmentation: a randomized clinical trial. JAMA Psychiatr. 79 (3), 193–200.

Franklin M, Foa E, March JS, 2003. The pediatric obsessive-compulsive disorder treatment study: rationale, design, and methods. J. Child Adolesc. Psychopharmacol. 13 (Suppl. 1), S39–S51. [PubMed: 12880499]

Franklin ME, Sapyta J, Freeman JB, Khanna M, Compton S, Almirall D, Moore P, Choate-Summers M, Garcia A, Edson AL, Foa EB, March JS, 2011. Cognitive behavior therapy augmentation of

pharmacotherapy in pediatric obsessive-compulsive disorder: the Pediatric OCD Treatment Study II (POTS II) randomized controlled trial. JAMA 306 (11), 1224–1232. [PubMed: 21934055]

Freeman J, Benito K, Herren J, Kemp J, Sung J, Georgiadis C, Arora A, Walther M, Garcia A, 2018. Evidence base update of psychosocial treatments for pediatric obsessive-compulsive disorder: evaluating, improving, and transporting what works. J. Clin. Child Adolesc. Psychol. 47 (5), 669–698. [PubMed: 30130414]

Garcia AM, Sapyta JJ, Moore PS, Freeman JB, Franklin ME, March JS, Foa EB, 2010. Predictors and moderators of treatment outcome in the pediatric obsessive compulsive treatment study (POTS I). J. Am. Acad. Child Adolesc. Psychiatry 49 (10), 1024–1033 quiz 1086. [PubMed: 20855047]

Geller DA, Biederman J, Stewart SE, Mullin B, Martin A, Spencer T, Faraone SV, 2003. Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. Am. J. Psychiatr. 160 (11), 1919–1928. [PubMed: 14594734]

Geller DA, March J, (CQI), T.A.C.o.Q.I, 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. [PubMed: 22176943]

Goldstein RB, Storch EA, Lehmkuhl H, Geffken GR, Goodman WK, Murphy TK, 2009. Successful medication withdrawal after cognitive-behavioral therapy in a treatment-resistant preadolescent male with obsessive-compulsive disorder. Depress. Anxiety 26 (1), E23–E25. [PubMed: 19067320]

Goodman WK, Murphy TK, Storch EA, 2007. Risk of Adverse Behavioral Effects with Pediatric Use of Antidepressants. Psychopharmacology 191, 87–96. [PubMed: 17180618]

Gordon M, Melvin G, 2013. Selective serotonin re-uptake inhibitors–a review of the side effects in adolescents. Aust. Fam. Physician 42 (9), 620–623. [PubMed: 24024221]

Guy W, 1976. ECDEU Assessment Manual for Psychopharmacology. U.S. Department of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs, United States.

Hamill Skoch S, Mills JA, Ramsey L, Strawn JR, 2021. Letter to the editor: sleep disturbances in selective serotonin reuptake inhibitor-treated youth with anxiety disorders and obsessive compulsive disorder-A bayesian hierarchical modeling meta-analysis. J. Child Adolesc. Psychopharmacol. 31 (5), 387–388. [PubMed: 33571033]

Horowitz LM, Bridge JA, Teach SJ, Ballard E, Klima J, Rosenstein DL, Wharff EA, Ginnis K, Cannon E, Joshi P, Pao M, 2012. Ask Suicide-Screening Questions (ASQ): a brief instrument for the pediatric emergency department. Arch. Pediatr. Adolesc. Med. 166 (12), 1170–1176. [PubMed: 23027429]

Hosenbocus S, Chahal R, 2011. SSRIs and SNRIs: a review of the discontinuation syndrome in children and adolescents. J Can Acad Child Adolesc Psychiatry 20 (1), 60–67. [PubMed: 21286371]

Jane Garland E, Kutcher S, Virani A, Elbe D, 2016. Update on the use of SSRIs and SNRIs with children and adolescents in clinical practice. J Can Acad Child Adolesc Psychiatry 25 (1), 4–10. [PubMed: 27047551]

Karno M, Golding JM, Sorenson SB, Burnam MA, 1988. The epidemiology of obsessive-compulsive disorder in five US communities. Arch. Gen. Psychiatr. 45 (12), 1094–1099. [PubMed: 3264144]

Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D, 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. [PubMed: 9204677]

Keeley ML, Storch EA, Dhungana P, Geffken GR, 2007. Pediatric obsessive-compulsive disorder: a guide to assessment and treatment. Issues Ment. Health Nurs. 28 (6), 555–574. [PubMed: 17613156]

Koran L, Simpson HB, 2013. Guideline Watch (March 2013): Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder. APA Pract. Guidel, pp. 1–22

Kordon A, Kahl KG, Broocks A, Voderholzer U, Rasche-Rauchle H, Hohagen F, 2005. Clinical outcome in patients with obsessive-compulsive disorder after discontinuation of SRI treatment: results from a two-year follow-up. Eur. Arch. Psychiatr. Clin. Neurosci. 255 (1), 48–50.

Leitenberg H, Yost LW, Carroll-Wilson M, 1986. Negative cognitive errors in children: questionnaire development, normative data, and comparisons between children with and without self-reported symptoms of depression, low self-esteem, and evaluation anxiety. J. Consult. Clin. Psychol. 54 (4), 528–536. [PubMed: 3745607]

Leonard HL, Meyer MC, Swedo SE, Richter D, Hamburger SD, Allen AJ, Rapoport JL, Tucker E, 1995. Electrocardiographic changes during desipramine and clomipramine treatment in children and adolescents. J. Am. Acad. Child Adolesc. Psychiatry 34 (11), 1460–1468. [PubMed: 8543513]

Lewin AB, De Nadai AS, Park J, Goodman WK, Murphy TK, Storch EA, 2011a. Refining clinical judgment of treatment outcome in obsessive-compulsive disorder. Psychiatr. Res. 185 (3), 394–401.

Lewin AB, Peris TS, Lindsey Bergman R, McCracken JT, Piacentini J, 2011b. The role of treatment expectancy in youth receiving exposure-based CBT for obsessive compulsive disorder. Behav. Res. Ther. 49 (9), 536–543. [PubMed: 21723534]

Lewin AB, McGuire JF, Murphy TK, Storch EA, 2014. The importance of considering parent's preferences when planning treatment for their children–the case of childhood obsessive-compulsive disorder. JCPP (J. Child Psychol. Psychiatry) 55 (12), 1314–1316. [PubMed: 25346230]

Mataix-Cols D, Fernandez de la Cruz L., Nordsletten AE., Lenhard F., Isomura K., Simpson HB., 2016. Towards an international expert consensus for defining treatment response, remission, recovery and relapse in obsessive-compulsive disorder. World Psychiatr. 15 (1), 80–81.

McGuire JF, Piacentini J, Lewin AB, Brennan EA, Murphy TK, Storch EA, 2015. A meta-analysis of cognitive behavior therapy and medication for child obsessive-compulsive disorder: moderators of treatment efficacy, response, and remission. Depress. Anxiety 32 (8), 580–593. [PubMed: 26130211]

Ogbaselase FA, Scelsa VL, Stoppelbein L, Becker SP, Fite PJ, Greening L, Luebbe AM, 2022. Psychometric properties of the children's emotion management scales within a psychiatric sample. Psychol. Assess. 34 (7), 620–630. [PubMed: 35357874]

Patton JH, Stanford MS, Barratt ES, 1995. Factor structure of the Barratt impulsiveness scale. J. Clin. Psychol. 51 (6), 768–774. [PubMed: 8778124]

Pediatric OCDTST, 2004. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. JAMA 292 (16), 1969–1976. [PubMed: 15507582]

Piacentini J, Bergman RL, Keller M, McCracken J, 2003. Functional impairment in children and adolescents with obsessive-compulsive disorder. J. Child Adolesc. Psychopharmacol. 13 (Suppl. 1), S61–S69. [PubMed: 12880501]

Piacentini J, Peris TS, Bergman RL, Chang S, Jaffer M, 2007. 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. [PubMed: 18088221]

Sallinen BJ, Nangle DW, O'Grady AC, 2004. Case study: successful medication withdrawal using cognitive-behavioral therapy for a preadolescent with OCD. J. Am. Acad. Child Adolesc. Psychiatry 43 (11), 1441–1444. [PubMed: 15502604]

Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, Cicchetti D, Leckman JF, 1997. Children's Yale-Brown obsessive compulsive scale: reliability and validity. J. Am. Acad. Child Adolesc. Psychiatry 36 (6), 844–852. [PubMed: 9183141]

Selles RR, Storch EA, Lewin AB, 2014. Variations in symptom prevalence and clinical correlates in younger versus older youth with obsessive-compulsive disorder. Child Psychiatr. Hum. Dev. 45 (6), 666–674.

Sheehan DV, Harnett-Sheehan K, Raj BA, 1996. The measurement of disability. Int. Clin. Psychopharmacol. 11 (Suppl. 3), 89–95.

Silverman WK, Ginsburg GS, Goedhart AW, 1999. Factor structure of the childhood anxiety sensitivity index. Behav. Res. Ther. 37 (9), 903–917. [PubMed: 10458052]

Simpson HB, Maher M, Page JR, Gibbons CJ, Franklin ME, Foa EB, 2010. Development of a patient adherence scale for exposure and response prevention therapy. Behav. Ther. 41 (1), 30–37. [PubMed: 20171325]

Simpson HB, Marcus SM, Zuckoff A, Franklin M, Foa EB, 2012. Patient adherence to cognitive-behavioral therapy predicts long-term outcome in obsessive-compulsive disorder. J. Clin. Psychiatry 73 (9), 1265–1266. [PubMed: 23059155]

Skarphedinsson G, De Nadai AS, Storch EA, Lewin AB, 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. Psychiatr. 26 (1), 47–55.

Storch EA, Merlo LJ, Larson MJ, Geffken GR, Lehmkuhl HD, Jacob ML, Murphy TK, Goodman WK, 2008a. Impact of comorbidity on cognitive-behavioral therapy response in pediatric obsessive-compulsive disorder. J. Am. Acad. Child Adolesc. Psychiatry 47 (5), 583–592. [PubMed: 18356759]

Storch EA, Milsom VA, Merlo LJ, Larson M, Geffken GR, Jacob ML, Murphy TK, Goodman WK, 2008b. Insight in pediatric obsessive-compulsive disorder: associations with clinical presentation. Psychiatr. Res. 160 (2), 212–220.

Storch EA, Khanna M, Merlo LJ, Loew BA, Franklin M, Reid JM, Goodman WK, Murphy TK, 2009. Children's Florida Obsessive Compulsive Inventory: psychometric properties and feasibility of a self-report measure of obsessive-compulsive symptoms in youth. Child Psychiatr. Hum. Dev. 40 (3), 467–483.

Storch EA, Lehmkuhl HD, Ricketts E, Geffken GR, Marien W, Murphy TK, 2010. An open trial of intensive family based cognitive-behavioral therapy in youth with obsessive-compulsive disorder who are medication partial responders or nonresponders. J. Clin. Child Adolesc. Psychol. 39 (2), 260–268. [PubMed: 20390817]

Storch EA, Caporino NE, Morgan JR, Lewin AB, Rojas A, Brauer L, Larson MJ, Murphy TK, 2011. Preliminary investigation of web-camera delivered cognitive-behavioral therapy for youth with obsessive-compulsive disorder. Psychiatr. Res. 189 (3), 407–412.

Storch EA, Wilhelm S, Sprich S, Henin A, Micco J, Small BJ, McGuire J, Mutch PJ, Lewin AB, Murphy TK, Geller DA, 2016. Efficacy of augmentation of cognitive behavior therapy with weight-adjusted d-cycloserine vs placebo in pediatric obsessive-compulsive disorder: a randomized clinical trial. JAMA Psychiatr. 73 (8), 779–788.

Storch EA, McGuire JF, Wu MS, Hamblin R, McIngvale E, Cepeda SL, Schneider SC, Rufino KA, Rasmussen SA, Price LH, Goodman WK, 2019. Development and psychometric evaluation of the children's Yale-Brown obsessive-compulsive scale second edition. J. Am. Acad. Child Adolesc. Psychiatry 58 (1), 92–98. [PubMed: 30577944]

Strawn JR, Geracioti L, Rajdev N, Clemenza K, Levine A, 2018. Pharmacotherapy for generalized anxiety disorder in adult and pediatric patients: an evidence-based treatment review. Expet Opin. Pharmacother. 19 (10), 1057–1070.

Summerfeldt, et al., 2019. English Translation of the Youth Version Adapted by Cervin and Perrin of the Obsessive-Compulsive Core Dimensions Questionnaire, Trait Version (OCCDQ-T).

Summerfeldt LJ, Kloosterman PH, Antony MM, Swinson RP, 2014. Examining an obsessive-compulsive core dimensions model: structural validity of harm avoidance and incompleteness. Journal of Obsessive-Compulsive and Related Disorders 3 (2), 83–94.

Torp NC, Dahl K, Skarphedinsson G, Compton S, Thomsen PH, Weidle B, Hybel K, Valderhaug R, Melin K, Nissen JB, Ivarsson T, 2015. Predictors associated with improved cognitive-behavioral therapy outcome in pediatric obsessive-compulsive disorder. J. Am. Acad. Child Adolesc. Psychiatry 54 (3), 200–207 e201. [PubMed: 25721185]

Turner C, O'Gorman B, Nair A, O'Kearney R, 2018. Moderators and predictors of response to cognitive behaviour therapy for pediatric obsessive-compulsive disorder: a systematic review. Psychiatr. Res. 261, 50–60.

Varni JW, Seid M, Rode CA, 1999. The PedsQL: measurement model for the pediatric quality of life inventory. Med. Care 37 (2), 126–139. [PubMed: 10024117]

Victor S, Klonsky ED, 2016. Validation of a brief version of the Difficulties in emotion regulation scale in five samples. J. Psychopathol. Behav. Assess. 38.

Whiteside SP, Gryczkowski M, Ale CM, Brown-Jacobsen AM, McCarthy DM, 2013. Development of child- and parent-report measures of behavioral avoidance related to childhood anxiety disorders. Behav. Ther. 44 (2), 325–337. [PubMed: 23611081]

Zohar J, 2008. Escitalopram in the treatment of obsessive-compulsive disorder. Expert Rev. Neurother. 8 (3), 339–349. [PubMed: 18345966]

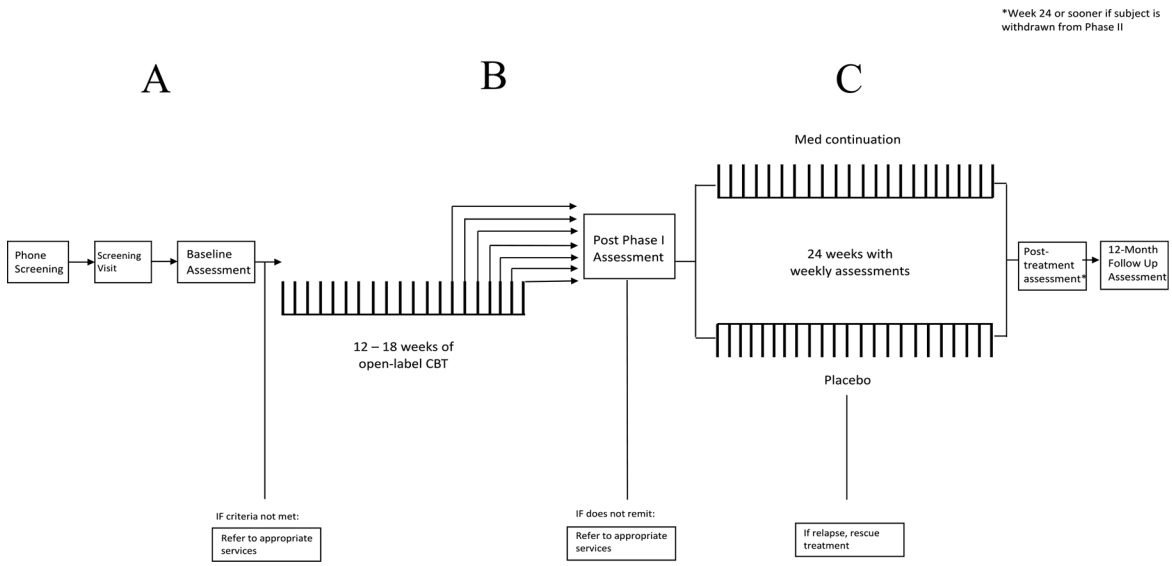

Fig. 1.

Study flow design depicting: A) Three step process to enroll patient. B) Phase I which includes 12–18 weeks with 14–20 sessions of open label CBT. C) Phase II which includes double blinded medication continuation or discontinuation titration to placebo.

Table 1

Inclusion/exclusion criteria.

Inclusion criteria	**Rationale**
Children and adolescents between 7 and 17 years of age at enrollment	Developmentally appropriate age
Primary OCD diagnoses for >6 months based on the KSADS-PL and have a CY-BOCS >/ = 16	Group of interest
Stable maximally tolerated non-liquid SRI medication (i.e. clomipramine, fluoxetine, fluvoxamine, sertraline, citalopram, escitalopram) for >/ = 12 weeks	Group of interest, time for medication to be maximally effective
Both parent and child are fluent in English	Ability to engage with CBT
Exclusion criteria	Rationale
Receiving concurrent psychotherapy for OCD	Confound outcomes
Taking other psychotropic medications other than for ADHD	Medication effects can confound treatment
SRI dose has changed in the last 4 weeks	Dose unstable or not had sufficient time to determine efficacy
Current clinically significant suicidality with intent and plan	Needs more acute care and care out of the scope of this study
Has one or more of the following diagnoses: conduct disorder, bipolar, psychotic disorders, substance use in the past 6 months	Confound outcomes and requires higher level of care
Primary or co-primary major depression	Not clinically advised to discontinue SRI
Pregnant or females engaging in unprotected sexual intercourse	Vulnerable population
Weighs <22.5 kg	Not able to tolerate adequate SRI dosage
Medically contraindicated	Unsafe
Cannot swallow capsules	Patient will be unable to take medication provided in phase II
Significant intellectual disability or learning disorder that would affect their ability to engage with CBT	Patient will be unable to partake in EX/RP

Table 2.

Study visits and assessment schedule.

	Phase I		Phase II	
Procedure	**Screening**	**Post**	**Weeks 4,8,12,16,20**	**Week 24[c]**
Kiddie Schedule for Affective Disorders and Schizophrenia Lifetime Version for DSM-5; Pregnancy Test (if applicable)	x			
Children's Yale-Brown Obsessive Compulsive Scale score[a e]; Clinical Global Improvement-Severity[a]; Sheehan Disability Scale; Ask Suicide-Screening Questions[a]; Revised Children's Anxiety and Depression Scale Child/Parent version; The Family Accommodation Scale for Anxiety; The Brown Assessment of Beliefs Scale-Modified for Children; Patient EX-RP Adherence Scale[b]; The Children's Florida Obsessive Compulsive Inventory-II[a]; Obsessive-Compulsive Inventory-Children's Version 5	x	x	x	x
The Child Obsessive Compulsive Impact Scale; The Pediatric Quality of Life Inventory; The Dimensional Obsessive-Compulsive Scale Child; Obsessive-Compulsive Trait Core Dimensions Questionnaire; Child Avoidance Measure-Parent-Report; The Child Avoidance Measure-Self-report; Child Anxiety Sensitivity Index; Child Negative Cognitive Error Questionnaire; Children's Emotion Management Scales (8–12); Difficulties in Emotion Regulation Scale-18 (12[e])		x		x
Clinical Global Impression-Improvement[a]		x	x	x
Wechsler Abbreviated Scale of Intelligence[d]				
Physical Exam, Laboratory Test, Urine Toxicology; Inhibition Tasks (Barratt Impulsiveness Scale and Stop Signal Task)	x	x		x

[a] Given during every CBT session and weekly during Phase II.

[b] Given during all CBT session.

[c] Week 24 or sooner if withdrawn from Phase II.

[d] As needed.

[e] After screening visit, only Severity scale of CY-BOCS will be administered.