

**Introduction to the Practice Guideline for the
Treatment of Patients with
Obsessive-Compulsive Disorder**

Task Force Membership

Deborah Heggie, Ph.D.
Shareh Ghani, M.D.
Gary M. Henschen, M.D., L.F.A.P.A.
Louis A. Parrott, M.D., Ph.D.
Mary Shorter, L.C.S.W.-C.

Table of Contents

| | |
|--|----|
| Purpose of This Document | 1 |
| Additional Recommendations Based on Recent Literature Review | 2 |
| Executive Summary | 2 |
| Introduction | 9 |
| Nosology, Epidemiology and Etiology | 10 |
| Office-based Treatment of OCD | 13 |
| Psychopharmacology | 14 |
| Neurostimulation | 19 |
| Complementary and Alternative Medicine | 22 |
| Psychotherapy | 23 |
| Combined Treatment | 27 |
| Healthcare Effectiveness Data and Information Set (HEDIS) | 29 |
| Obtaining Copies of the APA Guideline | 30 |
| Provider Feedback | 30 |
| References | 31 |

Purpose of This Document

This document is an introduction to the Magellan Healthcare (Magellan) adopted clinical practice guideline (CPG) for the treatment of individuals with Obsessive-Compulsive Disorder (OCD). As with all CPGs, this adopted guideline and this Introduction are intended to augment, not replace, sound clinical judgment. As a matter of good practice, providers should note clinically sound exceptions to this practice guideline in the member's treatment record, documenting the clinical reasoning used in making the exception. Magellan periodically requests clinical files from providers in order to monitor compliance with adopted guidelines. Clear documentation of the rationale for exceptions to the guideline's recommendations should be present in the member's treatment record whenever there is evidence of deviation from the guideline.

Additionally, this guideline does not supersede Food and Drug Administration (FDA) determinations or other actions regarding withdrawal or approval of specific medications or devices, and their uses. It is the responsibility of the treating clinician to remain current on medication/device alerts and warnings that are issued by the FDA and other regulatory and professional bodies, and to incorporate such information in his or her treatment decisions.

Magellan has adopted the American Psychiatric Association's (APA) *Practice Guideline for the Treatment of Patients With Obsessive-Compulsive Disorder*, First Edition (2007) and the APA Guideline Watch (March 2013) (APA 2007; APA 2013). These documents serve as a framework for practitioners' clinical decision-making with patients who have OCD. The adopted APA guideline is one of the most comprehensive and widely used evidence-based clinical practice guidelines for this disorder, incorporating developments in pharmacotherapy and other areas of psychiatric management of individuals with OCD. The APA guideline and Guideline Watch are research-based documents covering all areas of psychiatric management of patients with this disorder, from clinical features and epidemiology, to treatment approach and planning. Accepted by other managed behavioral healthcare companies, the APA guidelines and Guideline Watch reduce the burden on practitioners serving multiple organizations.

The APA *Practice Guideline for the Treatment of Patients With Obsessive-Compulsive Disorder*, First Edition contains a section entitled, "Specific Clinical Features Influencing the Treatment Plan" with information and discussion of clinical research findings on psychiatric features, demographic and psychosocial factors, and treatment implications of concurrent general medical conditions. While this section does include pertinent clinical information on treatment issues specific to the children and adolescents, the reader is referred to the American Academy of Child and Adolescent Psychiatry (AACAP) *Practice Parameter for the Assessment and Treatment of Children and Adolescents With Obsessive-Compulsive Disorder* (2012) for a detailed overview of assessment and treatment of the disorder in this population.

Additional Recommendations Based on Recent Literature Review

The APA guideline is based on a literature review through December 2004. It was approved by the APA in October 2006 and published in July 2007. The Guideline Watch reviewed the clinical literature between 2004 and 2013. Magellan's 2016 guideline update was based on a literature review conducted through May 2016. This guideline was updated to include additional research published through March 2018. Magellan encourages providers to be familiar with the information provided both in this Introduction and the published adopted APA guideline and Guideline Watch.

Executive Summary

(A discussion of additions/changes in this updated guideline.)

Epidemiology/Etiology

The 12-month prevalence of OCD in the United States has been reported as 1.2 percent, with severe cases representing almost one-third of all cases. Lifetime prevalence has been reported as 2.3 percent in the United States (Phillips and Stein, 2015). In a large epidemiological sample including individuals with OCD, the median age at onset was 19 years, with approximately one-fourth of cases beginning by age 10. Onset in males typically occurs at an earlier age than in females. A recent meta-analysis reported that pregnant and postpartum women, compared with women in the general population, are one and one-half to two times more likely to experience OCD (Phillips and Stein, 2015). An autoimmune process following infection with Group A β streptococcus has also been linked to some abrupt cases of childhood-onset OCD. The onset of OCD symptoms has also been linked to head trauma (Seibell and Hollander, 2014).

Genetic susceptibility to OCD has been suggested by twin and family studies. Greater genetic influence has been found in childhood-onset (OCD) than in adult-onset OCD. Genes most consistently implicated are serotonin 5-hydroxytryptamine (5-HT) and glutamate genes. Imaging studies have shown that the most consistently reported structural abnormalities in OCD involve the basal ganglia, orbitofrontal cortex, anterior cingulate cortex and striatum. Abnormalities in multiple neurotransmitter systems may be related to OCD symptoms with the cortico-striato-thalamo-cortical (CSTC) circuitry believed to contribute to the pathophysiology of OCD (Phillips and Stein, 2015).

A most recent genome-wide association study (GWAS) scanning the genomes of people with OCD, as well as close relatives of those with OCD, identified a significant association in patients with OCD near a gene, protein tyrosine phosphokinase (PTPRD) (Mattheisen et al, 2015). The study, OCD Collaborative Genetics Association Study (OC GAS), was comprised of patients (n=1406) with onset of OCD before aged 18 and a case control subsample (n = 1084). The most significant finding in the study was the signal near the PTPRD gene, "a member of the receptor protein tyrosine phosphatase family, which comprises transmembrane signaling molecules that regulate a variety of cellular processes including cell growth and differentiation. Pre-synaptic PTPRD promotes the differentiation of glutamatergic synapses" (Mattheisen et al., p. 344).

Researchers noted that plausible biologic hypotheses and prior genetic evidence has been shown for the finding related to PTPRD's association with OCD.

A large international study collected data from treatment centers across multiple countries and continents. Data points included comorbidity, age of onset, and suicidality (Brakoulias, V., et al, 2017). The authors found high rates of comorbidity with various conditions. The most common comorbid conditions included major depression, obsessive-compulsive personality disorder, generalized anxiety disorder, specific phobia and social phobia. The average age of onset for OCD was 17.9 years. This was earlier than the average age of onset for the comorbid conditions major depression, generalized anxiety disorder and psychotic disorders but was similar to social phobia and specific phobia. The similar age of onset led the researchers to conclude that there may be similarities between OCD and social phobia and specific phobia.

Office-Based Treatment

A recent cross-sectional study assessed the ability of primary care physicians to identify OCD utilizing an online vignette-based survey (Glazier et al., 2015). Primary care physicians (n = 208) reviewed vignettes focused on obsessions regarding aggression, contamination, fear of saying things, religion, pedophilia, somatic concern or symmetry and provided diagnoses and treatment recommendations for the individuals described in the vignettes. The study found that primary care physicians misidentified the vignettes with an overall misidentification rate of 50.5 percent. Of those misidentifying the vignettes, 46.7 percent and 8.6 percent recommended CBT or SSRI, respectively, while of participants correctly identifying the vignette, 66.0 percent and 35.0 percent recommended CBT or SSRI, respectively. Among those misidentifying the vignette, antipsychotic recommendation rates were elevated. Researchers concluded that “elevated OCD misdiagnosis rates and the impact of incorrect diagnoses on treatment recommendations highlight the need for greater training regarding OCD symptomatology and empirically supported treatments” (Glazier et al., p. 767).

Treatment-Psychopharmacology

In a study including patients with OCD (n=361) at different stages of treatment who were recruited in eight international tertiary care centers, researchers found that 317 patients reported use of at least one medication while 44 reported none (Van Ameringen et al, 2014). Of the sample receiving current medication, 77.6 percent were taking a selective serotonin reuptake inhibitor (SSRI) as their primary medication, either as monotherapy or an augmentation agent. Monotherapy agents also included tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors (SNRIs), antipsychotics and benzodiazepines. Authors reported no significant differences in clinical improvement or Yale Brown Obsessive Compulsive Scale (YBOCS) scores between the different monotherapy agents. Nearly one-half of those currently taking medication were using at least one augmentation agent, e.g., antipsychotics, benzodiazepines and antidepressants. When comparing monotherapy and the use of augmentation strategies, no significant differences were observed in clinical improvement or symptom severity. Authors concluded that while other clinical trials have provided evidence that pharmacological augmentation may be effective in OCD, many patients experience sub-optimal clinical improvement (Ameringen et al., 2014).

There have been varying reports as to whether SSRIs have a delayed response in the treatment of OCD. A meta-analysis of randomized, placebo-controlled trials of SSRIs measured the trajectory of the pharmacologic response (Issari Y et al 2016) and the relationship of the trajectory to the SSRI dose. The authors concluded that the greatest treatment gains occur early in the SSRI treatment and that a greater positive response is associated with higher doses of SSRIs ($P < .0001$).

Except for citalopram and escitalopram, all of the SSRIs have been approved by the FDA for the treatment of OCD in adults (Phillips and Stein, 2015). The FDA has approved only three SSRIs, i.e., fluoxetine, fluvoxamine and sertraline, in the treatment of children with OCD. Clomipramine, a tricyclic antidepressant, has been approved by the FDA for both adults and children, but SSRIs are the recommended first-line medication due to adverse side effects of clomipramine. SSRIs are typically used at higher doses and for longer periods in patients with OCD than in patients with depression. A particular SSRI is chosen based on side effect profiles, potential drug-drug interactions, comorbid medical conditions, patient age, prior treatment response, family history of treatment response and patient preference as no evidence has been shown for differential benefit among the SSRIs (Pittenger and Bloch, 2014; Seibell and Hollander, 2014). Although studies have shown the benefit of higher dose and longer treatment in treating patients with OCD, few studies suggest how long to continue pharmacotherapy after the achievement of a clinical response. Pittenger and Bloch noted that a meta-analysis of studies found relapse rates in individuals switched from pharmacotherapy to placebo were approximately twice as high as in those maintained on SSRI pharmacotherapy.

SNRIs, e.g., venlafaxine, have been shown in several studies to be highly effective in treating SSRI-refractory OCD (Pittenger et al., 2014). Other studies suggested that SNRIs, e.g., venlafaxine, are less effective than SSRIs, e.g., paroxetine in treating SSRI-refractory OCD. Pittenger and Bloch cautioned against recommending SNRIs for OCD monotherapy based on current data. SSRIs are generally the recommended first-line pharmacological treatment for OCD. According to the APA, when an eight- to 12-week trial of a SSRI does not result in a positive response, another trial of monotherapy with another SSRI or clomipramine should be given. They also noted that the likelihood of response decreases with an increased number of failed trials (Phillips and Stein, 2015).

Treatment – Augmentation of Serotonin Reuptake Inhibitors with Antipsychotics

A recent systematic review and meta-analysis investigated the effects of antipsychotic augmentation in OCD using as the primary outcome measure the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Veale et al., 2014). Adults with OCD ($n=493$) participated in fourteen studies, four of which were preceded by an open-label study of a SSRI, to determine its responsiveness prior to beginning treatment with an antipsychotic. The remaining ten studies involved patients receiving routine treatment with a SSRI. All studies were randomized controlled trials comparing an atypical antipsychotic, i.e., risperidone, olanzapine, quetiapine and aripiprazole, against a placebo for at least four weeks to augment SSRI treatment. The study found no evidence of the clinical effectiveness of olanzapine or quetiapine as augmenting agents, while aripiprazole and risperidone were found to be effective in the *short term*. They recommended against the use of olanzapine and quetiapine as augmenting agents in

OCD. Authors also noted evidence for the effectiveness of CBT or clomipramine to augment SSRIs before use of an anti-psychotic, but cautioned that the use of clomipramine combined with a SSRI requires electrocardiogram (ECG) monitoring.

Treatment – Augmentation of Serotonin Reuptake Inhibitors with Risperidone or Exposure and Ritual Prevention (EX/RP)

Based on meta-analyses, an estimate of up to one-third of adults with OCD respond acutely to augmenting SRIs with antipsychotics, but the *long-term* response to antipsychotic augmentation has not been studied (Foa et al., 2015). In a recent trial, patients with OCD (n=100) who were receiving either clomipramine or a SSRI for at least 12 weeks while remaining symptomatic were randomized to eight weeks of risperidone, EX/RP including twice-weekly 90-minute sessions, or pill placebo during the acute phase of the study. Patients (n=40) who responded (Y-BOCS scores decreased at least 25 percent) during the eight-week period entered a six-month maintenance phase where the two augmentation strategies continued. Of the patients receiving EX/RP during the acute phase, 60 percent were responders, whereas only 16 percent of those receiving risperidone were responders. However, those who responded to either EX/RP or risperidone maintained their gains over the six-month maintenance phase. Researchers concluded that these results “strongly support augmenting SRIs with EX/RP rather than risperidone in adults with OCD” and further suggested that “ongoing EX/RP treatment can help many patients maintain their acute gains” (Foa et al., p. 449).

A recent study included adults with OCD (n=32) who had failed to respond to 12 weeks of SRI treatment after which they were randomized to eight weeks of SRI augmentation with risperidone or pill placebo, again being classified as non-responders (McLean et al., 2015). Non-responders to risperidone and pill placebo (n=20 and 12, respectively) then elected to crossover to 17 twice weekly treatments of EX/RP. At posttreatment, more than half of the participants were responders with 15 percent achieving excellent response. Authors noted the importance of this study as it shows that EX/RP is effective for OCD patients who continue to report clinically significant OCD symptoms after SRI treatment and after SRI augmentation with either risperidone or placebo. Researchers found that the participants either maintained gains or showed improvement to week 32 follow-up. Researchers concluded, “This study adds to the body of evidence supporting the use of EX/RP with patients who continue to report clinically significant OCD symptoms after multiple pharmacologic trials” (McLean et al., 2015).

Cognitive Behavior Therapy

A recent meta-analysis investigation, including 16 randomized controlled trials with participants with OCD (n=756), examined the efficacy of cognitive behavior therapy (CBT) (Olatunji et al., 2015). Control conditions included the following: stress management training, relaxation, pill placebo, anxiety management and wait-list. Analysis of results found that CBT was superior to control conditions in the improvement of both OCD symptoms and depression symptoms at post-treatment showing a large effect size. Researchers noted the need for future studies to determine the extent to which CBT produces long lasting symptom changes for patients with OCD. They reported the lack of a significant association between higher pre-treatment OCD symptom severity or higher pre-treatment depression and lower CBT effect size. Findings were consistent with other studies showing relatively equivalent effects for

different treatment types, i.e., CT and ERP. The number of CBT sessions was unrelated to CBT effect sizes as were intensity of treatment and magnitude of treatment. Researches emphasize that “there may be no added benefit to extensive sessions given that standard CBT for OCD can stay cost-effective without losing efficacy” (Olatunji et al, p. 228).

Remote Cognitive Behavior Therapy

Using a meta-analytic approach, a recent study evaluated the efficacy of remote cognitive behavior therapy for OCD (Wootton, 2015). Included in this meta-analysis were 18 studies including individuals with OCD (n=823) whose mean age was 31 years. Treatments included 23 remote conditions, e.g., videoconferencing administered CBT (vCBT), telephone administered CBT (tCBT), computerized CBT (cCBT), internet administered CBT (iCBT), and bibliotherapy administered CBT (bCBT). *High intensity remote treatments* included vCBT and tCBT, both of which provide skills and length of sessions typically the same as in traditional face-to-face treatment with the patient and therapist interacting in real-time. *Low intensity remote treatments*, i.e., cCBT, iCBT and bCBT, also provide skills much the same as in face-to-face treatment and may include some clinician contact or be self-guided, although not in real time. All participants had moderate symptoms at baseline according to the Y-BOCS score. Control conditions included face-to-face treatment, attention controls, relaxation training and waitlist controls. Researchers found that remote treatment, regardless of methodology delivered, was more effective than no treatment, producing a decrease in symptoms of a large magnitude, with outcomes similar to face-to-face treatment. Researchers suggested that the amount of therapist contact may be a moderating factor and noted that the effect size in high intensity treatments was larger than in low intensity treatments although symptoms were decreased in both treatments. They concluded, “According to the findings of this meta-analysis an entirely remote stepped care treatment may be possible where low intensity remote treatments (such as iCBT or bCBT) are offered as a first step in a stepped care treatment for OCD, followed by higher intensity remote treatments (such as vCBT or tCBT if required” (Wootton, p.111). While suggesting that remote treatment may be as effective as face-to-face treatment, researchers also noted, “Across each of these studies the effect size differences are in the favor of face-to-face treatment and further research is required to elucidate the differences in outcome between different types of remote treatment and face-to-face treatment.” They suggested further investigation in the future due to the small number of randomized controlled trials that have been conducted to date comparing face-to-face and remote treatment.

Treatment – Augmentation of CBT with D-cycloserine

Researchers have hypothesized that the administration of D-cycloserine prior to use of CBT can enhance the treatment impact of CBT in children and adults. Earlier studies found promising results (Wilhelm et al, 2008, Farrell et al, 2013.) However, the studies used small sample sizes and truncated CBT protocols. A more recent study (Storch, 2016) found no added benefits from the administration of D-cycloserine in a population of children and adolescents with CBT. 142 children and adolescents with a diagnosis of OCD were randomly assigned to family CBT sessions with either a dose of D-cycloserine or placebo. Both groups responded well to the CBT as evidenced by a decline in the Yale-Brown Obsessive Compulsive Scale but the group receiving the medication did not display superior benefits over the group receiving the placebo. A later review and meta analysis of studies investigating the effect of D-cycloserine

augmentation with CBT found short term positive gains as compared to placebo and mixed findings in terms of continued positive impact at follow up (Mataix-Cols, 2017.)

Stepped Care and Lower Levels of Treatment (Self-Help)

Noting that although CBT with EX/RP is recognized as the most effective treatment for OCD, authors also pointed to the many barriers to accessibility, including restricted access in rural areas and to trained clinicians, as well as high cost (Pearcy et al., 2016). A meta-analysis, including eighteen studies (randomized controlled trials or quasi-experimental studies) that included adults with OCD (n=1570), investigated the efficacy of self-help treatment with a particular focus on therapeutic contact within the context of a stepped-care model (Pearcy et al., 2015). Studies were categorized depending on amount of therapeutic contact as follows: self-administered, predominately self-help, or minimal-therapist contact self-help. Researchers sought to determine the impact of the amount of therapist contact on outcomes, irrespective of whether the self-help treatments were mainstream or alternative. Results showed that as therapeutic contact increased, effect size increased:

- Self-administered self-help – pooled subgroup effect size at post-treatment - .33 (small total effect size)
- Predominantly self-help – pooled subgroup effect size at post-treatment - .68 (moderate total effect size)
- Minimal-therapist contact self-help – pooled subgroup effect at post-treatment -1.08 (large total effect size).

Researchers noted a downward trend in drop-out rates that occurred as therapeutic contact increased; the self-administered group had the highest dropout rate followed by the predominantly self-help group and the minimal self-help group. This study showed evidence of the efficacy of internet CBT for OCD with minimal-therapist contact self-help, but there is a lack of current randomized controlled trials for the treatment of OCD using CBT or ERP through self-administered self-help with no therapist contact. Researchers suggested the need for randomized controlled trials using CBT or ERP through self-administered self-help to investigate stepped care (Pearcy et al., 2016).

Brief Family Intervention to Reduce Accommodation in Obsessive-Compulsive Disorder

A recent, small randomized controlled study evaluated the feasibility, acceptability and efficacy of a brief adjunctive intervention for family members of adult patients with OCD (Thompson-Hollands et al., 2015). Patients (n=18) with a mean age of 35.44 years received standard ERP while a family member of each patient was randomized to either receive or not receive the brief adjunctive intervention. The intervention included two sessions for a family member within two weeks of the patient beginning ERP and another session two weeks later. The intervention began with psychoeducation, including the model of OCD and the rationale for ERP. Accommodation, as a common although maladaptive family response, was openly discussed. The sessions included skills training to reduce accommodation, which “serves the same maladaptive function as compulsions” (Thompson-Hollands et al., p. 222). Results of this 25 week study showed that the intervention successfully reduced family accommodation, based on scores on the Family Accommodation Scale for Obsessive-Compulsive Disorder. Average accommodation scores of family members in the control group remained little changed by the end of the study (remained at 78

percent of their baseline levels), while the scores of family members in the intervention group dropped substantially (dropped to 37 percent of baseline levels). Regression analysis found that “change in family accommodation from baseline accounted for a significant amount of variance in later OCD symptoms” in the intervention group and suggested, “this adjunctive intervention produces more rapid treatment response compared to traditional ERP alone” (Thompson-Hollands, et al., p. 218).

Deep Brain Stimulation in the Treatment of Obsessive-Compulsive Disorder

Deep Brain Stimulation has shown promise for the treatment of patients with severe treatment refractory OCD but there have been few studies that have monitored the long-term treatment impact. One recent study (Fayad et al, 2016) evaluated the long-term safety and effectiveness of DBS over the course of 73-112 months. Of the six adults who were enrolled in the original NIMH pilot study of use of DBS with OCD, four participants showed the same positive treatment response over time as they had after one year of the treatment. Positive response was defined as greater than 35% reduction in symptoms as measured by the Yale Brown Obsessive Compulsive Scale. An initial non-responder to the treatment achieved a 26% reduction in symptoms at the long-term follow up. (Fayad, SM, Guzick, AG, Reid, AM, Mason, DM, Bertone, A, Foote, KD, Okun MS, Goodman WK, Ward HE (2016, December 08). Six-Nine Year Follow-Up of Deep Brain Stimulation for Obsessive-Compulsive Disorder. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed?term=27930748>).

A recent study reviewed the modern literature regarding deep brain stimulation (DBS) in the treatment of therapy-refractory OCD (Blomstedt et al., 2015). Authors noted that based on current understanding of the pathophysiological mechanisms behind OCD, it is not possible to identify the best target for an intervention with DBS. Clinical effects of DBS for OCD have been presented in 25 publications including a total of 90 individual patients. As a result of their review of the studies, authors concluded, “A therapy that will improve about one-third of patients from severe to moderate OCD, and one-third from severe to mild or no OCD, is promising for many patients suffering from severe therapy-refractory symptoms. However, the presented study comes mainly from nonrandomized studies of limited size. Further, no consensus exists regarding the target of choice for DBS in this condition. It must therefore be emphasized that DBS for OCD is currently an *experimental therapy* that should only be performed in clinical studies by multidisciplinary teams with substantial experience with DBS from other conditions (Blomstedt et al., 2015).

Transcranial Magnetic Stimulation of the Supplementary Motor Area (SMA)

A recent randomized study of subjects (Pallanti et al, 2016) refractory to SSRI treatment assigned half of the subjects to a control group where the SSRI was augmented with an antipsychotic medication. The other half of the subjects were assigned to five 20-minute-long rTMS sessions per week for 3 weeks. Improvement was defined as at least 25% improvement from baseline as measured by the Yale Brown Obsessive Compulsive Scale. Of the group receiving rTMS, 68% met the “improved” definition. Of the group receiving the treatment as usual with augmented medication, 24% met the definition.

A recent randomized, double-blind placebo-controlled clinical trial investigated the efficacy of low-frequency (1 Hz) rTMS in patients with OCD (Hawken et al., 2016). Participants (n=22) were randomly assigned into one of two groups (ACTIVE or SHAM

groups). rTMS was applied bilaterally and simultaneously over the sensory motor area. The Y-BOCS score at the end of the six-week treatment period showed a clinically significant decrease for the ACTIVE group receiving treatment compared both to baseline as well as to the SHAM group, and the effect was maintained over the following six weeks after completion of treatment. Researchers suggested future studies are needed extending the follow-up period to determine the duration of clinical efficacy and to determine the generalizability of the findings (Hawken et al., 2016).

Exercise as an alternative and/or adjunctive treatment for OCD

A recent pilot study tested the feasibility and clinical benefits of 12-weeks of combined moderate-to-vigorous aerobic exercise and group CBT in patients whose mean age was 35 (n = 11) with moderate-to-severe, medication-refractory OCD (Rector et al., 2015). CBT was delivered in a group format incorporating exposure and response prevention with increasing emphasis on cognitive approaches for obsessions and compulsions. Adherence to exercise was measured by self-reported exercise session logs and weekly phone checks by research assistants and reported to exceed 80 percent. OCD symptom reduction measured from pre- to post-treatment by Y-BOCS scores showed large, clinically significant improvements in severity of symptoms. Researchers noted that the results of this study demonstrate the “possible value of aerobic exercise as an adjunctive treatment in OCD” and “are proceeding with a large-scale, multi-site randomized controlled trial that will aim to overcome the limitations associated with this pilot investigation” (Rector et al., p. 338).

Introduction

The Guideline Watch summarizes new evidence and recommendations since the publication of the Guideline, indicating that the changes in the definition of OCD in DSM-5 have no impact on the treatment recommendations of the Guideline. The recently published Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5™) no longer considers OCD as an “anxiety disorder.” Obsessive-compulsive and related disorders are now included in a separate chapter of the DSM-5. Related disorders include: body dysmorphic disorder; hoarding disorder; trichotillomania (hair pulling disorder); excoriation (skin picking) disorder; substance/medication-induced obsessive-compulsive and related disorder; obsessive-compulsive and related disorder due to another medical condition; other specified obsessive-compulsive and related disorder; and unspecified obsessive-compulsive and related disorder. The common thread running through OCD and related disorders are obsessions, compulsions or both. Although these disorders have features in common, they are considered distinct disorders as there are important differences between them. The DSM-IV OCD specifier “with poor insight” has been changed in DSM-5 to allow for some degrees on a spectrum of insight, including good or fair insight, poor insight and absent insight/delusional beliefs. A tic-related specifier is included in DSM-5 to identify individuals with a current or past comorbid tic disorder (APA, 2013).

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A most recent genome-wide association study (GWAS) scanning the genomes of people with OCD, as well as close relatives of those with OCD, identified a significant association in patients with OCD near a gene, protein tyrosine phosphokinase (PTPRD) (Mattheisen et al, 2015). The study, OCD Collaborative Genetics Association Study (OC GAS), was comprised of patients (n = 1406) with onset of OCD before age 18 years and a case control subsample (n = 1084). The most significant finding in the study was the signal near the PTPRD gene, “a member of the receptor protein tyrosine phosphatase family, which comprises transmembrane signaling molecules that regulate a variety of cellular processes including cell growth and differentiation. Pre-synaptic PTPRD promotes the differentiation of glutamatergic synapses” (Mattheisen et al., p. 344). Researchers noted that plausible biologic hypotheses and prior genetic evidence has been shown for the finding related to PTPRD’s association with OCD.

Related to OCD diagnosis and classification is an issue regarding the factor structure of the symptoms of OCD. The research team of Bloch et al. conducted a meta-analysis that included 21 studies and 5,124 participants with OCD and an exploratory factor analysis of the 13 Yale-Brown Obsessive-Compulsive Scale Symptom Checklist (Y-BOCS) categories (Bloch et al., 2008). Their findings showed that a four-factor structure explained a large proportion of the heterogeneity in the clinical symptoms of OCD, i.e., dimensions of symmetry, forbidden thoughts, cleaning and hoarding. In a published clinical review of current methods used in the assessment of OCD, these underlying symptom dimensions were noted to have important implications for the etiology, assessment and treatment of the disorder (Benito et al., 2011). Authors emphasized they have been associated with differential responses to cognitive-behavioral (CBT) and pharmacotherapy, different patterns of neural activity and

distinct patterns of familial transmission while playing an important role in tailoring treatments to the needs of individual patients (Benito et al., 2011). DSM-5 notes that while the specific content of obsessions and compulsions varies among individuals, symptom dimensions are common in OCD, i.e., cleaning, symmetry, forbidden or taboo thoughts, and harm, e.g., fears of harm to others or oneself and checking compulsions. Another dimension discussed in DSM-5 is the hoarding of objects as a consequence of obsessions and compulsions. Themes occur across different cultures and are relatively consistent in adults with OCD over time, and individuals with OCD often have symptoms in more than one dimension (American Psychiatric Association, 2013).

Risk factors for OCD have been analyzed using epidemiological data in order to more readily identify and effectively treat persons affected with this illness. In 2007, Fontenelle and Hasler conducted a large qualitative systematic review of community samples (90 studies and 16 reviews) and analyzed the correlates and risk factors associated with the development of OCD. These included demographic characteristics, innate features, e.g., familial background and intelligence levels, environmental factors and psychiatric comorbidities (Fontenelle et al., 2007). Major findings of their review showed that late adolescence is a period of increased vulnerability to OCD and that it affects predominantly female adults and male children and adolescents. Other key risk factors identified were being unmarried, non-white or abusing drugs. Additionally, researchers reported that OCD was found to be a familial and genetic disorder when one considers symptom dimensions instead of categorical diagnosis and when the disorder begins at an early age (Fontenelle et al., 2007).

Researchers examined data from the Swedish National Patient Register, Multi-Generation Register and Twin Register to provide unbiased estimates of familial risk for heritability of OCD at the population level (Mataix-Cols et al., 2013). The Swedish National Patient Register included data on individuals (n=24,000) diagnosed with OCD during four decades, and the Twin Register included data from a population-based sample of twins (n=16,000) with OCD symptoms. Analyses of family data and twin analyses were performed which led to the following conclusions: 1) OCD is a familial and heritable disorder; 2) unique, rather than shared, environment is important in OCD; and 3) non-biological relatives of patients with OCD are also at an elevated risk for OCD. Researchers concluded that the familiarity of OCD is explained for the most part by genetic factors and that non-shared environmental factors are at least as important. They suggested further studies to explore a finding of possible assortative mating in OCD (Mataix-Cols et al., 2013).

The adopted APA guideline indicates that mood disorders, i.e., depressive disorders and bipolar disorders, anxiety disorders, i.e., panic disorder, generalized anxiety disorder [GAD], social phobia, tics, Tourette's disorder and eating disorders, i.e., anorexia nervosa and bulimia nervosa, are conditions that commonly co-occur in patients with OCD. The guideline also specifies that other disorders with elevated prevalence in OCD include certain impulse-control disorders, i.e., skin picking and trichotillomania, attention-deficit/hyperactivity (ADHD) and oppositional defiant disorder (ODD). Since publication of the guideline, one family study of OCD with genetic probands found that major depressive disorder (MDD) was highly familial when comorbid with pediatric OCD (Hanna et al., 2011). A more recent study of 71

children and adolescents with primary OCD found that 21 percent of this sample exhibited depressive symptoms (confirmed by the Children's Depression Inventory) that were associated with higher levels of cognitive distortion and more severe OCD symptoms (Peris et al., 2010). Another study examining the effect of depression on refractory OCD and PTSD found that depression was related to higher levels of the OCD symptom cluster of obsessing, but not to other symptom clusters, i.e., hoarding, checking, neutralizing, ordering, washing and doubting, and to greater severity of PTSD (Merrill et al., 2011). In addition, the prevalence rate of PTSD and trauma exposure was higher in children with OCD (n=263) than in a comparative control group of non-OCD youth and those affected with concurrent disorders had more severe OCD symptoms (LaFluer et al., 2011).

The DSM-5 indicates that 76 percent of individuals with OCD have an anxiety disorder and 63 percent have a depressive or bipolar disorder, the most common being major depressive disorder. Another common comorbidity is personality disorder, occurring in 23 to 32 percent of individuals with OCD. A lifetime tic disorder occurs in up to 30 percent of individuals with OCD and is most common in males. Other comorbidities include related disorders of OCD, e.g., body dysmorphic disorder, trichotillomania and excoriation. An association between oppositional defiant disorder and OCD has also been reported. The DSM-5 advises that individuals with schizophrenia, schizoaffective disorder, bipolar disorder, eating disorders and Tourette's disorder should be assessed for OCD (American Psychiatric Association, 2013).

Age at onset (AAO) studies have been published demonstrating that early onset (EO) and late onset (LO) represent distinct subtypes of OCD. Results from the analysis of one Canadian OCD sample (n=252) found an association between earlier onset of illness and higher comorbidity with other obsessive compulsive spectrum disorders, suggesting greater severity and poorer outcome. In addition, subjects in the early-onset group (< 10 years) had a significant increase in comorbid tic and Tourette's disorder (Janowitz et al., 2009). A meta-analytic review of OCD studies confirmed these subtypes and found that EO compared to LO was more likely to occur in males, be associated with greater OCD global severity and higher prevalence of most types of OC symptoms, more likely to be comorbid with tics and other obsessive compulsive spectrum disorders and with greater prevalence of OCD in first degree relatives (Taylor 2011). Similar findings were reported in another study (n=196) where it was found that EO subjects tended more often to have comorbid panic disorder (de Luca et al., 2011). Likewise, findings from a retrospective chart review (n=132) conducted in Poland showed that specific types of obsessions and compulsions differed and were grouped by age of onset subtypes, i.e., adolescent, adults with early onset, adults with late onset. Investigators noted that more rigorous study of OCD symptom clusters by age of onset groups and duration of OCD is required (Butwicka et al., 2010). The DSM-5 indicates that a triad of attention-deficit/hyperactivity disorder (ADHD), tic disorder and OCD is often seen in early years of childhood (American Psychiatric Association, 2013).

Two studies focused on the key functions of compulsions for patients with OCD. An Australian study analyzed data from a structured psychiatric interview of 108 patients with OCD using the Y-BOCS and the Functions of Compulsions Interview (Starcevic et al., 2011). Investigators were able to verify the functions of 218 compulsions and

found that the mean number of functions per compulsion was 2.94 and were often performed automatically. Study results specified reasons for compulsions as follows: (1) hoarding performed for perceived need for collected objects; (2) order/symmetry/repeating performed to achieve a “just right” feeling; (3) checking performed to avert something bad from happening; (4) washing/cleaning performed to decrease stress or anxiety; and (5) mental compulsions (or compulsions without overt signs) were performed automatically (Starcevic et al., 2011). A longitudinal study of 225 patients with OCD followed over four years found that 12 percent of the sample presented with mental rituals, i.e., praying, counting, mental checking, thinking “good” or “safe” thoughts and neutralizing distressing images, as the primary compulsion (Sibrava et al., 2011). Further analysis of these findings indicated that for those patients endorsing mental rituals as their primary compulsion, the following were the most frequently endorsed obsession: (1) fear of harming self/other, being responsible for something bad happening, and (2) fears of offending God and sacrilegious thoughts. Investigators noted that praying and undoing bad thoughts with good thoughts were the most frequently endorsed mental ritual. In addition, the study found preliminary evidence that primary mental rituals were associated with an earlier onset of OCD and a more severe and chronic form of the disorder (Sibrava et al., 2011).

Parental rearing and response to OCD symptoms of children were studied in clinical trials in order to gain further understanding of relevant family dynamics experienced by individuals with OCD and develop effective therapeutic interventions (Lennertz et al., 2009; Albert et al., 2010). One controlled study conducted in Germany compared 122 subjects with OCD along with 41 of their siblings, to 59 healthy controls with 45 of their siblings. Analysis of findings from the German short-version of the Egena Minnen Befråff-ande Uppfostran (EMBU - translated to Own Memories of Parental Rearing Experiences in Childhood) tool showed that OCD cases reported less warm and more rejecting and controlling behavior by their parents compared with healthy control subjects. In addition, OCD subjects with early onset reported less maternal rejection than OCD subjects with late onset (Lennertz et al., 2009). Another study analyzed findings from the Family Accommodation Scale (FAS) administered to 141 psychopathology-free family members cohabitating with 97 patients with OCD. The results showed that family accommodation, i.e., a process whereby family members assist or participate in rituals, was common. Provision of reassurance, participation in rituals and assisting the patient in avoidance were the most frequent practices (occurring on a daily basis in 47 percent, 35 percent and 43 percent of family members respectively). In addition, study findings revealed that family accommodation is particularly frequent and distressing when the patient has prominent contamination/washing symptoms and/or when another family member has a history of an anxiety disorder (Albert et al., 2010).

Office-based Treatment of OCD

A recent cross-sectional study assessed the ability of primary care physicians to identify OCD utilizing an online vignette-based survey (Glazier et al., 2015). Primary care physicians (n = 208) reviewed vignettes focused on obsessions regarding aggression, contamination, fear of saying things, religion, pedophilia, somatic concern or symmetry and provided diagnoses and treatment recommendations for the

individuals described in the vignettes. The study found that primary care physicians misidentified the vignettes with an overall misidentification rate of 50.5 percent. Of those misidentifying the vignettes, 46.7 percent and 8.6 percent recommended CBT or SSRI, respectively, while of participants correctly identifying the vignette, 66.0 percent and 35.0 percent recommended CBT or SSRI, respectively. Among those misidentifying the vignette, antipsychotic recommendation rates were elevated. Researchers concluded that “elevated OCD misdiagnosis rates and the impact of incorrect diagnoses on treatment recommendations highlight the need for greater training regarding OCD symptomatology and empirically supported treatments” (Glazier et al., p. 767).

In one study, treatment of obsessive-compulsive disorder in U.S. office-based medical practices was studied (Patel et al., 2014). Examining data from the National Ambulatory Medical Care Survey (2003-2010), researchers found that among visits (n=316) with a diagnosis of OCD, 96 percent were to a physician seen previously by the patient and 86 percent of the visits were to a psychiatrist. Psychotropic medications, mostly SRIs, were prescribed at 84 percent of the visits and patients self-paying had higher chances of receiving psychotherapy. An imbalance in ethnic and racial distribution of OCD showed 91 percent of visits by non-Hispanic white patients, 1 percent by non-Hispanic black patients, 3 percent by Hispanic patients, and 4 percent by other non-Hispanic patients. Researchers suggested that research is needed to identify barriers to outpatient treatment of minority group members who have OCD. They suggested that efforts are also needed to better understand the recognition and treatment of OCD in primary care, especially given the potential shift to mental healthcare by primary care physicians under the Affordable Care Act (Patel et al., 2013).

Psychopharmacology

In a study including patients with OCD (n=361) at different stages of treatment who were recruited in eight international tertiary care centers, researchers found that 317 patients reported use of at least one medication while 44 reported none (Van Ameringen et al, 2014). Of the sample receiving current medication, 77.6 percent were taking a selective serotonin reuptake inhibitor (SSRI) as their primary medication, either as monotherapy or an augmentation agent. Monotherapy agents also included tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors (SNRIs), antipsychotics and benzodiazepines. Authors reported no significant differences in clinical improvement or Yale Brown Obsessive Compulsive Scale (YBOCS) scores between the different monotherapy agents. Nearly one-half of those currently taking medication were using at least one augmentation agent, e.g., antipsychotics, benzodiazepines and antidepressants. When comparing monotherapy and the use of augmentation strategies, no significant differences were observed in clinical improvement or symptom severity. Authors concluded that while other clinical trials have provided evidence that pharmacological augmentation may be effective in OCD, many patients experience sub-optimal clinical improvement (Ameringer et al., 2014).

Except for citalopram and escitalopram, all of the SSRIs have been approved by the FDA for the treatment of OCD in adults (Phillips and Stein, 2015). The FDA has approved only three SSRIs, i.e., fluoxetine, fluvoxamine and sertraline, in the

treatment of children with OCD. Clomipramine, a tricyclic antidepressant and potent SRI, has been approved by the FDA for both adults and children, but SSRIs are the recommended first-line medication due to adverse side effects of clomipramine. SSRIs are typically used at higher doses and for longer periods in patients with OCD than in patients with depression. A particular SSRI is chosen based on side effect profiles, potential drug-drug interactions, comorbid medical conditions, patient age, prior treatment response, family history of treatment response, and patient preference as no evidence has been shown for differential benefit among the SSRIs (Pittenger and Bloch, 2014; Seibell and Hollander, 2014). Although studies have shown the benefit of higher dose and longer treatment in treating patients with OCD, few studies suggest how long to continue pharmacotherapy after the achievement of a clinical response. Pittenger and Bloch noted that a meta-analysis of studies found relapse rates in individuals switched from pharmacology to placebo approximately were twice as high as in those maintained on their SSRI pharmacotherapy.

SNRIs, e.g., clomipramine and venlafaxine, have been shown in several studies to be highly effective in treating SSRI-refractory OCD (Pittenger et al., 2014). Other studies suggested that SNRIs, e.g., venlafaxine, are less effective than SSRIs, e.g., paroxetine in treating SSRI-refractory OCD. Pittenger and Bloch cautioned against recommending SNRIs for OCD monotherapy based on current data. SSRIs are generally the recommended first-line pharmacological treatment for OCD. According to the APA, when an eight- to 12-week trial of a SSRI does not result in a positive response, another trial of monotherapy with another SSRI or clomipramine should be given. They also noted that the likelihood of response decreases with an increased number of failed trials (Phillips and Stein, 2015).

A recent systematic review and meta-analysis investigated the effects of antipsychotic augmentation in OCD using as the primary outcome measure the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (et al., 2014). Adults with OCD (n=493) participated in fourteen studies, four of which were preceded by an open-label study of a SSRI, to determine its responsiveness prior to beginning treatment with an antipsychotic. The remaining ten studies involved patients receiving routine treatment with a SSRI. All studies were randomized controlled trials comparing an atypical antipsychotic, i.e., risperidone, olanzapine, quetiapine and aripiprazole, against a placebo for at least four weeks. The study found no evidence of the clinical effectiveness of olanzapine or quetiapine as augmenting agents, while aripiprazole and risperidone were found to be effective in the *short term*. They recommended against the use of olanzapine and quetiapine as augmenting agents in OCD. Authors also noted evidence for the effectiveness of CBT or clomipramine to augment SSRIs before use of an anti-psychotic, but cautioned that the use of clomipramine combined with a SSRI requires electrocardiogram (ECG) monitoring.

The adopted APA guideline specifies that both serotonin reuptake inhibitors (SRIs) and cognitive-behavioral therapy (CBT) are safe and effective first-line treatments for OCD. The guideline notes that the choice of initial treatment modality is individualized and depends on the following factors: (1) the nature and severity of the patient's symptoms; (2) co-occurring psychiatric and medical conditions; (3) the availability of CBT; and (4) the patient's past treatment history, current medications, capacities and preferences. The guideline also indicates that clomipramine, a mixed serotonin and

norepinephrine re-uptake inhibitor (SNRI) and selective serotonin re-uptake inhibitors (SSRIs) – specifically, fluoxetine, fluvoxamine, paroxetine and sertraline, are the recommended agents. However, the guideline notes that SSRIs are usually the preferred initial agents to be used because of their less troublesome side-effect profile. In addition to the guideline recommendations, other published information on SSRI treatment for OCD proposes their usage in significantly higher doses than those employed in depression and for at least six months or longer, recognizing that increased side-effect burden may be counterbalanced by increased treatment efficacy (Marazziti et al., 2010; Pampaloni et al., 2010).

Since release of the APA guideline, published meta-analytic findings continued to support SSRIs, e.g., citalopram (not approved by FDA for treatment of OCD), fluoxetine, fluvoxamine, sertraline and paroxetine, as a treatment for OCD (Soomro et al., 2009). Findings from the 17 studies (3097 participants) that were reviewed in this analysis showed that all of these drugs had similar efficacy with a modest treatment effect overall (Soomro et al., 2009). Additionally, other meta-analytic findings argued strongly for the efficacy of paroxetine and escitalopram (not approved by FDA for treatment of OCD), and to a somewhat lesser degree for fluoxetine, as a longer-term and maintenance treatment in the prevention of OCD relapse. Moreover, researchers suggested from their analysis that worsening by five Y-BOCS points be considered a threshold for relapse in patient with OCD (Fineberg et al., 2007; Donovan et al., 2010). The Guideline Watch notes an August 2011 Drug Safety Communication from the FDA advising that citalopram should not be used in doses greater than 40 mg/day due to its potential for QT_c prolongation (APA, 2013).

Since clomipramine has such a well-established basis in the treatment of OCD, the team of Dell’Osso et al. conducted a critical review of studies in order to determine the anti-obsessional properties of another SNRI, venlafaxine (Dell’Osso et al., 2006). In their critical review of research, the investigators noted that in two double-blind active-comparison studies, venlafaxine was found equally as effective as paroxetine and clomipramine in the short- and intermediate-term. Additionally, they identified one double-blind trial and two case reports where venlafaxine was shown to be particularly effective in OCD patients who had not responded to other SSRIs. These findings mirror the adopted guideline and its suggestion to consider switching to venlafaxine when the patient has an inadequate response to treatment with a single SSRI. Authors argued the need for more rigorous clinical trials to confirm the efficacy of venlafaxine in treating OCD due to its greater tolerability than clomipramine (Dell’Osso et al., 2006).

A study examined the longitudinal use of SRIs in adult outpatients (n=252) with OCD who were receiving treatment in clinical settings to determine whether discontinuation of SRIs results in a worsening of OCD symptoms in the majority of patients who had achieved either partial or full remission while taking the SRIs (Grant et al., 2013). Among those who had achieved either partial or full remission in the five year follow-up period, only 14.1 percent of those in partial remission and 12.1 percent of those in full remission had stopped SRI treatment. The cumulative incidence of worsening of OCD after discontinuing SRI treatment was only 33.3 percent. Researchers suggested that although most patients currently remain on the same SRI and same dose over many years, discontinuation of SRI treatment may not always result in significant

worsening of OCD symptoms. Researchers suggested future randomized trials where patients are randomized to placebo or continued SRI therapy over an extended period where resumption of SRIs would be offered to those who relapse or whose symptoms worsen. Other findings of this study showed factors associated with less likelihood of patients discontinuing treatment with SRIs including older age, receipt of CBT, reported improvement from SRIs, and longer periods of SRI treatment. Patients most likely to discontinue medication were patients receiving low dose SRIs and those taking citalopram (Grant et al., 2013).

Studies on augmentation strategies for treatment-resistant OCD were reviewed by Marazitti et al. They reported that about one-third of these patients may have a refractory condition and that the strongest predictor of poor response seemed to be the presence of higher Y-BOCS symptom checklist scores on hoarding obsessions and compulsions (Marazitti et al., 2010). These authors and others indicated that clinical studies supported the use of haloperidol and risperidone added to an SSRI, but acknowledged that the data were mixed on the use of olanzapine as an augmenting agent to SSRIs in the treatment of OCD (Bloch et al., 2006; Marazitti et al., 2010). More recent meta-analyses continue to support the efficacy of risperidone as an augmenting agent to antidepressants in the treatment of OCD, but efficacy was counterbalanced with adverse effects and increased sedation (Maher et al., 2011; Depping et al., 2010). Quetiapine added to an SSRI was also more recently studied where meta-analytic findings revealed that quetiapine as an additive to clomipramine, fluoxetine and fluvoxamine at the lowest doses was superior to placebo groups (Denys et al., 2007). The comparative efficacy of aripiprazole and risperidone as augmenting agents was investigated in patients (n=41) who did not respond after 12 weeks of monotherapy with SSRIs; findings suggested that risperidone was more effective than aripiprazole (Selvi et al., 2011).

The APA Guideline Watch discusses newer studies strengthening the evidence and supporting some of the augmentation strategies described in the 2007 guideline. The Guideline Watch cautions that the utility of some augmentation agents, e.g., exposure and response prevention (ERP) and some second-generation antipsychotics, should be reevaluated on an ongoing basis due to the modest evidence supporting their use in augmentation (American Psychiatric Association, 2013). In a randomized controlled trial (in press at time Guideline Watch was published) to compare the effects of two SRI augmentation strategies compared to pill placebo, adults (n=100) with OCD of moderate severity who had received a therapeutic SRI dose for at least 12 weeks before entering the trial were randomized to one of the following while continuing treatment with SRI: risperidone (up to 4 mg/d for eight weeks; cognitive behavioral therapy consisting of exposure and ritual prevention (EX/RP) over 17 sessions delivered twice weekly; or placebo (Simpson et al., 2013). Results showed that adding EX/RP to SRIs was more effective than adding risperidone or pill placebo in outcome measures, i.e., reducing symptoms of OCD; improving insight, functioning, and quality of life. Of patients receiving EX/RP, 80 percent responded to treatment compared to 22.5 percent and 15 percent of those receiving risperidone and placebo, respectively. On any outcome measure, risperidone was not significantly more superior to placebo. This study noted that long-term SRI treatment may itself not be benign as most patients receiving placebo, EX/RP, or risperidone to augment SRI treatment reported treatment-emergent adverse effects. The percentages of patients reporting treatment

emergent adverse effects were 88 percent, 72 percent and 58 percent for those receiving risperidone, placebo or EX/RP, respectively. Researchers suggested that EX/RP should be the first-line treatment due to its superior efficacy and less negative adverse effects when compared to risperidone. They questioned whether patients with OCD receiving SRIs who do not respond favorably to the addition of EX/RP can benefit from risperidone augmentation. Researchers note the need for alternative medication strategies for patients with OCD receiving SRIs (Simpson et al., 2013).

Ressler et al. suggested that Simpson et al.'s conclusion that EX/RP should be the agent considered first for SRI treatment augmentation is supported by current data (Ressler et al., 2013). Authors reviewed other studies finding that adding medication to EX/RP does not achieve better outcome than EX/RP alone for OCD, with only one exception, i.e., the use of D-cycloserine in addition to EX/RP. Authors discuss how EX/RP retrains the brain's habit-forming circuitry so that the compulsive habit will not be activated during the occurrence of an activating cue. In conclusion, authors suggested that "there are likely unique aspects of brain function that are differentially targeted by medication and psychotherapeutic approaches. As the neurobiology of OCD and other disorders are further dissected, we can hope for progress with targeted combined pharmacotherapy and psychotherapy in which rationally designed therapeutics can be fully derived from our understanding of the brain, its dysfunction, and mechanisms of recovery" (Ressler et al., pg 1130, 2013).

The APA Guideline Watch noted studies suggesting that quetiapine as an augmentation agent may be effective in only a small subset of patients with treatment-resistant OCD and that studies suggest that aripiprazole may be an effective augmentation agent (American Psychiatric Association, 2013).

The APA guideline presents a treatment algorithm of psychopharmacology that includes medication strategies that are to be used only in cases where the patient has shown little or no response to previous sequential treatment trials, i.e., augmentation with a second generation antipsychotic [SGA], adding CBT if not already provided, switching to a different SRI, augmentation with clomipramine or buspirone, pindolol, morphine sulfate, inositol or a glutamate antagonist. Drugs specified in the APA guideline for use with the most treatment-resistant patients include a switch to D-amphetamine, tramadol or ondansetron monotherapies or to a monoaminoxidase inhibitor (MAOI). Using ondansetron in combination with a SSRI was investigated in a small (n=42) double-blind, controlled pilot study comparing patients receiving fluoxetine (20 mg./day) plus the antiemetic agent, ondansetron (4 mg./day) versus fluoxetine (20 mg./day) plus placebo. Study findings demonstrated positive effects for both study groups on obsessions and compulsions. Patients treated with the ondansetron, however, had significantly lower Y-BOS scores in weeks two through eight than the placebo augmented group. In addition, there were no differences in frequency of side effects between the groups (Soltani et al., 2010).

The APA Guideline Watch notes evidence suggesting that dysregulation involving the neurotransmitter glutamate may be a contributor of the pathophysiology of OCD. The Guideline Watch discusses trials of augmentation agents, i.e., topiramate, lamotrigine, memantine, pregabalin, N-acetylcysteine and glycine, thought to modulate glutamate. Research after publication of the Guideline Watch has shown that intravenous

infusion of the N-methyl-D-aspartate (NMDA) antagonist ketamine has potential for relieving symptoms of OCD (Medscape, 2013). Researchers suggested that although modulating glutamate may be promising for OCD patients, ketamine is not yet at a stage that it can be given safely to outpatients due to its side effects. In this study where unmedicated adults with OCD (n=15) received one intravenous infusion of ketamine 0.5mg/kg over 40 minutes followed by an infusion of saline at least a week later (or received the two infusions in the opposite order), half of the participants reported improvement in obsessions after receiving the ketamine infusion. None of the patients receiving placebo met the criteria of improvement in obsessions. Researchers suggested that ketamine can rapidly relieve symptoms of OCD with the effect lasting at least one week in OCD patients with constant intrusive thoughts. They noted that this study hold promise for other research on further ways to modulate the NMDA receptor with the rapid effects minus the side effects of ketamine (Medscape, 2013).

Neurostimulation

Neurostimulation continues to be investigated as a potential efficacious treatment solution for refractory OCD. While recent studies suggest the treatment is promising, it has not yet been approved by the FDA for the treatment for OCD. One study reviewed the modern literature regarding deep brain stimulation (DBS) in the treatment of therapy-refractory OCD (Blomstedt et al., 2015). Authors noted that based on current understanding of the pathophysiological mechanisms behind OCD, it is not possible to identify the best target for an intervention with DBS. However, growing experience with rTMS through continued off label use has led some clinicians to state that the standard target area for rTMS is the supplementary motor area (SMA),(Hollander, 2016). Clinical effects of DBS for OCD have been presented in 25 publications including a total of 90 individual patients. As a result of their review of the studies, authors concluded, “A therapy that will improve about one third of patients from severe to moderate OCD, and one third from severe to mild or no OCD, is promising for many patients suffering from severe therapy-refractory symptoms.” However, the presented study comes mainly from nonrandomized studies of limited size. Further, no consensus exists regarding the target of choice for DBS in this condition. It must therefore be emphasized that DBS for OCD is currently an *experimental therapy* that should only be performed in clinical studies by multidisciplinary teams with substantial experience with DBS from other conditions (Blomstedt et al., 2015). A recent randomized study of subjects (Pallanti et al, 2016) refractory to SSRI treatment assigned half of the subjects to a control group where the SSRI was augmented with an antipsychotic medication. The other half of the subjects were assigned to five 20-minute-long rTMS sessions per week for 3 weeks. Improvement was defined as at least 25% improvement from baseline as measured by the Yale Brown Obsessive Compulsive Scale. Of the group receiving rTMS, 68% met the “improved” definition. Of the group receiving the treatment as usual with augmented medication, 24% met the definition.

The APA guideline reviews the initial research investigating the efficacy of Deep Brain Stimulation (DBS) on the treatment of treatment-resistant OCD. At time of publication, the adopted guideline specifies that early case reports and preliminary studies are promising and further research should be encouraged due “to the procedure’s reversibility and adjustability in comparison with ablative neurosurgery and the

absence to date of serious side effects” (p.56).

Since release of the guideline and based on a review of the peer-reviewed literature, Magellan considers DBS used in the treatment of treatment-resistant OCD to be an investigational treatment. This determination is based on an evaluation of the research findings where they did not support the effect of DBS on health outcomes, its safety and efficacy against existing alternative treatments, and its ability to demonstrate that benefits outweigh the risks (Nuttin BJ et al., 2003; Greenberg et al., 2006; Mallet et al., 2008; Denys et al, 2010; Goodman et al., 2010; Greenberg et al., 2010).

While there have been reported positive results in reducing symptoms of refractory OCD, these results have been associated with substantial risk of serious adverse events in patients with either VC/VS (ventral capsule/ventral striatum) or subthalamic nucleus stimulation implantation sites used for the treatment of refractory OCD. These include severe risk such as bleeding, infection or hemiparesis. More definitive tests of the safety, efficacy and tolerability of DBS will require larger controlled trials using matched healthy controls and double-blind on-off stimulation controls, other stimulation targets/surgical procedures, and evaluation of long-term benefits (Magellan, 2012).

The APA Guideline Watch reports that DBS continues to be explored and that benefits as well as serious adverse events, e.g., intracerebral hemorrhage and infections, have been observed during treatment (American Psychiatric Association, 2013). In a later study, authors investigated the proportion of treatment-seeking OCD patients who met criteria for DBS (Garnaat et al., 2014). Investigators suggested that patients who remain severely ill and impaired even after first- and second-line treatments may meet criteria for DBS. They examined the comprehensive baseline data on diagnosis, severity, and treatment history of OCD patients from the National Institute of Mental Health (NIMH)-supported Brown Longitudinal OCD Study and found that of 325 patients, only two met screening criteria for DBS. Their analysis, however, also highlighted an underutilization of efficacious treatments, showing that the most severely affected individuals had not been treated with sufficient variety of medications to rule out pharmacotherapy as a potentially effective option. Finding that behavioral psychotherapies were underutilized in treating OCD, they suggested that barriers to treatment need to be addressed. Investigators concluded that more information is needed on alternatives to DBS, e.g., intensive residential treatment programs, and that entry criteria for invasive treatments, e.g., DBS, need refinement.

An ablative procedure, i.e., limbic system surgery for treatment-refractory obsessive-compulsive disorder, was the subject of a study examining its efficacy and durability (Sheth et al., 2013). Changes in OCD and symptom severity were assessed at the initial and postoperative follow-up in patients (n=64) who underwent cingulotomy for refractory OCD. The definitions of full and partial symptom responses were Y-BOCS score reductions of ≥ 35 percent and 25 percent-34 percent, respectively. At the first postoperative follow-up, 35 percent of patients showed a full response and 7 percent had partial response. Repeat cingulotomy or subcaudate tractotomy was performed subsequently in 30 patients. At a five year follow-up, response rates were 47 percent and 22 percent for full and partial responses, respectively. Investigators concluded that limbic surgery based on initial cingulotomy is an effective treatment option for some

patients with severe OCD whose disease is refractory to conventional pharmacotherapy and psychotherapy.

A recent randomized, double-blind placebo-controlled clinical trial investigated the efficacy of low-frequency (1 Hz) rTMS in patients with OCD (Hawken et al., 2016). Participants (n=22) were randomly assigned into one of two groups: ACTIVE or SHAM groups. rTMS was applied bilaterally and simultaneously over the sensory motor area. The Y-BOCS score at the end of the six-week treatment period showed a clinically significant decrease for the ACTIVE group receiving treatment compared both to baseline as well as to the SHAM group, and the effect was maintained over the following six weeks after completion of treatment. Researchers suggested future studies are needed extending the follow-up period to determine the duration of clinical efficacy and to determine the generalizability of the findings (Hawken et al., 2016).

The APA guideline also discusses early research on the use of Repetitive Transcranial Stimulation (TMS) in the treatment of treatment-resistant OCD. The guideline notes that the four published trials evaluated had findings that were “inconsistent, perhaps because the studies differed in design, stimulation sites, duration and stimulation parameters” (p. 55). The APA guideline recommends that the overall strength of evidence for TMS is low.

A clinical review published subsequent to the adopted guideline indicated that these studies had stimulation parameters that varied as follows: (1) both right and left medial prefrontal cortex (PFC), (2) alternating left or right PFC, (3) bilateral stimulation of the supplementary motor area (SMA) and (4) left dorsolateral prefrontal cortex (DLPFC) (Pigot et al., 2008). In this report, the authors noted that the three sham-controlled trials in this group had negative results because the treatment courses may have been inadequate, underpowered (attributable to type II error) and not properly designed to control for comorbid depression in the OCD patients. Additionally, the authors stressed that the “neural circuitry implicated in the pathogenesis of OCD is not exclusively cortical. Given that TMS is a focal treatment that is known to result in cortical depolarization up to a depth of 2 cm, it is possible that prefrontal TMS is insufficient to modify abnormal subcortical circuitry in OCD, despite known trans-synaptic effects” (Pigot et al., 2008, p. 1451).

Another study (n=20) by Kang et al. where sequential TMS was performed alternating over the right DLPFC and SMA, showed no therapeutic effect for obsessive-compulsive symptoms (Kang et al., 2009). Conversely, a newer stimulation parameter and treatment protocol, i.e., bilateral SMA, was studied in a small double-blind sham-controlled study with more promising results and reduction in OCD symptomatology (Mantovani et al., 2010).

More recently, a published review of clinical trials on TMS treatment in the treatment of patients with OCD indicated that a total of 110 patients have been treated in 10 studies (Blom et al., 2011). Authors noted these results demonstrated only acute efficacy for obsessive-compulsive symptoms and no differences with sham treatment. Investigators also stressed that in order to generalize results of these studies, further research is necessary with more careful consideration of target regions and stimulation parameters, longer follow-up and use of double-blind, sham-controlled design in order

to draw conclusions about efficacy (Blom et al., 2011).

The APA Guideline Watch reports the findings of controlled trials of TMS that have produced negative results as well as suggestively positive results. Differences in these studies include the brain region stimulated as well as the frequency of the stimulus. In trials of high-frequency TMS in the right dorsolateral prefrontal cortex of patients with treatment-resistant OCD, no benefit was found from the treatment. In other studies, low-frequency stimulation in the supplemental motor area resulted in significantly greater reduction in OCD symptoms than sham treatment (after two weeks). Participants receiving active treatment had higher response rates at two weeks and at the 14-week follow-up (American Psychiatric Association, 2013).

Researchers performed an exploratory random-effects meta-analysis including 10 randomized controlled trials to assess the efficacy and acceptability of TMS in treating OCD (Berlim et al., 2013). Subjects with OCD (n=282), most with treatment resistant OCD, were randomized to active TMS or sham TMS in 14 sessions. This analysis found that neither high frequency TMS nor TMS targeted at the dorsolateral prefrontal cortex (DLPFC) were more effective than sham TMS whereas low frequency TMS and TMS applied over the non-DLPFC regions, i.e., supplemental motor area or orbitofrontal cortex, yielded significant improvements in Y-BOCS scores. Researchers suggested that the efficacy of TMS appears to be comparable to other alternative augmentation strategies. They also suggested that future studies are needed to investigate enhancement of the effects of TMS on OCD, e.g., identification of more stimulation parameters and predicting which patients might benefit from the treatment. They concluded that definitive conclusions about the clinical utility of TMS for OCD cannot yet be drawn and that larger-scale and sufficiently powered randomized controlled trials are needed (Berlim et al., 2013).

Complementary and Alternative Medicine

A recent pilot study tested the feasibility and clinical benefits of 12-weeks of combined moderate-to-vigorous aerobic exercise and group CBT in patients whose mean age was 35 (n = 11) with moderate-to-severe, medication-refractory OCD (Rector et al., 2015). CBT was delivered in a group format incorporating exposure and response prevention with increasing emphasis on cognitive approaches for obsessions and compulsions. Adherence to exercise was measured by self-reported exercise session logs and weekly phone checks by research assistants and reported to exceed 80 percent. OCD symptom reduction measured from pre- to post-treatment by Y-BOCS scores showed large, clinically significant improvements in severity of symptoms. Researchers noted that the results of this study demonstrate the “possible value of aerobic exercise as an adjunctive treatment in OCD” and “are proceeding with a large-scale, multi-site randomized controlled trial that will aim to overcome the limitations associated with this pilot investigation” (Rector et al., p. 338).

The only aspect of Complementary and Alternative Medicine (CAM) addressed by the APA guideline is yoga. The document briefly discusses the positive effects of a small study of Kundalini yoga versus mental mindfulness and relaxation response management as an established alternative treatment to OCD.

The CAM therapy of electroacupuncture (EA) was more recently studied in the treatment of refractory OCD in a small (n=19) pilot, waitlist-controlled trial (Zhang et al., 2009). All OCD patients participating had failed to fully respond to various classes of medications (e.g., anxiolytics, SSRIs/SNRIs, mood stabilizers, first and second generation antipsychotics), CBT or both and still exhibited persistent symptoms. Patients in the treatment group receiving EA (12 sessions) additional treatment to their current treatment displayed significantly greater improvements in OCD symptoms. Researchers speculated that EA could enhance the release of several endogenous neuropeptides in the hypothalamus and limbic regions, including endorphin, which may be deficient in patients suffering with OCD (Zhang et al., 2009).

Psychotherapy

A recent meta-analysis investigation, including 16 randomized controlled trials with participants meeting inclusion criteria (n=756), examined the efficacy of cognitive behavior therapy (CBT) for OCD (Olatunji et al., 2015). Control conditions included the following: stress management training, relaxation, pill placebo, anxiety management and wait-list. Analysis of results found that CBT was superior to control conditions in the improvement of both OCD symptoms and depression symptoms at post-treatment showing a large effect size. Researchers noted the need for future studies to determine the extent to which CBT produces long lasting symptom changes for patients with OCD. They reported the lack of a significant association between higher pretreatment OCD symptom severity or higher pretreatment depression and lower CBT effect size. Findings were consistent with other studies showing relatively equivalent effects for different treatment types, i.e., CT and ERP. The number of CBT sessions was unrelated to CBT effect sizes as were intensity of treatment and magnitude of treatment. Researches emphasize that “there may be no added benefit to extensive sessions given that standard CBT for OCD can stay cost-effective without losing efficacy” (Olatunji et al, p. 228).

Using a meta-analytic approach, a recent study evaluated the efficacy of remote cognitive behavior therapy for OCD (Wootton, 2015). Included in this meta-analysis were 18 studies including individuals with OCD (n=823) whose mean age was 31 years. Treatments included 23 remote conditions, e.g., videoconferencing administered CBT (vCBT), telephone administered CBT (tCBT), computerized CBT (cCBT), internet administered CBT (iCBT) and bibliotherapy administered CBT (bCBT). *High intensity remote treatments* included vCBT and tCBT, both of which provide skills and length of sessions typically the same as in traditional face-to-face treatment with the patient and therapist interacting in real-time. *Low intensity remote treatments*, i.e., cCBT, iCBT and bCBT, also provide skills much the same as in face-to-face treatment and may include some clinician contact or be self-guided, although not in real time. All participants had moderate symptoms at baseline according to the Y-BOCS score. Control conditions included face-to-face treatment, attention controls, relaxation training and waitlist controls. Researchers found that remote treatment, regardless of methodology delivered, was more effective than no treatment, producing a decrease in symptoms of a large magnitude, with outcomes similar to face-to-face treatment. Researchers suggested that the amount of therapist contact may be a moderating factor and noted that the effect size in high intensity treatments was larger than in low intensity treatments although symptoms were decreased in both treatments. They

concluded, “According to the findings of this meta-analysis an entirely remote stepped-care treatment may be possible where low intensity remote treatments (such as iCBT or bCBT) are offered as a first step in a stepped-care treatment for OCD, followed by higher intensity remote treatments (such as vCBT or tCBT if required” (Wootton, p.111). While suggesting that remote treatment may be as effective as face-to-face treatment, researchers also noted, “across each of these studies the effect size differences are in the favor of face-to-face treatment and further research is required to elucidate the differences in outcome between different types of remote treatment and face-to-face treatment.” They suggested further investigation in the future due to the small number of randomized controlled trials that have been conducted to date comparing face-to-face and remote treatment.

Noting that although CBT with EX/RP is recognized as the most effective treatment for OCD, authors also pointed to the many barriers to accessibility, including restricted access in rural areas and to trained clinicians, as well as high cost (Pearcy et al., 2016). A meta-analysis, including eighteen studies (randomized controlled trials or quasi-experimental studies) that included adults with OCD (n=1570), investigated the efficacy of self-help treatment with a particular focus on therapeutic contact within the context of a stepped care model (Pearcy et al., 2015). Studies were categorized depending on amount of therapeutic contact as follows: self-administered, predominately self-help, or minimal-therapist contact self-help. Researchers sought to determine the impact of the amount of therapist contact on outcomes, irrespective of whether the self-help treatments were mainstream or alternative. Results showed that as therapeutic contact increased, effect size increased:

- Self-administered self-help – pooled subgroup effect size at post-treatment - .33 (small total effect size)
- Predominantly Self-Help – pooled subgroup effect size at post-treatment - .68 (moderate total effect size)
- Minimal-Therapist Contact Self-Help – pooled subgroup effect at post-treatment - 1.08 (large total effect size).

Researchers noted a downward trend in drop-out rates that occurred as therapeutic contact increased; the self-administered group had the highest dropout rate followed by the predominantly self-help group and the minimal self-help group. This study showed evidence of the efficacy of internet CBT for OCD with minimal-therapist contact self-help, but there is a lack of current randomized controlled trials for the treatment of OCD using CBT or ERP through self-administered self-help with no therapist contact. Researchers suggested the need for randomized controlled trials using CBT or ERP through self-administered self-help to investigate stepped care (Pearcy et al., 2016).

A recent, small randomized controlled study evaluated the feasibility, acceptability and efficacy of a brief adjunctive intervention for family members of adult patients with OCD (Thompson-Hollands et al., 2015). Patients (n=18) with a mean age of 35.44 years received standard ERP while a family member of each patient was randomized to either receive or not receive the brief adjunctive intervention. The intervention included two sessions for a family member within two weeks of the patient beginning ERP and another session two weeks later. The intervention began with psychoeducation, including the model of OCD and the rationale for ERP.

Accommodation, as a common although maladaptive family response, was openly discussed. The sessions included skills training to reduce accommodation, which “serves the same maladaptive function as compulsions” (Thompson-Hollands et al., p. 222). Results of this 25 week study showed that the intervention successfully reduced family accommodation, based on scores on the Family Accommodation Scale for Obsessive-Compulsive Disorder. Average accommodation scores of family members in the control group remained little changed by the end of the study (remained at 78 percent of their baseline levels), while the scores of family members in the intervention group dropped substantially (dropped to 37 percent of baseline levels). Regression analysis found that “change in family accommodation from baseline accounted for a significant amount of variance in later OCD symptoms” in the intervention group and suggested, “this adjunctive intervention produces more rapid treatment response compared to traditional ERP alone” (Thompson-Hollands, et al., p. 218).

As noted earlier, the APA guideline recommends both SRIs and CBT as safe and effective first-line treatments for OCD. The guideline indicates that CBT used to treat patients with OCD relies primarily on exposure and response (aka relapse) prevention (ERP) or cognitive therapy (CT) techniques and acknowledges that the evidence base is strongest for ERP. Likewise, the guideline acknowledges supporting data on the use of CBT utilizing such techniques as identifying, challenging and modifying dysfunctional beliefs when combined with behavioral experiments or used in conjunction with ERP. A more recently published meta-analysis (seven studies) of CT, Behavior Therapy (BT) or CBT was consistent with the previous body of research in this area demonstrating their effectiveness, and also showed that baseline level of OCD severity and depressive symptom level predicted the degree of response (Gava et al., 2007).

Since the guideline’s release, the research team of Rosa-Alcazar et al. reported that although several meta-analyses have shown the benefits of CBT, the differential effectiveness of various approaches has been inconclusive thus far (Rosa-Alcazar et al., 2008). Results of this particular meta-analytic investigation of 19 studies showed that the treatment effect size estimates for exposure with response prevention (ERP) alone, cognitive restructuring (CR) alone and ERP plus CR were very similar. Also, their findings indicated that therapist-guided exposure was better than therapist- assisted self-exposure, and that exposure in vivo combined with exposure in imagination was better than exposure in vivo alone. Researchers have also noted that these techniques yield greater improvements for obsessions than for compulsions (Rosa-Alcazar et al., 2008). In addition, a systematic review of studies on exposure-in- vivo interventions was conducted on employed people with anxiety disorders, e.g., OCD, PTSD and mixed OCD with severe phobias. Findings showed that in the four OCD studies analyzed, work-related adverse outcomes, i.e., work functioning and sickness absence, were reduced with exposure-in-vivo treatment compared to other anxiety treatments, i.e., self-relaxation, anti-exposure therapy combined with clomipramine, response prevention and marital therapy, or a waiting list (Noordik et al., 2010).

The Guideline Watch reported a study comparing the efficacy of acceptance and commitment therapy (ACT) with relaxation therapy in patients (n=79) with OCD, finding significantly greater decrease in symptoms following ACT than relaxation therapy both posttreatment and at three month follow up. A later study compared the effects of two brief interventions for intrusive, obsession-like thoughts on psychological processes and obsessional symptoms: 1) exposure and response prevention (ERP) and

2) ACT (Fabricant et al., 2013). In this study, participants (n=56) who were college students with obsessional thoughts were randomly assigned to a single brief intervention with ERP, ACT or the control condition, i.e., expressive writing (EW). Findings showed that obsessional symptoms significantly declined from pretest to follow-up in all three conditions with no significant differences between the three conditions. All three conditions also reported decreased dysfunctional beliefs about intrusive thoughts with no significant between groups differences. Both the participants in ACT and ERP showed increased willingness to contact intrusive thoughts while the control group reported a slight decrease. Researchers suggested that the processes by which ACT and ERP promote change in obsessional symptoms may not be different, enacting change using similar mechanisms. They suggested more research is needed to understand how multisession ERP and ACT based treatments affect obsessional thoughts (Fabricant et al., 2013).

The APA guideline recognizes that there are limited clinical trial data on the efficacy of group behavioral therapies and acknowledges the need for additional research for this modality. Since then, a meta-analysis of 13 trials conducted by the team of Jónsson et al. examined the treatment effect sizes of group CBT/ERP against waitlist controls. Measuring clinical outcome using the Y-BOCS, their findings showed that group treatment is an effective treatment format in ERP or CBT for the treatment of OCD. However, researchers noted that these positive effects for CBT/ERP group treatment do not achieve change of the same magnitude as the individual formats of the respective treatments in previously reported studies (Jónsson et al., 2008; Jónsson et al., 2011).

After publication of the APA guideline, formats have been developed for behavioral therapies using new technology and with reported positive results. Findings from one study of 72 patients who received 10 weekly sessions of ERP delivered by telephone showed that clinical outcomes of this treatment was equally as effective as treatment delivered face to face (Lovell et al., 2006). Similarly, findings from a British systematic review of four studies evaluating the effectiveness of computer-guided therapy (using the software program, *BTSteps*), revealed that it was as good as therapist-led CBT for reducing time spent in rituals and obsessions (Tumur et al., 2007). Moreover, these researchers found that computerized CBT showed improved outcomes in work functioning, home management, social activities and private leisure activities and was superior to relaxation therapy in the treatment of patients with OCD (Tumur et al., 2007). Another pilot study (n=106 intervention; n=155 waitlist) on the effectiveness of an online CBT-based support group intervention showed promising results for people with compulsive hoarding (Muroff et al., 2010).

The Guideline Watch discusses studies examining the utility of telephone-based ERP, internet-based ERP, and computer-guided self-help for OCD. In a later study, authors reviewed the existing literature on the utility of computer-assisted assessment and treatment specific to OCD, examining the potential of the technology and addressing current challenges in the assessment and treatment of OCD (Lind et al., 2013). They acknowledged that the body of research on the utility of computers in the assessment and treatment of OCD is relatively small, but also acknowledged the potential of the use of a mobile phone to spontaneously simulate intrusive obsessional thoughts, allowing the patient to practice specific techniques outside of sessions with therapist.

In children and adolescents, the APA guideline indicates that treatment should often

start with CBT or with a combination of psychotherapy and an SRI. The guideline denotes ERP as an effective CBT approach for use in the pediatric population. More recently published meta-analytical findings continued to provide data supporting their value (Barrett et al., 2008; Watson et al., 2008; Munoz-Salmando et al. 2008; In-Albon et al., 2007). The research team of Barrett et al. reported that results from exposure-based CBT trials have consistently shown remission rates ranging from 40 percent to 85 percent across studies. Authors also acknowledged that individual exposure-based CBT had the strongest evidence of efficacy followed by family-focused individual or group formats for the treatment of child and adolescent OCD (Barrett et al., 2008). A retrospective case note review conducted in the United Kingdom of children and adolescents (n=75) treated for OCD with CBT reported that the total Children's Y-BOCS was significantly reduced and gains were maintained at long-term follow-up (mean f/u=5.5 yrs.). Positive outcomes did not differ for those either on concurrent or previously prescribed medication (Nakatani et al., 2009).

A more recent analysis was conducted to examine the links between insight and demographic, cognitive and clinical features among children and adolescents with OCD participating in a psychosocial treatment trial. Lewin et al. measured insight in youths with OCD (n=71; mean age = 11.7, 63 percent males) using a semi-structured interview along with several other validated clinical measurement tools for anxiety, OCD, depression, perceived control, intelligence and functioning. Results indicated that youths with OCD had poorer intellectual function, depressive symptomatology, and decreased perception of control over their environment. In addition, they possessed reduced adaptive functioning and were likely to have low insight into the irrational nature of their OCD symptoms. Investigators stressed that these issues were important to address in order to maximize therapeutic approaches tailored to this group (Lewin et al., 2010).

Combined Treatment

Based on meta-analyses, an estimate of up to one-third of adults with OCD respond acutely to augmenting SRIs with antipsychotics, but the *long-term* response to antipsychotic augmentation has not been studied (Foa et al., 2015). In a recent trial, patients with OCD (n=100) who were receiving either clomipramine or a SSRI for at least 12 weeks while remaining symptomatic were randomized to eight weeks of risperidone, EX/RP including twice-weekly 90-minute sessions, or pill placebo during the acute phase of the study. Patients (n=40) who responded (Y-BOCS scores decreased at least 25 percent) during the eight-week period entered a six-month maintenance phase where the two augmentation strategies continued. Of the patients receiving EX/RP during the acute phase, 60 percent were responders, whereas only 16 percent of those receiving risperidone were responders. However, those who responded to either EX/RP or risperidone maintained their gains over the six-month maintenance phase. Researchers concluded that these results “strongly support augmenting SRIs with EX/RP rather than risperidone in adults with OCD” and further suggested that “ongoing EX/RP treatment can help many patients maintain their acute gains” (Foa et al., p. 449).

A recent study included adults with OCD (n=32) who had failed to respond to 12 weeks of SRI treatment after which they were randomized to eight weeks of SRI augmentation

with risperidone or pill placebo, again being classified as non-responders (McLean et al., 2015). Non-responders to risperidone and pill placebo (n=20 and 12, respectively) then elected to crossover to 17 twice weekly treatments of EX/RP. At post-treatment, more than half of the participants were responders with 15 percent achieving excellent response. Authors noted the importance of this study as it shows that EX/RP is effective for OCD patients who continue to report clinically significant OCD symptoms after SRI treatment and after SRI augmentation with either risperidone or placebo. Researchers found that the participants either maintained gains or showed improvement to week 32 follow-up. Researchers concluded, “This study adds to the body of evidence supporting the use of EX/RP with patients who continue to report clinically significant OCD symptoms after multiple pharmacologic trials” (McLean et al., 2015).

The APA guideline specifies that combined treatment (SRI and CBT) is more effective than monotherapy for some patients but that it is *not* necessary for all patients. Herein, the document notes that combined treatment should be considered for patients who have had an unsatisfactory response to monotherapy, who have co-occurring psychiatric conditions for which SRIs are effective, or who wish to limit the duration of medication treatment. Additionally, the guideline denotes that combined treatment may also be considered for patients with severe OCD, since the medication may diminish symptom severity and allow the patient to engage in CBT.

One randomized controlled trial looked at the effects of sequencing the provision of behavioral therapy to patients already receiving an adequate SRI dose (Simpson et al., 2008). The study provided some 17 sessions of CBT (either twice weekly ERP or stress management) to 108 adult outpatients diagnosed with OCD while continuing SRI and adjuvant drug treatment, e.g., antipsychotics, benzodiazepine, mood stabilizer, stimulant and others. Results showed that the addition of ERP reduced OCD symptom severity more than the addition of stress management training in patients with clinically significant OCD despite an adequate SRI trial. Also, more patients who received ERP rather than stress management training were treatment responders and achieved minimal symptoms. Nonetheless, researchers concluded that the 17 sessions of CBT was not sufficient to help most of the patients in the study achieve minimal symptoms (Simpson et al., 2008).

A systematic review and meta-analysis examined the evidence from 13 head-to-head randomized controlled trials which compared behavioral therapy and SRI pharmacotherapy and their combination in the treatment of patients with OCD (n=959) in an outpatient setting (Romanelli et al., 2014). SRIs compared with behavioral therapy included SSRIs as well as clomipramine while behavioral therapy included exposure and response/ritual prevention (ExRP) and CBT. In trials comparing behavioral therapy with overall SRI pharmacotherapy (including both SSRIs and clomipramine), the results showed behavioral therapy was more effective. Researchers noted that where behavioral therapy was compared with SSRIs alone, it was not more effective. Combination of behavioral therapy and an SRI was more effective than treatment with SRI alone, whereas no difference in treatment effects was found between combination therapy and behavioral therapy alone. Researchers suggested more research is needed to evaluate the relative efficacy of the interventions (Romanelli et al., 2014).

The Cognitive Behavioral Therapy Augmentation of Pharmacotherapy in Pediatric Obsessive-Compulsive Disorder Treatment Study II (POTS II) was conducted in order to determine the efficacy of combined treatment in a pediatric population showing partial response to SRI medication, e.g., citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, (Franklin et al, 2011). This 12-week controlled trial of pediatric outpatients, (n=124) aged 7-17 years, randomized participants to one of three treatment strategies: (1) medication only, (2) medication management plus instructions in CBT, and (3) medication management plus full CBT sessions. All patients had a score of 16 or higher on the Children's Y-BOCS and positive outcome was determined by a change in this score of 30 percent or more. The modality of "instructions in CBT" included psychoeducation, establishing/reevaluating a simple stimulus hierarchy, identifying exposure plus response prevention targets, homework, and two telephone checks at home for guidance on implementation. Study results showed the medication management plus CBT was superior to the other two strategies on all outcome measures as an augmentation to SRI maintenance treatment. These findings corroborate results of the earlier POTS I, where combined treatment was also found to be superior in acute treatment of OCD in the pediatric population (Franklin et al., 2011).

Healthcare Effectiveness Data and Information Set (HEDIS) Measure: Follow-Up after Hospitalization (FUH)

The Healthcare Effectiveness Data and Information Set (HEDIS) is a set of performance measures developed and maintained by the National Committee for Quality Assurance (NCQA). The HEDIS measure that includes obsessive-compulsive disorder diagnoses is Follow-Up after Hospitalization for Mental Illness (FUH). This measure, like almost all HEDIS measures, focuses on processes, rather than on outcome measures. Patients with OCD who have been treated in an acute inpatient setting should receive a follow-up visit within 30 days of discharge, preferably within the first seven days after the discharge.

Obtaining Copies of the APA Guideline

Copies of the Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder, First Edition may be obtained through the APA at www.psych.org, or by calling (800) 368-5777, or by U.S. mail at:

American Psychiatric Publishing, Inc.
1000 Wilson Blvd., Suite 1825
Arlington, VA 22209-3901

Provider Feedback

Magellan welcomes feedback on our clinical practice guidelines. We take all suggestions and recommendations into consideration in our ongoing review of the guidelines. Comments may be submitted to:

Medical Policy Department
Magellan Healthcare
CPG@MagellanHealth.com

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