

Obsessive-Compulsive Disorder

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician, behavioral health professional, or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

John J. Whyte, MD, MPH, is currently the Chief Medical Officer at WebMD. In this role, he leads efforts to develop and expand strategic partnerships that create meaningful change around important and timely public health issues. Previously, Dr. Whyte was the Director of Professional Affairs and Stakeholder Engagement at the FDA's Center for Drug Evaluation and Research and the Chief Medical Expert and Vice President, Health and Medical Education at Discovery Channel, part of the media conglomerate Discovery Communications.

Prior to this, Dr. Whyte was in the Immediate Office of the Director at the Agency for Healthcare Research Quality. He served as Medical Advisor/Director of the Council on Private Sector Initiatives to Improve the Safety, Security, and Quality of Healthcare. Prior to this assignment, Dr. Whyte was the Acting Director, Division of Medical Items and Devices in the Coverage and Analysis Group in the Centers for Medicare & Medicaid Services (CMS). CMS is the federal agency responsible for administering the Medicare and Medicaid programs. In his role at CMS, Dr. Whyte made recommendations as to whether or not the Medicare program should pay for certain procedures, equipment, or services. His division was responsible for durable medical equipment, orthotics/prosthetics, drugs/biologics/therapeutics, medical items, laboratory tests, and non-implantable devices. As Division Director as well as Medical Officer/Senior Advisor, Dr. Whyte was responsible for more national coverage decisions than any other CMS staff.

Dr. Whyte is a board-certified internist. He completed an internal medicine residency at Duke University Medical Center as well as earned a Master's of Public Health (MPH) in Health Policy and Management at Harvard University School of Public Health. Prior to arriving in Washington, Dr. Whyte was a health services research fellow at Stanford and attending physician in the Department of Medicine. He has written extensively in the medical and lay press on health policy issues.

Faculty Disclosure

Contributing faculty, John J. Whyte, MD, MPH, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planners

John M. Leonard, MD
Mary Franks, MSN, APRN, FNP-C
Alice Yick Flanagan, PhD, MSW
Margaret Donohue, PhD

Senior Director of Development and Academic Affairs

Sarah Campbell

Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for healthcare professionals working with adults or adolescent patients who exhibit symptoms of obsessive-compulsive disorder.

Accreditations & Approvals



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INTERPROFESSIONAL CONTINUING EDUCATION

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 4 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit. Completion of this course constitutes permission to share the completion data with ACCME.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the learner to earn credit toward the CME and Self-Assessment requirements of the American Board of Surgery's Continuous Certification program. It is the CME activity provider's responsibility to submit learner completion information to ACCME for the purpose of granting ABS credit.

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Through an agreement between the Accreditation Council for Continuing Medical Education and the Royal College of Physicians and Surgeons of Canada, medical practitioners participating in the Royal College MOC Program may record completion of accredited activities registered under the ACCME's "CME in Support of MOC" program in Section 3 of the Royal College's MOC Program.

NetCE designates this continuing education activity for 4 ANCC contact hours.



IPCE CREDIT[™]

This activity was planned by and for the healthcare team, and learners will receive 4 Interprofessional Continuing Education (IPCE) credits for learning and change.

NetCE designates this continuing education activity for 4.8 hours for Alabama nurses.

NetCE designates this continuing education activity for 2 pharmacotherapeutic/pharmacology contact hours.

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Social workers completing this intermediate-to-advanced course receive 4 Clinical continuing education credits.

NetCE designates this continuing education activity for 1.5 NBCC clock hours.

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Special Approvals

This activity is designed to comply with the requirements of California Assembly Bill 1195, Cultural and Linguistic Competency, and California Assembly Bill 241, Implicit Bias.

About the Sponsor

The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

Disclosure Statement

It is the policy of NetCE not to accept commercial support. Furthermore, commercial interests are prohibited from distributing or providing access to this activity to learners.


Course Objective

The purpose of this course is to provide healthcare professionals with a basic understanding of obsessive-compulsive disorder (OCD), its clinical manifestations, and basic treatment approaches in order to facilitate optimum patient care and outcomes.

Learning Objectives

Upon completion of this course, you should be able to:

1. Review the epidemiology of obsessive-compulsive disorder (OCD).
2. Outline the diagnostic criteria and pathophysiology of OCD and possible barriers to diagnosis.
3. Describe the differential diagnosis and common comorbidities associated with OCD.
4. Discuss the use of pharmacotherapy in the management of OCD, including selection of treatment, duration, and how to address partial response or non-response.
5. Describe the use of cognitive-behavioral therapy in OCD treatment, with a focus on exposure and response prevention.
6. Identify appropriate interventions for treatment refractory OCD and experimental therapies.



Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a debilitating psychiatric illness affecting up to 2.5% of the population [1]. More than half (50.6%) of these cases are classified as “severe” [2]. Characterized by recurrent thoughts or worries (obsessions) and a strong desire to perform certain actions or activities (compulsions), OCD has a significant effect on day-to-day functioning and on quality of life.

Unfortunately, OCD often goes unrecognized [3]. Patients may hesitate to disclose their symptoms, and healthcare professionals unfamiliar with this disorder may confuse its manifestations with other psychiatric illnesses. Common comorbidities can further cloud the diagnosis.

This course will cover the epidemiology, diagnostic criteria, pathophysiology, and differential diagnosis of OCD. It will go on to discuss the first-line treatments, recommended duration of therapy, and options for patients who do not respond to initial therapy. Finally, it will address the role of inpatient treatment and experimental options.

EPIDEMIOLOGY

The exact prevalence of OCD is unknown. The National Comorbidity Survey Replication (NCS-R), a nationally representative household survey designed to assess the prevalence, severity, and comorbidity of various psychiatric disorders in the United States, found that OCD affects roughly 2.2 million American adults, or about 1% of adults in any given year [2; 4]. The NCS-R researchers used criteria from the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) to make the diagnosis, based on responses to a version of the World Health Organization’s Composite International Diagnostic Interview (CIDI). The Epidemiologic Catchment Area Study, conducted in the 1980s, found an OCD lifetime prevalence of 1.94% to 3.29% across five study sites [5]. This study employed lay interviewers to administer the National Institute of Mental Health Diagnostic

Interview Schedule (DIS). However, the reliability of the DIS-based diagnosis is open to question; at re-interview 12 months later, only 19.2% of patients who met OCD criteria on initial interview admitted to ever having had OCD-criteria symptoms. More recent nationally representative surveys confirm that OCD has a lifetime prevalence of 2% to 3% and that it is associated with substantial comorbidity and mortality [6]. OCD is estimated to make a significant contribution to the global burden of disease, with considerable uniformity of OCD symptoms across the globe [7; 8]. The incidence of OCD is reported to be higher in dermatology and cosmetic surgery patients [9].

OCD affects men and women about equally, and the prevalence appears to be similar across races and ethnicities [6]. It is not uncommon for women to experience the onset of OCD during pregnancy [9]. The NCS-R found a median age of onset of 19 years, with about one-fifth of cases starting before 10 years of age [4]. Other studies suggest a mean age of onset between 22 and 35 years, with one-third beginning before 15 years of age [10]. Early onset often leads to a long duration of untreated illness (around seven years on average), which leads to late interventions and poor response to therapy, particularly pharmacologic therapy [11]. Younger age at onset appears to be associated with more severe symptoms and higher rates of specific comorbidities, including attention deficit hyperactivity disorder, tic disorders, and other anxiety disorders. These patients may be less responsive to first-line pharmacologic treatment as adults [10].

SOCIOECONOMIC IMPACT

OCD can have significant effects on functioning, including work and personal relationships. It can adversely affect marriage, sexual functioning, family life, religious expression, leisure activities, and friendships [12]. Patients may avoid social situations due to embarrassment or anxiety. Carrying out compulsions may consume too much time to allow attending social events or may interfere with punctuality and efficiency at work. Several studies have shown a link between severity of OCD and decreased quality of life [13; 14; 15; 16].

In 2001, the World Health Organization rated OCD among the top 20 causes of disability for people 15 to 44 years of age worldwide [17]. Other studies indicate that OCD is among the top 10 most disabling of all disorders, accounting for 2.2% of all years lost to disability [18]. Studies of the costs of mental disorders are limited; however, in the mid-1990s it was estimated that lifetime indirect costs of OCD due to lost wages were \$40 billion [19]. A 2008 estimate on the economic cost of OCD in the United States showed \$10.6 billion in annual direct and indirect costs among those with a formal diagnosis who were in treatment [20]. This study noted that OCD had the lowest cost of all mental disorders, mainly due to the comparatively greater functionality of affected individuals and low frequency of the disorder.

NATURAL HISTORY

OCD tends to have a waxing and waning course. Most studies have followed patients for only a few months to years, making it difficult to draw conclusions about long-term outcomes.

Much of what is known about the course of OCD comes from a Swedish study that tracked more than 100 patients for a mean of 47 years, beginning in the mid-1950s [21]. Participants had been hospitalized for OCD between 1947 and 1953 and were examined for the study between 1954 and 1956, then again between 1989 and 1993. By the end of four decades, 83% had improved, with 20% recovering completely and 28% having minimal symptoms. Improvement was gradual in 65% and fast in only 9%; the rest had a course of improvement that was difficult to qualify. Among patients who had no symptoms at the first study examination, 37% had symptoms at the second. Conversely, among patients who did have symptoms at the first examination, only 58% had symptoms at the second.

DIAGNOSTIC CRITERIA

The first step in correctly diagnosing and treating OCD is understanding its definition. Although previously considered an anxiety disorder, OCD is classified as an obsessive-compulsive disorder in the revised fifth edition of the DSM (DSM-5-TR) along with other related conditions, including body dysmorphic disorder, hoarding disorder, trichotillomania, and excoriation disorder. Essentially, OCD involves obsessions and/or compulsions that cause distress or interfere with functioning. The obsessions are usually associated with anxiety, and compulsions often serve to ameliorate that anxiety. People with the disorder are usually aware, at least at some point in time, that their obsessions or compulsions are not reasonable.

The DSM-5-TR definition of OCD is based on four criteria [22]. The first criterion is the presence of either obsessions or compulsions. Obsessions are defined by [22]:

- Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted and cause marked anxiety or distress in most individuals.
- The person attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action.

Compulsions are defined by:

- Repetitive behaviors (e.g., handwashing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.

- The behaviors or mental acts are aimed at preventing or reducing anxiety or distress or preventing some dreaded event or situations; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive. Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

Secondly, diagnosis of OCD is dependent upon disruption of day-to-day life. The obsessions or compulsions are time consuming (take more than one hour per day) or significantly interfere with the person's normal routine, occupational (or academic) functioning, usual social activities or relationships, or other important areas of functioning.

The third diagnostic criterion is that the disturbance is not due to the direct physiologic effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Disease-specific manifestations are the fourth criterion. In order for OCD to be diagnosed in patients with another Axis 1 disorder, the content of the obsessions or compulsions may not be restricted to the other disorder (e.g., preoccupation with food in the presence of an eating disorder; hair pulling in the presence of trichotillomania; concern with appearance in the presence of body dysmorphic disorder; preoccupation with having a serious illness in the presence of hypochondriasis; preoccupation with sexual urges or fantasies in the presence of a paraphilia; or guilty ruminations in the presence of major depressive disorder).

The diagnosis of OCD may specify insight. At some point during the course of the disorder, the person may recognize that the obsessions or compulsions are excessive or unreasonable; this would be diagnosed as OCD with good or fair insight. If, for most of the time during the current episode, the person does not recognize that the obsessions and compulsions are excessive or unreasonable, the diagnosis is OCD with poor insight. If an individual is completely convinced that obsessions and compulsions are true or necessary, OCD with absent insight/delusional beliefs would be diagnosed.

Identifying the age of symptom onset as well as the age of OCD diagnosis can help predict the patient's prognosis [23].

COMMON THEMES

The DSM-5-TR diagnostic criteria do not specify the content of obsessions or any specific form of compulsion. However, several themes are common in OCD. These include being contaminated or spreading contamination, contracting a disease, causing harm to others, making an important mistake, committing a religious or moral sin, the possibility of committing homosexual or pedophilic acts, and being thought homosexual [10]. Common compulsions include cleaning or washing hands, checking to be sure a task was done, counting, arranging objects, confessing to sins or errors, making lists, and hoarding. Compulsions may be physical or mental, such as repeating a silent prayer.

Patients may have multiple, concomitant symptoms fitting more than one theme, and different symptoms may appear at different times. In addition, the possibility of OCD should not be dismissed merely because a patient's thoughts or behaviors do not fit these themes. Many patients will have obsessions involving other topics and compulsions with different manifestations.

INSIGHT

Most patients with OCD will have some insight into the fact that their obsessions or compulsions are not logical or reasonable. However, as noted, there is a subpopulation of patients for whom insight is absent. Lack of insight may be a manifestation of a particular bout with OCD symptoms, for example if the patient's level of anxiety overrules what, at another time, he or she might recognize as common sense. Occasionally, patients will report that they have never interpreted the fears or compulsions as less than reasonable. The actual number of patients who lack insight is unknown. In a DSM-IV field trial involving 431 patients at seven outpatient sites, 8% of participants had no insight at the time of inter-

view and 5% had never had insight [24]. Among the 250 subjects whose obsessions involved some feared consequence, only 13% felt certain that the consequence would not occur. Twenty-six percent were mostly certain that it would occur, and 4% were certain that it would occur. Poorer insight has been linked to poorer outcomes [22].

SUICIDE RISK

The risk of suicide appears to be elevated in patients with OCD compared to the population as a whole [10]. OCD symptoms and comorbid depression may be contributing factors. The precise risk of suicide is not known; in the NCS-R, the odds ratio for suicidal ideation in patients with OCD, compared to the general population, was 6.9 [25]. In the intake sample for the Brown Longitudinal Obsessive Compulsive Study, an ongoing, non-random, prospective study of the course of OCD, 52% of patients had a history of suicidal ideation and 15% had at least one suicide attempt [3]. A report from the International College of Obsessive-Compulsive Spectrum Disorders found a history of suicide attempt in approximately 15% of patients with OCD, with higher rates of psychiatric and medical comorbidities and previous hospitalizations in patients with a previous suicide attempt [26]. In general, patients with OCD should be carefully evaluated for suicidal ideation and any history of suicide attempts [10].



According to the American Psychiatric Association (APA), clinicians should understand that individuals with OCD are not immune to co-occurring disorders that may increase the likelihood of suicidal or aggressive behavior. When such co-occurring conditions are present, it is important to arrange treatments that will enhance the safety of the patient and others.

(https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf. Last accessed April 19, 2024.)

Strength of Recommendation: I (Recommended with substantial clinical confidence)

CHALLENGES TO DIAGNOSIS

While the criteria for OCD are straightforward, research has demonstrated that the diagnosis is often missed. Among the population in the Brown Longitudinal Obsessive Compulsive Study intake, subjects first received treatment an average of more than 17 years after having their first obsessive-compulsive symptoms and 11 years after meeting the diagnostic criteria [3].

Challenges to diagnosis include patients' own reluctance to discuss symptoms. They may be embarrassed to admit to their obsessions or ashamed of the extent to which they pursue compulsions, and they may be unaware that treatment is available. The wide differential diagnosis and the fact that comorbidities are common may also serve to obscure the diagnosis.

Symptoms resembling those of OCD can appear in the absence of disease [10]. Up to 80% of healthy people have intrusive or unwanted thoughts, and about 50% may have ritualized behaviors. The same themes common in OCD can appear in these thoughts and behaviors. However, the thoughts and behaviors do not cause marked distress and do not interfere greatly with functioning.

OVERCOMING

CHALLENGES TO DIAGNOSIS

Asking more than once about possible or suspected symptoms, perhaps at different visits, and making these questions part of routine history taking can help patients overcome embarrassment. Recalling that OCD can have widely varied themes, not merely the popularly recognized handwashing or counting, will help prevent missed diagnoses.

Most patients will have both obsessions and compulsions, but a small percentage will have only one or the other. In the DSM-IV field trial, about 2% of participants had mostly obsessions and 2% mostly compulsions [10]. Patients may be more troubled by obsessions, more concerned about compulsions, or equally disturbed by both.

When OCD is suspected, a thorough patient interview can both confirm the diagnosis and provide a baseline for evaluating treatment. The interview should include [10]:

- Current symptoms, including content of obsessions and manifestations of compulsions
- Effect of symptoms on functioning and quality of life
- Evaluation of safety of the patient and others
- Past psychiatric history, including any treatment
- Presence of other psychiatric symptoms
- General medical history and review of systems
- Family history, with attention to OCD and other psychiatric disorders

A physical exam is also important, both as an element of general medical care and to help establish that symptoms are not caused by an underlying neurologic problem. There are no distinctive physical signs of OCD, but an exam may reveal clues. Some patients will have chapped hands from handwashing or evidence of common comorbidities, such as skin picking or trichotillomania. However, most can be expected to have a normal physical exam.

The physical exam should include [10]:

- A mental status exam, with particular attention to thought process and content, illusions or hallucinations, suicide or homicide risk, insight, and judgment
- A neurologic exam, which may identify tics related to OCD

Neuropsychological assessment of patients with OCD suggests that there are deficits across a broad range of domains (e.g., poor performance on memory, visuospatial ability, and cognitive flexibility tests), with system/ordering behaviors more strongly related to poorer neuropsychological performance overall [27; 28].

Screening tools are available to help evaluate the impact of OCD. One of the best-known is the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). The Y-BOCS includes two components: a symptom checklist and a severity scale. The Y-BOCS is widely used in research studies of OCD treatment, with

reductions in severity used as markers of treatment success. The symptom checklist includes obsessions and both physical and mental compulsions. The severity scale is based on time spent on obsessions and compulsions, resistance to these symptoms, interference from symptoms, related distress, and level of control. Increasing numbers of points are assigned for increasing levels of impact. The scale is scored as follows [29]:

- Mild: 8–15 points
- Moderate: 16–23 points
- Severe: 24–31 points
- Extreme: 32–40 points

Other measurement tools are also available. The Obsessive-Compulsive Inventory-Revised is a brief, self-rated scale asking about specific symptoms and degrees of distress related to them [30]. A simple visual analog scale, with symptoms rated from “none” to “incapacitating,” may also be used.

LANGUAGE BARRIERS

As a result of the evolving racial and immigration demographics in the United States, interaction with patients for whom English is not a native language is inevitable. Because patient history is such a vital aspect of the assessment of OCD, it is each practitioner’s responsibility to ensure that information and instructions are explained in such a way that allows for patient understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient’s lack of proficiency in the English language, an interpreter is required.

In this multicultural landscape, interpreters are a valuable resource to help bridge the communication and cultural gap between clients/patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately

enhance the clinical encounter. In any case in which information regarding diagnostic procedures, treatment options, and medication/treatment measures are being provided, the use of an interpreter should be considered.

PATHOPHYSIOLOGY

The pathophysiology of OCD is not fully understood. A genetic component is apparent, with higher incidence in first-degree relatives of affected patients. In a meta-analysis of five family studies involving adult probands, researchers found a four-fold increase of OCD incidence among first-degree relatives [31; 32]. Twin studies consistently show higher concordance of OCD in monozygotic than in dizygotic twins [33]. Concordance ranges from 47% to 50% for dizygotic to 80% to 87% for monozygotic twins [10].

While the possibility of a specific genetic etiology has been considered, none has been identified with certainty, and research is limited. A 2017 study analyzing more than 600 genes thought to be associated with OCD among humans, dogs, and mice elicited the identification of four specific genes prominent in several of those with OCD [32]. These findings are consistent and provide evidence of the current common genetic theories of OCD [32].



Patients with OCD who are parents of young children may want advice regarding the genetic risk of OCD. The APA recommends that clinicians explain to such patients that the available data indicate an increased but modest risk of OCD in the children of affected individuals; patients wanting more information may be referred to a genetic counselor.

(https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf. Last accessed April 19, 2024.)

Strength of Recommendation: I (Recommended with substantial clinical confidence)

One theory is that a defect in neural pathways, likely including orbitofrontal-striatal circuits, may be involved, but specific pathology has not been consistently shown [34; 35]. The theory posits that hard-wired primal behaviors (e.g., checking, cleaning) are exacerbated due to a hyperstimulated thalamus [36]. Imaging studies of OCD brains have found increased metabolic activity in the caudate nucleus, cingulate gyrus, and orbital frontal cortex.

One study also showed defects in neural pathways, with a hyperactivation in the connections between the structures in the cortico-striato-thalamo-cortical (CSTC) circuit, which is primarily responsible for regulating complex behaviors [32; 37]. In addition, the cell-adhesion gene *CTTNBP2* was one of the commonly identified genes in those with OCD, supporting the potential that neural pathways play a significant role in OCD behaviors [32]. Another 2017 study showed results similar to previous studies, with inflammation occurring in the neurocircuitry in more than 30% of participants, especially in the orbitofrontal cortex and CSTC [38].

Another hypothesis regarding the underlying cause of OCD involves serotonin [36]. Research regarding a role for serotonin was spurred by studies of the effectiveness of antidepressants, such as clomipramine and desipramine, for OCD in non-depressed patients [34; 39]. Clomipramine, which acts primarily as a serotonin reuptake inhibitor (SRI), has proved to be more effective than desipramine, which is thought to act primarily by inhibiting norepinephrine reuptake [40]. The ability of selective serotonin reuptake inhibitors (SSRIs) to reduce OCD symptoms further supports a role for serotonin abnormalities in the pathogenesis of OCD, a theory supported by the 2017 study in which a gene that includes a serotonin receptor, *HTR2A*, was found to be among the most commonly associated in those with OCD [32]. A specific mechanism, however, has not been elucidated, and studies involving measures of serotonergic function have been inconsistent.

An important challenge to the serotonin hypothesis is that SSRIs fail to bring significant improvement for a substantial number of patients with OCD.

Other neurotransmitters, including dopamine and glutamate, are also being investigated for their influence in OCD [41]. The 2017 study supports this, showing that two of the four genes found to have a possible association with OCD, *NRXN1* and *REEP3*, are involved in a process that may cause OCD behaviors by creating an imbalance of excitatory glutamate and inhibitory GABAergic neuron differentiation [32]. Some researchers have raised the question of whether OCD may be an immune-related disorder [42; 43]. Exploration of this possibility began with the observation of an association between Sydenham chorea and OCD. Obsessive-compulsive symptoms have been observed in children following streptococcal infection, a condition termed pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS). Although the relationships between OCD and immune response remain unclear, available literature supports the role of immune processes in the pathophysiology of OCD, suggesting immunotherapeutic treatments may be useful in the treatment of OCD [43; 44].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of OCD is broad and includes other anxiety disorders, such as generalized anxiety disorder and post-traumatic stress disorder, as well as schizophrenia, delusional disorder, depression, Tourette syndrome, and obsessive-compulsive personality disorder (OCPD).

OCPD is characterized by preoccupation with order, perfection, and control, but not by the presence of obsessions or compulsions [24]. It is often compared to a “perfectionist” personality. Unlike OCD, symptoms must appear by early adulthood for the diagnosis to be made; however, OCD and OCPD may occur in the same person. The frequency of both diagnoses occurring together is not known, but studies suggest that it is not uncommon [45]. Estimates from OCD study populations indicate a concomitant rate between 23% and 32%, although these samples were not designed to be representative of all patients with OCD [45; 46]. For comparison, the prevalence of OCPD has been observed to be about 0.9% to 2% in community samples [45; 46].

There is also some evidence that OCPD is more common in people with OCD than in patients with other psychiatric disorders.

Post-traumatic stress disorder is characterized by onset in the wake of an extreme traumatic stressor. Symptoms include avoidance of stimuli associated with the trauma and persistent thoughts about the event, which may seem to resemble behaviors and obsessions seen in OCD [22]. However, the obsessions and compulsions of OCD are not related to a specific, preceding traumatic event.

Generalized anxiety disorder involves excessive anxiety and worry about feared events. Unlike OCD, the diagnostic criteria also include the presence of additional symptoms, including restlessness, a tendency to be easily fatigued, difficulty concentrating, irritability, muscle tension, and sleep disturbance [22]. Further, the anxiety in generalized anxiety disorder tends to focus on more realistic forthcoming problems and concerns.

Delusional disorder features the presence of one or more nonbizarre delusions. The content of the delusions may resemble that of an obsession in OCD; for example, a delusion that one has contracted an infection may resemble anxiety about contamination in OCD. Classically, a patient with OCD would have insight into his or her illness while a patient with delusional disorder would not; however, when insight is lacking, OCD may closely resemble delusional disorder. OCD with delusional beliefs may also superficially resemble schizophrenia. However, the additional symptoms of schizophrenia will generally be lacking.

Depression may be accompanied by intrusive, unpleasant thoughts, as in OCD, but these thoughts do not generally lead to compulsions. Depression may occur in conjunction with OCD, but OCD itself is not characterized by depressed mood and anhedonia. However, these conditions frequently co-occur, and careful evaluation is necessary [47].

Tourette syndrome is characterized by tics, which first manifest during childhood in the majority of patients. Tics in Tourette syndrome tend to be preceded by a physical sense of “needing” to do the

movement, but not by anxiety about a specific outcome or the desire to avert a feared event. However, the tics may be quite complex and may even resemble compulsions, leading to diagnostic confusion in some cases.

COMORBIDITIES

Most studies of comorbidities in OCD are based on case series or convenience samples, making it difficult to estimate the prevalence of comorbid conditions among patients with OCD overall. Available evidence does suggest that certain psychiatric illnesses are more common among people with OCD than among the general population. In one interview-based study of 334 patients with OCD, only 8% of participants had no psychiatric comorbidity [48]. In the Brown Longitudinal Obsessive Compulsive Study intake, 91% of subjects had at least one other Axis 1 disorder [3].

Comorbid disorders that begin prior to the onset of OCD symptoms may influence the occurrence of additional comorbidities over time [49]. In one study involving 1,001 patients with OCD, separation anxiety disorder preceded OCD in 17.5% of patients and was associated with a higher lifetime frequency of post-traumatic stress disorder. ADHD preceded OCD in 5.0% of patients and was associated with higher lifetime frequencies of substance abuse and dependence. Tic disorders preceded OCD in 4.4% of patients and were associated with higher lifetime frequencies of OCD spectrum disorders [50].

Depression is a particularly common comorbidity. A chart review of 120 patients with OCD in the Netherlands found depression in one-third, and a separate structured psychiatric interview found similar results (31%) for major depression [51; 52]. The Epidemiologic Catchment Area Study in the United States found 67% of individuals identified as having OCD had at least one episode of major depression [47]. In addition, OCD has been shown to comorbidly occur with social phobia (11% to 24%), simple phobia (including body dysmorphic disorder) (7% to 14%), and panic disorder (6% to 14%, 35% lifetime incidence) [9]. Associations have

also been observed between OCD and other conditions, including bipolar disorder, eating disorder, generalized anxiety disorder (20%), alcohol dependence/substance abuse, and Tourette syndrome (5% to 7%) [9; 10; 53]. Richter and colleagues looked at patients with OCD, social anxiety disorder, or panic disorder and found that trichotillomania, skin picking, body dysmorphic disorder, and tics were more strongly associated with OCD than with the other two anxiety disorders [54].

In addition to considering other psychiatric diagnoses in the setting of OCD, clinicians should be alert for OCD symptoms in patients who have already been diagnosed with a different psychiatric illness. For example, eating disorders are often accompanied by anxiety disorders, including OCD. One survey showed the comorbid rate of eating disorder and OCD to be roughly 8% [52]. OCD is also common in patients with Tourette syndrome. One large international registry found that 27% of people with Tourette syndrome also had OCD, and other studies have found percentages ranging from 28% to 62% [9; 10; 55; 56; 57]. A separate study showed that of patients with OCD, approximately 5% will have comorbid Tourette syndrome [52]. Childhood-onset OCD may have a higher rate of comorbidity with Tourette syndrome and ADHD [9].

TREATMENT

In the *Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder*, the American Psychiatric Association (APA) recommends two options for first-line therapy, either alone or in combination: SRIs and cognitive-behavioral therapy (CBT) [10].

Five SRIs are approved by the U.S. Food and Drug Administration (FDA) for OCD treatment, including four SSRIs and one serotonin-specific tricyclic antidepressant (TCA) [58]:

- Fluoxetine
- Fluvoxamine
- Paroxetine
- Sertraline
- Clomipramine

Two other SSRIs and one serotonin norepinephrine reuptake inhibitors (SNRIs) also appear to be effective, although they do not have an indication for OCD [59]:

- Citalopram (approved for depression)
- Escitalopram (approved for depression and generalized anxiety disorder in the United States; approved for OCD in Europe)
- Venlafaxine (approved for depression)

All of the SSRIs are recommended as options for first-line therapy by the APA. Pharmacologic therapy is also recommended for those patients whose symptoms may be exacerbated by CBT or when access to a mental healthcare professional is unavailable and severe symptoms are present [60]. Specific aspects of these medications, including efficacy and side effects, will be discussed further in this course.

The form of CBT most commonly studied in OCD involves exposure and response prevention [58]. Exposure and response prevention consists of talk therapy and specific exercises designed to reduce anxiety and dampen the need to perform compulsions. Unless otherwise specified, “CBT” will be used in this course to refer to forms of therapy that incorporate exposure and response prevention.

CBT should be initiated and monitored by a professional trained in this specific mode of treatment. The exercises often can and should be done by the patient at home, which requires a strong level of commitment. Patients who experience too much anxiety to do the exercises or are not willing to accept this form of participatory treatment may be better candidates for pharmacotherapy, at least as the first step.

Overall considerations for selecting pharmacotherapy or CBT include:

- Patient choice
- Failure of prior attempt with the other option
- Willingness to take medication
- Willingness to do the work of CBT

Another form of CBT commonly used is Internet-based self- or professional-guided therapy. This form of treatment may be beneficial for those in rural areas or whose behaviors make them resistant to seek traditional face-to-face treatment [60].

Whether SRIs, CBT, or their combination are more effective has not been widely studied. One meta-analysis suggested SRIs and CBT are equally effective, but the authors concluded that there was not enough evidence to draw a firm conclusion [61]. There also appears to be a benefit to combining SRI and CBT in some patients, although possibly not all. In addition, there is some limited evidence that CBT, alone or in combination with medication, may lead to lower symptom severity after treatment is discontinued [62; 63]. The APA recommends combining treatments for patients who do not respond adequately to monotherapy, who wish to limit the duration of SRI use, who have comorbidities that will benefit from SRIs, or who have severe OCD [10].

In 2008, Simpson and colleagues conducted a randomized controlled trial to examine the effects of augmenting SRIs with exposure and ritual prevention [62]. Participants were 108 adult outpatients with OCD. All had been taking an SRI at a therapeutic dose for at least 12 weeks prior to entry but still had a Y-BOCS total score of 16 or greater. The patients were provided with 17 biweekly sessions of CBT, either an OCD-specific program of exposure and ritual prevention or a control setting of stress management training, while still continuing the SRI. After eight weeks, patients receiving the exposure and response prevention sessions were more likely to have at least a 25% decrease in severity on the Y-BOCS scale. They were also more likely to have achieved a Y-BOCS score of 12 or less.


In 2011, the Pediatric OCD Treatment Study II (POTS II) compared SRI therapy combined with 14 one-hour CBT sessions over 12 weeks to both medication alone and medication plus CBT instructions given at in-person medication management visits [64]. Each of the three study groups consisted of 42 patients, and the measure for success was 30% improvement in initial Y-BOCS score over

the 12-week study period. The success rate of combination SRI and CBT (68.8%) was twice as high as either SRI plus instruction (34%) or medication alone (30%) [64].

A 2018 literature review assessed the efficacy of combining drug and psychological treatments for OCD [65]. The review included 10 controlled studies assessing the efficacy of using combination strategies from the start of treatment versus CBT alone; 6 assessing combination strategies from the start of treatment versus SSRIs alone; and 11 randomized controlled trials assessing treatments given sequentially [65]. The combination strategies administered from the start of treatment were not found to be superior to monotherapy alone, except for patients with severe depression. Sequential administration of CBT after medications was found useful in promoting remission in patients who partially responded to drugs and in promoting response in resistant patients [65].

TREATMENT GOALS

Unfortunately, OCD is a difficult disease to fully cure. Some patients will achieve full remission, but many will retain at least some obsessive or compulsive symptoms. In most cases, the goal is to allow the patient to return to normal or near-normal functioning, including the ability to work and to have healthy and satisfying social relationships. Elements of this process include decreasing the frequency and severity of symptoms and helping the patient to cope with residual disease. Discussing with patients the possibility that medication or CBT may not make OCD disappear entirely can help avoid disappointment and frustration.



Because the patient's beliefs about the nature of the illness and its treatments will influence adherence, the APA asserts that providing patient and family education may enhance adherence to treatment.

(https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf. Last accessed April 19, 2024.)

Strength of Recommendation: II (Recommended with moderate clinical confidence)

Improvement in OCD often occurs slowly, requiring months-long medication trials and/or many weeks or months of CBT. Patients may also need extra time to consider their treatment options, especially if their symptoms include “doubting,” as they may doubt their ability to make the right decision.

PHARMACOLOGIC THERAPY

When pharmacologic therapy is selected as first-line treatment, the APA recommends beginning with an SSRI instead of clomipramine, due to the better safety profile of the SSRIs [10]. Choice of SSRI should be individualized and should include consideration of [10]:

- Drug-specific side effects
- Drug-drug interactions
- Comorbidities
- Past response

Some have suggested that the response of first-degree relatives to a specific medication may indicate an increased chance for response. Additional research is necessary before a recommendation may be made. No data support the practice of combining two SSRIs [58].

Studies suggest that approximately 40% to 60% of patients will have a clinically useful response to SSRIs, with about a 20% to 40% decrease in symptoms [58; 60; 66]. Data on long-term improvement is limited. In a 3-year prospective follow-up study, researchers evaluated outcomes in 79 Italian patients with OCD treated with SSRIs [67]. Some patients also received augmented therapy with low doses of neuroleptics. They found a 65% probability of achieving at least partial remission and a 38% probability of achieving full remission. However, the rate of relapse was 60%. Worse outcomes were predicted by greater severity of illness, longer duration, and comorbid schizotypal personality disorder. In a systematic review of 17 studies involving 3,097 participants, researchers examined the efficacy and adverse effects of SSRIs versus placebo for the treatment of OCD [68]. They found that SSRIs were

more effective than placebo in achieving clinical response at six and 13 weeks post-treatment. The pooled relative risk was similar between individual SSRI drugs. Nausea, headache, and insomnia were the most commonly reported adverse effects in each of the studies. The long-term efficacy and tolerability of SSRIs for OCD has yet to be established [68].

Clomipramine

Clomipramine is a TCA with multiple actions, including significant activity as a serotonin reuptake inhibitor. It was the first medication approved in the United States for treatment of OCD [69]. Some studies have suggested that clomipramine is more effective than the SSRIs, but others have found equal effectiveness or more improvement with an SSRI [69; 70; 71; 72; 73]. Direct, controlled comparison studies have found fluvoxamine, paroxetine, and sertraline equal in efficacy to clomipramine. Patients with OCD who have comorbid tics or schizotypal personality are unlikely to respond to clomipramine or an SSRI alone [74]. Due to serious adverse effects, a high daily dose of clomipramine is not advised unless SSRI monotherapy is not adequate to control OCD behaviors [70]. In addition, clomipramine may be used as combination therapy with an SSRI to receive the benefits of the TCA without the problematic side effects of higher doses of the drug [70]. Concurrent use of clomipramine and fluoxetine is not advised, as fluoxetine inhibits the metabolism of clomipramine in the liver, creating high serum levels of clomipramine [70].

Clomipramine does have a higher potential for adverse effects than the SSRIs, particularly if used in combination with an SSRI [75]. Anticholinergic side effects are common, and overdose can lead to cardiac arrhythmias, seizures, hypotension, and death [76]. Risks of arrhythmogenic effects, cardiotoxicity, and seizure are concerns at doses greater than the maximum dose of 250 mg/day, and electrocardiograph monitoring is recommended for continued high dosages [59; 70].

SSRIs

The use of each SSRI in OCD is supported by placebo-controlled trials. Although available evidence suggests that efficacy is similar across this class of drugs, no trials have compared all the SSRIs under controlled conditions [69]. Thus, their actual relative efficacy is unknown. Further, different trials have used different definitions for response, making comparisons difficult.

Paroxetine

A multinational, double-blind, 12-week trial conducted by Zohar and colleagues compared flexible-dose paroxetine, 20–60 mg daily, to placebo [77]. Response was defined as a 25% decrease in the Y-BOCS score. Response rates were 55% for paroxetine and 35% for placebo.

Hollander and colleagues compared paroxetine 20 mg, 40 mg, or 60 mg per day to placebo in a 12-week, double-blind trial [78]. Response was considered to be a decrease of 25% in the Y-BOCS score or a decrease in Clinical Global Impression-Severity (CGI-S) score of two points or more. Response rates were 25% for the 40-mg dose, 29% for the 60-mg dose, and 13% for placebo. Improvement with the 20-mg dose was not statistically significant compared to placebo.

Another trial supports effectiveness in a Japanese population. In a 12-week, double-blind trial, Kamijima and colleagues compared flexible-dose paroxetine, starting at 20 mg and titrating to as high as 50 mg per day, to placebo [79]. Response rates were significantly higher for paroxetine.

Fluvoxamine

The largest study of fluvoxamine was conducted by Hollander and colleagues [80]. This double-blind, 12-week trial involved 253 subjects and identified two response levels: a 35% or 25% reduction in the Y-BOCS score. Response at both levels was significantly higher for the treatment group compared to the placebo group. Remission rates were also significantly higher: 44% versus 31% for a Y-BOCS score of 16 or less, and 18% versus 8% for a Y-BOCS score of 8 or less.

Two pivotal trials for fluvoxamine in OCD found that after 10 weeks of treatment, Y-BOCS scores decreased significantly more in the fluvoxamine group compared to the placebo group. Among patients who received one or more post-baseline ratings, the mean Y-BOCS score decreased by 21% in patients who received fluvoxamine and 7% in patients who received placebo [10].

Sertraline

A placebo-controlled trial of flexibly dosed sertraline for OCD was published by Kronig and colleagues in 1999 [81]. The trial involved 167 patients, with treatment for 12 weeks and doses ranging from 50–200 mg. The treatment group had significantly greater improvement on Y-BOCS scores, and significantly more sertraline patients showed a therapeutic response according to Clinical Global Impression-Improvement (CGI-I) scores (41% versus 23%).

An earlier trial, published by Greist and colleagues in 1995, compared different doses of sertraline in 325 patients [82]. Patients were randomized to 50 mg, 100 mg, or 200 mg per day for 12 weeks, and were assessed using the Y-BOCS, the National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH-GOCS), CGI-S and CGI-I, and the Maudsley Obsessive Compulsive Inventory. Overall, patients using sertraline did better than those prescribed placebo on all measures. The 50-mg and 200-mg groups also did better than placebo on all of the investigator-related scales, although the 100-mg group was better only on the NIMH-GOCS.

Fluoxetine

The largest trials of fluoxetine for OCD were published in the mid-1990s. Montgomery and colleagues followed 214 patients over eight weeks of treatment with daily fluoxetine doses of 20 mg, 40 mg, or 60 mg, or placebo [83]. At the 40-mg and 60-mg doses, the response rates, defined as a decrease in the Y-BOCS total score of at least 25% and a CGI-I rating of “much improved” or “very much improved,” were significantly higher with fluoxetine than with placebo. Response rate was 47% at the 60-mg dose, 48% at the 40-mg dose, and 26% with placebo.

Tollefson and colleagues studied 355 patients over 13 weeks, again comparing fluoxetine doses of 20 mg, 40 mg, 60 mg, or placebo [84]. At all doses, there was significant improvement on Y-BOCS scores compared to placebo.

A 2020 systematic review found that fluoxetine is well-tolerated and associated with significantly greater reduction in OCD severity in children and adolescents, as measured by the Children's Y-BOCS [85].

Citalopram

Citalopram is the most serotonin-selective of the SSRIs. Although it does not have an FDA-approved indication for OCD, it is included as an equivalent option to the other SSRIs in the APA guideline [10].

Montgomery and colleagues tested different doses of citalopram against placebo in 401 patients with OCD over 12 weeks, with "improvement" considered to be a 25% reduction in baseline Y-BOCS scores [86]. The percentage of patients who reached this endpoint was significantly higher in the treatment groups: 65% of subjects at 60 mg per day, 52% at 40 mg per day, and 57% for 20 mg per day, compared to 37% of subjects receiving placebo. The differences between the individual doses of citalopram were not statistically significant.

In 2011, the FDA issued a warning advising patients and prescribers that citalopram should no longer be used at a dosage greater than 40 mg due to risk of potentially fatal abnormal heart rhythms, including torsades de pointes and should not be used in patients with factors predisposing them to either of those conditions [87]. Additionally, doses of 60 mg per day have not been found to have reasonable benefit over doses of 40 mg per day [87; 88]. In 2012, a revised warning was issued to clarify that citalopram is "not recommended" rather than "contraindicated" in those with congenital long QT interval syndrome, should not be used at doses greater than 20 mg per day in patients older than 60 years of age, and should be discontinued in patients with a QTc measurement greater than 500 ms [88]. Citalopram must be dispensed with an FDA-approved patient medication guide [59].

Escitalopram

Escitalopram, an enantiomer of citalopram, is also not FDA approved for OCD. Like citalopram, it is included with the other SSRIs as an option in the APA recommendations [10].

A 24-week, double-blind, randomized trial, conducted by Stein and colleagues, showed a benefit of escitalopram over placebo in OCD [89]. Escitalopram at both 10 mg and 20 mg per day was superior to placebo on multiple measures, including remission at 12 weeks, defined as a Y-BOCS score of 10 or less. At 24 weeks, remission was significantly greater than placebo for escitalopram 10 mg per day, although only numerically greater than placebo for the 20-mg dose.

SRI in OCD

Although clomipramine and the SSRIs are also used to treat depression, their use in OCD has somewhat different parameters. Patients with OCD may require higher doses, and the onset of action may be slower. In depression, improvement may be expected as early as one week after initiating treatment. The APA guideline for the treatment of major depressive disorder recommends re-evaluating treatment if at least moderate improvement has not occurred after six to eight weeks [10]. In OCD, a full trial of SRI therapy takes 8 to 12 weeks, including 4 to 6 weeks on the highest tolerable dose [58; 70].

Starting at a low dose of an SRI helps to avoid side effects, including nausea, diarrhea, drowsiness, and headache. Many pills can be split, and some SRIs are available in liquid formulations that allow for even more flexible titration schedules. Usual doses of SRIs in OCD are provided in the APA guideline and updated manufacturer labeling (*Table 1*).

Side Effects

Many patients will tolerate SSRIs well, but for some, side effects can be significant. Some side effects, including nausea, agitation, and sleep disturbances, commonly occur when the medication is first started and disappear over the first few weeks to months. Explaining this to patients can help to encourage them to continue the medication, with the understanding that other options are available should the side effects fail to subside.

ADULT DOSING OF SSRIs FOR THE TREATMENT OF OCD ^a				
SSRI	Starting and Incremental Dose	Usual Target Dose	Usual Maximum Dose	Occasionally Prescribed Maximum Dose
Citalopram	20 mg	40 mg ^b	40 mg ^b	40 mg ^b
Escitalopram	10 mg	10–20 mg	40 mg	60 mg
Fluoxetine	20 mg	40–60 mg	80 mg	120 mg
Fluvoxamine	50 mg	100–300 mg	300 mg	450 mg
Paroxetine	20 mg	20–60 mg	60 mg	100 mg
Sertraline	50 mg	200 mg	200 mg	400 mg

^aDosages are for immediate-release formula, not controlled-release.
^bMaximum dose: 40 mg

Source: [10; 59] Table 1

In some cases, lowering the dose, changing the timing of doses, or changing to a different SRI will help to alleviate side effects; in others, adding an additional medication may be helpful [10]. Some side effects are particularly likely with certain SSRIs. For example, paroxetine is the most anticholinergic and appears to be more likely to cause weight gain than other SSRIs. Insomnia may be addressed by taking the SSRI in the morning instead of the evening or by the addition of a sleep-promoting agent. Modafinil may help with fatigue. Excessive diaphoresis may be improved by the addition of a low-dose anticholinergic.

Sexual symptoms, including decreased libido and difficulty with orgasm, may be difficult to overcome, but there are options that will work for some patients. In some cases, sexual symptoms will decrease over time. Some patients may be willing to wait until OCD symptoms have improved and weaning from the SSRI is appropriate. Some may benefit from a “drug holiday” up to once per week, stopping the SSRI for one day before a sexual encounter. In general, stopping an SSRI abruptly is not recommended due to the possibility of withdrawal effects, but with most of the SSRIs, missing one dose is not expected to affect outcomes adversely. The short half-life of paroxetine makes it a poor choice for this technique, and the half-life of fluoxetine may be too long for the one-day “holiday” to be useful.

SSRIs and clomipramine carry a warning from the FDA regarding a possible increased risk of suicidality in children, adolescents, and young adults [59]. Patients should be closely monitored for suicidality throughout therapy, particularly when beginning treatment or altering the dose.

Partial Response and Non-Response

As noted, the APA recommends a trial of at least 8 to 12 weeks with a given SRI, including at least four to six weeks at the highest tolerable dose [10]. For patients who fail to achieve a reduction in symptoms by the end of this time or who have only minimal response, there are several APA-recommended options [10]. One strategy is to offer a trial of a different SSRI. It may take multiple trials to find the right match for a given patient. Additional options include switching to clomipramine, switching to the serotonin-norepinephrine reuptake inhibitor venlafaxine, or adding a second-generation antipsychotic. Switching to mirtazapine is also offered as a strategy, although supporting evidence is limited. Switching to venlafaxine may be less effective than switching to a different SRI.

Some patients will be partial responders to SSRIs, with symptoms improving but still having a significant impact on functioning. For these patients, the APA recommends continuing the pharmacotherapy but augmenting it with either a second-generation antipsychotic or CBT. Antipsychotics alone have not proven useful in OCD. However, there is some

evidence to support their use to augment SRI therapy, with response rates of about 40% to 55% [10]. Unfortunately, the details of best use, including dose, duration, and subsets of patients who may benefit most, have not yet been established.

Duration of Treatment

The best duration for pharmacotherapy in OCD has not been determined. A minimum of one to two years has been recommended before withdrawal should be considered [10; 90]. Others recommend that pharmacotherapy should be continued indefinitely. Data suggest that patients' symptoms will return within one to two months after medications are stopped, even after two years of successful pharmacotherapy. Up to 20% of patients who discontinue a successful drug will not respond when the drug is restarted [74]. The presence of a comorbid diagnosis can interfere with clinical recovery and may guide the choice of interventions [58]. The decision to continue or to stop medication should be individualized and discussed with each patient.

As noted, neither SSRIs nor clomipramine should be stopped abruptly. Instead, these medications should be tapered slowly, decreasing by 10% to 25% every one to two months [10]. Sudden discontinuation can lead to a drug discontinuation syndrome, with symptoms that may include nausea and vomiting, headache, dizziness, insomnia, and agitation or lethargy. Patients may also experience paresthesias or myoclonic jerks.

PSYCHOLOGICAL THERAPY

Of all potential psychological therapies for OCD, CBT is supported by the best evidence. Most studies have used some form of exposure and response prevention as the mode of therapy, with variations in frequency, intensity, and guidance. These studies have generally been small, with at most a few dozen patients. One larger, multisite trial compared exposure and response prevention to clomipramine, placebo, or a combination of the two treatments [91]. This study involved intensive, daily exposure and response prevention for four weeks, followed by maintenance sessions for another eight weeks.

Overall, 71% of the 122 randomized patients completed treatment. Response rates at week 12, measured as improvement on the Y-BOCS, CGI-S, and NIMH-GOCS, were all significantly better for exposure and response prevention than for clomipramine. Exposure and response prevention plus clomipramine was not significantly better than exposure and response prevention alone. Based on the CGI-I measure, an "excellent" response was seen more often in the exposure and response prevention group and in the combination group than in the clomipramine-alone group.

Another large trial, involving 218 patients, compared two different techniques for exposure and response prevention to a control group [92]. One group received weekly instruction by therapists on performing exposure and response prevention techniques at home. The second group used a workbook and a computer program. The controls received relaxation training. In an intent-to-treat analysis, both the therapist-guided and computer-guided exposure and response prevention sessions were significantly superior to the control therapy, and the therapist-guided therapy was significantly more effective than the computer sessions.

In 2007, a Cochrane review compared psychological treatment for OCD with "treatment as usual" [93]. Eight relevant studies, all randomized trials, were identified, and in each one, patients on a waiting list were used as the controls. In all but one of the studies, some patients also received pharmacologic treatment. Study treatment duration ranged from six to 20 weeks. Patients receiving any type of CBT were found to have significantly fewer symptoms following treatment, with overall effect being influenced by baseline severity. The authors recommended further study to identify the best forms of CBT, predictors of response, and cost-effectiveness.

Not all patients will be able to complete a course of CBT. For some, the commitment level is too high. For others, the anxiety induced by facing or thinking about the feared objects or events is simply too strong. An estimated 22% to 30% of patients can be expected to drop out or refuse to comply with expo-

sure and response prevention therapy [58; 94]. For these patients, Internet-based self- or professional-guided therapy may be a beneficial alternative [60].

Some patients who are willing and able to attempt CBT will be stymied by insurance constraints. For these patients, and with appropriate guidance, self-help in the form of workbooks and exercises to be done at home is an option [58]. However, as experienced in the POTS II trial, CBT instruction-only response rates are likely much lower than that of weekly CBT sessions [64]. CBT available as online video teletherapy and through self-help apps are areas of current research for treatment of OCD [95; 96].

Techniques for CBT

Exposure and response prevention consists of a specific series of techniques. It may be offered as individual therapy or in a group setting. The APA recommends at least weekly sessions [10].

Exposure and response prevention is based on the idea that obsessions and compulsions serve to reinforce one another [97; 98]. The obsessions are associated with great anxiety; because compulsions serve to reduce that anxiety, the performance of these behaviors is reinforced with each cycle. At the same time, the use of ritualized behaviors to combat anxiety prevents the development of other methods of coping with the anxious feelings. Thus, repeated exposure to a feared stimulus while avoiding the use of ritualized behavioral responses should, over time, lead to a dampening of the anxiety response and a lessening of the need to perform compulsions. Exercises generally start with exposure to a situation that causes a moderate level of anxiety and progress to exposures that are more intensely feared. Patients are encouraged to think about the feared consequences of not performing their rituals. At the same time, they are asked to abstain from these ritualistic behaviors and encouraged to develop alternative ways of tolerating and overcoming anxiety. When exposure and response prevention is successful, patients gradually become accustomed to the idea that feared outcomes are unlikely to happen even though rituals are not performed. The patient's family should be

involved when possible. To be of most help to the patient, the family may need to be willing to change their responses to the patient (e.g., not provide requested reassurance to irrational doubts) [58]. Successful treatment depends in part on the family's willingness to reduce their accommodation of the patient's compulsive behaviors [99]. Additionally, a family history of OCD can significantly decrease the patient's response to CBT [100].

Recommended Duration of CBT

There is no strong evidence to support a given duration of CBT. However, the consensus, according to the APA guideline, is for an initial course of 13 to 20 weeks of weekly CBT or three weeks of daily sessions [10]. If treatment is successful, it may be tapered to monthly sessions for another three to six months. Some patients will benefit from occasional booster sessions as well. The APA recommends ongoing maintenance, although details are not specified [10]. The exact probability of relapse following CBT is unclear.

Patients who have not achieved benefit after an initial course of CBT should be re-evaluated. Lack of compliance with treatment may be a barrier to success, and reasons for noncompliance should be explored and, if possible, addressed. Some patients may require a longer duration of therapy. For partial responders, the APA recommends a trial of an SSRI to accompany CBT [10]. Other options include increasing the intensity of treatment or adding cognitive therapy to exposure and response prevention, although the effectiveness of these choices has not been established.

ADDITIONAL TREATMENT OPTIONS

Some patients will fail to respond to both standard pharmacologic options and to outpatient CBT. Others will achieve a partial response but remain unable to return to a satisfactory level of functioning. A subset of patients will be so disabled by symptoms that they are unable to participate in standard outpatient treatment. These patients should generally be referred to specialty psychiatric care, preferably to a physician with expertise in OCD.

One option for patients with severe OCD is inpatient therapy. Highly structured, intensive outpatient treatment may also be beneficial. Treatment-refractory patients may benefit from the use of other medications added to standard pharmacotherapy or from monotherapy with drugs other than SRIs. Limited evidence suggests that patients who are not helped by oral SRIs may benefit from oral morphine, IV clomipramine, IV citalopram, combinations of antidepressants, or other therapies; however, more research is needed to determine efficacy and identify appropriate use [40; 101; 102]. One randomized double-blind study tested the safety and efficacy of the central nervous system (CNS) stimulant methylphenidate extended-release (MPH-ER) as add-on therapy for SRI treatment-refractory OCD [103]. The study involved 44 adults (66% male) with SRI treatment-refractory OCD, receiving fluvoxamine pharmacotherapy, and with Y-BOCS scores higher than 20. Participants were randomized into two groups: group one received fluvoxamine (250 mg/day) plus MPH-ER (36 mg/day); group two received fluvoxamine (250 mg/day) plus identical placebo tablets. All participants were followed for eight weeks. Improvement in the Y-BOCS total score and Y-BOCS obsession subscale score was more prominent in the fluvoxamine plus MPH-ER group compared with those receiving placebo [103].

Psilocybin, cannabis, nicotine, and morphine for treatment of OCD were the subject of a systematic review of 16 observational and interventional studies. While the overall results were promising and showed a reduction in Y-BOCS scores, the authors concluded that further research and clinical trials are needed [104]. There is some evidence supporting augmentation with a second-generation antipsychotic (e.g., risperidone, paliperidone, aripiprazole); however, the use of these agents for OCD is off-label [59; 105].

Several other experimental treatments have been investigated. Cingulotomy, anterior capsulotomy, subcaudate tractotomy, limbic leucotomy, and deep brain stimulation may have benefit for select patients

with severe OCD who do not respond to less invasive treatment [36; 106]. However, best practice for these procedures has not been established, and the risk of serious adverse effects, including seizures, apathy, and executive dysfunction, must be weighed carefully against the potential benefit. There is conflicting evidence for transcranial magnetic stimulation (TMS), with some trials showing improvement while others show no effect. A 2003 Cochrane review concluded that there was too little evidence to draw conclusions about the usefulness of this treatment [107]. More recent analyses confirm that additional research, using large controlled trials, is needed to determine the usefulness of TMS for the treatment of OCD [49; 108; 109; 110].

CONCLUSION

OCD is a potentially debilitating illness that affects work, interpersonal relationships, and overall quality of life. In spite of straightforward criteria, evidence shows that the diagnosis is frequently missed. Varied presentations, comorbidities, and patients' own hesitation to discuss symptoms can cloud the diagnosis. Physicians must be familiar with the diagnostic criteria and with the variations in presentation in order to identify patients with OCD.

First-line therapies for OCD will relieve symptoms in some patients and provide partial improvement in others; however, some patients will prove to have illness that is refractory to established treatments. Changing or augmenting therapy, as according to recommendations in the APA guideline, can be helpful when initial therapy provides only partial improvement or no improvement at all. Patients with severe or treatment-refractory OCD should generally be referred to specialty care.

Although treating OCD can be challenging, recognition and appropriate care of this disorder can help a great many patients, reducing or even eliminating disability and improving their overall quality of life.

RESOURCES

American Psychiatric Association

<https://www.psychiatry.org>

Medical specialty society concerned with ensuring humane care and effective treatment for all persons with mental disorders.

American Psychological Association

<https://www.apa.org>

An association of professional psychologists actively involved in basic psychological research, applied research, and the treatment of psychological and mental disorders.

Anxiety and Depression Association of America

<https://adaa.org>

National nonprofit organization including clinicians, researchers, and consumers concerned with informing the public, healthcare professionals, and media about anxiety disorders.

Association for Behavioral and Cognitive Therapies

<https://www.abct.org>

An interdisciplinary organization for the scientific study of problems that may be treated by behavioral and/or cognitive therapies.

Behavioral Health Treatment Services Locator

<https://findtreatment.gov>

A service of the Substance Abuse and Mental Health Services Administration, part of the U.S. Department of Health and Human Services, that provides a listing of local mental health services throughout the United States and its territories.

National Institute of Mental Health

<https://www.nimh.nih.gov>

A division of the National Institutes of Health, a component of the U.S. Department of Health and Human Services, with the goal of improving the understanding and treatment of mental illnesses through basic and clinical research.

International OCD Foundation

<https://iocdf.org>

International not-for-profit organization offering education and support to people with OCD and supporting medical research and education about OCD and related disorders.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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