DEPARTMENT OF HEALTH

Obsessive-Compulsive Disorder Issue Brief

OCTOBER 2022

Introduction

This briefing was prepared in response to a petition to consider adding obsessive-compulsive disorder as a new condition to the list of qualifying conditions for the Minnesota medical cannabis program. The intention of these briefings is to present to the Commissioner of Health, members of the Medical Cannabis Review Panel, and interested members of the public, scientific studies of cannabis products as a therapy for the petitioned condition. Brief information on the condition and its current treatment are provided to help give context to the studies. The primary focus is on clinical trials and observational studies, but for many conditions there are few of these. A selection of articles on pre-clinical studies (typically laboratory and animal model studies) were included, especially if there are few clinical trials or observational studies. Interpretation of surveys can be difficult because it is unclear whether responders represent the population of interest and because of unknown validity of responses; however, surveys published in peer-reviewed journals were included for completeness. Published recommendations or opinions of national medical organizations were also included.

Searches for published clinical trials and observational studies of cannabis therapy were conducted using the National Library of Medicine's Medline key word searches appropriate for the petitioned condition. Articles identified as clinical trials, observational studies, or review articles were collected and reviewed. References in the identified articles were examined to ensure all the articles associated with the petitioned condition were identified and included. Moreover, ClinicalTrials.gov, a federal government-maintained website responsible for tracking current clinical trials funded, was used to identify any ongoing or completed clinical trials.

Definition

Obsessive-Compulsive Disorder (OCD) is a disorder characterized by recurring, intrusive thoughts (obsessions) that often cause significant emotional distress and anxiety. This can lead to behaviors (compulsions) that the affected individual feels compelled to perform to manage/reduce that distress. Contrary to popular belief, compulsions do not need to be observable behaviors. Compulsions can be mental. Some common OCD themes may involve the following:

1. Contamination (fear of germs, dirt, etc.)
2. Harm/violence (fear of hurting others or oneself)
3. Sexual themes (thoughts/mental images related to sex)
4. Religious/Moral scrupulosity (concerns about offending God or violating moral code)
5. Perfectionism themes ("just right" feelings, fear of making mistakes)
6. Identity-related themes (concerns about sexual orientation, gender identity, etc.)

Strict criteria for the diagnosis of OCD is defined in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5-TR; American Psychiatric Association [APA], 2022) and is presented verbatim below.

Diagnostic Criteria

A. Presence of obsessions, compulsions, or both:

   Obsessions are defined by (1) and (2):

   1. Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.
   2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).

   Compulsions are defined by (1) and (2):

   1. Repetitive behaviors (e.g., hand washing, 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.
   2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; 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.

B. The obsessions or compulsions are time-consuming (e.g., take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

D. The disturbance is not better explained by the symptoms of another mental disorder (e.g., excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder [repetitive or ritualistic movement, posture, or utterance]; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders;

guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).

Specify if:

With good or fair insight: The individual recognizes that obsessive-compulsive disorder beliefs are definitely or probably not true or that they may or may not be true.

With poor insight: The individual thinks obsessive-compulsive disorder beliefs are probably true.

With absent insight/delusional beliefs: The individual is completely convinced that obsessive-compulsive disorder beliefs are true.

Specify if:

Tic-related: The individual has a current or past history of a tic disorder.

The most commonly used and validated tool for measuring OCD severity is with the Yale-Brown Obsessive Compulsive Scale (YBOCS; Goodman et al., 1989). It is administered by a clinician and is used to assess for changes in severity during treatment. Scores can range from 0-40, with higher scores reflecting greater OCD severity.

Prevalence

OCD is estimated to affect 2-3% of the population (Stein et al., 2019). Within the U.S., 12-month prevalence is estimated to be at 1.2% (APA, 2022). Some speculate these estimates are low because individuals that present with mild symptoms may not seek treatment, and health care practitioners may not necessarily be knowledgeable about the various ways in which OCD can manifest, thus leading to inaccurate or delayed diagnosis (Fenske & Petersen, 2015; Hirschtritt et al., 2017). In addition, people who suffer from OCD often feel extreme shame about their obsessions, which makes them reluctant to come forward and receive treatment. It has been estimated that it can take roughly 8 years from the onset of symptoms before receiving any type of medication for treatment for the first time (Hirschtritt et al., 2017).

An oft-cited statistic from 1995 by DuPont et al. estimates the total economic cost of OCD to be $8.4 billion dollars—5.7% of the total $147.8 billion cost for all mental illness. This data are close to 30 years old, but even recent literature continues to cite it. It would be reasonable to expect these costs are significantly outdated and most likely low when factoring in inflation over time and decreased stigmatization over seeking mental health services.

Current Therapies

Both pharmacologic and non-pharmacologic treatments are used to manage OCD symptoms, and gold standards exist in both treatment domains. First-line medications for treating OCD are selective serotonin reuptake inhibitors (SSRIs), which are a class of drugs often used for treating major depressive disorder and anxiety disorders. Clomipramine, a tricyclic antidepressant (a historically older group of antidepressants than SSRIs) is another commonly prescribed

medication for OCD. A study using data from a Cochrane[1] database of randomized controlled trials found that the efficacy of SSRIs and clomipramine in treating OCD were relatively similar and considered moderately effective (Skapinakis et al., 2016). However, SSRIs are generally better tolerated than clomipramine, making SSRIs the more desirable choice in OCD patients.

Within cognitive-behavioral therapy (CBT), exposure and response prevention (ERP) is considered the gold standard for managing OCD. Individuals with OCD struggle to tolerate distress and uncertainty coming from obsessions, and the act of performing compulsions helps regulate that distress. In ERP training, the client goes through work to sit with and tolerate the distress or uncertainty coming from the obsessions and not perform compulsions. The idea is that clients should naturally allow their obsessions to occur as they do, but not to give in to compulsions to manage the distress coming from those obsessions. At first, this can be very challenging and highly uncomfortable for OCD sufferers because they are being told to *respond* differently to obsessions; they are to sit with the distress signals coming from their minds and, over time, they are retraining their nervous systems to process their obsessions as not a true threat. ERP can reduce OCD symptoms by 77% (Franklin et al., 2000), making it a fairly successful treatment. However, it has been estimated that 15% of patients will discontinue ERP treatment due to difficulty or intolerability of the treatment (Ong et al., 2016).

In summary, treatment with an SSRI alone or with CBT alone are moderately effective, with evidence suggesting superiority of CBT over SSRIs as monotherapy[2]. Given their independent successes, both SSRIs and CBT are sometimes combined for OCD treatment. At the same time, it is also important to acknowledge that roughly 25% of patients will not respond to either medication or psychotherapy, which means that a proportion of OCD sufferers remain treatment-resistant (Hirschtritt et al., 2017).

Preclinical Research

There has been some interest in finding new medications to treat OCD. One such area of interest includes exploring cannabis and cannabinoids in treating OCD symptoms. Firstly, cannabinoid receptor 1 (CB1-receptor)[3] is abundantly found in brain regions implicated in OCD, including in the prefrontal cortex (decision-making, goal-directed behaviors), amygdala (emotion regulation), hippocampus (memory, fear extinction), and the basil ganglia (repetitive behaviors). (Kayser et al., 2019). Secondly, cannabidiol (CBD; a cannabinoid found in the cannabis plant) has shown some promise in the preclinical literature for relieving fear and anxiety (Blessing et al., 2015). While OCD is not categorized under anxiety disorders in the DSM-

[1] Cochrane: a well-regarded not-for-profit organization that partners with the scientific and medical communities to provide up-to-date, high quality information about managing a range of healthcare conditions.
[2] Monotherapy: being on one type of treatment at one time, regardless of whether that's a medication or something else (e.g., psychotherapy).
[3] Receptor (neuronal receptor): refers to a site within bodily cells (neurons) that cannabinoids can bind to – like a key fitting into a specific lock (key = cannabinoid, lock = cannabinoid receptor). Cannabinoids are either produced within the body (*endo*cannabinoids or endogenous cannabinoids) or can be introduced into the body (cannabinoids like THC or CBD from the cannabis plant that a person may smoke, or man-made cannabinoids introduced into the body; exogenous cannabinoids).

5-TR, anxiety is often present in OCD even if it is not a primary manifestation of OCD. This suggests that there may be some potential for CBD to help with some of the anxiety-provoking aspects of OCD.

The endocannabinoid system may also be involved in the manifestation of compulsive-like behaviors. For example, it has been documented that the administration of CBD decreases compulsive-like behaviors, as measured in the marble-burying test in rats and mice (Dixit et al., 2020). In this paradigm, the bottom of a cage is covered in a layer of sawdust (typically no more than 5 centimeters deep), and several marbles are lain across the top of this pile evenly spaced apart. A rodent is subsequently placed in the cage, and the number of marbles that are buried are observed over a set amount of time. Burying is a common stereotyped behavior that is observed in rodents, and it has been considered to potentially map to stereotyped human behaviors like compulsions. Previous data has shown that administering CBD can decrease marble-burying in mice, suggesting CBD's anticompulsive-like effects (Dixit et al., 2020).

Overall, the preclinical literature indicates that the endocannabinoid system may have a role in anxiety and compulsive/repetitive behaviors, both of which are present in OCD. However, the science is still emerging, and it's important to keep in mind that, while animal studies play an important role in understanding the neurobiology underlying psychiatric disorders, the construct validity[4] of these models can come under scrutiny.

Clinical Trials

Five studies investigating the effects of cannabis/cannabinoids on OCD were identified, three of which were case studies/reports and the remaining two being clinical trials. Chronologically, the case study/report data are older than the two clinical trials reported here, and the perceived effectiveness of cannabis/cannabinoids in those case studies/reports may have provided some impetus to pursue the clinical trials that followed. While clinical trial data are extremely limited, one of the clinical trial results indicate that cannabinoids may not independently improve OCD symptoms but work to help in the exposure and response prevention (ERP) treatment in alleviating OCD symptoms. However, those particular findings are significantly limited by the lack of a placebo-controlled comparison. In fact, the other clinical trial which was a randomized controlled trial, showed that even if OCD symptoms were improved with cannabis, this was true for all conditions including the placebo arm. This supports prior evidence to suggest that expectancy effects[5] may noticeably influence perceived effectiveness of cannabis in treating obsessive-compulsive (OC) symptoms.

Overall, more clinical research is needed to better ascertain the effects of cannabis/cannabinoids on OCD symptomatology. Clinical trials should be designed with a greater number of participants than the current trials have included, and they should be placebo-controlled due to possible expectancy effects that have been documented previously.

[4] Construct validity: the strength with which one can say one's test or measure is actually capturing the thing one wants (e.g., "is marble-burying behavior in rodents actually a good measure of compulsions?").
[5] Expectancy effects: a phenomenon whereby one's expectations for a particular outcome unconsciously influences the actual outcome of the study.

Trials that investigate the individual contributions of specific cannabinoids (e.g., delta-9-tetrahydrocannabinol (THC) vs. CBD) to OCD symptomology are important, as well as trials using cannabis flower. The latter may be important from an external validity standpoint since cannabis flower (which contains phytochemicals beyond just THC/CBD that may contribute to overall perceived effects) is far more commonly used among both medicinal and recreational users than cannabis extract products (Sexton et al., 2016).

Kayser, R.R., Haney, M., Raskin, M., Arout, C., & Simpson, H.B. (2020). Acute effects of cannabinoids on symptoms of obsessive-compulsive disorder: A human laboratory study. *Depression & Anxiety, 37*(8), 801-811. https://doi.org/10.1002/da.23032

Kayser et al. (2020) was the first double-blind, placebo controlled randomized trial to examine acute effects of cannabis on OCD. In a crossover design[6], patients with severe OCD (n = 12) were exposed to three different smokeable cannabis pre-roll preparations with different THC:CBD ratios in randomized order: high THC to low CBD, low THC to high CBD, and placebo. Using a cued-smoking procedure to maximize dosing consistency among patients, patients were asked to smoke 50% of their preparation within a certain timed schedule, after which time patients' obsessions, compulsions, and anxiety levels were self-reported at 20, 40 60, 90, 120, and 180 minutes after smoking. Results indicated that, while OCD symptoms and anxiety levels were reduced over time, those reductions were similarly observed across all conditions including placebo. Therefore, the authors were unable to conclude that THC or CBD could alleviate acute OCD symptoms and anxiety. This study could benefit from replication with a larger sample size and longer study duration (study only investigated short-term, acute changes in OCD symptoms).

Kayser, R. R., Raskin, M., Snorrason, I., Hezel, D. M., Haney, M., & Simpson, H. B. (2020). Cannabinoid augmentation of exposure-based psychotherapy for obsessive compulsive disorder. *Journal of Clinical Psychopharmacology, 40*(2), 207–210. https://doi.org/10.1097/JCP.0000000000001179

This study investigated the efficacy of nabilone (a synthetic THC) on OCD, either in conjunction with ERP treatment or administering nabilone alone. Adult patients who scored at least moderately on the Yale-Brown Obsessive Compulsive Scale (YBOCS score >= 16) were included in the study (n = 11) and were randomized into one of the two treatment groups: nabilone alone vs. nabilone + ERP. Both treatment groups were in the study for 4 weeks, and third-party evaluators rated OCD symptoms in the patients using the YBOCS at baseline, 2-weeks, and 4-weeks (evaluators were blind to participants' treatment group). Results showed that those in the nabilone + ERP group showed significantly greater change in their YBOCS scores from baseline to 4-weeks, compared to those given nabilone alone. In fact, the nabilone alone condition did not result in significantly improved OCD symptoms within 4 weeks. Authors conclude that nabilone may enhance ERP efficacy to help treat OCD symptoms. However, the

[6] Crossover design: a study design where participants are assigned to all treatment conditions over different periods of time.

omission of a placebo control in this study along with its small sample size limit the interpretive power of this study.

Szejko, N., Fremer, C., & Müller-Vahl, K. R. (2020). Cannabis improves obsessive-compulsive disorder—case report and review of the literature. *Frontiers in Psychiatry, 11*. https://doi.org/10.3389/fpsyt.2020.00681

Szejko et al. (2020) published a case report on a young adult male with severe OCD since childhood. The motivation for this case report was spurred by this patient's prior experience with street cannabis and having reported that it had helped with OCD symptoms. Another reason for motivating this study was that he did not want to take SSRIs or seek out psychotherapy. Bedrocan (22% THC to <1% CBD; predominately available in Europe) was provided to this patient, and clinical assessments were administered at baseline and compared to results at 3-months, 6-months, and 20-months after treatment start. Due to a sample size of 1, no statistical tests were conducted, but the researchers noted that the patient reported a decrease in OCD symptoms over time, with a 90-95% reduction in obsessions and compulsions by the end of the study.

Schindler F., Anghelescu I., Regen F., & Jockers-Scherubl, M. (2008). Improvement in refractory obsessive compulsive disorder with dronabinol. *American Journal of Psychiatry, 165*(4), 536-537. https://doi.org/10.1176/appi.ajp.2007.07061016

This was a case study following two adult patients with treatment-resistant OCD; both had previously used paroxetine (an SSRI) for OCD symptoms with limited success. These individuals also suffered comorbid diagnoses, one with major depressive disorder and the other with schizophrenia. For the study, these patients augmented their existing medication regimen with dronabinol (a synthetic THC). At study outset, both were exhibiting moderate OCD symptoms according to YBOCS scores (scores of 20 and 23), and they had decreased to mild symptoms (scores of 10 and 15) within two weeks. Even with the apparent success in reducing OCD symptoms in the individual with comorbid schizophrenia, the authors caution treatment with cannabinoids in individuals with a history of, or predisposition to, psychoses.

Cooper J.J., & Grant J. (2017). Refractory OCD due to thalamic infarct with response to dronabinol. *Journal of Neuropsychiatry and Clinical Neurosciences, 29*(1), 77-78. https://doi.org/10.1176/appi.neuropsych.16030053

Cooper and Grant (2017) reported on a single patient (case report) who suffered from extreme OCD (YBOSC score: 39) after experiencing a stroke within a region of the thalamus that has been associated with the pathophysiology of OCD. He also had insulin-dependent diabetes and bipolar I disorder (both existed prior to the stroke) and was receiving medical treatment for both. A variety of treatments to curb OCD symptoms were unsuccessful, and dronabinol was started, with dosing titrated up to 20 mg a day. By the second week, the patient reported decreases in OCD symptoms, scoring as low as a 10 on the YBOSC at one point in time. In addition, this patient was able to tolerate starting cognitive-behavioral therapy which had been difficult previously.

Ongoing Clinical Trials

A search for ongoing clinical trials on ClinicalTrials.gov (https://ClinicalTrials.gov) was conducted using cannabis keywords ("cannabis", "cannabinoids", "marijuana", "thc", "cbd") and OCD keywords ("obsessive-compulsive disorder", "obsessions", "compulsions", "ocd"). The search led to the identification of two ongoing studies, both listed as being in the recruitment phase as of August 2022.

Multimodal Assessment of Cannabinoid Target Engagement in Adults With Obsessive-Compulsive Disorder (https://clinicaltrials.gov/ct2/show/NCT04880278)

This study is investigating the effects of nabilone (a synthetic THC) on neurocognitive processes associated with OCD. Adult patients with a prior diagnosis of OCD are being recruited for the study (target sample size: n = 60). Primary measures include brain imaging and neurophysiological measures performed during neurocognitive testing, while secondary measures include various anxiety-related measures, physiological measures (heart rate, blood pressure), and drug effects measures. Patients will be randomly assigned to either nabilone or placebo (parallel assignment), and between-subjects comparisons will be made. This study is estimated to be completed July 2026 and is being conducted by Kayser and colleagues, who are the authors of the two published clinical trials mentioned previously in this brief.

Epidiolex in Obsessive Compulsive Disorder and Related Disorders (https://clinicaltrials.gov/ct2/show/NCT04978428)

This study is examining the effects and safety profile of Epidiolex (CBD) on adult OCD patients and related disorders such as skin picking, trichotillomania (hair pulling), tic disorder, and hoarding. The description of the study does not indicate whether the patients are being sampled from the clinical populations of interest, or if it is relying on participant self-report for having one of those diagnoses. Nonetheless, authors are primarily interested in measuring for the severity of OCD, skin picking, hoarding, and tics at baseline and at Week 2 of the study. Patients (target sample size: n = 15) will start with a twice daily, 2.5 mg/kg dose of Epidiolex for Week 1. Week 2 will be at an increased dosage of 5 mg/kg of Epidiolex twice per day. This is not a placebo-controlled study. Estimated study completion date is listed as September 2023, and it is being conducted by Grant and colleagues (Grant is a co-author in the case report mentioned previously in this brief).

Observational Studies

A handful of observational studies have been published investigating the relationship between cannabis use and OCD symptomatology. Taking the literature altogether, while some evidence suggests that individuals who use cannabis/cannabinoids perceive benefits to obsessive-compulsive symptoms, this finding is accompanied by literature indicating that these users may also be at greater risk for developing cannabis problems or cannabis use disorder (CUD). Therefore, the perceived benefits of cannabis in this population are tempered by potential harmful public health effects. This section presents some representative observational studies on the current state of knowledge.

A review of the literature also shows some limitations. For example, many observational studies use a cross-sectional design which makes the directionality of any observable associations unclear. Furthermore, a number of studies have targeted non-clinical populations for their sample (e.g., college students, general population) to answer questions about OCD symptomatology. This limits the generalizability of findings to actual clinical populations. Even if the authors administered validated tools to identify participants exhibiting obsessive-compulsive symptomatology, this is not verified by a professional evaluation, and some studies include patients who self-report having OCD. There may also be selection bias depending on recruitment methods.

Spradlin, A., Mauzay D., & Cuttler, C. (2017). Symptoms of obsessive-compulsive disorder predict cannabis misuse. *Addictive Behaviors, 72*, 159-164. https://doi.org/10.1016/j.addbeh.2017.03.023

Spradlin et al. (2017) conducted an anonymous, online survey recruiting college students who had prior experience with using cannabis. These participants (n = 430), who were sampled from a non-clinical population (university), were administered the Obsessive-Compulsive Inventory-Revised (OCI-R; Foa et al., 2002) and asked to report on their cannabis usage (frequency of use, quantity consumed), cannabis misuse (measures to address cannabis problems and cannabis use disorder symptoms), and their levels of anxiety, stress, and depression. Results indicated that higher obsessive-compulsive (OC) scores were correlated with increased cannabis problems (detrimental personal, social, and occupational issues due to cannabis use), cannabis use disorder (CUD) symptoms, and coping motives (the use of cannabis to cope with distress). However, OC scores were not associated with cannabis use (how frequently they used cannabis or the quantity consumed). When researchers controlled for the participants' reported anxiety, stress, and depression, the positive association between OC scores and cannabis problems, CUD symptoms, and coping motives remained. Furthermore, their analysis indicated that coping motives may mediate the association between OC symptomatology and cannabis misuse/problems. It may be that, in an effort to cope with stress and anxiety induced by obsessions and compulsions, they may seek out cannabis and thereby increase their risk for cannabis-related problems.

In summary, while the frequency and quantity consumed is not associated with OC symptomatology, those who display OC symptoms may be more prone to cannabis misuse/problems. Those effects remain even when controlling for participants' reported anxiety, stress, and depressive symptoms. Despite these findings, it should be noted that the cross-sectional nature of this study makes claims on the directionality of these associations challenging. In addition, their study could benefit from sampling methods that target a clinical population rather than a non-clinical population. They do, however, point out that 13% of their sample reached clinical cut-off scores indicative of OCD according to the OCI-R.

Bakhshaie, J., Storch, E.A., Tran, N., & Zvolensky, M.J. (2020). Obsessive-compulsive symptoms and cannabis misuse: The explanatory role of cannabis use motives. *Journal of Dual Diagnosis, 16*(4), 409-419. https://doi.org/10.1080/15504263.2020.1786616

Bakhshaie et al.'s (2020) cross-sectional study was somewhat similar to Spradlin et al.'s (2017) study in its objective: to examine for associations between OC symptomatology and cannabis

misuse, along with any mediating effects of coping to explain cannabis misuse. Unlike Spradlin et al., however, they included a few additional measures. Most notably, they also measured other substance usage, specifically whether they were recent tobacco users as well as a measure to assess for alcohol use problems. Their study sample consisted of college students (non-clinical sample) which is similar to Spradlin et al. (2017), but their sample was roughly 40% smaller (n = 177) and more racially diverse. Results from their online survey showed a significant positive association between OC symptomatology and risky cannabis use; greater OC symptomatology was correlated with increased risky cannabis use (self-reported difficulty in controlling, decreasing, or ceasing cannabis use). Unlike Spradlin et al. (2017), however, OC symptomatology was not correlated with cannabis problems (self-reported detrimental effects to personal, social, occupational, and physical circumstances due to cannabis use). In other words, while greater OC symptoms were associated with self-reported difficulties in controlling their cannabis usage, it was not associated with any detrimental effects to their personal, occupational, or social lives. When controlling for problematic alcohol use and tobacco smoking status, coping motives (usage of cannabis to cope with distress) were not found to mediate the association between OC symptomatology and cannabis misuse. This diverges from Spradlin et al. (2017); however, Spradlin et al. did not collect data on problematic alcohol use or tobacco smoking status to control for in their study.

Nicolini, H., Martínez-Magaña, J.J., Genis-Mendoza, A.D., Villatoro Velásquez, J.A., Camarena B., Fleiz Bautista, C., Bustos-Gamiño, M., Aguilar Garcia, A., Lanzagorta, N., & Medina-Mora, M.E. (2021). Cannabis use in people with obsessive-compulsive symptomatology: Results from a Mexican epidemiological sample. *Frontiers in Psychiatry, 12*, 664228. https://doi.org/10.3389/fpsyt.2021.664228

This cross-sectional study investigated the association between OC symptomatology and cannabis dependence via a large nationally-representative survey conducted in Mexico (non-clinical population). As a part of a household survey and among the subset of individuals who agreed to provide a DNA sample, questions on drug, alcohol, and tobacco use were collected along with questions on psychiatric history – namely prior history of obsessive-compulsive, anxiety, depression, hypomania (milder form of mania), and psychosis symptomatology. Cannabis dependence was identified in participants exhibiting three or more of the following: "tolerance, abstinence, a longer time or greater amount of use, persistent or uncontrollable cravings, excessive time spent in getting drugs or recuperating from their effects, reduction in social, work, or recreational activities, or continued use in spite of awareness of harmful effects". Of the total sample (n = 13,130), 2.4% (n = 288) exhibited OC symptomatology. In addition, the prevalence of ever having used cannabis in those exhibiting OC symptomatology was greater than in those found in the population as a whole (24.4% vs. 9.7%). Another interesting finding was that those who had ever exhibited OC symptomatology reported higher rates of ever having used cannabis than those who had ever exhibited symptoms for anxiety, depression, and hypomania. Those having ever experienced psychosis symptomology were the only group to have higher rates of ever having used cannabis, compared to those ever experiencing OC symptomology. The authors found this finding interesting given prior evidence to indicate that cannabis use is higher in many psychiatric populations than in non-psychiatric populations, yet where OCD may specifically fall along this spectrum among other psychiatric

conditions has been relatively unknown. Lastly, DNA analysis revealed that those who have ever exhibited OC symptomatology were at greatest risk for becoming cannabis-dependent, as measured by polygenic risk scores. Those who displayed OC symptomatology but had never used cannabis had statistically lower risk of becoming cannabis-dependent, which the authors interpreted to mean the following: the mere act of using cannabis in OC-vulnerable individuals may elevate their risk for developing cannabis dependence.

Kayser, R.R., Senter, M.S., Tobet, R., Raskin, M., Patel, S., & Simpson, H.B. (2021). Patterns of cannabis use among individuals with obsessive-compulsive disorder: Results from an internet survey. *Journal of Obsessive-Compulsive and Related Disorders, 30*, 100664. https://doi.org/10.1016/j.jocrd.2021.100664

Unlike the previously mentioned observational studies in this brief, the authors of this study tried to recruit adults who 1) had a professional OCD diagnosis or had a score ≥ 21 on the Obsessive-Compulsive Inventory-Revised (OCI-R; previously established to be a potential clinical cut-off for OCD diagnosis), and 2) had used cannabis at least once in any preparation (flower, extracts, edibles). Recruitment for this online survey was through extensive public advertising through popular online websites (e.g., Reddit), various social media platforms (e.g., Facebook, Instagram), and OCD-related organizations (e.g., International OCD Foundation). Analysis was conducted on 601 patients (average age: 29 years old) who completed the entire survey and fit the above criteria. The survey included questions to measure cannabis use disorder (CUD), their patterns of cannabis usage (frequency, quantity, forms of cannabis used, methods of administration), and questions about current OCD symptomology. Forty-four percent (44%) of participants reported to come from states with both recreational and medical cannabis programs, 41% from states with only medical cannabis programs, and 15% from states where cannabis was completely illegal. Roughly 90% reported using cannabis at least once over the past month, with 57% reporting using cannabis at least daily. Mean age of OCD onset was 9.9 years of age, with first cannabis use reported on average to be at 17 years old; therefore, onset of OCD typically occurred prior to first cannabis use in this sample. Participants' primary formulation of choice for consuming cannabis was cannabis flower followed by cannabis extracts (65% and 25% of participants, respectively). When asked about THC and CBD concentrations (e.g., reporting on percentage of THC and CBD in products they consume), participants seemed generally more knowledgeable about THC concentrations in their preparations compared to CBD concentrations. THC concentrations were often reported to fall in the "high THC" range (>10% THC) for cannabis flower and cannabis extracts; whereas, it was more common for participants to report not knowing CBD concentrations or that CBD concentrations were low (<10% CBD) for those same formulations. For those who reported using edibles at least a quarter of the time, 75% reported not knowing the concentrations of THC and CBD in those products.

The majority of participants reported that cannabis helped their obsessions (68%) and compulsions (65%), and a smaller proportion either reported worsening of obsessions (17%) and compulsions (14%) or no change to obsessions (8%) and compulsions (21%). When assessing for CUD symptomatology, 42% met probable CUD diagnosis. Another 66% fell under the threshold for probable CUD but were high enough to be categorized as having problematic cannabis use. These results suggest that, while a decent proportion of participants experience

some OCD relief, this is also accompanied by problematic cannabis use. Lastly, the majority of participants (62%) were currently not in any evidence-based OCD treatment, with increases in cannabis usage frequency being associated with a decreased likelihood of seeking those treatments. While speculative, authors propose that the usage of cannabis may demotivate individuals from seeking those evidence-based treatments due to beliefs that cannabis could be an adequate replacement. Some limitations of this study include the cross-sectional nature of the study along with no independent verification of OCD diagnosis in participants. In addition, selection bias may have been present in the study and may not be representative of the wider OCD population. It is also possible for expectancy effects to have affected the results.

National Medical Organization Recommendations

No guidance documents or statements were found to recommend the therapeutic use of cannabis or cannabinoids in the management of OCD. However, Allina Health has submitted a letter to the Minnesota Department of Health expressing their opposition to adding OCD to the list of approved medical conditions. The National Academies of Sciences, Engineering, and Medicine produced a report on the health effects of cannabis in 2017, but the committee did not specifically speak to the health effects of cannabis on OCD.

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