

The Voice of the Patient

A series of reports from the U.S. Food and Drug Administration's (FDA's)
Patient-Focused Drug Development Initiative

Opioid Use Disorder

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Introduction

On April 17, 2018, the Food and Drug Administration (FDA) held a public meeting to hear perspectives from individuals with opioid use disorder (OUD), caregivers, and other patient representatives on the most significant health effects and available therapies to manage opioid use disorder. FDA conducted the meeting as part of the agency's Patient-Focused Drug Development (PFDD) initiative,¹ an effort to systematically gather patients' perspectives on their condition and available therapies to treat their condition. This initiative began as part of the fifth authorization of the Prescription Drug User Fee Act (PDUFA V). FDA collaborated with National Institute on Drug Abuse (NIDA) to identify the opportunity for this PFDD meeting and engage the stakeholder community in preparing for the meeting.

More information on FDA's PFDD initiative can be found at <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm579400.htm>.

Overview of Opioid Use Disorder

Opioid analgesics (termed opioids in this report) are a class of drugs commonly prescribed to treat moderate to severe pain. Opioids include drugs available by prescription such as oxycodone, hydrocodone, codeine, morphine, and fentanyl. Opioids also include illicit substances such as heroin and fentanyl. Although often prescribed to control pain, opioids may also produce feelings of euphoria and sedation which may lead to misuse of opioids resulting in opioid use disorder.

In 2016, an estimated 2.1 million people from age 12 years and older in the United States had opioid use disorder (OUD).² OUD is the diagnostic term used for a chronic, neurobiological disease characterized by a problematic pattern of opioid use leading to significant impairment or distress. OUD includes signs and symptoms that reflect compulsive, prolonged self-administration of opioid substances for no legitimate medical purpose, or, if another medical condition is present that required opioid treatment, opioid use in doses far greater than the amount needed for treatment of that medical condition. OUD can affect persons from all educational and socioeconomic backgrounds. Persons with OUD may experience periods of exacerbation and remission, making symptom control difficult.

Individuals with OUD may pursue various routes to management of recovery during their condition. Treatment for OUD often involves medication-assisted treatment (MAT). MAT is the use of medications in combination with counseling and behavior therapies. This integrated approach can help individuals with OUD achieve and sustain recovery. There are three FDA-approved drugs for opioid dependence: buprenorphine, methadone, and naltrexone. All three FDA-approved therapies have been demonstrated as safe and effective in combination with other supports. Due to the chronic nature of OUD, there is no maximum duration of maintenance treatment, and some patients may continue MAT indefinitely.

¹ The Federal Register Notice for the Patient-Focused Drug Development Initiative can be found here: <https://www.gpo.gov/fdsys/pkg/FR-2015-07-02/pdf/2015-16359.pdf>.

² Results from the 2016 National Survey on Drug Use and Health conducted by Substance Abuse and Mental Health Services Administration (SAMHSA) can be found here: <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>.

Meeting overview

This meeting provided FDA with the opportunity to hear directly from individuals, caregivers, and other stakeholders about their experiences and perspectives with OUD. The discussion focused on two key topics: (1) health effects and daily impacts of OUD, and (2) individuals' and families' perspectives on current approaches to treating OUD. The questions for the meeting discussion (Appendix 1) were published in a [Federal Register notice](#) that announced the meeting.

For each topic, a panel of individuals (Appendix 2) shared comments to begin the dialogue. Panel comments were followed by large-group facilitated discussions inviting comments from other individuals and caregivers in the audience. An FDA facilitator led the discussion, and a panel of FDA staff (Appendix 2) asked follow-up questions. Participants who joined the meeting via the live webcast (referred to in this report as web participants) also contributed comments. In addition, in-person and web participants were periodically invited to respond to polling questions (Appendix 3), which provided a sense of the demographic makeup of participants and how many participants shared a particular perspective on a given topic.

Approximately 100 individuals with OUD or caregivers of individuals with OUD attended the meeting in-person. Approximately 85 individuals with OUD or caregivers provided input through the live webcast. Meeting participants (in-person and webcast) varied in gender, race, age, history of opioid use, experiences with OUD, and time in recovery. Participants also varied in their overarching perspectives on substance use and treatment. Although participants at this meeting may not fully represent the overall population of individuals with OUD, the input received reflects a range of experiences with and perspectives on OUD and OUD management approaches.

To supplement the input gathered at the meeting, individuals with OUD and others were encouraged to submit comments on the topic to a public docket,³ which was open until June 18, 2018. Seventy-two comments were submitted to the public docket, the majority by individuals with OUD or caregivers of individuals with OUD, and patient advocacy organizations.

More information, including the archived webcast and meeting transcript, is available on the meeting website: <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm591290.htm>.

Report overview and key themes

This report summarizes the input shared by individuals with OUD, caregivers, and other stakeholders during the meeting or through the webcast. It also includes a summary of comments submitted to the public docket. To the extent possible, the terms used in this report to describe specific health effects, impacts, treatment experiences, and perspectives reflect the words used by in-person participants, web participants, or docket commenters. The report is not meant to be representative in any way of the views and experiences of any specific group of individuals or entities. There may be health effects, impacts, treatments, or other aspects of OUD not included in this report.

The input from the meeting and docket comments underscore the diversity in experiences with OUD, the complexity of selecting an appropriate treatment, and the broader challenges individuals with OUD face in accessing care and support. Several key themes emerged from this meeting:

³ A *docket* is a repository through which the public can submit electronic and written comments on specific topics to U.S. federal agencies such as FDA. More information can be found at www.regulations.gov.

- OUD is a chronic, neurobiological disease with devastating impacts. Participants reiterated both the acute and chronic health effects of OUD, which sometimes last decades into their recovery. Participants described “being a prisoner” to opioid withdrawals often accompanied by nausea, vomiting, and uncontrollable muscle spasms. Participants also offered insight on opioid “cravings,” or desire to use. They highlighted the relationship between craving and anxiety and stressed that cravings are more than a physical liking for a substance. Cravings were described as “the act of doing it, preparing it, consuming it, the immediate relief afterwards.” Participants also stressed that cravings may last well beyond acute withdrawal and can be triggered unpredictably. Other long-term effects included scarring due to IV drug use, insomnia, anxiety, and fear.
- OUD affects all aspects of individuals’ lives. Participants described significant impact on their work and ability to care for themselves and family. Many participants described the devastating loss of meaningful relationships with family and friends due to their OUD. Some participants commented that mending relationships with family and friends was often a key motivator for their journey to recovery. Participants also expressed their worries of relapse in the future.
- Participants emphasized that effective management of OUD requires a holistic approach tailored to the needs of the individual. They expressed varying perspectives on the desired outcomes of treatment, ranging from complete abstinence from opioid use to better managing or controlling use of opioids. The shared focus, however, was to improve their functioning, well-being, and safety. Participants also expressed mixed views on the role of MAT in their journey. Some participants said that they accept the need to stay on MAT for the long term. Some, however, hope to “detox off MAT” once they have stabilized in recovery. And some participants said they do not see a role for the currently available MAT in their recovery.
- Participants identified several challenges and barriers to accessing and sustaining MAT. They highlighted the impact of stigma on their interactions with healthcare providers and others, particularly when being perceived as “an addict” or when being labeled as “dirty” or “clean.” Participants also highlighted challenges in access to MAT, including long wait times, difficulty finding facilities that provide MAT, strict requirements for entry into MAT programs, medication cost, and concerns about safety at the facility. They described the added challenges to maintaining recovery due to the intensity of withdrawal and craving, the significant pain or mental health needs, and their own difficulty in coming to terms with their illness.
- More broadly, participants stressed the need for greater awareness of OUD and understanding of their needs as a community. Participants offered insights on how to better help individuals with OUD manage their condition, including working toward development of non-opioid treatment options, integrating MAT into primary care, and implementing holistic approaches that integrate mental health, social support, and medical treatment. Most importantly, participants stressed the need to reduce the stigma of OUD, help individuals create “situations of stability”, and to not lose sight of their underlying pain, trauma, or mental health needs.

The patient input generated through this PFDD meeting and the public docket comments strengthens FDA’s understanding of the impact of OUD on individuals and the treatments currently used to manage OUD. FDA staff will carefully consider this input during the drug development process, including when advising sponsors on their drug development programs and when assessing products under review for

marketing approval. This input may also be of value to the drug development process more broadly. For example, it may be useful to drug developers as they explore treatments more specific to symptoms of OUD, or in designing interventions that can facilitate enhanced management of OUD.

Topic 1: Health Effects and Daily Impacts That Matter Most to Patients

The first topic discussion focused on gathering perspectives on the impacts of OUD on individuals' health and daily life. FDA was particularly interested in understanding how participants describe the health effects of OUD in their own words. FDA was also interested in learning how OUD affects individuals' ability to perform daily activities normally and as fully as they would like to.

Four panelists provided comments to start the dialogue. They included:

- A 36-year-old man who developed OUD 11 years ago following a back injury. He highlighted the emotional impacts of OUD which led to feelings of depression, low self-esteem, compulsive behavior, and an attempted suicide.
- A 52-year-old woman who shared her journey of struggling with OUD for nearly 30 years and her experiences with frequent hospitalizations and severe infections leading to sepsis due to intravenous opioid use.
- A 30-year-old woman with OUD also shared her experience as a caregiver of an individual with chronic pain. She highlighted the challenges of maintaining recovery as a caregiver with access to opioids, as well as the impacts of witnessing inadequate pain management of a loved one.
- A 58-year-old woman with chronic pain managing OUD who highlighted her difficulties with stigma, cognitive issues, and inadequate pain management. In addition, she also shared the challenge of coping with the death of her daughter from an opioid overdose.

The panelists' opening comments provided a range of perspectives on daily impacts of OUD. Their stories provided rich insight into the physical, social, and psychological impacts of OUD. During the large-group facilitated discussion that followed the panel discussion, nearly all individuals and caregivers indicated by a show of hands that their experiences (or those of their loved ones) were reflected in the panelists' comments. The remainder of this section summarizes in more depth the input from in-person and web participants on the topics related to the health effects and impacts of OUD.

Perspectives on health effects of OUD

To set context, participants described their paths to developing OUD. Participants' experiences ranged from individuals who struggled with other substance use disorders in their adolescence and eventually became addicted to heroin, to individuals who developed OUD following use of prescription opioids for acute injury or chronic pain, to individuals who began experimenting with recreational use of opioids within the past 10 years. These varying histories highlight the complexity of opioid use, misuse, addiction, and recovery. They also provide insight on how experiences and perspectives of OUD and its management may be shaped by individuals' personal situations.

In a polling question (Appendix 3, Q8), participants were asked to identify the most burdensome health effects of their OUD. In response, participants described several serious and chronic effects on their overall health. Participants attributed these health effects to numerous underlying aspects: opioid withdrawal, opioid “cravings,” side effects of opioid use, and underlying health conditions.

Throughout the discussion, participants illustrated the overlap between opioid withdrawal, cravings, and anxiety. Participants noted this overlap as causing difficulty in determining the root cause of the health effects they experience. For example, some meeting participants described experiencing anxiety due to opioid withdrawal, whereas others associated anxiety with opioid cravings, underlying mental health conditions, or trauma. Throughout the large-group facilitated discussion, meeting participants shared the severity of the impacts of their condition in various areas of their lives. The summary below attempts to highlight these complexities, using the participants’ own words.

Effects of opioid withdrawal

Impacts of opioid withdrawal were raised by meeting participants as one of the most significant and bothersome symptoms of their condition. They described withdrawal as consisting of multiple symptoms such as nausea, diarrhea, and vomiting in addition to a myriad of intense physical manifestations, including uncontrollable movements. Meeting participants referred to the symptoms of opioid withdrawal as feeling “drug sick.” Throughout the large-group discussion participants highlighted avoiding the feeling of being “drug sick” during opioid withdrawals often hindered their recovery. One participant shared, “Always the withdrawals drove me back to opioids.” Another participant described the “unsurmountable” challenges of opioid withdrawal stating, “Opioid use sort of drove my daily activities as I would be drug sick if I didn’t [obtain opioids].” During meeting discussion individuals described opioid withdrawal in vivid detail in the statements below:

- “The feeling of these bugs like crawling underneath my skin and chewing their way through my body.”
- “Skin crawls where you can’t lay still...your body just jerks. You feel like a cat on a hot tin roof.”

In-person and web participants also highlighted the intense emotional impacts of opioid withdrawal. Participants shared that withdrawal also led to anxiety, depression, low self-esteem, and, at times, suicidal ideation. One participant highlighted this concept, stating, “[Without opioids] I seemed just completely useless and worthless, weak, and pathetic.” Meeting participants also noted that due to their past dependence on opioids, OUD affects how they experience anxiety. One participant highlighted this concept, stating, “For the addict mind [anxiety] is resemblance of withdrawal symptoms. My mind will tell my body that I need drugs to manage the anxiety.”

Throughout the discussion, meeting participants highlighted the feeling of experiencing opioid withdrawals due to illicit opioid use as well as use of FDA-approved treatments for MAT, which is described in further detail in the Topic 2 discussion.

Effects of opioid “cravings”

Throughout the meeting, individuals and families described numerous challenges they experience due to opioid “cravings.” Many meeting participants described their experience of opioid cravings as a lasting effect of OUD, which many still experience years into their recovery journey. One participant

highlighted this, stating, “Over 20 years [in recovery] have problems with various kinds of cravings.” A parent at the meeting described needing to “wrap our mind” around this invisible facet of the illness.

FDA was particularly interested in hearing how individuals with OUD described the experience of “cravings” and if this term accurately portrays their experience. Meeting participants indicated, by show of hands, that the term cravings captured their experience. In-person and web participants also described the cravings using other terms such as “urges,” “obsession,” and “feening.” Similar to the discussion of withdrawal, participants noted how cravings can also lead to anxiety due to the fear of being “drug sick.” One participant stated, “Being scared you’re not going to get it [opioids] brings the anxiety in because you don’t want to be sick.”

Participants also noted throughout the large-group discussion that cravings are not limited to opioid use but also include the process and actions which led up to their development of OUD. One participant highlighted, “It’s not just the substance craving itself. It’s the act of doing it, preparing it, consuming it, the immediate relief after.” Another participant in OUD recovery for ten years shared experiencing physical cravings when using ATM machines due to frequenting ATMs during her past opioid use. She stressed the impact of this experience years later, noting, “When I put my credit card in an ATM. I would still feel physical sickness about that longing and that craving.” Participants also shared how their cravings may be triggered by various experiences, such as seeing products they were formerly addicted to or vivid descriptions of opioid use discussed in recovery meetings. A participant shared, “The more stressful a situation is, the more physically painful a situation is, the worst that craving feeling.”

Participants also noted the fear of experiencing cravings due to current or upcoming medical procedures which may require opioids. Participants highlighted this in the statements below:

- “During recent rotator cuff surgery, I had to stay on opioids . . . [I was] just counting the footsteps of the person managing the medicine.”
- “When I was getting ready to have my first child. My concern was how am I going to handle being in pain because it’s going to cause cravings.”

Throughout the discussion, meeting participants highlighted the feeling of experiencing opioid cravings due to illicit opioid use as well as use of FDA-approved treatments for MAT, which is described in further detail in the Topic 2 discussion.

Other Effects

In addition to opioid withdrawal and craving, participants highlighted other health effects that have a significant impact on their daily lives. Throughout the meeting, participants expressed difficulty in delineating if health effects they experience were specific to opioid use, side effects of medical treatments, or underlying health conditions.

- Several participants noted issues with **falling asleep and staying asleep**. Several meeting participants highlighted that, even in recovery, they do not actually obtain typical amounts of sleep. One participant in long-term recovery for twelve years shared, “On average I sleep about 4 to 5 hours a night.” Another participant shared, “I take 15, 20-minute naps.” In particular, a few meeting participants highlighted an overlap between anxiety and sleep issues. One participant shared, “I used to be anxious. That would keep me awake.”

- Many meeting participants described **compulsive behaviors**, often illicit, due to OUD. For example, one participant described becoming “the return lady for stolen goods at stores.” Other participants shared instances of compulsive overspending leading to significant debt. Participants highlighted several reasons for their behaviors including avoidance of opioid withdrawal, intensity of opioid cravings, and underlying emotional issues. Many described their experiences with these behaviors as a catalyst for seeking medical treatment for OUD.
- Many participants shared experiencing underlying **acute or chronic pain** which led to their initial exposure to opioids and caused difficulties in their recovery. One participant described beginning high-dose opioids due to a back injury. Another participant described the difficulties in pain management during recovery, stating, “I need to get off the opioids . . . but [I’m] not given any alternative.” Another participant, also a caregiver for a chronic pain patient, expressed similar concerns.

Other health effects identified include **cognitive issues and medical complications** due to OUD. Participants noted that cognitive issues were often experienced during periods of active opioid use. One participant attributed opioid use with “taking away my stamina, making my speech slow, making everything foggy.” Participants also shared the effects of OUD on their overall health. One participant shared experiencing sepsis, several abscesses, and severe infections requiring hospitalization due to intravenous drug use. Another participant shared experiencing visible scarring on her arms due to intravenous drug use.

Overall Impacts on Daily Life

Participants throughout the meeting, both in-person and webcast, described in rich detail the impact that OUD has on daily life, including:

- **Stigma.** Most participants shared experiencing stigma due to OUD. Participants vividly described labels and terms often used to describe their condition, such as “addict” or “junkie,” which impact their self-esteem. Participants particularly highlighted the use of the terms “clean” and “dirty” to refer to their current recovery status. One participant stressed, “None of us are dirty. We don’t have to say clean.” Another participant described the challenge of “hearing things like I’m an addict and an abuser and the disrespect that goes with it.” A few participants also attributed illicit behaviors often associated with OUD as a trigger for some of the stigma experienced by individuals with OUD. One participant highlighted this stating stigma is “never going to end without the criminal justice component removed.” A few participants also discussed the impact of stigma when securing housing or pursuing career opportunities due to criminal convictions on their record.
- **Emotional Impacts.** Several participants discussed emotional impacts of OUD. Throughout the large-group discussion, participants highlighted three categories for the emotional issues they experience: those unmanaged prior to OUD, those which developed during OUD, and those which became apparent during recovery. Participants described the impact of traumatic experiences, including, but not limited to, anxiety, depression, and abuse, which may have led to their OUD. One participant shared experiencing social anxiety as a child which led to heroin use, stating, “I didn’t like being withdrawn. Heroin took care of that.” Another participant shared being diagnosed with depression, anxiety, and an eating disorder, which “manifested into

opioids for me.” Another participant described developing “a very, very, severe depression along with OUD” leading to an attempted suicide through intentional overdose. Participants also described emotional impacts due to physical scars from past drug use. One participant shared instances of not leaving her home even in the summer without long sleeves to hide scars from drug use. Participants stressed recovery as critical in addressing other emotional issues.

- **Impact on relationships.** Many participants addressed how OUD impacted their interactions with family and friends. Participants described being unable to maintain relationships. One participant characterized this, stating, “Most of my family members turned their backs on me.” Another participant highlighted how the side effects of opioids affected her marriage, noting, “My husband has to sleep in another room so at least one of us can get some rest.” Throughout this discussion, participants stressed how pursuing recovery has allowed them to restore relationships with family and friends. One participant shared that their efforts in recovery also translate to establishing relationships on a broader level, stating, “Where you find recovering people, you find recovering families, you find recovering communities.” Throughout the discussion, many meeting participants credited MAT with “giving their life back” in regard to maintaining and restoring meaningful relationships.
- **Impact on work, school, and careers.** Many participants discussed experiencing hardships at work due to OUD. Some participants attributed their difficulties at work or school to experiencing intense opioid withdrawal symptoms. Others attributed their difficulties to opioid use. One participant highlighted this, stating, “I can’t perform the functions of my job because I am unable to get [through] a lengthy meeting or make presentation [due to the withdrawal].” Another participant shared missing work for days and being “almost fired many times.” One participant described becoming “restricted to the living room essentially and becom[ing] a slave to my OUD.”
- **Worry about the future.** Many meeting participants also stressed the concern of relapse as a source of worry throughout their recovery. One participant shared that he relapsed following the death of his father due to lack of support, stating, “I had no support structure around me [following his death].” Another participant shared her fears of relapse while being a caregiver for a loved one with chronic pain. She stated, “What happens when I’m not strong enough to not go to the lockbox [where the opioids are] . . . and decide to use again.” Another participant highlighted fear of another relapse, stating, “second relapse has a much higher chance of me dying.” However, a few participants expressed less concern for relapse, because of their commitment to recovery. For example, one participant stated, “I am not at risk for relapse, that is not even a possibility.”

During the large-group facilitated discussion, FDA expressed interest in how individuals with OUD perceive their ability to take care of themselves (Appendix 3, Question 10). Although some individuals stated they felt that caring for themselves was important but not top of mind, other participants expressed that other impacts were more important and exceeded their need to care for themselves. One participant noted this, stating, “Maybe it’s a part of the OUD that, my brain disease doesn’t even make me think, I need to take care of myself.”

Topic 2: Patient Perspectives on Treatment for Opioid Use Disorder

The second topic discussion gathered perspectives from individuals with OUD on their experiences with approaches to management. Five panelists (Appendix 2) provided comments to start the dialogue. The panelists shared their experiences, not only in the treatments they used, but also the factors they considered when making decisions about their recovery. Panelists included:

- A 50-year-old man who described his complex recovery journey, transitioning from a harm reduction program to methadone and later buprenorphine, and the challenges he faced obtaining medication management and medical care for OUD.
- A 42-year-old man who shared his experiences of switching from levomethadyl acetate (LAAM)⁴ to methadone over his eighteen-year recovery journey.
- A 53-year-old woman who shared her experience of transitioning from naltrexone to more communal and family support networks to maintain her 30-year recovery journey without MAT.
- A 58-year-old woman who shared her experience with non-drug interventions to manage her OUD following unsuccessful attempts with MAT during her 20-year recovery journey.
- A man who shared his experience of tapering himself from Suboxone and the value of a support system and stability in maintaining his recovery over the past three years.

In the large-group facilitated discussion that followed, individuals with OUD, caregivers, and families discussed their experiences with prescription drugs, non-drug therapies and medical devices utilized during their recovery. Overall, many participants expressed that the journey to recovery is multifaceted and personal. Participants described a variety of approaches as part of their recovery which included family and peer support, counseling or behavioral therapy, online support groups, in addition to medication. Participants highlighted throughout discussion that their approach to recovery was often framed by their treatment goals, which in some cases changed over time. Several participants stressed that their comments represent the treatment and management approaches which worked best for them personally and may not be applicable to all individuals with OUD. Throughout the meeting discussion, participants indicated by show of hands that their experiences (or those of loved ones) were reflected in the panelists' comments. Participants emphasized the need for improved access to medical treatment as well as counseling and behavioral support services for their condition.

Perspectives on current treatments

Participants described a range of treatment approaches to manage their OUD. Participants detailed a complex process of finding a suitable approach to recover from OUD. Participants provided diverse perspectives on a range of treatment goals for OUD management, which included complete abstinence from opioids and/or MAT, reduced opioid use on a temporary or casual basis, as well as addressing underlying causes of their OUD through additional social support and mental health services.. Overall,

⁴ Levomethadyl Acetate Hydrochloride [LAAM] is a synthetic opioid structurally related to methadone, but with a longer duration of action. LAAM is not currently marketed in the United States.

meeting participants stressed that staying on MAT long-term was a preferable alternative than returning to unmanaged OUD.

Meeting participants expressed mixed viewpoints on abstinence from opioids as a reasonable goal for OUD management. One participant noted, “Why are we only looking at abstinence? . . . there’s a lot of the room in the middle.” Throughout the large-group discussion, some meeting participants questioned whether abstinence from opioids is a feasible as a goal of OUD management. One participant likened OUD to management of anxiety, sharing, “[If a doctor said] you will never be anxious again [following treatment] you would say, ‘You’re crazy.’ But that’s what we do with drug treatment.”

Participants’ perspectives on the benefits and downsides of their therapies, as well as what they would look for in an ideal treatment, are summarized below.

Medication Assisted Treatment: Benefits of MAT

Participants described in detail their experiences with MAT, including opioid agonists (such as methadone), opioid antagonists (such as naltrexone), opioid partial agonists (such as buprenorphine, buprenorphine/naloxone). Many began their discussion by explaining the complex series of events leading to their introduction to MAT. For example:

- “I figured, you know let’s give [LAAM] a shot, I tried detox, I tried rehabs, I tried 12 step programs, I could never get clean for longer than may be a couple weeks.”
- “I went to at least 10 different detoxes. I would do 90 days programs, 90 meetings in 90 days then relapse. Then finally a doctor said to me... go on to a methadone treatment.
- “[After going to jail] I was put into a pretrial intervention program. I elected to do Suboxone treatment because it was one of the [program] conditions.”
- “I was watching the car of that transaction [involving a woman I did drugs with]. I didn’t know how long it was going to be until I decided [illicit behavior] was something I was willing to do [for heroin]. I went into treatment.”

In describing their experiences with MAT, many focused on the benefits of treatment. Several attributed MAT with getting their “life back.” Participants commented on MAT reducing their desire to use opioids illicitly and enhancing their ability to withstand withdrawal and cravings. For example:

- “[After starting methadone] I didn’t feel it anymore. I bought the heroin and I injected, I just had no euphoric rush whatsoever.”
- “The treatment[naltrexone] worked well for me . . . I did not return to active addiction and I also experienced no cravings.”
- “I was able to get my life in order [with methadone]. . . able to arrest the cravings and the compulsiveness around the disease and the chasing, you know, the insanity of it.”

Participants also shared experiences of establishing meaningful relationships following MAT. One participant highlighted this, stating, “[I] had my family back, meaningful relationships and it was just incredible.” Others also shared being able to fulfill work and school obligations after beginning MAT.

Medication Assisted Treatment: Goals for OUD Management

Throughout the meeting, participants provided a diverse range of treatment goals for OUD. Participants highlighted their approach to MAT was often based on their treatment goals throughout recovery. One participant highlighted this, stating, “Recovery is not static. What I needed in the beginning didn’t necessarily look like what I needed further down the road.”

Some participants described exploring temporary self-medication or casual use of MAT in lieu of formal treatment. Participants described the goal for casual use was to “manage” or “control” their use of opioids temporarily. One participant explained, “[In the beginning] I was wishing that it was a methadone program where you could just go on a weekend. Like you say you just want to get to a certain stage [of opioid use].” Another participant shared attempting to control use on special occasions: “You need to appear normal. I could do [Suboxone] for a short period of time and then taper myself back on whatever I was using.” A few participants also shared early experiences of using opioids or other prescriptions when initially beginning medication assisted treatment. One participant shared using clonidine to “get high” while using methadone.

Some meeting participants described “tapering” from MAT at some point in their recovery. One participant shared their transition from five years of managing OUD with Suboxone to currently no longer using MAT to maintain recovery. Another participant shared her journey of using naltrexone for seven years before eventually tapering away from MAT. One web participant described tapering methadone during pregnancy, sharing that “her dose constantly changes” throughout her pregnancy.

Other meeting participants, however, described unsuccessful attempts of tapering from MAT due to the presence of withdrawal or craving symptoms. One participant shared, “I tried to taper off methadone before. I was always unsuccessful. The withdrawal symptoms were extremely high and my tolerance was very low.” Another participant shared, “When I would try to get off the methadone I relapse sometimes. I would find myself out there [using drugs], back in jail.”

FDA was also interested in participants’ perspectives on the perception that MAT is a “replacement” for previous opioid use. One participant explained this perception of MAT as “somewhat like exchanging one opioid addiction for another.” Overall participants expressed various perspectives on this topic but stressed the use of MAT as a favorable alternative to untreated OUD.

Treatment downsides of MAT

Participants highlighted several challenges to sustaining MAT use, as described below:

- Several participants described experiencing **bothersome side effects** with MAT, particularly methadone. Participants described experiences with profuse sweating, sexual dysfunction, weight gain, and constipation. Participants particularly highlighted sweating as problematic: “On methadone you sweat a lot and it can come out [of] nowhere.” Another participant highlighted sweating as her reason to discontinue methadone, stating, “Not really dainty or feminine to be sweating profusely. Your clothes have these big stains.” Participants also

highlighted using other medications to deal with long-term side effects of MAT. A few participants stated that the side effects of MAT factored into their decision to switch to another MAT option. One web participant highlighted that switching between MAT products led to more manageable side effects.

- Several meeting participants identified **barriers to care** impacting their ability to manage OUD, which included cost of medication and overall access to treatment. One participant stressed that “people don’t go to methadone or Suboxone, because we decide to put so many barriers in their way to make it so hard to engage those systems.” Specific challenges mentioned included long-wait times, strict payment types for services, and the requirement of a positive opioid lab result to begin the program. For example, one participant shared that he “had to go out and score heroin [and experience overdose] to get into a methadone program.” Another participant shared issues in obtaining naltrexone due to cost (“\$1000 per month”) and consistent low stock of MAT at her local pharmacy.
- Many meeting participants also highlighted the challenge due to **locations of their MAT programs**. A participant who discontinued methadone shared, “It [the MAT clinic] was in a part of town where you could cop other drugs. It was not a great recovery path for me.” Another participant shared his experience of going to a methadone clinic located at a police station, sharing, “My neighbors would say, ‘Why are you at the police station every morning?’” One participant also shared fearing for his safety, stating, “My most scary moment on methadone was going into the clinics to pick up my take-homes that someone might jump me.”

Other therapies for OUD

Meeting participants, in-person and via webcast, emphasized the importance of other therapies beyond MAT in the management of OUD. Meeting participants stressed “no one size of treatment fits all.” Meeting participants described recovery as a process that encompassed a combination of several therapies which may include individual counseling or behavioral therapy, family support, and peer support in addition to or without drug therapy. One meeting participant described this as a “culture of recovery.” Specific therapies discussed are described in further detail below.

- Several meeting participants described their experiences utilizing different **types of health services** to manage OUD. Types of health services mentioned by meeting participants include individual and group counseling services, detox and residential treatment programs, weekly recovery meetings, and other recovery focused programs such as 12-step programs. Several participants shared the impact of therapy and counseling in addressing the mental health issues associated with their recovery. One participant highlighted this stating, “I had needed mental health to help me realize and to come out of denial about being on drugs.”
- Many meeting participants stressed **support from peers, family, friends, faith** as critical to their recovery. Meeting participants described their support networks including community organizations, accountability partners, family, and friends. Participants stressed the value in interacting with others in recovery as important to staying committed to managing OUD. One participant highlighted that, “Meeting other people in recovery and them helping me. That really made my recovery strong.”

- Many meeting participants also shared experiences using **other prescription drugs** to manage their OUD. Participants again highlighted incorporating medications as part of a multifaceted approach. One participant shared using antidepressants as part of a holistic approach to recovery, which also included meditation, yoga, and exercise. Another participant shared her experiences of using Trazodone and Seroquel to manage sleep issues.
- A few participants also shared experiences using **medical devices and mobile applications** to assist in their recovery. Participants shared various reasons for incorporating apps into their recovery, which included managing anxiety, managing stressful situations, regulating sleep, and monitoring variability in heart rate. One participant also shared their experience with using a cranial electrotherapy stimulation device to assist with pain control.
- A few participants identified **other substances**, such as kratom and ibogaine, that they considered to support their management of OUD.

Perspectives on improving the management of OUD

Participants provided a range of perspectives on areas which could be improved to assist management of OUD. Meeting participants stressed that enhanced management of OUD begins by improving the medical community's understanding of OUD and increased awareness of their condition.

Participants stressed that OUD is a chronic condition. Throughout the meeting, participants described differences in management of OUD compared to other chronic conditions, which they attributed to stigma. One participant highlighted this sharing his personal experience of treating his OUD as he would diabetes and recognizing the importance of understanding his condition. Participants also highlighted use of terms that reinforce stigma such as "clean" vs "dirty" to refer to recovery status and instances of being perceived as an "addict" which altered the care they received during recovery.

In discussion of an ideal treatment, participants stressed the desire for non-opioid treatment options and the need for continued research. Participants also expressed a desire to broaden MAT to include other products that are not currently FDA-approved. In response an FDA panel member highlighted the agency's desire "to understand how a medication could be evaluated for effectiveness [in OUD] that might be completely different from anything we already have available." Participants stressed the need for easier access to currently available treatments and less regulations surrounding access to MAT.

Meeting participants also stressed the importance of ensuring the availability of support networks to meet the changing needs of individuals with OUD. Participants noted that recovery is not one-size-fits-all and the need for OUD management tailored to individual treatment goals. Participants highlighted that treatment goals change and a "situation of stability" is needed to prevent relapse and continue recovery. Several participants highlighted managing chronic pain, emotional issues, personal traumas, stigma, and restoring meaningful relationships as key areas of their recovery which are challenging to address holistically without changes in overall approaches to management of OUD.

Summary of Comments Submitted to the Public Docket

Seventy-two comments were submitted to the public docket that supplemented the Patient-Focused Drug Development Meeting on Opioid Use Disorder. The docket comments reiterated the significant and burdensome health effects of OUD on every aspect of individuals' lives. Most comments were submitted by individuals with OUD or their caregivers, individuals with chronic pain, healthcare providers, professional organizations, and academic researchers.

Overall, the comments received reflected the experiences or perspectives shared during the public meeting. The following highlights of these comments focus mainly on experiences or perspectives that were not raised or addressed in detail at the meeting.

Submitted comments on the health effects of OUD

The docket comments reiterated the health effects of OUD on the lives of individuals and their caregivers. The health effects described were generally consistent with those discussed at the meeting and included opioid withdrawal, opioid cravings, and other health effects. Symptoms of opioid withdrawal mentioned by docket commenters included chills, painful cramping, nausea, vomiting, and uncontrollable movements. Commenters also mentioned opioid cravings. For example, one commenter described "an intense mental desire to secure the drug at all cost." A caregiver described opioid cravings as "very disruptive in daily life and creat[ing] strong pressures to relapse." Similar to in-person and web meeting participants, commenters also shared experiences of opioid cravings and withdrawals.

Docket commenters also briefly mentioned other health effects due to OUD, such as sleep issues, which included irregular sleep patterns and inability to fall asleep, issues managing chronic and acute pain, and other health complications due to past opioid use. Docket commenters particularly highlighted challenges with compulsive behaviors due to OUD. One commenter described being "in and out of jail." Another commenter shared, "I was a woman living in a tent behind a hotel, selling my body for heroin."

Submitted comments on the overall impacts of OUD

The docket comments reflected the input received related to the debilitating impact of OUD on individuals' daily lives and families. Docket reiterated many of the impacts of OUD including stigma, emotional impacts, relationships, impact on work and careers and worry about the future.

Similar to in-person participants, docket commenters highlighted the impact of experiencing stigma. One commenter stressed the need to "remove stigma and the discrimination that comes with OUD." Another commenter shared experiencing discrimination in employment due to OUD.

Commenters also shared the impact of OUD on relationships. One commenter described the toll of being a caregiver, sharing, "In constantly bearing the burden of his disease I neglected my own needs, and my mental and emotional health suffered greatly." Another commenter highlighted the emotional impacts of families affected by OUD sharing the experience of "paralyzing pain, fear and hopelessness felt by families when they learn their child is sick and suffering." Another commenter shared, "When a loved one struggles, the entire family struggles."

Several commenters stressed the impact of OUD on their ability to carry out important activities. One parent commented that OUD “totally derailed” the life of her son leading to his eventual withdrawal from college. Other commenters also shared experiences of being “unable to function” due to OUD. An individual with OUD highlighted this, stating, “Even though I knew the real me, the addiction wouldn’t allow me to live a normal productive life.”

A few commenters also shared other impacts of OUD on daily life. A few commenters described intense emotional impacts, such as depression and experiences of suicidal ideation due to OUD. One commenter described the emotional impacts as a “sense of hopelessness and failure.” A few commenters also mentioned worry about the future and possible changes that may restrict treatment for acute or chronic pain as well as OUD. One commenter currently using MAT shared, “I get very afraid . . . helpful treatments will be limited or revoked.”

Submitted comments on management of OUD

The submitted comments reflected the challenges of managing OUD. Docket commenters highlighted the journey to recovery as highly personal and very dependent on the level of support and multi-faceted care individuals with OUD receive. Commenters reiterated that “no single treatment is right for everyone.” Docket commenters also stressed the need for counseling and mental health support to manage their OUD. One commenter attributed recovery success with meeting with her counselor every morning. She shared those meetings allowed her to “get on a regular schedule” and develop “good habits to replace the bad.” Commenters also reiterated the importance of a strong support system of families and peers when managing OUD.

Similar to comments from meeting participants, perspectives varied regarding MAT. Several commenters highlighted numerous barriers to accessing MAT, including cost, insurance, clinic locations, and lack of inclusion of MAT into particular detox and opioid rehabilitation programs. One commenter shared her experience of buying Suboxone “off the street” to manage withdrawal due to lack of availability and experiencing a severe infection requiring over three weeks of hospitalization.

Commenters described varying levels of success with MAT. Similar to the perspectives of meeting participants, many credited MAT with enabling them to live a “normal and exceling life.” Commenters also shared experiences of managing their OUD with other therapies due to unsuccessful experiences or barriers to MAT. Other drugs and therapies mentioned included acupuncture, kratom, and ibogaine.

Suggestions to enhance management of OUD shared by commenters included increased awareness of OUD as a chronic condition, reduction in barriers to care and access to MAT, and broader acceptance of harm reduction approaches.

Conclusion

The perspectives shared by participants at this meeting provided a vivid portrayal of the challenges and burdens facing individuals with OUD. FDA recognizes that individuals with OUD and caregivers have a unique ability to contribute to our understanding of their condition and treatment management. FDA is grateful to all the participants for attending the meeting and sharing their perspectives. This Patient-

Focused Drug Development meeting provided FDA the opportunity to hear from individuals and caregivers first-hand the impact of OUD.

FDA is grateful to the individuals and caregivers who thoughtfully and bravely provided such personal insight into their lives. Through this meeting, FDA learned more about what matters most to individuals and caregivers impacted by OUD. FDA recognizes the importance of supporting those with OUD by using their personal experiences to inform drug development and review considerations. FDA shares the desire and commitment expressed by meeting participants to advancing the development and appropriate use of safe and effective treatment options for managing OUD.

Appendix 1: Meeting Agenda

Public Meeting on Patient-Focused Drug Development for Opioid Use Disorder (OUD)

April 17, 2018

10:00 – 10:05 am	Welcome Sara Eggers, PhD <i>Office of Strategic Programs (OSP), Center for Drug Evaluation and Research (CDER), FDA</i>
10:05 – 10:10 am	Opening Remarks Theresa Mullin, PhD <i>Associate Director for Strategic Initiatives, CDER, FDA</i>
10:10 – 10:20 am	Background on Opioid Use Disorder and Treatment Maryam Afshar, MD <i>Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) Office of New Drugs (OND), CDER, FDA</i>
10:20 – 10:25 am	The Road from PFDD Meetings to Clinical Trial Endpoints Elektra Papadopoulou, MD, MPH <i>Associate Director, Clinical Outcomes Assessments Staff, OND, CDER, FDA</i>
10:25 – 10:35 am	Overview of Discussion Format Sara Eggers, PhD <i>OSP, CDER, FDA</i>
10:35 – 11:05 am	Panel #1 Discussion on Topic 1: Health Effects and Daily Impacts of OUD A panel of individuals and families will provide comments to start the discussion on significant health effects and daily impacts of opioid use disorder.
11:05 – 12:00 pm	Large-Group Facilitated Discussion on Topic 1 Individuals and families in the audience will be invited to add to the dialogue.
12:00 – 1:00 pm	Lunch
1:00 – 1:05 pm	Afternoon Welcome Sara Eggers, PhD <i>OSP, CDER, FDA</i>
1:05 – 1:35 pm	Panel #2 Discussion on Topic 2: Current Approaches to Treatment of OUD A panel of individuals and families will provide comments to start the discussion on current approaches to treating opioid use disorder.
1:35 – 2:20 pm	Large-Group Facilitated Discussion: Topic 2 Individuals and families in the audience will be invited to add to the dialogue.
2:20 – 2:35 pm	Break
2:35 – 3:15 pm	Large-Group Facilitated Discussion: Topic 2 Continued
3:15 – 3:45 pm	Open Public Comment
3:45 – 4:00 pm	Closing Remarks Mitra Ahadpour, MD, DABAM <i>Deputy Director, Office of Translational Sciences (OTS) CDER, FDA</i>

Discussion Questions

Topic 1: Health effects and daily impacts of Opioid Use Disorder (OUD)

1. Of all the ways that OUD negatively affects your health and well-being, which effects have the most significant impact on your daily life? Examples of negative effects may include:

- Effects of using opioids, such as confusion, constipation, or other symptoms;
- Effects of opioid withdrawal, such as nausea, diarrhea, or other symptoms;
- Effects of opioid “cravings;”
- Impacts on ability to function in personal or professional life;
- Emotional or social effects; and
- Other potential effects.

2. How does OUD affect daily life on your best days? On your worst days?

3. How has your OUD changed over time?

4. What worries you most about your condition?

Topic 2: Current approaches to treatment of Opioid Use Disorder (OUD)

1. Are you currently using, or have you used in the past, any prescription medical treatments to treat your OUD? Such treatments may include buprenorphine, methadone, naltrexone, and others that your health care provider has prescribed. If so, please describe your experiences with these treatments.

- How well have these treatments worked for you? How well have they helped address the effects of OUD that are most bothersome to you?
- What are the biggest problems you have faced in using these treatments? Examples may include bothersome side effects, challenges getting the medicines, concern about stigma, and other possible problems.

2. Besides prescription medical treatments, are there other treatments or therapies that you currently use to address your OUD? If so, please describe. How well do these treatments or therapies help address the effects of OUD that are most bothersome to you?

3. Of all treatments, therapies, or other steps that you have taken to address your OUD, what have you found to be most effective in helping you manage your OUD?

4. What are the biggest factors that you take into account when making decisions about seeking out or using treatments for OUD?

5. What specific things would you look for in an ideal treatment for OUD?

6. If you had the opportunity to consider participating in a clinical trial studying experimental treatments for OUD, what factors would you consider when deciding whether or not to participate?

Appendix 2: Patient and FDA Panel Participants

Patient Panel, Topic 1

- Andrew
- Pamela
- Amanda
- Jody

Patient Panel, Topic 2

- David
- Paul
- Carol
- Jan
- Daniel

FDA Panel

- Sharon Hertz, Division of Anesthesia, Analgesia, and Addiction Products (DAAAP), Center for Drug Evaluation and Research (CDER)
- Celia Winchell, DAAAP, CDER
- Maryam Afshar, DAAAP, CDER
- Mitra Ahadpour, Office of Translational Sciences, CDER
- Elektra Papadopoulos, Clinical Outcomes and Assessment Staff (COA), CDER
- Michelle Tarver, Office of the Center Director, Center for Devices and Radiological Health (CDRH), FDA
- Theresa Mullin, Office of Strategic Programs, CDER

Appendix 3: Meeting Polling Questions

Patient-Focused Drug Development Meeting on Opioid Use Disorder (OUD)

Demographic Questions

1. Where do you live?
 - a. Within Washington, D.C. metropolitan area (including the Virginia and Maryland suburbs)
 - b. Outside of the Washington, D.C. metropolitan area

2. Which statement best describes you?
 - a. An individual who currently struggles with OR has struggled in the past with opioid addiction or abuse
 - b. A family member or caregiver of an individual(s) who currently struggles with or has struggled in the past with opioid addiction or abuse
 - c. An advocate for individuals who struggle with opioid addiction or abuse.

We will ask that the remainder of the questions be answered individuals with opioid use disorder or a family member or caregiver on behalf of an individual with opioid use disorder.

3. What is your/your loved one's age?
 - a. Younger than 18 years old
 - b. 18 – 29 years old
 - c. 30 – 39 years old
 - d. 40 – 49 years old
 - e. 50 – 59 years old
 - f. 60 years old or older

4. Do you/your loved one identify as:
 - a. Female
 - b. Male
 - c. Other

5. How long has it been since you/your loved one first started using opioids, of any kind?
 - a. Less than 5 years ago
 - b. 5-10 years ago
 - c. 11 – 20 years ago
 - d. 21 – 30 years ago

- e. More than 30 years ago
 - f. I'm not sure
6. Have you/your loved one ever been diagnosed by a healthcare professional as having opioid use disorder or addiction?
- a. Yes
 - b. No
7. Have you/your loved one ever had any of the following conditions? **Check all that apply.**
- a. Acute pain for which medical treatment was sought (such as broken bones, dental work, post-surgery)
 - b. Chronic pain (such as neuropathic, cancer, posttraumatic)
 - c. Other substance use disorder (e.g., alcohol, amphetamines, cocaine, hallucinogens)
 - d. Psychiatric or mental health conditions (such as depression, anxiety or mood disorders)
 - e. Other health conditions that I believe are relevant to today's discussion

Questions for Topic 1: Symptoms and Daily Impact of OUD That Matter Most to Patients

8. In general, what are the most bothersome health effects related to your/your loved one's opioid use disorder? **Please choose up to two answers.**
- a. Health effects associated with use of opioids (such as confusion, constipation, sleepiness)
 - b. Symptoms associated with opioid withdrawal (such as nausea, diarrhea)
 - c. Symptoms associated with opioid "cravings"
 - d. Symptoms related to an underlying health condition (such as unmanaged pain)
 - e. Other health effects not mentioned
9. Thinking specifically of reducing use or abstaining from opioids, what have been the most bothersome symptoms? **Please choose up to three answers.**
- a. Fatigue or lack of energy
 - b. Cognitive effects (such as inability to concentrate, or "brain fog")
 - c. Anxiety, irritability, or jitteriness
 - d. Depression, apathy, or boredom
 - e. Insomnia or sleep issues

- f. Nausea, vomiting, or diarrhea
 - g. Flu-like symptoms, such as fever or body aches
 - h. Pain
 - i. Other symptoms not mentioned
10. What do you find to be the most significant impacts of your/your loved one's opioid use disorder on your/your loved one's daily life? **Please choose up to three answers.**
- a. Ability to carry out important activities (such as go to work, school, hobbies)
 - b. Ability to care for myself or family
 - c. Having days when I am barely able to function at all
 - d. Risks to safety of self or others
 - e. Impact on relationships with family and friends
 - f. Stigma or discrimination
 - g. Worry about the future (such as relapse, overdose)
 - h. Emotional impacts (such as self-esteem, self-identify)
 - i. Other impacts not mentioned

Questions for Topic 2: Patients' Perspectives on Current Approaches to Treatment of OUD

11. Have you/your loved one ever used any of the following medicines to manage your/your loved one's opioid use disorder? **Check all that apply.**
- a. Opioid Agonist (such as methadone)
 - b. Opioid Antagonist (such as naltrexone)
 - c. Opioid Partial Agonist (such as buprenorphine, buprenorphine/naloxone)
 - d. Other prescription or over-the-counter medications
 - e. Other drug therapies not mentioned
 - f. I've never used any drug therapies
12. When considering a new treatment for opioid use disorder, which of the following benefits would you consider to be most meaningful? **Please choose two.**
- a. Help me control my use of opioids so that I can better function
 - b. Help me achieve complete abstinence of opioids
 - c. Reduce effects of opioid withdrawal
 - d. Reduce opioid "cravings"
 - e. Reduce how often I have to take the treatment
 - f. Ability to take my medication at home
 - g. Other benefit not mentioned