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Hearing on

"Combatting the Opioid Abuse Epidemic:

Professional and Academic Perspectives."

Statement of

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Introduction

Chairman Murphy and members of the Subcommittee, thank you for the opportunity to provide an academic perspective concerning the medical management of opioid use disorders as it relates to the current epidemic.

My name is Adam Bisaga. I am a Research Psychiatrist at the New York State Psychiatric Institute and a Professor of Psychiatry at Columbia University Medical Center. My research, supported by the National Institute on Drug Abuse, is focused on the development of new medications to treat opioid use disorder. I am also educating clinicians with regards to safe and effective use of medications to treat opioid use disorder. This effort is supported by SAMHSA with a national training program called Provider's Clinical Support System for Medication Assisted Treatment or PCSS-MAT. [1] Finally, I am also a physician, taking care of patients with substance use disorders and co-occurring mental health disorders for the past 20 years.

Addiction as a behavioral disorder

Substance Use Disorder, also known as addiction, is a brain disorder manifested by an abnormal behavior around the use of alcohol or drugs. At its core, it is the loss of control over substance use. When we examine brain function in a person who is addicted, we see unusually low or high activity in the brain centers responsible for pleasure, learning and memory, and motivation to perform and inhibit certain behaviors. As a result of these changes, individuals with Substance Use Disorders have intense responses to certain external stimuli, such as passing by the liquor store, and to internal experiences, such as feelings of sadness or anger. In response, they experience powerful urges to use the given substance, and cannot stop thinking

about it. Their ability to resist these intense urges is limited, even though they well know that using drugs can have catastrophic consequences. These exaggerated responses persist for a long time, even in people who were able to abstain from use, and as a result many individuals repeatedly relapse.

This set of abnormal responses and behaviors is at the center of the pathology associated with addiction. Some individuals with this problem, like those using substances every day, may also have unpleasant withdrawal symptoms when they do not take their daily dose. But the presence of withdrawal symptoms is neither sufficient nor necessary for a diagnosis of a Substance Use Disorder. As such, patients taking pain medicines every day as directed by physicians are not addicted, they still have control over their use, even though they will experience withdrawal if they miss taking the medication. A baby born to a woman treated with an opioid medication, a baby that is exhibiting signs of opioid withdrawal, is not addicted to opioids. Similarly, using psychoactive substances on daily basis is not sufficient for a diagnosis of addiction. Many people will have one or two drinks everyday after work and do not have any of the abnormal responses and behaviors that characterize addiction. They do not have an Alcohol Use Disorder, associated brain pathology, or the associated loss of control.

Our understanding of addiction as a chronic brain disorder is similar to our understanding of many other psychiatric disorders, in which symptoms and behaviors can be linked to abnormal brain function.

Like with many other disorders, vulnerability to addiction differs from person to person. The balance of risk and protective factors determines whether a person can drink everyday or be treated with painkillers on a ongoing basis with no subsequent problems, while another person will develop abnormal brain responses and over time causing the individual to lose control over

their substance use. We estimate that approximately half of the risk to develop these abnormal brain responses to substances is genetically determined. The remainder of the risk is related to life experiences, co-existing medical and psychiatric problems, and to the exposure to addictive substances.

Prior to the development of the current scientific understanding, addiction was seen as either a moral failing or a character weakness, as a criminal behavior, or as purposeful self-indulgence. However, research has now shown us otherwise. We developed strategies to more effectively treat addicted individuals that match the understanding of the nature or cause of the problem. At present, while there is a public recognition of the role of genetic and biological factors in the development of addiction, approximately one-third of Americans continue to view addiction as a sign of simple lack of will power. [2] This view has undermined efforts to implement the most effective and ethical strategies to reduce the impact of addiction on society.

Treatment

Research into mechanisms involved in maintaining addiction has led to multiple effective treatments. Informed by the scientific evidence, the most effective treatment for opioid addiction involves a combination of a medication that targets the brain, and psychosocial interventions (counseling, skills development) aimed at reducing abnormal behaviors. This combination of medicine and therapy has success rates similar to treatments for many other psychiatric and medical disorders such as depression or high blood pressure. However, in stark contrast to treatments for most other disorders, where using evidence-based medication assisted treatments is the standard of care, very few of the patients with opioid addiction receive treatments that have

been proven to be most effective. Instead, patients are treated with an outdated and mostly ineffective approach; a rapid detoxification of the substance followed by a so-called "drug-free" or "abstinence only" approach, a treatment that does not allow for medications to stabilize recovery. This approach is not only ineffective but can also be dangerous as patients face a significantly elevated risk of dying by overdose during the first month of abstinence. Tolerance, a resistance to drug effects after repeated exposure, is the main mechanism that the brain uses to protect itself against toxic effects of drugs. But during early abstinence, the "protective" effect of tolerance is lost and the brain becomes vulnerable to the effects of opioids. This rapid loss of established tolerance is one of the mechanisms contributing to post-detoxification deaths in patients that are not treated with medication.

Medications to treat Opioid Use Disorder

Three medications are currently used in the treatment of opioid use disorder; methadone, buprenorphine, and naltrexone. The FDA approved these medications, considering them safe and effective.

Methadone was approved over 40 years ago and was first widely used, with great success in the 1970s to treat returning veterans addicted to heroin. It works by stimulating opioid receptors in the brain which normalizes function in several key brain systems.[3] Compared to treatment without medication, methadone-treated patients show marked reductions in heroin and other drug use, have lower mortality, fewer medical complications, decreased criminal activity , and have improved social and occupational functioning. [4,5] Patients who respond to methadone report loss of craving for heroin and have no withdrawal symptoms. It is important to note that

when patients remain on the appropriate dose, they most often experience no sedation or euphoria from this medication and are able to live a normal life. However, methadone is a potent medication and if misused it can produce sedation, euphoria, and even death. To minimize these risks, dispensing methadone is highly regulated and occurs only in specialized treatment programs. However, these regulations can restrict access to methadone and there are waitlists to receive it in many areas of the country. Methadone is often misunderstood and stigmatized making access to treatment difficult.

Buprenorphine was approved in 2000 to treat opioid use disorder in primary care office settings by physicians who complete an additional training course. Buprenorphine works similarly to methadone but only causes partial activation of opioid receptors, limiting its risk of overdose. It also strongly binds to receptors blocking effects of heroin. Patients treated with buprenorphine experience similar reduction in drug use and have health benefits as seen with methadone, though methadone is generally more effective at retaining patients in treatment.[6] Patients on buprenorphine continue to benefit from ongoing treatment even though some may continue to use illicit opioids intermittently. Buprenorphine is safer than methadone; therefore less monitoring in needed. Nevertheless, buprenorphine, like methadone, is a controlled substance as it can be abused. Both methadone and buprenorphine stimulate opioid receptors and individuals taking them remain physically dependent. When these medications are stopped abruptly patients experience symptoms of withdrawal and discontinuation effects as is the case with many medications in use today like antidepressants or antihypertensives.

Methadone and buprenorphine are widely used around the world and are on the World Health Organization's list of essential medicines with the recommendation that they should *"... be available at all times in adequate amounts and in appropriate dosage forms, at a price the*

community can afford." [7] WHO recognizes that methadone and buprenorphine should be used in the setting of established treatment programs.

The third medication approved by FDA for treatment of Opioid Use Disorder is naltrexone. It was first available over 30 years ago as a daily tablet and was approved as a monthly injection in 2010. Naltrexone works differently from buprenorphine or methadone. It attaches to opioid receptors, and while it produces no effect on its own, it prevents heroin or opioid painkillers from exerting any effects. Naltrexone is used following detoxification to reduce cravings for heroin[8] and also block the impact of any relapse. Because it acts as a total blocker, it assures periods of abstinence where patients can learn to live without heroin and engage in therapy to learn new skills to regain control of their lives.

Given the challenge of treatment non-adherence in this population, a monthly injection assures longer periods of abstinence, compared to missing a daily dose of medication. Therefore the injectable form of naltrexone is now the preferred formulation by expert clinicians. Since this is a new form of medication, we have less experience with it as compared to methadone or buprenorphine, and fewer providers are aware of it. Naltrexone does not produce physical dependence so there is no withdrawal when it is stopped and it is not a controlled substance since it has no abuse potential.

Importance of Individualized Treatment

The response to medication-assisted treatments varies, similar to treatment in other medical or psychiatric disorders, such as hypertension or depression. Many individuals respond best to one of the three medications and it may take one or two attempts to determine the best fit. Occasionally, individuals may get better with treatment that includes only therapy and a self-help

group meetings (like Alcoholics Anonymous (AA) or Narcotic Anonymous (NA)). Such 12-step programs can be very helpful for patients who remain involved, but have very high drop-out rates. At this time we don't know how to predict which individuals will respond to a specific medication and which individuals will get better with psychosocial treatments alone.

Methadone, buprenorphine, and naltrexone have different pharmacological effects, they are not simply duplicative. Patients seeking treatment need all three available medication options. Hopefully, as all of these medications come into broader use, we will be able to carry out research to determine a process for matching the most effective medication to an individual patient based on drug use history, genetic factors, psychiatric profiles, and environmental exposures. However, as long as we are using one of the medications known to be effective, the odds of success will be greater than with a treatment approach without medication support. Unfortunately, treatment without medication support is currently the dominant approach in the United States. High quality evidenced-based medication-assisted treatment is only available at a few select programs or with high cost private practitioners.

Duration of medication-assisted treatment

The primary goals of treatment for opioid use disorder are similar to treatment goals for other chronic illnesses such as diabetes or hypertension. These are: 1) To reduce or eliminate the primary symptoms of the illness, in this case compulsive use of opioids, 2) To decrease the risk of illness-related complications, such as overdose, or incarceration, and 3) To improve the overall well-being of the patient to maintain a healthy life and contribute to society.

Treatment with methadone or buprenorphine works best as a maintenance intervention,

used at adequate doses without a predefined length of treatment duration. There is no scientific evidence showing benefits to limiting the time someone takes the medications. [3] Rather the evidence shows that the longer a patient remains in treatment, the more likely they are successful during treatment and after it is discontinued. [9] Opioid addiction is a chronic brain disease requiring ongoing treatment to achieve the best outcomes.

Aiming towards cessation of medications at some point in the future is important, due to concerns about costs and side effects that are always important to consider in medicine, but it should only be a goal of secondary importance, after all other goals were accomplished and patients have stabilized in their recovery. When it comes to using medications in the treatment of chronic medical problems, as long as the patient benefits from treatment, and benefits outweigh risks of continuing the medication, most physicians would advise against stopping it. For example, in management of hypertension, stopping medication is not a primary goal of treatment. The main objective is to maintain normal blood pressure and prevent complications such as stroke and heart attacks. If a patient lost weight, exercised regularly, and the dose of medication needed to maintain normal blood pressure was gradually decreased without problems, then stopping the medication could be a goal. But would we ever discontinue or refuse prescribing the medication because the patient is not willing to lose weight or exercise? Such an approach would be unethical and ineffective, not meeting the standard of care in medicine. Sadly, this situation is a common occurrence in the treatment of opioid use disorders.

Reduction in overdose deaths

The risk of death because of untreated opioid addiction is very high, approximately 1 in a 100 of individuals addicted to opioids dies every year as a result of this illness. This risk is greatly reduced in patients that are treated with medications. [10-12] Another important strategy to reduce the number of overdose deaths involves the distribution of overdose prevention kits with the opioid blocker naloxone. Reversing overdoses with naloxone can be certainly successful in saving lives, but this is not a treatment of opioid addiction. It should be promoted along side medications to treat this disorder. Unless these individuals enter treatment and receive medication to normalize their brain function, they will remain at very high risk of another overdose. Medication-assisted treatment is the best way to reduce the number of overdose deaths on a large scale. More than a hundred individuals, many of them young adults, die every day as a result of this devastating disorder. But unlike many other disorders with high mortality rates, opioid use disorder is treatable, and a joint effort of health professionals, community advocates, and policy makers is urgently needed to reverse this tragic trend.

Recommendations

Chairman Murphy and members of the Subcommittee, I respectfully submit the following recommendations for your consideration.

1) Encourage the expansion of medication-assisted treatments with methadone, buprenorphine, and naltrexone to maximize chances that every patient will have the best possible outcomes. Every licensed drug treatment program should offer these medications alongside evidence-based behavioral treatments and other supportive strategies.

2) Ensure that both public and commercial insurance companies pay for treatment that is evidence-based to encourage creation of new treatment programs that offer the most effective treatments.

3) Provide additional financial support, if insurance coverage is lacking, to lower the threshold for treatment entry and increase access to effective medications for all those that would like to receive help, including veterans, adolescents, and prisoners. .

4) Provide funding for the education of a new generation of medical professionals: medical students, physicians, nurses, psychologists, social workers and counselors to be able to treat both mental health and substance use disorders. Include up-to-date training curricula in medication-assisted psychosocial treatments of substance use disorders.

5) Provide funding for research into developing new treatments and to improving the effectiveness of existing treatments such as protocols for patient-treatment matching to further maximize treatment effectiveness

I would like to thank the committee for the opportunity to testify on this very important issue.

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