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Responses to Questions for the Record

House Energy and Commerce Subcommittee on
Oversight and Investigations

"What is the Federal Government Doing to Combat the Opioid Abuse Epidemic?"

May 1, 2015

I. Additional Questions for the Record

The Honorable Michael C. Burgess

1. **While technology has the potential to solve many problems in healthcare, we are hearing similar complaints about PDMPs as we do with EHRs. Some doctors suggest that PDMPs interrupt clinical workflow. The Health IT Policy Committee sought public comment on whether HER certification could enable and support streamlined access to PDMPs. Because PDMPs are a critical tool for patient care and clinical decision making, ONC suggested in their September 2013 report to Congress that they would explore a PDMP requirement in certification of EHRs. Can anyone speak to further discussion regarding including PDMPs as a requirement for certification of EHRs?**

   Answer: I refer you to the response provided on behalf of the Department by Assistant Secretary Frank.

2. **Some have raised questions about the efficacy of medication assisted treatment. Can you please comment on what the standard of care is for treating individuals with opioid dependence?**

   Answer: The standard of care for treating individuals with opioid dependence includes treatment with medication in combination with psychosocial supports. The evidence strongly demonstrates that methadone, buprenorphine, and injectable naltrexone (*e.g.*, Vivitrol), when administered in the context of an addiction treatment program, all effectively help maintain abstinence from other opioids, reduce opioid use disorder-related symptoms, and reduce the risk of infectious disease and crime. Two comprehensive Cochrane reviews, a process that statistically combines data from multiple studies, one analyzing data from 11 randomized clinical trials that compared the effectiveness of methadone to placebo and another analyzing data from 31 trials comparing buprenorphine or methadone treatment to placebo, found that:

- Patients on methadone were over four times more likely to stay in treatment and had 33 percent fewer opioid-positive drug tests compared to patients treated with placebo;[1]

- Long-term (beyond six months) outcomes are better for patients receiving methadone when compared to patients treated with placebo, independent of counseling received;[1]

- Buprenorphine treatment significantly decreased the number of opioid-positive drug tests when compared to patients treated with placebo, with some studies finding up to a 75-80 percent reduction in opioid positive drug tests;[2]

Broadly, the *Standards of Care for the Addiction Specialist Physician*, released by the American Society for Addiction Medicine (ASAM) in 2014, include comprehensive assessment and diagnosis, withdrawal management, treatment planning, treatment management, care transitions and care coordination, and continuing care management[3]. In the case of opioid use disorders, physicians should discuss and offer evidence based pharmacological therapies to all patients. To be clear, the evidence supports long term maintenance with these medicines in the context of behavioral treatment and recovery support, not short term detoxification programs aimed at abstinence from drugs of abuse. As stated in the Standards of Care:

> "Maintenance treatments of addiction are associated with the development of a pharmacological steady-state in which receptors for addictive substances are occupied, resulting in relative or complete blockade of central nervous system receptors such that addictive substances are no longer sought for reward and/or relief….Integration of pharmacotherapy via maintenance treatments with psychosocial treatments generally is associated with the best clinical results."[3]

Abstinence from all medicines may be a particular patient's goal and that goal should be discussed between patients and providers. However the scientific evidence suggests the relapse rates are high when tapering off of these medications and abstinence orientations popular in many treatment programs do not facilitate patients' long term, stable recovery.

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[1] Mattick, R. P., Breen, C., Kimber, J. & Davoli, M. in *Cochrane Database of Systematic Reviews* (ed. The Cochrane Collaboration) (John Wiley & Sons, Ltd, 2009), at http://doi.wiley.com/10.1002/14651858.CD002209.pub2

[2] Mattick, R. P., Breen, C., Kimber, J. & Davoli, M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst. Rev.* **2,** CD002207 (2014).

[3] American Society of Addiction Medicine (ASAM). The ASAM Standards of Care for the Addiction Specialist Physician. (2014), at http://www.asam.org/docs/default-source/practice-support/quality-improvement/asam-standards-of-care.pdf?sfvrsn=10

The Honorable Larry Buschon

1. **What are the implications of most opioid-dependent patients not getting treatment in programs that use medication?**

   Answer: As treatment plans that incorporate medication are the standard of care for opioid use disorder (OUD), patients in programs without access to medications are not being treated with the best-available evidence-based treatments for addiction (see our response to Rep. Burgess' second question). A treatment plan that includes medication has the highest probability for being effective,[4] yet only around 13 percent of all clients in treatment for OUD receive any of the three FDA-approved medications for this purpose.[5] Even for patients who have access to programs offering medications, preauthorization and other administrative requirements can prevent timely care.[6]

   Methadone, buprenorphine, and naltrexone have all been FDA-approved for treatment of OUD, which means that they have demonstrated clinically and statistically significant effectiveness.[3] These medications improve a wide variety of outcomes; they increase retention in treatment and social functioning, while reducing opioid use, criminal activity, risk of HIV infection and risk of overdose. These benefits are seen in comparison to psychosocial therapeutic approaches that do not incorporate pharmacotherapies. A clinical trial comparing buprenorphine plus psychosocial treatment to psychosocial treatment alone found that none of the patients receiving psychosocial treatment alone were retained in treatment after two months, whereas 75 percent of patients in the buprenorphine group were retained in treatment for a full year and showed a 75-percent reduction in positive urine screens for other opioids. Of patients not retained in treatment, there was a 20 percent mortality rate.[7] Outcomes are similarly improved in patients receiving methadone independent of counseling provided.[7,8,9]

   One implication of restricted access to MAT can be seen in studies that compare deaths due to opioid overdose before and after regional policy changes that expand access to MAT. Expansion of patients receiving MAT in Baltimore County was associated with a 66 percent reduction in heroin overdose deaths.[10] While direct causation cannot be determined from this type of study, the results align with evidence from clinical studies to suggest that patients without access to MAT have poorer treatment outcomes.

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[4] National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. Effective Medical Treatment of Opiate Addiction. *JAMA J. Am. Med. Assoc.* **280,** 1936–1943 (1998).
[5] Knudsen, H. K., Abraham, A. J. & Roman, P. M. Adoption and implementation of medications in addiction treatment programs. *J. Addict. Med.* **5,** 21–27 (2011).
[6] The American Society of Addiction Medicine. Advancing Access to Addiction Medications. (2013). at <http://www.asam.org/docs/default-source/advocacy/aaam_implications-for-opioid-addiction-treatment_final>
[7] Kakko, J., Svanborg, K. D., Kreek, M. J. & Heilig, M. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. *The Lancet* **361,** 662–668 (2003).
[8] Schwartz, R. P. *et al.* A randomized controlled trial of interim methadone maintenance. *Arch. Gen. Psychiatry* **63,** 102–109 (2006).
[9] Kinlock, T. W. *et al.* A randomized clinical trial of methadone maintenance for prisoners: results at 1-month post-release. *Drug Alcohol Depend.* **91,** 220–227 (2007).
[10] Schwartz, R. P. *et al.* Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. *Am. J. Public Health* **103,** 917–922 (2013).

2. I noticed the draft NIH National Pain Strategy did not mention technologies like SCS. What is NIH doing to promote FDA approved, non-pharmaceutical chronic pain treatments?

Answer: Chronic pain affects more than 100 million people in the United States and costs up to $635 billion per year in medical treatment and lost productivity and contributing to poor quality of life.[11] Although opioid medications have a legitimate role in the treatment of acute pain and some chronic pain conditions, it is clear that they often are overprescribed or are prescribed without adequate safeguards and monitoring and that their misuse can have devastating effects. The development of more effective treatment interventions with lower risks is a significant research priority for NIH. The NIH spends over $400 million annually to support chronic pain research ranging from basic science studies to understand the causes of chronic pain, to translational studies to develop novel treatments and clinical studies to determine optimal pain management approaches.

Spinal cord stimulation (SCS), is approved by the FDA for management of intractable chronic pain. It can be an effective non-pharmacological treatment option for some forms of chronic pain including complex regional pain syndrome. However, SCS is more invasive than other treatment options and is associated with risks for complications including leakage of cerebrospinal fluid, damage to nerves that come out of the spine, infection, nerve injury, etc. While these risks may be acceptable for some patients with severe chronic pain this may not be an ideal treatment option for many patients. In addition, 25-50 percent of patients report a loss of analgesia (pain relief) within 12-24 months of implantation.[12,13] More larger scale research studies are needed to determine which patients are most likely to experience long term benefit from SCS. In the shorter term, however, it is important that all providers who treat chronic pain are educated on current evidence based treatment options for chronic pain including SCS and other non-pharmacological treatments.

One role of NIH is to fund research to determine whether an approach/device, which has already been shown to be safe for other conditions, is efficacious for pain management in particular settings. Several brain stimulation devices that are non-invasive (*e.g.*, Transcranial Direct Current Stimulation, Transcutaneous Magnetic Stimulation, ultrasound, and combinations thereof) as well as a plethora of electrical stimulation devices for peripheral nerves/tissues have been cleared by FDA, but are not specifically indicated for pain management. NIH supports research on the effectiveness of these devices for use in treating chronic pain.

In addition, NIH also supports clinical trials to assess the use of natural products, as well as "mind and body" interventions such as mindfulness approaches, yoga, etc., for pain

[11] Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. Washington (DC): National Academies Press (US); 2011. ISBN-13: 978-0-309-21484-1.
[12] Doleys DM. Neurosurg Focus. Psychological factors in spinal cord stimulation therapy: brief review and discussion. 2006 Dec 15;21(6):E1.
[13] Cameron T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: 20 year literature review. J Neurosurg 2004; 100:254-267.

management, and some of these products require FDA clearance.

3. **How do we increase patient access to these advanced non-opioid treatments?**

   Answer: NIH is not only focused on the development of next-generation pain treatment modalities, but also their effective dissemination and implementation so they reach patients who can benefit from them. Educating clinicians and clinicians-in-training regarding the most effective treatment modalities for pain is a critical element of this objective. In an effort to coordinate research on pain, and enhance clinician education, NIH established the NIH Pain Consortium, a collaboration of 25 NIH Institutes, Centers and Offices which coordinates collaborative pain research initiatives activities at NIH. The Consortium is funding the development of the first open-access chronic pain data registry to help identify pain management interventions that are most effective for specific patient-types with chronic pain. In addition, NIDA is leading an NIH Pain Consortium initiative to enhance pain education among physicians, nurses, and other health care providers. The Consortium currently supports 12 Centers for Excellence for Pain Education (CoEPEs) that act as hubs for the development, evaluation and distribution of pain management curriculum resources for medical, dental, nursing and pharmacy schools. The curriculum resources developed by this program not only teach medications to treat specific pain conditions and factors that contribute to both under- and over-prescribing of pain medications, but also the latest research in complementary and integrative pain management options.

   The National Pain Strategy, developed by the Interagency Pain Research Coordinating Committee and the NIH, on behalf of HHS, calls for a patient centered approach to pain management, which includes multidisciplinary, multimodal, and integrated care. Such an approach includes non-pharmacological interventions. Several recommendations in the strategy support the implementation of means to achieve this type of care.

The Honorable Jan Schakowsky

1. **The current standard of care for treating pregnant women with opioid dependence, according to the American College of Obstetricians and Gynecologists, is medication assisted therapy, such as buprenorphine or methadone. Medically supervised tapered doses of opioids or abrupt discontinuation are contrary to the current standard of care and are only appropriate in a highly controlled research setting.**

   Can you tell us more about the standard of care for treating these patients?

   Answer: The standard of care for treating pregnant women with opioid use disorder (OUD) involves use of the medications methadone or buprenorphine in combination with psychosocial support and prenatal care. Untreated OUD during pregnancy can have devastating effects on the fetus. The fluctuating levels of opioids in the blood of mothers with opioid use disorder expose the fetus to repeated periods of in-utero withdrawal[14], and can result in restricted growth, preterm labor, convulsions, and

[14] Kaltenbach, K., Berghella, V. & Finnegan, L. Opioid dependence during pregnancy. Effects and management. *Obstet. Gynecol. Clin. North Am.* **25,** 139–151 (1998).

even in the death of the fetus. In addition to these direct physical effects, untreated OUD is also associated with increased risk of complications from untreated maternal infections, such as HIV,[15] malnutrition and poor prenatal care,[16] and dangers conferred by active use of illicit drugs and non-medical use of prescription drugs, including violence and incarceration.[14, 17]

To mitigate the negative effects of OUD on the fetus, treatment with methadone has been used for pregnant women with OUD since the 1970s, and has been recognized as the standard of care since 1998. Official statements from the National Institutes of Health National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction,[13] along with The American College of Obstetricians and Gynecologists and the American Society of Addiction Medicine,[15] document methadone treatment as best practice for opioid use disorder in pregnancy. The Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Improvement Protocols (TIP 40, 43) indicate that methadone and buprenorphine treatment stabilizes fetal levels of opioids, reducing repeated prenatal withdrawal[12,18], increases maternal HIV treatment to reduce the likelihood of transmittal to the fetus,[13-15] and links mothers to better prenatal care,[14,15] Even though neonatal abstinence syndrome (NAS) may occur in babies whose mothers have received MAT, it is less severe than it would be in the absence of treatment.

Both methadone and buprenorphine reduce the incidence and severity of NAS, resulting in a shorter treatment time for the baby.[19,20] However, recent evidence suggests Buprenorphine may be a better treatment option for opioid use disorders in pregnant women. Comparing buprenorphine to methadone treatment (in a meta-analysis),[18] buprenorphine treatment resulted in:

- 10 percent lower incidence of NAS
- shorter treatment time (an average of 8.46 days shorter)
- lower amount of morphine used for NAS treatment (an average of 3.6mg lower)
- higher gestational age, weight and head circumference at birth.

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[15] National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. Effective Medical Treatment of Opiate Addiction. *JAMA J. Am. Med. Assoc.* **280,** 1936–1943 (1998).

[16] Center for Substance Abuse Treatmentl. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) Series 43. (2005). at <http://www.ncbi.nlm.nih.gov/books/NBK64164/pdf/TOC.pdf>

[17] The American College of Obstetricians and Gynecolosits & The American Society of Addiction Medicine. Opioid Abuse, Dependence and Addiction in Pregnancy. (2012). at <http://www.acog.org/-/media/Committee-Opinions/Committee-on-Health-Care-for-Underserved-Women/co524.pdf?dmc=1&ts=20150429T1228129639>

[18] Kandall, S. R., Doberczak, T. M., Jantunen, M. & Stein, J. The methadone-maintained pregnancy. *Clin. Perinatol.* **26,** 173–183 (1999).

[19] Fajemirokun-Odudeyi, O. *et al.* Pregnancy outcome in women who use opiates. *Eur. J. Obstet. Gynecol. Reprod. Biol.* **126,** 170–175 (2006).

[20] Brogly, S. B., Saia, K. A., Walley, A. Y., Du, H. M. & Sebastiani, P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. *Am. J. Epidemiol.* **180,** 673–686 (2014).

II. Member Requests for the Record

The Honorable David McKinley

1. **What one thing would you recommend that we could do to try to start reversing this epidemic and this problem?**

   Answer: We are pleased that this Subcommittee is interested in finding ways that the Congress can have a positive impact on tackling this important issue.

   The causes of the current opioid use disorder epidemic and related overdose deaths in the United States are complex and include an amalgam of medical, social, and economic factors. The consequences are also far reaching, affecting the health, social, and economic welfare of individuals with opioid addiction, as well as their families and the larger community.

   Unfortunately, the consensus among experts is that there is no single approach or initiative that will solve this complicated problem. Furthermore, no single organization or entity can address this problem alone; a coordinated, multifaceted response involving the Federal Government, state governments, public health officials, medical and other health partners, and community organizations is required.

   Addressing this crisis is a top priority for HHS and to do so, the Department has developed an aggressive, multi-pronged initiative that focuses on three priority areas, grounded in the best research and clinical science available, to combat opioid abuse. By leveraging the distinct strengths of the HHS agencies, HHS's three part plan aims to:

   - Improve opioid prescribing practices to address the over-prescribing of opioids;
   - Expand the use of naloxone, used to treat opioid overdoses, to help reduce the number of deaths associated with opioid overdose; and
   - Expand the use of Medication-assisted Treatment (MAT), a comprehensive treatment model that combines the use of medication with counseling and behavioral therapies to treat substance use disorders.

   These priorities represent activities and interventions where evidence suggests that HHS has the greatest opportunity for measureable impact.

   NIDA's top priority in contributing to this coordinated HHS strategy is to improve the education of healthcare providers on evidence-based practices for treating pain. There is still much we don't know about the best methods for treating chronic pain, and NIDA is supporting significant ongoing research to better understand this issue. However, we do know that opioids are typically not the best treatment for chronic non-cancer pain, yet they are still frequently prescribed as a first line treatment in this context. The United States makes up only 4.6 percent of the world's population, but consumes 80 percent of

its opioids, resulting in disproportionately high rates of opioid use disorders and overdose deaths.

To improve the education of providers on evidence based strategies for addressing pain NIDA, in partnership with the NIH Pain Consortium, is helping to fund 12 Centers of Excellence in Pain Education that act as hubs for the development and dissemination of pain management curriculum resources for medical, dental, nursing and pharmacy schools to enhance and improve how health care professionals are taught about pain and its treatment. The FY 2016 President's Budget includes a proposal for continued funding for these centers of excellence, and we encourage the Congress to fully fund this program.

In addition, NIDA, in partnership with the Office of National Drug Control Policy, developed two online continuing medical education courses on safe prescribing for pain and managing patients who abuse prescription opioids. To date, these courses have been completed by over 100,000 clinicians combined. NIDA also strongly supports mandatory prescriber education in this area. Pain can be a component of nearly every medical issue and every provider should be well-trained in how to appropriately address pain while minimizing risk for negative outcomes including addiction and overdose.

The opioid abuse epidemic is a critical issue for HHS, the Administration, and the Nation as a whole, and we know we cannot solve it alone. We look forward to continuing to partner with the Congress, the states, and other stakeholders to continue to make progress on this vital issue and prevent further morbidity and mortality from opioid related overdoses.