Final Report: Opioid Use, Misuse, and Overdose in Women

July 19, 2017

OFFICE ON WOMEN'S HEALTH

Final Report: Opioid Use, Misuse, and Overdose in Women

Table of Contents

U.S. Department of Health and Human Services
200 Independence Avenue, SW, Room 712E, Washington, DC 20201

www.womenshealth.gov | 800-994-9662

OFFICE ON WOMEN'S HEALTH

Executive Summary

This report was developed as part of an initiative of the U.S. Department of Health and Human Services (HHS) Office on Women's Health (OWH) to examine prevention, treatment, and recovery issues for women who misuse opioids, have opioid use disorders (OUDs), and/or overdose on opioids. Since this work began in March 2015, OWH developed a *White Paper: Opioid Use, Misuse, and Overdose in Women (*https://www.womenshealth.gov/files/documents/white-paper-opioid-508.pdf) and convened a national meeting in September 2016 and a Region I (New England) meeting in October 2016 to discuss these critical issues.

Opioids, both illegal (e.g., heroin, illicitly manufactured synthetic opioids) and legal (e.g., oxycodone, hydrocodone) are drugs that reduce the body's perception of pain. The *Diagnostic and Statistical Manual of Mental Disorders* (5th ed., *DSM-5*) defines opioid use disorder as a problematic pattern of opioid use leading to significant impairment or distress. Opioid use disorder is increasing at alarming rates for both men and women in the United States. While the epidemic is being addressed at many different levels, much still needs to be done. The prevalence of prescription opioid and heroin use among women is substantial. Between 1999 and 2015, the rate of deaths from prescription opioid overdoses increased 471 percent among women, compared to an increase of 218 percent among men, and heroin deaths among women increased at more than twice the rate than among men.[1] Most alarmingly, there has been a startling increase in the rates of synthetic opioid-related deaths; these deaths increased 850 percent in women between 1999 and 2015. At the same time, the differences between how opioid misuse and use disorder impact women and men are often not well understood. Even in areas where differences between the sexes are apparent, such as women appearing to progress more quickly to addiction than men, very little is understood about *why* those differences occur.

This Report highlights the key background and findings from the white paper, provides a summary of the September 2016 national meeting, and concludes with a section focused on findings and takeaways from both the national and regional meetings.

Introduction

On March 26, 2015, HHS announced a department-wide initiative to combat the opioid epidemic.[2] The first HHS opioid initiative focused on three priority areas:

- "Opioid prescribing practices to reduce opioid use disorders and overdose,
- The expanded use of naloxone, used to treat opioid overdoses,
- Expanded use of Medication-assisted Treatment (MAT) to reduce opioid use disorders and overdose."[3]

In April 2017, Dr. Thomas Price, HHS secretary, identified the opioid epidemic as a top Department priority. To address the epidemic, Secretary Price announced a revised and expanded HHS Strategy, which includes five priorities for fighting the opioid crisis:

- "Improving access to treatment and recovery services;
- Promoting use of overdose-reversing drugs;
- Strengthening our understanding of the epidemic through better public health surveillance;
- Providing support for cutting-edge research on pain and addiction; and
- Advancing better practices for pain management."[4]

In support of the HHS opioid initiative, OWH has been working to examine prevention, treatment, and recovery issues for women who misuse opioids, have opioid use disorders, and/or overdose on opioids. OWH sought to explore the opioid epidemic with the overall mission to:

- Foster a national conversation on best practices to prevent, diagnose, and treat opioid-related hazards and deaths among women in the U.S.;
- Bridge gaps between researchers and public health practitioners by creating platforms to share best practices, promising approaches, and priority questions;
- Consolidate what is already known about opioid use and hazards of opioid-related harms that are specific to or more pronounced among women, as well as the research on prevention, diagnosis, and treatment of OUD among women; and

- Explore options for federal, state, and local governments; health insurers; law enforcement; and clinicians to address dependence, disability, and death related to opioid use.

Since this work began in March 2015, OWH developed a White Paper and convened a national meeting in September 2016 and a Region I (New England) meeting in October 2016. This Final Report highlights the key background and findings from the White Paper, provides a summary of the national meeting, and concludes with a section focused on findings and takeaways from both the national and regional meetings.

White Paper

The *White Paper: Opioid Use, Misuse, and Overdose in Women* was developed with the goal of ensuring that all stakeholders attending the September 2016 national meeting started from a shared level of understanding of how the unique aspects of this epidemic impact women across age, race, geography, and income. To develop the White Paper, OWH conducted a review of the literature focused on topics around OUDs and women, as well as consulted with subject matter experts within and outside HHS. The White Paper was released on January 16, 2017, and is available at: https://www.womenshealth.gov/files/documents/white-paper-opioid-508.pdf.

National Meeting

On September 29 and 30, 2016, HHS OWH convened experts and stakeholders to examine issues associated with the opioid epidemic through the lens of women's health. The meeting provided an opportunity to foster a national conversation about best practices in OUD prevention and treatment for women, and it supported a vigorous collaboration among researchers, public health practitioners, clinicians, policymakers, women with lived experience, and others to bring this epidemic to an end. The national meeting's specific goals were to:

- Build upon the work being done under the HHS opioid initiative while examining the unique and specific needs of women with regard to opioid use;
- Foster a national conversation on best practices to address opioid-related dependence and death among women in the U.S.; and

- Bridge an existing gap between data and practice while providing opportunities to share best practices from around the country.

Regional Meeting

In partnership with OWH, on October 24 and 25, 2016, the HHS Region I (New England) Office, led by regional staff from the Office of the Assistant Secretary for Health (OASH), convened a Region I Invitational Symposium in Nashua, NH to focus on the unique needs of women in the New England area. Invitees participated in facilitated state-specific breakout sessions with resource experts on women's health and opioid addiction. This approach enabled states to identify key areas for improvement and action steps for change, as well as to develop a framework to apply lessons learned in other regions and states. The specific goals of the Region I Invitational Symposium were to:

- Build upon the previous Region I work focused on the opioid epidemic by the New England governors, state programs, community and academic partners, and regional OASH/HHS leadership;
- Provide a forum to share information and findings from the national OWH meeting on women and opioids (September 29 and 30, 2016);
- Facilitate a regional conversation to identify gaps in services, barriers, and best practices;
- Build on a history of innovative substance abuse programming for women in the New England states; and
- Provide an opportunity to bring key stakeholders in Region I together to share data, identify needs, and develop state-specific action steps/plans.

Background

Opioid use disorder is increasing at alarming rates for both men and women in the United States. The prevalence of prescription opioid, heroin, and illicit synthetic opioid use among women is substantial. Between 1999 and 2015, the rate of deaths from prescription opioid overdoses increased 471 percent among women, compared with an increase of 218 percent among men, and heroin deaths among women increased at more than twice the rate than among men. [5] Most alarmingly, there has been a startling increase in the rates of synthetic opioid-related deaths; these deaths have increased 850 percent in women between 1999 and 2015.[6] While the epidemic is being addressed at many different levels, much still needs to be done. The differences in how prescription opioid and heroin use impacts women and men are often not well understood. There is emerging knowledge about the many factors that affect a woman's path to opioid misuse and OUD, including biological and social influences, past experiences, geography, and demographic characteristics, but gaps in knowledge about these factors remain.

The picture of substance use is different for women and men. According to the Centers for Disease Control and Prevention (CDC), women are more likely than men to experience chronic pain and use prescription opioid pain medications for longer periods and in higher doses.[7] Women tend to use substances differently than men, sometimes using a smaller amount of drugs for a shorter amount of time before they become dependent.[8] For example, a national multisite effectiveness trial suggests that women who use opioids not only progress to dependence more quickly than men, but they also experience more cravings than men.[9] Psychological and emotional distress have been identified as risk factors for hazardous prescription opioid use among women but not among men.[10] Many people with a substance use disorder may transition to injection drug use, thereby putting themselves at risk for viral hepatitis and HIV. Notably, new cases of hepatitis C among women increased more than 260 percent from 2010 to 2014,[11] likely increasing the risk of perinatal hepatitis C transmission to their infants.[12] Finally, women who are parents and family caregivers may face additional barriers to treatment for substance use disorders (SUDs), such as lack of child care.[13]

Issues in Prevention

As discussed earlier, many factors may affect a woman's diagnosis of OUD, including biological and social influences, past experiences, geography, and demographic characteristics. In this section, we explore some of these issues as they relate to the prevention of opioid misuse and use disorder in women.

Biological Pathways to Substance Use Disorder

Women's paths to substance use are complicated, and relatively little information is available regarding biological pathways in women. The biological differences between men and women in substance use are better understood with regard to nicotine and alcohol than for opioids. For instance, women metabolize nicotine faster than men, which may be related to why women generally do not respond as well as men to nicotine replacement therapies. With alcohol, evidence shows that women often become intoxicated after fewer drinks and in a shorter amount of time than men. Women tend to have smaller amounts of water in the body due to higher proportions of body fat. This can lead to higher blood alcohol concentrations after drinking compared with men of similar weight.[14, 15] In addition, evidence shows that women develop heart and nerve damage and cirrhosis after fewer years of heavy drinking than men, as well as experience more lung damage than male smokers.[16, 17] These physiological differences between the sexes may also put women at a higher risk for medical problems associated with substance use disorders.[18]

Women may also become physically dependent on opioid pain medication more quickly than men, a phenomenon known as "telescoping." Telescoping refers to the progression of time from first use of an addictive substance to physical dependence on that substance.[19] Women tend to use substances differently than men, sometimes using a smaller amount of drugs for a shorter amount of time before they become dependent.[20] These differences in use and basic physiological differences (e.g., body fat percentages, metabolic rate, and hormonal fluctuations) between the sexes are what likely lead to telescoping.

Some research has shown that women also may be more sensitive to cravings. For example, one study demonstrated that women are more sensitive to cue-induced cravings for cocaine.[21, 22] Another study examining cigarette smoking found women's smoking was more intensely influenced by craving than by mood, with the converse being true for men.[23] A study specifically examining opioids found cravings were significantly higher among women than among men.[24]

Social Pathways to Substance Use Disorder — Adverse Childhood and Adult Experiences

Relationships and family history can also play a critical role in women's introduction to substance use. Women are more likely to initiate hazardous drug use while in some type of intimate partner relationship, particularly after introduction of the substance by a boyfriend or spouse.[25] Additionally, psychological and emotional distress have been identified as risk factors for prescription opioid nonmedical use among women but not among men.[26] For example, victims of violence and/or sexual abuse are at an increased risk for adverse outcomes from substance use.[27] Research indicates that OUDs are associated with intimate partner violence victimization, particularly among women, and that women also may be particularly susceptible to such violence when under the influence of opioids.[28]

A history of traumatic childhood events, such as physical or sexual abuse, has been associated with the initiation of substance use among women.[29] Research has shown that physical and sexual trauma followed by post-traumatic stress disorder (PTSD) is more common in drug-misusing women than in drug-misusing men.[30]

Studies have repeatedly found that rates of both childhood and adult sexual abuse are higher among women than among men[31] and that this abuse is correlated with substance use disorders. A research review by Najavits et al. found that a lifetime history of trauma was found in 55 percent to 99 percent of women who misused substances, compared with rates of 36 percent to 51 percent in the general population.[32] Compared with men, a higher proportion of women with substance use disorders have histories of trauma, including sexual and/or physical abuse. Often this abuse was perpetrated by people the women knew and trusted.[33]

Adverse childhood experiences are not limited to physical and sexual abuse; they also may include other forms of trauma such as emotional abuse, neglect, substance use disorders among family members, mental illness in the home, separation/divorce of parents, an incarcerated household member, or having a mother who was treated violently.[34] CDC's Adverse Childhood Experiences Study has demonstrated a strong relationship between adverse childhood experiences and a variety of negative health outcomes including smoking, alcohol use, and harmful drug use.[35]

Social Determinants and Demographics

Factors such as geography, race/ethnicity, and socioeconomic status are determinants for rates of opioid use and misuse in U.S. women. Although these factors are often generally correlated with rates of opioid use and misuse, some differences appear to exist based on sex and gender.[i]

Geography

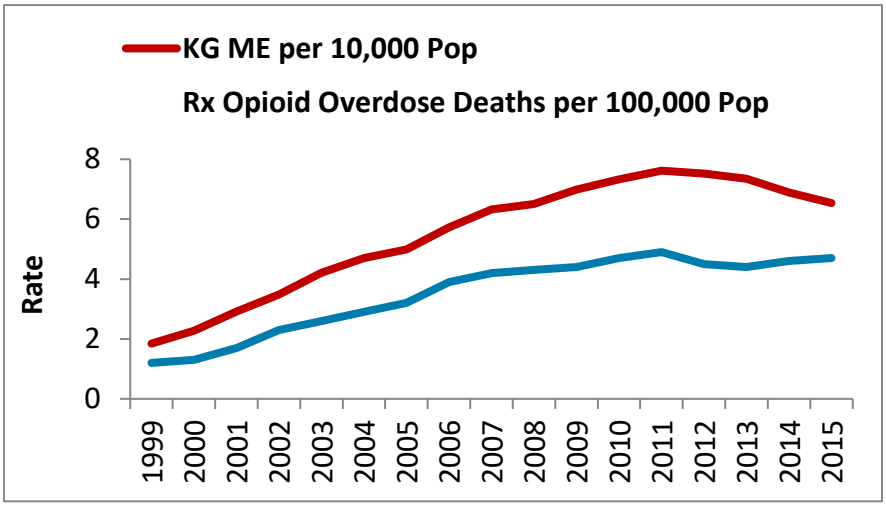
Over the last 15 years, prescription opioids have been increasingly prescribed to treat acute and chronic pain; they have also been increasingly misused and implicated in drug overdose deaths. After a sharp increase in the number of opioid prescriptions filled in the U.S. during the first decade of the 21st century, opioid prescribing and related deaths began to level out around 2012, though each remain high (see Exhibit 1).[36, 37, 38, 39, 40] In fact, in 2015 almost 30 percent of all drug overdose deaths, and close to half of all opioid overdose deaths, involved a prescription opioid.[41] Alcohol increases the risk of harm from opioid misuse. It contributes to 18.5 percent of emergency department visits involving opioids and roughly 15 to 20 percent of deaths due to opioid overdoses.[42, 43]

Opioid prescribing rates vary widely across the U.S. When controlling for gender, rates are generally highest in Appalachia, along with counties in Southern and Western states.[44] CDC analysis of geographic region data from private insurance claims illustrated similar trends for women, finding opioid

[i] This report utilizes the NIH guidelines for defining sex and gender. According to the NIH, "'Sex' refers to biological differences between females and males, including chromosomes, sex organs, and endogenous hormonal profiles. 'Gender' refers to socially constructed and enacted roles and behaviors which occur in a historical and cultural context and vary across societies and over time. All individuals act in many ways that fulfill the gender expectations of their society. With continuous interaction between sex and gender, health is determined by both biology and the expression of gender." (Sex/Gender. National Institutes of Health, Office of Research on Women's Health. https://orwh.od.nih.gov/research/sex-gender/.)

prescription rates were highest among 15- to 44-year-old women in the South and were lowest in the Northeast. Death rates from drug overdose for women are more pronounced in rural areas in the South and Midwest.

Exhibit 1: Increases in Rx opioid prescribing coincide with increases in Rx opioid overdose deaths



In an effort to improve appropriate prescribing of opioid pain medication, some states are seeing success in instituting prescription drug monitoring programs (PDMPs) to track a patient's prescriptions and identify potential prescription problems, such as multiple doctors prescribing opioid pain medications to the same patient.[45] PDMPs, which are statewide electronic databases that track the dispensing of certain controlled substances including prescription opioids to patients, can help prescribers and pharmacists identify patients who are at risk for substance use disorders. Evidence suggests that PDMPs are also effective as clinical support tools and aid in public health surveillance. PDMPs appear to be effective in changing prescriber behavior and reducing the number of patients who visit multiple providers seeking the same or similar drugs.[46, 47, 48] Additionally, recent data indicates that PDMPs have had an impact on opioid-related overdose deaths and other adverse events.[49] Although 49 states currently have established PDMPs, not all are mandatory, and uptake is much lower in states where use is voluntary.[50] PDMPs appear to have had the most impact in reducing deaths in states where they are mandatory, are updated more frequently, and/or require information about a broader range of drugs.[51, 52]

Race, Ethnicity, and Socioeconomic Status

Racial and ethnic background can be determinants in substance use disorder development. Though Americans in general are living longer, death rates are increasing for white, non-Hispanic women. Death rates for white, non-Hispanic women ages 15 to 54 between 2005 and 2013 for accidental poisoning, a category that includes drug overdoses (largely comprised of prescription drug overdoses), increased 121 percent compared with 80 percent for men.[53, 54] Though men are more likely to die from a drug overdose, the rate at which women, especially white women, are closing that gap is alarming. The increase in death rates for white American women has coincided with a shift toward prescribing opioids for more types of chronic pain rather than purely acute pain and cancer treatments, as was the case in the late 1980s to mid-1990s. There is little epidemiological evidence as to why death rates among white women have increased while death rates among other racial groups have decreased. Further, white women, specifically in the middle class, are more likely to be treated for chronic pain compared with minority women, including increasing prescription of opioids.[55] Research has shown that prescriber bias may contribute to the disparity in prescribing rates, with minorities less likely to be prescribed opioids.[56] For Medicaid beneficiaries, CDC researchers found opioid prescriptions were nearly one and a half times higher among white, non-Hispanic women ages 15–44, compared with non-Hispanic black or Hispanic women.[57] In general, however, American Indian or Alaska Native women have the highest risk of dying from a prescription opioid overdose.[58]

Although middle class white women are more likely to be treated for chronic pain, women with substance use disorders are more likely to have lower incomes, be unemployed, and have less education compared with women without substance use disorders.[59] Generally, socioeconomically disadvantaged minority drug users experience a disproportionate number of overall health consequences from harmful drug use.[60]

Chronic Pain and Pain Management

The 2012 National Health Interview Survey (NHIS) reported that approximately 25 million adults in the United States had daily pain. When pain is chronic and continuous, people can experience emotional responses including anxiety and depression, which can in turn lead to more pain.[61] Of adults who report daily pain, the NHIS found an association between pain severity and gender, as women were more likely

than men to report any pain.[62] Results from epidemiologic and clinical studies support these survey findings, and they demonstrate women are at increased risk for chronic pain. Some evidence suggests that women may experience more severe clinical pain (pain as a direct result of injury or ailment).[63] While the sex/gender differences in chronic pain are not clearly understood, possible explanations include biological and psychosocial mechanisms. Some studies have found a link between sex hormones and pain sensitivity, including changes in pain perception across the menstrual cycle.[64, 65]

In addition to being at increased risk for chronic pain, women are more likely to be prescribed opioids, be given higher doses of opioid pain medication, and use them for a longer duration of time than men.[66] Research suggests women may also be more likely to use prescription opioids to self-medicate for other problems including anxiety or stress.[67] Childhood abuse has also been linked to chronic pain later in life; individuals who have reported a history of abuse early in life are more likely to experience chronic pain.[68]

The March 2016 CDC Guideline for Prescribing Opioids for Chronic Pain summarizes the research literature about the benefits and risks associated with prescription opioids, and it provides an evidence-based guide for clinicians and patients in shared decision-making about the use of these medications and alternative treatment options for chronic pain management.[69] The Guideline states, "long-term opioid use has uncertain [pain management] benefits but known, serious risks."[70]

The Guideline acknowledges that prevention, assessment, and treatment of chronic pain are challenges for health care providers. The Guideline also reports that patients within certain groups, including women, can be at risk for inadequate pain treatment and can experience persistent pain that is not well controlled. Clinical, psychological, and social consequences are associated with chronic pain — including limitations in complex activities, lost work productivity, reduced quality of life, and stigma — that emphasize the importance of appropriate and compassionate patient care. The CDC Guideline recommends patients receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options.[71]

Although the CDC Guideline focuses specifically on opioids and chronic pain, acute and postoperative pain are also important to consider. In fact, Recommendation 6 of the CDC Guideline notes that long-term opioid use often begins with treatment of acute pain, stating specifically, "[w]hen opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed."[72]

In February 2016, the American Pain Society released a clinical practice guideline similar to the CDC Guideline, but it focused on post-surgical pain management.[73, 74] The American Pain Society's guideline includes recommendations to limit use of opioids to manage post-operative pain. The guideline also discusses the need for education aimed at correcting misperceptions including "that opioids are always required for postoperative pain, or that opioid use inevitably leads to addiction."[75] Although the recommendations do not focus specifically on women, they do include guidance around opioid use following cesarean sections, as well as a discussion of the need to educate parents and caregivers about issues around post-operative pain management for children, such as assessing pain and concern about OUD.

In 2010, the National Institutes of Health (NIH) contracted with the Institute of Medicine (IOM) to undertake a study and make recommendations "to increase the recognition of pain as a significant public health problem in the United States." The report called for a cultural transformation in pain prevention, care, education, and research. In response to the report, the HHS Assistant Secretary for Health directed the Interagency Pain Research Coordinating Committee to oversee creation of a National Pain Strategy (NPS), which was released in March 2016. The objectives of the NPS are to decrease the prevalence of pain across its continuum from acute to high-impact chronic pain and its associated morbidity and disability across the lifespan. The NPS addresses the public health significance of opioid use and misuse, and it notes that public health concerns related to the misuse or diversion of prescription opioid pain medications and risk for dependence and overdose with long-term opioid

prescribing need to be considered during the development of policies and programs related to pain management.[76]

Alternative Approaches to Opioid Pain Management

The first recommendation in the CDC Guideline discusses how nonpharmacological therapies, including physical therapy and exercise therapy, are preferred for chronic pain.[77] The Guideline notes evidence that both physical and exercise therapy can reduce chronic pain, noting high-quality evidence of exercise therapy for knee,[78] hip,[79] and low back pain.[80] The Guideline also discusses psychological therapies combined with exercise as a strategy that can reduce long-term pain.

The Substance Abuse and Mental Health Administration's (SAMHSA) *Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders* also discusses nonpharmacological therapies for managing chronic pain, including therapeutic exercise, physical therapy, cognitive behavioral therapy, and complementary and alternative medicine. There is some evidence that exercise can help manage various types of pain as well as reduce anxiety and depression, which, as previously noted, women cite as reasons for using opioids.[81] Some studies have shown that cognitive behavioral therapy can help patients manage and reduce pain, often while addressing the depression and anxiety that frequently accompany chronic pain.[82, 83, 84] Alternative and complementary strategies for pain management are also discussed throughout a number of the objectives of the National Pain Strategy, particularly as an element of comprehensive and patient-centered pain management.[85]

Women as Family Caregivers and Parents

According to the Family Caregiver Alliance's National Center on Caregiving, approximately 66 percent of caregivers are women.[86] Caregiving for a family member can have a significant impact on the mental and physical health of the caregiver herself and has been shown to lead to increased levels of depression, anxiety, and other mental health symptoms.[87] As psychological and emotional distress have also been identified as risk factors for hazardous prescription opioid use among women, caregiving may place women at a greater risk of substance misuse. Given the importance that women place on their role as family caregivers, they are more likely to seek and stay in treatment longer if they are able to maintain their caregiving role while in treatment, and they are more likely to either stay within the same

treatment services or retain relationships with treatment providers throughout the provision of services.[88]

Becoming pregnant can also have an effect on women's substance-misusing behaviors. Oftentimes, women will stop using harmful substances during pregnancy, only to begin hazardous substance use shortly after birth.[89] SAMHSA's *Advancing the Care of Pregnant and Parenting Women With Opioid Use Disorder and Their Infants: A Foundation for Clinical Guidance* reports that, from 2000 to 2009, prenatal maternal opioid use increased from 1.19 to 5.63 per 1,000 hospital births per year.[90] Opioid misuse during pregnancy is especially risky as it not only impacts the health of the woman, but it also can impact that of her unborn child.[91] Among other things, opioid use puts the neonate at risk of neonatal abstinence syndrome (NAS) — hyperactivity of the central and autonomic nervous system. SAMHSA's *Advancing the Care of Pregnant and Parenting Women With Opioid Use Disorder and Their Infants: A Foundation for Clinical Guidance* reports a nearly twofold increase in the incidence of NAS from 2009 to 2012. Further, a 2015 study found the rate of neonatal intensive care unit admissions with NAS from 2004 through 2013, increased from seven cases per 1000 admissions to 27 cases per 1000 admissions.[92] Infants born to mothers who misused opioids during pregnancy must be monitored and treated accordingly. The recommended treatment for pregnant women with an OUD is methadone or buprenorphine assisted therapy. These treatments improve pregnancy outcomes and can potentially reduce risky behavior associated with illicit drug use in the mother; while they still confer some risk of NAS, the risk is less severe than it would be in the absence of treatment.[93, 94]

Adolescents

In 2015, 3.9 percent (n=969,000) of adolescents ages 12 to 17 misused pain relievers in the previous year. More than half of those adolescents who misused pain relievers in the last year are female (n=518,000). Further, 122,000 adolescents age 12 to 17 had a use disorder due to prescription pain relievers in the last year.[95] Most adolescents who misuse prescription pain relievers get them from a friend or relative (54.2% for free and 16.6% taken/bought). Only a small percentage of those who use these pain relievers obtain a prescription from a medical professional (18.1%).[96, 97] Teens may misuse opioids to experience the euphoria and high; lessen the feelings of anxiety, stress, and physical pain;

and/or use them in response to peer pressure.[98] The primary reasons teens listed for using opioids rather than other drugs are that they are easy to get from their parents' medicine cabinets, are easily available, are not illegal drugs, and/or can be claimed as their own prescription if caught.[99] There is evidence that the use of these drugs in adolescence can evolve into OUD in adulthood. A University of Michigan study found people who have taken prescription opioids for legitimate medical purposes during high school have a 33 percent greater risk of opioid misuse by the age of 23.[100] Youth who misuse prescription medications are also more likely to report other drug use.[101]

Adolescent girls ages 12–17 are more likely than boys in that age group to use all psychotherapeutics, including pain relievers, for nonmedical reasons. Moreover, of the nonmedical users of prescription drugs, girls in this age range are more likely to become dependent. This gender difference is not the same for all age groups, however. For individuals ages 18 and older, as previously stated, males are more likely than females to misuse prescription drugs.[102] Little research has been done to account for why adolescent girls ages 12–17 display such a unique trend towards nonmedical use, as compared with their male counterparts and as compared to other age groups.

Older Adults

Some 40 to 50 percent of adults age 65 and older report the presence of a chronic pain disorder.[103] Approximately one-third of all prescription drugs in the U.S. are used by individuals in this age range. Specifically, among patients 65 and older, 19 percent of men and 23 percent of women take at least five prescription drugs.[104] Women age 65 years and older have a higher percentage of long-term use of prescription opioids than women below 65 years and then men in all age groups 18 years and older.[105] In general, OUD often goes unrecognized and untreated in this age group and research on treatment of substance use disorders for this population is limited.[106]

Recently Incarcerated Women

In 2014, 1,508,600 individuals were sentenced to more than one year in state and federal facilities. Of those, 109,200 were women.[107] According to data from the U.S. Department of Justice, approximately half of state and federal prisoners meet the DSM-IV criteria for substance use disorders.[108] Although the

need for safe and effective detoxification or continuing medication-assisted treatment for opioid use disorders is appropriate for these individuals, studies have found that these types of services are infrequently available. The majority of jails report that they do not provide medications for opioid detoxification and those that do often do not use evidence-based practices.[109] Failure to provide safe and effective detoxification, treatment, and counseling for incarcerated individual's dependence on heroin also puts them at high risk for HIV and viral hepatitis transmission through unsafe injection in prisons, possible loss of tolerance after detoxification that could result in fatal overdoses, and recidivism upon release.[110]

Increasing Use of Naloxone for Women

Naloxone is a medication called an "opioid antagonist," used to reverse the physical effects of opioid overdose. Specifically, naloxone is administered during an opioid overdose to reverse life-threatening depression of the central nervous system and respiratory system, restoring normal breathing for the person experiencing the overdose. Naloxone is a prescription medication with no potential for physical or psychological dependence. Although traditionally administered by emergency response or hospital personnel, naloxone can be administered by Good Samaritans or minimally trained bystanders, such as family and peer networks, which makes it a valuable resource in reversing the epidemic of opioid overdose deaths.

Some state laws, including laws allowing standing orders for naloxone in community pharmacies and in many states and tribes, and strong support by HHS for naloxone's use aim to make naloxone more available.[111, 112] However, women may not be benefiting as much as they could from the expanding availability of naloxone. A 2016 study found that men were nearly three times more likely than women to receive naloxone in Emergency Medical Services (EMS) opioid overdose resuscitation efforts.[113] Reasons for this lower use among women are not well understood. In 2014 and late 2015, the Food and Drug Administration (FDA) approved an auto-injector version and a nasal spray version of naloxone, respectively. With multiple formulations now available, increased availability and usage will hopefully follow for both men and women. Given the trends in increased heroin use among women, increased

availability and usage of naloxone may soon be that much more critical to prevent death from overdose among women.

Issues in Treatment

Expanding Medication-assisted Treatment for Women

Medication-assisted treatment (MAT) is "the use of medications with counseling and behavioral therapies to treat substance use disorders and prevent opioid overdose."[114] There are currently three FDA-approved drugs used for MAT of OUDs (methadone, buprenorphine, and naltrexone), each with different advantages and disadvantages as well as different uses and effects. Each medication also has different prescription requirements.

The evidence of the effectiveness of MAT is overwhelmingly positive.[115, 116, 117] However, despite a 2015 Practice Guideline from the American Society of Addiction Medicine that focuses on the use of medications in the treatment of substance use disorders involving opioid use, and a recommendation within the CDC prescribing Guideline that clinicians offer or facilitate MAT for patients with OUD,[118] MAT remains underutilized. Only 20 percent of adults with OUD get the treatment they need each year, with cost and access reported as a primary barrier.[119] Many substance use treatment programs are reluctant to offer opioid dependent patients MAT. Stigma and negative attitudes towards MAT (based on the misconception that buprenorphine or methadone "substitute a new dependence for an old one")[120] persist among clinic staff and administrators. This leads to insufficient dosing or limitations on the duration of use of these medications (when they are used at all), which often leads to treatment failure and the perception that the drugs are ineffective, further reinforcing the negative attitudes toward their use.[121]

The comprehensive nature of MAT, when implemented as recommended, lends itself well to addressing the many physiological, psychological, and psychosocial factors facing women with OUD. For example, individual, group, and family therapy may help address psychosocial complications associated with family dynamics or guilt over the adverse effects of addiction on the family.[122] To increase the use of MAT for women, services need to be both comprehensive and woman-focused, and barriers, such as

concerns about what will happen to a woman's children if she seeks treatment, need to be addressed. SAMHSA has issued guidance about the types of services that should be included in comprehensive MAT for women, such as:

- "Special groups to address problems of pregnant women who are opioid addicted;
- Available treatments for women addicted to opioids, including pharmacotherapies;
- Education and discussion groups on parenting and childcare;
- Special groups and services for children and other family members;
- Couples counseling; and
- Case management and assistance in locating safe, affordable housing."[123]

In addition, the Health Resources and Services Administration (HRSA) awarded $94 million to health centers in 2016 to improve and expand the delivery of substance abuse services in health centers. The awards will increase the number of patients screened for substance use disorders and connected to treatment, increase the number of patients with access to MAT for substance use disorder treatment, and provide training to help health professionals make informed prescribing decisions.[124] In 2017, SAMHSA will award $485 million to states through the State Targeted Response to the Opioid Crisis Grants Congress authorized as part of the 21st Century Cures Act. This funding will support a range of prevention and treatment services, including MAT.[125]

Unique Needs of Women in Treatment

In general, there tends to be a lack of substance use disorder treatment to meet overall demand, particularly in rural areas, and this is particularly true for OUDs.[126, 127, 128, 129] Looking at treatment for both men and women, approximately 96 percent of states, including the District of Columbia, have opioid use or dependence rates higher than their treatment capacity rates.[130] Many states are also already operating at significant capacity; 38 states (77.6%) have at least 75 percent of their opioid treatment programs (OTPs) operating at 80 percent capacity.[131] According to SAMHSA's 2014 National Survey of Substance Abuse Treatment Services (N-SSATS), 44 percent of treatment programs provided special programs or groups for adult women and only 20 percent offered programs or groups for pregnant or postpartum women.[132] Analysis of data from over 50,000 participants in the National Survey

on Drug Use and Health found that, among prescription opioid users, men reported significantly higher rates of treatment utilization (11% lifetime, 5% past year) compared with women (6% lifetime, 3% past year).[133] The reasons are not well understood, although the N-SSATS research suggests a lack of services for women may play a role. When women do enter treatment for substance use disorder, they typically present with medical, behavioral, psychological, and social problems that are generally more severe than for men, suggesting a need for gender-specific treatment approaches.[134]

Women as Caregivers and the Impact on Treatment

Many women who are in caregiving roles often will not seek treatment or do not complete treatment because they are unable to manage their caregiving responsibilities and participate in treatment programs at the same time. Women with children may also fear that their children will be removed from their custody. In addition, the responsibilities of caregiving, in addition to undergoing treatment, can become overwhelming for some women. Successful treatment programs may need to consider providing increased supports to address this barrier.[135]

Approximately 70 percent of women entering substance use disorder treatment services have children,[136] yet many of the existing, traditional residential drug treatment programs do not allow children to be present. As a result, parenting women may feel torn between seeking the needed treatment and caring for children. A family-centered treatment model looks at the role of the family in the treatment of women with substance use disorders. In addition to clinical treatment, this model includes a continuum of family-based clinical and community support services that address many factors for women and their families, such as substance misuse; mental health; physical health; developmental health; and social, economic, and environmental needs. Because women place high values on their relationships and families, treatment should focus on promoting and supporting healthy attachment and relationships between parents and children and on women's relationships with others. Family-centered treatment helps not only the woman dealing with adverse outcomes of drug use — it also helps her family and their needs.

Women, Treatment, and the Justice System

In many states, pregnant women or women with children can be reported to child protective services for using illicit drugs, which may lead to their loss of child custody. Involvement with the child welfare system plays a critical role in a woman's decision to seek care, because admitting to a substance use disorder may lead to involvement with the criminal justice system and potential loss of custody. The 2011 National Drug Control Strategy has acknowledged the importance of women not having to choose between seeking treatment and caring for their children.[137]

The Office of National Drug Control Policy has encouraged sentencing alternatives to incarceration, expanding family-based treatment programs, and treatment interventions that are trauma-informed.[138] Drug courts are one sentencing alternative that has shown strong evidence in reducing drug-related recidivism.[139] Drug courts provide offenders with substance use disorders an alternative to jail by providing intense supervision, drug testing, and treatment. These new approaches may be helpful in addressing women's needs.

Health Insurance Coverage Issues for Women in Treatment

Public and private coverage for treatment may serve as barriers to access. Private insurance policies are inconsistent in their coverage of MAT, the duration or number of episodes of treatment they will cover, or the requirements that patients much "fail" (meaning relapse) before MAT is approved.[140] Many private health plans also exclude coverage of methadone maintenance treatment altogether, even though it is proven to be the most effective treatment option for many people with OUD.[141] The Mental Health Parity and Addiction Equity Act (MHPAEA) requires insurance plans that cover SUD to offer coverage for services that are no more restrictive than the coverage for medical and surgical conditions. However, MHPAEA does not require insurance plans to offer coverage for SUD in general, nor does it require coverage for specific treatments or services for SUDs.[142] Medicaid state pharmacy programs must cover buprenorphine, buprenorphine naloxone combination products, and naltrexone products; however, state Medicaid programs may use drug utilization management techniques such as prior authorization, step therapy, or preferred drug lists.

Although Medicaid is encouraging state efforts to prevent and treat opioid use disorders, limitations and requirements for Medicaid reimbursement may serve as real or perceived barriers to treatment. For example, some states place limits on the length of treatment with buprenorphine-naloxone, after which time prior authorization is required for continued treatment. A number of states also require evidence that patients are receiving behavioral therapy with their medications; however, care needs to be taken that documentation does not become burdensome and turn into a barrier to accessing medications.[143]

Insurance coverage can be challenging with respect to non-pharmaceutical pain management, as well. Because there is limited evidence of effectiveness of some alternative treatments such as yoga, chiropractic and osteopathic manipulation, meditation, or massage therapy, Medicaid and private insurance plans may not cover such treatments, making these methods expensive for individuals choosing to use them. Some states and private insurers, however, are moving towards coverage of alternative treatments. In July 2016, Oregon's Medicaid program, for example, began covering acupuncture, chiropractic and osteopathic manipulation, and cognitive behavioral therapy for patients with chronic back pain, if these treatments are appropriate upon initial evaluation.[144]

Training

HHS is actively working to stem the overprescribing of opioids by providing prescribers with access to the tools and education they need to make informed decisions. In particular, HHS has developed a number of activities that support opioid prescriber education.[145] The Office of the Surgeon General launched a national campaign in 2016 called "Turn the Tide Rx," which encourages improved prescribing practices and acknowledges the role of clinicians in addressing the opioid epidemic. The campaign seeks to "educate and mobilize prescribers to take immediate action to stem the opioid epidemic, provide patients with information to protect themselves and their families from opioid misuse and overdose, learn from communities around the country that are finding creative ways to tackle the epidemic, and change the cultural perceptions about addiction so that it is not seen as a moral failing but a chronic illness."[146] The website, TurnTheTideRx.org, informs providers about different treatment options, including a pain treatment toolbox, and offers an educational section for patients that discusses different types of opioids and risks associated with their use.[147]

SAMHSA funding has also been used to create continuing medical education courses on prescribing opioids for chronic pain developed by local and state health organizations across the United States. These courses offer training on practice management, legal and regulatory issues, opioid pharmacology, and strategies for managing challenging patient situations.[148] With respect to training around acute pain prescribing, some states have developed provider training to correspond with their acute pain prescribing guidelines. In June 2016, for instance, prescribers in Ohio were asked to complete an online training program around their new acute pain opioid prescribing guidelines.[149] Beginning in fall 2016, over 60 medical schools started requiring students to take some type of prescriber education based on the CDC Guideline.[150] Similarly, almost 200 nursing schools and more than 50 pharmacy schools have committed to requiring prescriber training in their educational programs. Beginning in fall 2016, participating schools of nursing will require advanced practice registered nursing students to take some form of prescriber education in line with the CDC Guideline by the time they graduate. Colleges and schools of pharmacy will also provide education in their curricula on overdose interventions and how to counsel patients on appropriate use of naloxone.[151]

Meeting Summary

As noted in the introduction, this paper and the national and regional meetings convened in September and October 2016 by HHS OWH provided an opportunity to bridge knowledge and gaps among researchers, public health practitioners, and other stakeholders by creating opportunities to share best practices and promising approaches and identify areas for further research and evaluation. This section presents a summary of the September 2016 national meeting convened by HHS OWH. The meeting was held in Arlington, Virginia, streamed via webcast (recording available at https://www.youtube.com/user/USGOVHHS/videos), and live tweeted using the hashtag #OWHOpioidSummit.

Day One

Welcome and Opening Remarks

Nancy Lee, M.D. (Deputy Assistant Secretary for Health-Women's Health, Director of Office on Women's Health [OWH], U.S. Department of Health and Human Services [HHS][ii]) welcomed participants and noted that the meeting would provide an opportunity to explore issues and best practices unique to women within the context of the opioid epidemic. After reviewing logistics, she provided an overview of OWH, key facts about the opioid crisis that would drive the discussions at this meeting, and the role of OWH in addressing the crisis. She reemphasized OWH's main goals in addressing opioid use in women:

- Foster a national conversation on best practices to prevent, diagnose, and treat opioid misuse and death among women;
- Bridge gaps between researchers and public health practitioners by creating platforms to share best practices, promising approaches, and priority questions;
- Consolidate what is already known about opioid use and opioid-related harm specific to, or more pronounced in, women; and

[ii] Dr. Lee retired from federal service after the meeting.

- Explore priorities and policy options that federal, state, and local government, health insurers, law enforcement, and clinicians can take to address this crisis of death, disability, and disruption among women.

By including participants who are experts in the opioid crisis, OWH hoped to support a vigorous collaboration among researchers, public health practitioners, clinicians, policymakers, and women with lived experience to bring this crisis to an end.

Cortney Lovell, Owner, WRise Consulting, provided opening remarks on what the opioid epidemic means for women and the unique needs and opportunities for women in treatment and recovery, from the perspective of someone in long-term recovery from opioid addiction. She provided a dramatic recounting of her own experiences with opioid and heroin addiction and discussed how recovery programs need to walk women through the transtheoretical model of change (Prochaska and DiClemente, 1983) at their own pace rather than pushing or penalizing women when they are not ready for change. Her presentation included potential opportunities to meet the unique needs of women in treatment and recovery programs. She also now serves as a consultant on substance use prevention, youth engagement, and leadership.

Panel I: What Does the HHS Initiative Mean for Women?

Dr. Lee (Moderator) opened the panel by reintroducing HHS's opioid initiative.

Karen A. Scott, M.D., M.P.H., Chief Medical Officer, Office of the Assistant Secretary for Health (OASH), HHS[iii]

Dr. Scott's presentation stressed the need to explore the issues unique to women within the broader opioid epidemic and discussed best practices in opioid use disorder prevention and treatment for women. Her presentation included statistics around opioid misuse and use disorders, including growing evidence that suggests a relationship between the increased nonmedical use of opioid analgesics and

[iii] Dr. Scott also served as Interim Acting Director of OWH from October 2016 to January 2017.

heroin abuse in the U.S. Opioid abuse is complex because providers need to manage individuals' pain, particularly chronic pain. It is important to relieve pain and suffering without doing so in a way that leads to inappropriate access to, or use of, opioid medications. Dr. Scott stressed the need to invest in alternatives to pain management and in training physicians to have conversations with patients about approaches to pain management. The epidemic is complex, and its impact on and implications for women make it essential to engage providers in the response, and Dr. Scott mentioned how the Surgeon General led the country in mobilizing physicians and other health care providers and prescribers. She discussed the importance of considering all the components of life that make us healthy and the role of social determinants of health in prevention.

CDR Christopher Jones, Pharm.D., M.P.H., Director, Division of Science Policy, Office of the Assistant Secretary for Planning and Evaluation (ASPE), HHS

CDR Jones highlighted progress made in the three major areas of the HHS opioid initiative:

- Opioid prescribing practices: In March 2016, CDC released prescribing guidelines and the Office of the Assistant Secretary for Health released the National Pain Strategy (NPS). The NPS has six areas (population research, prevention and care, disparities, service delivery and payment, professional education and training, and public education and communication), with short-, medium-, and long-term strategies in each area. Specific strategies include:
    - Making alternative methods for pain management available;
    - Focusing on upstream drivers and maximizing prescription drug monitoring programs (PDMPs); and
    - Engaging the prescribing community through increased education and training on substance use and pain management for practitioners across the spectrum of health professions.
- Expanded use of Naloxone: The Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), of the National Institutes of Health, are working with manufacturers to create products that can be used by nonmedical personnel. An example of this initiative is the FDA approval of the auto-injector formulation in April 2014, and the FDA expedited review and

approval of the NARCAN nasal spray in 2015. The Health Resources and Services Administration (HRSA) also provided funding to expand access to, and use of, naloxone by nonmedical personnel in rural communities; and the Office of the Assistant Secretary for Planning and Evaluation (ASPE) is supporting state and local governments in their efforts to respond to the changing policy environment.

In 2016, ASPE compiled a comprehensive inventory of opioid research across HHS, organized according to the three areas of the opioid initiative (http://www.hhs.gov/opioids/about-the-epidemic/inventory-hhs-research-pain-and-opioid-misuse-and-overdose.html). The list includes intramural and extramural research and provides a brief description of each project. Additionally, in July 2013, CDC devoted an issue of *Vital Signs* to prescription painkiller overdoses among women (http://www.cdc.gov/vitalsigns/PrescriptionPainkillerOverdoses/index.html).

Vice-Admiral Vivek H. Murthy, M.D., M.B.A., Surgeon General, U.S. Public Health Service Commissioned Corps, HHS

Dr. Murthy provided an overview of the opioid crisis as influenced by his country-wide listening tour during his first days as Surgeon General, his clinical experience treating patients with substance use disorder, and the pleas of his former colleagues. He noted many people played a part in contributing to the opioid crisis. Doctors, nurses, and other clinicians were urged to be more aggressive about treating pain, but they were not given the training and support they needed to do it safely and effectively. Dr. Murthy and his medical school classmates were taught opioid medications were not addictive if they were given to someone with legitimate pain. In addition, pharmaceutical companies marketed these medications aggressively, and most people get opioids through legal prescription written for themselves or for a family member or friend.

Dr. Murthy noted the path to the opioid crisis was paved with good intentions. He discussed how overdose deaths have quadrupled since 1999, nearly 2 million people are addicted to prescription opioids, and we lose more than 40 people every day to a prescription opioid overdose. He also noted the epidemic is contributing to the spread of HIV and hepatitis C and the growing use of heroin, which is

cheaper than prescription opioids in many parts of the U.S. Dr. Murthy discussed how speeches and articles about the opioid crisis rarely talk about the impact on women, and he stated that we must recognize there are differences between men and women, and that women face unique barriers to treatment, such as caregiving responsibilities.

Dr. Murthy also talked about the recently launched "Turn the Tide Rx" campaign, which is engaging clinicians to be part of a national movement. As part of the campaign, Dr. Murthy sent a letter to 2.3 million health care practitioners with a call to action to sharpen their prescribing practices and to connect people to treatment, if needed. Thousands of clinicians in all 50 states have already pledged to participate and take an active role in addressing opioid misuse. Dr. Murthy also visited treatment centers across the country to help communities recognize that those centers are a key part of the solution.

According to Dr. Murthy, we need to do five things to address the epidemic:

- Increase access to treatment for those who have an opioid use disorder;
- Treat pain simply and effectively by sharpening prescribing practices, conducting more research on alternatives to opioid medications, and paying for those alternatives;
- Make naloxone more available, including to first responders and community and family members. A good example is a pilot program in Seattle, in which police officers on bicycles are equipped with naloxone and trained to respond to emergencies;
- Help people protect themselves, their families, and their communities from addiction by informing them about the dangers of opioids, how to use them safely, and how to dispose of them properly; and
- Change how we think about addiction in this country, to see substance use disorders (SUDs) as a chronic illness, not a bad choice or character flaw.

Dr. Murthy closed by noting that compassion is one of our most powerful weapons in the fight against addiction, because it allows us to stop judging and start helping, going beyond our own bias to extend

the help and support that people need. He concluded that compassion does not require a medical degree.

Panel Discussion

Following his remarks, Dr. Murthy led a panel discussion with Ms. Lovell and Mishka Terplan, M.D., M.P.H. (Medical Director, Behavioral Health Systems Baltimore), on the need for effective treatment, charges for practitioners and community members, how the epidemic is affecting pregnant women, and hopes for the future.

Ms. Lovell noted that many people with SUDs hesitate to speak up because they are afraid of judgment. Ms. Lovell then expanded on her personal motivation to speak up. Like many individuals struggling with substance use disorder, she started experimenting as a teenager when it seemed more socially acceptable. However, she did not realize that she was genetically pre-disposed to addiction or that she had a mood disorder, and she did not understand the impact of adverse childhood experiences, all of which created a "perfect storm" for social experimentation to turn into years of physical dependency. Ms. Lovell discussed how treatment and recovery should focus on helping people understand what the drugs and substances are doing for them (e.g., providing an escape, detracting from depression) and on helping them find ways to address those things without substances. She struggled with depression and feelings of inadequacy, combined with low energy levels that were numbed by substances. The initial stages of withdrawal and post-acute withdrawal took a long time and required a great deal of support from doctors, therapists, counselors, and family to find healthier ways to have more energy and feel better. She explained that nutrition, exercise, spiritual practice, and connecting with other women are important parts of maintaining her recovery. She lives in a rural area where resources are limited, so she participates in a weekly recovery group with other women that is held via webcast.

The next discussion focused on the number of individuals and clinicians who are not aware that effective treatment is available for substance use and addiction. Dr. Terplan described what treatment is like, how long it takes to achieve recovery, and what is entailed in maintaining recovery. He noted that most physicians do not have a comprehensive understanding of addiction. In a training context, clinicians tend

to encounter individuals with SUDs in the emergency room. Treatment systems have not adapted to the current understanding that addiction is a public health condition and a chronic illness. Therefore, there is a need to develop systems of care that incorporate different dimensions, such as the Substance Abuse and Mental Health Administration (SAMHSA) model, and emphasize recovery as part of treatment over the life course. The change in terminology from medication-assisted *treatment* to medication-assisted *recovery* is an example of that shift. Dr. Terplan also discussed the discrepancies in treatment between men and women citing that some differences are biological while others are due to social roles and expectations. Providers rarely ask patients what benefit they receive from drug use, which is a question that can help with developing an appropriate pain management strategy or addiction assessment.

Ms. Lovell provided advice to healthc are providers on how to get people into recovery and advice for families and friends who want to be helpful in the journey of recovery. Providers need to learn what addiction is, how it manifests itself, how to ask about it, and what to do when a patient says he or she is addicted. Providers should know the resources available in the community, and if resources are not available, they should be a part of the team to build them. Families can join support groups, look at online guides on how to address substance use disorder with a loved one and get connected to recovery community centers and organizations. Community groups are especially important for young people, because they help them create a sense of purpose.

Dr. Terplan commented on the opioid epidemic's impact on pregnant women and providers' reluctance to prescribe methadone out of concern for the fetus. Data on how to care for pregnant women with opioid use disorder indicate that the most effective approach is to integrate prenatal care with treatment for substance use disorder, including Medication Assisted Treatment (MAT), historically with methadone, more recently with buprenorphine. He described how the epidemic of neonatal abstinence syndrome has been misunderstood and how important it is to differentiate withdrawal from addiction. Babies are not born addicted because chronic diseases cannot be present at birth, but they do undergo withdrawal. Neonatal abstinence syndrome is treatable with no long-term consequences. The primary concern, especially for state Medicaid programs, is the cost of care ($65,000 for a newborn with NAS, versus $10,000 for a newborn without it). He noted that providers should engage a pregnant woman

with SUD in whatever level of care she will accept. Medication is an essential component, but prenatal care and behavioral treatment are also required for a successful pregnancy. The health of the mother is vital to the health of the baby, and health care policies and treatment interventions should treat them as one unit.

Dr. Murthy stressed that abstinence is not the only strategy for pregnant women living with substance use disorder. There is significant evidence that medication-assisted approaches do not cause harm and, in fact, the mother and baby ultimately do better than they would have done otherwise. He noted that our health care system is not set up to allow people to get all necessary and affordable care in one place and that there needs to be more affordable alternatives to opioids available.

Ms. Lovell stressed that there is hope as long as we can keep people with SUDs alive so that they can find recovery. She emphasized that people need to speak to policymakers and legislators about increasing funding for opioid use, misuse, overdose prevention services, and the continuum of care beyond brick and mortar treatment settings. Dr. Murthy added that there is a positive shift in our country about how people are thinking about this issue and the actions they are taking.

<u>Open Discussion</u>

- Kelly Thibert, National Medical Student Association (NMSA) noted that though care of someone impacted by the epidemic is common in medical school, curriculum focus on addiction and opioids is minimal. NMSA, representing more than 40,000 clinicians in training, is conducting advocacy for curriculum reform and wants input on how to address this need for more training.
    - Dr. Terplan noted all physicians will care for someone whose life has been affected by substance use or substance use disorder. Despite its prevalence, however, it is not prioritized in research and training. Curriculum reform is essential, but the key predictor of whether a physician will incorporate addiction into medical practice is exposure. Addiction medicine should be integrated within the existing structures of medical care delivery and hospitals. Medical students need contact with people who are in recovery,

they need to see chronic care treatment in an outpatient setting, and they need to be exposed to the continuum of community-based providers.

  - Dr. Murthy added that, beyond curricular change, we need to integrate behavioral health treatment into the traditional health care system, we need insurers to support changes in payment systems, and we need pharmacies to play a greater role in supporting access to treatment. Medical students and health care provider trainees can be an important voice for change, and their voice is needed again.

- Sharon Stancliff, Harm Reduction Coalition, asked how primary care physicians in communities with limited resources can be given the confidence to use the tools they learn about if they do not have access to the full spectrum of services.
  - Dr. Terplan stated that prevention tends to be focused on primary care providers and not sufficiently on systems of care. Physicians are responsible for prescribing medications such as buprenorphine, but behavioral counseling and other providers within the clinical context can do a brief intervention. He noted that we should also look at using peer networks and providing reimbursement for non-traditional models of care. He stated that the opioid epidemic could have been anticipated as an unintended consequence of opioid prescribing. He noted that pregnant women often have a complex array of conditions and that even where guidelines exist, they should not be used to take patients off a medication that they need. Providers need to ask questions to understand the patient and address a series of concerns based upon her condition, not upon population-level norms.
  - Dr. Murthy stated that if clinicians are asked to take on a new practice, they need a combination of training, technical assistance, payment incentives, and support. HHS recently issued a rule that increased the number of patients that a buprenorphine-registered provider can treat from 100 to 275. That will be challenging for clinicians who are not part of a large system that can provide the full complement of services their patients need, and we need to find a better way to support clinicians in that process.

- Melinda Ray, National Association of Clinical Nurse Specialists (NACNS), expressed concern that clinical nurse specialists who work in chronic care and primary care across the country were not included in the legislation for prescribing buprenorphine. This created a large gap of potential providers, particularly in rural and underserved areas. Additionally, there is a lack of adequate guidelines for diagnosis and treatment of pregnant and lactating women with chronic pain. There are many strong opinions about what medications they should or should not take, but there is very little evidence in that area, particularly regarding lactation.

Panel II: Exploring Issues in Prevention for Women

Moderator:

- Jennifer Bishop-Crawford, Sc.D., M.P.H., Director, Division of Strategic Communications, OWH

Mishka Terplan, MD, MPH: Prevention Through Integration — Life Course Observations

Dr. Terplan remarked that there are significant opportunities for prevention by focusing on the intersection of reproductive health and addiction. The Baltimore City Health Department (BCHD), for example, has integrated reproductive health services and substance use/addiction programs in several ways:

- BCHD trained Planned Parenthood staff in Screening, Brief Intervention, Referral, and Treatment (SBIRT) and expanded the program to screen all Title X clients, male or female, for substance use. Those who are using opioids at an unhealthy level receive a brief intervention, and those who meet the SBIRT criteria are referred to treatment;
- The "Reproductive Health Project on the Van" incorporated needle exchange services into a mobile family planning clinic for female exotic dancers. The program cost $85 per client, including clinician costs and supplies; and
- The Baltimore Reproductive Health Initiative integrated family planning screening, education, and service delivery within substance use/addiction programs. The program uses a screening tool for substance use providers that consists of a single, non-judgmental question ("Would you like to get pregnant in the next year?"), making it easy to provide (or refer for) family planning

services if the person needs or wants them. In the first four months of the program, 60 percent of clients indicated a need for contraceptives; of those, 83 percent received them.

He concluded that language influences how others think of addition and public health. Terms such as "opioid abuse" are judgmental and lead to stigma. Scientifically accurate, person-centered terms such as "substance use/misuse" and "addiction" or "substance use disorder" increase support for public health goals and help to further the struggle for equal rights and justice in our society.

Brian T. Bateman, M.D., M.Sc., Associate Professor, Anesthesia, Harvard Medical School: Opioids after Cesarean Delivery

Dr. Bateman presented his research about opioids and cesarean delivery. About 1.3 million women undergo Cesarean delivery (CD) each year in the U.S. Nearly all patients are prescribed opioids upon discharge, making this a common source of opioid exposure among young women and a good example of issues associated with opioid prescribing for acute indications. The following studies have explored the issues of opioid prescribing in women:

- A survey of 720 patients explored the amount of opioid that is typically required following discharge (Kennedy-Hendricks et al, JAMA Intern Med. 2016; 176[7]: 1027-1029). Researchers concluded that: a) the amount of opioid prescribed following CD generally exceeds the amount consumed by a significant margin; b) a higher number of pills dispensed predicted higher levels of opioid consumption; c) strategies to reduce the amount of opioid medication prescribed should be pursued; and d) patients should be informed about the importance of properly disposing of leftover medication.
- A study that looked at CD as a risk factor for persistent opioid use (Bateman et al. Am J Obstetrics and Gynecology. 2016 Mar 17) used a cohort of 80,000 opioid-naïve women who were prescribed opioids following CD. The study found that opioids after CD may be a precipitant for persistent use as 1 in 300 opioid-naïve women were persistent users one year following CD. Younger age, smoking, prior non-opioid substance misuse, back pain, fibromyalgia, migraines, depression, and anxiety were predictors of persistent use.

- Massachusetts General Hospital (MGH) conducted a pilot study of a shared decision-making approach for opioid prescribing after CD. Women in the hospital were asked to reflect on their use of opioid medication and to choose the number of pills they wanted, from zero to 40 (the standard protocol at MGH was 40 tablets). On average, women in the study chose 20 tablets, consumed 16, and had six left over — far less than the findings of the survey study. The researchers concluded that shared decision-making appears to be a better way to align what patients are prescribed with what they actually need.

Kelly Barth, DO, Associate Professor, Division of Bio-Behavioral Medicine, Medical University of South Carolina: Gender Differences in Pain — The Role of Sleep

Dr. Barth described how the Medical University of South Carolina has a comprehensive pain management clinic within the Department of Psychiatry. Patients with chronic abdominal pain are treated initially for pain, not for addiction. They often present with co-morbid depression and anxiety, including history of early life trauma, as well as poor sleep, and opioid use.

Dr. Barth conducted a study funded by the NIH Office of Research on Women's Health (ORWH) to determine whether improving sleep could decrease pain. Sleep disturbance is one of the most potent predictors of developing chronic pain. Research subjects were healthy males and females with one night of sleep deprivation. The study found that females had a significant decrease in both their mechanical pain threshold and their thermal pain thresholds after sleep disruption. Males did not experience similar changes in their pain thresholds. The study suggests that addressing a patient's need for sleep prior to surgery could decrease the need for opiates post-operatively, which in turn would lower the risk of chronic opiate use. Cognitive behavioral therapy for insomnia has also been shown to decrease chronic pain for people undergoing knee surgery, and napping has been shown to improve pain tolerance for people who are sleep deprived.

Traci Craig Green, Ph.D., Associate Professor, Emergency Medicine (Research), Brown University: Women, Opioids, Pain, and Overdose

Dr. Green described how predisposing factors, especially histories of violence, play important roles in women's exposure to opioids and risk. Patterns of help-seeking behaviors and opioid use suggest prevention and intervention points within the health care setting and could provide opportunities for research. Sex differences in the epidemiology of opioid use, misuse, and overdose, especially transitions to heroin and fentanyl, are not well understood and are a ripe area for future research. Several studies have provided evidence on these factors and sex differences to help guide research:

- The Massachusetts Linked Analysis compares multiple sets of data from 2013–2014 to understand opioid overdose from a population level. A comparison of data from the Medical Examiner's office with toxicological lab data showed severe gender disparities. Heroin toxicity was significantly higher among men, while women bore the burden of prescription opioid toxicity. Women with opioid toxicity were predominantly in their 40s and 50s. PDMP data show that women are more likely than men to have prescriptions from multiple providers and to fill them from multiple pharmacies, increasing their risk of opioid-related death.
- Rhode Island data from 2009 to 2015 showed that fentanyl has been a significant driver in the increase in overdose deaths since 2011. While medical examiner data show that heroin is more likely to be involved in male deaths, gender does not predict fentanyl-involved overdoses.
- A CDC-funded study to understand the causal factors in prescription opioid overdose and misuse in Connecticut and Rhode Island found that intimate partner violence (IPV) was a driving factor in women's exposure to prescription opioids, whether for physical pain or to cope with the situation. Opioid use also contributed to partner conflict, with prescription opioids used as an instrument of power and control by the abuser. The bi-directionality of misuse and IPV, combined with social isolation, increases overdose risk for women.
- A study of young, nonmedical prescription opioid users in Rhode Island found that childhood sexual abuse was a key factor in the frequency of opioid use by young women.
- A NIDA-funded study looked at the impact of an overdose prevention and naloxone distribution program in a criminal justice setting by showing female inmates a video on overdose prevention and naloxone administration prior to their release from prison. Eighty-nine percent of those who viewed the video demonstrated skills in administering naloxone during a post-assessment and were given naloxone following their release. Subsequent follow-up found that seven

women had non-fatal overdoses. Results suggest that this protocol should be extended to all women upon their release.

Open Discussion

- Denise Holden, The RASE Project, noted that some older patients in long-term recovery from addiction still need relief from pain and asked if there was research on alternative treatment to opioids. Dr. Barth clarified there are times when patients need opioids for post-surgical or acute pain, but those with SUDs need increased support and a structure to get off the opioids afterwards. People with SUDs should not receive opioids for chronic pain. Research is needed to find other options. The CDC guidelines suggest that non-opioid pharmacologic treatments are equally effective, with much less risk. Cognitive behavioral therapy has been found to be as effective as medication for insomnia or mild chronic pain, such as osteoarthritis. It is important to evaluate alternatives to determine the standard of care for non-opioid pain management.
- Steve Sumner, CDC, asked if researchers were looking at whether women who receive opioids at the time of delivery are at greater risk for IPV, particularly if their partner has substance use issues, and if any of the panelists were involved in upstream projects that look at preventing violence to prevent substance use. Panelists were not aware of current research and identified it as an area of need.
- Carole Warshaw, National Center on Domestic Violence, Trauma & Mental Health (NCDVTMH), reported a study on substance use coercion that found that more than 27 percent of callers to the national domestic violence hotline said their partners coerced them into using more than they wanted to, and 60 percent of those in treatment said their partners sabotaged their recovery. NCDVTMH will pilot a substance use-related coercion scale this year. They are working with a women's services coordinator in Colorado on some of these issues and would be interested in partnering with others to develop interventions that make a difference.

Report Out and Discussion From Day One Breakout Sessions

Breakout Session I: The HHS Initiative

Use of Naloxone for Women (Responses to Overdoses): Key Points

- The gap in research on gender disparities in receiving naloxone from first responders should be addressed. This could be done by stratifying existing data and conducting informational interviews with women who have been through the process.
- Education about naloxone should involve the community and stakeholders, in addition to providers and the emergency department.
- Insurance coverage and increasing costs are barriers to expanding the use of naloxone.
- The lack of understanding about naloxone and its impact leads to stigma.
- A Rhode Island program that connected an emergency department with peer recovery coaches is a promising approach.

Medication-assisted Treatment: Key Points

- Women in treatment who have children or are pregnant face challenges, including the need to arrange child care, daily scrutiny, stigma, and the threat of visits by child protective services.
- Treatment should be provided for incarcerated women and those who are returning to the community.
- Policies vary from state to state. In one state, women are refused entry into opioid treatment if they are pregnant. Another state prohibited women on methadone from living in public housing.
- Funding should be provided for primary care as an additional source of treatment.
- The role of arresting women for drug use when they are pregnant should be examined.

Open Discussion

- Nancy Campbell, Rensselaer Polytechnic Institute, expressed concern that many activist groups and organizations that are advocating for increased use and access to naloxone are not thinking in gender-specific terms. The movement to get gender-specific treatment for other conditions has gone through many iterations over many decades. There needs to be a connection between women's issues and the opioid overdose problem.
- Ms. Stancliff, Harm Reduction Coalition, noted that mothers of children who are at risk or have been lost to overdose are a powerful voice and might be a source of information for research.

- Suzanne Haynes, OWH, noted that the National EMS Information System (NEMSIS) has a database of 911 calls in at least 40 states with data on conditions for which calls are made and diagnoses made by providers who see the patients.
- A meeting participant noted that there may be uncertainty among first responders regarding whether to administer naloxone during pregnancy. A program in Massachusetts trains parents of adolescents who have had one overdose episode to administer naloxone. SOLACE (Surviving Our Loss and Continuing Everyday), the national organization of people who lost a loved one to opioid overdose, could be a resource.
- Loretta Finnegan, M.D., Finnegan Consulting, clarified that naloxone Is not contraindicated in pregnancy and should be used in pregnant women. She added that when treating pregnant women there should be a focus on the mother as well as the child.

Breakout Session II: Issues in Prevention

Research: Key Points

- There are significant research gaps in the area of prevention.
- Some of the data are not well developed. Some small studies may be informative.
- Much of the data are not disaggregated by sex or gender. A new NIH policy that sex should be treated as a biological variable should help to identify sex and gender differences.
- Data gaps are compounded by the need to coordinate data sources.
- Some data gaps are due to issues in the history of research on women's health (i.e., not conducting research on pregnant women in order to protect babies).
- Areas for further research include:
    - The role of opioids in pain management for aging populations, and women in particular.
    - The impact of sleep on pain and gender differences associated with that.
    - Contextual factors that are different for women (e.g., women as caretakers) and their impact on prevention and treatment.
    - Cohort studies that follow individuals by gender across the life course, beginning with naïve exposure, could help to understand differences in the stages of dependency.

- The evidence base should be developed for prevention approaches in different areas of practice (e.g., pediatrics, psychiatry, pain management).
- Approaches to measure or monitor prevention efforts related to hazardous opioid use could track outcomes such as dispensing of prescriptions, increased use of MAT, overdose and repeat overdose, preventable death, and risky prescribing practices.
- Prevention cannot be approached with a one-size-fits-all mindset. Goals to reduce opioid problems should not interfere with providing appropriate care for pain management.

Promising Practices: Key Points

- Prescribing practices do not recognize that women in their 40s and 50s have different needs from younger women. Providers need screening tools and education.
- Many patients receive their first opioid prescription following wisdom tooth removal. Dentists should be included in provider education.
- There is a lack of communication among treatment providers in interdisciplinary health care teams; electronic health records might help in the future.
- The full natal cycle (i.e., pre-conception, pregnancy, post-natal) provides many opportunities for risk screening and education.
- Financing and sustainability are critical issues.
- Providers who prescribe opioids should teach patients how to come off them.
- Racially motivated bias leads to under-prescribing for minority women due to assumptions that they are seeking opioids.
- A screening tool is needed that every prescriber could use to identify, prevent, and treat appropriately.

Promising practices include:

- Population-based approaches for outreach.
- Mayo Clinic's Interdisciplinary approach to take patients off opioids using occupational therapy, physical therapy, and psychotherapy.
- Collaboration with BlueCross Blue Shield in Florida to fund alternative therapies.

- Treatment program for college-age women that includes training in self-defense and empowerment.
- Early screening for childhood trauma.
- Providers should screen patients every time they come in.
- Patient- and family-centered approaches.

Policy Approaches: Key Points

- Policies should be developed for all levels (i.e., federal and state) and in many areas (e.g., reimbursement and health care providers, support for families, and treatment and screening).
- Data are needed on gender and race to understand more about the populations that are at risk for hazardous opioid use or OUDs, particularly the women in those groups.
- Policies have intended and unintended consequences.

Metrics for Evaluation: Key Points

- There are not enough gender-specific prevention programs to evaluate.
- Good research requires a well-defined population. However, patients in opioid prevention programs present at many stages of addiction and with many co-morbidities (e.g., domestic violence, HIV, pregnancy, trauma, and mental health). Research based on a more general population is not applicable.
- Addiction takes many forms, and patients are at all stages of life.
- Systems and agencies that address the range of co-morbidities do not talk to each other, making it difficult to share best practices.
- It is important to evaluate a woman within the context of family and intimate partners. Most evaluation designs do not address these situations.
- Many patients do not disclose their opioid use due to stigma, similar to the early days of the HIV epidemic.
- Many prevention programs are funded by SAMHSA and other federal agencies. There are no normative data about how the measures used by these agencies perform in women-sensitive programs. This makes it difficult to compare programs.

Suggestions for further work include:

- Development of communication mechanisms between agencies that deal with women and families (e.g., child development, child protective services, mental health services, substance use services, courts).
- Development of a person-centered approach to evaluation. Use conversations with women to generate evaluation instruments that reflect their values.
- Women should be entrusted to provide feedback on the quality of care they receive.
- Measures that improve the quality of care are more critical than pure research measures.
- Normative data about these measures are needed so we can compare programs.

Open Discussion

- Hendrée Jones, University of North Carolina School of Medicine, asked if any of the breakout groups discussed the newer, "designer" opioids, such as fentanyl, and whether social media could be used to anticipate the next wave of overdoses so that practitioners can be proactive. The Promising Practices breakout group discussed the role of media and agreed that they could help with the prevention effort. Dr. Goplerud stated that social media is a promising approach. NORC developed a tool by doing early analysis of websites of enthusiasts and found early mentions of "Molly" well before the epidemic hit. Data visualization tools can be helpful in finding word associations. However, people use different terms (e.g., MDMA, ecstasy, Molly) in different ways; prevention approaches will depend upon how they describe that term.
- Dr. Goplerud stressed that money is the key driver for quality improvement. Insurance providers can drive change by agreeing upon what they will pay for or the type of training providers must have in order to be reimbursed.

Day Two

Recap of Day One and Charge for Day Two

Dr. Lee opened the meeting and welcomed participants. She emphasized that the work of OWH is focused on sex- and gender-specific medicine and research. That means that sex, which is biological, and

gender, which is a social construct, should be primary variables that are considered from the outset. Too often, health statistics are not broken out by sex. Within that, other important variations (e.g., race and ethnicity) are associated with different risk factors and disease incidence. Researchers at NIH are now required to use both male and female animals and cell cultures in their studies and to report the findings by sex. It is essential to reach both men and women who are affected by the opioid crisis, and it is essential to understand the barriers for both.

Mary Fleming, M.A. (Associate Administrator for Women's Services, SAMHSA) noted that SAMHSA is the federal agency within HHS that is charged with overseeing behavioral health, which includes mental health and substance use treatment and recovery services. SAMHSA uses discretionary grants, block grants, and collaboration with other agencies and stakeholders to bring best practices to scale and support the policy goals of HHS. SAMHSA has been very involved with the HHS opioid initiative, especially in the area of treatment.

Ms. Fleming discussed key issues that emerged during Day One and noted that Day Two would focus on:

- Engagement in treatment and financing strategies for sustainability and impact;
- Determining how to best use peers in recovery and support, keeping in mind social determinants;
- Partnering with and supporting families, including approaches to help them deal with the stigma of having a family member with substance use disorder; and
- Financing and sustainability issues; working with the Centers for Medicare & Medicaid Services (CMS).

Dr. Lee closed the session by noting the importance of acknowledging the linkages between violence against women, trafficking, and drug use, including opioid misuse. Women who experience violence or trafficking may be at increased risk for coerced drug use and have unique and specific treatment and prevention needs. OWH recently developed a curriculum in partnership with the Administration for Children and Families (ACF) to help health care providers recognize and provide services for trafficked individuals.

Panel III: Exploring Issues in Treatment for Women

Moderator:

- Aaron Polacek, Fellow, OWH

Deborah Werner, M.A., PMP, Project Director, Women, Children and Families Training and TA Center; Senior Program Manager, Advocates for Human Potential: Issues in Treatment for Women

Ms. Werner emphasized three key points:

- There are gender differences, and women benefit from gender-responsive SUD services.
- Access to medication-assisted treatment/recovery and effective behavioral interventions are both important.
- Recovery supports are also essential.

She emphasized that adapting substance use services that were designed for men and assuming they will be appropriate for women is misguided. The history of substance use services for women started with programs designed for men. The realization that women need different content led to gender-responsive approaches. Current program efforts are focused on adapting those approaches initially designed for men in order to reflect gender differences. She also noted that women differ from men in terms of risk factors for SUDs, consequences of use, motivations and barriers to accessing help, and treatment and recovery support needs. Intimate Partner Violence (IPV) can be both a risk factor and a consequence. Doctors play an important role in helping women access services, because women go to them more often than men do.

Ms. Werner reviewed the gender-responsive principles developed by SAMHSA to assess substance use services for women:

- Address women's unique experience;
- Trauma-informed;
- Use relational approaches;
- Comprehensive and address women's multiple needs as well as the needs of families; and
- Provided in a healing environment.

She also discussed SAMHSA's six principles of trauma-informed care:

- Safety;
- Trustworthiness and transparency;
- Peer support and mutual self-help;
- Collaboration and mutuality;
- Empowerment, voice, and choice; and
- Cultural, historical, and gender issues.

SAMHSA has four pillars for ongoing recovery: home, health, purpose, and community. SAMHSA's comprehensive treatment model for women and children combines the full range of treatment in concentric rings of clinical treatment services, clinical support services, and community support in concentric rings.

Hendrée Jones, Ph.D., Executive Director, UNC Horizons, Professor, Department of Obstetrics and Gynecology, University of North Carolina School of Medicine: Opioid Use Disorder: Treatment in the Perinatal Period

Dr. Jones discussed treatment for opioid use disorder in the perinatal period. Her presentation addressed four areas:

- The use of opioid agonist treatment as a part of a comprehensive treatment program for women who have OUDs;
- Integration of maternal child dyad care as a part of a complete treatment approach;
- Integration of sexual health education and contraceptive choice as a part of a whole-health approach for women enrolled in treatment for substance use disorders; and
- Actions everyone can take to help improve the care of women and children who are touched by opioid use disorder.

Neonatal abstinence syndrome (NAS) often results when a woman uses opioids during pregnancy. NAS is not the same as Fetal Alcohol Syndrome (FAS). It is treatable, children can recover from it, and the condition and the treatment are not known to have long-term effects. Interactions between the mother

and child can impact resiliency and risk, with potential long-term impacts. The sooner we intervene, the better it will be for secure, attachment-based bonding.

Dr. Jones reviewed the following key findings from studies on the use of MAT and neonates:

- The Maternal Opioid Treatment: Human Experimental Research (MOTHER) Study found both methadone and buprenorphine, when used as a part of comprehensive care, benefit the mother and baby.
- A 2015 study by Wiegand et al. that compared buprenorphine, buprenorphine plus naloxone, and methadone outside of a controlled trial found even more dramatic advantages for buprenorphine.
- The UNC Horizons model combines opioid agonist medication plus a range of services to promote secure attachment between mother and child. The model incorporates trauma-informed care, peer support, and medical care along a continuum that includes prevention, residential and outpatient treatment, and continuing care. Support services (e.g., child care, transportation, parenting education, and vocational rehabilitation) help to create the most secure attachment possible between mothers and babies.

Dr. Jones also noted there are several ways to move the needle forward:

- Challenge assumptions (e.g., every level of illicit substance use is harmful; legal substances are less harmful than illegal ones; pregnant women who use substances do not care about their fetus, are not motivated for treatment, or have a magical motivation for treatment; if a woman really wanted treatment, she would get it; separating mother from baby is best for baby).
- Remember there is no such thing as a baby without a mother. Practitioners should embrace the mother-baby dyad and provide treatment that accepts both of them. Researchers should address the myriad of issues and contextualize their results, findings, and discussions.
- Remember the continuum of drug use. Not every woman who uses a drug has a substance use disorder, and not every woman needs treatment.
- Remember that toxicology tests for illicit substances are not parenting tests, and they are not sufficient for a diagnosis of a substance use disorder.

At the structural level, support is needed for policies that provide:

- Reimbursement of comprehensive services
- Access to appropriate identification, assessment, and treatment across the lifespan
- Access to whole health care
- Responsible prescribing by providers and training for providers in substance use disorders and their treatments
- Tobacco cessation support
- Hospital policies and protocols for NAS that support mother and child together and avoid unnecessary stays in the neonatal intensive care unit.

Sandra Springer, M.D., Associate Professor of Medicine, Department of Internal Medicine, Section on Infectious Diseases, Yale School of Medicine: Medication Assisted Therapy for Opioid Use Disorders Can Improve the HIV Continuum of Care for Women

Dr. Springer discussed how medication-assisted therapy for opioid use disorders can improve the HIV continuum of care for women. She noted, in addition to the risk of overdose, opioid use among women is highly associated with the acquisition and transmission of blood-borne infectious diseases such as HIV and hepatitis C virus (HCV) due to syringe sharing and unprotected sex. Opioid use interferes with the continuum for care for those who are already living with HIV. The use of alcohol or drugs can lead to reduced adherence to anti-retroviral therapy (ART) and increased viral load, which can result in disease progression to AIDS.

She further described that opioid agonist therapies (methadone and buprenorphine) have been demonstrated to reduce opioid use and craving and opioid-related mortality and to reduce drug- and sex-related HIV risk behaviors, improve retention in treatment, and improve HIV viral suppression. Retention on buprenorphine has been associated with high levels of maximal viral suppression among HIV-infected, opiate-dependent individuals at the time of their release from prison compared to those who went on and off treatment and those who did not start treatment. Extended-release naltrexone

improves HIV viral load suppression three months post-release. Naltrexone is also approved by the FDA for alcohol use disorders making it possible to treat two SUDs simultaneously.

She concluded by noting that women represent one-third of drug users, but only one in five drug users in treatment. Barriers to drug treatment among women who use drugs include incarceration, the lack of discreet and gender-sensitive services, widespread societal stigma of women who use drugs, and the lack of women in drug research.

Finally, Dr. Springer suggested the following steps could improve drug treatment and the HIV continuum of care for women with OUDs:

- Include women who use drugs in comprehensive surveillance data to document the prevalence of OUDs and uptake of pharmacologic treatments.
- Decriminalize drug use among women, and offer drug treatment and drug diversion programs.
- Develop and implement interventions that facilitate women and girls to engage in drug treatment services and receive MAT.
- Provide on-site, integrated HIV and HCV testing and treatment along with drug treatment for women.

Steven Allan Sumner, M.D., Medical Epidemiologist, Division of Violence Prevention, CDC, National Center for Injury Prevention and Control: Use of Naloxone by Emergency Medical Services

Dr. Sumner presented a 2014 study on the use of naloxone by EMS providers in Rhode Island. He noted that EMS providers play a key role in the discussion of how to improve naloxone administration in the field, because they are often among the first to arrive on the scene of a medical emergency. Historically, overdoses have largely been among heroin users, who have generally been younger males who inject the drug. EMS providers have been trained on that scenario and are accustomed to seeing it. Based on that prior experience, they can more easily miss opioid overdoses among women, older adults, and chronically ill patients.

He noted the growing diversity of individuals who are victims of opioid overdose makes it likely that there are cases in which opioid intoxication may not be recognized by EMS providers or clinicians. The study points to the need for increased clinical suspicion of opioid overdose, especially among women. A final consideration is the potential impact of changes in the naloxone protocol. At the time of his study, only 12 states permitted EMS providers to administer naloxone, and many states require providers to contact Medical Control. States are now beginning to reconsider this protocol.

Open Discussion

- Substance use treatment programs can provide a range of preventive and harm reduction services, including rapid, on-site, point-of-care testing for HIV and HCV, and PrEP.
- CDC guidelines for PrEP identify three major risk groups: men who have sex with men, heterosexual couples, and injection drug users. Additional risk factors are unprotected sex with an unknown-status partner or a known-positive partner or sharing drug paraphernalia.
- Coverage for naltrexone varies by state.
- The Veterans Administration also covers some medications. Extended-release naltrexone is FDA-approved for alcohol disorders as well as for opioid use disorders, but it is used infrequently for that purpose.
- Expanding MAT to rural communities goes beyond the ability of providers to prescribe. Many factors impact the feasibility of MAT, including payment and the conditions that are required to administer it.
- The distribution strategy of naloxone is broad. Some programs provide it to patients who use opioids; others provide it to bystanders or to police.

Panel IV: Approaches and Opportunities for Sustainable Impact

Suzette Tucker, M.H.S., Program Manager Women's Services, Maryland Department of Health and Mental Hygiene (MDHMH), Behavioral Health Administration: Approaches in Women's Services for Sustainable Impact

Ms. Tucker described behavioral health programs for women at MDHMH. Behavioral health and substance use treatment services for women in Maryland including:

- Contracted residential treatment for women with children;
- Detoxification service for women with dependent children, including child care while the mother is in detoxification;
- Supportive recovery housing;
- Substance Abuse and Treatment Services (SATS): A legislative mandate that provides SUD counselors who screen, assess, and refer to treatment any person applying for temporary cash assistance who might have a substance use disorder;
- Children in Need of Assistance/Substance-exposed Newborn: A legislative mandate that works with mothers in the hospital to ensure they get into treatment; and
- Child Welfare Project: A legislative mandate that provides screening, assessment, and referral to treatment for anyone in the home who might be using substances.

Maryland provides supportive recovery housing services to keep families together. Mothers can bring all of their children under age 18 into recovery housing, regardless of the number. Women must complete outpatient and residential services and must be abstinent from drug use and in the recovery process.

Maryland launched a Women's Coalition in May 2016 to ensure that women's services continue to thrive and move forward in Maryland. The mission of the coalition is to provide advocacy, collaboration, education, and services to the providers who work with them. It includes state and local agencies, treatment providers, housing providers, drug court providers, trauma and grief providers, homeless services providers, faith-based organizations, and women in recovery.

Bernestine Jeffers, Substance Abuse, Women/Special Populations Contact, Wisconsin Department of Health Services: The Opioid Epidemic

Ms. Jeffers described actions to address the opioid crisis in rural Wisconsin. Access to services is challenging due to geography, weather, and workforce shortages. Actions to prevent opioid harm and abuse include education, tracking and monitoring, enforcement, treatment options, medication disposal, and reversal (naloxone access). State departments collaborate to provide those services. Specific examples include:

- Medication disposal: The medication disposal system is housed in the Department of Justice, and the Department of Health helps to provide the service. Walgreens opened five drop-off sites for medication disposal across the state, in addition to a state facility.
- Education: Provider education includes an annual dinner for primary care physicians to increase understanding of the opiate problem in the state.
- Tracking and Monitoring: Wisconsin's PDMP is housed in the Department of Health Services (DHS) and is operated in partnership with the Division of Public Health. Funding was recently awarded to expand these services.
- Enforcement: A Drug-endangered Children steering committee at the Department of Justice includes clinicians, policymakers, and all levels of law enforcement.
- Medication-assisted Treatment: Options include all FDA-approved medications (buprenorphine products, naltrexone, methadone). A program for infants born to untreated opiate-addicted women provides in-home services by care coordinators. A new opioid treatment program is focused on non-methadone treatments.

HOPE programs provide MAT and residential detoxification and stabilization services to underserved and high-need communities in the northern tier of Wisconsin. The program goal is to reduce the rate of relapse and number of deaths and to reduce the number of infants born to untreated opioid-addicted women. The program creates relationships with community providers to improve treatment availability.

Valerie L. Mielke, Assistant Commissioner for Mental Health and Addiction Services, New Jersey Division of Mental Health and Addiction Services: OWH National Meeting on Opioid Use, Abuse, and Misuse in Women

Ms. Mielke described efforts at the New Jersey Division of Mental Health and Addiction Services to improve programs and increase staff training for women's SUD treatment.

New Jersey received women's set-aside funding under the federal Substance Abuse Block Grant to provide gender-specific treatment for substance use disorder. New Jersey's comprehensive approach includes:

- Assessment and treatment for co-occurring disorders;
- Family-centered treatment;
- Individual and family counseling sessions;
- Trauma-informed/trauma-specific treatment using the “Seeking Safety” program;
- Group and educational counseling sessions;
- Case management services, including referrals and follow-up through the continuum of care;
- Evidence-based parenting skills curriculum;
- Child care focused on developmental needs and age-appropriate activities;
- Medical care referrals for children, including immunizations and psychological care, as needed;
- Primary medical care, including referral for prenatal care;
- Strengthening Families program;
- Life skills training (budgeting, nutrition, household, and child safety);
- Linkages and recovery management support;
- Housing support and assistance to help women with children access permanent housing; and
- Transportation.

New Jersey appropriates $17.5 million in state and federal Block Grant funds to support a statewide network of licensed SUD treatment providers for pregnant and parenting women and women with dependent children under child welfare supervision. The network includes intensive outpatient and outpatient treatment programs (with and without methadone), long- and short-term residential programs, and a halfway house.

The New Jersey Policy Academy Team developed a statewide opioid workgroup with additional state representation (state police, Medicaid, High Intensity Drug Trafficking Area, Juvenile Justice Commission, and the Governor’s Council on Alcoholism and Drug Abuse). The workgroup meets monthly to implement the goals and objectives of the strategic approach developed through the Policy Academy. The workgroup is looking at ways to share data across departments in order to have a more collaborative approach to individuals who are addicted to opioids.

Laurie Krom, M.S., Director, ATTC Network Coordinating Office, University of Missouri-Kansas City, School of Nursing and Health Studies: Addiction Technology Transfer Center (ATTC) Network

Ms. Krom described the Addiction Technology Transfer Center (ATTC) network and highlighted resources that are available through the program. The network, established by SAMHSA in 1993, consists of:

- ATTC Regional Centers: The Regional Centers are aligned with the 10 HHS regions and are funded through cooperative agreements with SAMHSA. They address multi-system issues, provide education and training, develop region-specific products, and utilize regional advisory boards.
- National Focus Area Centers: National SBIRT ATTC, National Hispanic & Latino ATTC, National Rural & Frontier ATTC, National Native American & Alaska Native ATTC.
- National Centers of Excellence:
    - ATTC Center of Excellent on Racial and Ethnic Minority Young Men Who Have Sex with Men and Other Lesbian, Gay, Bisexual, and Transgender Populations; and
    - ATTC Center of Excellence on Behavioral Health for Pregnant and Postpartum Women and their Families.

The mission of the ATTC Network is to:

- Accelerate the adoption and implementation of evidence-based and promising addiction treatment and recovery-oriented practices and services;
- Heighten the awareness, knowledge, and skills of the workforce that addresses the needs of people with substance use and/or other behavioral health disorders; and
- Foster regional and national alliances among culturally diverse practitioners, researchers, policy makers, funders, and the recovery community.

ATTC resources include:

- Local resources: Users can find their regional centers or search a national focus area by searching the “Find an ATTC” link at ATTCnetwork.org.

- Events calendar: This online calendar lists training and events across the country, with links for information and registration.
- Health*e*Knowledge.org: A database of free online learning and low-cost continuing education courses for health care providers that includes courses on women's services and substance abuse in women.
- ATTCppwtools.org: The ATTC Center of Excellence on Behavioral Health for Pregnant Women and Their Families provides a variety of tools, such as 30-minute "webinettes," including one on the opioid epidemic from November 2016.

Open Discussion: Key Points

- Importance of including older women, non-pregnant women, or non-parenting women.
- Older women are particularly vulnerable and have different needs from women in general.

Report Out and Discussion From Day Two Breakout Sessions

Breakout Session III: Treatment

Policy Approaches: Key Points

- Funding streams, including block grants and State Medicaid, tend to get siloed. Federally qualified health centers, chronic care, complex patient models, and patient-centered medical homes are successful approaches to bridge those silos.
- Access to treatment in rural areas is difficult for all, but women are particularly impacted due to their family roles and secondary status for transportation. Medicaid rules regarding transportation vary from state to state. Mobile MAT is one approach to bridge that gap.
- Access to housing can be a barrier for women.
- Women with substance use disorders face extreme consequences, including criminalization and family disruption. Women may be referred to protective services because they are in treatment. There needs to be clear guidance about how harmful those policies are, and the policies themselves should be removed wherever possible.
- Engagement and outreach efforts for women should begin much earlier.

Promising Practices: Key Points

- Dissemination of promising practices is a key issue — many are not familiar with the resources available. One solution would be to create a non-governmental website to disseminate promising practices at the community level. Examples should include case studies and stories in addition to evidence-based practices.
- Community-based programs do not have time to write funding applications, evaluate programs, and publish articles. HHS should fund evaluation of community-based programs to help disseminate and replicate promising practices.
- Fidelity to practice is important, but it is time consuming and expensive.
- Outreach and engagement are important. Home-based programs help with engagement and serve the whole family, but it is difficult to sustain with third-party payers. One option would be to link substance use treatment with an existing home-visiting program.
- Tennessee's correctional release model and safe consumption sites in New York are examples of promising practices.
- It is important to assist women in transition.
- Empowering women to continue this work can sustain peer recovery programs.

Research: Key Points

- Importance of using of existing datasets, studies, and programs, aggregating existing information by factors such as gender or age, and considering elements that contribute to programmatic successes and failures.
- An analysis of economic outcomes that can drive funding, and looking for subgroups where there might be cost savings could be beneficial.
- Programs often demonstrate effectiveness in areas that are not of interest to insurance or health care providers. Use those findings to bring a larger constituency to the table, including criminal justice and child protective services, to talk about research and funding.
- Continuation of coordination between MAT/medication-assisted recovery (MAR) and psychosocial and behavioral therapies to study the impact on access, engagement, and retention.

- Need for multidisciplinary, interdisciplinary, and transdisciplinary research. Include basic science researchers, such pain researchers, addiction researchers, and clinicians. Look for opportunities to link findings in one area of research with another.
- Need for research into how technology and mobile health might promote engagement, retention, and social support, particularly in rural areas.
- Outcome measures should not focus exclusively on abstinence.
- For pregnant women, we need to go beyond infant birth outcomes to look at both the mother and the baby and continue to look at the impact of treatment for mothers postpartum.
- Need for linkages between researchers and advocacy groups. Apply what is working in one area and find ways to build it into a larger scale federal initiative.
- The opioid epidemic is bringing other groups to the table, including pain patients and parents who have lost children to overdose. However, efforts to have conversations about important issues often stop before they begin because of stigma.
- Research should be driven by what is important to funders and society. If we really care about opiate-related overdose death, we should be looking for opportunities to study it.

Metrics for Evaluation: Key Points

- Block grant reporting data do not provide the information needed to truly measure the effectiveness of these programs. We need information on pregnancy, from jails, and from child protective services.
- Data are siloed and do not lend themselves to cross-analysis.
- A White House initiative used a model for sharing data from criminal justice, treatment programs, and third-party payers.
- Many individuals in treatment are on their parents' health insurance, which adds complexity and concerns about confidentiality.
- Providers have multiple funding sources, and each requires different data. There is no uniform set of data with common definitions.
- There is a need for national measures and ways to compare success or failure within states; more federal evaluation funding is needed.

- Studies must consider how to best evaluate different types of providers (e.g., navigators) as programs become more innovative.
- Pay-for-success is the new model. "Success" needs to be defined and is difficult to measure when treatment consists of a lifetime intervention for a chronic disease.
- Baseline information is important. We cannot measure progress unless we know where we started, and we cannot know where we are starting unless we have a common set of definitions.

Breakout Session IV: Approaches and Opportunities

Regional Approaches: Key Points

- The Ohio Supreme Court convened Ohio and its six border states to look at opioid addiction from a criminal justice perspective. The conference addressed issues such as interstate compacts, treatment across state lines, and transit of drugs across state lines, but it did not address public health or sex and gender issues.
- Many people live in one state and work in another, and health care systems often cross state lines. This has implications for the Prescription Drug Monitoring Program (PDMP).
- Regulations for naloxone access can be different across state lines.
- Many innovative programs are in Medicaid expansion states. OWH could host a dialogue for non-expansion states to discuss potential programs and interventions.

Cross-sector Collaboration and Partnerships: Key Points

- Challenges and barriers to collaboration include silos and lack of integration, stigma (from providers, families, and communities), a shortage of resources for recovery, and a lack of data on sustained recovery.
- More data, including local and state-based data, are needed on how to respond to stigma, including effective messages to inform health care providers, communities, and faith communities about what addiction really is and how to support people.
- Potential partners include people working in domestic violence, professional medical associations, foster care, foundations, colleges and universities, law enforcement, patient advocates and peer mentors, housing, and harm reduction.

- Co-location of services is an excellent opportunity for collaboration and partnerships. Best practices include training people working in injury response/prevention in addiction screening, linking prenatal care to addiction services, providing infectious disease screenings in MAT, and combining trauma-informed care with psychological support from mentors and peer navigators.
- Law enforcement is a critical partner.
- Health care settings need peer recovery specialists.
- Guidance documents and standardized language to inform people about quality care and quality integration are needed.
- Documentation of best practices is needed so people know where buy-in exists within their communities.
- Develop a one-stop shop with resources for collaboration.

Targeted Opportunities for High-risk Women: Key Points

- Identification and screening of potentially high-risk women are those who are in re-entry or involved in the criminal justice system, victims of sexual abuse and trauma, HIV-positive women, women with psychiatric illness, women who are homeless or at risk of homelessness, and women who are currently in recovery.
- Native-American women are at very high risk, as are many African-American women and girls ages 12 to 17, especially when family drug use is involved.
- Geriatric women may have trouble with medication management, may be isolated, and are at risk for falls and exploitation.
- There are insufficient resources and attention to opportunities to address problems among high-risk women.
- Some private insurance policies cover medications and opioids, but they do not cover alternatives such as acupuncture and massage.
- Providers should conduct screenings at intake, especially for women who have experienced trauma.
- Providers should not assume that patients have a supportive network or family environment.
- More support is needed for sober living environments.

- Need for a website or resource clearinghouse for women in recovery, like those for other chronic disease states, that includes information on opioids, interactions, and maintaining recovery.
- Need for cross-training of pharmacists.
- Patients should be screened for family drug use, mental illness, and homelessness. Electronic health records could be enhanced to alert the provider if those conditions were identified upon intake or previous clinical care, so the provider can consider prescribing fewer pills or an alternative to opioids.
- OWH should collaborate with the Department of Housing and Urban Development (HUD) on housing for high-risk women and their families.
- OWH can support and sustain cross-sector collaboration and partnerships by testing and disseminating the trauma-informed curriculum that is currently in development; supporting primary care medical homes, particularly considering those that target women; promoting wrap-around services and strategies to sustain them; utilizing peers and patient navigators to assist in identifying and referring women who are at high risk; and developing and promoting a public re-education program on how we should be managing pain, versus how we currently manage it.
- Comprehensive services should be provided for women who have been involved in sex work or human trafficking (there is a successful example in Delaware).

<u>Federal, State, and Local Policy Approaches: Key Points</u>

- The culture around substance use disorders is shifting. Treatment is more patient-oriented, harm reduction is part of the conversation, and there are efforts to eliminate parallel systems and to collaborate with the right sets of partners. There is recognition that services should be integrated in a comprehensive way.
- Policies that are working include national partnership grants funded by ACF and MAT expansion.
- MAT expansion results in more babies with NAS, with many babies taken from their mothers. Stakeholders recommended that HHS and the Department of Justice should issue a clear, joint statement in support of the mother-baby dyad.

- Treatment on demand is an area of interest. However, rules may be different across states or at the county level, making it difficult to find a point of entry.
- The National Alliance for Model State Drug Laws is a resource that allows states to research laws pertaining to naloxone use, naloxone use by women, and Good Samaritan laws.
- Develop licensing laws for provision of women-specific treatment.
- Strengthen referral mechanisms between obstetric and primary care providers.
- Remove potential barriers related to malpractice insurance and liability laws.
- Develop safe care models to keep mothers and babies out of the child welfare system.

Open Discussion

- If OWH could demonstrate that outreach to women can identify risk factors that would not surface in a provider's office, it would help with funding and would convince providers of the importance of this approach. A Care Path plan showing how an individual moves through an integrated system from treatment, to recovery, to continual recovery would help to educate providers and caregivers.
- There is concern about the lack of peer services and the need for an updated training curriculum. Peer services should provide gender- and sex-specific peers. The most widely accepted basic training for becoming a certified peer is almost a decade old. It does not include MAT or harm reduction, and it is not gender-specific.
- Providers and payers need to take into account 42 CFR Part 2, which provides privacy for women in substance use treatment. Most non-substance use disorder providers are not aware of the regulation. Inclusion of that information in electronic medical records is in direct violation of the regulation, and the regulation is a barrier to communication between providers. Lawyers she spoke with had conflicting interpretations regarding how that regulation can be applied in today's world.
    - The Legal Action Center in New York has an up-to-date compendium of all the regulations related to 42 CFR Part 2. The concern is not about collecting the information,

but about sharing it without consent. SAMHSA has made recommendations to revise the regulation, but the changes have not been approved as of this meeting.[iv]

Next Steps/Closing/Call to Action

Moderator's Comments

Nicole E. Greene, Deputy Director, Office of Women's Health, summarized highlights from the meeting. Ms. Greene noted that OWH will utilize the information that was presented during the meeting in its future efforts. Ms. Greene then introduced Dr. Finnegan.

Speaker: Loretta Finnegan, M.D., President/Executive Officer, Finnegan Consulting, LLC/The College on Problems of Drug Dependence, Inc.

Dr. Finnegan reviewed issues related to addiction in women and offered findings and recommendations regarding substance use treatment for women and specifically for pregnant women and their babies. She spoke about how addiction in women has many layers. Dr. Finnegan spoke of how the cycle of addiction begins with illicit and licit drug use, which can lead to medical complications, family dysfunction, psychiatric disorders, physical and sexual abuse, social issues, legal problems, educational deficits, employment failure, and economic loss. Those complications lead back to more drug use. It is not enough to treat drug use without addressing those other layers.

She spoke about how addiction is a brain disease and a chronic, relapsing disorder. Many studies have shown changes in the brains of those who are addicted. Six months of methadone or buprenorphine is not sufficient to reverse those changes any more than six months of insulin is sufficient to treat diabetes, yet that is what we prescribe for women with addiction. Common medical problems in opioid-addicted women include HIV and other sexually transmitted diseases, hepatitis B and C, cellulitis or

[iv] On January 18, 2017 SAMHSA published a final rule, *Confidentiality of Substance Use Disorder Patient Records*, updating CFR Part 2 and addressing many of these concerns. The text of the final rule is available at: https://www.federalregister.gov/documents/2017/01/18/2017-00719/confidentiality-of-substance-use-disorder-patient-records.

phlebitis, pneumonia, septicemia, urinary tract infections, and overdose death. Those conditions must be treated along with the addiction itself. Opioid-dependent women also face numerous psychosocial issues. Psychiatric disorders such as depression, anxiety disorder, and psychosis are common. Many suffer from physical or sexual abuse, which often leads to post-traumatic stress disorder. Homelessness, prostitution, and drug dealing are also common.

She emphasized that effective SUD treatment requires a comprehensive approach with a wide range of components, such as those included in the comprehensive treatment model discussed in the 2009 NIDA publication*, Principles of Drug Abuse Treatment (A Research Based Guide)* (NIH Publication #09-4180). Interventions for pregnant women must recognize that the mother and fetus are a dyad; services for one member of that dyad must consider the other. Opioid-dependent women require special services, because they are at extremely high risk. NAS should not be defined as abuse or harm by the mother, especially when it results from compliance with treatment. A host of issues influence the occurrence and severity of NAS, including genetics. Drugs taken by the mother, including those related to MAT, are just one factor. In the past, a baby with NAS was taken away from the mother and placed in neonatal intensive care. That is no longer the case, unless the baby has another condition. Comprehensive services for the pregnant mother provide the best outcomes for the mother, her baby, and her other children. A multidisciplinary team approach is very important. None of the providers will be involved 100 percent of the time, but all are necessary to provide the array of services that are needed to get the woman healthy.

Dr. Finnegan issued the following challenges for meeting participants:

- Educate the public, children, adolescents, physicians and other medical disciplines, and lawyers and judges regarding the facts about opioid use and abuse and the necessary treatments for recovery.
- Consider opioid dependent women as having a brain disease complicated by psychosocial issues.
- Ensure that treatment programs have the facilities and appropriate disciplines to treat women who are opioid dependent.

- Provide best practices treatment in prisons.
- Develop an educational campaign to eliminate the stigma associated with opioid dependence and addiction, in general.
- Stop considering opioid dependence as a criminal justice issue and place it in the category of a chronic, relapsing disorder.
- Provide more education on the pharmacology of methadone and buprenorphine use in women, especially when pregnant.
- Make a national and state commitment to increase the number and quality of treatment facilities for women in general and when they are pregnant.

Dr. Finnegan concluded by encouraging participants to share their own lists of challenges and recommendations with OWH.

Key Findings

Themes and Potential Areas for Further Exploration

Emerging knowledge about the many factors that affect a woman's path to opioid use and misuse, including biological and social influences, past experiences, and demographic characteristics, is fundamental to continued progress in addressing the opioid epidemic in women. As we learn more about complex factors of opioid use that are specific to women, evidence-based strategies aimed towards prevention and treatment can be evaluated and disseminated. Through the development of the White Paper and during the national and regional meetings, OWH and stakeholders identified six key findings, themes, and potential areas for further exploration. These are highlighted below.

Theme 1 — Research on Unique Needs of Women

Research, from basic to applied, can help all stakeholders to better recognize and understand the unique biological and sociological aspects of opioid use in women across age, race, and socioeconomic spectrums in prevention, pain management, and treatment.

Implications for Policy and Practice

There are significant research gaps regarding the impact of gender on substance use disorders. Current data are often not disaggregated by sex or gender, some of which is the result of historical issues associated with research on women. A new NIH policy that sex must be treated as a biological variable should help to enhance research that can help identify sex and gender differences. Researchers can be encouraged to make better use of existing and emerging datasets, studies, and programs to better analyze information by gender, age, and other factors.

At the same time, more data are needed on gender and race, particularly when it comes to women who are most at risk for hazardous opioid use, OUDs, and overdose, including women with co-occurring mental health disorders, such as anxiety disorders or depression. More information is also needed on women who are pregnant, incarcerated, or recently released from jail. Data sharing across sectors is also critical to help understand complex systems impacting opioid use and treatment. A White House initiative focused on sharing data from criminal justice, treatment programs, and third-party payers may

serve as a model for opioid-related research. Cohort studies that follow individuals by gender across the life course, beginning with naïve exposure, could also help to better understand differences in the stages of and factors impacting dependency.

Biological and environmental differences related to physical dependence and risk of death from opioids among women is also not well understood. For example, research indicates that women may become physically dependent on opioids more quickly and after having used smaller amounts than men. Basic physiological differences between the sexes (e.g., body fat percentages, metabolic rate, and hormonal fluctuations) are what likely leads to a faster progression from opioid use to OUDs, but more research is needed.

Theme 2 — Provider Tools and Education

Providers need improved screening tools and education to understand, identify, and treat OUDs appropriately.

Implications for Policy and Practice

Health care and other social service providers play an important role in both the prevention and treatment of OUDs among women. To improve the effectiveness of their care, it is important to better identify and implement evidence-based approaches to help providers prevent, diagnose, and treat OUDs.

As part of this process, efforts to help opioid prescribing providers to better inform their patients about the dangers of opioids, how to use them safely, how to safely discontinue, and how to dispose of them properly can be expanded. All health care providers should be trained to recognize the risks and signs associated with OUDs and understand their options for referral to treatment. Training should also encompass consideration about compounding social determinant factors such as intimate partner violence or trauma, and related health outcomes such as HIV, viral hepatitis, and overdose risk. Electronic health records are an emerging tool that may enhance communication among providers and ensure critical information is relayed between different parties.

Effectively addressing OUDs among women will take a multidisciplinary approach and effective communication across disciplines. Partnerships can be fostered between health care and other service providers, including those who work in domestic violence, foster care, law enforcement, and others. Communication mechanisms and policy alignment can also be enhanced for social service agencies that deal with women and families (e.g., child development, child protective services, mental health services, substance use services, courts) to improve treatment approaches and outcomes. Providers and communities may also benefit from more education on how to best respond to stigma about substance use disorders, including effective messaging about what addiction really is and how to best support those who need it.

Finally, co-location of services is a good opportunity for collaboration and partnerships. Best practices include training people working in injury response/prevention in addiction screening or providing infectious disease screenings in treatment. Primary care medical homes, particularly those that target women and utilize peers and patient navigators to assist in identifying and referring women who are at high-risk, are other potential opportunities for cross-sector collaboration and partnerships.

Theme 3 — Access to Gender Responsive Support

There is growing awareness that women benefit from access to gender-responsive behavioral interventions, medication assisted treatment, and recovery supports.

Implications for Policy and Practice

There is no one-size-fits-all solution for appropriate interventions, treatment, and recovery supports. Goals to reduce opioid dependence should be balanced with providing appropriate care that is gender-responsive. Many of these factors can severely limit women's ability to access and remain in treatment safely. In addition, discrimination against women in treatment, especially pregnant women, may persist, particularly in traditional, non-gender responsive treatment models.

For example, policies and practices can benefit from further exploration of gender differences in motivations for treatment utilization and barriers to seeking treatment for substance use disorders. Women with substance use disorders often face extreme consequences including criminalization and

family disruption, referral to child protective services because they are in treatment, and trauma and intimate partner violence.

Enhanced efforts can be made to identify and disseminate best practices in state and local policies and practices for women who misuse opioids, which may help ensure better access and outcomes. Such best practices could help address disparities in availability of, and access to, treatment for pregnant women, including refusal to provide services; access to public housing for women on methadone; and services for women with children who may be threatened with removal of their children for seeking treatment, which create barriers that significantly inhibit opportunities for recovery.

Theme 4 — Expanded Access to Naloxone

Expanded access to naloxone, with supporting education about its use among first responders, community, and family members, represents an important tool in combatting overdose deaths.

Implications for Policy and Practice

Naloxone is widely recognized as a tool to help reverse the acute effects of overdose and prevent death. For it to be most effective in combatting the opioid epidemic among women, naloxone should be made more readily available, along with supporting education about recognizing overdose in women. Education about naloxone should also involve the community, family members, and stakeholders, in addition to providers and emergency departments.

Although recognition of the value of naloxone is becoming more widespread, increasing costs, as well as state and local laws and regulations, continue to represent barriers to expanded use of naloxone. Pilot programs, such as one in Seattle in which police officers on bicycles were equipped with naloxone and trained to respond to emergencies, can be studied and replicated if successful. In addition, research on overcoming gender disparities in recognizing overdose in women and providing naloxone by first responders can help assure effective access for/by women. Finally, the National Alliance for Model State Drug Laws has developed resources that allow states to research laws pertaining to naloxone use and access, including Good Samaritan laws, as well as a model state naloxone access law. These resources are intended to help expand access to this important tool.[152]

Theme 5 — Opioid Dependence as a Chronic Disorder

Emerging scientific evidence recognizes that opioid dependence is a chronic and relapsing disorder that benefits from a variety of treatment approaches.

Implications for Policy and Practice

Opioid dependence has historically been considered a criminal justice issue, as opposed to one best addressed through the public health and health care systems. However, increasing evidence suggests that in order to ensure appropriate supports and help reduce associated stigma, stakeholders must recognize that opioid dependence is a chronic disorder with high chance of relapse (similar to depression or hypertension). It is also a life-long condition, like diabetes, that cannot be solved with a single, one-time intervention. As with other chronic conditions, people with OUDs may not move in a straight line through the continuum of dependence, treatment, and recovery, and, in fact, relapse is often a part of the illness.

As emerging science recognizes that opioid dependence is a chronic brain disease complicated by psychosocial issues, some of which are unique for women, the culture around use disorders is shifting. Treatment is becoming more patient-oriented, harm reduction is being incorporated into prevention and treatment, and there are efforts to integrate SUDs into primary and mental health care systems of care. Systems of care should be aligned to support behavioral interventions and medication-assisted treatment that is gender-responsive, supports patients and families, and recognizes that people with these conditions may relapse. There is growing recognition that, in order to be most effective, health care services should be integrated and linked with community resources, including support groups, faith-based organizations, and safe places for high-risk groups including adolescents.

Theme 6 — Financing for Prevention and Treatment

In order for prevention and treatment to succeed for women at different levels of care, financing will be critical to implementation and sustainability of successful interventions.

Implications for Policy and Practice

Innovative and emerging approaches to working with opioid dependence should continue to be supported, evaluated, sustained, and brought to scale if successful. Federally qualified health centers,

chronic care and complex patient models, home visiting, and patient-centered medical homes are among a range of evidence-based and successful approaches that integrate approaches to care for women with opioid dependence. Flexible, integrated funding streams can better ensure comprehensive approaches to prevention and care.

Appropriate, evidence-based insurance coverage policies are also a key component to addressing opioid dependence and recovery. As evidence to support new alternatives to opioid pain management and treatment are emerging, insurance coverage policies can support access to care by considering ways to cover evidence-based practices. Finally, as pay-for-success models continue to develop, appropriate outcomes of “success” for opioid treatment and recovery need to be defined and measured, recognizing that opioid dependence is a chronic disease. Currently, there is no uniform set of data with common definitions and there is an absence of reliable baseline information. In order to move forward on scaling effectively, there is a need for national measures and methods to compare success or failure within and across states and provider settings.

Conclusion

Since March 2015, when HHS launched the ongoing department-wide effort to address the opioid epidemic, OWH has examined the impact of the opioid crisis on women and women's health. Hazardous and deadly opioid use, including misuse of prescription opioids, heroin, and fentanyl, is increasing at alarming rates for both men and women in the United States. While the crisis is being addressed at many different levels, much still needs to be done, including efforts designed to address the specific and unique needs of women. Even in areas where differences between the sexes is apparent, such as women appearing to progress more quickly to addiction than men, very little is understood about *why* those differences occur. Through this Report, the White Paper, and the national and regional meetings, OWH has highlighted promising practices that specifically address opioid prevention and treatment for women. These efforts have also identified numerous areas that are may be able to serve as a platform for further research and evaluation. Recognition of the nature and scope of the opioid crisis, including the unique needs of women, is emerging at a rapid pace, and the discussion and findings from these national and regional activities will serve as a stepping-off point for further actions and support robust prevention and treatment for all women.

References

[1] Centers for Disease Control and Prevention. Analysis of the National Vital Statistics System Multiple Cause of Death data, Wide-ranging OnLine Data for Epidemiologic Research (WONDER). 2017.

[2] HHS takes strong steps to address opioid-drug related overdose, death and dependence [news release]. U.S. Department of Health & Human Services; March 26, 2015. http://www.hhs.gov/about/news/2015/03/26/hhs-takes-strong-steps-to-address-opioid-drug-related-overdose-death-and-dependence.html. Accessed September 28, 2016.

[3] Opioid abuse in the U.S. and HHS actions to address opioid-drug related overdoses and deaths. Office of the Assistant Secretary for Planning and Evaluation Web site. https://aspe.hhs.gov/opioid-abuse-us-and-hhs-actions-address-opioid-drug-related-overdoses-and-deaths. Accessed October 31, 2016.

[4] Secretary Price Announces HHS Strategy for Fighting Opioid Crisis [speech]. U.S. Department of Health and Human Services; April 19, 2017. https://www.hhs.gov/about/leadership/secretary/speeches/2017-speeches/secretary-price-announces-hhs-strategy-for-fighting-opioid-crisis/index.html. Accessed July 11, 2017.

[5] Centers for Disease Control and Prevention. Analysis of the National Vital Statistics System Multiple Cause of Death data, Wide-ranging OnLine Data for Epidemiologic Research (WONDER). 2017.

[6] Centers for Disease Control and Prevention. Analysis of the National Vital Statistics System Multiple Cause of Death data, Wide-ranging OnLine Data for Epidemiologic Research (WONDER). 2017.

[7] Prescription Painkiller Overdoses. *CDC Vital Signs*; July 2013. http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html. Accessed September 28, 2016.

[8] Substance Use in Women. National Institute on Drug Abuse Web site. https://www.drugabuse.gov/publications/drugfacts/substance-use-in-women. Updated September 2015. Accessed October 31, 2016.

[9] Back SE, Payne RL, Wahlquist AH, et al. Comparative Profiles of Men and Women with Opioid Dependence: Results from a National Multisite Effectiveness Trial. The American journal of drug and alcohol abuse. 2011;37(5):313-323. doi:10.3109/00952990.2011.596982.

[10] Back, SE, Lawson, K, Singleton, L, and Brady, KT. Characteristics and Correlates of Men and Women with Prescription Opioid Dependence. Addict Behav. 2011; August; 36(8): 829-834. doi:10.1016/j.addbeh.2011.03.013.

[11] Surveillance for Viral Hepatitis - United States, 2014. CDC Web site. https://www.cdc.gov/hepatitis/statistics/2014surveillance/index.htm. Updated September 22, 2016. Accessed October 31, 2016.

[12] Koneru A, Nelson N, Hariri S, et al. Increased Hepatitis C Virus (HCV) Detection in Women of Childbearing Age and Potential Risk for Vertical Transmission — United States and Kentucky, 2011–2014. *MMWR Morb Mortal Wkly Rep* 2016;65:705–710. DOI: http://dx.doi.org/10.15585/mmwr.mm6528a2

[13] Substance Use While Pregnant and Breastfeeding. NIDA Web site. https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/substance-use-while-pregnant-breastfeeding. Updated September 2016. Accessed October 31, 2016.

[14] Center for Substance Abuse Treatment. Substance Abuse Treatment: Addressing the Specific Needs of Women. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2009. (Treatment Improvement Protocol (TIP) Series, No. 51.) Available from: http://www.ncbi.nlm.nih.gov/books/NBK83252/

[15] Jones H, Goler N, Werner D. Women's Health, Wellness, and Recovery: An Introduction to Women's Substance Use Disorders and Health [webinar]. May 6, 2015. In the Substance Abuse and Mental Health Services Administration's Women Matter! series. Retrieved from: http://www.samhsa.gov/women-children-families/trainings/women-matter.

[16] Jones H, Goler N, Werner D. Women's Health, Wellness, and Recovery: An Introduction to Women's Substance Use Disorders and Health [webinar]. May 6, 2015. In the Substance Abuse and Mental Health Services Administration's Women Matter! series. Retrieved from: http://www.samhsa.gov/women-children-families/trainings/women-matter.

[17] Brady, KT.; Back, SE.; Greenfield, SF., editors. *Women and Addiction: A Comprehensive Handbook*. New York, NY: Guilford Press; 2009.

[18] Back, SE, Lawson, K, Singleton, L, and Brady, KT. Characteristics and Correlates of Men and Women with Prescription Opioid Dependence. *Addict Behav*. 2011; August; 36(8): 829-834. Doi:10.1016/j.addbeh.2011.03.013.

[19] Substance Abuse and Mental Health Services Administration, National Survey of Substance Abuse Treatment Services (N-SSATS): 2014. Data on Substance Abuse Treatment Facilities. BHSIS Series S-79, HHS Publication No. (SMA) 16-4963. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2015.

[20] Hernandez-Avila, CA, Rounsaville, BJ, Kranzler, HR. Opioid-, cannabis- and alcohol-dependent women show more rapid progression to substance abuse treatment. *Drug Alcohol Depend*. 2004 Jun 11; 74(3): 265-72. doi: 10.1016/j.drugalcdep.2004.02.001

[21] Hitschfeld MJ, Schneekloth TD, Ebbert JO, et al. Female smokers have the highest alcohol craving in a residential alcoholism treatment cohort. *Drug Alcohol Depend*. 2015;150:179-182.

[22] Kennedy AP, Epstein DH, Phillips KA, Preston KL. Sex differences in cocaine/heroin users: drug-use triggers and craving in daily life. *Drug Alcohol Depend*. 2013;132(0):29-37.

[23] Shiffman S, Rathbun SL. Point process analyses of variations in smoking rate by setting, mood, gender, and dependence. *Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors*. 2011;25(3):501-510. doi:10.1037/a0022178.

[24] Back, SE, Lawson, K, Singleton, L, and Brady, KT. Characteristics and Correlates of Men and Women with Prescription Opioid Dependence. *Addict Behav*. 2011; August; 36(8): 829-834. Doi:10.1016/j.addbeh.2011.03.013.

[25] Brecht ML, O'Brien A, Mayrhauser CV, Anglin MD. Methamphetamine use behaviors and gender differences. *Addictive Behaviors*. 2004;29(1):89–106.

[26] Back, SE, Lawson, K, Singleton, L, and Brady, KT. Characteristics and Correlates of Men and Women with Prescription Opioid Dependence. *Addict Behav*. 2011; August; 36(8): 829-834. Doi:10.1016/j.addbeh.2011.03.013

[27] 2013 Trans-HHS Intimate Partner Violence Screening and Counseling: Research Symposium. Women's Health Resources. https://sis.nlm.nih.gov/outreach/2013IPVsymposium.html. Updated October 5, 2015. Accessed June 16, 2016.

[28] Smith PH, Homish GG, Leonard KE, Cornelius JR. Intimate partner violence and specific substance use disorders: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol Addict Behav*. 2012 Jun; 26(2). Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3883081/

[29] Agrawal A, Gardner CO, Prescott CA, Kendler KS. The differential impact of risk factors on illicit drug involvement in females. *Social Psychiatry and Psychiatric Epidemiology*.2005;40(6):454–466.

[30] U. S. Department of Health and Human Services, National Institutes of Health, National Institute of Mental Health. (2012) Principles of Drug Addiction Treatment: A Research-Based Guide. (NIH Publication No. 12-4180). Retrieved from https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/what-are-unique-needs-women-substance-use.

[31] Jones H, Goler N, Werner D. Women's Health, Wellness, and Recovery: An Introduction to Women's Substance Use Disorders and Health [webinar]. May 6, 2015. In the Substance Abuse and Mental Health Services Administration's Women Matter! series. Retrieved from: http://www.samhsa.gov/women-children-families/trainings/women-matter.

[32] Najavits LM, Weiss RD, Shaw SR. The link between substance abuse and posttraumatic stress disorder in women: A research review. *American Journal on Addictions*. 1997;6(4):273–283.

[33] Covington, SS. Women and Addiction: A Trauma-Informed Approach. *Journal of Psychoactive Drugs*. SARC Supplement 5, November 2008: 377-385.

[34] Adverse Childhood Experiences. Substance Abuse and Mental Health Services Administration website http://www.samhsa.gov/capt/practicing-effective-prevention/prevention-behavioral-health/adverse-childhood-experiences. Updated March 7, 2016. Accessed June 17, 2016.

[35] About Adverse Childhood Experiences. Centers for Disease Control and Prevention's website http://www.cdc.gov/violenceprevention/acestudy/about_ace.html. Updated April 1, 2016. Accessed June 2, 2016.

[36] Paulozzi L, Jones CM, Mack KA, Rudd RA, Chou R. Vital Signs: Overdoses of Prescription Opioid Pain Relievers --- United States, 1999—2008. *MMWR Morb Mortal Wkly Rep*. 2011 Nov 4;60(43):1487-92. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6043a4.htm?s_cid=mm6043a4_w

[37] Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths – United States, 2000-2014. *MMWR Morb Mortal Wkly Rep* 2016;64(50);1378-82. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm?s_cid=mm6450a3_w. Accessed on October 31, 2016.

[38] National Institute on Drug Abuse. Research Report Series "Prescription Opioids and Heroin: A Subset of People who Abuse Prescription Opioids May Progress to Heroin Use." December 2015. Available at https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/subset-users-may-naturally-progress-rx-opioids-to-heroin

[39] CDC Wonder. Atlanta, GA: Centers for Disease Control and Prevention; 2015. http://wonder.cdc.gov/.

[40] Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). http://www.samhsa.gov/data/client-level-data-teds.

[41] Rudd RA, Seth P, David F, Scholl, L (2016). Increases in Drug and Opioid-Involved Overdose Deaths — United States, 2010–2015. Morbidity and Mortality Weekly Report, 65(50-51);1445–1452. Available: https://www.cdc.gov/mmwr/volumes/65/wr/mm655051e1.htm.

[42] Jones CM, Paulozzi LJ, Mack KA (2014). Alcohol Involvement in Opioid Pain Reliever and Benzodiazepine Drug Abuse–Related Emergency Department Visits and Drug-Related Deaths — United States, 2010. Morbidity and Mortality Weekly Report, 63(40), 881-885. Available: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6340a1.htm.

[43] Warner M, Trinidad JP, Bastian BA, et al. Drugs most frequently involved in drug overdose deaths: United States, 2010–2014. National vital statistics reports; vol 65 no 10. Hyattsville, MD: National Center for Health Statistics. 2016. Available: https://www.cdc.gov/nchs/data/nvsr/nvsr65/nvsr65_10.pdf.

[44] McDonald DC, Carlson K, Izrael D. Geographic Variation in Opioid Prescribing in the U.S. J Pain. 2012 Oct; 13(10): 988-996. doi: 10.1016/j.jpain.2012.07.007

[45] Rettner R. Southern States Have the Highest Painkiller Prescription Rates. Scientific American. July 1, 2014. http://www.scientificamerican.com/article/southern-states-have-the-highest-painkiller-prescription-rates/. Accessed October 31, 2016.

[46] PDMP Center of Excellence. Brandeis University. Briefing on PDMP Effectiveness. September 2014. http://www.pdmpassist.org/pdf/COE_documents/Add_to_TTAC/Briefing%20on%20PDMP%20Effectiveness%203rd%20revision.pdf. Accessed October 31, 2016.

[47] Patrick SW, Fry CE, Jones TF, Buntin MB. Implementation of Prescription Drug Monitoring Programs Associated with Reductions in Opioid-Related Death Rates. *Health Aff.* June 2016; 35(6). doi: 10.1377/hlthaff.2015.1496

[48] Bao Y, Pan Y, Taylor A, et al. Prescription Drug Monitoring Programs are Associated with Sustained Reductions in Opioid Prescribing by Physicians. *Health Aff.* June 2016; 35(6):1045-1051. doi: 10.1377/hlthaff.2015.1673

[49] Patrick SW, Fry CE, Jones TF, Buntin MB. Implementation Of Prescription Drug Monitoring Programs Associated With Reductions In Opioid-Related Death Rates. *Health Aff*. 2016 Jul 1; 35(7): 1324–1332. doi: 10.1377/hlthaff.2015.1496

[50] Prescription Drug Monitoring Frequently Asked Questions (FAQ). Prescription Drug Monitoring Program Training and Technical Assistance Center Web site. http://www.pdmpassist.org/content/prescription-drug-monitoring-frequently-asked-questions-faq. Accessed October 31, 2016.

[51] Dowell D, Zhang K, Noonan RK, Hockenberry JM. Mandatory Provider Review And Pain Clinic Laws Reduce The Amounts Of Opioids Prescribed And Overdose Death Rates. *Health Aff*. Oct 2016; 35(10):1876-1883. doi: 10.1377/hlthaff.2016.0448

[52] Patrick SW, Fry CE, Jones TF, Buntin MB. Implementation Of Prescription Drug Monitoring Programs Associated With Reductions In Opioid-Related Death Rates. *Health Aff*. 2016 Jul 1; 35(7): 1324–1332. doi: 10.1377/hlthaff.2015.1496

[53] Schrager A. What's killing white, middle-aged women in America? *Quartz*. December 1, 2015. http://qz.com/552760/why-are-white-middle-aged-women-dying-in-america/. Accessed October 31, 2016.

[54] Aron L, Dubay L, Waxman E, Martin S. To Understand Climbing Death Rates Among Whites, Look to Women of Childbearing Age. *Health Affairs Blog*. November 10, 2015. http://healthaffairs.org/blog/2015/11/10/to-understand-climbing-death-rates-among-whites-look-to-women-of-childbearing-age/. Accessed October 31, 2016.

[55] Schrager A. What's killing white, middle-aged women in America? *Quartz*. December 1, 2015. http://qz.com/552760/why-are-white-middle-aged-women-dying-in-america/. Accessed October 31, 2016.

[56] Committee on Advancing Pain Research, Care, and Education. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Institute of Medicine of the National Academies, Washington, DC; 2011.

[57] Opioid painkillers widely prescribed among reproductive age women [press release]. CDC; January 22, 2015. http://www.cdc.gov/media/releases/2015/p0122-pregnancy-opioids.html

[58] Centers for Disease Control and Prevention (CDC). Vital Signs: Overdoses of Prescription Opioid Pain Relievers and Other Drugs Among Women – United States, 1999-2010. *MMWR Morb Mortal Wkly Rep*. 2013;62(26);537-542.

[59] Jones H, Goler N, Werner D. Women's Health, Wellness, and Recovery: An Introduction to Women's Substance Use Disorders and Health [webinar]. May 6, 2015. In the Substance Abuse and Mental Health Services Administration's Women Matter! series. Retrieved from: http://www.samhsa.gov/women-children-families/trainings/women-matter

[60] Galea S, Vlahov D. Social determinants and the health of drug users: socioeconomic status, homelessness, and incarceration. *Public Health Reports*. 2002;117(Suppl 1):S135-S145.

[61] Substance Abuse and Mental Health Services Administration. Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders. Treatment Improvement Protocol (TIP) Series 54. HHS Publication No. (SMA) 12-4671. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011. http://store.samhsa.gov/shin/content/SMA12-4671/TIP54.pdf. Accessed June 9, 2016.

[62] Nahin, RL. Estimates of pain prevalence and severity in adults: United States, 2012. *Journal of Pain*. 2015; 16(8): 769-780. http://www.jpain.org/article/S1526-5900(15)00679-3/pdf

[63] Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *BJA: British Journal of Anaesthesia.* 2013; 111(1): 52–58. doi: 10.1093/bja/aet127

[64] Craft RM. Modulation of pain by estrogens. *Pain*. 2007;132:S3–S12. doi:10.1016/j.pain.2007.09.028

[65] Cairns BE, Gazerani P. Sex-related differences in pain. *Maturitas*. 2009;63:292–6. doi: 10.1016/j.maturitas.2009.06.004

[66] Prescription Painkiller Overdoses. CDC Vital Signs; July 2013. http://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html. Accessed September 28, 2016.

[67] McHugh RK, DeVito EE, Dodd D, et al. Gender differences in a clinical trial for prescription opioid dependence. *J Subst Abuse Treat*. 2013;45(1):38-43. doi: 10.1016/j.jsat.2012.12.007

[68] Walsh CA, Jamieson E, MacMillan H, Boyle M. Child abuse and chronic pain in a community survey of women. *J Interpers Violence*. 2007;22:1536–54. doi:10.1177/0886260507306484.

[69] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. doi: http://dx.doi.org/10.15585/mmwr.rr6501e1

[70] Why Guidelines for Primary Care Providers? CDC Web site. http://www.cdc.gov/drugoverdose/pdf/guideline_infographic-a.pdf. Accessed October 31, 2016.

[71] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. doi: http://dx.doi.org/10.15585/mmwr.rr6501e1

[72] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. doi: http://dx.doi.org/10.15585/mmwr.rr6501e1

[73] Anson P. Post-Surgical Pain Guidelines Reduce Use of Opioids. Pain News Network Web site. February 18, 2016. http://www.painnewsnetwork.org/stories/2016/2/18/guidelines-for-post-surgical-pain-discourage-use-of-opioids. Accessed October 31, 2016.

[74] Chou, R. et al. Management of Postoperative Pain: A Clinical Practice Guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. February 2016, Volume 17, Issue 2, Pages 131-157. Available at http://www.jpain.org/article/S1526-5900%2815%2900995-5/fulltext#back-bib18

[75] Committee on Advancing Pain Research, Care, and Education. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Institute of Medicine of the National Academies, Washington, DC; 2011

[76] The Office of the Assistant Secretary for Health at the U.S. Department of Health and Human Services. National Pain Strategy. The Interagency Pain Research Coordinating Committee Web site. https://iprcc.nih.gov/National_Pain_Strategy/NPS_Main.htm. Published March 2016. Accessed October 31, 2016.

[77] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep.* 2016;65(No. RR-1):1–49. doi:http://dx.doi.org/10.15585/mmwr.rr6501e1

[78] Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2015;1:CD004376

[79] Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev.* 2014;4:CD007912

[80] Hayden JA, van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. *Cochrane Database Syst Rev.* 2005;3:CD000335

[81] Weinstock J, Barry D, Petry NM. Exercise-related activities are associated with positive outcome in contingency management treatment for substance use disorders. *Addictive Behaviors*. 2008; 33(8), 1072–1075. doi: 10.1016/j.addbeh.2008.03.011

[82] McCracken LM, MacKichan F, Eccleston C. Contextual cognitive-behavioral therapy for severely disabled chronic pain sufferers: Effectiveness and clinically significant change. *European Journal of Pain*. 2007; 11(3), 314–322. doi: 10.1016/j.ejpain.2006.05.004

[83] Thorn, BE, Pence LB, Ward LC, et al. A randomized clinical trial of targeted cognitive behavioral treatment to reduce catastrophizing in chronic headache sufferers. *Journal of Pain*. 2007; 8(12), 938–949. doi: 10.1016/j.jpain.2007.06.010

[84] Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. *Journal of Studies on Alcohol and Drugs*. 2009; 70(4), 516–527.

[85] The Office of the Assistant Secretary for Health at the U.S. Department of Health and Human Services. National Pain Strategy. The Interagency Pain Research Coordinating Committee Web site. https://iprcc.nih.gov/National_Pain_Strategy/NPS_Main.htm. Published March 2016. Accessed October 31, 2016.

[86] Women and Caregiving: Facts and Figures. Family Caregiver Alliance National Center on Caregiving Web site. www.caregiver.org/women-and-caregiving-facts-and-figures. Accessed October 31, 2016.

[87] Women and Caregiving: Facts and Figures. Family Caregiver Alliance National Center on Caregiving Web site. www.caregiver.org/women-and-caregiving-facts-and-figures. Accessed October 31, 2016.

[88] Jones H, Goler N, Werner D. Women's Health, Wellness, and Recovery: An Introduction to Women's Substance Use Disorders and Health [webinar]. May 6, 2015. In the Substance Abuse and Mental Health Services Administration's Women Matter! series. Retrieved from: http://www.samhsa.gov/women-children-families/trainings/women-matter.

[89] Jones H, Goler N, Werner D. Women's Health, Wellness, and Recovery: An Introduction to Women's Substance Use Disorders and Health [webinar]. May 6, 2015. In the Substance Abuse and Mental Health Services Administration's Women Matter! series. Retrieved from: http://www.samhsa.gov/women-children-families/trainings/women-matter.

[90] Substance Abuse and Mental Health Services Administration, Advancing the Care of Pregnant and Parenting Women With Opioid Use Disorder and Their Infants: A Foundation for Clinical Guidance, Rockville, MD: Substance Abuse and Mental Health Services Administration, 2016. http://www.regulations.gov/document?D=SAMHSA-2016-0002-0001. Accessed August 8, 2016.

[91] Opioid abuse, dependence, and addiction in pregnancy. Committee Opinion No. 524. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2012;119:1070–6. http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Health-Care-for-Underserved-Women/Opioid-Abuse-Dependence-and-Addiction-in-Pregnancy#13.

[92] Tolia VN, Patrick SW, Bennett NM, et al. Increasing incidence of the neonatal abstinence syndrome in US neonatal ICUs. *New England Journal of Medicine*. 2015; 372(22), 2118-2126. doi: 10.1056/NEJMsa1500439

[93] Fajemirokun-Odudeyi O, Sinha C, Tutty S, *et al.* Pregnancy outcome in women who use opiates. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2006; 126(2): 170–175. doi: 10.1016/j.ejogrb.2005.08.010

[94] Brogly SB, Saia KA, Walley AY, Du HM, Sebastiani P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. *Am. J. Epidemiol.* 2014; 180(7): 673–686. doi: 10.1093/aje/kwu190

[95] Center for Behavioral Health Statistics and Quality. (2016). 2015 National Survey on Drug Use and Health: Detailed Tables. Substance Abuse and Mental Health Services Administration, Rockville, MD. Retrieved from: https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf

[96] Opioid Addiction 2016 Facts & Figures. American Society of Addiction Medicine Web site. http://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf. Accessed October 31, 2016.

[97] Popping Pills A Drug Abuse Epidemic. NIDA Web site. https://www.drugabuse.gov/sites/default/files/poppingpills-nida.pdf. Accessed October 31, 2016.

[98] Why do adolescents take drugs? NIDA Web site. https://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/frequently-asked-questions/why-do-adolescents-take-drugs. Updated January 2014. Accessed October 31, 2016.

[99] Medication and Counseling Treatment. SAMHSA Web site. http://www.samhsa.gov/medication-assisted-treatment/treatment. Updated September 28, 2015. Accessed October 31, 2016.

[100] Miech R, Johnston L, O'Malley PM, Keyes KM, Heard K. Prescription opioids in adolescence and future opioid misuse. *Pediatrics.* 2015; 136(5). http://pediatrics.aappublications.org/content/136/5/e1169

[101] Why do adolescents take drugs? NIDA Web site. https://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/frequently-asked-questions/why-do-adolescents-take-drugs. Updated January 2014. Accessed October 31, 2016.

[102] Research Report Series: Prescription Drug Abuse. NIDA Web site. https://www.drugabuse.gov/sites/default/files/prescriptiondrugrrs_11_14.pdf. Accessed October 31, 2016.

[103] Sullivan MA. Prescription Opioid Addiction and Chronic Pain in Older Adults [webinar]. Providers' Clinic Support System for Opioid Therapies Web site. http://pcss-o.org/wp-content/uploads/2014/10/Prescription-Opioid-Addiction-and-Chronic-Pain-in-Older-Adults.pdf. Accessed October 31, 2016.

[104] Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. *JAMA*. 2002;287(3):337–344. doi:10.1001/jama.287.3.337

[105] Campbell C, Weisner C, LeResche L, et al. Age and gender trends in long-term opioid analgesic use for noncancer pain. *American Journal of Public Health*. 2010; 100(12):2541–47. doi: 10.2105/AJPH.2009.180646

[106] Sullivan MA. Prescription Opioid Addiction and Chronic Pain in Older Adults [webinar]. Providers' Clinic Support System for Opioid Therapies Web site. http://pcss-o.org/wp-content/uploads/2014/10/Prescription-Opioid-Addiction-and-Chronic-Pain-in-Older-Adults.pdf. Accessed October 31, 2016.

[107] Carson EA. Prisoners in 2014. Bureau of Justice Statistics Web site. http://www.bjs.gov/content/pub/pdf/p14.pdf. Published September 2015. Accessed October 31, 2016.

[108] Mumola CJ, Karberg JC. Drug Use and Dependence, State and Federal Prisoners, 2004. Bureau of Justice Statistics Special Report: October 2006. U.S. Department of Justice. Retrieved from: http://www.bjs.gov/content/pub/pdf/dudsfp04.pdf

[109] Mitchel SG, Kelly SM, Brown BS, et al. Incarceration and opioid withdrawal: the experiences of methadone patients and out-of-treatment heroin users. *J Psychoactive Drugs*. 2009 Jun; 41(2): 145–152. doi: 10.1080/02791072.2009.10399907

[110] Mitchel SG, Kelly SM, Brown BS, et al. Incarceration and opioid withdrawal: the experiences of methadone patients and out-of-treatment heroin users. *J Psychoactive Drugs*. 2009 Jun; 41(2): 145–152. doi: 10.1080/02791072.2009.10399907

[111] Which States Have 911 Good Samaritan Laws and/or Naloxone Access Laws? Drug Policy Alliance Web site. http://www.drugpolicy.org/resource/which-states-have-911-good-samaritan-laws-andor-naloxone-access-laws. Published January 25, 2016. Accessed October 31, 2016.

[112] Mahoney, C. FDA Supports Greater Access to Naloxone to Help Reduce Opioid Overdose Deaths. FDA Voices Blog; August 10, 2016. http://blogs.fda.gov/fdavoice/index.php/2016/08/fda-supports-greater-access-to-naloxone-to-help-reduce-opioid-overdose-deaths/. Accessed January 27, 2017.

[113] Sumner SA, Mercardo-Crespo MC, Spelke MB, at al. Use of naloxone by emergency medical services during opioid drug overdose resuscitation efforts. Prehospital Emergency Care. 2016; 20(2): 220-225. http://www.tandfonline.com/doi/full/10.3109/10903127.2015.1076096

[114] Medication and Counseling Treatment. Substance Abuse and Mental Health Services Administration Web site. http://www.samhsa.gov/medication-assisted-treatment/treatment. Updated September 28, 2015. Accessed October 31, 2016.

[115] Addiction Treatment Forum. MAT with Methadone or Burprenorphine: Assessing the Evidence for Effectiveness. February 10, 2014. http://atforum.com/2014/02/mat-with-methadone-or-buprenorphine-assessing-the-evidence-for-effectiveness/. Accessed October 31, 2016.

[116] Fullerton CA, Kim M, Thomas CP, et al. Medication-assisted treatment with methadone: assessing the evidence. *Psychiatric Services*. 2014 Feb 1;65(2):146-57. doi: 10.1176/appi.ps.201300235.

[117] Thomas CP, Fullerton CA, Kim M, et al. Medication-assisted treatment with buprenorphine: Assessing the Evidence. *Psychiatric Services*. 2014 Feb 1;65(2):158-70. doi: 10.1176/appi.ps.201300256

[118] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49. doi: http://dx.doi.org/10.15585/mmwr.rr6501e1

[119] Nurse Practitioners in Women's Health. Position Statement: Prevention and Management of Opioid Misuse and Opioid Use Disorder Among Women Across the Lifespan. Available at: https://www.npwh.org/lms/filebrowser/file?fileName=NPWH%20Opioid%20Position%20Statement%20for%20public%20comment.pdf

[120] Addiction Experts Battle Stigma Attached to Medication-Assisted Treatment. National Council on Alcoholism and Drug Dependence Web site. https://www.ncadd.org/blogs/in-the-news/addiction-experts-battle-stigma-attached-to-medication-assisted-treatment. Published May 18, 2016. Accessed October 31, 2016.

[121] Knudsen HK, Abraham AJ, Roman PM. Adoption and implementation of medications in addiction treatment programs. *J Addict Med* 2011; 5:21-27.

[122] Center for Substance Abuse Treatment. Chapter 13 - Medication-Assisted Treatment for Opioid Addiction During Pregnancy. In: Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Rockville, MD: Substance Abuse and Mental Health Services Administration (US); 2005. (Treatment Improvement Protocol (TIP) Series, No. 43.) http://www.ncbi.nlm.nih.gov/books/NBK64148/

[123] Center for Substance Abuse Treatment. Chapter 13 - Medication-Assisted Treatment for Opioid Addiction During Pregnancy. In: Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Rockville, MD: Substance Abuse and Mental Health Services Administration (US); 2005. (Treatment Improvement Protocol (TIP) Series, No. 43.) http://www.ncbi.nlm.nih.gov/books/NBK64148/#

[124] HHS awards $94 million to health centers to help treat the prescription opioid abuse and heroin epidemic in America [news release]. U.S. Department of Health and Human Services; March 11, 2016. https://www.hhs.gov/about/news/2016/03/11/hhs-awards-94-million-to-health-centers.html. Accessed January 27, 2017.

[125] Trump Administration awards grants to states to combat opioid crisis [news release]. U.S. Department of Health and Human Services. April 19, 2017. https://www.hhs.gov/about/news/2017/04/19/trump-administration-awards-grants-states-combat-opioid-crisis.html. Accessed July 12, 2017.

[126] Lenardson JD, Gale JA. Distribution of Substance Abuse Treatment Facilities Across the Rural – Urban Continuum. Maine Rural Health Research Center; Working Paper #35. https://muskie.usm.maine.edu/Publications/rural/wp35b.pdf. Published October 2007. Accessed October 31, 2016.

[127] Americans Concerned About Lack of Access to Opioid Addiction Treatment. New Beginnings Drug & Alcohol Rehabilitation Web site. http://www.newbeginningsdrugrehab.org/prescription-drugs/americans-concerned-about-lack-of-access-to-opioid-addiction-treatment/. Published May 9, 2016. Accessed October 31, 2016.

[128] Jones CM, Campopiano M, Baldwin G, and McCance-Katz E. National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment. *Am J Public Health*. 2015 Aug; 105(8): e55-63. doi: 10.2105/AJPH.2015.302664

[129] Dick AW, Pacula RL, Gordon AJ, et al. Growth in buprenorphine waivers for physicians increased potential access to opioid agonist treatment, 2002-11. *Health Aff (Millwood)*. 2015 Jun; 34(6): 1028-34. doi: 10.1377/hlthaff.2014.1205

[130] Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment. *American Journal of Public Health*. 2015;105(8):e55-e63. doi: 10.2105/AJPH.2015.302664

[131] Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment. *American Journal of Public Health*. 2015;105(8):e55-e63. doi: 10.2105/AJPH.2015.302664

[132] Substance Abuse and Mental Health Services Administration, National Survey of Substance Abuse Treatment Services (N-SSATS): 2014. Data on Substance Abuse Treatment Facilities. BHSIS Series S-79, HHS Publication No. (SMA) 16-4963. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2015.

[133] Back, SE, Payne RL, Simpson AN, Brady, KT. Gender and prescription opioids: findings from the National Survey on Drug Use and Health. *Addict Behav*. 2010 Nov; 35(11): 1001-1007. doi: 10.1016/j.addbeh.2010.06.018

[134] Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in women. *The Psychiatric clinics of North America* 33.2 (2010): 339–355. doi: 10.1016/j.psc.2010.01.004

[135] Substance Use in Women. National Institute on Drug Abuse website https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/summary. Updated July 2015. Accessed May 27, 2016.

[136] Werner, D., Young, N.K., Dennis, K, & Amatetti, S. Family-Centered Treatment for Women with Substance Use Disorders – History, Key Elements and Challenges. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, 2007.

[137] National Drug Control Strategy. Office of National Drug Control Policy website https://www.whitehouse.gov/sites/default/files/ondcp/ndcs2011.pdf. Accessed May 27, 2016.

[138] Women and Treatment. Office of National Drug Control Policy website https://www.whitehouse.gov/ondcp/women-treatment. Accessed May 27, 2016.

[139] Drug courts. County Health Rankings & Roadmaps website http://www.countyhealthrankings.org/policies/drug-courts. Updated October 19, 2016. Accessed October 31, 2016.

[140] Legal Action Center. Confronting the Epidemic: The Case for Eliminating Barriers to Medication-Assisted Treatment of Heroin and Opioid Addiction. March 2015. http://lac.org/wp-content/uploads/2014/07/LAC-The-Case-for-Eliminating-Barriers-to-Medication-Assisted-Treatment.pdf. Accessed October 31, 2016.

[141] Legal Action Center. Confronting the Epidemic: The Case for Eliminating Barriers to Medication-Assisted Treatment of Heroin and Opioid Addiction. March 2015. http://lac.org/wp-content/uploads/2014/07/LAC-The-Case-for-Eliminating-Barriers-to-Medication-Assisted-Treatment.pdf. Accessed October 31, 2016.

[142] Implementation of the Mental Health Parity and Addiction Equity Act (MHPAEA). SAMHSA web site. https://www.samhsa.gov/health-financing/implementation-mental-health-parity-addiction-equity-act

[143] The Center for Medicaid and CHIP Services. Medication Assisted Treatment for Substance Use Disorders [informational bulletin]. July 11, 2014. https://www.medicaid.gov/Federal-Policy-Guidance/Downloads/CIB-07-11-2014.pdf. Accessed October 31, 2016.

[144] Meier B, Goodnough A. New Ways to Treat Pain Meet Resistance. *New York Times*. June 22, 2016. http://www.nytimes.com/2016/06/23/business/new-ways-to-treat-pain-without-opioids-meet-resistance.html?_r=0. Accessed October 31, 2016.

[145] HHS takes strong steps to address opioid-drug related overdose, death and dependence [news release]. U.S. Department of Health & Human Services; March 26, 2015. http://www.hhs.gov/about/news/2015/03/26/hhs-takes-strong-steps-to-address-opioid-drug-related-overdose-death-and-dependence.html. Accessed September 28, 2016.

[146] AAFP Supports Turn the Tide Rx Campaign to End Opioid Abuse. August 9, 2016. American Academy of Family Physicians Web site. http://www.aafp.org/news/health-of-the-public/20160809turntide.html. Accessed October 31, 2016.

[147] Treatment Options. Turn the Tide Rx Web site. http://turnthetiderx.org/treatment/#. Accessed October 31, 2016.

[148] Opioid Prescribing Courses for Health Care Providers. SAMHSA Web site. http://www.samhsa.gov/medication-assisted-treatment/training-resources/opioid-courses. Updated February 16, 2016. Accessed October 31, 2016.

[149] Ohio Osteopathic Association Practice Solutions Program. Ohio Offers Online Training for New Acute Pain Prescribing Guidelines. June 23, 2016. http://www.ooanet.org/aws/OOSA/pt/sd/news_article/124063/_PARENT/psp_layout_details/false. Accessed October 31, 2016.

[150] The White House. Fact Sheet: Obama Administration Announces Additional Actions to Address the Prescription Opioid Abuse and Heroin Epidemic. March 29, 2016. https://www.whitehouse.gov/the-press-office/2016/03/29/fact-sheet-obama-administration-announces-additional-actions-address. Accessed October 31, 2016.

[151] The White House. Fact Sheet: Obama Administration Honors Americans Leading Efforts to Stop the Prescription Opioid and Heroin Epidemic. April 29, 2016. https://www.whitehouse.gov/the-press-office/2016/04/29/fact-sheet-obama-administration-honors-americans-leading-efforts-stop. Accessed October 31, 2016.

[152] Naloxone. National Alliance for Model State Drug Laws website. http://www.namsdl.org/naloxone.cfm. Accessed July 12, 2017.