Summer 2018

Volume 34, Number 2

American Academy of Addiction Psychiatry

Translating Science. Transforming Lives.

The Official Newsletter of the American Academy of Addiction Psychiatry

President's Column - Women and Opioid Use Disorders

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In 2016, more than 11 million Americans misused prescription opioids and more than 42,000 died of opioid poisonings – an increase of approximately 28% over 2015. Fatal overdoses on fentanyl and other synthetic opioids more than doubled from 9,580 in 2015 to 19,413 in 2016. Deaths from heroin increased 20% and those from other opioid prescription drugs increased by 4%.[1] In spite of this, there remains a wide treatment implementation gap with only a minority gaining access to evidence based treatment including medication for opioid use disorders (OUD).

The changing and complex nature of this epidemic is a critical consideration for implementing and disseminating evidence-based policies and practices and closing the treatment implementation gap. Converging data reveal an emerging epidemic in women, highlighting some of the unique treatment needs of women with opioid use disorders as well as their children and families. Women are more likely to be prescribed opioids and more likely to use them for a longer period of time overall.[2] Women have experienced sustained significant increases in heroin use over the past four decades such that by 2010, women were using heroin at rates similar to men[3] with a doubling of heroin use among women between 2002 and 2013. While more men die from prescription opioid overdoses than women, since 1999 deaths from prescription opioid overdoses increased 471% among women compared with 218% in men. Approximately 48,000 women died of prescription painkiller overdoses between 1999 and 2010. For every woman who dies of a prescription overdose, at least 30 women go to the emergency department for prescription opioid misuse or poisonings. The death rate from heroin overdoses among women is twice that of men.[4]

Additional data on deaths from prescription opioid overdoses show that women between 45 and 54 years have the highest risk of dying from a prescription opioid overdose. In addition, women between 25 and 54 years are more likely than any other age group to visit an emergency department with opioid misuse or OUD. Non-Hispanic white and Native American or Alaskan Native women have the highest risk of dying from opioid poisonings.[5]

With the increasing prescription opioid use among women, there has been a corresponding increase of use in women of reproductive age. The 2017 National Survey of Drug Use and Health reported that 2.3% of women of reproductive age reported non-medical opioid use in the last 30 days and 0.8% of pregnant women reported non-

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medical opioid use in the past 30 days.[6] Among pregnant women, one 2014 study showed that 0.4% had opioid dependence or misuse at the time of delivery.[7]

Because of this increase in opioid use and OUD among women of reproductive age,[8] there has also been an unprecedented rise in the number of infants born with neonatal opioid withdrawal syndrome (NOWS). Nationwide, this increase in NOWS affected 5-6 infants for each 1,000 live births in 2015 compared with 1 infant per 1,0000 live births in 2000.[9,10] While these are national statistics, some states in Appalachia and New England where OUD is most prevalent have rates of NOWS that have exceeded 30 per 1000 live births.[10] In West Virginia, the 2017 prevalence of NOWS was 5.12% of all live births or 10 times the national rate. A 2017 article in JAMA Pediatrics reported the sharp increase in both maternal opioid use and infant NOWS between 2004 and 2013 with the steepest increases in rural compared with urban areas.[11]

In order to narrow the treatment gap for women with OUDs, it will be important to address significant, specific clinical and demographic characteristics of women with OUDs. Women with OUDs have higher rates of co-occurring psychiatric disorders, especially depression, anxiety, and post-traumatic stress disorder (PTSD). There is converging data demonstrating that women have an accelerated course of addiction to opioids (i.e., telescoping course). Treatment barriers for women with OUDs include that women are more likely than their male counterparts to have co-occurring psychiatric disorders and histories of trauma, a partner who is using opioids or other drugs, financial vulnerability, dependent children living with them, minimal social support, and an intense level of stigma and discrimination.[12]

While some of these characteristics may be similar to gender differences observed for other substance use disorders, the escalating rate of OUD in women is distinct in a number of ways. The first is that the death rate from opioid poisonings is unprecedented and rising among women. Given the prevalence of depression, anxiety, and PTSD in women, among these deaths, it is likely that an excess of 10% represents intentional suicide. Women with prescription OUD are more likely to have chronic pain, psychiatric comorbidity, and decreased functional status.[13] Gender responsive treatment for women with OUD requires attention to integrated treatment of co-occurring psychiatric disorders such as anxiety, depression, and PTSD. In addition, attention to social circumstances that include financial dependence, dependent children, and vulnerability to partners who use drugs and alcohol is also critical to initiating, engaging and retaining women with OUD in evidence based treatment.

Women of reproductive age who have OUD and become pregnant have limited access to evidence based pregnancy and post-partum treatment for themselves and their infants. Instead, in many instances, they face stigma and discrimination and fear of losing custody of their children. The rate of OUD in pregnant women has increased and there is currently an unprecedented rate of neonatal opioid withdrawal syndrome among infants nationwide. There is great need for an integrated approach to provide both prenatal care and evidence based treatment for OUD in pregnancy for which the standard is stabilization on agonist medication (i.e., either methadone or buprenorphine).[14] In addition to agonist treatment and prenatal care, post-partum treatment of the mother and newborn infant will need to extend beyond acute treatment of NOWS. The current epidemic requires that our field innovate the care model for women and infants affected by OUD and set new standards for best practices for the treatment of the maternal-infant dyad. Such consideration should result in new models of care that might include housing stabilization, parent skills coaching, home visits to mother and infant, among other known effective interventions that target increasing the health and well-being of vulnerable mothers and their newborns.

Solutions to the current opioid epidemic will require that we address both the clinical and social needs of specific populations of patients with OUD in order to provide and retain patients in evidence-based treatment. For women with OUD, gender-responsive care targeted at the specific needs of women will be critical to early treatment initiation as well as engagement and retention in treatment. ■

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Science Leading the Way to Help Curb the Opioid Crisis

The opioid crisis claimed over 42,000 lives in our country in 2016.[1] Beyond the deaths from overdose, over 2 million people live with an opioid use disorder.[2] Entwined with opioid misuse and addiction is the even larger problem of pain in America: 25 million people in the US suffer from pain on a daily basis.[3] Fortunately, the dire scope of these crises has prompted Congress to dedicate funds to conduct the science necessary to find real and workable solutions. In June, the Helping to End Addiction Long-term (HEAL) Initiative was launched, using $500 million Congress added to the NIH budget in fiscal year 2018. The money will fund several ambitious NIH projects, falling under two broad umbrellas: improving opioid addiction treatment and enhancing pain management.[4]

The search for new ways of treating opioid use disorder (OUD), including new OUD medications, improved formulations of existing medications, and new overdose-reversal tools, is already a priority at NIDA. With the HEAL funds, the Focused OUD Medications Development Research Project will be able to accelerate this process. It will support a series of high-impact studies with the aim of producing roughly 15 investigational new drugs and then, ideally, around five New Drug Applications to be submitted to the Food and Drug Administration. Meanwhile, the NIDA Clinical Trials Network Opioid Research Enhancement Project will use HEAL funds to expand the ability to conduct studies on new medications and new ways of implementing treatments effectively.[5]

Although more treatment options for OUD are badly needed, one of the factors that has led to the escalating crisis is the failure to deliver existing treatments. Because of infrastructure barriers and misinformation still perpetuated around medications like buprenorphine and methadone (e.g., the myth that being maintained on an agonist is no different from a new addiction), medication-assisted treatment (MAT) remains grossly underutilized,[6] despite being repeatedly shown to be highly effective at reducing opioid use and associated outcomes including overdose. Thus, a few HEAL projects will center on finding models of better delivering existing treatments.

In collaboration with the Substance Abuse and Mental Health Services Administration, NIDA will conduct a major pilot project called the HEALing Communities Study. In up to three hard-hit communities, this study will apply an integrated set of interventions to address the opioid problem at each of several stages: prevention, screening, engagement in MAT, retention in treatment, and recovery supports. Lessons learned from this project can then be applied in communities across the nation. In addition, the Justice Community Opioid Innovation Network will study ways to better deliver OUD treatment in justice settings; and a pilot study already underway at the National Institute of Child Health and Human Development is exploring best practices for treating neonatal opioid withdrawal syndrome (NOWS), called ACT NOW, will be expanded.

Because it began—and for many individuals, still begins—with opioid pain medications, the problem of opioid addiction cannot be disentangled from the problem of pain. All patients with pain, whether from dental procedures or surgery or any other condition, need more effective and safer options than what is currently available. Thus, a large portion of the HEAL funding is going to support a series of pain-related research initiatives under the direction of the National Institute of Neurological Disorders and Stroke. Projects will seek objective signatures of both acute and chronic pain and intensify the ongoing search for new, nonaddictive pain treatments, as well as finding ways of speeding new treatments through the drug-approval pipeline.

The rapidly evolving opioid and pain crises in America demand science-driven solutions. Good science requires an investment in resources, which is why the HEAL Initiative is such a promising development. We can hope that in the next few years we will see many promising new advances in addiction and pain treatment as a result of this initiative, as well as more effective modes of delivering them. ■

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We hope that our members and *The AJA* readers will recognize the opportunities offered by *The AJA* to publish your clinical and research work. *The AJA* continues to prioritize Review Articles and to solicit Special Issue collections of manuscripts. Our Special Issue last year on ethnic diversity in the genetics of alcoholism (co-edited by Drs. Karen Chartier, and Drs. Michie and Victor Hesslebrock), had a tremendous response in clinician views and scientific citations. We welcome our AAAP members to submit their own outlines of Special Issues, which should include the topics for the proposed papers and related authors, who ideally have also been recruited and tentatively agreed to submit the 8-15 papers needed for such a Special Issue. Our emails for contacting us about such Special Issue proposals are: kosten@bcm.edu and cdomingo@bcm.edu.

We, as clinicians and researchers, can help journalists and the visibility of AAAP and *The AJA* by proactively promoting the "news worthiness" of our work in clear, succinct language that highlights the value and application of our findings to everyday life. When a clear press release about our work lands in a journalist's inbox, we can, in turn, exponentially increase the likelihood of our news piece being chosen for further media exposure over hundreds of other potential leads on that day. Keep in mind that news can be defined in a single sentence:

"News is something which will interest a large part of the community and which has never been brought to their attention." Charles Dane, Editor of New York Sun, 1920

Finally, we would like to take this opportunity to extend a most sincere THANK YOU to all the AJA's peer reviewers who continue to make outstanding contributions to the life of our AAAP flagship Journal. They have markedly facilitated the growth and strength of Addiction Psychiatry as much as the many authors, both within and outside the U.S., who continue to submit their research findings for publication in *The AJA*. We appreciate the opportunity to publish your work and to educate our growing AAAP membership. ■

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of using research data and emphasizing the death rate. We had a tremendously high early discharge rate among patients with opioid use disorders. These patients were not staying in an outpatient setting; they were bringing drugs onto campus. We reviewed the literature on buprenorphine/naloxone and extended-release naltrexone and decided to go down this path, which was the basis of COR-12.[3] At first, the only discussion was about adding these two medications. However, we determined that if that is all we do, we would not be successful in addressing this problem.

Just because we recommend medication-assisted treatment (MAT) does not mean the patient will take it. We have just under 1/3 of patients who refuse medications. We have just over 1/3 of patients on extended-release naltrexone and just under 1/3 of patients on buprenorphine/naloxone. We did a study that we have submitted for publication which is a 6-month outcome on these groups. What we found was no statistical difference among the 3 groups.

My goal with COR-12 primarily is engagement. To have engagement in an outpatient setting that is long enough for a patient to get into good recovery and reach a point where the need for medication becomes less of an issue. In our study, at up to 6 months, if patients are talking about discontinuing MAT, it usually results in relapse. Therefore, we want them to stay on MAT for longer than 6 months, but for how long we are not sure. My job as chief medical officer is to figure out how we can improve outcomes for the people who come to us for help. COR-12 is a great example of that. ■

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mindfulness training. Furthermore, ayahuasca intake also led to a significant increase in "decentering," or "the capacity to observe one's thoughts and emotions as temporary events of the mind," which is another core component of mindfulness. These findings suggest that ayahuasca use may have therapeutic potential through increasing mindfulness capacities.[15]

Liester and colleagues[10] have described several hypotheses for potential mechanisms by which ayahuasca use may be useful in the treatment of addictions. One suggested mechanism is that ayahuasca use reduces dopamine levels in the mesolimbic pathway, thereby reducing activity in the reward pathway in the brain. A second hypothesis is that the reduced dopamine signaling interferes with synaptic plasticity that is associated with learning and development and maintenance of addiction. A third hypothesis suggests that ayahuasca use contributes to improved decision-making ability. The final hypothesis is that the ayahuasca-induced transcendent experiences allow the user to overcome problematic substance use.[10]

These recent findings suggest that further research is needed into the potential efficacy of ayahuasca in the treatment of psychiatric and substance use disorders as well as to clarify risks of use. Furthermore, the increasing discussion of ayahuasca in the media and the growing popularity of its consumption are indications that clinicians must be prepared to discuss this substance with patients. ■

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