

Opioids: Overprescribing, alternatives, and clinical guidance

PART 2

Optimal management of pregnant women with opioid misuse

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Ob.Gyn. News

More deliveries now include opioid use disorder

The prevalence of opioid use disorder more than quadrupled among pregnant women at labor and delivery from 1999 to 2014, according to the Centers for Disease Control and Prevention

Richard Franki

The national prevalence of opioid use disorder increased by 333% as it went from 1.5 cases per 1,000 delivery hospitalizations in 1999 to 6.5 cases per 1,000 in 2014. At the state level, there were significant increases in all 28 states with data available for at least 3 consecutive years during the study period, Sarah C. Haight, MPH, and her associates at the CDC in Atlanta said in the *Morbidity and Mortality Weekly Report*.

Average annual rate changes for those states ranged from a low of 0.01 per 1,000 delivery hospitalizations per year in California to 5.37 per year in Vermont, with the national rate change coming in at 0.39 per year. Of the 14 states with data available in 1999, Iowa had the lowest rate at 0.1 per 1,000 deliveries and Maryland had the highest at 8.2. In 2014, when data were available for 26 states and the District of Columbia, the highest rate was Vermont's 48.6 per 1,000 deliveries and the lowest was 0.7 in Washington, D.C., the investigators reported.

Although "increasing trends might represent actual increases in prevalence or improved screening and diagnosis," Ms. Haight and her associates added that "these estimates also correlate with state opioid prescribing rates in the general population. West Virginia, for example, had a prescribing rate estimated at 138 opioid prescriptions per 100 persons in 2012."

"These findings illustrate the devastating impact of the opioid epidemic on families across the U.S., including on the very youngest," said CDC Director Robert R. Redfield, MD. "Untreated opioid use disorder during pregnancy can lead to heartbreaking



results. Each case represents a mother, a child, and a family in need of continued treatment and support."

Data for the analysis came from the Agency for Healthcare Research and Quality's National Inpatient Sample and State Inpatient Databases. ■

SOURCE: Haight SC, et al. *MMWR*. 2018 Aug 10;67(31):845-849.

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Obstetric patients with opioid use disorder fare well with medication-assisted treatment

Of the 78% of pregnant patients on opioids who chose detoxification, 152 (53%) fully detoxified

Kari Oakes

A prospective study of pregnant women with opioid use disorder showed good success with tapering or discontinuation of medication-assisted treatment (MAT) for women who wished to reduce or eliminate opioids while pregnant.

In related work, naltrexone showed promise for MAT in pregnancy, with rapid fetal clearance and no neonatal abstinence syndrome (NAS) seen in women who were adherent to naltrexone.

Presenting early experiences from an obstetric clinic dedicated to care of women with opioid use disorder (OUD), Craig Towers, MD, said that the clinic began seeing patients in November, 2016. "Eastern Tennessee has a high rate of opioid use disorder," so the clinic at the University of Tennessee, Knoxville, fills an unmet need, he said, speaking during a poster session at the meeting sponsored by the Society for Maternal-Fetal Medicine.

Women who enroll at the clinic are offered MAT; those who are stable on MAT and adherent to prenatal care also are offered the choice to taper from MAT and detoxify, said Dr. Towers, professor in the division of maternal-fetal medicine in the department of obstetrics and gynecology at the University of Tennessee, Knoxville.

The prospective observational cohort study found that, of a total of 367 compliant patients, 286 (78%) chose opioid tapering/detoxification, and of these, 152 (53%) did detoxify fully. Of these patients, 126 (83%) were taking no opioids at delivery, and their infants experienced no NAS.

At the time of delivery, 26 patients (17%) were taking opioids at delivery; 18 were back on MAT, and 8 were using illicit opioids. A total of 116 patients chose to continue MAT, whether they stayed on the regimen or converted back to stable MAT doses after beginning to taper.

Another option offered women at the OUD-dedicated obstetric clinic is the use of the Bridge device, a percutaneous nerve field stimulator, for OUD. Dr. Tower said that, in early use in 14 patients, the Bridge was successful in helping women transition off opioids completely in 10 (71%) patients.

About the larger study, Dr. Towers said, "This is the first study

to prospectively report outcome data on a designated OUD clinic that offers detoxification during pregnancy.

"With a structured program that includes behavioral health and offers the option of detoxification, fetal risks are negligible, relapse rates by delivery are low, and NAS rates are greatly decreased," wrote Dr. Towers and colleagues in the abstract accompanying the study.

In a related poster presentation, Dr. Towers reported outcomes for a subset of pregnant women with OUD who received naltrexone as MAT. Previously, said Dr. Towers, retrospective work showed no significant harm using naltrexone, which is one of the three approved options for MAT to manage OUD, along with buprenorphine and methadone. Naltrexone has the advantage of helping reduce cravings.

Of the 108 patients, 82 (76%) remained on naltrexone until delivery; in these pregnancies, there were no cases of NAS. However, among the 26 pregnancies in which women stopped taking naltrexone before delivery, there were 6 (23%) NAS cases.

Fifty-one patients were started on naltrexone before 24 weeks' gestation, and of those patients, no changes were seen with fetal monitoring. There were no instances of spontaneous abortion or intrauterine demise in any participants.

The investigators tracked gestational age at the point of full detoxification and gestational age at the point naltrexone was started. Additionally, fetal response to naltrexone and maternal and neonatal outcomes were recorded.

"This is the first prospective study and largest to date on the use of naltrexone in pregnancy," Dr. Towers and his colleagues wrote in the poster accompanying the presentation. "These data demonstrate that naltrexone MAT is a viable option for managing OUD in pregnancy." ■

Dr. Towers reported no conflicts of interest and no outside sources of funding.

SOURCE: Towers C, et al. SMFM 2019, Posters 141 & 142.

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Treating the pregnant patient with opioid addiction

Women are increasingly the face of the opioid epidemic, says this addiction expert, and not receiving the care they need. Here, how to help close the gap on treatment.

Q&A with Mishka Terplan, MD

OBG MANAGEMENT: How has the opioid crisis affected women in general?

Mishka Terplan, MD: Everyone is aware that we are experiencing a massive opioid crisis in the United States, and from a historical perspective, this is at least the third or fourth significant opioid epidemic in our nation's history.¹ It is similar in some ways to the very first one, which also featured a large proportion of women and also was driven initially by physician prescribing practices. However, the magnitude of this crisis is unparalleled compared with prior opioid epidemics.

There are lots of reasons why women are overrepresented in this crisis. There are gender-based differences in pain—chronic pain syndromes are more common in women. In addition, we have a gender bias in prescribing opioids and prescribe more opioids to women (especially older women) than to men. Cultural differences also contribute. As providers, we tend not to think of women as people who use drugs or people who develop addictions the same way as we think of these risks and behaviors for men. Therefore, compared with men, we are less likely to screen, assess, or refer women for substance use, misuse, and addiction. All of this adds up to creating a crisis in which women are increasingly the face of the epidemic.

OBG MANAGEMENT: What are the concerns about opioid addiction and pregnant women specifically?

Dr. Terplan: Addiction is a chronic condition, just like diabetes or depression, and the same principles that we think of in terms of optimizing maternal and newborn health apply to addiction. Ideally, we want, for women with chronic diseases to have stable disease at the time of conception and through pregnancy. We know this maximizes birth outcomes.

Unfortunately, there is a massive treatment gap in the United States. Most people with addiction receive no treatment. Only 11% of people with a substance use disorder report receipt of treatment. By contrast, more than 70% of people with

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Keypoints

- Only up to one-quarter of pregnant women with opioid addiction receive treatment for that addiction.
- Untreated addiction is a serious medical condition associated with preterm delivery and low-birth weight infants; treated addiction is associated with term delivery and normal-weight infants.
- Medically supervised withdrawal is not recommended during pregnancy. In addition to appropriate prenatal care, the standard treatment of opioid use disorder in pregnancy is pharmacotherapy with either methadone or buprenorphine plus behavioral counseling.
- As with many other medications, fetal dependence may occur with methadone or buprenorphine, resulting in neonatal abstinence syndrome (NAS) at birth. NAS is treatable, time-limited, and not associated with long-term harms.
- ObGyns should express empathy for pregnant women with addiction, in order to counter the discrimination these women experience from society and other health care providers.

depression, hypertension, or diabetes receive care. This treatment gap is also present in pregnancy. Among use disorders, treatment receipt is highest for opioid use disorder; however, nationally, at best, 25% of pregnant women with opioid addiction receive any care.

In other words, when we encounter addiction clinically, it is often untreated addiction. Therefore, many times providers will have women presenting to care who are both pregnant and have untreated addiction. From both a public health and a clinical practice perspective, the salient distinction is not between people with addiction and those without but between people with treated disease and people with untreated disease.

Untreated addiction is a serious medical condition. It is associated with preterm delivery and low birth weight infants. It is associated with acquisition and transmission of HIV and hepatitis C. It is associated with overdose and overdose death. By contrast, treated addiction is associated with term delivery and normal weight infants. Pharmacotherapies for opioid use disorder stabilize the intrauterine environment and allow for normal fetal growth. Pharmacotherapies for opioid use disorder help to structure and stabilize the mom's social circumstance, providing

a platform to deliver prenatal care and essential social services. And pharmacotherapies for opioid use disorder protect women and their fetuses from overdose and from overdose deaths. The goal of management of addiction in pregnancy is treatment of the underlying condition, treating the addiction.

OBG Management: What should the ObGyn do when faced with a patient who might have an addiction?

Dr. Terplan: The good news is that there are lots of recently published guidance documents from the World Health Organization,² the American College of Obstetricians and Gynecologists (ACOG),³ and the Substance Abuse and Mental Health Services Administration (SAMHSA),⁴ and there have been a whole series of trainings throughout the United States organized by both ACOG and SAMHSA.

There is also a collaboration between ACOG and the American Society of Addiction Medicine (ASAM) to provide buprenorphine waiver trainings specifically designed for ObGyns. Check both the ACOG and ASAM pages for details. I encourage every provider to get a waiver to prescribe buprenorphine. There are about 30 ObGyns who are also board certified in addiction medicine in the United States, and all of us are more than happy to help our colleagues in the clinical care of this population, a population that all of us really enjoy taking care of.

Although care in pregnancy is important, we must not forget about the postpartum period. Generally speaking, women do quite well during pregnancy in terms of treatment. Postpartum, however, is a vulnerable period, where relapse happens, where gaps in care happen, where child welfare involvement and sometimes child removal happens, which can be very stressful for anyone much less somebody with a substance use disorder. Recent data demonstrate that one of the leading causes of maternal mortality in the US is from overdose, and most of these deaths occur in the postpartum period.⁵ Regardless of what happens during pregnancy, it is essential that we be able to link and continue care for women with opioid use disorder throughout the postpartum period.

OBG MANAGEMENT: How do you treat opioid use disorder in pregnancy?

Dr. Terplan: The standard of care for treatment of opioid use disorder in pregnancy is pharmacotherapy with either methadone or buprenorphine (TABLE) plus behavioral counseling—ideally, co-located with prenatal care. The evidence base for pharmacotherapy for opioid use disorder in pregnancy is supported by every single professional society that has ever issued guidance on this, from the World Health Organization to ACOG, to ASAM, to the Royal College in the UK as well as Canadian and Australian obstetrics and gynecology societies; literally every single professional society supports medication.

The core principle of maternal fetal medicine rests upon the fact that chronic conditions need to be treated and that treated

TABLE My preferred pharmacologic regimen for managing opioid addiction during pregnancy

Day 1	<ul style="list-style-type: none"> • Assess withdrawal using clinical opiate withdrawal scale (COWS) • Begin medication when COWS score ≥ 8 <ul style="list-style-type: none"> —COWS score 8–10: Give buprenorphine 2 mg^a —COWS score >10: Give buprenorphine 4 mg • Repeat COWS every 1–2 hours and give additional buprenorphine when COWS score ≥ 8 • Typical Day 1 total dosage = 6–8 mg
Day 2	<ul style="list-style-type: none"> • Assess withdrawal using COWS • Give total Day 1 dosage of buprenorphine • Assess withdrawal using COWS 1 hr later and give additional buprenorphine dosage based on COWS score • Typical Day 2 dose = 12–16 mg • If patient is stable, write up to a 7-day prescription for buprenorphine

^aBuprenorphine regulation varies by state.

illness improves birth outcomes. For both maternal and fetal health, treated addiction is way better than untreated addiction. One concern people have regarding methadone and buprenorphine is the development of dependence. Dependence is a physiologic effect of medication and occurs with opioids, as well as with many other medications, such as antidepressants and most hypertensive agents. For the fetus, dependence means that at the time of delivery, the infant may go into withdrawal, which is also called neonatal abstinence syndrome. Neonatal abstinence syndrome is an expected outcome of in-utero opioid exposure. It is a time-limited and treatable condition. Prospective data do not demonstrate any long-term harms among infants whose mothers received pharmacotherapy for opioid use disorder during pregnancy.⁶

The treatment for neonatal abstinence syndrome is costly, especially when in a neonatal intensive care unit. It can be quite concerning to a new mother to have an infant that has to spend extra time in the hospital and sometimes be medicated for management of withdrawal. There has been a renewed interest amongst ObGyns in investigating medically-supervised withdrawal during pregnancy. Although there are remaining questions, overall, the literature does not support withdrawal during pregnancy—mostly because withdrawal is associated with relapse, and relapse is associated with cessation of care (both prenatal care and addiction treatment), acquisition and transmission of HIV and hepatitis C, and overdose and overdose death. The pertinent clinical and public health goal is the treatment of the chronic condition of addiction during pregnancy. The standard of care remains pharmacotherapy plus behavioral counseling for the treatment of opioid use disorder in pregnancy.

Clinical care, however, is both evidence-based and person-centered. All of us who have worked in this field, long before there was attention to the opioid crisis, all of us have provided medically-supervised withdrawal of a pregnant person, and that is because we understand the principles of care. When evidence-based care conflicts with person-centered care, the ethical course is the provision of person-centered care. Patients have the right of refusal. If someone wants to discontinue medication, I have tapered the medication during pregnancy, but continued to provide (and often increase) behavioral counseling and prenatal care.

Treated addiction is better for the fetus than untreated addiction. Untreated opioid addiction is associated with preterm birth and low birth weight. These obstetric risks are not because of the opioid per se, but because of the repeated cycles of withdrawal that an individual with untreated addiction experiences. People with untreated addiction are not getting “high” when they use, they are just becoming a little bit less sick. It is this repeated cycle of withdrawal that stresses the fetus, which leads to preterm delivery and low birth weight.

Medications for opioid use disorder are long-acting and dosed daily. In contrast to the repeated cycles of fetal withdrawal in untreated addiction, pharmacotherapy stabilizes the intrauterine environment. There is no cyclic, repeated, stressful withdrawal, and consequentially, the fetus grows normally and delivers at term. Obstetric risk is from repeated cyclic withdrawal more than from opioid exposure itself.

OBG MANAGEMENT: Research reports that women are not using all of the opioids that are prescribed to them after a cesarean delivery. What are the risks for addiction in this setting?

Dr. Terplan: I mark a distinction between use (ie, using something as prescribed) and misuse, which means using a prescribed medication not in the manner in which it was prescribed, or using somebody else’s medications, or using an illicit substance. And I differentiate use and misuse from addiction, which is a behavioral condition, a disease. There has been a lot of attention paid to opioid prescribing in general and in particular postdelivery and post-cesarean delivery, which is one of the most common operative procedures in the United States.

It seems clear from the literature that we have overprescribed opioids postdelivery, and a small number of women, about 1 in 300 will continue an opioid script.⁷ This means that 1 in 300 women who received an opioid prescription following delivery present for care and get another opioid prescription filled. Now, that is a small number at the level of the individual, but because we do so many cesarean deliveries, this is a large number of women at the level of the population. This does not mean, however, that 1 in 300 women who received opioids after cesarean delivery are going to become addicted to them. It just means that 1 in 300 will continue the prescription. Prescription continuation is

a risk factor for opioid misuse, and opioid misuse is on the pathway toward addiction.

Most people who use substances do not develop an addiction to that substance. We know from the opioid literature that at most only 10% of people who receive chronic opioid therapy will meet criteria for opioid use disorder.⁸ Now 10% is not 100%, nor is it 0%, but because we prescribed so many opioids to so many people for so long, the absolute number of people with opioid use disorder from physician opioid prescribing is large, even though the risk at the level of the individual is not as large as people think.

OBG MANAGEMENT: From your experience in treating addiction during pregnancy, are there clinical pearls you would like to share with ObGyns?

Dr. Terplan: There are a couple of takeaways. One is that all women are motivated to maximize their health and that of their baby to be, and every pregnant woman engages in behavioral change; in fact most women quit or cutback substance use during pregnancy. But some can’t. Those that can’t likely have a substance use disorder. We think of addiction as a chronic condition, centered in the brain, but the primary symptoms of addiction are behaviors. The salient feature of addiction is continued use despite adverse consequences; using something that you know is harming yourself and others but you can’t stop using it. In other words, continuing substance use during pregnancy. When we see clinically a pregnant woman who is using a substance, 99% of the time we are seeing a pregnant woman who has the condition of addiction, and what she needs is treatment. She does not need to be told that injecting heroin is unsafe for her and her fetus, she knows that. What she needs is treatment.

The second point is that pregnant women who use drugs and pregnant women with addiction experience a real specific and strong form of discrimination by providers, by other people with addiction, by the legal system, and by their friends and families. Caring for people who have substance use disorder is grounded in human rights, which means treating people with dignity and respect. It is important for providers to have empathy, especially for pregnant people who use drugs, to counter the discrimination these women experience from society and from other health care providers.

OBG MANAGEMENT: Are there specific ways in which ObGyns can show empathy when speaking with a pregnant woman who likely has addiction?

Dr. Terplan: In general when we talk to people about drug use, it is important to ask their permission to talk about it. For example, “Is it okay if I ask you some questions about smoking, drinking, and other drugs?” If someone says, “No, I don’t want you to ask those questions,” we have to respect that. Assessment of substance use should be a universal part of all medical care, as substance use, misuse, and addiction are essential domains of wellness, but I think we should ask permission before screening.

One of the really good things about prenatal care is that people come back; we have multiple visits across the gestational period. The behavioral work of addiction treatment rests upon a strong therapeutic alliance. If you do not respect your patient, then there is no way you can achieve a therapeutic alliance. Asking permission, and then respecting somebody's answers, I think, goes a really long way to establishing a strong therapeutic alliance, which is the basis of any medical care. ■

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