



Table of Contents

| Overview | 2 | | |
|--|----|--|--|
| Background on Maternal Substance Use and Overdose | | | |
| Unintentional Overdose Among Women of Reproductive Age | 4 | | |
| PAMR Findings | 5 | | |
| Drug Type | 7 | | |
| Demographics | 8 | | |
| Contributing Factors | 11 | | |
| Vignette | 13 | | |
| PAMR Initiatives | 14 | | |
| References | 15 | | |

Overview

The Ohio Department of Health (ODH) established the Ohio Pregnancy-Associated Mortality Review (PAMR) to identify and review pregnancy-associated deaths with the goal of developing interventions to reduce maternal mortality, particularly for pregnancy-related deaths.

A pregnancy-related death is the death of a woman while pregnant or within one year of pregnancy from any cause related to or aggravated by the pregnancy or management, excluding accidental or incidental causes such as a car accident that occurred within a year of the end of pregnancy. A pregnancy-associated death is the broader category and includes the death of a woman while pregnant or anytime within one year of pregnancy regardless of cause.

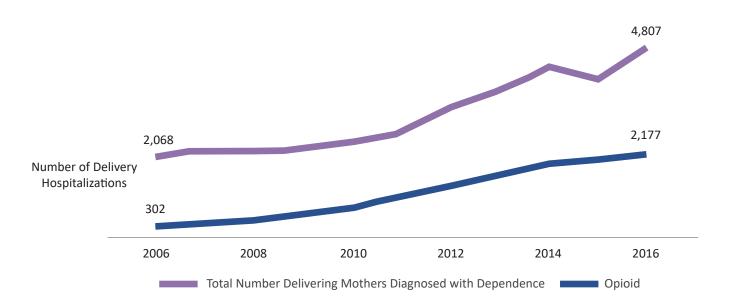
The purpose of this PAMR special topics data brief is to supplement the comprehensive report, A Report on Pregnancy-Associated Deaths in Ohio 2008-2016, with additional information about leading causes of pregnancy-related deaths.

Background on Maternal Substance Use and Overdose

Substance use is associated with a more than four-fold increased risk of maternal death (Maeda, 2014). Opioid abuse contributes to maternal mortality by increasing the risk of anesthesia complications, cardiac arrest, and overdose (Maeda, 2014). Among women aged 30-64 (not specific to pregnancy), deaths due to synthetic opioids overdose increased 1,643% and heroin overdose deaths increased by 915% between 1999 and 2017 in the United States (VanHouten, 2019). In Ohio, opioid overdose deaths increased nearly 4,000% for women in general during the same time period (U.S. Department of Health and Human Services [HHS] 2018). Women are more likely than men to self-medicate for anxiety with prescription opioids and are more susceptible to cravings and relapse (NIDA, 2018). Women are most likely to abuse substances

during their reproductive years (McHugh et. al., 2014). Women with substance-use disorders have a higher unintended pregnancy rate than women who do not have substance-use disorders, resulting in a higher incidence of drug use among pregnant and postpartum women (Terplan, 2015). Opioid-use disorder is associated with late entry into prenatal care, missed appointments, increased risk of preterm birth and Caesarean section, growth restriction, and neonatal abstinence syndrome (Parlier, 2014). In 2018, 33.2% of unintentional overdose deaths in Ohio were women, and of those 62.4% were of reproductive age (18-44 years old). Thirteen percent of reproductive-age women report illicit drug use and 6.3% report continuing use during pregnancy (McHugh, 2014). In Ohio, the number of women with a diagnosis of opioid dependence at time of delivery rose from 302 to 2,177 from 2006 through 2016 (Figure 1).

Figure 1: Number of Delivery Hospitalizations with a Drug Abuse Dependence Diagnosis, Ohio 2006-2016

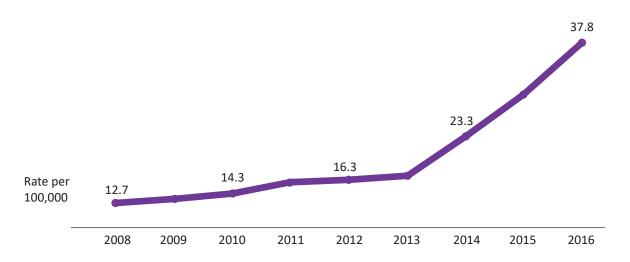


Source: Ohio Neonatal Abstinence Report (2015, 2017), Ohio Hospital Association, Ohio Department of Health, Violence and Injury Prevention Program. Data based on International Statistical Classification of Diseases and Related Health Problems (ICD). ICD-9-CM codes were used from 2006 through September 2015, and ICD-10-CM codes were used from October 2015 through 2016.

Unintentional Overdose Among Women of Reproductive Age

Among reproductive-aged women in Ohio, there were 748 deaths due to unintentional overdose during 2016 alone (http://publicapps.odh.ohio.gov/EDW/DataCatalog). Death rates increased from 12.7 per 100,000 in 2008 to 37.8 in 2016; over half the deaths since 2008 occurred during 2014 through 2016 (Figure 2). The increase is driven by the rapid rise in deaths involving opiates, especially illicit fentanyl (Figure 3). In 2016, non-Hispanic white women were overrepresented, comprising 77.1% of women of reproductive age, and 89% of unintentional overdose deaths. In contrast, non-Hispanic Black women comprised 14.9% of the population, but only 7.2% of deaths. In 2015, the greatest number of female overdose deaths occurred among those aged 50-54. By 2016, however, the highest number of female overdose deaths were aged 35-39. As overdoses among age groups with the highest pregnancy rates rise, it is reasonable to expect maternal mortality due to overdose to increase.

Figure 2: Death Rate from Unintentional Overdose Among Women of Reproductive Age (18-44 Years), Ohio 2008-2016



Source: Ohio Department of Health, Bureau of Vital Statistics; analysis conducted by ODH Violence and Injury Prevention Section. Includes Ohio residents who died due to unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44).

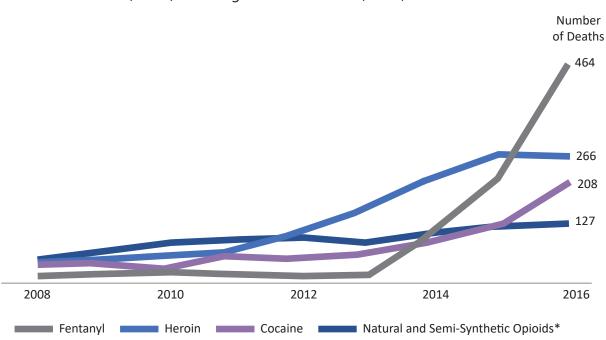


Figure 3: Unintentional Drug Overdose Deaths Among Reproductive-Aged Females (18-44) Involving Select Substances, Ohio, 2008-2016

Source: Ohio Department of Health, Bureau of Vital Statistics, analysis conducted by Violence and Injury Prevention Section. *Natural and semi-synthetic opioids (e.g. oxycodone, hydrocodone) correspond to code T40.2. Multiple drugs are usually involved in overdose deaths. Individual deaths may be reported in more than one category.

PAMR Findings: Overdose Among Women Who Were Pregnant or within One Year of Delivery at Time of Death

There were 116 unintentional overdose deaths among women who were pregnant or within one year of pregnancy in Ohio from 2008 through 2016 (Figure 4). Pregnancy-associated deaths were deemed unintentional overdoses when the cause of death on the death certificate was unintentional drug poisoning (i.e. ICD-10 codes X40-X44). Four of the deaths were determined to be pregnancy-related, 106 deaths were determined to be pregnancy-associated, but not related, and the causes of the remaining six deaths were undetermined. Over half of all pregnancy-associated overdose deaths occurred in 2015 and 2016 (Figure 4).

Previous research has found substance use and overdose to decrease during pregnancy (Forray, 2015). Despite the decrease in substance use during pregnancy (Forray, 2015), the increase of substance use by all women of reproductive age has led to an overall increase in the incidence of substance use during pregnancy (Terplan, 2015). For most of the last decade, women who were pregnant or within one year of pregnancy in Ohio had a lower rate of overdose deaths than women of reproductive age as a whole; for example, there were 4.7 pregnancy-associated overdose deaths per 100,000 live births in 2008, versus 12.7 overdose deaths per 100,000 women of reproductive age in the same year. However, in 2016, the rates of overdose deaths among the two populations were nearly equal, at 33.3 overdose deaths per 100,000 live births and 37.8 overdose deaths per 100,000 women of reproductive age. If fentanyl use continues to increase as witnessed from 2013-2016, it is possible that the rate of overdose will also continue to increase in pregnant and postpartum women.

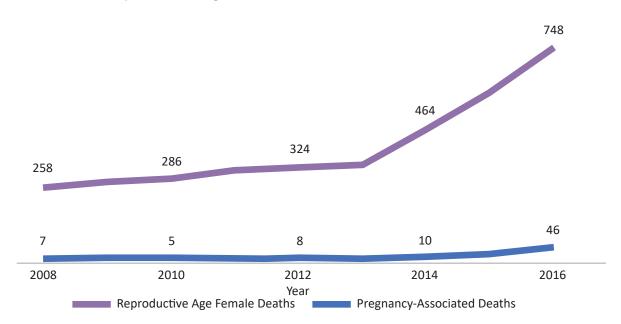
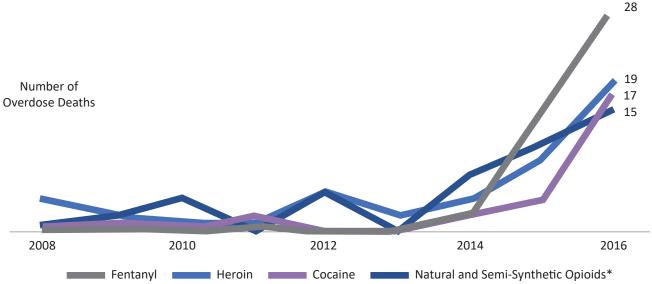


Figure 4: Number of Unintentional Drug Overdose Deaths Among Reproductive-Aged Females (18-44), Ohio, 2008-2016

Source: Pregnancy-associated deaths identified by the Ohio Department of Health, Pregnancy-Associated Mortality Review Program. Other data from the Ohio Department of Health, Bureau of Vital Statistics; analysis conducted by ODH Violence and Injury Prevention Program and the ODH Pregnancy-Associated Mortality Review Program. Includes Ohio residents who died of unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44).

Figure 5: Number of Pregnancy-Associated Deaths Due to Unintentional Overdose, by Year and Select Drug, Ohio, 2008-2016



Source: Pregnancy-associated deaths identified by the Ohio Department of Health, Pregnancy-Associated Mortality Review Program. Other data from the Ohio Department of Health, Bureau of Vital Statistics; analysis conducted by ODH Pregnancy-Associated Mortality Review Program. Includes Ohio residents who died of unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44).

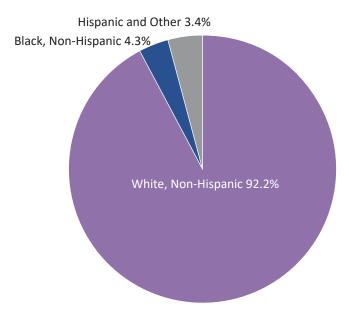
*Natural and semi-synthetic opioids (e.g. oxycodone, hydrocodone) correspond to code T40.2.

Multiple drugs are usually involved in overdose deaths. Individual deaths may be reported in more than one category.

PAMR Findings | Demographics

When examining the data by race and ethnicity, overdose deaths during pregnancy and the postpartum period follow the same trends that have previously been identified among all women of reproductive age in Ohio. Whites are overrepresented among overdose deaths, comprising 92.2% of pregnancy-associated overdose deaths but only 75.5% of live births (Figure 6).

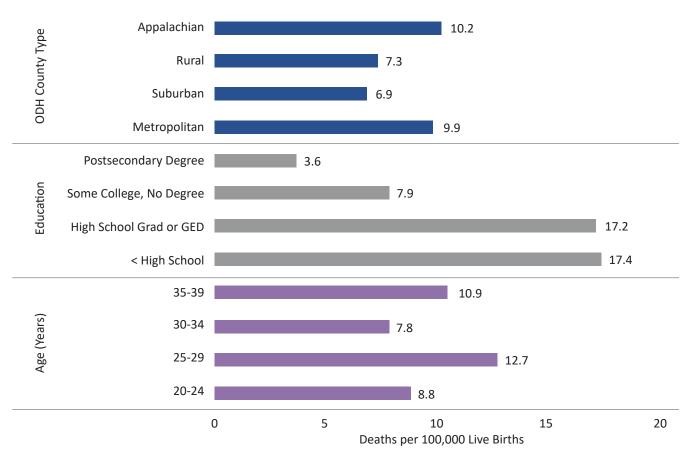
Figure 6: Pregnancy-Associated Deaths due to Unintentional Overdose, by Race and Ethnicity, Ohio 2008-2016



Source: Unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44 as indicated on the death certificate, Ohio Department of Health, Bureau of Vital Statistics). Other data from the Ohio Department of Health Pregnancy-Associated Mortality Review Program.

Women 25-29 years old and from Appalachian counties have the highest rate of pregnancy-associated overdose death (Figure 7). The average pregnancy-associated mortality ratio due to overdose for Appalachian counties from 2008 through 2016 is 10.2; however, when considering only the mortality ratio from 2015 and 2016, the ratio is 33.7 (data not shown). Despite having the lowest average mortality ratio from 2008 through 2016 by community type, the mortality ratio among suburban counties was almost equivalent to that for Appalachia from 2015 through 2016 (32.4).

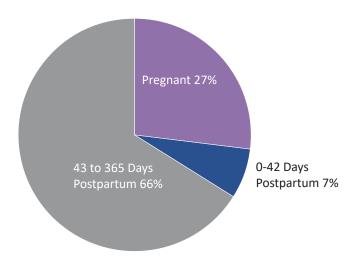
Figure 7: Pregnancy-Associated Mortality Ratios due to Unintentional Overdose, by County Type, Educational Level, and Age, Ohio 2008-2016



Source: Unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44 as indicated on the death certificate, Ohio Department of Health, Bureau of Vital Statistics). Other data from the Ohio Department of Health Pregnancy-Associated Mortality Review Program.

Overall, 27% of pregnancy-associated deaths occurred during pregnancy, while 66% occurred 43-365 days postpartum and 7% occurred from within 42 days postpartum (Figure 8).

Figure 8: Pregnancy-Associated Deaths due to Unintentional Overdose, by Timing Related to Pregnancy, Ohio 2008-2016



Source: Unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44 as indicated on the death certificate, Ohio Department of Health, Bureau of Vital Statistics). Other data from the Ohio Department of Health Pregnancy-Associated Mortality Review Program.

Women with a history of opioid abuse are more vulnerable to perinatal overdose in at least two scenarios involving tolerance. Tolerance is a physiological response to a substance the body is exposed to regularly in which resistance to the effects of the substance develops, requiring greater amounts of the substance to achieve the same effect. In the first scenario, a woman continues substance use during pregnancy. Tolerance can build because the woman's metabolism increases due to pregnancy, requiring greater opiate doses during pregnancy to achieve an equivalent effect. Her metabolism decreases postpartum, and she becomes more sensitive to opioid agonists. Thus, postpartum exposure to the same dose that she tolerated during pregnancy could result in unintentional overdose. In the second scenario, a woman abstains from substance use during pregnancy. Tolerance gradually decreases the longer the body goes without exposure to the substance. Women who use and stop or reduce their use during pregnancy are also more likely to overdose in the postpartum. If they relapse, they often do so with their old dose, which has a greater effect on the body after a period of abstinence or reduced use due to waning tolerance. In addition, women receiving treatment for substance use during pregnancy may not have equivalent access to treatment postpartum (HHS, 2016), and even if remaining in treatment, maintaining optimum pharmacological dosage during the postpartum can be challenged by hormonal changes (Pace et. al., 2014).

Factors identified that contributed to unintentional overdose deaths

There were 285 contributing factors identified across the 69 reviewed overdose deaths. Substance use was the most common contributing factor identified across all pregnancy-associated reviewed overdoses (Table 1). We also examined factors by timing of the death related to pregnancy. Among women who died while pregnant, the next most common contributing factors were adherence to medication recommendations and the presence of a mental health condition. Among women who died in the postpartum period whose cases were reviewed, the most common contributing factors after substance use were presence of a mental health condition, continuity or coordination of care, and barriers to accessing care. The most common barriers to access were no or inadequate insurance, a shortage of providers, and transportation difficulties. Deaths in the postpartum period were most often deemed preventable due to a recent point of contact with the healthcare system, such as a delivery hospitalization or postpartum visit.

Table 1. Contributing factors among 69 Reviewed Pregnancy-Associated Deaths due to Unintentional Overdose, 2008-2016

| Factor Class | Count (%) | Representative Themes | | |
|---|-----------|---|--|--|
| Provider Factor Level | | | | |
| Assessment | 8 (3) | Failure to screen; inadequate assessment for risk; lack of toxicity screen | | |
| Continuity of Care/Care Coordination | 5 (2) | Lack of care continuity | | |
| Referral | 5 (2) | Failure to refer or seek consultation | | |
| Communication | 3 (1) | Lack of communication between providers that led to lack of continuity of care | | |
| Delay | 2 (1) | Delay in or lack of diagnosis, treatment or follow-up care | | |
| SUBTOTAL | 28 (10) | | | |
| System / Facility Factor Level | | | | |
| Access / Financial | 15 (5) | Barriers to accessing care including insurance, provider shortages, and transportation, unavailable facilities and difficulty getting an appointment | | |
| Continuity of Care/Care Coordination | 12 (4) | Continued access to prescription medications due to non-coordinated care; lack of continuity of care; poor case management | | |
| Outreach | 5 (2) | Inadequate community outreach | | |
| Policies and Procedures | 5 (2) | Lack of standardized policies and procedures; lack of policy to reach out to the psychiatric department when a patient shows signs of mental health issues; no procedure to test for toxicity during prenatal care and at birth | | |
| Communication | 4 (1) | Poor communication between providers | | |
| SUBTOTAL | 49 (17) | | | |

Table 1 (continued)

| Factor Class | Count (%) | Representative Themes |
|-------------------------------|-----------|---|
| Patient / Family Factor Level | | |
| Substance Use Disorder | 67 (24) | Woman's substance abuse directly compromised woman's health status; individual or combination abuse of alcohol, illicit drugs, or prescriptions |
| Mental Health Conditions | 36 (13) | Anxiety; depression; suicide attempt |
| Adherence | 25 (9) | Nonadherence to medical recommendations |
| Violence | 13 (5) | Intimate partner violence; other history of violence |
| Delay | 12 (4) | Delay in seeking care; failure to seek care |
| Chronic Disease | 10 (4) | Chronic pain; obesity |
| Knowledge | 9 (3) | Lack of knowledge regarding importance of event, treatment, or follow-up |
| Childhood Abuse / Trauma | 7 (2) | |
| Social Support / Isolation | 7 (2) | Lack of social support |
| Unstable Housing | 5 (2) | |
| Tobacco Use | 4 (1) | |
| SUBTOTAL | 208 (73) | |
| TOTAL | 285 (100) | |

Source: Unintentional drug poisoning (underlying cause of death ICD-10 codes X40-X44 was identified from the death certificate). Totals may be greater than the sum of individual categories, as some small categories were not listed.

Challenges and opportunities in addressing unintentional overdose among women around the time of pregnancy

When considering public-health strategies to combat overdoses among women during pregnancy and postpartum, many challenges arise. Efforts to address the problem are decentralized, with several different agencies and stakeholder groups forming separate collaboratives and working on singular initiatives. Overdoses in Ohio have risen at such a rapid rate as to make a coordinated response on the necessary scale difficult to achieve both logistically and financially. In addition, women who are pregnant and in the postpartum period are a special population with specific needs; it is not easy to decide who is the most appropriate medical provider, increasing the necessity of well-coordinated and continuous care before, during and after pregnancy.

In addition to contributing to almost all deaths due to overdose, substance use is also a contributing factor in many maternal deaths due to causes other than overdose. The term substance use encompasses tobacco and alcohol, as well as drugs. Substance use may contribute to deaths with an underlying cause of cardiomyopathy, hypertensive disorder, another cardiovascular or cerebrovascular cause, or motor vehicle accidents, among others. It may directly affect the physical progression of a disease or may interfere with a woman's ability to access and adhere to treatment. Often accompanying a mental health condition, substance use is a significant contributing factor in many maternal suicides.

Melissa's Story: Opioid Use Disorder in Pregnancy

"Melissa" was a 28-year-old, non-Hispanic, white woman who had six pregnancies and five children and was 28 weeks pregnant at the time of her death. Her medical history included postpartum depression with three prior pregnancies, cocaine and heroin abuse, intimate partner violence, Hepatitis C, and tobacco use.

Prenatal Period: She began prenatal care when she was 16 weeks pregnant and had two prenatal care visits. No referrals were made during the prenatal period.

In the year following delivery of her fifth child, she visited the same emergency department 11 times with differing complaints of pain, for which she was repeatedly prescribed opioid medication. She requested medication-assisted treatment (MAT) more than once, but her providers were not comfortable treating pregnant women. One month after receiving her last prescription, she overdosed on heroin. She was resuscitated and discharged with an appointment scheduled for three days later at a suboxone clinic. She missed that appointment and fatally overdosed seven days after discharge.

Her death certificate listed the cause of death as acute heroin intoxication and the manner as an accident. An autopsy was done by a medical examiner.

Key Questions Answered by the Review Committee

Was the Death Pregnancy-Related?

Yes. The committee determined that her death was related to an inability to access drug or mental health treatment.

What was the Cause of Death?

Mental Health Condition. Melissa suffered from opiate-use disorder, a mental health condition that was the underlying cause of death in the system used for maternal mortality review.

Was there Some Opportunity to Alter Outcome?

Yes. Melissa engaged frequently with the healthcare system including being seen in the same emergency department multiple times in the months prior to death. A review of her medical record or her controlled prescription history via the Ohio Automated Rx Reporting System (OARRS) would have shown a pattern consistent with opioid abuse. Each visit was a potential intervention point.

Additionally, Melissa requested MAT during her last visit. She was evaluated by a social worker and discharged to follow up at a MAT clinic three days later. A more effective strategy would have been to initiate MAT prior to discharge, which is done in some facilities.

| What were the Factors that Contributed to this Death? | What are the Recommendations and Actions that Address those Contributing Factors? |
|--|--|
| Substance abuse (patient/family level) | Increase accessibility of naloxone (Narcan) for pregnant women with Opioid Use Disorder (OUD) and their household. |
| Misdiagnosis (provider level) | Offer education about diagnosis and treatment of OUD in pregnancy and the postpartum period to healthcare providers. |
| Failure to screen or adequately assess for risk (system level) | Improve coordination of medical care and substance abuse/mental health treatment. |
| Failure to refer for treatment (system level) | Promote the institution of more comprehensive resources and treatment programs for reproductive-aged women. |

Case is fictitious but based on real events



PAMR Initiatives

In response to the rise in pregnancy-associated and pregnancy-related opioid deaths, the PAMR program at the Ohio Department of Health, with a Rapid Maternal Overdose Review (RMOR) grant from the Centers for Disease Control and Prevention (CDC), is improving identification and surveillance of pregnancy-associated overdose deaths. The RMOR initiative aims to ascertain details surrounding maternal deaths due to unintentional overdose to ensure a comprehensive review is conducted. This review helps PAMR identify potential for programmatic interventions to prevent maternal overdose deaths.

References

Forray, A, Merry, B, Lin H, Ruger, JP, Yonkers, KA. (2015, May). Perinatal substance use: a prospective evaluation of abstinence and relapse. Drug and Alcohol Dependence, 150, 147-155.

Maeda, A, Bateman, B, Clancy, CR, Creanga, AA, Leffert, LR. (2014, December). Opioid abuse and dependence during pregnancy. Anesthesiology, 121(6): 1158-1165.

McHugh, RK, Wigderson, S, Greenfield, SF. (2014, June). Epidemiology of substance use in reproductive-age women. Obstetrics and Gynecology Clinics of North America, 41(2), 177-189.

National Institute on Drug Abuse (NIDA). (2018, July). Substance use in women. Retrieved from https://www.drugabuse.gov/ publications/research-reports/substance-use-in-women. Accessed November 29, 2018.

Ohio Department of Health, Violence and Injury Prevention Program. Neonatal abstinence syndrome (NAS) in Ohio: 2006-2015 report. Retrieved from https://odh.ohio.gov/wps/wcm/connect/gov/b0099f42-4c41-44ac-87ec-5abd96390685/Ohio NAS Report 2006-2015.pdf?MOD=AJPERES&CONVERT TO=url&CACHEID=ROOTWORKSPACE.Z18 M1HGGIK0N0JO00Q09DDDDM3000-b0099f42-4c41-44ac-87ec-5abd96390685-miTIPrw. Accessed November 29, 2018.

Pace, CA, Kaminetzky, LB, Winter, M, Cheng, DM, Saia, K, Samet, JH, Walley, AY. (2014, September). Postpartum changes in methadone maintenance dose. Journal of Substance Abuse Treatment, 47(3), 229–232.

Parlier, AB, Fagan, B, Ramage, M, Galvin, S. (2014, November). Prenatal care, pregnancy outcomes, and postpartum birth control plans among pregnant women with opiate addictions. Southern Medical Journal, 107(11), 676-683.

Substance Abuse and Mental Health Services Administration (SAMHSA). (2017, September 7). Results from the 2016 National Survey on Drug Use and Health: Detailed tables. Retrieved from https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf. Accessed December 5, 2018.

Terplan, M, Hand, DJ, Hutchinson, M, Salisbury-Afshar, E, Heil, SH. (2015, November). Contraceptive use and method choice among women with opioid and other substance use disorders: A systematic review. Preventative Medicine, 80, 23-31.

United States Department of Health and Human Services (DHHS), Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released 2018. Retrieved from http://wonder.cdc.gov/ucd-icd10.html. Accessed December 10, 2018.

VanHouten JP, Rudd RA, Ballesteros MF, Mack KA. (January 2019). Drug Overdose Deaths Among Women Aged 30–64 Years — United States, 1999–2017. MMWR Morb Mortal Wkly Rep 2019; 68:1–5.