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Maternal and Infant Characteristics Associated with Maternal Opioid Overdose in the Year Following Delivery

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Abstract

Background and Aims—Opioid-related overdose is increasingly linked to pregnancy-associated deaths, but factors associated with postpartum overdose are unknown. We aimed to estimate the strength of the association between maternal and infant characteristics and postpartum opioid-related overdose.

Design—Retrospective cohort study using a linked, population-level dataset.

Setting—Massachusetts, United States.

Participants—Women who delivered one or more live births from 2012–2014 (n=174,517).

Measurements—The primary outcome was opioid-related overdose in the postpartum year. We used multivariable logistic regression to explore the independent associations of maternal

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(demographics, substance use, pregnancy) and infant (gestational age, birthweight, neonatal abstinence syndrome (NAS)) characteristics with postpartum opioid overdose. Findings were stratified by maternal opioid use disorder (OUD) diagnosis.

Findings—There were 189 deliveries to women who experienced ≥1 opioid overdose in the first year postpartum (11/10,000 deliveries). Among women with postpartum opioid overdose, 46.6% had an OUD diagnosis within twelve months before delivery. In our adjusted model, maternal diagnosis of OUD (aOR 3.61, 95% CI 1.73–7.51) and prior non-fatal overdose (aOR 2.40, 95% CI 1.11–5.17) were most strongly associated with postpartum overdose. After stratifying by OUD status, infant diagnosis of NAS (OUD+ aOR 2.03, 95% CI 1.26–3.27; OUD- aOR 2.79, 95% CI 1.12–6.93), and high unscheduled healthcare utilization (OUD+ aOR 2.27, 95% CI 1.38–3.73; OUD- aOR 2.11, 95% CI 1.24–3.58) were positively associated with postpartum overdose in both groups.

Conclusion—Among women who delivered live infants in Massachusetts, USA between 2012 and 2014, maternal diagnosis of OUD, prior non-fatal overdose, infant diagnosis of NAS, and high unscheduled health care utilization appeared to be positively associated with postpartum opioid overdose. However, over half of postpartum overdoses in that period were to women without a diagnosis of OUD. Engagement in methadone or buprenorphine treatment in the month prior to delivery was not sufficient to reduce the odds of postpartum overdose.

Keywords

Pregnancy; postpartum; opioid use disorder; overdose; women; maternal; neonatal abstinence syndrome; non-fatal

Introduction

In the United States, opioid-related overdose events are increasingly implicated in pregnancy-associated deaths, defined as deaths occurring during or within a year of the end of pregnancy, contributing to 11 to 25% of deaths in several states.[1–6] The majority of the reported deaths occur later in the postpartum period; in Massachusetts, over 90% of substance-use related pregnancy-associated deaths occurred after six weeks postpartum, compared with 60% of all other pregnancy-associated deaths.[1–5] In Massachusetts, the seven to twelve months following delivery were found to be a period of increased risk of both fatal and non-fatal opioid overdose events (12.3/100,00 person-days) compared with the trimester just prior to delivery (3.3/100,00 person-days).[7]

The postpartum period is a vulnerable period where overdose can pose significant risks to maternal and child health and well-being. This time can be particularly challenging for mothers with opioid use disorder (OUD) given high rates of postpartum depression, fragmented transitions of care from prenatal to postpartum providers, lapses in insurance following delivery, physiologic changes impacting medication dose for treatment of OUD, and the shame and stigma experienced by women secondary to neonatal opioid withdrawal or loss of child custody.[8–13]

Overdose risk factors in the general population have been well described, including prior non-fatal overdose, greater severity of opioid use disorder, receipt of prescription opioids,

recent incarceration, depression, female gender, and housing instability.[14–22] Yet unique risk factors for overdose among postpartum women in the year following delivery have not been specifically examined. The purpose of this study was to identify the extent to which maternal and infant characteristics identifiable at time of delivery were associated with opioid-related fatal and non-fatal overdose in the first postpartum year utilizing a linked-statewide population-level dataset in Massachusetts. We hypothesized that in addition to the factors previously described in the general population, inadequate prenatal care and preterm delivery would be associated with opioid-related overdose in the postpartum period. Additionally, among women who experienced postpartum overdose, we aimed to compare characteristics by OUD diagnosis, an important benchmark in identification of at-risk women during pregnancy.

Methods

Design

We performed a retrospective cohort study utilizing a statewide linked-dataset, called the Public Health Data Warehouse, previously described as the Chapter 55 database. This dataset was established as part of a Massachusetts (MA) legislative mandate and is overseen by the Massachusetts Department of Public Health (MDPH).[23–25] Linkage across several state data sets from 2011–2015, including the All Payer Claims Database (APCD), Vital Records (birth and death certificates), Bureau of Substance Addiction Services (BSAS) licensed substance use disorder treatment data, the Center for Health Information and Analysis Case Mix records (inpatient hospitalization, observation encounters, and emergency department discharges), the Prescription Monitoring Program (PMP), MA Ambulance Trip Record Information System, and state Medicaid (MassHealth), among others, was performed by the MDPH to allow further exploration of factors that influence opioid overdoses. A full description of the datasets linked, data structure, and linkage rates across datasets has been described previously.[26]

Participants

Our cohort included all MA residents who delivered a live birth in MA and a documented gestational age ≥ 20 weeks, identified using birth certificates. Birth certificate linkage rates for our study period were 91.7%. Fetal death records were excluded. Our study cohort was limited to deliveries that occurred between January 2012 and September 2014, to allow for a full year of available data before and after each delivery. The study population included birth of both singleton and multiples (treated as a single delivery episode), as well as multiple deliveries to the same woman during the study period.

Measures

Our primary outcome of interest was any fatal or nonfatal opioid-related overdose during the 365 days following delivery. Opioid-related overdose events were defined by identification of any of the following: (1) A discharge from an inpatient unit, observation unit, or an emergency department encounter with an indication of opioid overdose based on *International Classification of Disease* (ICD) *Ninth Edition* diagnosis codes for opioid poisoning (Supplementary Table 1); (2) An ambulance encounter with an indication of

opioid overdose based on an algorithm created by MPDH and the Centers for Disease Control and Prevention (available only from 2013–2015); or (3) A death certificate indicating opioid overdose as cause of death.

Maternal characteristics extracted from the birth certificate include age at time of delivery, race/ethnicity, highest educational level, marital status, and the adequacy of prenatal care utilization index.[27] Enrollment in MassHealth (Medicaid) during the month of delivery was identified from the MassHealth insurance database. Additional characteristics were defined dichotomously based on any evidence in the 12 months before delivery, inclusive of month of delivery – homelessness, defined as an active casefile in the MA Department of Housing and Community Development (DHCD) dataset; incarceration, defined as release from incarceration in a prison or a jail in MA; and anxiety and depression, defined by APCD and Case Mix data. Finally, high utilization of unscheduled care, defined as three or more emergency department and/or obstetric triage visits in the 12 months before delivery, exclusive of the month of delivery based on Case Mix data.

Maternal OUD in the year prior to delivery was defined as an ICD-9 or ICD-10 code for opioid use disorder (Supplementary Table 1) in either APCD claims or Case Mix records. Women were defined as enrolled in an opioid treatment program if they had any evidence of enrollment in a state-funded program in the 12 months before delivery from BSAS records, which includes acute treatment services, crisis stabilization, residential, and intensive outpatient programs. Women were defined as receiving medication for OUD (MOUD) in the 12 months before delivery and the month of delivery if they had a claim for methadone maintenance treatment (Supplementary Table 1), record of methadone treatment from BSAS, or had filled a prescription for buprenorphine or buprenorphine/naloxone. Non-fatal overdose in the year prior to delivery was defined as a claim or ambulance record for opioid overdose in the 365 days before delivery not linked to a death record. Finally, an opioid prescription filled in the 3 months prior to delivery, excluding buprenorphine, was determined from PMP data. Prescriptions in the month of delivery were excluded to avoid opioid prescriptions for postpartum pain control.

Mothers who delivered infants with neonatal withdrawal symptoms were identified by infant diagnosis claim of neonatal abstinence syndrome (NAS) (Supplementary Table 1). Gestational age, birthweight, delivery type, and receipt of breastmilk prior to discharge were identified from birth certificate data. To account for the collinearity between gestational age and birthweight, infants were described as preterm/low birthweight if they were born before 37 weeks and/or weighed less than 2,500 grams. In order to have a single value for each delivery, infant characteristics were combined for multiple gestations (e.g., if one twin was diagnosed with NAS, the delivery was coded as NAS positive).

Analyses

We used descriptive statistics, including counts, percentages, and rates per 10,000 live births to compare the characteristics of women with postpartum overdose to women who delivered a live birth in Massachusetts but had no documented postpartum overdose for each covariate. We used generalized estimating equations logistic regression with an unstructured correlation structure to account for multiple deliveries to the same woman throughout the

study period. We developed three models: an unadjusted model, a model which controlled for maternal diagnosis of OUD, and a multivariable model that evaluated the association of all *a priori* maternal and infant covariates described earlier and postpartum overdose. Multivariable models were examined for potential collinearity by calculating variance inflation factors and condition indices. To examine the effect of a prior diagnosis of OUD, we assessed potential interactions between OUD diagnosis and each covariate in our multivariate models. Significant interactions were identified, so the final model was stratified by prior OUD diagnosis. All analyses were performed in SAS Studio version 3.6 (Cary, NC). The Partners Institutional Review Board deemed this study exempt as non-human subjects research.

Results

We identified 179,407 deliveries resulting in a live birth in Massachusetts during our study period. We excluded 4,890 (2.7%) deliveries that were missing maternal or infant covariates, leaving 174,517 deliveries (170,678 singleton and 3,839 multiples) in our final cohort among 164,765 unique women. There were 189 deliveries (all among unique women) with at least one postpartum opioid overdose in the year following delivery, affecting approximately 11/10,000 deliveries. Ninety-three percent of initial overdose events (176) were non-fatal and 58% (109) occurred in the 7–12 months following delivery (Figure 1).

Descriptive statistics for women in the study population are presented in Table 1. Women who had an overdose in the year following delivery were significantly more likely to be younger than age 25, white/non-Hispanic, less educated, unmarried, receiving public insurance at delivery, and have less than adequate prenatal care, when compared to all women in MA who delivered a live birth. In terms of opioid use and treatment in the year prior to delivery, women who had a postpartum overdose were significantly more likely to: have a diagnosis of OUD, enroll in a treatment program for an opioid problem, receive MOUD during the month of delivery, and fill an opioid prescription (excluding buprenorphine) in the three months prior to delivery. With respect to psychosocial history in the year before delivery, women with an overdose were significantly more likely to have a diagnosis of depression and anxiety, high unscheduled healthcare utilization, a history of incarceration, and evidence of homelessness. Finally, deliveries among women with a postpartum overdose were more likely to result in a preterm or low birthweight infant, diagnosis of NAS, and less initiation of breastfeeding.

We compared the characteristics of the deliveries of women who had an overdose who had evidence of OUD in the year before delivery (n=88) with those who did not have evidence of OUD (n=101) in Table 2. Women without prior evidence of OUD but who experienced a postpartum overdose were more likely to have adequate prenatal care and breastfeed their infant compared with women with a prior OUD diagnosis. Additionally, this group was less likely to have high unscheduled healthcare utilization and less likely to have a prior diagnosis of anxiety or depression, compared with deliveries to women with a prior OUD diagnosis.

Our unadjusted model (Model 1) identified that diagnosis of OUD and opioid-related variables were most highly associated with a postpartum overdose. After adjusting for OUD status (Model 2) and all other covariates (Model 3) we found a significant reduction in the magnitude of the adjusted odds ratios (Supplementary Table 2). We identified evidence of a significant interaction between OUD diagnosis and the association between multiple covariates and postpartum overdose in our adjusted model. These findings led us to present our final model stratified by OUD diagnosis (Figure 2).

In the OUD positive group, infant NAS diagnosis, prior overdose in last 12 months, high ED utilization, and maternal anxiety were associated with postpartum overdose. In the OUD negative group, in addition to infant NAS diagnosis and higher ED utilization, we found that marital status, public insurance, preterm/low birthweight, C-section delivery, opioid treatment program involvement, opioid prescribing, and incarceration status were positively associated with postpartum overdose (Figure 2). For three covariates, marital status, enrollment in Medicaid, and opioid prescription three months before delivery, the direction of the adjusted odds ratio differed by OUD status, but they were not statistically significant in the final models. In both models, MOUD during the month of delivery was not statistically significantly associated with postpartum overdose.

Discussion

In a population-level cohort of more than 174,000 deliveries resulting in live births between 2012–2014 in Massachusetts using a linked administrative dataset, postpartum overdose occurred at a rate of 11/10,000 deliveries. In our cohort, less than half of women with a postpartum overdose had a documented OUD diagnosis in the year prior to or during their delivery hospitalization, and maternal and infant characteristics associated with overdose differed by OUD status. In our final stratified models, factors significantly associated with postpartum overdose in both groups included infant diagnosis of NAS and high unscheduled healthcare utilization. For women in the OUD negative group, additional characteristics positively associated with postpartum overdose included public insurance, being unmarried, enrollment in a public opioid treatment program, preterm/low birth weight, cesarean delivery, and history of incarceration; conversely, older age and non-white race were associated with decreased odds of postpartum overdose.

We found that postpartum overdose is an uncommon event that occurs at a lower rate than overdose in the general population in Massachusetts (31/10,000 in 2015).[25] While this rate was lower than reported national rates of other conditions affecting postpartum women in the United States such as depression (impacting 9–20% of all deliveries)[28] or obstetrical complications requiring readmission (1–2% of all deliveries),[29] we found the postpartum opioid-related overdose rate was similar to that of postpartum psychosis (0.1–0.5% of deliveries).[28,30] Given postpartum overdose can result in significant morbidity and mortality for women and the prevalence of OUD in pregnancy continues to rise,[31] identifying women at risk of overdose is important to offer harm reduction services such as naloxone distribution and provide addiction treatment.[32,33]

Similar to prior studies, we found that a known history of an OUD and prior overdose were substantially associated with increased odds of postpartum overdose.[15–19,34] Unique to postpartum women, we identified that an infant diagnosis of NAS at delivery and preterm/low birthweight at delivery were associated with a greater likelihood of postpartum overdose. For infant NAS diagnosis, we hypothesize that this association is most likely a proxy for maternal evidence of opioid use or recent opioid prescribing (70% of cases of NAS were to women with evidence of OUD). However, the shame and stigma women experience from watching their infant display withdrawal symptoms, grief from loss of parental custody, and stresses of caring for a potentially fussier baby could also contribute to this positive association. There remains great heterogeneity in the way providers classify opioid-exposed infants as having a diagnosis of NAS.[35] Based on NAS claims diagnoses alone, we were unable to determine if an infant required pharmacologic treatment or not, and if differences in overdose exist by infant treatment status. Preterm or low birthweight infants may have special health care needs that increase the burden on caretakers in the year postpartum. Additionally, higher unscheduled health care utilization, but not inadequate prenatal care receipt, was associated with postpartum overdose. A qualitative study of low-income pregnant women with high unscheduled care found utilization may be driven by experiences of illness insufficiently addressed by outpatient prenatal care.[36] The experience of women having unmet health needs may portend future postpartum overdose risk, regardless of whether a diagnosis of OUD is identified at delivery.

In our stratified analysis among women with an OUD diagnosis, we found that a diagnosis of anxiety, but not depression in the year before delivery was significantly associated with postpartum overdose. In the OUD negative group, we found a similar but not statistically significant association between prior mental health diagnosis and postpartum overdose, likely due to insufficient power to detect an association. A history of psychopathology during pregnancy has been previously shown to be strongly associated with postpartum depression, which could contribute to postpartum relapse and overdose.[8,37]

Notably, there was no independent association between receiving MOUD the month of delivery and adjusted odds of postpartum overdose. This suggests that engagement in treatment with methadone or buprenorphine at time of delivery is not sufficient to reduce the odds of postpartum overdose. While our study design focused on factors identifiable at delivery, research has shown that discontinuation of MOUD increases overdose risk in the general population.[33,38] Pregnancy represents a time where many women newly engage in treatment and receive MOUD, and the exploration of factors contributing to postpartum disengagement from treatment is an underexplored area for future research. For example, research exploring how caretaking responsibilities may interfere with the ability to engage in treatment and recovery supports, particularly as few treatment centers nationally have gender-specific and child care supports for women and their families.[39]

Finally, there has been an increasing body of literature examining opioid prescribing in women after delivery, as prescribing is routine after cesarean delivery[40] but also common after vaginal delivery.[41] In our stratified analysis among women without a diagnosis of OUD, we found a statistically significant association between cesarean delivery and postpartum overdose, which could be a proxy for postpartum opioid prescribing. However, a

recent analysis by Ladha and colleagues assessed overdose risk for 90 days following several common surgical procedures, and found post-cesarean delivery had one of the lowest odds of overdose among 22 surgical procedures studied.[42] Future research examining specific postpartum prescribing patterns and overdose risk is warranted.

Compared with our prior work that restricted analyses to individuals with an OUD diagnosis in the year prior to delivery,[7] this analysis included all live births in MA. Our study was designed to look at maternal and infant factors identifiable at time of delivery associated with postpartum overdose, to help identify individuals who may be at higher risk in the postpartum period, and thus be able to offer more intensive services and resources tailored to this population. While we found that OUD diagnosis was strongly associated with increased odds of postpartum overdose, over half the deliveries with a postpartum overdose were to women with no documented OUD diagnosis in the year prior to and including month of delivery. We hypothesize several explanations for this finding. First, women with an existing OUD may not have received prenatal substance use screening, or disclosed their substance use history fully during pregnancy for fear of losing custody of their child or stigma surrounding substance use disorder during pregnancy, and thus were not identified prior to delivery. Second, given our reliance on administrative rather than clinical data, women with OUD may not have been properly characterized/documented with a diagnosis code of OUD despite being known to have one, as prior work showed that OUD is underdocumented in claims data in Massachusetts.[43] Third, women may have developed a new OUD or newly used opioids resulting in an overdose following delivery but did not have OUD prior to delivery. Finally, not all women who overdose meet criteria for OUD, particularly as overdose becomes more frequent due to contamination of fentanyl into the opioid and non-opioid drug supply.[15]

Our subgroup analysis comparing those with a postpartum overdose by OUD status showed that these two groups of women had important differences in their characteristics. Those without a diagnosis claim for OUD had more adequate prenatal care engagement, less psychiatric comorbidity, less unscheduled health care utilization, higher rates of breastfeeding, and were less likely to deliver an infant with NAS, suggesting either less in-utero opioid exposure during pregnancy or a lack of appropriate prenatal identification rather than absence of diagnosis due to lack of access to care. For this group of women, identifying ways in the postpartum period to have increased contact for screening for substance use disorder is important, particularly given 25–35% of all women do not attend their postpartum visit.[44] Pediatric providers who have frequent visits with families in the first year following delivery could play an important role in screening for OUD and identifying risk factors among families including postpartum depression, isolation, and limited supports in caring for a new baby.[45]

Our study has several important limitations. First, our observational cohort using administrative data is subject to both selection bias and misclassification bias. We attempted to minimize this risk by removing deliveries with an implausible gestational age and controlling for maternal demographics in our final adjusted model. Second, as overdose was a rare event, we may not have had enough power in our model to show all factors associated with postpartum overdose, such as homelessness and depression. Third, our study design

focused on maternal and infant factors identifiable at time of delivery, but given more than half of the overdoses happened greater than six months after delivery, important characteristics just prior to the overdose such as engagement in MOUD were not known. Fourth, ambulance trip overdose data were only available from 2013–2015, so it is possible overdoses that did not result in hospital visits were missed, resulting in an underestimation of the overdoses in 2012. Fifth, stratifying our analysis by OUD status likely limited our ability to fully detect associations. Despite these limitations, our analysis is strengthened by the ability to report population-level data in Massachusetts and utilize a novel linked public health dataset.

We identified that maternal diagnosis of OUD, prior non-fatal overdose, infant diagnosis of NAS, and high unscheduled health care utilization are associated with postpartum overdose. Engagement in methadone or buprenorphine treatment in the month prior to delivery was not sufficient to reduce the odds of postpartum overdose, suggesting that early screening, continuous access to health care, and tight linkage to postpartum care providers are essential for women to maintain treatment adherence. Finally, more than 50% of women with a postpartum overdose did not have prior evidence of OUD, suggesting that an additional focus on screening women for OUD at delivery and postpartum, with sustained postpartum maternal support, is critical to efforts to reduce pregnancy-associated morbidity and improve the health of families.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Literature Cited

1. MacDorman MF, Declercq E, Thoma ME. Trends in Texas maternal mortality by maternal age, race/ethnicity, and cause of death, 2006–2015. Birth. 1 2018. doi:10.1111/birt.12330.
2. Kavanaugh V Pregnancy-Associated Deaths From Drug Overdose in Virginia, 1999–2007: A Report from the Virginia Maternal Mortality Review Team; 2015.
3. Metz TD, Rovner P, Hoffman MC, Allshouse AA, Beckwith KM, Binswanger IA. Maternal Deaths From Suicide and Overdose in Colorado, 2004–2012. Obstet Gynecol. 2016;128(6):1233–1240. doi:10.1097/AOG.0000000000001695. [PubMed: 27824771]
4. Mehta PK, Bachhuber MA, Hoffman R, Srinivas SK. Deaths From Unintentional Injury, Homicide, and Suicide During or Within 1 Year of Pregnancy in Philadelphia. Am J Public Health. 2016;106(12):2208–2210. doi:10.2105/AJPH.2016.303473. [PubMed: 27736205]
5. Massachusetts Department of Public Health. Substance Use among Pregnancy-Associated Deaths — 2005–2014. In: Maternal Mortality and Morbidity Review in Massachusetts: 2018.
6. Smid MC, Stone NM, Baksh L, et al. Pregnancy-Associated Death in Utah. Obstet Gynecol. 2019;133(6):1131–1140. doi:10.1097/AOG.0000000000003279. [PubMed: 31135726]

7. Schiff DM, Nielsen T, Terplan M, et al. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018;132(2):466–474. doi:10.1097/AOG.0000000000002734. [PubMed: 29995730]
8. Chapman SLC, Wu L-T. Postpartum substance use and depressive symptoms: a review. Women Health. 2013;53(5):479–503. doi:10.1080/03630242.2013.804025. [PubMed: 23879459]
9. Benningfield MM, Dietrich MS, Jones HE, et al. Opioid dependence during pregnancy: relationships of anxiety and depression symptoms to treatment outcomes. Addiction. 2012;107 Suppl:74–82. doi:10.1111/j.1360-0443.2012.04041.x. [PubMed: 23106929]
10. Klaman SL, Isaacs K, Leopold A, et al. Treating Women Who Are Pregnant and Parenting for Opioid Use Disorder and the Concurrent Care of Their Infants and Children: Literature Review to Support National Guidance. J Addict Med. 2017;11(3):178–190. doi:10.1097/adm.0000000000000308. [PubMed: 28406856]
11. Pace CA, Kaminetzky LB, Winter M, et al. Postpartum changes in methadone maintenance dose. J Subst Abuse Treat. 2014;47:229–232. doi:10.1016/j.jsat.2014.04.004. [PubMed: 24953167]
12. Auguste T, Gulati M. Recommendations and Conclusions Presidential Task Force on Redefining the Postpartum Visit Committee on Obstetric Practice Optimizing Postpartum Care Committee Opinion Optimizing Postpartum Care E141. Vol 131.; 2018 https://www.acog.org/-/media/Committee-Opinions/Committee-on-Obstetric-Practice/co736.pdf?dmc=1&ts=20180731T0225509403. Accessed July 30, 2018.
13. Daw JR, Hatfield LA, Swartz K, Sommers BD. Women In The United States Experience High Rates Of Coverage 'Churn' In Months Before And After Childbirth. Health Aff. 2017;36(4):598–606. doi:10.1377/hlthaff.2016.1241.
14. Walley AY, Cheng DM, Coleman SM, et al. Risk factors for recent nonfatal overdose among HIV-infected Russians who inject drugs. AIDS Care. 2014;26(8):1013–1018. doi:10.1080/09540121.2013.871218. [PubMed: 24382133]
15. Somerville NJ, O'Donnell J, Gladden RM, et al. Characteristics of Fentanyl Overdose — Massachusetts, 2014–2016. MMWR Morb Mortal Wkly Rep. 2017;66(14):382–386. doi:10.15585/mmwr.mm6614a2. [PubMed: 28406883]
16. Mack KA, Jones CM, Ballesteros MF. Illicit Drug Use, Illicit Drug Use Disorders, and Drug Overdose Deaths in Metropolitan and Nonmetropolitan Areas — United States. MMWR Surveill Summ. 2017;66(19):1–12. doi:10.15585/mmwr.ss6619a1.
17. Caudarella A, Dong H, Milloy MJ, Kerr T, Wood E, Hayashi K. Non-fatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. Drug Alcohol Depend. 2016;162:51–55. doi:10.1016/j.drugalcdep.2016.02.024. [PubMed: 26993373]
18. Powis B, Strang J, Griffiths P, et al. Self-reported overdose among injecting drug users in London: extent and nature of the problem. Addiction. 1999;94(4):471–478. http://www.ncbi.nlm.nih.gov/pubmed/10605843. Accessed February 23, 2018. [PubMed: 10605843]
19. Martins SS, Sampson L, Cerdá M, Galea S. Worldwide Prevalence and Trends in Unintentional Drug Overdose: A Systematic Review of the Literature. Am J Public Health. 2015;105(11):e29–e49. doi:10.2105/AJPH.2015.302843.
20. Chahua M, Sordo L, Barrio G, et al. Non-fatal opioid overdose and major depression among street-recruited young heroin users. Eur Addict Res. 2014;20(1):1–7. doi:10.1159/000346787. [PubMed: 23921233]
21. Bohnert ASB, Valenstein M, Bair MJ, et al. Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths. JAMA. 2011;305(13):1315. doi:10.1001/jama.2011.370. [PubMed: 21467284]
22. Larochelle MR, Liebschutz JM, Zhang F, Ross-Degnan D, Wharam JF. Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose. Ann Intern Med. 2016;164(1):1. doi:10.7326/M15-0038. [PubMed: 26720742]
23. Massachusetts Department of Public Health. An Assessment of Opioid-Related Deaths in Massachusetts (2013–2014).; 2016 https://www.mass.gov/files/documents/2016/09/pg/chapter-55-report.pdf. Accessed April 11, 2018.
24. Commonwealth of Massachusetts. An Act Requiring Certain Reports for Opiate Overdoses; 2015 https://malegislature.gov/Laws/SessionLaws/Acts/2015/Chapter55. Accessed October 8, 2017.

25. MA Department of Public Health. An Assessment of Fatal and Nonfatal Opioid Overdoses in Massachusetts (2011 – 2015). Boston; 2017 https://www.mass.gov/files/documents/2017/08/31/legislative-report-chapter-55-aug-2017.pdf. Accessed October 8, 2017.
26. Massachusetts Department of Public Health. Data Brief: Opioid-Related Overdose Deaths among Massachusetts Residents. Boston, MA; 2017.
27. Kotelchuck M An Evaluation of the Kessner Adequacy of Prenatal Care Index and a Proposed Adequacy of Prenatal Care Utilization Index. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1615177/pdf/amjph00460-0056.pdf. Accessed December 10, 2017.
28. Vesga-López O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry. 2008;65(7):805–815. doi:10.1001/archpsyc.65.7.805. [PubMed: 18606953]
29. Clapp MA, Little SE, Zheng J, Robinson JN. A multi-state analysis of postpartum readmissions in the United States. Am J Obstet Gynecol. 2016;215(1):113.e1–113.e10. doi:10.1016/j.ajog.2016.01.174. [PubMed: 27829570]
30. VanderKruik R, Barreix M, Chou D, et al. The global prevalence of postpartum psychosis: a systematic review. BMC Psychiatry. 2017;17(1):272. doi:10.1186/s12888-017-1427-7. [PubMed: 28754094]
31. Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. Opioid Use Disorder Documented at Delivery Hospitalization — United States, 1999–2014. MMWR Morb Mortal Wkly Rep. 2018;67(31):845–849. doi:10.15585/mmwr.mm6731a1. [PubMed: 30091969]
32. Hawk KF, Vaca FE, D'Onofrio G. Reducing Fatal Opioid Overdose: Prevention, Treatment and Harm Reduction Strategies. Yale J Biol Med. 2015;88(3):235–245. http://www.ncbi.nlm.nih.gov/pubmed/26339206. Accessed May 10, 2019. [PubMed: 26339206]
33. Larochelle MR, Bernson D, Land T, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality. Ann Intern Med. 2018;169(3):137. doi:10.7326/M17-3107. [PubMed: 29913516]
34. Bagley SM, Cabral H, Saia K, et al. Frequency and associated risk factors of non-fatal overdose reported by pregnant women with opioid use disorder. Addict Sci Clin Pract. 2018;13(1):26. doi:10.1186/s13722-018-0126-0. [PubMed: 30547833]
35. Wachman EM, Schiff DM, Silverstein M. Neonatal Abstinence Syndrome: Advances in Diagnosis and Treatment. JAMA. 2018;319(13):1362–1374. doi:10.1001/jama.2018.2640. [PubMed: 29614184]
36. Mehta PK, Carter T, Vinoya C, Kangovi S, Srinivas SK. Understanding High Utilization of Unscheduled Care in Pregnant Women of Low Socioeconomic Status. Women's Heal Issues. 2017;27(4):441–448. doi:10.1016/j.whi.2017.01.007.
37. O'hara MW, Swain AM. Rates and risk of postpartum depression—a meta-analysis. Int Rev Psychiatry. 1996;8(1):37–54. doi:10.3109/09540269609037816.
38. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ. 2017;357:j1550. doi:10.1136/BMJ.J1550. [PubMed: 28446428]
39. Terplan M, Longinaker N, Appel L. Women-Centered Drug Treatment Services and Need in the United States, 2002–2009. Am J Public Health. 2015;105(11):e50–e54. doi:10.2105/AJPH.2015.302821. [PubMed: 26378825]
40. Bateman BT, Franklin JM, Bykov K, et al. Persistent opioid use following cesarean delivery: patterns and predictors among opioid-naïve women. Am J Obstet Gynecol. 2016;215(3):353.e1–353.e18. doi:10.1016/j.ajog.2016.03.016. [PubMed: 26996986]
41. Prabhu M, Garry EM, Hernandez-Diaz S, MacDonald SC, Huybrechts KF, Bateman BT. Frequency of Opioid Dispensing After Vaginal Delivery. Obstet Gynecol. 2018;132(2):459–465. doi:10.1097/AOG.0000000000002741. [PubMed: 29995732]
42. Ladha KS, Gagne JJ, Patorno E, et al. Opioid Overdose After Surgical Discharge. JAMA. 2018;320(5):502. doi:10.1001/jama.2018.6933. [PubMed: 30087999]
43. Barocas JA, White LF, Wang J, et al. Estimated Prevalence of Opioid Use Disorder in Massachusetts, 2011–2015: A Capture–Recapture Analysis. Am J Public Health. 2018;108(12):1675–1681. doi:10.2105/AJPH.2018.304673. [PubMed: 30359112]

44. National Committee for Quality Assurance. Prenatal and Postpartum Care (PPC) - NCQA. https://www.ncqa.org/hedis/measures/prenatal-and-postpartum-care-ppc/. Published 2017 Accessed May 10, 2019.

45. Earls MF, Yogman MW, Mattson G, Rafferty J, COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH COPAOCAF. Incorporating Recognition and Management of Perinatal Depression Into Pediatric Practice. Pediatrics. 2019;143(1):e20183259. doi:10.1542/peds.2018-3259. [PubMed: 30559120]

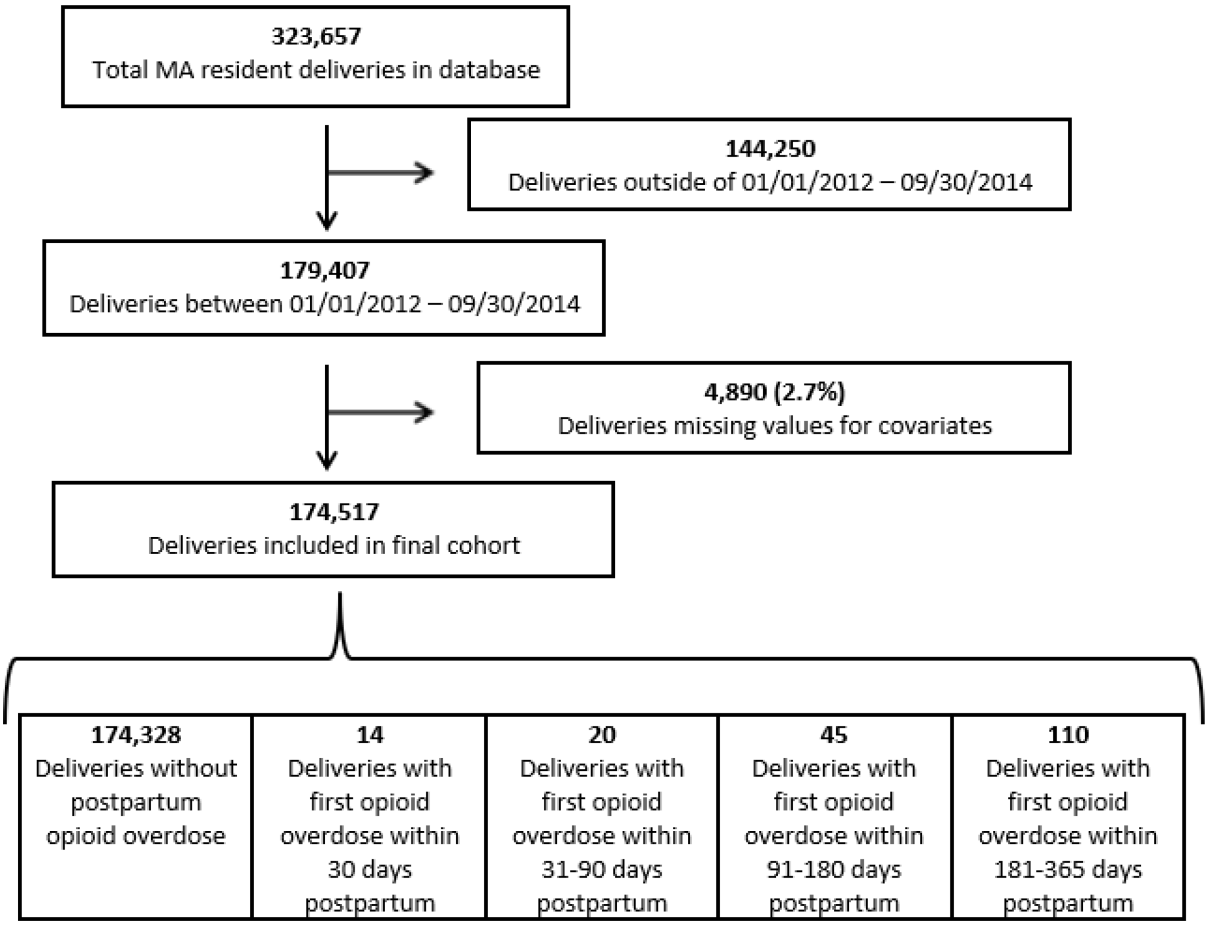
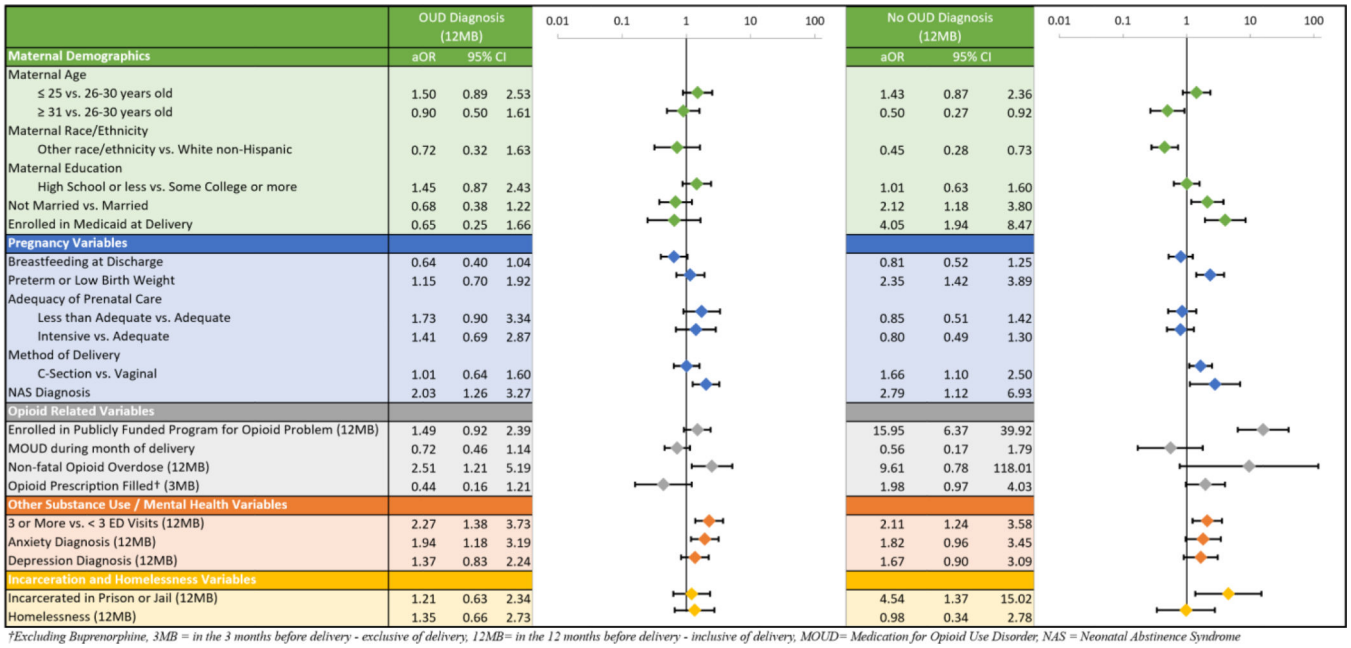


Figure 1:
Study Schema



	OUD Diagnosis (12MB)			No OUD Diagnosis (12MB)		
Maternal Demographics	aOR	95% CI		aOR	95% CI	
Maternal Age						
≤ 25 vs. 26-30 years old	1.50	0.89	2.53	1.43	0.87	2.36
≥ 31 vs. 26-30 years old	0.90	0.50	1.61	0.50	0.27	0.92
Maternal Race/Ethnicity						
Other race/ethnicity vs. White non-Hispanic	0.72	0.32	1.63	0.45	0.28	0.73
Maternal Education						
High School or less vs. Some College or more	1.45	0.87	2.43	1.01	0.63	1.60
Not Married vs. Married	0.68	0.38	1.22	2.12	1.18	3.80
Enrolled in Medicaid at Delivery	0.65	0.25	1.66	4.05	1.94	8.47
Pregnancy Variables						
Breastfeeding at Discharge	0.64	0.40	1.04	0.81	0.52	1.25
Preterm or Low Birth Weight	1.15	0.70	1.92	2.35	1.42	3.89
Adequacy of Prenatal Care						
Less than Adequate vs. Adequate	1.73	0.90	3.34	0.85	0.51	1.42
Intensive vs. Adequate	1.41	0.69	2.87	0.80	0.49	1.30
Method of Delivery						
C-Section vs. Vaginal	1.01	0.64	1.60	1.66	1.10	2.50
NAS Diagnosis	2.03	1.26	3.27	2.79	1.12	6.93
Opioid Related Variables						
Enrolled in Publicly Funded Program for Opioid Problem (12MB)	1.49	0.92	2.39	15.95	6.37	39.92
MOUD during month of delivery	0.72	0.46	1.14	0.56	0.17	1.79
Non-fatal Opioid Overdose (12MB)	2.51	1.21	5.19	9.61	0.78	118.01
Opioid Prescription Filled† (3MB)	0.44	0.16	1.21	1.98	0.97	4.03
Other Substance Use / Mental Health Variables						
3 or More vs. < 3 ED Visits (12MB)	2.27	1.38	3.73	2.11	1.24	3.58
Anxiety Diagnosis (12MB)	1.94	1.18	3.19	1.82	0.96	3.45
Depression Diagnosis (12MB)	1.37	0.83	2.24	1.67	0.90	3.09
Incarceration and Homelessness Variables						
Incarcerated in Prison or Jail (12MB)	1.21	0.63	2.34	4.54	1.37	15.02
Homelessness (12MB)	1.35	0.66	2.73	0.98	0.34	2.78

†Excluding Buprenorphine, 3MB = in the 3 months before delivery - exclusive of delivery, 12MB= in the 12 months before delivery - inclusive of delivery, MOUD= Medication for Opioid Use Disorder, NAS = Neonatal Abstinence Syndrome

Figure 2:

Adjusted Odds Ratios for Postpartum Opioid Overdose, Stratified by OUD Diagnosis (N=174,517)

Table 1:

Maternal and Infant Characteristics by Postpartum Opioid Overdose (N=174,517)

	OD event during 365 days following delivery (n= 189)		No OD event during 365 days following delivery (n= 174,328)		OD Rate per 10,000 live births
Characteristics	**n**	**%**	**n**	**%**	**Rate (95% CI)**
Maternal Demographics					
Maternal Age					
≤ 25 years old	88	46.6%	34,662	19.9%	25.3 (20.0, 30.6)
26–30 years old	61	32.3%	45,994	26.4%	13.2 (9.9, 16.6)
≥ 31 years old	40	21.2%	93,672	53.7%	4.3 (2.9, 5.6)
Maternal Race/Ethnicity					
White non-Hispanic	153	81.0%	111,031	63.7%	13.8 (11.6, 15.9)
Other race/ethnicity	36	19.1%	63,297	36.3%	5.7 (3.8, 7.5)
Maternal Education					
High School or less	117	61.9%	47,295	27.1%	24.7 (20.2, 29.1)
Some College or more	72	38.1%	127,033	72.9%	5.7 (4.4, 7.0)
Marital Status					
Married	35	18.5%	114,985	66.0%	3.0 (2.0, 4.1)
Not Married	154	81.5%	59,343	34.0%	25.9 (21.8, 30.0)
Enrolled in MassHealth at Delivery					
Yes	173	91.5%	73,045	41.9%	23.6 (20.1, 27.1)
No	16	8.5%	101,283	58.1%	1.6 (0.8, 2.4)
Pregnancy Variables					
Breastfeeding at Discharge					
Yes	90	47.6%	145,117	83.2%	6.2 (4.9, 7.5)
No	99	52.4%	29,211	16.8%	33.8 (27.1, 40.4)
Preterm or Low Birth Weight (% Yes)					
Yes	50	26.5%	16,707	9.6%	29.8 (21.6, 38.1)
No	139	73.5%	157,621	90.4%	8.8 (7.3, 10.3)
Adequacy of Prenatal Care*					
Less than Adequate	80	42.3%	36,888	21.2%	21.6 (16.9, 26.4)
Adequate	50	26.5%	72,899	41.8%	6.9 (5.0, 8.8)
Intensive	59	31.2%	64,541	37.0%	9.1 (6.8, 11.5)
Method of Delivery					
Vaginal	120	63.5%	120,866	69.3%	9.9 (8.1, 11.7)
C-Section	69	36.5%	53,462	30.7%	12.9 (9.8, 15.9)
NAS Diagnosis					
Yes	66	34.9%	1,892	1.1%	337.1 (255.8, 418.4)
No	123	65.1%	172,436	98.9%	7.1 (5.9, 8.4)
Opioid Related Variables					

	OD event during 365 days following delivery (n= 189)		No OD event during 365 days following delivery (n= 174,328)		OD Rate per 10,000 live births
Characteristics	**n**	**%**	**n**	**%**	**Rate (95% CI)**
Enrolled in BSAS Program for Opioid Problem (12MB) (% Yes)	67	35.5%	1,233	0.7%	515.4 (392.0, 638.8)
Type of MOUD (12MB)					
Buprenorphine only	32	16.9%	1,210	0.7%	257.6 (158.4, 346.9)
Methadone only	32	16.9%	1,071	0.6%	290.1 (189.6, 390.6)
Mixed	14	7.4%	233	0.1%	566.8 (269.9, 863.7)
None	111	58.7%	171,814	98.6%	6.5 (5.3, 7.7)
MOUD during month of delivery (% Yes)	56	29.6%	1,935	1.1%	281.3 (207.6, 354.9)
Non-fatal Opioid Overdose (12MB) (% Yes)	12	6.4%	67	0.04%	1519.0 (659.5, 2378.4)
OUD Diagnosis (Casemix or APCD) (12MB)					
Yes	88	46.6%	2,431	1.4%	349.3 (276.4, 422.3)
No	101	53.4%	171,897	98.6%	5.9 (4.7, 7.0)
Opioid RX† Filled (3MB‡)					
Yes	14	7.4%	4,347	2.5%	32.1 (15.3, 48.9)
No	175	92.6%	169,981	97.5%	10.3 (8.8, 11.8)
Healthcare Utilization					
Any Emergency department visit (12MB‡					
Yes	116	61.4%	36,280	20.8%	31.9 (26.1, 37.7)
No	73	38.6%	138,048	79.2%	5.3 (4.1, 6.5)
Any Hospital admission (12MB‡)					
Yes	51	27.0%	8,637	5.0%	58.7 (42.6. 74.8)
No	138	73.0%	165,691	95.1%	8.3 (6.9, 9.7)
Any Observational Stay (12MB‡)					
Yes	24	12.7%	7,925	4.6%	30.2 (18.1, 42.3)
No	165	87.3%	166,403	95.5%	9.9 (8.4, 11.4)
Any Inpatient or ED utilization (12MB‡)					
Yes	122	64.6%	43,711	25.1%	27.8 (22.9, 32.8)
No	67	35.5%	130,617	74.9%	5.2 (3.9, 6.4)
High Utilization of ED (12MB‡)					
3 or more ED or OB triage visits	77	40.7%	9,292	5.3%	82.2 (66.8, 100.5)
Less than three visits	112	59.3%	165,036	94.7%	6.8 (5.5, 8.0)
Mental Health Variables					
Anxiety Diagnosis (12MB)					
Yes	69	36.5%	7,821	4.5%	87.5 (66.8, 108.1)
No	120	63.5%	166,507	95.5%	7.2 (5.2, 8.5)
Depression Diagnosis (12MB)					
Yes	71	37.6%	9,646	5.5%	73.1 (56.1, 90.1)

	OD event during 365 days following delivery (n= 189)		No OD event during 365 days following delivery (n= 174,328)		OD Rate per 10,000 live births
Characteristics	**n**	**%**	**n**	**%**	**Rate (95% CI)**
No	118	62.4%	164,682	94.4%	7.2 (5.2, 8.5)
Incarceration and Homelessness Variables					
Incarcerated in Prison or Jail (12MB)					
Yes	18	9.5%	359	0.2%	477.5 (256.9, 698.0)
No	171	90.5%	173,969	99.9%	9.8 (8.3, 11.3)
Homelessness - shelter/hotel case file (12MB)					
Yes	15	7.9%	2,049	1.2%	72.7 (35.9, 109.5)
No	174	92.1%	172,279	98.8%	10.1 (8.6, 11.6)

† Excluding Buprenorphine, 3MB‡ = in the 3 months before delivery - exclusive, 12MB= in the 12 months before delivery - inclusive, 12MB‡ = in the 12 months before delivery - exclusive, SP=in study period (2011–2015)

APCD = All Payer Claims Database, BSAS = Bureau of Substance Addiction Services, Casemix = Hospital discharge data, DHCD = Department of Housing and Community Development, DPH = Department of Public Health, MOUD=Medication for Opioid Use Disorder NAS = Neonatal Abstinence Syndrome

Table 2:

Comparison of Maternal and Infant Characteristics among Women with Postpartum Overdose by Evidence of Opioid Use Disorder (N=189)

	Evidence of OUD in 12 months before delivery, inclusive (n= 88)		No Evidence of OUD in 12 months before delivery, inclusive (n= 101)		
Characteristics	**n**	**%**	**n**	**%**	**p-value**
Maternal Demographics					
Maternal Age					0.200
≤ 25 years old	35	39.8%	53	52.5%	
26–30 years old	31	35.2%	30	29.7%	
≥ 31 years old	22	25.0%	18	17.8%	
Maternal Race/Ethnicity					0.001
White non-Hispanic	*	*	73	72.3%	
Other race/ethnicity	*	*	28	27.7%	
Maternal Education					0.024
High School or less	62	70.5%	55	54.5%	
Some College or more	26	29.6%	46	45.5%	
Marital Status					0.911
Married	16	18.2%	19	18.8%	
Not Married	72	81.8%	82	81.2%	
Enrolled in MassHealth at Delivery (% Yes)	*	*	11	10.9%	0.199
Pregnancy Variables					
Breastfeeding at Discharge (% Yes)	28	31.8%	62	61.4%	<0.001
Preterm or Low Birth Weight (% Yes)	25	28.4%	25	24.8%	0.570
Adequacy of Prenatal Care					<0.001
Less than Adequate	51	58.0%	29	28.7%	
Adequate	13	14.8%	37	36.6%	
Intensive	24	27.3%	35	34.7%	
Method of Delivery					0.344
Vaginal	59	67.1%	61	60.4%	
C-Section	29	33.0%	40	39.6%	
NAS Diagnosis (% Yes)	56	63.6%	*	*	<0.001
Opioid Related Variables					
Enrolled in BSAS Program for Opioid Problem (12MB) (% Yes)	50	56.8%	17	16.8%	<0.001
Any MOUD (12MB) (% Yes)	67	76.1%	11	10.9%	<0.001
MOUD during month of delivery (% Yes)	50	56.8%	*	*	<0.001
Non-fatal Opioid Overdose (12MB) (% Yes)	11	12.5%	*	*	0.001
Healthcare Utilization					
Any Emergency department visit (12MB‡) (% Yes)	67	76.1%	49	48.5%	<0.001

	Evidence of OUD in 12 months before delivery, inclusive (n= 88)		No Evidence of OUD in 12 months before delivery, inclusive (n= 101)		
Characteristics	**n**	**%**	**n**	**%**	**p-value**
Any Hospital admission (12MB‡) (% Yes)	38	43.2%	13	12.9%	<0.001
Any Observational Stay (12MB‡) (% Yes)	19	21.6%	*	*	0.001
Any Inpatient or ED utilization (12MB‡) (% Yes)	70	79.6%	52	51.5%	<0.001
ED Visits (12MB‡) (% Yes)	48	51.4%	29	28.7%	<0.001
Mental Health Variables					
Anxiety Diagnosis (12MB) (% Yes)	50	56.8%	19	18.8%	<0.001
Depression Diagnosis (12MB) (% Yes)	50	56.8%	21	20.8%	<0.001
Incarceration and Homelessness Variables					
Incarcerated in Prison or Jail (12MB) (% Yes)	11	12.5%	*	*	0.193
DHCD shelter/hotel case file (12MB) (% Yes)	11	12.5%	*	*	0.030

* Values suppressed due to privacy restrictions. Any non-zero value < 11 is suppressed. If only one value is suppressed in a category, the next smallest value is also suppressed to prevent back calculation.

3MB‡ = in the 3 months before delivery - exclusive, 12MB= in the 12 months before delivery - inclusive, 12MB‡ = in the 12 months before delivery - exclusive, SP=in study period (2011–2015)

APCD = All Payer Claims Database, Casemix = Hospital discharge data, DHCD = Department of Housing and Community Development, MOUD=Medication for Opioid Use Disorder, NAS = Neonatal Abstinence Syndrome