HHS Public Access

Author manuscript

Drug Alcohol Depend. Author manuscript; available in PMC 2022 June 01.

Published in final edited form as:

Drug Alcohol Depend. 2021 June 01; 223: 108704. doi:10.1016/j.drugalcdep.2021.108704.

Maternal opioid exposure, neonatal abstinence syndrome, and infant healthcare utilization: A retrospective cohort analysis

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Abstract

Background: We sought to describe healthcare utilization of infants by maternal opioid exposure and neonatal abstinence syndrome (NAS) status.

Methods: A longitudinal cohort of 81,833 maternal-infant dyads were identified from Oregon's 2008–2012 linked birth certificate and Medicaid eligibility and claims data. Chi-square tests compared term infants (≥37 weeks of gestational age) by maternal opioid exposure, defined using International Classification of Diseases, Ninth Revision, Clinical Modification (*ICD-9-CM*) diagnosis codes or prescription fills, and NAS, defined using *ICD-9-CM* codes, such that infants were categorized as Opioid+/NAS+, Opioid+/NAS−, Opioid−/NAS+, and Opioid−/NAS−.

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Contributors

Dr. Ko conceptualized and designed the study, coordinated data acquisition, analyzed and interpreted data, and drafted, revised, and finalized the manuscript for submission. Dr. Yoon conceptualized and designed the study, coordinated data acquisition, created the analytic dataset, and critically reviewed and provided edits in preparation for submission. Ms. Tong conceptualized and designed the study, assisted with interpretation of data, and critically reviewed and provided edits to the manuscript in preparation for submission. Ms. Rockhill designed analytic methods for the study and critically reviewed and provided edits to the manuscript in preparation for submission. Ms. Haight and Ms. Patel carried out analyses, provided interpretation of the data, and critically reviewed and the manuscript in preparation for submission. Dr. Luck is the principal investigator of the study from which data were acquired and was instrumental in the acquisition of the data for this project; he also critically reviewed the manuscript in preparation for submission; and Dr. Shapiro-Mendoza contributed to the design and acquisition of the data, critically reviewed the manuscript, and provided edits that contributed to the interpretation of the data. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Publisher's Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC. The following study is not being considered for publication elsewhere and has not been published previously.

Declaration of Competing Interest

No conflicts declared

Modified Poisson regression was used to calculate adjusted risk ratios (aRR) and 95 % confidence intervals (CI) for healthcare utilization for each infant group compared to Opioid−/NAS− infants.

Results: The prevalence of documented maternal opioid exposure was 123.1 per 1000 dyads and NAS incidence was 5.8 per 1000 dyads. Compared to Opioid−/NAS− infants, infants with maternal opioid exposures were more likely to be hospitalized within 4 weeks (Opioid+/ NAS+: [aRR: 4.7; 95 % CI: 4.3–5.1]; Opioid+/ NAS−: [aRR: 3.7; 95 %CI: 3.1–4.5]) and a year after birth (Opioid+/ NAS+: [aRR: 3.7; 95 %CI: 3.4–4.0]; Opioid+/ NAS−: [aRR: 2.8; 95 %CI: 2.3–3.4]). Infants with maternal opioid exposure and/or NAS were more likely than Opioid−/NAS− infants to have ≥2 sick visits and any ED visits in the year after birth.

Conclusions: Infants with NAS and/or maternal opioid exposure had greater healthcare utilization than infants without NAS or opioid exposure. Efforts to mitigate future hospitalization risk and encourage participation in preventative services within the first year of life may improve outcomes.

Keywords

Opioids; Neonatal abstinence syndrome; Infant; Medicaid; Pregnancy; Healthcare

1. Introduction

Maternal opioid exposure is thought to have driven recent increases in the incidence of neonatal abstinence syndrome (NAS), a newborn withdrawal syndrome (Patrick et al., 2020; Patrick et al., 2015a). Other substances (e.g., antidepressants, benzodiazepines, tobacco) have also been implicated in newborn withdrawal signs such as tremors, dehydration, and poor weight gain (Hudak et al., 2012). NAS risk and severity is dependent on multiple factors (Patrick et al., 2020, 2015a), including cumulative opioid exposure (Patrick et al., 2015a; Desai et al., 2015), maternal smoking history or daily cigarettes smoked (Patrick et al., 2015a; Desai et al., 2015), maternal history of opioid or alcohol dependence (Desai et al., 2015), and psychotropic medication exposure (Desai et al., 2015). Benzodiazpaines and gabapentine co-exposures have been found to increase length of hospitalization stay and the need for pharmacological treatment of infants with NAS (Wachman et al., 2018a).

Infants with NAS typically have longer mean birth hospitalizations than infants without NAS (Winkelman et al., 2018). However, less is known regarding hospitalization and healthcare utilization in the first year of life for infants with NAS and whether it differs from infants exposed to opioids but without NAS. Only a few studies have estimated the risk of hospitalization or readmission among U.S. infants with NAS (Liu et al., 2019; Patrick et al., 2015b; Percy et al., 2020) or maternal opioid exposure (Percy et al., 2020). A New York state study found that infants with NAS were more than twice as likely as uncomplicated term infants without NAS to have a hospital readmission 30 days after birth hospitalization (Patrick et al., 2015b). In data from commercial healthcare plans, children with NAS were found to have increased inpatient hospitalizations within the first year of life which persisted into early childhood (Liu et al., 2019). Maternal opioid exposure were not available in these studies. Compared to non-exposed infants in an Ohio county, infants with opioid exposure but without a NAS diagnosis had increased odds of hospitalization during the first year of

life; however, infants with NAS did not have increased hospitalization odds (Percy et al., 2020).

Utilization of other healthcare services during the first year of life, such as emergency department visits (Hwang et al., 2020; Percy et al., 2020), sick visits, and routine well-child visits (Goyal et al., 2020; Jarlenski et al., 2020), by infants exposed to opioids or diagnosed with NAS is not well understood. Among opioid-exposed infants, 40 % had an emergency department visit in their first year of life (Hwang et al., 2020). In a study comparing opioid exposed and unexposed infants, similar rates of emergency department visits were observed (Percy et al., 2020).

As an estimated 80 % of infants with NAS are Medicaid-financed (Winkleman et al., 2018, Patrick et al., 2012), understanding healthcare utilization of infants by maternal opioid exposure and NAS diagnosis status would be useful in planning for health care utilization and services for affected infants who remain publicly insured. Further, understanding hospitalization risk can be informative in guiding optimal management of NAS during birth hospitalization and discharge planning. Thus, using maternal-infant linked data of a Medicaid-enrolled population, we sought to: 1) describe sociodemographic and clinical characteristics; and 2) examine infant healthcare utilization (i.e., hospitalization and well-child, sick-child, and ED visits) within a year of birth by maternal opioid exposure and NAS status.

2. Material and methods

2.1. Study design and sample

A longitudinal cohort was constructed by deterministically linking birth certificate data to Medicaid eligibility, healthcare claims, and pharmaceutical claims data of women and their children (aged<3 years) in Oregon during 2008–2012 (Fig. 1); linkage was >90 %. Of the 113,106 Medicaid-financed births occurring during 2008–2012 with up to 10 months of pregnancy data, 94,959 maternal-infant dyads (84.0 %) had 1-year infant follow-up data. Mothers <15 or >44 years of age, infants who may require different healthcare needs (non-singleton deliveries, infants with iatrogenic withdrawal or congenital abnormalities, infants born <22 or >42 weeks or missing gestational age, premature infants [gestational age <37 weeks], infants with non-hospital births), and infants not eligible for our outcomes of interest (infants with birth hospitalization greater than 4 weeks or who died within a year of birth) were excluded (n = 13,126), yielding 81,833 mother-infant dyads.

2.2. Measures

2.2.1. Opioid exposure and NAS—Maternal opioid exposure was identified as opioid-related (abuse, dependence, poisoning, or adverse effect of opioids, heroin, or analgesics) *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis codes occurring during pregnancy (Appendix A) or ≥1 opioid prescription filled during pregnancy from Medicaid claims and pharmaceutical data (National Drug Codes [NDC] available upon request). NAS was identified with an *ICD-9-CM* code (779.5) in Medicaid claims data, which has been found to have a positive predictive value of 91 %

(Maalouf et al., 2019). Dyads were grouped into four categories: infants with documented maternal opioid exposure with (Opioid+/NAS+) and without NAS (Opioid+/NAS−), and infants without documented maternal opioid exposure with (Opioid−/ NAS+) and without NAS (Opioid−/NAS−).

2.2.2. Maternal sociodemographic and comorbidities and infant birth outcomes—

Maternal characteristics were identified from the birth certificate (2003 version) and categorized as: maternal age at delivery (15–25, 26–35, 36–44 years), race and Hispanic origin (Non-Hispanic white, Non-Hispanic black, Hispanic, Non-Hispanic other/ unknown), highest education level obtained (≤ high school, ≥ some college), marital status at delivery (married, unmarried), residence at delivery (urban, rural; categorization based on the US Department of Agriculture's 2013 Rural-Urban Continuum Codes), previous live births (0, 1, ≥2), and trimester of entry into prenatal care (1st, 2nd, 3rd, none). Tobacco use during pregnancy was self-reported on the birth certificate and tobacco use diagnoses were obtained from maternal Medicaid claims data. Medicaid claims were used to identify diagnoses during pregnancy of depression, anxiety, drug-induced mental health disorder, alcohol use disorder, other substance use disorder, and fills for selective serotonin reuptake inhibitors (SSRIs) (Appendix A: *ICD-9-CM* codes; NDC available upon request). Birthweight (<2500 or ≥2,500 g) was obtained from the birth certificate.

2.2.3. Infant hospitalization and healthcare utilization—

Birth hospitalization and associated length of stay (days) were identified from infant Medicaid claims that had a birth code (*ICD-9-CM:* V30-V39). Subsequent hospitalizations were identified as inpatient hospital admissions that occurred after birth hospitalization discharge, among infants discharged from their birth hospitalization before 4 weeks. The following variables were created from infant Medicaid claims data: hospitalization within 4 weeks of birth (yes/no), hospitalization within a year after birth (yes/no), number of hospitalizations, and average length of hospitalization stay (days). Hospitalization reasons were identified and categorized based on existing relevant literature and most frequently observed reasons: feeding issues or dehydration, seizures or other life threatening events, respiratory conditions, jaundice or hemolytic events, fever, non-respiratory infections, respiratory infections, diarrhea, and injuries (Patrick et al., 2015a, b; Tomashek et al., 2006)(Appendix A: *ICD-9-CM* and Current Procedural Terminology [CPT] codes). Similar to previous studies, attendance at well-child visits within a year after birth was categorized as <5 or ≥5 visits to account for longer birth and other hospitalizations (Farr et al., 2013). Number of sick-child visits (<2 or ≥2) were identified from CPT codes (Appendix A) and ED visits (none or any) were identified as services in an ED occurring after birth hospitalization discharge.

2.3. Statistical analysis

We estimated the prevalence of maternal opioid exposure and the incidence of NAS. Chi-square tests were conducted to assess differences in maternal sociodemographic, mental health, and substance use characteristics and infant gestational age and birthweight among the four categories (herein referred to as Opioid+/NAS+, Opioid+/NAS−, Opioid−/NAS+, Opioid−/NAS− infants). Median hospitalization lengths of stay were compared using Kruskal-Wallis tests. Timing of first hospitalization and healthcare utilization (well-child

visit attendance, sick-child, and ED visits) was assessed across the four categories using chi-square tests. Among hospitalized infants, differences in reasons for hospitalization and the number and length of stay of hospitalizations were assessed, respectively, using chi-square tests and ANOVA tests.

Modified Poisson regression with robust error variance was used to calculate unadjusted and adjusted risk ratios for Opioid+/NAS+, Opioid+/NAS−, Opioid−/NAS + infants compared to Opioid−/NAS− infants and five outcomes: hospitalization within four weeks after birth (Model 1), hospitalization within one year after birth (Model 2), attendance at <5 vs. 5+ well-child visits (Model 3), attendance at ≥2 vs. < 2 sick visits (Model 4), and any vs. no ED visits within one year of birth (Model 5). All models were adjusted for infant sex, and maternal race/ethnicity, age, education, marital status, residence at delivery, trimester of entry into prenatal care, depression, anxiety, SSRI use, tobacco use, alcohol use disorder, and other substance use disorder based on a directed acyclic graph.

Missing values for education (n = 406; 0.5 %), marital status (n = 71; 0.1 %), tobacco use during pregnancy (n = 800; 1.0 %), and residence (n = 261; 0.3 %) were imputed with average values to allow for inclusion of these observations in the models. All analyses were performed using SAS 9.3 Statistical Software and SAS-callable SUDAAN. All cells with fewer than 10 dyads were suppressed to prevent identification.

3. Results

3.1. Maternal opioid exposure and NAS

Of the 81,833 maternal-infant dyads in our sample, the prevalence of maternal opioid exposure was 123.1/1000 and the incidence of NAS was 5.8 per 1000 infants during 2008–2012. Among infants with maternal opioid exposure, 3.5 % had NAS. Maternal opioid exposure was present more frequently among infants with NAS (74.8 %) than among infants without NAS (12.0 %). Among the Opioid+/NAS + group, 25.4 % had maternal prescription opioid exposure only, 43.8 % had maternal opioid use disorder only, and 30.8 % had both maternal prescription opioid use and opioid use disorder exposure. Among the Opioid+/NAS− group, 92.8 % had maternal prescription opioid use exposure only, 4.2 % maternal opioid use disorder only, and 3.0 % had both maternal prescription opioid use and opioid use disorder exposure (data not shown).

Compared to Opioid−/NAS− infants, Opioid+/NAS + infants were more likely to be born to mothers who were 26–35 years of age; identified as Non-Hispanic white; had some college education or more; were unmarried; were urban residents; initiated prenatal care in the 3rd trimester or not at all; and had mental health and/or substance use diagnoses during pregnancy ($p < 0.01$ for all, Table 1). Compared to the other groups, Opioid+/NAS + infants had the highest prevalence of documented maternal major and minor depression (8.2 %), anxiety (5.9 %), drug-induced mental health disorder (10.7 %), report of tobacco use (72.9 %), alcohol use disorder (9.3 %) and other substance use disorder (51.7 %), as well as infant diagnosis of narcotics affecting infants (16.4 %). Opioid−/NAS + infants had the second highest report of maternal tobacco use (64.7 %), diagnosis of other substance use disorder (30.3 %) as well as infant diagnosis of narcotics affecting infant (17.7 %). The Opioid−/NAS

+ infants had the highest prevalence of infant diagnosis of noxious substance affecting infant (19.3 %).

3.2. Infant characteristics and healthcare utilization

The Opioid+/NAS + infants were more likely to be <2,500 g (7.6 %) at birth than Opioid−/NAS− infants (1.9 %, $p < 0.01$, Table 2). The median length of stay at birth hospitalization was greater for Opioid+/NAS + infants (4 days) and Opioid−/ NAS + and Opioid+/NAS− infants (both 3 days) than for Opioid−/NAS− infants (2 days; $p < 0.01$ for all).

Overall, 12.3 % and 16.3 % of our study population was hospitalized within 4 weeks and a year of birth, respectively. A greater proportion of Opioid+/NAS + infants were hospitalized within 4 weeks after birth (60.7 %) than Opioid−/NAS+ (47.9 %), Opioid+/NAS− (12.9 %), and Opioid−/NAS− infants (11.9 %; $p < 0.01$; Table 2). A greater proportion of opioid+/ NAS + infants were hospitalized within a year after birth (65.5 %) than Opioid−/NAS+ (48.7 %), Opioid+/NAS− (18.7 %), and Opioid−/NAS− infants (15.7 %; $p < 0.01$). The average number of hospitalizations within a year after birth was greatest for Opioid+/NAS + infants, followed by Opioid−/NAS+, Opioid+/NAS−, and Opioid−/NAS− infants (respectively, 9.8, 9.4, 3.3, and 3.1 hospitalizations; $p < 0.01$). The average length of hospitalization stays after birth hospitalization did not significantly differ by Opioid/NAS group (p's>0.05). Hospitalization reasons, with the exceptions of seizures/life-threatening event, respiratory condition, fever, and non-respiratory infection, differed across Opioid/NAS groups. Feeding issues or dehydration were more prevalent among infants with NAS, regardless of maternal opioid exposure, compared to infants without NAS ($p < 0.01$).

Overall, 55.4 % of our sample had <5 well-child visits, 53.9 % had ≥ 2 sick visits, and 18.4 % had any ED visit within a year of birth. A greater proportion of opioid+/NAS + infants had <5 well-child visits (68.6 %) than Opioid−/NAS+ (57.1 %), Opioid+/ NAS− (56.4 %), and Opioid−/NAS− infants (55.2 %; $p < 0.01$; Table 2). A greater proportion of Opioid+/NAS + infants had ≥2 sick child visits (65.8 %) than Opioid−/NAS− infants (52.6 %; $p < 0.01$). Additionally, a greater proportion of Opioid+/NAS + infants had an ED visit within a year of birth (26.0 %) than Opioid−/NAS− infants (17.7 %; $p < 0.01$).

3.3. Adjusted models

Compared to Opioid−/NAS− infants, Opioid+/NAS + infants were 4.67 (95 % CI: 4.25–5.13) times, Opioid+/NAS− infants were 3.73 (95 % CI: 3.09–4.52) times, and Opioid−/ NAS + infants were 1.07 (95 % CI: 1.01–1.13) times as likely to be hospitalized within four weeks after birth in models adjusting for potential confounders (Table 3). Similarly, relative to Opioid−/NAS− infants, Opioid+/NAS + infants (aRR: 3.68; 95 % CI: 3.39–4.01), Opioid+/NAS− infants (aRR: 2.77; 95 %: 2.30–3.35), and Opioid−/NAS+ (aRR: 1.15; 95 % CI: 1.09–1.20) infants were more likely to be hospitalized within one year after birth. Additionally, Opioid+/NAS + infants were 1.16 (95 %CI: 1.08–1.24) times as likely to have <5 well-child visits within one year after birth compared to Opioid−/NAS− infants. Infants with maternal opioid exposure and/or NAS were more likely to have ≥2 sick visits and at

least 1 ED visit within the first year of life compared to Opioid−/NAS− infants; the 95 % confidence intervals overlapped for the three exposed groups.

4. Discussion

In our retrospective cohort of continuously Medicaid-enrolled mothers and term infants in Oregon, we found that approximately half of infants with NAS, regardless of documented maternal opioid exposure, were hospitalized within 4 weeks or up to a year of birth, which was more likely than non-opioid exposed infants without NAS (Opioid−/NAS−). On average, infants with NAS had a greater number of hospitalizations within a year after birth than infants without NAS. After accounting for potential confounders, opioid-exposed infants with NAS had the highest magnitude of risk for hospitalization within 4 weeks and up to a year after birth, followed by infants with maternal opioid exposure without NAS, and non-opioid exposed infants with NAS. Our findings differ from another study which found that infants with opioid exposure, but without NAS had an increased risk of hospitalization within a year, whereas infants with NAS did not have a stastically significant higher risk (Percy et al., 2020). However, other studies have found that infants with NAS have an increased risk of hospital readmission within 30-days (Patrick et al., 2015b) as well as increased hospitalization risk within a year (Liu et al., 2019). In the context of these other studies, our findings indicate a need for better assessment of the dyad's readiness for discharge and of continued risk over the first year of life. Feeding issues/dehydration were more common among infants with NAS; feeding problems are common reasons for hospitalization among all infants and considered preventable (Young et al., 2013). Additionally, diagnoses of maternal depression and anxiety, and other substance use/use disorder were more common among opioid-exposed infants with NAS. Together, these findings suggests that affected mother-infant dyads may benefit from additional support and services post-discharge (e.g., home-visiting) and from early, accessible, collaborative pediatric care.

Well-child visits are opportunities to monitor and assess growth, screen for and initiate early intervention for problematic development, and provide guidance to caregivers. In our study, which excluded infants with birth hospitalizations greater than 4 weeks, over half of our overall Medicaid sample attended <5 well-child visits within a year after birth. Attendance at well-child visits differed by NAS and opioid exposure with nearly 70 % of infants with NAS and maternal opioid exposure only attending <5 well-child visits. These estimates are similar to another study of 8 large pediatric academic health centers in Delaware, Pennsylvania, and Florida which found that half of their sample and three- quarters of infants with intrauterine opioid exposure did not adhere to recommendations for well child visits defined as attendance at 1-, 2-, 4-, 6-, 9- and 12-month visits (Goyal et al., 2020). Medicaid-enrolled children are less likely to complete the recommended well-child schedule (Freed et al., 1999; Chi et al., 2013), and over 80 % of births with NAS are financed by Medicaid (Patrick et al., 2012; Winkelman et al., 2018). These data suggest a need to understand barriers to well-child attendance for families of infants with opioid exposure or NAS.

Further, we found that infants with maternal opioid exposure and/or NAS were more likely to have ≥2 sick visits and at least one ED visit than infants without maternal opioid exposure

or NAS. A study of Medicaid-enrolled children in New York and Texas found an increased healthcare utilization ratio for ED visits in children with NAS within the first two years of life, even after matching demographically and clinically similar infants without NAS (healthcare utilization ratio: 1.06; 95 %CI: 1.01, 1.11) (Taylor et al., 2020). In conjunction with lower well-child attendance, our findings of higher sick and ED visits suggest a need to encourage use of preventative services. Public health strategies such as reducing stigma and improving continuity of care for the mother and infant dyad may be beneficial.

Less than 5% of infants with documented maternal opioid exposure had an NAS diagnosis. However, among infants with NAS, approximately 3 out of 4 infants had a documented maternal opioid exposure at any time during pregnancy. In the quarter of infants with NAS without maternal opioid exposure, it is possible that maternal opioid use was undocumented (e.g., undiagnosed opioid use disorder, diverted opioid prescriptions, undisclosed illicit use) or that another possible exposure, like benzodiazepines, was not considered (Desai et al., 2015). This is consistent with another study that found 65 % of infants with NAS had a documented maternal prescription opioid exposure (Patrick et al., 2015a); our higher proportion may be due to the inclusion of opioid-related diagnosis codes in our exposure. Opioid-related diagnostic codes (including opioid use disorder) and prescriptions were included in our study as both exposures may result in NAS. The composition of the Opioid+/NAS + and Opioid+/NAS− groups differed in that the Opioid+/NAS + group had a greater proportion of women with opioid use disorder; sample sizes restricted further analysis regarding type of maternal opioid exposure and infant healthcare utilization. Our findings may also reflect a more vulnerable population of continuous Medicaid-enrolled maternal-infant dyads than previous study samples of Medicaid-financed births, which allows for higher income levels to be eligible for Medicaid for pregnancy.

NAS is an expected condition that may result from medication-assisted treatment which is the recommended treatment for opioid use disorder during pregnancy (American College of Obstetricians and Gynecologists, 2017). Collaboration between addiction specialists, obstetrician-gynecologists, and pediatric care teams is essential for the dyad’s health (Ko et al., 2017). However, currently, there is no national standard for assessment or care of infants with NAS at birth hospitalization. In 2016, the total hospital cost of U.S. infants with NAS at birth hospitalization was an estimated $572.7 million (Strahan et al., 2019) attributed in part to longer length of stays. To reduce length of stay and costs, innovative protocols like outpatient tapering and non-pharmaceutical interventions are being explored (Backes et al., 2012; MacMillan et al., 2018; Smirk et al., 2014; Wachman et al., 2018b). However, it is important to evaluate the impact of these protocols on subsequent hospitalizations in the first year of life. Our data suggest a need to improve the transition from hospital to home. Interventions, discharge guidelines, and research related to other populations of at-risk infants (i.e., preterm infants) (Engle et al., 2007; Kuzniewicz et al., 2013; Phillips et al., 2013) may yield lessons on how best to support maternal-infant dyads, considerations for additional follow-up, and outreach to promote engagement in preventative services and reduce hospitalizations and healthcare costs (Winkleman et al., 2018).

4.1. Strengths and limitations

A strength of this study is linked maternal and infant data allowing for the unique capture of both maternal exposure and infant outcome and healthcare utilization data. In our cohort of Medicaid-financed births in Oregon, the incidence of NAS was 5.8 per 1000 dyads during 2008–2012. This estimate is higher than another published Oregon-specific NAS estimate during the same time frame (Ko et al., 2016), which encorporated all births, regardless of payer source. Linkage of multiple data sources provided data on numerous confounders and allowed for follow-up of infant healthcare utilization through the first year of life.

This study has a few limitations. First, the study relies on administrative data from Medicaid records and pharmaceutical claims. Diagnoses and pharmaceutical fills may not represent use or other opioid exposures (heroin use, use of diverted opioid prescriptions, etc.); thus, estimates of maternal opioid exposure may be biased. Second, at the time of these data, a standard definition for NAS did not exist (Chiang et al., 2019); thus, there is likely unaccounted variability and potential underestimation of identification of NAS through ICD-9-CM codes. In this analysis, we were unable to distinguish the need for pharmacologic treatment or NAS severity which likely influences an individual infant's hospitalization risk. Finally, results may not be generalizable as analyses focused on Medicaid-financed deliveries in Oregon. Given public health and clinical quality improvement efforts related to NAS, analyses may not reflect post-2012 infant healthcare utilization.

4.2. Conclusions

Limitations withstanding, this study provides estimation of healthcare utilization in the first year after birth among dyads with and without maternal opioid exposure by NAS status. Infants with documented maternal opioid exposure and NAS had approximately four times the risk of hospitalization within a year after birth compared to infants without NAS or maternal opioid exposure. Nearly 70 % of opioid-exposed infants with NAS had less than 5 well-child visits in a year. Infants with NAS and/or maternal opioid exposure were more likely to have at least 2 sick-child and 1 ED visit than their counterparts.

Given our findings, efforts to mitigate future hospitalization risk and encourage participation in preventative services may improve outcomes.

Acknowledgements

The authors would like to acknowledge Kelsey Coy for her assistance in data analyses.

Funding source

This publication was supported through the Centers for Disease Control and Prevention's Cooperative Agreement 1U01DP004783-01 to the College of Public Health and Human Sciences at Oregon State University.

Role of funding source

The manuscript underwent clearance within the Centers for Disease Control and Prevention (CDC). However, CDC had no further role in the preparation of the manuscript, or in the decision to submit the manuscript for publication.

Appendix A: ICD-9-CM and CPT codes for maternal and infant variables from Medicaid claims

Maternal Variables		
	ICD-9-CM (Diagnosis Codes)	Prescription Opioid Fills
Maternal opioid exposure	304.00–304.03, 304.70–304.73, 305.50–305.53, 760.72, 965.00, 965.01, 965.02, 965.09, 970.1, 995.29, E850.0, E850.1, E850.2, E935.0, E935.1, E935.2, E980.0	Full Opioid Agonists, Partial Opioid Agonists. List of NDC codes available upon request.
	ICD-9-CM (Diagnosis Codes)	
Tobacco	305.1, 649.00–649.04, 989.84, V15.82, E869.4	
Depression	296.20–296.26, 296.30–296.36, 296.82, 298.0, 300.4, 309.0–309.1, 309.28, 311	
Anxiety	300.00–300.09, 300.20–300.29, 300.7, 308.0–308.9, 309.21, 309.81	
Drug-induced mental health disorder	292.0, 292.11–292.12, 292.2, 292.81–292.89, 292.9, 307.49, 310.1	
Alcohol use disorder	291.0–291.5, 291.81–291.89, 291.9, 303.00–303.03, 303.90–303.93, 305.00–305.03, 357.5, 425.5, 535.30–535.31, 571.0–571.3, 760.71, 790.3, 980.0, E860.0-E860.1, E980.9, V11.3, V79.1	
Other substance use disorder	304.10–304.13, 304.20–304.23, 304.30–304.33, 304.40–304.43, 304.50–304.53, 304.60–304.63, 304.80–304.83, 304.90–304.93, 305.20–305.23, 305.30–305.33, 305.40–305.43, 305.60–305.63, 305.70–305.73, 305.80–305.83, 305.90–305.93, 760.73, 791.9, 995.29, E850.8, E851, E852.0–E852.9, E853.0–E853.9, E855.1–E855.2, E855.4, E858.8, E929.2, E937.0, E937.8, E938.5, E940.8, E950.1–E950.3, E962.0, E995.22	
	Selective Serotonin Reuptake Inhibitor Prescription Fills	
Selective Serotonin Reuptake Inhibitor use during pregnancy	Tricyclic Antidepressants, Benzodiazepines, Monoamine Oxidase Inhibitors, Monoamine Oxidase Type B Inhibitors, Serotonin Reuptake Inhibitors, Serotonin Uptake Inhibitors, Atypical Antipsychotic, Norepinephrine Uptake Inhibitors, Serotonin and Norepinephrine Reuptake Inhibitors, Cytochrome P450 2D6 Inhibitors, Aminoketone, Dopamine Uptake Inhibitors, Increased Dopamine Activity, Increased Norepinephrine Activity. List of NDC codes available upon request.	
Infant Variables		
	ICD-9-CM (Diagnosis Codes)	
Neonatal abstinence syndrome	779.5	
Feeding issues/ dehydration	276.50–276.52, 315.9, 775.5–775.6, 779.31–779.34, 783.1, 783.21–783.22, 783.3, 783.40–783.43	
Seizures/life threatening events	345.00–345.01, 345.10–345.11, 345.2–345.3, 345.40–345.41, 345.50–345.51, 345.60–345.61, 345.70–345.71, 345.80–345.81, 345.90–345.91, 780.31–780.39	
Respiratory conditions	V29.2, 478.11, 478.9, 490, 493.0–493.92, 518.0, 518.81, 519.11, 769, 770.10–770.18, 770.2–770.7, 770.81–770.89, 786.00–786.09, 786.1–786.2, 786.30–786.39, 786.4, 786.50–786.59, 786.6–786.9	
Jaundice/ Hemolytic Events	773.0–773.2, 774.0–774.2, 774.30–774.39, 774.4–774.7, 782.4	
Fever	V29.0, 778.4, 780.60–780.66	
Non-respiratory infections	027.2, 034.0–034.1, 035, 036.0–036.3, 036.40–036.43, 036.81–036.89,036.9, 037, 038.0, 038.10–038.19, 038.2–038.3, 038.40–038.49, 038.8–038.9, 039.0–039.9, 040.0–040.3, 040.41–040.42, 040.81–040.89, 041.00–041.09, 041.10–041.19, 041.2–041.3, 041.41–041.49, 041.5–041.7, 041.81–041.89, 041.9, 047.0, 047.1, 047.8, 047.9, 048, 049.0, 049.1, 049.2, 049.8, 049.9, 050.0–050.2, 050.9, 051.01–051.02, 051.1–051.9, 054.40–054.49, 057.0, 057.8–057.9, 074.0–074.1, 074.20–074.23, 074.3, 074.8, 077.99, 78.89, 079.0–079.4, 79.50–079.59, 79.6, 079.81–079.89, 079.98–079.99, 112.0–112.5, 112.81–112.89, 112.9, 320.0–320.7, 320.81–320.89, 320.9, 322.0–322.9, 372.00, 372.30–372.39, 376.01, 590.10, 590.80–590.81, 599.0, 682.1–682.9, 684, 686.8–686.9, 730.28, 771.0–771.7, 771.81–771.89, 785.52, 790.7, 995.91–995.92	
Respiratory infections	032.0–032.3, 033.0–33.9, 79.6, 460, 461.9, 462, 464.00–464.01, 464.10–464.11, 464.20–464.21, 464.30–464.31, 464.4, 464.50–464.51, 465.0–465.9, 466.0, 466.11–466.19, 480.0–480.9, 481,	

Maternal Variables	
	482.0–482.2, 482.30–482.39, 482.40–482.49, 482.81–482.89, 482.9, 483.0–483.8, 484.1–484.8, 485, 486, 487.0–487.8, 488.01–488.09, 488.11–488.19, 488.81–488.89, 770.0
Diarrhea/ Gastrointestinal Issues	003.0, 008.69, 008.8, 530.81, 537.0, 550.9, 553.9, 558.3, 558.9, 564.00, 564.09, 565.0, 566, 569.3, 573.8, 574.20, 575.2, 576.2, 576.8, 577.0, 578.0–578.9, 579.3, 579.8, 750.5, 772.4, 777.8, 779.32–779.33, 787.01–787.04, 787.3, 787.7, 787.91, 787.99, 789.00, 789.09
Injury	800.00–800.09, 800.10–800.19, 800.20–800.29, 800.30–800.39, 800.40–800.49, 800.50–800.59, 800.60–800.69, 800.70–800.79, 800.80–800.89, 800.90–800.99, 801.00–801.09, 801.10–801.19, 801.20–801.29, 801.30–801.39, 801.40–801.49, 801.50–801.59, 801.60–801.69, 801.70–801.79, 801.80–801.89, 801.90–801.99, 802.0–802.1, 802.20–802.29, 802.30–802.39, 802.4–802.9, 803.00–803.09, 803.10–803.19, 803.20–803.29, 803.30–803.39, 803.40–803.49, 803.50–803.59, 803.60–803.69, 803.70–803.79, 803.80–803.89, 803.90–803.99, 804.00–804.09, 804.10–804.19, 804.20–804.29, 804.30–804.39, 804.40–804.49, 804.50–804.59, 804.60–804.69, 804.70–804.79, 804.80–804.89, 804.90–804.99, 805.00–805.08, 805.10–805.18, 805.2–805.9, 806.00–806.09, 806.10–806.19, 806.20–806.29, 803.30–806.39, 806.4–806.5, 806.60–806.69, 806.70–806.79, 806.8–806.9, 807.00–807.09, 807.10–807.19, 807.2–807.6, 808.0–808.3, 808.41–808.49, 808.51–808.59, 808.8–808.9, 809.0–809.1, 810.00–810.03, 810.10–810.13, 811.00–811.09, 811.10–811.19, 812.00–812.09, 812.10–812.19, 812.20–812.21, 812.30–812.31, 812.40–812.49, 812.50–812.59, 813.00–813.08, 813.10–813.18, 813.20–813.23, 813.30–813.33, 813.40–813.47, 813.50–813.54, 813.80–813.83, 813.90–813.93, 814.00–814.09, 814.10–814.19, 815.00–815.09, 815.10–815.19, 816.00–816.03, 816.10–816.13, 817.0–817.1, 818.0–818.1, 819.0–819.1, 820.00–820.09, 820.10–820.19, 820.20–820.22, 820.30–820.32, 820.8–820.9, 821.00–821.01, 821.10–821.11, 821.20–821.29, 821.30–821.39, 822.0–822.1, 823.00–823.02, 823.10–823.12, 823.20–823.22, 823.30–823.32, 823.40–823.42, 823.80–823.82, 823.90–823.92, 824.0–824.9, 825.0–825.1, 825.20–825.29, 825.30–825.39, 826.0–826.1, 827.0–827.1, 828.0–828.1, 829.0–829.1, 830.0–830.1, 831.00–831.09, 831.10–831.19, 832.00–832.09, 832.10–832.19, 832.2, 833.00–833.09, 833.10–833.19, 834.00–834.02, 834.10–834.12, 835.00–835.03, 835.10–835.13, 836.0–836.4, 836.50–836.59, 836.60–836.69, 837.0–837.1, 838.00–838.09, 838.10–838.19, 839.00–839.08, 839.10–839.18, 839.20–839.21, 839.30–839.31, 839.40–839.49, 839.50–839.59, 839.61–839.69, 839.71–839.79, 839.8–839.9, 840.0–840.9, 841.0–841.3, 841.8–841.9, 842.00–842.02, 842.09, 842.10–842.13, 842.19, 843.0–843.9, 844.0–844.9, 845.00–845.09, 845.10–845.19, 846.0–846.9, 847.0–847.9, 848.0–848.3, 848.40–848.49, 848.5–848.9, 850.0, 850.11–850.12, 850.2–850.9, 851.00–851.09, 851.10–851.19, 851.20–851.29, 851.30–851.39, 851.40–851.49, 851.50–851.59, 851.60–851.69, 851.70–851.79, 851.80–851.89, 851.90–851.99, 852.00–852.09, 852.10–852.19, 853.00–853.09, 853.10–853.19, 854.00–854.09, 854.10–854.19, 860.0–860.5, 861.00–861.03, 861.10–861.13, 861.20–861.22, 861.30–861.32, 862.0–862.1, 862.21–862.29, 862.31–862.39, 862.8–862.9, 863.0–863.1, 863.20–863.29, 863.30–863.39, 863.40–863.49, 863.50–863.59, 863.80–863.89, 863.90–863.99, 864.00–864.09, 864.10–864.19, 865.00–865.09, 865.10–865.19, 866.00–866.03, 866.10–866.13, 867.0–867.9, 868.00–868.09, 868.10–868.19, 869.0–869.1, 870.0–870.9, 871.0–871.9, 872.00–872.02, 872.10–872.12, 872.61–872.69, 872.71–872.79, 872.8–872.9, 873.0–873.1, 873.20–873.29, 873.30–873.39, 873.40–873.49, 873.50–573.59, 573.60–873.69, 873.70–873.79, 873.8–873.9, 874.00–874.02, 874.10–874.12, 874.2–874.9, 875.0–875.1, 876.0–876.1, 877.0–877.1, 878.0–878.9, 879.0–879.9, 880.00–880.09, 880.10–880.19, 880.20–880.29, 881.00–881.02, 881.10–881.12, 881.20–881.22, 882.0–882.2, 883.0–883.2, 884.0–884.2, 885.0–885.1, 886.0–886.1, 887.0–887.7, 890.0–890.2, 891.0–891.2, 892.0–892.2, 893.0–893.2, 894.0–894.2, 895.0–895.1, 896.0–896.3, 900.00–900.03, 900.1, 900.81–900.89, 900.9, 901.0–901.3, 901.40–901.42, 901.81–801.89, 901.9, 902.0, 902.10–902.19, 902.20–902.29, 902.31–902.39, 902.40–902.49, 902.50–902.59, 902.81–902.89, 902.9, 903.00–903.02, 903.1–903.9, 904.0–904.3, 904.40–904.42, 904.50–904.54, 904.6–904.9, 910.0–910.9, 911.0–911.9, 912.0–912.9, 913.0–913.9, 914.0–914.9, 915.0–915.9, 916.0–916.9, 917.0–917.9, 918.0–918.9, 919.0–919.9, 920, 921.0–921.9, 922.0–922.2, 922.31–922.33, 922.4–922.9, 923.00–923.09, 923.10–923.11, 923.20–923.21, 923.3–923.9, 924.00–924.01, 924.10–924.11, 924.20–924.21, 924.3–924.9, 925.1–925.2, 926.0, 926.11–926.19, 926.8–926.9, 927.00–927.09, 927.10–927.11, 927.20–927.21, 927.3–927.9, 928.00–928.01, 928.10–928.11, 928.20–928.21, 928.3–928.9, 929.0–929.9, 930.0–930.9, 931, 932, 933.0–933.1, 934.0–934.9, 935.0–935.2, 936, 937, 938, 939.0–939.9, 940.0–940.9, 941.00–941.09, 941.10–941.19, 941.20–941.29, 941.30–941.39, 941.40–941.49, 941.50–941.59, 942.00–942.09, 942.10–942.19, 942.20–942.29, 942.30–942.39, 942.40–942.49, 942.50–942.59, 943.00–943.09, 943.10–943.19, 943.20–943.29, 943.30–943.39, 943.40–943.49, 943.50–943.59, 944.00–944.08, 944.10–944.18, 944.20–944.28, 944.30–944.38, 944.40–944.48, 944.50–944.58, 945.00–945.09, 945.10–945.19, 945.20–945.29, 945.30–945.39, 945.40–945.49, 945.50–945.59, 946.0–946.5, 947.0–947.9, 948.00, 948.10–948.11, 948.20–948.22, 948.30–948.33, 948.40–948.44, 948.50–948.55, 948.60–948.66, 948.70–948.77, 948.80–948.88, 948.90–948.99, 949.0–949.5, 950.0–950.9, 951.0–951.9, 952.00–952.09, 952.10–952.19, 952.2–952.9, 953.0–953.9, 954.0–954.9, 955.0–955.9, 956.0–956.9, 957.0–957.9, 960.1–960.9, 961.0–961.9, 962.0–962.9, 963.0–963.9, 964.0–964.9, 965.00–965.09, 965.1–965.5, 965.61–965.69, 965.7–965.9, 966.0–966.4, 967.0–967.9, 968.0–968.9, 969.00–969.09, 969.1–969.6, 969.70–969.79, 969.8–969.9, 970.0–970.1, 970.81–970.89, 970.9, 971.0–971.9, 972.0–972.9, 973.0–973.9, 974.0–974.7, 975.0–975.8, 976.0–976.9, 977.0–977.9, 978.0–978.9, 979.0–979.9, 980.0–980.9, 981, 982.0–982.8, 983.0–983.9, 984.0–984.9, 985.0–985.9, 986, 987.0–987.9, 988.0–988.9, 989.0–989.7, 989.81–989.89, 989.9

***ICD-9-CM* (diagnosis codes)**

Maternal Variables		
CPT (service codes)		
Well-child visits	V20.2, V20.31-V20.32	99381–99382, 99391–99392, 99432, 83655, 99,438
	CPT (service codes)	
Sick-child visit	99201–99205, 99211–99215, 99241–99245	

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; CPT = Current Procedural Terminology.

Abbreviations:

NAS	neonatal abstinence syndrome
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
aRR	adjusted risk ratio
CI	confidence interval
ED	emergency department
SSRI	Selective Serotonin Reuptake Inhibitor
NDC	national drug codes
CPT	current procedural terminology.

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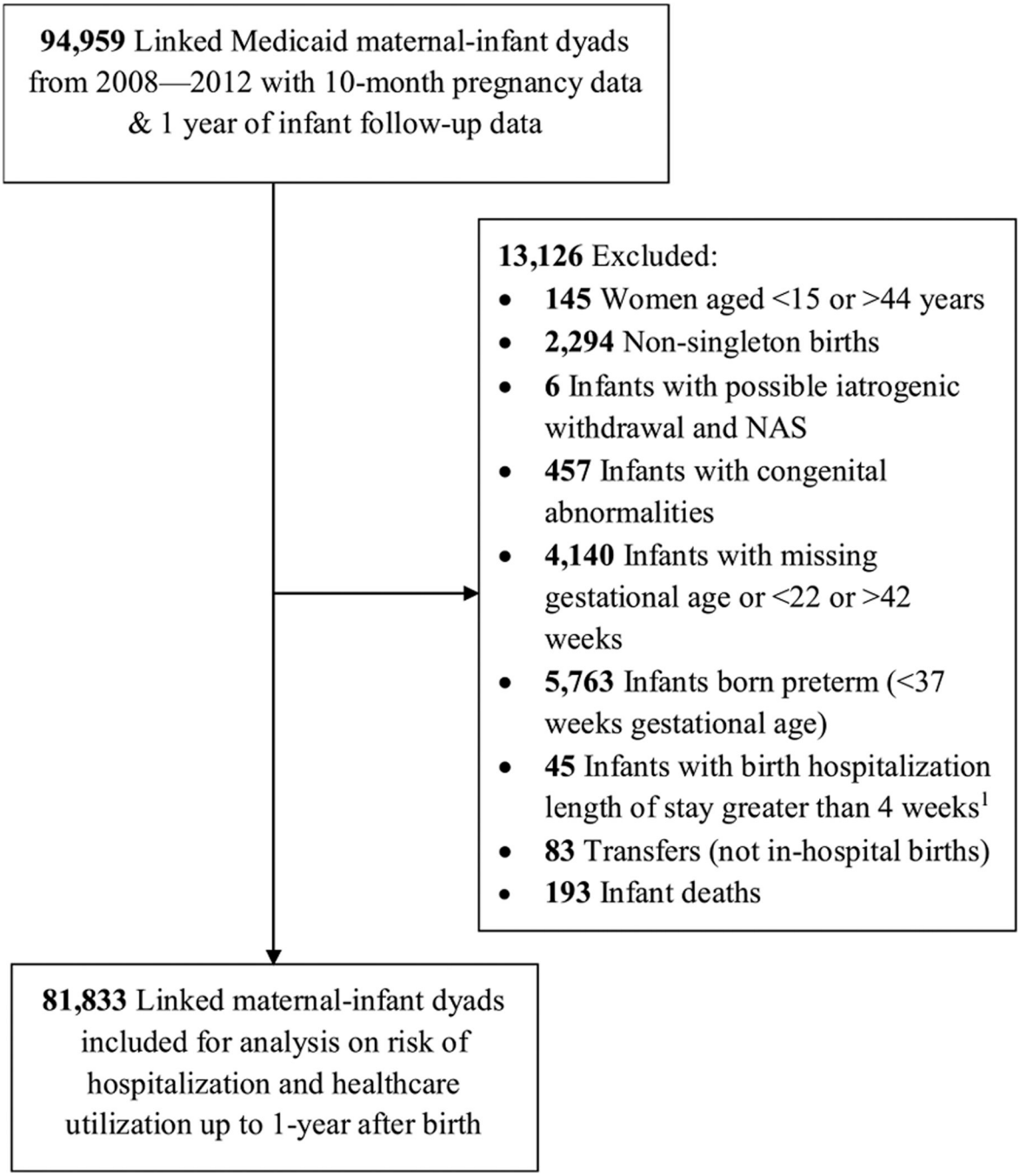

Fig. 1.
Sample flow diagram of Medicaid financed hospital deliveries, Oregon, 2008–2012.

Table 1

Characteristics of Medicaid financed hospital deliveries, Oregon, 2008—2012, N = 81,833[1].

Maternal Characteristics	Total %	Opioid+/ NAS+ (n = 354) %	Opioid+/ NAS− (n = 9724) %	Opioid−/ NAS+ (n = 119) %	Opioid−/NAS− (n = 71,636) %	p-value[2]
Age (years)						<0.01
15–25	52.5	34.2	53.2	__[3]	52.5	
26–35	40.8	59.6	41.4	__[3]	40.6	
36–44	6.7	6.2	5.5	__[3]	6.9	
Race/Ethnicity						<0.01
Non-Hispanic White	56.9	83.1	74.7	__[3]	54.4	
Non-Hispanic Black	3.1	3.7	3.7	__[3]	3.0	
Hispanic	32.1	6.8	14.4	__[3]	34.7	
Non-Hispanic Other	7.8	6.5	7.1	__[3]	7.9	
Education						<0.01
≤ High school	64.4	55.1	63.6	63.9	64.6	
≥ Some College	35.6	44.9	36.4	36.1	35.4	
Marital Status						<0.01
Married	43.3	24.6	33.7	27.7	44.7	
Unmarried	56.8	75.4	66.3	72.3	55.3	
Residence at delivery						<0.01
Urban	85.7	91.2	84.2	88.2	85.9	
Rural	14.3	8.8	15.8	11.8	14.1	
Previous Live Births						<0.01
0	37.8	31.6	34.5	26.9	38.3	
1	29.3	26.3	29.6	29.4	29.3	
≥2	32.9	42.1	36.0	43.7	32.4	
Trimester of Entry into Prenatal Care						<0.01
1 st	70.1	58.8	74.6	__[3]	69.6	

Maternal Characteristics	Total %	Opioid+/ NAS+ (n = 354) %	Opioid+/ NAS− (n = 9724) %	Opioid−/ NAS+ (n = 119) %	Opioid−/NAS− (n = 71,636) %	p-value[2]
2nd	23.3	26.8	20.1	__[3]	23.7	
3rd	4.8	10.7	3.5	__[3]	5.0	
No Prenatal Care	1.7	3.7	1.8	__[3]	1.7	
Mental Health and Substance Use During Pregnancy	%	%	%	%	%	**p-value** [1]
Diagnosis of depression						<0.01
Major and Minor	1.5	8.2	3.6	__[3]	1.1	
Major only	4.5	12.4	8.8	__[3]	3.9	
Minor only	5.1	15.8	9.9	__[3]	4.4	
None	88.9	63.6	77.7	__[3]	90.6	
Diagnosis of anxiety						<0.01
Yes	1.5	5.9	3.6	__[3]	1.1	
No	98.5	94.1	96.4	__[3]	98.9	
SSRI use						<0.01
Yes	1.2	6.5	4.3	__[3]	0.8	
No	98.8	93.5	95.7	__[3]	99.2	
Diagnosis of drug-induced mental health disorder						<0.01
Yes	0.2	10.7	0.6	__[3]	0.1	
No	99.8	89.3	99.4	__[3]	99.9	
Report or diagnosis of tobacco use						<0.01
Yes	22.7	72.9	45.5	64.7	19.3	
No	77.3	27.1	54.5	35.3	80.7	
Diagnosis of alcohol use disorder						<0.01
Yes	1.6	9.3	4.0	__[2]	1.2	
No	98.4	90.7	96.0	__[2]	98.8	
Diagnosis of other substance use disorder[4]						<0.01

Maternal Characteristics	Total %	Opioid+/ NAS+ (n = 354) %	Opioid+/ NAS− (n = 9724) %	Opioid−/ NAS+ (n = 119) %	Opioid−/NAS− (n = 71,636) %	p-value[2]
Yes	9.5	51.7	23.6	30.3	7.3	
No	90.5	48.3	76.4	69.8	92.7	
Diagnosis of narcotics affecting infant						<0.01
Yes	0.5	28.3	1.3	17.7	0.2	
No	99.5	71.7	98.7	82.4	99.8	
Diagnosis of any noxious substance affecting infant						<0.01
Yes	0.5	16.4	2.0	19.3	0.7	
No	99.5	83.6	98.0	80.7	99.3	

[1] Prevalence of maternal opioid exposure was [(354+9724)/81,833]*1000 = 123.2/1000; incidence of NAS was [(354+119)/81,833]*1000 = 5.8/1000 births.

[2] Chi-square test comparing all four Opioid use/NAS delivery categories.

[3] Per data use agreement, cells with observations less than 10 cannot be presented.

[4] Includes diagnoses of amphetamine, cannabis, cocaine, sedative, hallucinogen use disorder as well as diagnosis of other drug dependence in mother during pregnancy.

Table 2

Infant hospitalization and health care utilization among Medicaid financed hospital deliveries, Oregon, 2008–2012, N = 81,833.

	Total	Opioid+/ NAS+ (n = 354)	Opioid+/NAS− (n = 9724)	Opioid−/ NAS+ (n = 119)	Opioid−/ NAS− (n = 71,636)	
Infant Characteristics	**%**	**%**	**%**	**%**	**%**	**p-value**[1]
Birthweight (grams)						
≥2500	98.0	92.4	97.4	__[2]	98.1	<0.01
<2500	2.0	7.6	2.7	__[2]	1.9	
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**p-value** [1]
Length of stay at birth hospitalization (days)	2 (2)	4 (8)	3 (2)	3 (4)	2 (2)	<0.01
Characteristics of Hospitalizations [3]	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**p-value** [1]
Hospitalization within 4 weeks after birth						<0.01
Yes	12.3	60.7	12.9	47.9	11.9	
No	87.7	39.3	87.1	52.1	88.1	
Hospitalization within a year after birth						<0.01
Yes	16.3	65.5	18.7	48.7	15.7	
No	83.7	34.5	81.3	51.3	84.3	
Number of hospitalizations						
Within 4 weeks after birth	2.0 (3.2)	8.7 (7.9)	1.8 (3.2)	7.2 (8.3)	1.9 (2.8)	<0.01
Within a year after birth	3.3 (6.5)	9.8 (9.2)	3.3 (6.6)	9.4 (11.9)	3.1 (6.4)	<0.01
Average length of stay of hospitalizations (days)						
Within 4 weeks after birth	1.1 (0.7)	1.2 (0.6)	1.1 (0.7)	1.1 (0.4)	1.1 (0.7)	0.63
Within a year after birth	1.1 (0.7)	1.2 (0.5)	1.2 (0.7)	1.1 (0.3)	1.1 (0.7)	0.87
Reasons for Hospitalizations [3]	**%**	**%**	**%**	**%**	**%**	**p-value** [1]
Feeding issues/dehydration						
Yes	20.9	28.5	20.4	29.3	20.8	0.01
No	79.1	71.6	79.6	70.7	79.2	
Seizures/life-threatening event						0.41
Yes	3.2	__[2]	3.1	__[2]	3.2	

	Total	Opioid+/ NAS+ (n = 354)	Opioid+/NAS− (n = 9724)	Opioid−/ NAS+ (n = 119)	Opioid−/ NAS− (n = 71,636)	
Infant Characteristics	**%**	**%**	**%**	**%**	**%**	**p-value**[1]
No	96.8	__[2]	96.9	__[2]	96.8	
Respiratory condition						0.10
Yes	18.3	18.5	19.7	27.6	18.1	
No	81.7	81.5	80.3	72.4	81.9	
Jaundice/Hemolytic Events						<0.01
Yes	20.7	14.7	16.3	__[2]	21.6	
No	79.3	85.3	83.7	__[2]	78.4	
Fever						0.17
Yes	8.0	11.2	7.8	__[2]	8.0	
No	92.0	88.8	92.2	__[2]	92.0	
Non-respiratory infection						0.59
Yes	9.9	7.8	10.5	__[2]	9.8	
No	90.1	92.2	89.5	__[2]	90.2	
Respiratory infection						<0.01
Yes	16.5	9.5	19.6	__[2]	16.1	
No	83.5	90.5	80.4	__[2]	83.9	
Diarrhea						0.01
Yes	7.4	4.3	9.1	__[2]	7.1	
No	92.6	95.7	90.9	__[2]	92.9	
Injury						0.03
Yes	2.4	__[2]	3.3	__[2]	2.3	
No	97.6	__[2]	96.7	__[2]	97.7	
Healthcare utilization within a year after birth	**%**	**%**	**%**	**%**	**%**	**p-value** [1]
Number of well-child visits						<0.01
<5	55.4	68.6	56.4	57.1	55.2	

Infant Characteristics	Total %	Opioid+/ NAS+ (n = 354) %	Opioid+/NAS− (n = 9724) %	Opioid−/ NAS+ (n = 119) %	Opioid−/ NAS− (n = 71,636) %	p-value[1]
≥5	44.6	31.4	43.6	42.9	44.8	
Number of sick-child visits						<0.01
≥2	53.9	65.8	62.6	63.0	52.6	
<2	46.1	34.2	37.4	37.0	47.4	
Emergency department visit						<0.01
Yes	18.4	26.0	23.3	30.3	17.7	
No	81.6	74.0	76.7	69.8	82.3	

[1] Chi-square test comparing all four Opioid use/NAS delivery categories; ANOVA used for continuous variables.

[2] Per data use agreement, cells with observations less than 10 cannot be presented.

[3] Denominator only includes those with a hospitalization (n=13,341).

NAS= Neonatal Abstinence Syndrome; SD= Standard Deviation.

Drug Alcohol Depend. Author manuscript; available in PMC 2022 June 01.

Table 3

Adjusted risk ratios for NAS and health care utilization among Medicaid financed hospital deliveries, Oregon, 2008–2012 (N = 81,833).

Opioid/NAS associated with healthcare utilization	RR (95 % CI)[1]	aRR[1,2] (95% CI)
Model 1: Hospitalization within four weeks after birth		
Opioid+/NAS+	5.10 (4.68–5.55) [3]	4.67 (4.25–5.13) [3]
Opioid+/NAS-	4.02 (3.33–4.85) [3]	3.73 (3.09–4.52) [3]
Opioid−/ NAS+	1.08 (1.02–1.14) [3]	1.07 (1.01–1.13) [4]
Model 2: Hospitalization within one year after birth		
Opioid+/NAS+	4.18 (3.87–4.51) [3]	3.68 (3.39–4.01) [3]
Opioid+/NAS−	3.11 (2.58–3.74) [3]	2.77 (2.30–3.35) [3]
Opioid−/NAS+	1.19 (1.14–1.24) [3]	1.15 (1.09–1.20) [3]
Model 3: <5 well-child visits within one year after birth[5]		
Opioid+/NAS+	1.24 (1.16–1.34) [3]	1.16 (1.08–1.24) [3]
Opioid+/NAS−	1.04 (0.89–1.21)	0.94 (0.80–1.11)
Opioid−/ NAS+	1.02 (1.00–1.04) [4]	0.99 (0.97–1.01)
Model 4: ≥2 sick visits within one year after birth[6]		
Opioid+/NAS+	1.25 (1.16–1.35) [3]	1.19 (1.10–1.29) [3]
Opioid+/NAS−	1.20 (1.04–1.37) [4]	1.19 (1.04–1.36) [4]
Opioid−/NAS+	1.19 (1.17–1.21) [3]	1.15 (1.13–1.17) [3]
Model 5: any ED visits within one year after birth[7]		
Opioid+/NAS+	1.47 (1.23–1.76) [3]	1.25 (1.05–1.49) [4]
Opioid+/NAS−	1.71 (1.30–2.25) [3]	1.46 (1.10–1.92) [3]
Opioid−/NAS+	1.32 (1.27–1.37) [3]	1.23 (1.18–1.28) [3]

[1]Reference is Opioid−/NAS− dyads.

[2]Models are adjusted for infant sex, trimester of entry into prenatal care, SSRI use, maternal age, race, education, marital status, urban/rural residence, depression, anxiety, tobacco use, alcohol use disorder, and other substance use disorder.

[3] $p<0.01$.

[4] $p<0.05$.

[5] Compared to ≥5 well-child visits within one year after birth.

[6] Compared to <2 sick visits within one year after birth.

[7] Compared to no ED visits within one year after birth.

RR = Risk Ratio; aRR= Adjusted Risk Ratio; CI= Confidence Interval; NAS= Neonatal Abstinence Syndrome.