



Opioid use disorder and maternal outcomes following cesarean delivery: a multistate analysis, 2007–2014

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Aim: To examine the association between opioid use disorder (OUD) and maternal outcomes following cesarean delivery. **Methods:** Retrospective analysis of over 2.4 million discharge records for in-patient cesarean delivery across five states from 2007 to 2014. Primary outcome was in-hospital mortality. Secondary outcomes included length of stay (LOS) and 30- and 90-day readmission rates. **Results:** OUD patients were 148% more likely than non-OUD patients to die during hospitalization (adjusted odds ratios [aOR]: 2.48, 95% CI: 1.20, 5.10; $p < 0.05$). OUD was associated with increased odds of 30-day readmission (aOR: 1.46, 95% CI: 1.30, 1.65; $p < 0.001$) and 90-day readmission (aOR: 1.70, 95% CI: 1.55, 1.88; $p < 0.001$); LOS was not significantly different. **Conclusion:** OUD predicts increased in-patient mortality and odds of 30- and 90-day readmission following cesarean delivery.

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Opioid use disorder (OUD) is a public health crisis in USA with more than 42,000 opioid overdose deaths in 2016 and over 47,000 deaths in 2017 [1]. The number of women who use opioids at the time of delivery has significantly increased and a large percentage of those with OUD are women of childbearing age [2–4]. According to one study, opioids are dispensed to 14% of women during the antepartum period with approximately 6% of women receiving opioids during each of the three trimesters [5]. During 2008–2013, an average of 20.0% of reproductive-aged women enrolled in Medicaid in New York received at least one prescription for opioids [6]. Women may also use opioids as part of medication-assisted treatment for OUD [7].

Opioid use during pregnancy creates the potential for adverse outcomes. Research examining the association of opioid use during pregnancy with maternal mortality and morbidity shows an increase in death during hospitalization, cardiac arrest and obstetric complications [8,9]. Fetal risks associated with maternal opioid use include intrauterine growth restriction, placental abruption, preterm delivery, oligohydramnios, stillbirth and neonatal abstinence syndrome [8,10–14]. OUD is a problem that affects pregnant women across all demographic and socioeconomic strata, racial/ethnic groups and geographical areas [15].

Cesarean delivery has increased in prevalence over the past several decades and is the most commonly performed surgical procedure both in USA and worldwide; as such, many women with OUD may undergo a cesarean delivery in their lifetime [16–19]. Opioids are the mainstay for post-cesarean pain management both during hospitalization and upon discharge. In a nationwide survey of women undergoing cesarean delivery, 85% received an opioid prescription upon discharge [20]. Among pregnant women with pre-existing OUD, increased pain sensitivity and opioid tolerance may complicate treatment and management of pain following cesarean delivery [21]. As such, women with OUD who undergo cesarean delivery make up a particularly vulnerable population that warrants further research to guide management and reduction of opioid use and improve recovery during the postpartum period.

Both the deleterious effects and increased prevalence of maternal opioid use are well described, as is the frequency of cesarean delivery in USA. Yet, there are no known studies that have investigated the relationship between OUD and maternal outcomes in the context of cesarean delivery, although prior studies have shown that overall pregnant women with OUD generally experience worse outcomes compared with women without OUD [8,13,14,22,23]. Using a national cohort of parturients from five diverse states representing about 28% of the US population, we aimed to examine the rates of maternal mortality and other post-delivery outcomes associated with OUD among women undergoing cesarean delivery.

Methods

Study database & population

We conducted a retrospective analysis of 2007–2014 discharge data from California, Florida, Kentucky, New York and Maryland using the State Inpatient Databases (SID), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality [24]. All California data were unavailable for 2012–2014 cases; readmission data were unavailable for Kentucky (2007–2014) and Maryland (2012–2014). The SID is an administrative database that encompasses approximately 97% of all hospital discharges in USA and consists of clinical and nonclinical data. A present-on-admission (POA) identifier is used to delineate pre-existing medical diagnosis from medical complications that arise during hospitalization. Each in-patient hospital admission correlates to an individual record; unique identification codes are used to link patient records for identifying patient readmissions and calculating readmission time in days. HCUP has implemented safeguards to protect the privacy of patients and providers included in the data, as well as quality control measures to confirm the validity and internal consistency of the SID data [24]. All study activities were approved by the Institutional Review Board at Weill Cornell Medicine.

Using International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) codes, we identified discharge data for adult patients (≥ 18 years) undergoing cesarean deliveries (ICD-9-CM 669.7). Exclusion criteria included missing demographic data and missing data on length of stay and readmission.

Our primary variable of interest was POA OUD. We queried cases using ICD-9-CM codes to identify patients with opioid dependence or nondependent opioid use (ICD-9-CM 304.00–304.03, 304.70–304.73, 305.50–305.53, E935.1, E935.2, E940.1, 965.00, 965.09, 970.1, E850.1, E850.2). For each admission, we extracted the following variables: age, sex, race (white, black, Hispanic, other, missing), primary insurance payer (Medicare, Medicaid, private insurance, other insurance, uninsured), state, year of delivery, median household income by quartile, elective operation status, disposition at discharge, hospital delivery volume by quartile, and POA indicators using the obstetric comorbidity index developed and validated by Bateman *et al.* [25]. The Bateman index includes weighted measures that predict severe maternal morbidity and mortality, including severe pre-eclampsia or eclampsia, chronic congestive heart failure, congenital heart disease, pulmonary hypertension, chronic ischemic heart disease, sickle cell disease, multiple gestation, cardiac valvular disease, systemic lupus erythematosus, human immunodeficiency virus, mild or unspecified pre-eclampsia, drug abuse, placenta previa, chronic renal disease, pre-existing hypertension, previous cesarean delivery, gestational hypertension, alcohol abuse, asthma, pre-existing diabetes mellitus and maternal age older than 35 years [25]. Previous studies have used this validated comorbidity index to assess the relationships between potential obstetric risk factors and maternal outcomes among large national sample sizes [26–29].

Study outcomes

Our primary outcome was in-hospital mortality. Our secondary outcomes included length of stay (LOS) of the initial hospitalization and 30- and 90-day readmissions. For both 30- and 90-day readmissions we recorded the top five diagnosis codes as listed on the readmission record for OUD and non-OUD patients.

Statistical analysis

Demographic characteristics and POA comorbidities were compared through bivariate analysis between patients with and without OUD. We also compared unadjusted rates of our primary and secondary outcomes by OUD status. Pearson's χ^2 test or Fisher's exact test was used to compare categorical variables and t-test (for parametric variables) or Wilcoxon Rank-Sum test (for nonparametric variables) was used to compare continuous variables.

For our multivariable analyses, we modeled our primary and secondary outcomes using generalized linear models. Demographic variables (e.g., age, race, primary insurance payer), hospital characteristics (e.g., hospital delivery volume by quartile), clinical characteristics (e.g., LOS for readmissions models) and obstetric comorbidities that

were significantly associated with OUD status at $p < 0.05$ in our unadjusted analysis were included in our multivariate models to reduce confounding bias. Adjusted odds ratios (aOR) and adjusted incidence rate ratios (aIRR) with 95% CIs were reported for binary outcomes (e.g., in-patient hospital mortality, 30-day readmission, 90-day readmission) and count outcomes (e.g., LOS), respectively.

Because obesity and admission status are well-established risk factors for adverse maternal outcomes [30–34], we included obesity (ICD-9-CM: 278.00), admission status (coded as elective surgery, urgent/emergent/other surgery and missing [this includes all of California, which does not code for this variable]) and both obesity and admission status as covariates in our multivariate models as a sensitivity analysis. We recoded admission status from the elective operation status variable. All p-values were two-sided with an alpha value of 0.05. All statistical analysis was conducted using SAS 9.4 (SAS Institute, Inc., NC, USA) and Stata SE 15 (TX, USA).

Results

Bivariate results

Bivariate results of demographic characteristics and POA comorbidities of patients who underwent cesarean delivery compared by OUD status are shown in Table 1. Our cohort included a total of 2,425,527 parturients of which 10,703 (0.4%) were identified with OUD. The prevalence of OUD among patients who underwent cesarean delivery increased fourfold from 0.25% in 2007 to 0.90% in 2014. White patients made up 75.9% of patients with OUD. Private insurance was the most common primary payer for non-OUD patients (50.2%), whereas Medicaid was the primary payer for the majority of patients with OUD (74.6%). Patients with OUD were also more likely to be in the bottom two quartiles for median household income and presented more obstetric comorbidities compared with those without OUD.

Bivariate and multivariate outcomes compared by OUD status are shown in Table 2. In-hospital mortality was greater among OUD patients (<11, 0.1%) in comparison to non-OUD patients (367, 0%). Further, a greater proportion of patients with OUD were readmitted 30 and 90 days following discharge compared with those without OUD (30-day readmission: 4.2% OUD vs 1.9% non-OUD; 90-day readmission: 6.7% OUD vs 2.6% non-OUD). OUD patients had similar LOS following cesarean delivery in comparison to patients without OUD.

The top five diagnoses listed for 30-day readmission among OUD patients were mental disorders of mother, postpartum condition or complication (ICD-9-CM 648.44), other complications of obstetrical surgical wound, postpartum condition or complication (ICD-9-CM 674.34), other current conditions complicating pregnancy, childbirth or the puerperium (ICD-9-CM 648.94), anemia in the mother complicating pregnancy, childbirth or the puerperium (ICD-9-CM 648.24), and tobacco use disorder complicating pregnancy, childbirth, or the puerperium, postpartum condition or complication (ICD-9-CM 649.04). These diagnoses were also listed among the top reasons for 90-day readmission among OUD patients with tobacco use disorder (ICD-9-CM 305.1) being the most common reason for readmission. Among non-OUD patients, the top five diagnoses listed for 30-day readmission were other complications of obstetrical surgical wounds (ICD-9-CM 674.34), anemia in the mother complicating pregnancy, childbirth or the puerperium (ICD-9-CM 648.24), other current conditions complicating pregnancy, childbirth or the puerperium (ICD-9-CM 648.94), unspecified anemia (ICD-9-CM 285.9), and other complications of the puerperium, postpartum condition or complication (ICD-9-CM 674.84); the top five diagnoses for non-OUD patients remained the same for 90-day readmission. Frequencies and percentages of the top five reasons for both 30- and 90-day readmissions compared by OUD status are shown in Tables 3a and 3b.

Multivariate results

After adjusting for potential confounding variables, patients with documented OUD who underwent cesarean delivery were nearly 2.5-times more likely than patients without OUD to die during the delivery hospitalization (aOR: 2.48, 95% CI: 1.20, 5.10; $p < 0.05$). Patients with OUD during pregnancy were also 46% more likely to be readmitted 30 days following discharge (aOR: 1.46, 95% CI: 1.30, 1.65; $p < 0.001$) and 70% more likely to be readmitted 90 days following discharge (aOR: 1.70, 95% CI: 1.55, 1.88; $p < 0.001$). Patients with OUD did not have statistically significant longer LOS (aIRR: 1.02, 95% CI: 1.00, 1.04; $p = 0.10$; Table 2).

Sensitivity analysis

In an effort to account for other potential confounders, we ran our main model with two additional variables: obesity and admission status (elective surgery, urgent/emergent/other surgery and missing). After adjusting for obesity,

Table 1. Demographic and present-on-admission obstetric comorbidities of patients undergoing cesarean delivery by opioid use disorder status.

Characteristic	OUD (%)	No OUD (%)	Overall (%)	p-value
Total	10,703 (0.4)	2,414,824 (99.6)	2,425,527 (100)	
Age in years				<0.0001
– Mean (SD)	28.72 (5.43)	29.66 (6.08)	29.66 (6.08)	
Race				<0.0001
– White	8,119 (75.9)	1,011,928 (41.9)	1,020,047 (42.1)	
– Black	950 (8.9)	366,673 (15.2)	367,623 (15.2)	
– Hispanic	970 (9.1)	679,785 (28.2)	680,755 (28.1)	
– Other	459 (4.3)	294,325 (12.2)	294,784 (12.2)	
– Missing	205 (1.9)	62,113 (2.6)	62,318 (2.6)	
Year				<0.0001
– 2007	941 (8.8)	374,862 (15.5)	375,803 (15.5)	
– 2008	1,014 (9.5)	371,767 (15.4)	372,781 (15.4)	
– 2009	1,177 (11)	367,710 (15.2)	368,887 (15.2)	
– 2010	1,372 (12.8)	356,799 (14.8)	358,171 (14.8)	
– 2011	1,527 (14.3)	353,936 (14.7)	355,463 (14.7)	
– 2012	1,350 (12.6)	197,513 (8.2)	198,863 (8.2)	
– 2013	1,539 (14.4)	195,786 (8.1)	197,325 (8.1)	
– 2014	1,783 (16.7)	196,451 (8.1)	198,234 (8.2)	
State				<0.0001
– California	1,659 (15.5)	814,027 (33.7)	815,686 (33.6)	
– Florida	3,207 (30)	641,978 (26.6)	645,185 (26.6)	
– Kentucky	1,649 (15.4)	146,234 (6.1)	147,883 (6.1)	
– Maryland	1,846 (17.2)	182,570 (7.6)	184,416 (7.6)	
– New York	2,342 (21.9)	630,015 (26.1)	632,357 (26.1)	
Median household income state quartile for patient zip code – by quartile				<0.0001
– First quartile	3,685 (34.4)	658,531 (27.3)	662,216 (27.3)	
– Second quartile	2,783 (26)	586,756 (24.3)	589,539 (24.3)	
– Third quartile	2,246 (21)	567,932 (23.5)	570,178 (23.5)	
– Fourth quartile	1,546 (14.4)	519,684 (21.5)	521,230 (21.5)	
– Missing	443 (4.1)	81,921 (3.4)	82,364 (3.4)	
Payer				<0.0001
– Medicare	259 (2.4)	14,250 (0.6)	14,509 (0.6)	
– Medicaid	7,980 (74.6)	1,072,647 (44.4)	1,080,627 (44.6)	
– Private insurance	1,946 (18.2)	1,213,247 (50.2)	1,215,193 (50.1)	
– Other	228 (2.1)	45,858 (1.9)	46,086 (1.9)	
– Self-pay/no charge	287 (2.7)	68,550 (2.8)	68,837 (2.8)	
– Missing	<11 (0.1)	272 (0)	<283 (0)	
Elective operation status				<0.0001
– Emergency	1,373 (12.8)	217,129 (9)	218,502 (9)	
– Urgent	3,577 (33.4)	553,001 (22.9)	556,578 (22.9)	
– Elective	4,048 (37.8)	828,033 (34.3)	832,081 (34.3)	
– Newborn	<11 (0.1)	234 (0)	<245 (0)	
– Trauma center	<11 (0.1)	179 (0)	<190 (0)	
– Other	<11 (0.1)	336 (0)	<347 (0)	
– Missing	1,686 (15.8)	815,912 (33.8)	817,598 (33.7)	
Disposition at discharge				<0.0001
– Routine	10,182 (95.1)	2,370,000 (98.1)	2,380,182 (98.1)	
– Transfer to short-term hospital	52 (0.5)	2,893 (0.1)	2,945 (0.1)	

Percent may not sum to 100 due to rounding.
OUD: Opioid use disorder.

Table 1. Demographic and present-on-admission obstetric comorbidities of patients undergoing cesarean delivery by opioid use disorder status (cont.).

Characteristic	OUD (%)	No OUD (%)	Overall (%)	p-value
– Home healthcare	302 (2.8)	37,943 (1.6)	38,245 (1.6)	
– Died	<11 (0.1)	367 (0)	<378 (0)	
– Transfer to other, against medical advice, or destination unknown	159 (1.5)	3,621 (0.1)	3,780 (0.2)	
Hospital volume				<0.0001
– First quartile	2,957 (27.6)	569,325 (23.6)	572,282 (23.6)	
– Second quartile	2,877 (26.9)	615,767 (25.5)	618,644 (25.5)	
– Third quartile	2,599 (24.3)	598,905 (24.8)	601,504 (24.8)	
– Fourth quartile	2,270 (21.2)	630,827 (26.1)	633,097 (26.1)	
Obstetric comorbidities per Bateman (2013)				
– Alcohol abuse	206 (1.9)	2,308 (0.1)	2,514 (0.1)	<0.0001
– Asthma	958 (9)	94,770 (3.9)	95,728 (3.9)	<0.0001
– Cardiac valvular disease	81 (0.8)	11,055 (0.5)	11,136 (0.5)	<0.0001
– Chronic congestive heart failure	<11 (0.1)	70 (0)	<81 (0)	0.0028
– Chronic ischemic heart disease	<11 (0.1)	415 (0)	<426 (0)	0.0023
– Chronic renal disease	56 (0.5)	7,056 (0.3)	7,112 (0.3)	<0.0001
– Congenital heart disease	14 (0.1)	1,966 (0.1)	1,980 (0.1)	0.0742
– Drug abuse	9,192 (85.9)	24,943 (1)	34,135 (1.4)	<0.0001
– Gestational hypertension	332 (3.1)	80,060 (3.3)	80,392 (3.3)	0.2184
– HIV	99 (0.9)	5,924 (0.2)	6,023 (0.2)	<0.0001
– Mild or unspecified pre-eclampsia	334 (3.1)	92,279 (3.8)	92,613 (3.8)	0.0002
– Multiple gestation	309 (2.9)	88,618 (3.7)	88,927 (3.7)	<0.0001
– Placenta previa	159 (1.5)	36,684 (1.5)	36,843 (1.5)	0.777
– Pre-existing diabetes mellitus	133 (1.2)	39,734 (1.6)	39,867 (1.6)	0.0011
– Pre-existing hypertension	421 (3.9)	76,828 (3.2)	77,249 (3.2)	<0.0001
– Previous cesarean delivery	5,117 (47.8)	1,060,509 (43.9)	1,065,626 (43.9)	<0.0001
– Pulmonary hypertension	19 (0.2)	954 (0)	973 (0)	<0.0001
– Severe pre-eclampsia	213 (2)	62,066 (2.6)	62,279 (2.6)	0.0002
– Sickle cell disease	39 (0.4)	6,077 (0.3)	6,116 (0.3)	0.0203
– Systemic lupus erythematosus	43 (0.4)	4,073 (0.2)	4,116 (0.2)	<0.0001
– Bateman obstetric comorbidity index				<0.0001
Median (Q1, Q3)	3 (2, 3)	1 (0, 2)	1 (0, 2)	
Obesity	730 (6.8)	159,027 (6.6)	159,757 (6.59)	0.328

Percent may not sum to 100 due to rounding.
OUD: Opioid use disorder.

admission status and both obesity and admission status in our multivariate models, OUD remained significantly associated with increased risk of in-hospital mortality and 30- and 90-day readmissions ([Supplementary Table 1](#)).

Discussion

In this retrospective study of over 2.4 million parturients using SID data for California, Florida, Kentucky, New York and Maryland, we found that patients with OUD who underwent cesarean delivery experienced significantly greater risk of inpatient mortality and 30- and 90-day readmissions in comparison to non-OUD patients after adjusting for patient- and hospital-level characteristics. LOS was not significantly longer among OUD patients compared with patients without OUD.

Several studies have examined the effects of OUD on maternal and perinatal outcomes, although none have specifically examined outcomes in patients with OUD who undergo cesarean delivery [8,13,14,22,23]. Whiteman *et al.* [22] found that opioid use during pregnancy was associated with longer hospital stays, higher healthcare costs and increased adverse perinatal outcomes. Maeda *et al.* [8] found that OUD patients, compared with non-

Table 2. Bivariate and multivariate outcomes for patients undergoing cesarean delivery by opioid use disorder status.

Outcome	No. (%)	aOR (95% CI)
In-hospital mortality		
– OUD	<11 (0.1)	2.48 (1.20, 5.10) [†]
– No OUD	367 (0)	1.00 (reference)
30-day readmission		
– OUD	299 (4.2)	1.46 (1.30, 1.65) [‡]
– No OUD	34,620 (1.9)	1.00 (reference)
90-day readmission		
– OUD	479 (6.7)	1.70 (1.55, 1.88) [‡]
– No OUD	47,791 (2.6)	1.00 (reference)
Length of stay in days		
– OUD	3 (3,4) [¶]	1.02 (1.00, 1.04) ^{§, #}
– No OUD	3 (3,4) [¶]	1.00 (reference)

[†]p < 0.05.
[‡]p < 0.001.
[§]p = 0.10.
[¶]Median (Q1, Q3).
[#]aIRR (95% CI).
aOR: Adjusted odds ratios; OUD: Opioid use disorder.

Table 3a. Top five diagnoses listed for 30-day readmission among patients undergoing cesarean delivery by opioid use disorder status.

OUD		No OUD	
ICD-9-CM diagnosis code	No. (%)	ICD-9-CM diagnosis code	No. (%)
648.44: mental disorders of mother, postpartum condition or complication	72 (3.49%)	674.34: other complications of obstetrical surgical wounds	8136 (5.39%)
674.34: other complications of obstetrical surgical wound, postpartum condition or complication	67 (3.25%)	648.24: anemia in the mother complicating pregnancy, childbirth or the puerperium	6047 (4.01%)
648.94: other current conditions complicating pregnancy, childbirth or the puerperium	64 (3.10%)	648.94: other current conditions complicating pregnancy, childbirth or the puerperium	5844 (3.87%)
648.24: anemia in the mother complicating pregnancy, childbirth or the puerperium	62 (3.01%)	285.9: unspecified anemia	4429 (2.94%)
649.04: tobacco use disorder complicating pregnancy, childbirth or the puerperium, postpartum condition or complication	59 (2.86%)	674.84: other complications of the puerperium, postpartum condition or complication	3921 (2.60%)

ICD-9-CM: International Classification of Disease, 9th Revision, Clinical Modification; OUD: Opioid use disorder.

Table 3b. Top five diagnoses listed for 90-day readmission among patients undergoing cesarean delivery by opioid use disorder status.

OUD		Non-OUD	
ICD-9-CM diagnosis code	N (%)	ICD-9-CM diagnosis code	N (%)
305.1: tobacco use disorder	123 (3.97%)	674.34: other complications of obstetrical surgical wounds	8425 (4.23%)
648.44: mental disorders of mother, postpartum condition or complication	83 (2.68%)	648.24: anemia in the mother complicating pregnancy, childbirth or the puerperium	6338 (3.19%)
674.34: other complications of obstetrical surgical wound, postpartum condition or complication	70 (2.26%)	648.94: other current conditions complicating pregnancy, childbirth or the puerperium	6261 (3.15%)
648.94: other current conditions complicating pregnancy, childbirth or the puerperium	67 (2.16%)	285.9: unspecified anemia	5384 (2.71%)
648.24: anemia in the mother complicating pregnancy, childbirth or the puerperium	66 (2.13%)	674.84: other complications of the puerperium, postpartum condition or complication	4503 (2.26%)

ICD-9-CM: International Classification of Disease, 9th Revision, Clinical Modification; OUD: Opioid use disorder.

OUD patients, experienced greater odds of obstetric morbidities and were 4.6-times more likely to die during hospitalization. OUD also appears to be a risk factor for cesarean delivery [8] with research showing that opioid use during pregnancy is associated with increased odds of cesarean delivery [23].

We found a bivariate unadjusted association between socioeconomic status and OUD. The majority of women with OUD was insured by Medicaid and in the bottom two quartiles of median household income. Conversely, non-OUD patients tended to be privately insured and were less likely to be in the lowest median income quartile. Despite controlling for patient-level characteristics in our multivariable analyses, potential confounders concerning such social determinants of health may remain unaccounted for in our statistical models.

Social determinants of health may explain the observed disparity in maternal outcomes following cesarean delivery [35,36]. Numerous studies have documented greater misuse of opioids among pregnant women and women of childbearing age who are socioeconomically disadvantaged compared with their more affluent counterparts [4,6,37,38]. Desai *et al.* [39] noted a significant increase from 2000–2007 in opioid use among a cohort of 1.1 million pregnant women enrolled in Medicaid, with a fifth of the cohort filling a prescription for an opioid medication. Disadvantaged populations face significant barriers to accessing treatment for OUD, including lack of access to treatment facilities [40]. This is further compounded by social stigma [41,42] and geographic discordance [43], both of which have been shown to discourage patients with OUD from seeking help and returning for follow-up appointments. Consequently, expecting mothers who have OUD and come from low socioeconomic backgrounds likely experience worse maternal outcomes due to absence or delay in treatment [40,42].

Differences in post-cesarean delivery outcomes may also be explained secondary to OUD patients having poorer baseline health compared with non-OUD patients. Previous studies have shown that pregnant women with OUD have greater rates of pre-existing conditions, such as substance use, depression, anxiety, HIV, anemia, hypertension, diabetes and renal disease [8,22]. Increased obstetric comorbidities among patients who use opioids during pregnancy have been associated with increased maternal mortality and increased maternal intensive care unit admission [25]. In our study, we similarly observed a significantly greater prevalence of POA obstetric comorbidities in our cohort of OUD patients who underwent cesarean delivery. We also found that patients with OUD were more likely than non-OUD patients to be readmitted to the hospital for reasons relating to obstetric comorbidities, such as mental illnesses and tobacco use disorder. Although we controlled for comorbidities in our multivariable analyses, it is possible that we did not adjust for other comorbidities that perceivably could contribute to the disparity in maternal outcomes between OUD patients and patients without OUD.

Our findings highlight the need for a multipronged approach to address the prevalence of opioid use during pregnancy and the occurrence of adverse maternal outcomes following cesarean delivery. Currently, opioid agonist treatment is the standard treatment for pregnant women with OUD [4,44]. Opioid agonist treatment involves the administration of medications, such as methadone and buprenorphine, to reduce symptoms of opioid use in mothers [44,45] and to prevent the fetus from experiencing recurrent opioid withdrawal and toxicity [4]. However, less than half of the states in the USA have targeted programs designed to treat pregnant women with OUD, and only a fifth of all states prohibit publicly funded drug treatment programs from discriminating against pregnant women [46]. Policymakers should focus on expanding the availability and access of opioid treatment programs for pregnant women on both a federal and state level [47]. Outreach programs should educate pregnant women about the adverse outcomes of opioid use and assist women, especially those from disadvantaged backgrounds, with navigating the healthcare system [4]. Given the co-occurrence of OUD with substance abuse, mood disorders and history of trauma, additional efforts should focus on expanding services to address these issues among pregnant women [44].

Clinicians also play a significant role in managing opioid use and preventing adverse maternal and fetal outcomes. Clinicians should practice responsible opioid prescribing, routinely screen all pregnant women for OUD, develop tailored treatment plans with addiction specialists and other members of the care team, and establish a strong rapport with patients to ensure regular follow-up and successful intervention [47–49].

Enhanced recovery after surgery (ERAS) protocols may likewise address adverse outcomes following cesarean delivery among women with OUD. ERAS can be applied to all surgical types (emergent, urgent, elective) and provides a multidisciplinary, evidence-based approach to standardize perioperative care and reduce healthcare cost and provider implicit bias [50]. The implementation of ERAS protocols has been shown to improve postoperative outcomes across a range of surgical procedures [51–54] and attenuate disparities in perioperative care and outcomes [55–57]. An ERAS protocol targeting women who undergo cesarean delivery could enhance quality of perioperative care, improve maternal and fetal outcomes and reduce disparities and healthcare costs [58]. ERAS also has the potential to address pre-existing OUD and future risks for OUD by reducing the amount of opioids prescribed to patients following cesarean delivery, further improving care during the postpartum period [59]. Future research elucidating

the underlying mechanisms linking OUD with adverse post-cesarean outcomes is necessary for the development of a comprehensive ERAS protocol that justly recognizes and considers all obstetric risk factors preoperatively.

Our study has multiple strengths. The SID data represents approximately 97% of all hospital discharges in USA and has been validated by quality control measures established by HCUP, ensuring both internal and external data consistency [24]. Our study cohort consisted of over 2.4 million parturients from five diverse states (representing more than a quarter of the nation's population) over the span of 8 years. This robust sample size strengthens the external validity of our results and provides sufficient statistical power to adjust for potential confounding bias on both a patient and hospital level. Finally, our study is a novel addition to the existing literature on the relationship between OUD and maternal outcomes; it is to our knowledge the first study to assess the association between OUD and maternal outcomes in the context of cesarean delivery.

Our study is also subject to limitations. Patient readmissions can only be identified in the SID if they occurred in the same state as the initial procedure. Since out-of-state readmissions cannot be identified, readmissions may be undercounted. Further, coding of administrative data may vary based on differences in coding practice [60], and errors in data collection and input may also influence our findings. There are also potential confounding variables, such as nutrition and patient compliance, which cannot be adjusted for. Any associations between OUD and maternal outcomes in our study represent correlation and cannot be interpreted in a framework of causality. Due to limitations of the SID, we were unable to determine cause of maternal mortality. The SID also does not provide explicit reasons for unplanned readmissions; we determined the top diagnoses listed for 30- and 90-day readmissions by comparing readmission records with initial discharge records to identify new ICD-9-CM codes [36]. We therefore acknowledge that our insight into the potential underlying pathways between OUD and maternal mortality and readmissions is strongly limited.

Conclusion

In conclusion, our data suggest that OUD status predicts adverse maternal outcomes following cesarean delivery. Specifically, women with OUD experience increased in-patient mortality and readmissions in comparison to non-OUD patients. Given the large number of women with OUD, as well as the high rate of cesarean delivery in this country, it is necessary to develop targeted solutions spanning the patient, provider, hospital and community level to prevent adverse post-delivery outcomes. Expanding treatment and outreach services is one potential way to address complex issues of treatment accessibility, socioeconomic factors, and stigma in this high-risk patient population. Obstetricians can also engage in routine screening of pregnant women and provide counseling regarding risks associated with opioid use. Finally, development of ERAS protocols targeting OUD patients who undergo cesarean delivery may improve postpartum care and recovery through standardization of care and use of best available medical evidence.

Summary points

- Opioid use disorder (OUD) status predicts adverse maternal outcomes following cesarean delivery.
- Compared with non-OUD patients, patients with OUD were nearly 2.5-times more likely to die during hospitalization.
- OUD patients were also 46 and 70% more likely to be readmitted 30 days and 90 days following discharge, respectively.
- Social determinants of health and differences in baseline health may potentially explain the observed disparity in maternal outcomes.
- Targeted solutions to prevent future adverse post-delivery outcomes among OUD patients include expanding treatment and outreach services, recognizing the important role of obstetricians in managing the use of opioids during pregnancy and implementing Enhanced Recovery After Surgery protocols.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2144/cer-2020-0050

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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