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New persistent opioid use after acute opioid prescribing in pregnancy: a nationwide analysis

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Abstract

Objective: To evaluate the association between opioid prescribing during pregnancy and new persistent opioid use in the year following delivery.

Study Design: This nationwide retrospective cohort study included patients ages 12–55 in Optum's de-identified Clinformatics® Data Mart Database, undergoing vaginal birth (VB) or cesarean birth (CB) from 2008–2016, with continuous enrollment from 2-years before birth to 1-year post-discharge. Women were included if they were opioid-naïve in pregnancy (i.e. did not fill

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Condensation: Of opioid-naïve women who fill an opioid prescription during pregnancy, 1 in 25 will develop new persistent opioid use in the year after delivery.

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an opioid prescription 2-years to 9-months before delivery) and did not undergo a procedure within the year after discharge. The exposure was filling an opioid prescription in pregnancy.

The primary outcome was new persistent opioid use (NPOU), defined as a pharmacy claim for 1 opioid prescription between 4–90 days post-discharge and 1 prescription between 91–365 days post-discharge. Clinical and demographic covariates were included. Analyses included descriptive statistics and multivariable logistic regression, adjusting for clinical and demographic covariates.

Results: Of 158,425 childbirths identified, 101,013 (63.8%) were VB and 57,412 (36.2%) were CB. Among all patients, 6.0% (9,429) filled an opioid prescription during pregnancy. The factors associated with filling an opioid in pregnancy were having a non-delivery procedure in pregnancy [adjusted OR (aOR) 9.60, 95% CI (8.81–10.47)] and having an emergency room visit during pregnancy [aOR 2.48, 95% CI (2.37–2.59)]. Of women who received an opioid in pregnancy, 4% (379) developed NPOU. The factors most associated with NPOU were receiving an opioid prescription during pregnancy [aOR 3.45 95% CI (3.04–3.92)] and filling a peripartum opioid prescription (1-week prior to 3-days post-discharge) [aOR 2.28, 95% CI (2.02–2.57)]. Though having a procedure during pregnancy was associated with increased receipt of an opioid prescription, it was also associated with reduced NPOU [aOR 0.72, 95% CI 0.52–0.99].

Conclusion: Women who receive an opioid prescription during pregnancy are more likely to experience new persistent opioid use. Maternity care providers must balance pain management in pregnancy with potential risks of opioids.

Keywords

pregnancy; vaginal delivery; cesarean delivery; opioid; pain management

Introduction:

As maternity care providers have recognized the role of peripartum opioid prescribing in the opioid epidemic, reducing opioid prescribing following delivery has become a national priority.^{1–4} This increased focus is warranted, as 1 in 75 women in the United States who fill an opioid prescription in the peripartum period will continue filling prescriptions up to one year postpartum.⁵ In fact, exposure to postpartum opioids has been linked to new persistent use after delivery, independent of the type of birth (vaginal vs. cesarean), suggesting the risk is inherent to the opioid prescription.⁵

Less is known, however, about the long-term consequences of acute opioid prescribing *during* pregnancy, outside of the delivery episode. It is possible that opioid prescribing for pain in pregnancy could have a similar effect as postpartum opioid prescribing. Women may experience pain from physiologic changes of pregnancy (e.g. round ligament pain), recurrence of chronic conditions (e.g. back pain), or pathologic pain related to new conditions (e.g. appendicitis).^{6–9} Pain management in pregnancy must balance risks to both the pregnant women and fetus. As opioid-alternatives like non-steroidal anti-inflammatory medications (NSAIDs), may cause fetal complications including miscarriage and renal dysfunction,^{10,11} pregnant patients may be more likely to receive opioids because of potential differences in safety profile during pregnancy. However, there is a growing body of evidence that acute opioid exposure can lead to long-term use.^{12,13}

In order to understand the effects of opioid prescribing during maternity care, we assessed rates of opioid prescribing during pregnancy and their impact on long-term opioid use following delivery in opioid-naïve patients.

Methods:

In this retrospective cohort study, we analyzed claims from a national single private-payer including medical and prescription drug coverage, aggregated in Optum's de-identified Clinformatics® Data Mart Database. We included women ages 12–55 who underwent vaginal or cesarean birth from 2008–2016, with continuous enrollment from 2-years before birth to 1-year after discharge. We selected patients with 2-years of continuous enrollment prior to birth in order to identify women who were opioid-naïve in the year prior to pregnancy. Similarly, we required an additional year of enrollment postpartum to assess opioid use in the year following delivery. Women were excluded if they 1) filled an opioid prescription from 2-years to 9-months before delivery admission (i.e. were not opioid-naïve in the year before pregnancy); 2) underwent a procedure as identified by anesthesia codes within 1-year of discharge, or 3) had an index hospitalization length of stay (defined as time from cesarean delivery to discharge) of >7 days, as these deliveries were not thought to represent routine care. If patients had multiple deliveries in the specified time period, only the first birth was included.

The main exposure in this analysis was filling an opioid prescription in pregnancy. The primary outcome was new persistent opioid use (NPOU) after vaginal or cesarean delivery, defined as at least two pharmacy claims after discharge: 1 opioid prescription between 4–90 days post-discharge and 1 prescription between 91–365 days post-discharge.^{5,14} This definition of NPOU is consistent with prior work, and represents a time when patients are expected to have recovered from their initial delivery episode.

To assess the factors associated with filling an opioid prescription during pregnancy and developing NPOU, we included demographic and clinical characteristics as covariates in adjusted models. Demographic variables included age, race, education, region, and year of delivery. Clinical characteristics included pregnancy comorbidities as measured by the Bateman comorbidity index¹⁵, delivery type (vaginal vs. cesarean), and delivery specific complications/additional procedures defined by billing codes for both vaginal delivery (e.g. prolonged labor, bilateral tubal ligation) and cesarean delivery (e.g. unscheduled delivery and repeat cesarean). Characteristics of opioid exposure during pregnancy included receipt of an opioid prescription during pregnancy and oral morphine equivalents prescribed. We also report if patients received a peripartum opioid prescription (defined as 1-week prior to 3-days after discharge), as this has previously been independently associated with NPOU.⁵ Health care utilization measures including emergency department visits, inpatient hospitalizations, and procedures in pregnancy (as defined by non-delivery anesthesia codes) were also included as dichotomous variables. To determine the diagnoses associated with opioid prescriptions, we reported the diagnosis codes from encounters 3-days prior to prescription fills, with a frequency of 50 across the included population.

Analyses included descriptive statistics for cohort characteristics, rates of opioid prescription fills in pregnancy, diagnoses associated with opioid prescriptions, and rates of NPOU. Multivariable logistic regression models were used to separately estimate the adjusted odds ratio (aOR) for filling an opioid prescription in pregnancy and developing NPOU. We also conducted a sensitivity analysis using two additional definitions of NPOU from the literature: 1) Brummett et al defined NPOU in patients undergoing major and minor procedures as 2 opioid prescriptions filled after the perioperative period, 1 prescription before 90 days, and 1 prescription between 90–180 days post-discharge; and 2) Bateman et al defined NPOU as 1 opioid prescription filled in at least 4 of 12 months after the perioperative period to 365 days after discharge.^{16,17} All statistical analyses were performed using SAS version 9.4. Statistical significance was set at $P<0.05$ with 2-sided tests. This study was deemed exempt by the University of Michigan Institutional Review Board.

Results:

We identified 988,036 women who underwent vaginal or cesarean delivery from 2008–2016, of whom, 158,425 met inclusion criteria [101,013 (63.8%) vaginal deliveries; 57,412 (36.2%) cesarean deliveries]. [Figure 1] Descriptive data for the cohort is presented in Table 1. Among all deliveries, 6.0% (9,429) of women filled an opioid in pregnancy [vaginal delivery, 5.6% (5,619); cesarean delivery, 6.6% (3,810)]. Of patients who filled an opioid prescription during pregnancy, the median OMEs per patient was 108 (IQR 81–146), and 16% filled 2 prescriptions during pregnancy (range 1–22 prescriptions in pregnancy). Only 1.8% (2,871) of patients in the cohort had a procedure with anesthesia during pregnancy.

Patients were more likely to receive an opioid prescription during pregnancy if they received non-delivery anesthesia [aOR=9.60, 95% CI (8.81–10.47)], presented for an emergency room visit [aOR=2.48, 95% CI (2.37–2.59)] or underwent an inpatient hospitalization [aOR=1.92, 95% CI (1.78–2.08)]. Women who used tobacco [aOR=1.48, 95% CI (1.37–1.60)], had comorbid psychiatric diagnoses such as mood disorders [aOR=1.23, 95% CI (1.13–1.33)], and had comorbid pain disorders such as back pain [aOR=1.57, 95% CI (1.48–1.65)], were also more likely to receive an opioid prescription than women without these characteristics. [Table 2] The most common diagnoses associated with receiving an opioid in pregnancy were abdominal pain [4,278(14.5%)], urinary tract infections (UTI) [1,997(6.8%)], and back pain [1,470 (6.3%)]. Diagnoses associated with opioid prescriptions were unspecified for 10,071 (34.2%).

Of patients who received an opioid in pregnancy, 4.0% (379) developed new persistent opioid use. Of those undergoing vaginal birth who received an opioid during pregnancy, 3.2% (179) had postpartum NPOU. Among women undergoing cesarean delivery who received an opioid during pregnancy, 5.2% (200) had postpartum NPOU. Rates of NPOU after vaginal delivery and cesarean delivery in women who did not receive an opioid prescription in pregnancy were 0.6% (545) and 1.3% (682) respectively.

We identified several risk factors associated with new persistent opioid use. [Figure 2] Women were more likely to develop NPOU if they received an opioid during pregnancy [aOR 3.45 95% CI (3.04–3.92)] or filled a peripartum opioid prescription [aOR 2.28, 95%

CI (2.02–2.57)]. While having an emergency department visit during pregnancy was associated with NPOU [aOR 1.19, 95% CI (1.06–1.33), inpatient hospitalization was not [aOR 1.15, 95% CI (0.94–1.42)]. Though undergoing a procedure in pregnancy was the factor most strongly associated with filling an opioid prescription, it was associated with a decreased rate of NPOU after delivery [aOR 0.72, 95% CI 0.52–0.99]. Patients who had lower education, history of substance abuse, and cesarean delivery were also more likely to have NPOU.

NPOU after delivery was higher in patients who filled an opioid prescription during pregnancy across all definitions of NPOU included in the sensitivity analysis. Even using the most conservative definition of new persistent opioid use¹⁶, rates were higher in those with opioid use during pregnancy compared to those without (vaginal and cesarean delivery combined: 1.2% (115) vs. 0.1% (176); vaginal delivery 1.2% (70) vs. 0.1% (96); cesarean delivery 1.2% (45) vs. 0.1% (80)) [p<0.01 for all comparisons].

Structure Discussion/Comment:

Principal Findings: In our study, receipt of an opioid prescription during pregnancy was independently associated with new persistent opioid use in the year following delivery. Undergoing a procedure with anesthesia was most strongly associated with receiving an opioid prescription during pregnancy, but with lower rates of NPOU. In contrast, emergency department visits were associated with both receipt of an opioid prescription in pregnancy and NPOU. We also confirmed factors previously associated with NPOU, including prescription factors (e.g. filling a peripartum prescription) and individual factors (e.g. younger age, lower education, race, tobacco use, and psychiatric and pain diagnoses).^{5,14,17} Going forward, future efforts targeting opioid reduction throughout pregnancy, in addition to the peripartum period, are critical to reduce the long-term harms of opioid exposure.¹⁸

Results: Previous estimates suggest 14–22% of patients fill opioid prescriptions during pregnancy.^{19,20} We only included women in our study who were opioid-naïve in the year before pregnancy and had 3 years of continuous enrollment to isolate the independent effect of opioid prescribing during pregnancy. These criteria explain the lower rates of opioid prescribing seen in our population when compared to previous groups. Thus, our findings likely underestimate national rates of NPOU, as prior work has demonstrated higher rates of prescribing for patients who have Medicaid or are not opioid-naïve prior to pregnancy.^{19–21} Thus, almost 1 in 5 women in the general population are exposed to opioids during pregnancy, a particularly vulnerable period often associated with stress and anxiety that may further potentiate the risk of prolonged use.¹⁸

Clinical Implications: There are many potential consequences of opioid prescribing in pregnancy for both women and their children. For women who are opioid-naïve, opioid prescribing can be associated with NPOU and greater risk for opioid harms in the future.^{5,16} Additionally, some data suggest a possible increased risk of neural tube defects, congenital heart defects, and gastroschisis in fetuses exposed to opioids during the first trimester.^{22,23} Exposure to opioids near the time of birth may also contribute to neonatal abstinence syndrome (NAS), NICU admissions, and potential neurodevelopmental effects.^{24,25,26}

While adequate pain management must be a priority, approaches should also balance the potential maternal and fetal risks and benefits of treatment.

Research Implications: While there are now clear recommendations for post-delivery prescribing for pregnant women, current recommendations for pain management in pregnancy provide little guidance on appropriate management of acute pain.^{3,6} There are several reasons for this omission: 1) efforts to reduce post-operative prescribing in other surgical specialties have paved the way for post-delivery recommendations but have not been as well developed for prenatal pain management; 2) there are potential concerns about the safety of opioid-alternatives (such as NSAIDs and acetaminophen) in pregnancy. There are data linking use of NSAIDs with complications in the third trimester, including premature closure of the ductus arteriosus and oligohydramnios from impaired renal function.^{27–29} In contrast, the validity of studies that associate NSAIDs with miscarriage and acetaminophen with increased rates of ADHD, is limited by recall bias and inadequate adjustment for confounding.^{24,30,31} Still, in the absence of robust safety data, providers may resort to using opioids for acute pain, though these medications are not without harm. Acute pain management guidelines will require a clearer understanding of the actual risks of non-opioid medications, and the potential benefits of non-pharmacologic treatments for acute pain such as deep breathing, visualization, massage, and physical therapy in the context of pregnancy.
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In our study, the most common diagnoses associated with opioid fills in pregnancy were unspecified, or attributable to visits for non-specific abdominal pain, urinary tract symptoms, and back pain. It is difficult to assess which of these indications is “appropriate” for opioid prescribing, particularly because we cannot see alternative pain strategies utilized by patients: opioid-sparing medications are frequently prescribed over-the-counter and non-pharmacologic regimens leave no footprint in claims data. Interestingly, undergoing a procedure in pregnancy was associated with a reduced risk of NPOU; this may be because surgical management provided definitive treatment of patients’ pain (e.g. performing a cholecystectomy for a patient with cholelithiasis or the surgical management of nephrolithiasis), or the pain related to non-surgical diagnoses conferred unique risks of NPOU. More granular understanding of the diagnoses associated with opioid prescribing will be crucial for setting best practices for pain management.

Strengths and Limitations: Our study has several important limitations. First, the generalizability of our study is limited by our requirement for 3 years of continuous insurance enrollment; however, this was necessary to clearly define the impact of opioid prescribing in pregnancy, and likely underestimates rates of NPOU. Additionally, we assessed pharmacy claims for women with commercial insurance, limiting the generalizability of our findings. As half of all births in the United States are covered by private insurance, these results are applicable to a wide group. Second, the number of eligible births in our cohort decreased between 2008–2016. While decreased fertility rates may account for a portion of this reduction, it does not fully explain the 40% decline. It is possible that fewer women in 2016 were opioid-naïve entering pregnancy, or continuous enrollment for our prespecified period is less common in 2016 compared to prior years.

Future analyses will investigate these findings in broader cohorts. Finally, using pharmacy claims allows us to identify only prescriptions filled. We cannot identify if prescriptions were written but not filled, prescriptions were filled but not all opioid pills consumed, or if opioids were consumed that were not prescribed. Future work including direct patient inquiry will be helpful for elucidating these differences.

Still, we believe these limitations are outweighed by our study's strengths. These include the novel evaluation of pregnancy opioid exposure as a risk factor for NPOU, the large sample size, and the longitudinal assessment of risk across pregnancy up to one year postpartum. This work fills an important knowledge gap about the long-term effects of opioid prescribing during pregnancy, and represents the best currently available data.

Conclusions:

Many women receive opioid prescriptions during pregnancy, of whom, 1 in 25 develop new persistent opioid use after childbirth. Future work is needed to clarify the safety of opioid alternatives, define prescribing guidelines in pregnancy, and implement opioid-sparing regimens not just at the time of delivery, but also throughout pregnancy.

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AJOG at a Glance:**Why was this study conducted?**

- A.** Between 14–22% of patients fill an opioid prescription in pregnancy, however, little is known about the consequences of this acute prescribing in pregnancy. We evaluated rates of NPOU after delivery in opioid-naïve women who received an opioid prescription during pregnancy, and the factors most associated with NPOU.
- B.** What are the key findings? In opioid-naïve patients who received an acute opioid prescription during pregnancy, 4% developed new persistent opioid use in the year after delivery. Filling an opioid in pregnancy and postpartum were associated with NPOU, while having surgery in pregnancy was associated with lower NPOU.
- C.** What does this study add to what is already known? These data suggest opioid prescribing during pregnancy poses a risk of postpartum persistent opioid use. Maternity providers will need to consider how to best balance adequate pain management in pregnancy with the risk of long-term opioid harms.

Figure 1:
Flowchart of Patient Inclusions and Exclusions

Figure 2:

Plot of adjusted odds ratios of characteristics associated with new persistent opioid use after delivery

Table 1:

Characteristics of patients undergoing vaginal or cesarean delivery, with and without new persistent opioid use

	Vaginal Delivery (n=101,013)		Persistent Opioid Use (n=724)		No Persistent Opioid Use (n=100,289)		P* Value	Cesarean Delivery (n=57,412)		Persistent Opioid Use (n=882)		No Persistent Opioid Use (n=56,530)		P* Value	Vaginal and Cesarean Delivery (n=158,425)		Persistent Opioid Use (n=1,606)		No persistent Opioid Use (n=156,819)		P* Value
	n	%	n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%	
Age							<0.001							<0.001							<0.001
<20	3802	3.8	58	8.0	3744	3.7		1131	2.0	40	4.5	1091	1.9		4933	3.1	98	6.1	4835	3.1	
20-29	34423	34.1	312	43.1	34111	34.0		14916	26.0	276	31.3	14640	25.9		49339	31.1	588	36.6	48751	31.1	
30-39	58153	57.6	324	44.8	57829	57.7		36454	63.5	504	57.1	35950	63.6		94607	59.7	828	51.6	93779	59.8	
>=40	4635	4.6	30	4.1	4605	4.6		4911	8.6	62	7.0	4849	8.6		9546	6.0	92	5.7	9454	6.0	
Race							<0.001							<0.001							<0.001
White	50032	49.5	75	51.8	49657	49.5		26641	46.4	70	53.3	26171	46.3		76673	48.4	845	52.6	75828	48.4	
Black	6561	6.5	74	10.2	6487	6.5		4524	7.9	91	10.3	4433	7.8		11085	7.0	165	10.3	10920	7.0	
Hispanic	10361	10.3	66	9.1	10295	10.3		6466	11.3	96	10.9	6370	11.3		16827	10.6	162	10.1	16665	10.6	
Asian	7621	7.5	24	3.3	7597	7.6		4794	8.4	18	2.0	4776	8.5		12415	7.8	42	2.6	12373	7.9	
Unknown	26438	26.2	185	25.6	26253	26.2		14987	26.1	207	23.5	14780	26.2		41425	26.2	392	24.4	41033	26.2	
Region							<0.001							<0.001							<0.001
Northeast	11499	11.4	33	4.6	11466	11.4		7201	12.5	49	5.6	7152	12.7		18700	11.8	82	5.1	18618	11.9	
Midwest	27182	26.9	162	22.4	27020	26.9		12732	22.2	186	21.1	12546	22.2		39914	25.2	348	21.7	39566	25.2	
South	40142	39.7	362	50.0	39780	39.7		26095	45.5	70	53.3	25625	45.3		66237	41.8	832	51.8	65405	41.7	
West	21876	21.7	165	22.8	21711	21.7		11238	19.6	176	20.0	11062	19.6		33114	20.9	341	21.2	32773	20.9	
Unknown	314	0.3	2	0.3	312	0.3		146	0.3	1	0.1	145	0.3		460	0.3	3	0.2	457	0.3	
Education Level							<0.001							<0.001							<0.001
Less than 12th Grade	555	0.6	6	0.8	549	0.6		325	0.6	7	0.8	318	0.6		880	0.6	13	0.8	867	0.6	
HighSchool	18815	18.6	196	27.1	18619	18.6		11350	19.8	240	27.2	11110	19.7		30165	19.0	436	27.2	29729	19.0	
Diploma																					
Less than Bachelor Degree	53682	53.1	401	55.4	53281	53.1		29826	52.0	467	53.0	29359	51.9		83508	52.7	868	54.1	82640	52.7	
Bachelor Degree Plus	27105	26.8	116	16.0	26989	26.9		15364	26.8	161	18.3	15203	26.9		42469	26.8	277	17.3	42192	26.9	

	Vaginal Delivery (n=101,013)		Persistent Opioid Use (n=724)		No Persistent Opioid Use (n=100,289)		P* Value	Cesarean Delivery (n=57,412)		Persistent Opioid Use (n=882)		No Persistent Opioid Use (n=56,530)		P* Value	Vaginal and Cesarean Delivery (n=158,425)		Persistent Opioid Use (n=1,606)		No persistent Opioid Use (n=156,819)		P* Value
	n	%	n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%	
Unknown	856	0.9	5	0.7	851	0.9		547	1.0	7	0.8	540	1.0		1403	0.9	12	0.8	1391	0.9	
Household Income Range	<0.001																				<0.001
<\$40K	9192	9.1	97	13.4	9095	9.1	9192	9.1	97	13.4	9095	9.1	9192	9.1	97	13.4	9095	9.1	9192	9.1	97
\$40K-\$49K	4716	4.7	41	5.7	4675	4.7	4716	4.7	41	5.7	4675	4.7	4716	4.7	41	5.7	4675	4.7	4716	4.7	41
\$50K-\$59K	5040	5.0	52	7.2	4988	5.0	5040	5.0	52	7.2	4988	5.0	5040	5.0	52	7.2	4988	5.0	5040	5.0	52
\$60K-\$69K	7932	7.9	55	7.6	7877	7.9	7932	7.9	55	7.6	7877	7.9	7932	7.9	55	7.6	7877	7.9	7932	7.9	55
\$70K-\$74K															3				7		
\$75K-\$99K	12102	12.0	79	10.9	12023	12.0		6813	11.9	106	12.0	6707	11.9		18915	11.9	185	11.5	18730	11.9	
\$100K+	39219	38.8	218	30.1	39001	38.9		21822	38.0	264	29.9	21558	38.1		61041	38.5	482	30.0	60559	38.6	
Unknown	22812	22.6	182	25.1	22630	22.6		13098	22.8	208	23.6	12890	22.8		35910	22.7	390	24.3	35520	22.7	
Delivery Year	<0.001																				<0.001
2008	14326	14.2	102	14.1	14224	14.2		7662	13.4	147	16.7	7515	13.3		21988	13.9	249	15.5	21739	13.9	
2009	14883	14.7	133	18.4	14750	14.7		8567	14.9	168	19.1	8399	14.9		23450	14.8	301	18.7	23149	14.8	
2010	13054	12.9	123	17.0	12931	12.9		7827	13.6	146	16.6	7681	13.6		20881	13.2	269	16.8	20612	13.1	
2011	11760	11.6	90	12.4	11670	11.6		6907	12.0	110	12.5	6797	12.0		18667	11.8	200	12.5	18467	11.8	
2012	10931	10.8	72	9.9	10859	10.8		6380	11.1	106	12.0	6274	11.1		17311	10.9	178	11.1	17133	10.9	
2013	9608	9.5	66	9.1	9542	9.5		5441	9.5	70	7.9	5371	9.5		15049	9.5	136	8.5	14913	9.5	
2014	9250	9.2	52	7.2	9198	9.2		4927	8.6	51	5.8	4876	8.6		14177	9.0	103	6.4	14074	9.0	
2015	8989	8.9	52	7.2	8937	8.9		4967	8.7	49	5.6	4918	8.7		13956	8.8	101	6.3	13855	8.8	
2016	8212	8.1	34	4.7	8178	8.2		4734	8.3	35	4.0	4699	8.3		12946	8.2	69	4.3	12877	8.2	
Tobacco use history	5695	5.6	91	12.6	5604	5.6		3704	6.5	120	13.6	3584	6.3		9399	5.9	211	13.1	9188	5.9	
Mental Health Disorder	<0.001																				<0.001
Adjustment	3514	3.5	44	6.1	3470	3.5		2119	3.7	45	5.1	2074	3.7		5633	3.6	89	5.5	5544	3.5	
Anxiety	7895	7.8	121	16.7	7774	7.8		4657	8.1	141	16.0	4516	8.0		12552	7.9	262	16.3	12290	7.8	
Mood	6369	6.3	116	16.0	6253	6.2		3772	6.6	121	13.7	3651	6.5		10141	6.4	237	14.8	9904	6.3	
Suicide or self-harm	282	0.3	8	1.1	274	0.3		87	0.2	1	0.1	86	0.2		369	0.2	9	0.6	360	0.2	

	Vaginal Delivery (n=101,013)		Persistent Opioid Use (n=724)		No Persistent Opioid Use (n=100,289)		P* Value	Cesarean Delivery (n=57,412)		Persistent Opioid Use (n=882)		No Persistent Opioid Use (n=56,530)		P* Value	Vaginal and Cesarean Delivery (n=158,425)		Persistent Opioid Use (n=1,606)		No persistent Opioid Use (n=156,819)		P* Value
	n	%	n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%	
Personality	176	0.2	5	0.7	171	0.2	<0.001	71	0.1	1	0.1	70	0.1	0.930	247	0.2	6	0.4	241	0.2	0.026
Disruptive	1588	1.6	34	4.7	1554	1.6	<0.001	828	1.4	25	2.8	803	1.4	<0.001	2416	1.5	59	3.7	2357	1.5	<0.001
Psychosis	156	0.2	5	0.7	151	0.2	<0.001	74	0.1	3	0.3	71	0.1	0.078	230	0.2	8	0.5	222	0.1	<0.001
Alcohol or substance use	1874	1.9	45	6.2	1829	1.8	<0.001	1145	2.0	48	5.4	1097	1.9	<0.001	3019	1.9	93	5.8	2926	1.9	<0.001
Other mental disorder	2664	2.6	47	6.5	2617	2.6	<0.001	1551	2.7	52	5.9	1499	2.7	<0.001	4215	2.7	99	6.2	4116	2.6	<0.001
Pain Disorders																					
Arthritis	27381	27.1	276	38.1	27105	27.0	<0.001	16476	28.7	309	35.0	16167	28.6	<0.001	43857	27.7	585	36.4	43272	27.6	<0.001
Back	20065	19.9	216	29.8	19849	19.8	<0.001	11587	20.2	248	28.1	11339	20.1	<0.001	31652	20.0	464	28.9	31188	19.9	<0.001
Neck	9062	9.0	90	12.4	8972	9.0	0.001	5409	9.4	112	12.7	5297	9.4	<0.001	14471	9.1	202	12.6	14269	9.1	<0.001
Other Pain	23257	23.0	249	34.4	23008	22.9	<0.001	14358	25.0	315	35.7	14043	24.8	<0.001	37615	23.7	564	35.1	37051	23.6	<0.001
Roteman's Comorbidity Index																					
0	57407	56.8	372	51.4	57035	56.9	0.062	22197	38.7	326	37.0	21871	38.7		79604	50.3	698	43.5	78906	50.3	
1	23043	22.8	177	24.5	22866	22.8		14715	25.6	214	24.3	14501	25.7		37758	23.8	391	24.4	37367	23.8	
2	12302	12.2	103	14.2	12199	12.2		9997	17.4	167	18.9	9830	17.4		22299	14.1	270	16.8	22029	14.1	
3	4595	4.6	38	5.3	4557	4.5		5121	8.9	79	9.0	5042	8.9		9716	6.1	117	7.3	9599	6.1	
4	1911	1.9	19	2.6	1892	1.9		2521	4.4	39	4.4	2482	4.4		4432	2.8	58	3.6	4374	2.8	
>=5	1755	1.7	15	2.1	1740	1.7		2861	5.0	57	6.5	2804	5.0		4616	2.9	72	4.5	4544	2.9	
Care Utilization in Pregnancy																					
AnyEmergency room visit	22203	22.0	247	34.1	21956	21.9	<0.001	13829	24.1	302	34.2	13527	23.9	<0.001	36032	22.7	549	34.2	35483	22.6	<0.001
Any non-delivery	3456	3.4	54	7.5	3402	3.4	<0.001	2605	4.5	59	6.7	2546	4.5	0.002	6061	3.8	113	7.0	5948	3.8	<0.001
Inpatient hospitalization																					
Opioid filled during pregnancy	5619	5.6	179	24.7	5440	5.4	<0.001	3810	6.6	200	22.7	3610	6.4	<0.001	9429	6.0	379	23.6	9050	5.8	<0.001
Quartile of the first Opioid prescription (mg of OME equivalent)														<0.001							

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	Vaginal Delivery (n=101,013)		Persistent Opioid Use(n=724)		No Persistent Opioid Use (n=100,289)		p* Value	Cesarean Delivery (n=57,412)		Persiste nt Opioid Use (n=882)		No Persistent Opioid Use (n=56,530)		p* Value	Vaginal and Cesarean Delivery (n=158,425)		Persistent Opioid Use (n=1,606)		No persistent Opioid Use (n=156,819)		p* Value
	n	%	n	%	n	%		n	%	n	%	n	%		n	%	n	%	n	%	
<75	96567	95.6	577	79.7	95990	95.7		54358	94.7	711	80.6	53647	94.9		150925	95.3	1288	80.2	149637	95.4	
75–108	1656	1.6	51	7.0	1605	1.6		1097	1.9	62	7.0	1035	1.8		2753	1.7	113	7.0	2640	1.7	
108–150	804	0.8	26	3.6	778	0.8		579	1.0	26	3.0	553	1.0		1383	0.9	52	3.2	1331	0.9	
>=150	1986	2.0	70	9.7	1916	1.9		1378	2.4	83	9.4	1295	2.3		3364	2.1	153	9.5	3211	2.1	
AnyAnesthesiaprocedure	1443	1.4	15	2.1	1428	1.4	0.143	1428	2.5	29	3.3	1399	2.5	0.124	2871	1.8	44	2.7	2827	1.8	0.005
Delivery Characteristics																					
Hospital Length of Stay for delivery							0.376							0.094							<0.00>1
<=3 days	97310	96.3	693	95.7	96617	96.3		33831	58.9	544	61.7	33287	58.9		131141	82.8	1237	77.0	129904	82.8	
4–7 days	3703	3.7	31	4.3	3672	3.7		23581	41.1	338	38.3	23243	41.1		27284	17.2	369	23.0	26915	17.2	
Opioid filled duringperipartumperiod	25943	25.7	382	52.8	25561	25.5	<0.001	42899	74.7	753	85.4	42146	74.6	<0.001	68842	43.5	1135	70.7	67707	43.2	<0.001

Table 2.

Logistic regression model for filling an opioid prescription during pregnancy

Characteristic	Vaginal Delivery Cohort (n=101,013)			Cesarean Delivery Cohort (n=57,412)			VD & CD Combined Cohort (n=158,425)		
	Adjusted OR	95% CI	P Value	Adjusted OR	95% CI	P Value	Adjusted OR	95% CI	P Value
Age									
20-29 (reference)	1	NA	NA	1	NA	NA	1	NA	NA
<20	0.88	(0.77-	0.081	0.88	(0.69-	0.281	0.88	(0.78-	0.035
30-39	0.93	(0.87-	0.023	0.93	(0.86-	0.081	0.94	(0.89-	0.008
>=40	0.92	(0.79-	0.280	0.97	(0.84-	0.683	0.96	(0.86-	0.403
Race									
White (reference)	1	NA	NA	1	NA	NA	1	NA	NA
Black	1.06	(0.96-	0.260	0.99	(0.88-	0.900	1.04	(0.96-	0.389
Hispanic	0.77	(0.69-	<.001	0.79	(0.70-	<.001	0.78	(0.72-	<.001
Asian	0.84	(0.74-	0.008	0.81	(0.70-	0.005	0.83	(0.76-	<.001
Unknown	0.93	(0.87-	0.044	0.92	(0.84-	0.046	0.93	(0.88-	0.006
Region									
Northeast (reference)	1	NA	NA	1	NA	NA	1	NA	NA
Midwest	1.93	(1.70-	<.001	1.81	(1.57-	<.001	1.87	(1.70-	<.001
South	2.29	(2.04-	<.001	2.15	(1.89-	<.001	2.23	(2.05-	<.001
West	2.27	(2.01-	<.001	2.07	(1.79-	<.001	2.18	(1.98-	<.001
Unknown	3.50	(2.23-	<.001	1.27	(0.51-	0.606	2.66	(1.78-	<.001
Education Level									
Less than Bachelor Degree	1	NA	NA	1	NA	NA	1	NA	NA
Less than 12th Grade	0.96	(0.65-	0.821	1.11	(0.70-	0.650	1.02	(0.76-	0.890
High School Diploma	1.07	(0.99-	0.077	1.09	(0.99-	0.071	1.08	(1.02-	0.010
Bachelor Degree Plus	0.84	(0.78-	<.001	0.95	(0.87-	0.206	0.88	(0.83-	<.001
Unknown	0.93	(0.68-	0.628	0.88	(0.60-	0.508	0.91	(0.72-	0.449
Delivery Year									
2008	1	NA	NA	1	NA	NA	1	NA	NA
2009	0.99	(0.89-	0.796	1.01	(0.89-	0.856	1.00	(0.92-	0.949

Characteristic	Vaginal Delivery Cohort (n=101,013)			Cesarean Delivery Cohort (n=57,412)			VD & CD Combined Cohort (n=158,425)		
	Adjusted OR	95% CI	P Value	Adjusted OR	95% CI	P Value	Adjusted OR	95% CI	P Value
2010	1.03	(0.93-	0.600	1.06	(0.93-	0.372	1.04	(0.96-	0.295
2011	0.98	(0.88-	0.741	0.94	(0.82-	0.322	0.97	(0.89-	0.392
2012	0.83	(0.74-	0.001	0.91	(0.80-	0.168	0.86	(0.79-	<.001
2013	0.83	(0.74-	0.001	0.78	(0.67-	0.001	0.81	(0.74-	<.001
2014	0.60	(0.53-	<.001	0.64	(0.55-	<.001	0.62	(0.56-	<.001
2015	0.55	(0.48-	<.001	0.59	(0.50-	<.001	0.57	(0.51-	<.001
2016	0.53	(0.46-	<.001	0.56	(0.47-	<.001	0.54	(0.49-	<.001
Tobacco Use	1.48	(1.34-	<.001	1.46	(1.30-	<.001	1.48	(1.37-	<.001
Psychiatric diagnoses									
Adjustment disorder	1.06	(0.92-	0.455	1.03	(0.87-	0.763	1.04	(0.94-	0.443
Anxiety disorder	1.04	(0.94-	0.483	1.18	(1.05-	0.005	1.10	(1.02-	0.020
Mood disorder	1.27	(1.14-	<.001	1.17	(1.03-	0.015	1.23	(1.13-	<.001
Substance use disorder	1.16	(0.98-	0.088	1.29	(1.06-	0.013	1.21	(1.06-	0.004
Pain Condition									
Arthritis	1.14	(1.07-	<.001	1.13	(1.04-	0.003	1.13	(1.08-	<.001
Back	1.57	(1.46-	<.001	1.56	(1.43-	<.001	1.57	(1.48-	<.001
Neck	0.95	(0.86-	0.288	0.90	(0.80-	0.073	0.93	(0.87-	0.054
Other pain	1.44	(1.35-	<.001	1.47	(1.37-	<.001	1.45	(1.38-	<.001
Bateman's Comorbidity Index	1.02	(1.00-	0.045	1.02	(1.00-	0.077	1.03	(1.01-	0.002
Emergency room visit during	2.59	(2.44-	<.001	2.31	(2.15-	<.001	2.48	(2.37-	<.001
Inpatient during pregnancy	2.07	(1.87-	<.001	1.73	(1.54-	<.001	1.92	(1.78-	<.001
Any Anesthesia procedure during	10.96	(9.72-	<.001	8.23	(7.27-	<.001	9.60	(8.81-	<.001