OBSTETRICS

Persistent opioid use following cesarean delivery: patterns and predictors among opioid-naïve women

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BACKGROUND: The incidence of opioid-related death in women has increased 5-fold over the past decade. For many women, their initial opioid exposure will occur in the setting of routine medical care. Approximately 1 in 3 deliveries in the United States is by cesarean, and opioids are commonly prescribed for postsurgical pain management.

OBJECTIVE: The objective of this study was to determine the risk that opioid-naïve women prescribed opioids after cesarean delivery will subsequently become consistent prescription opioid users in the year following delivery and to identify predictors for this behavior.

STUDY DESIGN: We identified women in a database of commercial insurance beneficiaries who underwent cesarean delivery and who were opioid naïve in the year prior to delivery. To identify persistent users of opioids, we used trajectory models, which group together patients with similar patterns of medication filling during follow-up, based on patterns of opioid dispensing in the year following cesarean delivery. We then constructed a multivariable logistic regression model to identify independent risk factors for membership in the persistent user group.

RESULTS: A total of 285 of 80,127 (0.36%, 95% confidence interval, 0.32—0.40), opioid-naïve women became persistent opioid users (identified using trajectory models based on monthly patterns of opioid dispensing) following cesarean delivery. Demographics and baseline comorbidity predicted such use with moderate discrimination (c statistic = 0.73). Significant predictors included a history of cocaine abuse (risk, 7.41%; adjusted odds ratio, 6.11, 95% confidence interval, 1.03—36.31) and other illicit substance abuse (2.36%; adjusted odds ratio, 2.78, 95% confidence interval, 1.12—6.91), tobacco use (1.45%; adjusted odds ratio, 3.04, 95% confidence interval, 2.03—4.55), back pain (0.69%; adjusted odds ratio, 1.74, 95% confidence interval, 1.33—2.29), migraines (0.91%; adjusted odds ratio, 2.14, 95% confidence interval, 1.58—2.90), antidepressant use (1.34%; adjusted odds ratio, 3.19, 95% confidence interval, 2.41—4.23), and benzodiazepine use (1.99%; adjusted odds ratio, 3.72, 95% confidence interval, 2.64—5.26) in the year prior to the cesarean delivery.

CONCLUSION: A very small proportion of opioid-naïve women (approximately 1 in 300) become persistent prescription opioid users following cesarean delivery. Preexisting psychiatric comorbidity, certain pain conditions, and substance use/abuse conditions identifiable at the time of initial opioid prescribing were predictors of persistent use.

Key words: cesarean delivery, cohort, opioids, pain, pregnancy studies

The rapidly escalating increase in the incidence of opioid medication overdose among women in the United States has received much recent attention from the US Centers for Disease Control and Prevention and other leading health care organizations.[1,2] From 1999 to 2010, the rate of death from this cause increased 5-fold among women. Opioid-related emergency room visits also increased substantially over this time period. These risks were particularly high among women of reproductive age.

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Whereas for some women the initial exposure to opioids comes from illicit purchase and use, for many others it occurs in the course of routine medical care. A common medical event in such patients is cesarean delivery. Approximately 1.3 million women undergo cesarean delivery each year in the United States,[3] making it the most common inpatient surgical procedure,[4] as it is in many other developed countries. Women who undergo this procedure typically have postoperative pain[5] and are frequently discharged with prescriptions for opioid analgesics. Such prescriptions therefore represent a common source of exposure to opioids in young women, many of whom may have never used these drugs previously.

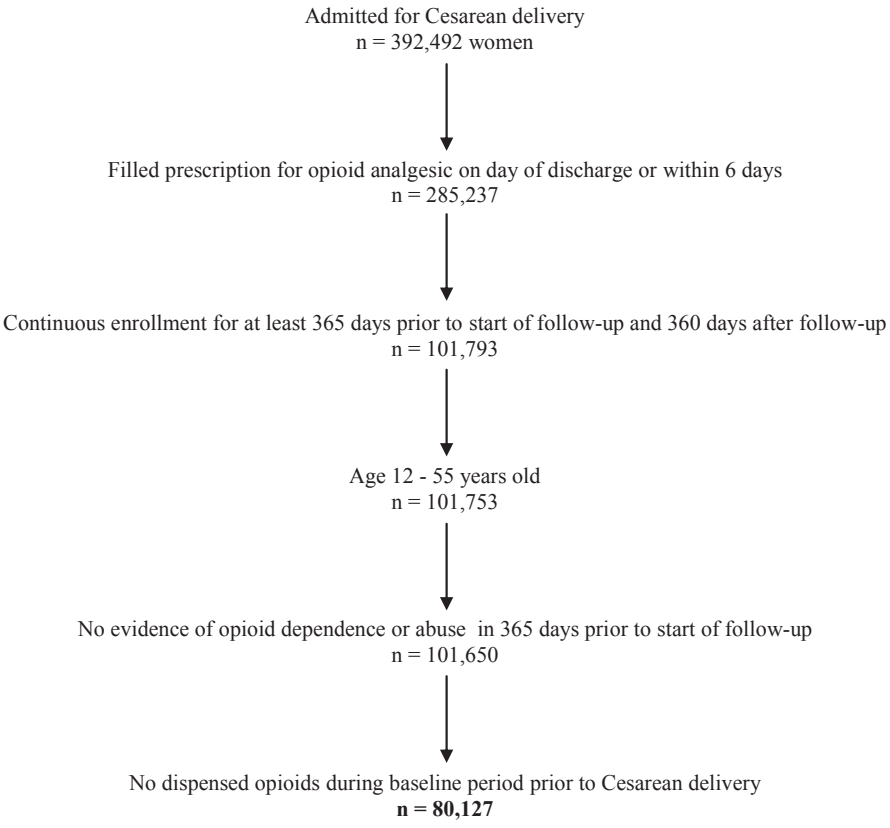
Given concerns about prescription opioid use and abuse in women of reproductive age, we sought to determine the risk that opioid-naïve women prescribed these medications after cesarean delivery will subsequently become persistent users of prescription opioid medications and to identify potentially actionable predictors of this outcome.

Materials and Methods

Data source

Study data were derived from the Clinformatics Data Mart, a database of health care utilization drawn from the transactions of the nationwide commercial US health insurer, UnitedHealthcare, for the years 2003—2011. The database contains transactional data on reimbursement for outpatient pharmacy dispensings, inpatient and outpatient services, and procedures and associated diagnoses (recorded using *International Classification of Diseases*, ninth edition CM codes). Only those beneficiaries with both medical and

FIGURE 1
Cohort selection



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prescription drug coverage are included in the database.

Claims submitted for payment by providers and pharmacies are verified, adjudicated, adjusted, and deidentified prior to inclusion in the database. The use of this deidentified database for research was approved by the Institutional Review Board of the Partners Healthcare System (Boston, MA).

Cohort

We included all women who underwent a Cesarean delivery identified by the procedure codes 74.0, 74.1, 74.2, 74.4, and 74.99 from the *International Classification of Diseases*, ninth edition, and who filled a prescription for an opioid medication on the day of hospital discharge or within 6 days thereafter. This was done based on the assumption that a filled prescription during this window would likely be to treat acute postoperative pain related to the cesarean delivery.

Opioids considered in the analysis included hydrocodone, oxycodone, codeine, meperidine, hydromorphone, morphine, fentanyl, methadone, and oxymorphone. Follow-up began on the seventh day following discharge from the delivery hospitalization.

To allow for adequate ascertainment of baseline characteristics and assessment of persistent postdelivery opioid use, the analysis was restricted to patients with continuous enrollment with the insurer for at least 365 days prior to and 360 days after the beginning of follow-up. We further restricted our cohort to women aged 12−55 years at the time of delivery. Because the focus of the study was on the risk of persistent opioid use after initial exposure to opioids following cesarean delivery, we excluded women who had filled outpatient prescriptions for opioids during the baseline period prior to delivery or who had diagnoses in the baseline period indicating opioid abuse or dependence (although it is possible that the woman may have used opioids prior to the baseline period). If a woman met the inclusion criteria for more than 1 delivery, only the first delivery was considered in the analysis. The final cohort consisted of 80,127 women (Figure 1).

To identify persistent users of opioids after cesarean delivery, we used trajectory models, which group together patients with similar patterns of medication filling during follow-up. The trajectory model approach has previously been applied to the evaluation of medication adherence.[6]

To define the trajectory groups for opioid use in our cohort, we first determined whether a woman filled a prescription for an opioid medication during each of 12 consecutive 30 day periods of follow-up. Based on this definition, we then fit a group-based trajectory model to define 5 distinct groups of opioid use.[7,8] In this model, the log odds of filling an opioid during each 30 day period was estimated as a third-order polynomial of time separately within each group, as in prior evaluations of 12 month trajectories.[6] The model also estimated the probability of group membership for each patient; patients were assigned to the group with the highest membership probability.

Based on this model, we defined the group of patients with the highest probability of filling over time as persistent users. The other 4 trajectory groups were considered nonpersistent users. The model was estimated using Proc Traj, in SAS (version 9.2; SAS Institute, Cary, NC). A 5 group model was chosen based on a combination of the Bayesian information criterion and clinical interpretability of resulting trajectory groups; models with other numbers of groups were also considered.

Trajectory models make it possible to use the observed data to define distinct filling patterns of opioids in our cohort during the year after delivery and classify