



## Association of Anesthesia Modality with Opioid Prescriptions After Cesarean Delivery: A Comparative Study of General and Epidural Techniques

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### Abstract

**Background:** Cesarean section (C-section) is the most common surgical procedure performed in the United States and a known contributor to initial opioid exposure among women of reproductive age. While neuraxial (epidural) anesthesia is the preferred technique for cesarean delivery, general anesthesia is still used in select clinical scenarios. Given the ongoing opioid crisis, it is critical to understand how anesthesia modality influences postoperative opioid prescribing patterns.

**Objective:** To evaluate the association between anesthesia type (general vs. epidural) and postoperative opioid prescription rates in women aged 18 to 50 undergoing cesarean delivery, with follow-up extending to 90 days after surgery.

**Methods:** We conducted a retrospective cohort study using the TriNetX Global Collaborative Network, a federated health research platform of electronic medical records from 148 healthcare organizations. Women aged 18–50 who underwent cesarean delivery between 2005 and 2025 were identified. Patients were grouped based on anesthesia type using CPT codes: general anesthesia (01961 only) and epidural anesthesia (01967 or 01968). Propensity score matching was performed on demographics, comorbidities, and prior medication exposures, resulting in two balanced cohorts each containing 78,572 patients. The primary outcome was receipt of an opioid prescription (morphine, oxycodone, hydromorphone, codeine, or tramadol) from day 1 to day 90 after surgery. Risk and survival analyses were conducted using TriNetX tools.

**Results:** Opioid prescriptions were more common in the general anesthesia group (74.3%) compared to the epidural group (64.2%), with a risk difference of 10.1% and an odds ratio of 1.616. Kaplan-Meier survival analysis showed a significantly lower probability of remaining opioid-free at 90 days in the general anesthesia group (25.4% vs. 35.5%, log-rank  $p < 0.001$ ). The hazard ratio for opioid use was 1.264 (95% CI: 1.249–1.279).

**Conclusion:** Women receiving general anesthesia for cesarean section were more likely to receive postoperative opioids and had a higher overall risk of opioid use within 90 days compared to those receiving epidural anesthesia. These findings underscore the importance of anesthesia choice in minimizing opioid exposure and guiding perioperative pain management strategies.

**Keywords:** Cesarean Delivery; General Anesthesia; Epidural Anesthesia; Opioid Prescribing; Postoperative Pain Management

### Introduction

The opioid epidemic continues to be a pressing public health crisis in the United States, with prescription opioids frequently serving as the initial point of exposure for individuals who go on to develop misuse or dependency. Among the various settings where opioids are introduced, surgical procedures represent a major gateway. Cesarean delivery (C-section), in particular, is the most commonly performed surgical procedure in the U.S., accounting for nearly one-third of all births and approximately 1.2 million operations annually [1]. As such, the postpartum period following C-section represents a critical window in which opioid stewardship can have meaningful public

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health impact [2].

Traditionally, pain management after cesarean delivery has relied heavily on short-term opioid prescriptions. However, substantial evidence now indicates that the number of opioids prescribed often far exceeds what patients actually use, leading to a surplus of unused medication that is vulnerable to diversion, misuse, and long-term sequelae including persistent opioid use [3, 4]. While recent initiatives have aimed to curb excessive prescribing, much of the existing research has focused on prescription quantity and refill rates, with less attention given to the role that anesthetic choice may play in shaping postoperative opioid use.

Epidural anesthesia is widely used in obstetric care and offers the dual benefit of intraoperative anesthesia and prolonged postoperative analgesia by blocking nociceptive transmission at the spinal level [5, 6]. This regional technique may reduce the perceived need for systemic pain control in the immediate postoperative period. Conversely, general anesthesia, while necessary in certain clinical situations, lacks the extended analgesic properties of neuraxial techniques and may result in higher pain intensity after surgery, thereby increasing reliance on systemic opioids [7, 8]. Despite this clear physiological basis for differing analgesic trajectories, few large-scale studies have directly compared postoperative opioid prescribing patterns between general and epidural anesthesia in the cesarean population.

As clinicians and policymakers continue to seek strategies that balance effective pain management with the imperative to reduce unnecessary opioid exposure, understanding the relationship between anesthesia type and opioid prescribing is essential. This study aims to evaluate the association between anesthetic modality—general versus epidural—and postoperative opioid prescribing among women undergoing cesarean delivery. We hypothesize that patients receiving general anesthesia will be more likely to receive opioids postoperatively, and to initiate use earlier, than those who receive epidural anesthesia. By clarifying how anesthetic approach influences opioid use, this study may inform both clinical decision-making and institutional opioid stewardship efforts in obstetric care.

## Methods

This retrospective cohort study utilized de-identified electronic health record data from the TriNetX Global Collaborative Network, a federated research platform aggregating clinical information from 148 healthcare organizations. The data encompass a wide range of clinical domains, including demographics, procedures, diagnoses, medication use, and laboratory results. The analysis was conducted on July 1, 2025, using the Compare Outcomes feature on the TriNetX platform.

The study population included women aged 18 to 50 years who underwent cesarean delivery at participating institutions between 2005 and 2025. Patients were categorized into two mutually exclusive cohorts based on the type of anesthesia received during their cesarean delivery. The general anesthesia cohort included women with a recorded CPT code 01961 (anesthesia for cesarean delivery only) and no record of neuraxial labor analgesia or epidural conversion, which were excluded using CPT codes 01967 and 01968. The epidural anesthesia cohort included women who received neuraxial anesthesia, defined by the presence of either CPT code 01967 (neuraxial labor analgesia) or 01968 (anesthesia for cesarean delivery following neuraxial labor analgesia). All patients in both cohorts had to have procedural codes indicating cesarean delivery (CPT 59510, 59514, or

59515).

The index event for analysis was defined as the first recorded occurrence of cesarean delivery. To evaluate postoperative outcomes, the time window for outcome measurement began one day after the index event and ended 90 days later. Patients whose index event occurred more than 20 years prior to the analysis date were excluded.

Propensity score matching was performed to balance the cohorts on baseline demographics and comorbidities, including age, race, obesity, hypertensive disorders of pregnancy, depressive episodes, recurrent major depressive disorder, and other anxiety disorders, as well as prior exposure to each opioid medication. These factors were selected because they represent established confounders that may independently influence both the choice of anesthesia technique and postoperative opioid prescribing patterns. Age and race are known to impact both anesthetic decision-making and pain management practices. Obesity and hypertensive disorders of pregnancy can affect anesthesia risk profiles and surgical complexity, potentially leading to differing analgesic needs. Psychiatric conditions such as depression and anxiety have been consistently linked to increased postoperative opioid use and a higher likelihood of persistent opioid therapy. Additionally, matching on prior exposure to specific opioid medications was essential to account for baseline differences in opioid tolerance and preoperative prescribing behaviors. After matching, each cohort contained 78,572 patients, resulting in well-balanced groups with standardized differences below accepted thresholds.

## Event of Interest Definition

The primary outcome was receipt of an opioid prescription following cesarean delivery. Opioid medications were identified using RxNorm codes and included morphine, oxycodone, hydromorphone, codeine, and tramadol. The presence of any of these medications in the electronic health record following the index event and within the 90-day window was considered evidence of postoperative opioid exposure.

## Statistical Analysis

Two types of statistical analyses were performed using the TriNetX platform. First, a risk analysis was conducted to calculate the proportion of patients in each cohort who received an opioid prescription. The analysis generated a risk difference, risk ratio, and odds ratio, each with corresponding 95% confidence intervals. Statistical significance was determined using z-tests. Second, a Kaplan-Meier survival analysis was performed to estimate the time to first opioid prescription postoperatively. This analysis included all patients, regardless of whether they had opioid prescriptions prior to the index event. The log-rank test was used to compare survival distributions between the two cohorts, and hazard ratios were calculated to quantify the relative instantaneous risk of opioid prescribing over time.

All analyses were conducted within the TriNetX platform. This study received exemption from formal IRB review due to the use of de-identified data.

## Ethical Considerations

This retrospective study is exempt from informed consent. The data reviewed is a secondary analysis of existing data, does not involve intervention or interaction with human subjects, and is de-identified according to the de-identification standard defined in the HIPAA Privacy Rule.

## Results

A total of 157,144 women aged 18 to 50 who underwent cesarean delivery were included in the analysis after propensity score matching, with 78,572 patients in each cohort. Within the 90-day postoperative period, 58,382 patients (74.3%) in the general anesthesia group filled at least one opioid prescription, compared to 50,407 patients (64.2%) in the epidural group.

This represents an absolute risk difference of 10.1%, a risk ratio of 1.158, and an odds ratio of 1.616, suggesting a significantly greater likelihood of postoperative opioid exposure among patients who received general anesthesia.

Both groups had a median time to first opioid prescription of 2 days, but Kaplan-Meier survival analysis revealed a distinct difference in opioid-free survival across the 90-day period. By day 90, only 25.4% of patients in the general anesthesia group remained opioid-free, compared to 35.5% in the epidural group. This difference was statistically significant based on the log-rank test ( $\chi^2 = 1905.140$ ,  $p < 0.001$ ). The hazard ratio for opioid use in the general anesthesia group was 1.264 (95% CI: 1.249–1.279), indicating a 26.4% higher instantaneous risk of initiating opioid therapy at any point during the follow-up period compared to those who received epidural anesthesia.

These outcomes are summarized in Table 1, with Figure 1 depicting the comparative risk of postoperative opioid prescription by anesthesia type, and Figure 2 illustrating the Kaplan-Meier survival curves for remaining opioid-free over the 90-day period.

## Discussion

This study evaluated the relationship between anesthetic modality and postoperative opioid prescribing following cesarean delivery, revealing that general anesthesia is associated with significantly greater rates of opioid prescriptions within 90 days postoperatively. Even after matching and adjusting for clinical characteristics, the general anesthesia cohort had higher absolute and relative risks of receiving opioids, as well as a shorter opioid-free survival. These

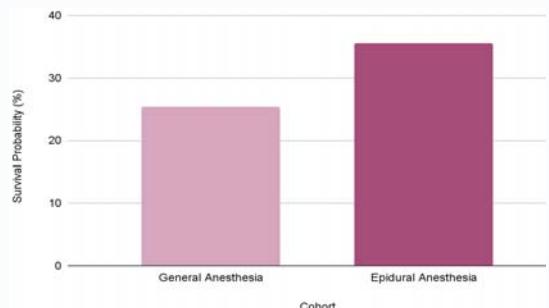


Figure 2: Probability of Remaining Opioid-Free at 90 Days.

findings underscore anesthetic choice as an underrecognized but modifiable factor in postpartum opioid exposure, particularly relevant in the context of the ongoing opioid epidemic [2, 4].

### Physiologic Mechanisms Underpinning Anesthesia Type and Postoperative Pain

The observed differences in opioid prescribing likely stem from fundamental physiologic distinctions between neuraxial and general anesthesia. Epidural anesthesia provides direct, segmental blockade of nociceptive afferent pathways at the spinal cord level, offering superior intraoperative and extended postoperative analgesia. This localized analgesic effect reduces the central sensitization associated with surgical pain, thereby diminishing the need for systemic opioids [5, 6]. In contrast, general anesthesia induces unconsciousness but does not target the same neural pathways involved in pain transmission and modulation. Consequently, patients often emerge from general anesthesia with unmitigated nociceptive signaling and higher pain intensity, prompting earlier and more frequent opioid administration [7, 8].

Additionally, neuraxial anesthesia may attenuate the neuroendocrine stress response to surgery by suppressing hypothalamic-pituitary-adrenal axis activation. Reduced secretion of cortisol and catecholamines contributes to better pain control and more stable hemodynamics in the perioperative period [5, 6]. In contrast, general anesthesia allows full expression of this stress response, which may exacerbate postoperative pain and hyperalgesia. These physiologic effects explain why epidural techniques, especially those involving adjunct local anesthetics or opioids, offer durable postoperative pain control without systemic exposure [6, 7].

### Clinical Implications for Opioid Stewardship

The clinical implications of these findings are especially salient given the growing body of literature on postpartum opioid overprescription. Prior work has shown that most women use fewer opioids than prescribed, leaving substantial quantities of unused medication in circulation, posing a risk for diversion and misuse [3, 4]. By reducing initial opioid exposure through strategic anesthetic planning, clinicians may mitigate long-term risks, including persistent opioid use and opioid use disorder. Our results align with these data and support broader institutional adoption of neuraxial techniques when not contraindicated.

Further, anesthetic decision-making should be considered in the development of opioid stewardship initiatives, particularly in obstetric settings where cesarean delivery is among the most commonly performed surgical procedures [1]. Our findings also suggest a need for enhanced education of clinicians and patients

Table 1: Postoperative Opioid Use Outcomes by Anesthesia Type.

Metric	General Anesthesia	Epidural Anesthesia
Patients in Cohort	78,572	78,572
Patients with Opioid Use	58,382	50,407
Opioid Use Risk (%)	74.3%	64.2%
Median Time to Opioid Use (days)	2	2
Survival Probability at End (%)	25.4%	35.5%
Hazard Ratio (95% CI)	1.264 (1.249–1.279)	1.0 (Reference)

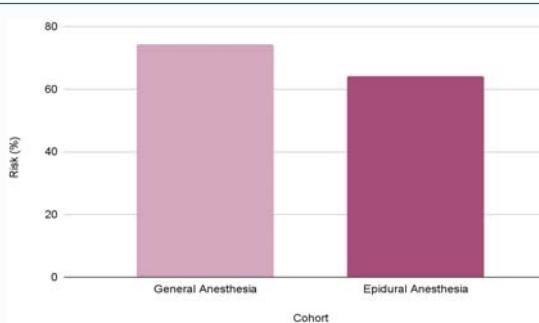


Figure 1: Postoperative Opioid Prescription Risk by Anesthesia Type.

regarding the implications of anesthetic choice on postoperative pain and recovery trajectories.

### Limitations and Future Directions

Despite robust methodology, our study has several limitations. The use of administrative data restricts the granularity of our analysis—actual opioid consumption, patient-reported pain scores, and satisfaction with pain control were not available. Additionally, institutional pain protocols, prescriber variability, and patient preferences may have introduced unmeasured confounding. However, our results remain consistent with existing guidelines recommending neuraxial anesthesia as the preferred method for cesarean delivery when clinically feasible [9].

Moreover, while epidural anesthesia is associated with improved postoperative pain outcomes, it is not without risk. Potential complications include maternal hypotension, inadequate block, urinary retention, and rare but serious neurologic injury [10, 11]. Therefore, anesthetic choice must remain individualized, taking into account patient comorbidities, surgical factors, and shared decision-making principles.

### Conclusion

In conclusion, this study reinforces the role of anesthetic choice as a key determinant of postoperative opioid exposure following cesarean delivery. General anesthesia was associated with significantly higher opioid prescribing rates, shorter opioid-free survival, and greater instantaneous risk of initiating opioid use. These findings reflect the physiologic advantages of neuraxial anesthesia in modulating postoperative pain and minimizing systemic opioid requirements.

As healthcare systems seek to combat the opioid crisis through preventive strategies, anesthetic planning may serve as a simple yet powerful lever for intervention. Optimizing pain control through regional anesthesia not only improves maternal outcomes but also reduces the broader societal burden of opioid misuse. Future prospective studies should investigate real-world opioid consumption, patient satisfaction, and long-term pain trajectories to further refine best practices for perioperative care in obstetric populations.

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