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Short Report

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Persistent opioid use after cesarean delivery in the United States of America: a systematic review

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ABSTRACT

Background: This systematic review assessed the incidence of persistent opioid use after cesarean delivery in opioid-naïve individuals in the United States of America (USA).

Methods: A literature search identified articles that reported persistent opioid use after cesarean delivery between January 2000 and February 2022. Studies were manually reviewed, and data pertaining to rates of persistent postpartum opioid use and methodologic information were qualitatively analyzed. Sixty studies were identified, and four met inclusion criteria. All four studies were retrospective reviews of insurance claims data among individuals naïve to opioids. Data from 486 263 individuals delivering between 2001 and 2016 were included. The criteria to define persistent opioid use in opioid-naïve individuals generally involved two or more opioid prescriptions filled within the first year after cesarean delivery, with each definition including additional varying criteria.

Results: Rates of persistent opioid use after cesarean delivery ranged from 0.12% to 2.2%, with the highest rate reported in private insurance claims between 2008 and 2016. Findings suggest a substantial number of individuals are at risk (from 1:1000 to 1:50) for persistent opioid use up to 12 months postpartum. With 1.2 million individuals undergoing cesarean delivery annually in the USA, as few as 1440 and as many as 26 400 may continue using opioids past the fourth trimester.

Conclusions: Findings emphasize the importance of developing a standardized definition of persistent opioid use to accurately assess the risk, rate, and trends for persistent opioid use among opioid-naïve individuals undergoing cesarean delivery.

Introduction

The rate of persistent opioid use following cesarean delivery (CD) is unclear. Cesarean delivery is the most common inpatient surgical procedure, accounting for 31.9% of births in the United States of America (USA) and an average of 18.6% of births worldwide.¹⁻³ In the USA, oral opioids are commonly prescribed at hospital discharge⁴ and exposure to high doses of opioids after CD may be associated with persistent opioid use.^{5,6} Importantly, as few as five days of prescription opioid use can increase the probability of acute use converting into long-term use.⁷

In the absence of prospective studies, the rate of persistent opioid use following CD is estimated using retrospective data. To obtain an estimate of persistent opioid use after CD, this systematic review of the literature evaluated studies reporting the incidence of persistent opioid use in opioid-naïve individuals in the USA.

Methods

A systematic literature review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were identified using a search string (see Supplemental Material 1) to identify all articles available in the PubMed database with published reporting on persistent opioid use after CD in opioid-naïve patients in the USA between January 2000 and February 2022. The literature search was restricted to articles published in the English language.

Studies were manually assessed and were included if they had primary data, evaluated >10 patients, reported opioid use or a prescription for seven or more days, or were USA-based. The remaining studies were selected for manual review of data extraction. Reference lists of chosen studies were reviewed to identify any additional studies not identified with the search string. Included studies were manually reviewed to identify relevant details. No formal meta-analysis was conducted.

Bias was assessed using the tool for assessing the risk of bias developed by the Clinical Advances Through Research and Information Translation Group at McMaster University.⁸ This tool provides guidance and examples of low- and high-risk bias across eight aspects of research design to facilitate the assessment of bias in cohort studies.

Results

Study selection

Sixty studies were identified from PubMed; one additional study was identified from the references of an included study (Fig.1). Four studies met inclusion criteria for further evaluation (Table 1). Fifty-seven studies were excluded: seven had patient numbers <10 (including case studies), 17 were not primary data, 31 did not report persistent opioid use, one reported only patients who had vaginal delivery, and one reported data from outside the USA.

Study characteristics and synthesis of results

Included studies were three retrospective reviews of insurance claims data from two claims databases and one Tennessee Medicaid query. Analyzed data spanned 2001 to 2016 and comprised 486 263 individuals undergoing CD.^{6,9-11} All studies reported data that included opioid-naïve individuals. Although definitions of 'opioid-naïve' differed for all four studies, individuals were opioid-naïve if they had not taken any opioid for ≥ 6 months before delivery. Definitions and analytic approaches used to assess persistent opioid use varied, with criteria generally involving two or more opioid prescriptions filled within the first year after CD (Table 1). Across studies, rates of persistent opioid use after CD ranged from 0.12% to 2.2%.^{6,9-11}

Across studies, there was a generally low risk of bias⁸ because each study included patient data obtained from secure records (i.e. insurance claims records) and provided sufficient information for reproducibility of results. However, as claims data may not capture all sources of opioids, some risk of bias existed due to the inability to completely exclude persistent opioid use being present at baseline. Similarly, the inability to identify sources of opioids that are not captured in claims data may have impacted the ability to estimate persistent opioid use after CD.

Discussion

Main findings

This systematic review identifies differences in existing definitions of “persistent opioid use” used in the literature to characterize the extent of persistent use more comprehensively. Despite heterogeneity of definitions, our review suggests that a substantial number of individuals are at risk for persistent opioid use up to 12 months after CD (approximate ratios of 1:1000 to 1:50). The heterogeneity of definitions used to report persistent opioid use after surgery was previously assessed in a systematic literature review, in which 29 different definitions of persistent opioid use were found within 39 studies, therefore it is not surprising to have found different definitions of persistent opioid use in each of the four studies included in this systematic review.¹²

The lack of a standardized definition of, and varying criteria for, persistent opioid use make direct comparisons of reported rates challenging. The highest rate of persistent opioid use (2.2%) was based on a definition requiring ≥ 1 opioid prescription from postsurgical days 91 to 365; by contrast, the lowest rate (0.12%) reported was based on a definition of >10 prescriptions or a supply of >120 days.¹¹ Although this review was restricted to the USA, a study in Denmark reported a persistent opioid use rate of 0.16% in a subgroup of opioid-naïve individuals undergoing scheduled or pre-labor CD. This falls within the range observed in the current analysis.¹³

On the basis of the highest reported rate in this review,¹⁰ these data suggest that as few as 1440 and as many as 26 400 individuals from the 1.2 million undergoing CD each year² may have persistent opioid use past the fourth trimester (total range from studies, 1440¹¹ to 26 400¹⁰).

Limitations

The review’s conclusions are limited as a result of the small number of peer-reviewed studies that evaluate persistent opioid use in the obstetric population. All included studies were retrospective reviews of opioid prescriptions, limiting the ability to assess whether reported rates of opioid prescription accurately reflect actual rates of opioid use. Furthermore, these studies assessed data from commercial or private insurance claims, with only one study assessing Medicaid claims and this being limited to the state of Tennessee. Because opioid prescribing rates can vary based on private or public insurance coverage, and across different geographic regions of the USA, the generalizability of these findings is limited.^{14,15} Similarly, opioid-naïve patients were defined as those not filling a prescription for opioids within six months of CD. Because many insurance providers do not pay for opioid maintenance prescriptions,¹⁶ it is possible that some individuals classified as opioid-naïve had received opioid medications via other programs (e.g. medication-assisted treatment with methadone or buprenorphine).

Of note, three studies found that individuals with histories of pain¹⁰ or illicit substance use,^{6,10,11} conditions possibly associated with prior opioid use or maintenance treatment, were at risk for developing persistent opioid use. Additionally, one study including opioid-naïve patients permitted opioid prescriptions up to one week

prior to CD to account for a pre-operative prescription for postoperative pain. These patients, although otherwise opioid-naïve for the year before CD, were found to be at increased risk for developing persistent opioid use.¹⁰ Because peripartum opioid use appeared to be associated with persistent opioid use, inclusion of these patients in this analysis may have impacted the overall reported opioid persistence rates in this study. Further, although one study excluded patients with additional medical procedures in the year following discharge, it is not possible to determine from the remaining studies whether opioid prescriptions were written for other indications (such as a dental procedure or pain secondary to injury).¹⁰ Finally, the most recent data included in this systematic review were from 2008 to 2016,¹⁰ so it is possible that patterns of opioid prescription, refills, and persistent opioid use have changed since then, particularly in the setting of the COVID-19 pandemic which was initially associated with increased opioid prescription.¹⁷

All four studies reported persistent opioid use among opioid-naïve individuals;^{6,9-11} as such, the generalizability of these findings to the estimated 0.65% of pregnant individuals with opioid use disorder in the USA is uncertain.¹⁸ Studies evaluating current rates of persistent opioid use in obstetric patients when postoperative analgesia management is individualized and shared-decision making is used are needed.¹⁹

Conclusions and implications

This systematic review suggests thousands of individuals in the USA who are prescribed opioids after CD are at risk for developing persistent opioid use, however differences in estimates are likely driven by different criteria used to define persistent opioid use disorder. Inconsistencies in the literature highlight the need for a standard definition to accurately assess the risk, rate, and trends for persistent opioid use in individuals who have undergone CD. Such a definition may require consensus from several key stakeholders.¹² Because both effective pain management and judicious prescribing of opioids are key factors for obstetric patients, a standard definition of persistent postsurgical opioid use is crucial for epidemiologic studies. Understanding the rate of persistent opioid use can aid in defining prescribing practices and policies to help minimize the occurrence of unnecessary exposure to opioid harms and, consequently, the likelihood of developing persistent use beyond the fourth trimester.^{10,12}

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Declaration of interests

None.

References

1. Betran AP, Ye J, Moller AB, Zhang J, Gulmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. *PLoS One*. 2016;11:e0148343. 10.1371/journal.pone.0148343.
2. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK. Births: final data for 2018. *Natl Vital Stat Rep*. 2019;68:1–47.
3. Healthcare Cost and Utilization Project. Most common operations during inpatient stays. Available at: <https://www.hcup-us.ahrq.gov/faststats/NationalProceduresServlet>. Accessed November 12, 2020.
4. Badreldin N, Grobman WA, Chang KT, Yee LM. Opioid prescribing patterns among postpartum women. *Am J Obstet Gynecol*. 2018;219:103 e1–03 e8.
5. Bateman BT, Cole NM, Maeda A, et al. Patterns of opioid prescription and use after cesarean delivery. *Obstet Gynecol*. 2017;130:29–35. 0.1097/aog.0000000000002093.
6. Bateman BT, Franklin JM, Bykov K, et al. Persistent opioid use following cesarean delivery: patterns and predictors among opioid-naive women. *Am J Obstet Gynecol*. 2016;215:353.e1–e18.
7. Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use — United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66:265–69. 10.15585/mmwr.mm6610a1.
8. Methodological resources: tool to assess risk of bias in cohort studies. Available at: <https://www.evidencepartners.com/resources/methodological-resources/>. Accessed February 12, 2021.
9. Osmundson SS, Wiese AD, Min JY, et al. Delivery type, opioid prescribing, and the risk of persistent opioid use after delivery. *Am J Obstet Gynecol*. 2019;220:405–407. 10.1016/j.ajog.2018.10.026.
10. Peahl AF, Dalton VK, Montgomery JR, Lai YL, Hu HM, Waljee JF. Rates of new persistent opioid use after vaginal or cesarean birth among US women. *JAMA Netw Open*. 2019;2:e197863. 10.1001/jamanetworkopen.2019.7863.
11. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. *JAMA Intern Med*. 2016;176:1286–1293. 10.1001/jamainternmed.2016.3298.
12. Jivraj NK, Raghavji F, Bethell J, et al. Persistent postoperative opioid use: a systematic literature search of definitions and population-based cohort study. *Anesthesiology*. 2020;132:1528–1539. 10.1097/ALN.0000000000003265.

13. Thomsen BSV, Edwards HM, Clausen TD, et al. Incidence of persistent postpartum opioid use by mode of delivery: a 2016 cohort study of Danish women. *Int J Obstet Anesth.* 2022;50:103254. 10.1016/j.ijoa.2022.103254.
14. Centers for Disease Control and Prevention. U.S. opioid prescribing rate maps. Available at: <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html>. Accessed November 13, 2020.
15. Mikosz CA, Zhang K, Haegerich T, et al. Indication-specific opioid prescribing for US patients with Medicaid or private insurance, 2017. *JAMA Netw Open.* 2020;3:e204514. 10.1001/jamanetworkopen.2020.4514.
16. Abraham AJ, Andrews CM, Harris SJ, Friedman PD. Availability of medications for the treatment of alcohol and opioid use disorder in the USA. *Neurotherapeutics.* 2020;17:55–69.
17. Lee B, Yang K-C, Kaminski P, et al. Substitution of nonpharmacologic therapy with opioid prescribing for pain during the COVID-19 pandemic. *JAMA Netw Open.* 2021;4:e2138453. 10.1001/jamanetworkopen.2021.38453.
18. Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. Opioid use disorder documented at delivery hospitalization — United States, 1999–2014. *MMWR Morb Mortal Wkly Rep.* 2018;67:845–849. 10.15585/mmwr.mm6731a1.
19. Prabhu M, McQuaid-Hanson E, Hopp S, et al. A shared decision-making intervention to guide opioid prescribing after cesarean delivery. *Obstet Gynecol.* 2017;130:42–46. 10.1097/AOG.0000000000002094.

Figure legend**Fig.1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram

Figure1

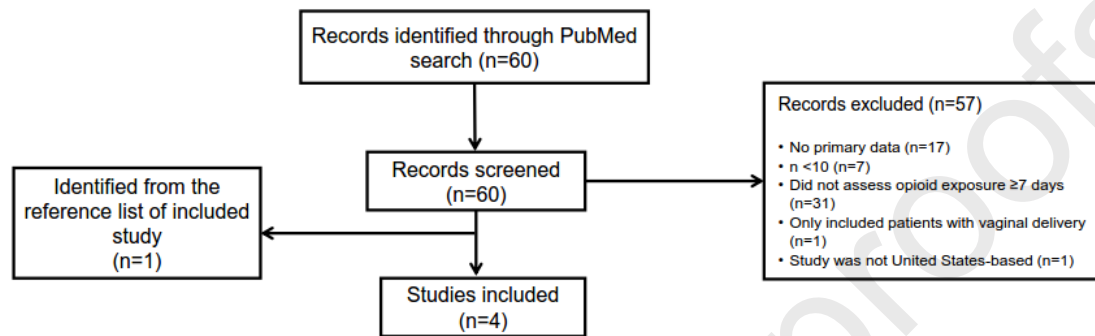
[Click here to access/download:Figure,D-22-00223Fig.1.pptx](#)

Table 1. Studies of persistent opioid use after cesarean delivery

Publication	Data source (years analyzed)	Cohort (n)	Definition of “opioid-naïve”	Definition	
				Definition of “persistent opioid use”	Prevalence (%)
Peahl et al ¹⁰	Private payer claims from Clinformatics Data Mart (2008-2016)	113 213	No opioid prescription filled ≤12 m prior to cesarean delivery	≥2 prescription claims - 1 claim 4 to 90 days after discharge - 1 claim 91-365 days after discharge	
Osmundson et al ⁹	Filled prescriptions through Tennessee Medicaid ^a (2007-2015)	91 261	Opioid-naïve for six or more months prior to cesarean delivery	≥7 prescription claims - One filled prescription in ~45 days intervals during postpartum days 43-365	
Bateman et al ⁶	Commercial claims from Clinformatics Data Mart (2003-2011)	80 127	No opioid prescription filled ≤12 months prior to cesarean delivery or diagnosis of opioid dependence or abuse	Trajectory model grouping patients with similar patterns of prescription filling - Analyzed filled prescriptions during 12 consecutive 30-day periods to define five distinct groups Group with the highest probability of filling prescription over first postpartum year was considered to have persistent use	0.3%
Sun et al ¹¹	Administrative private insurance health claims from MarketScan (2001-2013)	201 662	No opioid prescription filled ≤12 months prior to cesarean delivery	Either a prescription or supply quantity during postsurgical days 91-365 - ≥10 prescriptions - or supply of >120 days	0.1%

CD: cesarean delivery; CI: confidence interval. ^a Estimate based on reported rate of persistent opioid use assuming an estimated 1 million CDs per year.⁵ ^b CI not reported.

SUPPLEMENTAL MATERIAL 1. Search string.

(((((long-term[Title/Abstract] OR longitudinal[Title/Abstract] OR prolonged[Title/Abstract] OR chronic[Title/Abstract] OR persistent[Title/Abstract] OR recurrent[Title/Abstract]) AND (((surg*[Title/Abstract] OR postsurg*[Title/Abstract] OR postoperat*[Title/Abstract] OR operat*[Title/Abstract] OR after surg* [Title/Abstract] OR following surg*[Title/Abstract]))) AND (((opioid*[Title/Abstract] OR opiate* [Title/Abstract] OR narcotic*[Title/Abstract]) AND (abuse[Title/Abstract] OR misuse[Title/Abstract] OR prescri*[Title/Abstract] OR use[Title/Abstract] OR usage[Title/Abstract]))) OR (chronic opioid after surgery[Title/Abstract] OR persistent opioid after surgery[Title/Abstract]))) AND ("2000"[Date - Publication] : "3000"[Date - Publication]) AND english[Language] AND (Cesarean OR cesarean OR C-section OR "Cesarean Section"[MESH])

Highlights

- This review evaluated persistent opioid use after cesarean delivery (POUCD)
- POUCD assessed in opioid-naïve individuals up to one year post-cesarean delivery
- POUCD rate was reported in four studies conducted in the United States
- POUCD rates ranged from 0.12%–2.2% and may affect up to 26 400 individuals annually
- Criteria for POUCD varied, emphasizing the need for a standard definition