


# Effect of a stepwise opioid-sparing analgesic protocol on in-hospital oxycodone use and discharge prescription after cesarean delivery

Ruth Landau,<sup>1</sup> Erik Romanelli,<sup>2</sup> Bahaa Daoud,<sup>1</sup> Ben Shatil,<sup>3</sup> Xiwen Zheng,<sup>1</sup> Beatrice Corradini,<sup>1</sup> Janice Aubey,<sup>1</sup> Caroline Wu,<sup>1</sup> Catherine Ha,<sup>1</sup> Jean Guglielminotti <sup>1</sup>

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/rapm-2020-102007>).

<sup>1</sup>Anesthesiology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York, USA

<sup>2</sup>Anesthesiology, Montefiore Medical Center, Bronx, New York, USA

<sup>3</sup>Anesthesiology, Emory University, Atlanta, Georgia, USA

## Correspondence to

Dr Jean Guglielminotti, Anesthesiology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York, USA; [jg3481@cumc.columbia.edu](mailto:jg3481@cumc.columbia.edu)

Received 7 August 2020

Revised 18 September 2020

Accepted 8 October 2020

Published Online First

10 November 2020

## ABSTRACT

**Introduction** Opioid exposure during hospitalization for cesarean delivery increases the risk of new persistent opioid use. We studied the effectiveness of stepwise multimodal opioid-sparing analgesia in reducing oxycodone use during cesarean delivery hospitalization and prescriptions at discharge.

**Methods** This retrospective cohort study analyzed electronic health records of consecutive cesarean delivery cases in four academic hospitals in a large metropolitan area, before and after implementation of a stepwise multimodal opioid-sparing analgesic computerized order set coupled with provider education. The primary outcome was the proportion of women not using any oxycodone during in-hospital stay ('non-oxycodone user'). In-hospital secondary outcomes were: (1) total in-hospital oxycodone dose among users, and (2) time to first oxycodone pill. Discharge secondary outcomes were: (1) proportion of oxycodone-free discharge prescription, and (2) number of oxycodone pills prescribed.

**Results** The intervention was associated with a significant increase in the proportion of non-oxycodone users from 15% to 32% (17% difference; 95% CI 10 to 25), a decrease in total in-hospital oxycodone dose among users, and no change in the time to first oxycodone dose. The adjusted OR for being a non-oxycodone user associated with the intervention was 2.67 (95% CI 2.12 to 3.50). With the intervention, the proportion of oxycodone-free discharge prescription increased from 4.4% to 8.5% (4.1% difference; 95% CI 2.5 to 5.6) and the number of prescribed oxycodone pills decreased from 30 to 18 (–12 pills difference; 95% CI –11 to –13).

**Conclusions** Multimodal stepwise analgesia after cesarean delivery increases the proportion of oxycodone-free women during in-hospital stay and at discharge.

## INTRODUCTION

Opioid use and abuse during pregnancy and the post partum has increased fivefold in the USA between 1999 and 2014.<sup>1,2</sup> Meanwhile, pregnancy-associated mortality involving opioids has more than tripled from 1.3 per 100 000 in 2007 to 4.2 in 2016.<sup>3</sup> From a public health perspective, it is particularly alarming since childbirth is the most common indication for hospitalization nationwide with about 4 million annual births, and cesarean

delivery being the most performed inpatient procedure with about 1.3 million annual cases.<sup>4</sup>

Opioid exposure during in-hospital stay after cesarean delivery may contribute to the observed increase in opioid use and opioid-related deaths. The incidence of persistent opioid use among opioid-naïve women after a hospitalization for cesarean delivery varies but can be as high as 2.2% (1 per 50),<sup>5–8</sup> and that of an opioid overdose 0.9 per 100 000.<sup>9</sup> The likelihood for new persistent opioid use increases with each additional day of opioid medication supplied as of the third day,<sup>10,11</sup> which underscores that persistent opioid use can be triggered by the initial postpartum opioid exposure. The American College of Obstetricians and Gynecologists (ACOG) therefore recommended in 2018 to limit the 'duration of use of opiate prescriptions (after childbirth) to the shortest reasonable course expected for treating acute pain'.<sup>12</sup>

Multimodal stepwise protocols are currently recommended for in-hospital and postdischarge analgesia after cesarean delivery; they should include intraoperative neuraxial opioids given at the time of anesthesia, scheduled postoperative non-opioid medications, and rescue postoperative systemic opioids.<sup>12</sup> Discharge opioid prescription should also take into account intrahospital opioid consumption.<sup>13</sup> However, the three premises that non-opioid analgesic medications should be administered in a scheduled manner regardless of the pain score intensity, that opioids should be offered only if and when the patient experiences severe breakthrough pain, and that discharge prescription should be individualized based on in-hospital opioid use are not universally adopted.<sup>14</sup> Non-stepwise protocols have resulted in patients receiving opioids without having the opportunity to have their pain managed with non-opioid analgesics. It has become more and more apparent that some women may not even need any systemic opioids post partum,<sup>15</sup> or that split doses will reduce overall opioid consumption.<sup>16</sup> Furthermore, two recent studies report a decreased in-hospital opioid use after the implementation of multimodal stepwise analgesic prescriptions for postpartum pain but did not include a control group and did not examine discharge prescription.<sup>17,18</sup>

We conducted this study to test the hypotheses that a stepwise multimodal opioid-sparing analgesic computerized order set coupled with provider



© American Society of Regional Anesthesia & Pain Medicine 2021. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Landau R, Romanelli E, Daoud B, et al. *Reg Anesth Pain Med* 2021;**46**:151–156.

education is associated with significantly decreased oxycodone use during cesarean delivery hospitalization and significantly decreased oxycodone prescriptions at discharge.

## METHODS

The Strengthening the Reporting of Observational Studies in Epidemiology and the Reporting of Studies Conducted Using Observational Routinely Collected Health Data statements were followed.

The stepwise multimodal opioid-sparing analgesic computerized order set was implemented in medical center A (hereafter referred to as intervention hospitals) but not in medical center B (control hospitals).

## Participating hospitals

Four hospitals from two distinct healthcare systems (A and B) located in the same major metropolitan area contributed data in this study. A has two labor and delivery units: one in hospital 1, an academic center (5000 annual deliveries and 35% cesarean delivery rate), and one in hospital 2, a community-based hospital (2200 annual deliveries and 25% cesarean delivery rate). B has two labor and delivery units: one in hospital 3 (2200 annual deliveries and 32% cesarean delivery rate) and one in hospital 4 (4800 annual deliveries and 36% cesarean delivery rate). A is the first birth center in the area for the annual number of births. B was chosen for its geographic proximity and relative overlapping catchment populations to provide a control cohort, and as the third birth center in the area.

## Intervention

The intervention was implemented in hospitals 1 and 2 of the medical center A in two stages (online supplemental appendix 1). First, between April and October 2017 obstetric and anesthesia providers (nurses, nurse practitioners, physician assistants, residents, fellows, and physician attendings) were educated about pain after cesarean delivery, stepwise multimodal opioid-sparing analgesia, judicious in-hospital and discharge opioid prescribing in the setting of the opioid crisis, and the new in-hospital order

sets were presented. Information was presented during Obstetrics and Gynecology Departmental Grand Rounds in April 2017 and 12 presentations on the labor and delivery unit. All nursing staff attended 1 of 12 in-person presentations with a mandatory and flagged presence. Second, in November 2017, the new computerized order set with stepwise opioid-sparing analgesia after cesarean delivery was implemented in the recovery and postpartum units.

There was no specific patient information beyond the usual information provided by the care team; postcesarean delivery women are educated about analgesic options in the postanesthesia recovery unit (PACU) and the postpartum unit, which include non-opioid (acetaminophen and ibuprofen) and opioid (oxycodone) medications. Additional discharge information about recovery and pain management was provided by nurse practitioners.

## Analgesic order set after cesarean delivery in intervention hospitals 1 and 2 (medical center A)

The computerized order sets before and after the intervention are presented in figure 1. The four major changes in the new order set were that (1) the two non-opioid pain medications (acetaminophen and ibuprofen) were given every 6 hours (unless contraindicated) irrespective of pain score intensity, (2) for mild pain, additional ibuprofen was available before escalating to an opioid, (3) oxycodone 5 mg was available for moderate to severe pain, with a maximum daily dose of 30 mg, based on the 2018 ACOG recommendations,<sup>12</sup> which could be over-ridden if deemed indicated, and (4) all analgesic medications were prescribed by the obstetric anesthesia team until discharge. The obstetric anesthesia team evaluated each patient on postoperative day 1 and was called to reassess women reporting moderate or severe pain after having already received 20 mg of oxycodone in the last 24 hours.

## Adherence to the protocol in intervention hospitals 1 and 2 (medical center A)

All medications given by a nurse to a patient are scanned (bar code) and reported in the electronic medical record. Therefore, all analgesic medications taken in the recovery room and on the

Computerized Order Sets for Post-Cesarean Pain Management		
Intervention Hospitals		Control Hospitals
Before Intervention Multimodal analgesia	After Intervention Stepwise opioid-sparing multimodal analgesia	Before and after intervention Multimodal analgesia
For planned cesarean deliveries, obstetric admission orders did not include preoperative PO acetaminophen	For planned cesarean deliveries, obstetric admission orders included: preoperative PO acetaminophen 975mg	For planned cesarean deliveries, obstetric admission orders did not include preoperative PO acetaminophen
For the first 16 postoperative hours, all pain medications were prescribed by the Obstetric Anesthesia team and then by the Obstetric team afterwards as follows:	Until hospital discharge (typically 72 hours), all pain medication were prescribed by the OB Anesthesiology team as follows:	Until hospital discharge, all pain medication were prescribed by the Obstetric team as follows:
<ul style="list-style-type: none"> <li>▪ IV ketorolac 30mg, per need 3-4 doses in the first 24 hours, then PO ibuprofen 600mg every 4-6 hours per need</li> <li>▪ For breakthrough pain (every 4 hours per need):               <ul style="list-style-type: none"> <li>- If pain score 1-3: PO acetaminophen 650mg</li> <li>- If pain score 4-6: oxycodone 5mg</li> <li>- If pain score 7-10: oxycodone 10mg</li> </ul> </li> <li>▪ No limit for daily oxycodone dose.</li> </ul>	<ul style="list-style-type: none"> <li>▪ Scheduled every 6 hours to be taken together: PO ibuprofen 600mg + PO acetaminophen 975mg</li> <li>▪ For breakthrough pain:               <ul style="list-style-type: none"> <li>- If pain score 1-3: PO ibuprofen 200mg (up to 2 tablets)</li> <li>- If pain score 4-6: oxycodone 5mg every 4 hours per need</li> <li>- If pain score 7-10: oxycodone 5mg every 3 hours per need</li> </ul> </li> <li>▪ Daily oxycodone dose limited to 30mg (unless ordered otherwise by the Obstetric Anesthesia team)</li> </ul>	<ul style="list-style-type: none"> <li>▪ IV ketorolac 30mg IV, per need 3-4 doses in the first 24 hours</li> <li>▪ For breakthrough pain, every 4-6 hours, per need:               <ul style="list-style-type: none"> <li>- If mild to moderate pain: ibuprofen 600mg</li> <li>- If moderate pain: acetaminophen 650mg</li> <li>- If moderate to severe pain: oxycodone 5mg (or Percocet 5-325) 1-2 tablets</li> </ul> </li> <li>▪ No limit for daily oxycodone dose.</li> </ul>

**Figure 1** Computerized order sets for postcesarean pain management. IV, intravenous; PO, per os (oral).

postpartum unit are recorded. Adherence to the protocol was determined by evaluating the intake of acetaminophen, since it is extremely rare for patients to have a contraindication to acetaminophen after cesarean delivery. Non-adherence to the new order set was defined if the patient did not take any acetaminophen in the first 24 hours while taking oxycodone pills.

#### Opioid prescription at discharge in intervention hospitals 1 and 2 (medical center A)

All prescribers received education on judicious opioid prescription after cesarean delivery, and that prescriptions of 40–60 pills had been shown to result in approximately 50% left-over unused pills.<sup>19</sup> The education covered the potential impact of left-over opioid pills which include persistent use, misuse and diversion. The amount of prescribed opioid pills was left to the discretion of the prescriber.

#### Analgesic order set after cesarean delivery in control hospitals 3 and 4 (medical center B)

The computerized order set in control hospitals is shown in [figure 1](#). Major differences with new order set in intervention hospitals were (1) the absence of standing orders for non-opioid analgesics, (2) absence of a daily oxycodone dose limit, and (3) all analgesic medications beyond the PACU were prescribed by the obstetric providers.

#### Anesthesia for cesarean delivery

In the four participating hospitals, before and after the intervention, all women undergoing cesarean delivery with neuraxial anesthesia received neuraxial morphine (spinal dose 150–200 mcg or epidural dose 3 mg) as part of their anesthetic, and intravenous ketorolac 30 mg at the end of the case, unless contraindicated. Women with general anesthesia typically received intraoperative intravenous opioids (fentanyl, morphine or hydromorphone). In addition to the usual order set, a minority of women received a truncal regional block (transversus abdominis plane block), and/or hydromorphone intravenous patient-controlled analgesia for 24–48 hours.<sup>20</sup>

#### Outcomes

The primary outcome was binary and related to whether oxycodone was used or not during in-hospital stay (ie, non-oxycodone user). The in-hospital secondary outcomes were: (1) time to first oxycodone pill since delivery (in hours), and (2) total in-hospital oxycodone dose (in milligrams). The discharge secondary outcomes were: (1) the proportion of oxycodone-free discharge prescriptions, and (2) the number of oxycodone pills prescribed at discharge.

The information on in-hospital oxycodone use was abstracted from the electronic medical record. Every oxycodone pill is scanned (bar code) when given to the patient, and nurses are present when patients take the oxycodone pill(s). Therefore, the electronic medical record provides reliable and accurate information about oxycodone use during delivery hospitalizations. The information on discharge prescription was abstracted from the institutional opioid prescription dashboard. This information was available in intervention hospitals 1 and 2 but not in control hospitals 3 and 4.

#### Study samples and study periods

The study sample included all women undergoing scheduled or not scheduled cesarean delivery in the four hospitals, with neuraxial or general anesthesia, before and after the intervention.

No exclusion criteria were applied. The two study periods (before and after the intervention) are described in online supplemental appendices 1 and 2.

#### Patient and cesarean delivery characteristics

The following patient characteristics were abstracted from the electronic health record: maternal age, race (categorized as non-Hispanic White vs other), body mass index at term (expressed in kilogram per square meter), parity, gestational age (expressed in weeks of amenorrhea), and diagnosis of pre-eclampsia during the current pregnancy. The following cesarean delivery characteristics were also abstracted: previous cesarean delivery, planned cesarean delivery, cesarean delivery performed during night shift (defined as between 17:01 and 07:59), associated tubal ligation, and type of anesthesia (categorized as general vs other types).

#### Statistical analysis

Statistical analysis was performed with R V.3.4.1 (R Foundation for Statistical Computing, Vienna, Austria). Results are expressed as median (IQR), mean (1 SD), or count (%). Two independent analyses were performed: one for cesarean deliveries performed in intervention hospitals and one for cesarean deliveries performed in control hospitals.

Univariate comparisons of women characteristics and of the outcomes between the two time periods (before and after the intervention) used  $\chi^2$  test for categorical variables and Wilcoxon rank-sum test for continuous variables. The 95% CI for the difference in the outcomes examined between the two time periods was calculated using bootstrap with replacement ( $B=2000$ ) and the percentile method. Subgroup analysis was also performed in the two intervention hospitals (hospital 1 and hospital 2) and according to the anesthesia mode (general anesthesia or neuraxial anesthesia).

The effect of the intervention on the primary outcome (proportion of non-oxycodone users) was further assessed with the OR from a logistic regression model. In this model, the dependent variable was oxycodone status (user or non-user) and the independent variable was the two periods (before or after intervention). The model was further adjusted for the following seven variables with a  $p$  value  $<0.20$  in the univariate comparison before and after the intervention, along with the hospital identifier: non-White race, body mass index, parity, gestational age, primary cesarean delivery, planned cesarean delivery, and shift (night vs day). Missing values for variables used for adjustment used multiple imputations.

#### A priori effect size calculation

We expected to include at least 500 and 2000 cesarean delivery cases in the intervention hospitals before and after the intervention, respectively. With a prevalence of 10% non-oxycodone users before the intervention, an alpha of 5%, a power of 90%, and a two-sided test, we would be able to demonstrate a 50% or greater relative increase in the proportion of non-oxycodone users (15% or greater) after the intervention.

#### RESULTS

In intervention hospitals, 2983 cesarean deliveries were performed and analyzed, including 2255 after the intervention (75.6%) (online supplemental appendix 2). In control hospitals, 470 cesarean deliveries were performed and analyzed, including 224 in 2018 (47.6%).

In intervention hospitals, statistically significant changes were observed in patient characteristics after the intervention

**Table 1** Comparison of patient and cesarean delivery characteristics before and after the intervention

	Intervention hospitals			P value*†	Control hospitals			P value*†
	Missing, n	Before	After		Missing, n	Before	After	
Sample size, n		728	2255			246	224	
Patient								
Median (IQR) age (years)	0	32 (27–36)	32 (27–36)	0.65	0	30 (26–35)	30 (26–35)	0.92
Non-White race including Hispanics, n (%)	746	421 (74.8)	889 (53.1)	<0.01	76	198 (95.2)	173 (93.0)	0.48
Median (IQR) BMI (kg/m <sup>2</sup> )	16	31.2 (27.7–35.3)	31.6 (28.2–35.7)	0.10	0	33.4 (29.1–37.7)	32.8 (29.3–37.7)	>0.99
Parity ≥1, n (%)	1	379 (52.1)	1313 (58.2)	<0.01	0	142 (57.7)	133 (59.4)	0.79
Median (IQR) gestational age in weeks of amenorrhea	5	39 (37–39)	39 (37–40)	<0.01	0	39 (38–39)	39 (38–40)	0.30
Pre-eclampsia, n (%)	2	71 (9.8)	212 (9.4)	0.82	0	36 (14.6)	21 (9.4)	0.11
Cesarean delivery								
Primary CD, n (%)	0	436 (59.9)	1221 (54.1)	<0.01	0	140 (56.9)	111 (49.6)	0.13
Planned CD, n (%)	0	389 (53.4)	956 (42.4)	<0.01	0	133 (54.1)	133 (59.4)	0.19
Night-time (17:01 to 07:59), n (%)	25	318 (43.7)	906 (40.6)	0.16	0	91 (37.0)	91 (40.6)	0.48
Bilateral tubal ligation, n (%)	1	94 (12.9)	255 (11.3)	<0.01	0	25 (10.2)	27 (12.1)	0.61
General anesthesia, n (%)	0	30 (4.1)	85 (3.8)	<0.01	0	7 (2.8)	6 (2.7)	>0.99

\*P value compares before and after the implementation of the new order set.

†Univariate comparisons used  $\chi^2$  test for categorical variables and Wilcoxon rank-sum test for continuous variables. BMI, body mass index; CD, cesarean delivery.

including a decrease in the proportion of racial and ethnic minority women, an increase in the proportion of multiparous women, and an increase in gestational age (table 1). Statistically significant changes were also observed in cesarean delivery characteristics with a decrease in the proportion of both primary and planned cesarean deliveries. No change was observed in the control hospitals between the two study periods.

### Primary outcome

In intervention hospitals, the proportion of non-oxycodone users increased after the intervention (from 15.5% to 32.7%; <0.001), yielding a 17.2% difference (95% CI 9.7% to 25%) (table 2). The difference was greater in hospital 1 (20.3%; 95% CI 17.4% to 23.1%), the academic hospital, than in hospital 2 (8.7%; 95% CI 2.6% to 14.4%), the community hospital. The adherence to the new order set after its implementation was 71.3%, with no difference between hospital 1 and hospital 2 (72.1% vs 69.5%, respectively;  $p=0.219$ ). After adjustment for patient and cesarean delivery characteristics, the OR of being a non-oxycodone user associated with the intervention was 2.67 (95% CI 2.12 to 3.50) (figure 2); for cesarean deliveries under neuraxial anesthesia, the adjusted OR was 2.61 (95% CI 2.08 to 3.30), and for cesarean deliveries under general anesthesia 4.91 (95% CI 1.01 to 23.79). In control hospitals, there was no change in the proportion of non-oxycodone users between the two study periods.

### In-hospital secondary outcomes

In intervention hospitals, there was a significant decrease in total mean in-hospital oxycodone dose among users but not of the time to first oxycodone dose (table 2). No change was observed in control hospitals.

### Discharge secondary outcomes

In intervention hospitals, there was an increase in oxycodone-free discharge prescriptions and a significant decrease in the number of oxycodone pills prescribed at discharge (table 2).

## DISCUSSION

The major findings of our study are that implementation of a stepwise opioid-sparing analgesic computerized order set for cesarean delivery coupled with provider education resulted in a twofold increase in the proportion of women not using oxycodone during hospital stay (from 15.5% to 32.7%), and a twofold reduction in the mean oxycodone dose among women using opioids (from 59 to 25 mg). Furthermore, the number of oxycodone pills prescribed at discharge decreased almost twofold (from 32 to 18 pills). These findings were consistent across the two intervention hospitals and across anesthesia type.

### In-hospital opioid use

Recent data show that up to 54% of women after cesarean delivery do not use any systemic opioids,<sup>15</sup> highlighting that postoperative analgesic protocols should be tailored to individual opioid use. One study even reported that pain scores were higher among women who were prescribed opioids compared with those among women prescribed ibuprofen and acetaminophen.<sup>21</sup> Such findings are particularly important since non-opioids are usually perceived to be weaker analgesics than opioids and relatively ineffective in the setting of moderate to severe pain.

Stepwise pain management entails taking scheduled acetaminophen combined with non-steroidal anti-inflammatory drugs, usually every 6 hours, with opioids to be taken only if breakthrough pain. In clinical practice, the nurse will record pain intensity evaluated by the patient using a numerical scale, ranging from 0 (no pain) to 10 (worst pain imaginable), and give an opioid pill if pain intensity is greater than 7. In a small cohort study, separating acetaminophen from opioids and limiting the use of opioids for breakthrough pain achieved a significant reduction in in-hospital opioid use,<sup>17</sup> confirming a previous study that had implemented the same approach.<sup>22</sup> In a larger study, a power plan included new methods of pain assessment as well as standardized order sets, resulting in a 30% reduction in in-hospital opioid use after both vaginal and cesarean deliveries.

**Table 2** Comparison of the primary and secondary outcomes before and after the intervention

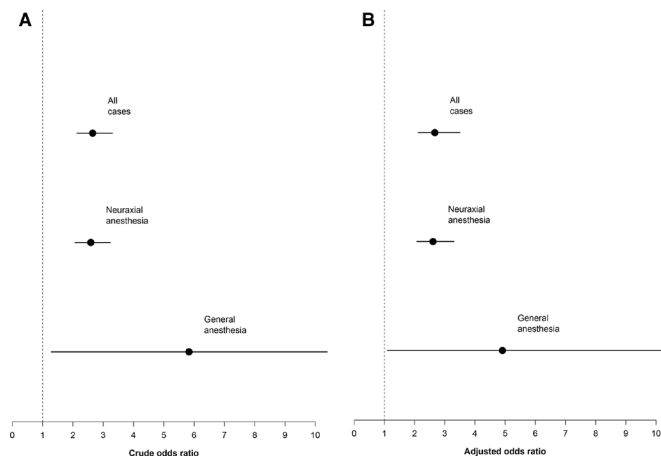
	Intervention hospitals				Control hospitals			
	Before	After	P value*†	Difference (95% CI)	Before	After	P value*†	Difference (95% CI)
<b>In-hospital primary and secondary outcomes</b>								
Sample size, n	728	2255			246	224		
Missing values, n	0	0			0	0		
Non-oxycodone user, n (%)	113 (15.5)	738 (32.7)	<0.01	17.2% (9.7% to 25%)	9 (3.7)	10 (4.5)	0.83	1.8% (−2.2% to 3.8%)
Hospital 1	48/520 (9.2)	458/1553 (29.5)	<0.01	20.3% (17.4% to 23.0%)	–	–	–	–
Hospital 2	65/208 (31.2)	280/702 (39.9)	0.03	8.7% (2.3% to 14.6%)	–	–	–	–
Median (IQR) total oxycodone dose (mg)	45 (20–80)	20 (10–35)	<0.01	–	70 (45–100)	70 (45–100)	0.96	–
Mean dose (mg)	58.6	25.3	–	−33.3 mg (−29.9 to −37.0)	73.8	74.4	–	0.6 mg (−5.5 to 6.8)
Median (IQR) time to first oxycodone dose (hour)	18.7 (5.2–28.8)	19.9 (6.8–30.1)	0.06	–	14 (7–20)	12 (5–20)	0.05	–
Mean time (hour)	20.2	22.4	–	2.2 hours (0.0 to 3.5)	15.6	14.4	–	1.2 hours (−2.9 to 0.4)
<b>Discharge secondary outcomes</b>								
Sample size, n	702	2214						
Missing values, n	26	41						
Oxycodone-free prescription, n (%)	31 (4.4)	188 (8.5)	<0.01	4.1% (2.5% to 5.6%)				
Median (IQR) number of oxycodone pills prescribed	32 (24–40)	18 (16–20)	<0.01					
Mean number of pills	30	18		−12 pills (−11 to −13)				

\*P value compares before and after the implementation of the new order set.

†Univariate comparisons used  $\chi^2$  test for categorical variables and Wilcoxon rank-sum test for continuous variables.

However, women were less likely to reach acceptable pain levels post partum, and discharge opioids were not evaluated.<sup>18</sup> Beyond reducing maternal exposure to opioids and possibly persistent opioid use, reducing in-hospital and persistent opioid use will

also decrease newborn opioid exposure related to breast feeding, which has been associated with neonatal sedation, respiratory depression and opioid overdose fatalities.<sup>23</sup>



**Figure 2** OR for the risk of being non-oxycodone user associated with the new order set, overall and according to anesthesia mode. (A) Crude OR. (B) Adjusted OR. Adjustment used the following seven variables with a p value  $\leq 0.20$  in the univariate analysis, along with the hospital identifier: non-White race, body mass index, parity, gestational age, primary cesarean delivery, planned cesarean delivery, and shift (night vs day).

### Discharge opioid prescription

Unnecessarily high opioid prescription after childbirth is frequent and may lead to the introduction of unused opioids in households, and increases the likelihood of persistent opioid use, abuse, misuse and accidental ingestion. The median number of dispensed opioid pills after cesarean delivery was reported to be in the order of 40 with 15 left-over pills in 2016, yielding an estimate of approximately 20 million opioid tablets introduced into communities from left-over medication in the USA.<sup>19</sup> In the current study, we observed a modest 4% increase in the proportion of oxycodone-free discharge prescriptions. Our intervention was primarily targeted to reduce in-hospital oxycodone use and while judicious opioid prescription was explained and described during all educational sessions, we did not provide specific guidance on how to tailor the discharge prescriptions to patients' in-hospital oxycodone use. Furthermore, we did not provide individualized patient education during hospitalization nor at discharge. However, there was a marked decrease in the number of oxycodone pills prescribed from 30 to 18. The mean 12 pills reduction per discharge prescription would lead to 15.6 million opioid tablets not introduced into communities. We acknowledge that we did not analyze patient oxycodone use after discharge or new prescriptions filled after discharge.

## Limitations

Our findings should be interpreted in the context of several limitations. First, we compared the proportion of non-oxycodone users before and after the intervention and adjusted for the changes in patients and hospital characteristics between the two study periods. With only two participating healthcare systems, it is not possible to use the difference-in-differences approach that would have compared the changes in the proportion of non-users in a group of intervention hospitals to the changes in a group of control hospitals.<sup>24</sup> To address this limitation, we included two control hospitals since it was thought that the abundant coverage on the opioid crisis in the lay and medical press in 2017 could in itself induce a change in opioid use and prescriptions or spillover effect. Second, our intervention did not target oxycodone prescriptions at discharge, and as such, the proportion of women who did not use oxycodone (in the order of 30%) but were nonetheless sent home with an oxycodone prescription remained high (in the order of 90%). Third, the adherence to the new order set was in the order of 70% in both intervention hospitals despite robust provider education, which suggests that in order to improve patient-reported outcomes, individualized patient education is also required. Fourth, we did not follow-up women after discharge and cannot establish whether reduced in-hospital oxycodone exposure and reduced pills prescribed at discharge lead to a reduction in persistent opioid use. Last, given the retrospective nature of our study, we did not gather information on patients' self-reported outcomes such as satisfaction with pain management and pain outcomes. Striking the right balance to avoid insufficient opioid prescriptions and patient dissatisfaction may be an unintended consequence of opioid-sparing approaches. This should be viewed as an incentive for further research focusing on patient-reported outcomes.

## CONCLUSION

Implementation of a multimodal stepwise analgesic regimen after cesarean delivery was associated with a significant increase in oxycodone-free women during in-hospital stay and at discharge. This simple and low-cost intervention could be generalized to prevent introduction of unused opioids in households and development of persistent opioid use.

**Twitter** Ben Shatil @drbenshatil

**Contributors** RL had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: RL, ER, JG. Acquisition and statistical analysis: RL, ER, BD, BS, XW, BC, CH, CW, JG. Interpretation of data: RL, JG. Drafting of the manuscript: RL, JG. Critical revision of the manuscript for important intellectual content: JA. Administrative, technical, or material support: BC. Study supervision: RL

**Funding** Support for this study was provided solely from institutional and/or departmental sources.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** This study was approved by the Institutional Review Boards of Columbia University Irving Medical Center (New York, NY, USA) and of Montefiore Medical Center (New York, NY, USA) as part of quality assurance programs using analysis of computerized medical records. Waiver for informed consent was obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request.

## ORCID iD

Jean Guglielminotti <http://orcid.org/0000-0002-8699-0724>

## REFERENCES

- Maeda A, Bateman BT, Clancy CR, et al. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. *Anesthesiology* 2014;121:1158–65.
- Haight SC, Ko JY, Tong VT, et al. Opioid Use Disorder Documented at Delivery Hospitalization - United States, 1999-2014. *MMWR Morb Mortal Wkly Rep* 2018;67:845–9.
- Gemmill A, Kiang MV, Alexander MJ. Trends in pregnancy-associated mortality involving opioids in the United States, 2007-2016. *Am J Obstet Gynecol* 2019;220:115–6.
- Martin JA, Hamilton BE, Osterman MJK, et al. Births: final data for 2018. *Natl Vital Stat Rep* 2019;68:1–47.
- Bateman BT, Franklin JM, Bykov K, et al. Persistent opioid use following cesarean delivery: patterns and predictors among opioid-naïve women. *Am J Obstet Gynecol* 2016;215:353.e1–353.e18.
- Sun EC, Darnall BD, Baker LC, et al. Incidence of and risk factors for chronic opioid use among opioid-naïve patients in the postoperative period. *JAMA Intern Med* 2016;176:1286–93.
- 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;220:405–7.
- Peahl AF, Dalton VK, Montgomery JR, et al. Rates of new persistent opioid use after vaginal or cesarean birth among US women. *JAMA Netw Open* 2019;2:e197863.
- Ladha KS, Gagne JJ, Patorno E, et al. Opioid overdose after surgical discharge. *JAMA* 2018;320:502–4.
- 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;66:265–9.
- Mosher HJ, Hofmeyer BA, Hadlandsmyth K, et al. Predictors of long-term opioid use after opioid initiation at discharge from medical and surgical hospitalizations. *J Hosp Med* 2018;13:243–8.
- ACOG. ACOG Committee opinion no. 742: postpartum pain management. *Obstet Gynecol* 2018;132:e35–43.
- Prabhu M, Dubois H, James K, et al. Implementation of a quality improvement initiative to decrease opioid prescribing after cesarean delivery. *Obstet Gynecol* 2018;132:631–6.
- Neuman MD, Bateman BT, Wunsch H. Inappropriate opioid prescription after surgery. *Lancet* 2019;393:1547–57.
- Holland E, Bateman BT, Cole N, et al. Evaluation of a quality improvement intervention that eliminated routine use of opioids after cesarean delivery. *Obstet Gynecol* 2019;133:91–7.
- Nanji JA, Guo N, Riley ET, et al. Evaluation of opioid use with split doses of oral opioids in a postcesarean delivery analgesia order set. *Obstet Gynecol* 2019;134:120–7.
- Smith AM, Young P, Blosser CC, et al. Multimodal stepwise approach to reducing in-hospital opioid use after cesarean delivery: a quality improvement initiative. *Obstet Gynecol* 2019;133:700–6.
- Rogers RG, Nix M, Chipman Z, et al. Decreasing opioid use postpartum: a quality improvement initiative. *Obstet Gynecol* 2019;134:932–40.
- Bateman BT, Cole NM, Maeda A, et al. Patterns of opioid prescription and use after cesarean delivery. *Obstet Gynecol* 2017;130:29–35.
- Shatil B, Zheng X, Daoud B, et al. A case-series describing analgesic approaches in women receiving general anesthesia for cesarean delivery. 51st Annual Meeting of the Society for Obstetric Anesthesia and Perinatology (SOAP); May 1-5, Phoenix (AZ), 2019.
- Dinis J, Soto E, Chauhan SP, et al. 42: non-opioid versus opioid analgesia after hospital discharge from a cesarean delivery: a randomized clinical trial. *Am J Obstet Gynecol* 2019;220:S34.
- Valentine AR, Carvalho B, Lazo TA, et al. Scheduled acetaminophen with as-needed opioids compared to as-needed acetaminophen plus opioids for post-cesarean pain management. *Int J Obstet Anesth* 2015;24:210–6.
- Martin E, Vickers B, Landau R, et al. ABM Clinical Protocol #28, Peripartum Analgesia and Anesthesia for the Breastfeeding Mother. *Breastfeed Med* 2018;13:164–71.
- Dimick JB, Ryan AM. Methods for evaluating changes in health care policy: the difference-in-differences approach. *JAMA* 2014;312:2401–2.