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REVIEW ARTICLE

Personalized analgesic management for cesarean delivery

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ABSTRACT

Current pain and analgesic management strategies apply a standardized one-size-fits-all approach to women undergoing cesarean delivery. These standardized protocols do not account for significant variability in women's pain and may lead to under-treatment in patients with high analgesic needs and overtreatment, associated with increased analgesic-related side effects, in women with low analgesic needs and higher analgesic drug sensitivity. Pre-operative identification of patients at-risk of developing severe pain might allow clinicians to optimize care by offering personalized, stratified or targeted analgesic treatment protocols. Pre-operative pain prediction tools are only of moderate value in this regard. Pain reporting during local anesthetic infiltration and answering simple rating questions about anticipated pain and analgesic needs are the easiest tools to apply and show some promise for post-cesarean delivery pain prediction. Patient-driven analgesic dose and protocol selection (based on individual preferences for pain relief and for avoidance of side effects after cesarean delivery) may optimally balance individual pain needs and side effect concerns compared to standardized postoperative pain treatment protocols. Individualized or stratified post-discharge opioid prescribing practices have been shown to reduce unnecessary opioid analgesic prescriptions and consumption, so should be implemented routinely. Outcomes other than pain and analgesic use, including recovery measures and maternal satisfaction metrics, should be considered when evaluating personalized or patient-selected pain treatment protocols.

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Introduction

Most women report pain and require opioid analgesia following cesarean delivery.^{1–3} Pain and analgesic requirements have been reported to be equivalent to those experienced after a hysterectomy.⁴ Women undergoing cesarean delivery rank avoidance of pain during and after surgery as their highest anesthetic priority.⁵ Postoperative pain is associated with greater opioid use, and excessive opioid utilization increases maternal and breast-fed neonatal adverse effects.^{6–8} Approximately 20% of women who undergo a cesarean delivery experience severe acute postoperative pain.^{2,9} These women may report severe pain for months after cesarean delivery¹⁰ and may never stop taking the opioids they were prescribed.¹¹ Severe postoperative pain is associated with delayed functional recovery and an increased risk of postpartum depression, both of which may negatively impact the mother's ability to care for her neonate and decrease her breastfeeding suc-

cess.^{2,7,9,12} Early mobilization is particularly important in this obstetric population because of an increased risk of thrombo-embolic complications.¹³ Severe acute postoperative pain is also a significant predictor of the development of more persistent or chronic surgical pain.^{9,14} Chronic pain after cesarean delivery is estimated to occur in 9–18% of women.^{15–17}

Current analgesic management strategies apply a standard one-size-fits-all approach to women undergoing cesarean delivery. These strategies are often inadequate for the significant proportion of patients who experience severe postoperative pain.^{2,9} This review examines the concept of applying a more personalized pain management plan following cesarean delivery, in order to adapt management for the cohort of women who might be expected to experience more severe pain and to have greater analgesic requirements. Pre-operative methods to help identify those women at-risk of experiencing more severe pain, as well as ways to involve women in decisions about their analgesic preferences, will be outlined.

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Standardized versus personalized analgesic management

In an effort to optimize postoperative analgesia, pain management protocols have moved towards a standardized approach that has become embedded in enhanced recovery after surgery pathways.^{18–21} These evidence-based multimodal analgesic protocols are intended to reduce the variability in care, improve pain management, decrease opioid utilization and accelerate recovery to normal presurgical function. In principle, this is the optimal approach to managing surgical pain. However, standardized one-size-fits-all postoperative pain management protocols treat all patients the same and assume all women will have similar pain experiences after delivery. Additionally, the drugs included in these analgesic protocols are chosen based on evidence from randomized studies that are designed to assess mean analgesic effect differences between study groups. Such an approach does not account for the variability of analgesic needs and drug response within a population recovering from surgery.^{2,9,10} Standardized peri- and postoperative pain management protocols may lead to undertreatment of patients with high analgesic needs and overtreatment, with associated increased analgesic-related side effects, of patients with low analgesic requirements.

In a large cohort, assessed after cesarean delivery the median number of days required for pain resolution was 21 but the reported range was 0–85 days. There was also much variability in the pain burden (defined as the area-under-the-curve of daily numerical verbal 0–10 pain scores multiplied by the duration of pain in days), with a range of six to 140.² Similarly, the median number of days until opioid and all analgesics cessation was nine and 16 days respectively, whereas the range was 0–39 days for cessation of opioid and 7–55 days for cessation of all analgesics.² A further analysis of this vaginal and cesarean delivery patient cohort that was followed daily after discharge from hospital until pain- and opioid-free recovery was reported, found that the upper 20th percentile of patients experienced a significantly greater pain burden (both higher intensity and longer duration) than the remainder (lower 80th percentile) of the study cohort (Fig. 1).¹⁰ These findings suggest that a one-size-fits-all approach is not appropriate for the entire postpartum population, and that, at a minimum, analgesic protocols should be adjusted or stratified to target the proportion of women at-risk of severe or prolonged pain.

Physician versus patient-driven care

Standardized one-size-fits-all postoperative pain management protocols are physician-selected and prescribed to all women without soliciting patient input. This

physician-oriented model requires the treating clinicians to select the patient's analgesic drugs and doses without, or with minimal, patient consultation or involvement. There is, however, considerable variability in the preferences of pregnant women with regard to both pain relief expectations and side effect avoidance after cesarean delivery.^{5,22} The patient's input as to their desires can provide valuable information to help meet the balance between pain minimization and the potential analgesic drug-related side effects. Although a cohort of peripartum women on average rank pain during and after cesarean delivery as top priorities they wish to avoid, many women rank opioid-related side effects such as vomiting, nausea and pruritus as more important than pain.⁵ Women would tolerate a visual analog pain scale 0–100 mm score of 56 ± 22 mm (mean \pm standard deviation) before exposing their baby to the potential effects of the analgesics they receive. If women are given a choice about the intrathecal morphine dose administered for cesarean delivery, fear of pain after surgery is the key reason that a higher dose is chosen; and concern about side effects such as nausea and vomiting is the overwhelming reason cited by women selecting a low dose.²²

Involving patients in their health care decisions is also important from a clinical, ethical and public health perspective.^{23–25} Patients' involvement in analgesic drug and dosage selection, based on individual preferences, can help align physician-proposed treatment with these patient preferences, values and expectations. A patient-centered approach increases adherence to treatment recommendations^{24,26} and may consequently improve patient outcomes.

Determining women at-risk of experiencing severe pain and having high opioid requirements after cesarean delivery

If patients could be identified pre-operatively to be at greater risk of developing severe postoperative pain, physicians could optimize care by offering personalized, stratified or targeted analgesic treatment plans. Drugs and doses that would otherwise not be suitable for all women undergoing cesarean delivery due to their side effect profiles or cost could be utilized in selected at-risk patients.^{27,28} Examples of a personalized approach include: at-risk women prophylactically receiving larger intrathecal morphine doses than standardly administered; additional adjunctive medications such as gabapentin, clonidine or ketamine (which show modest efficacy when given to all and have associated side effects that preclude widespread usage); and local anesthetic techniques such as wound infiltration or transversus abdominis plane or quadratus lumborum blocks (that involve additional time, equipment and cost but only limited analgesic benefit if provided to all women

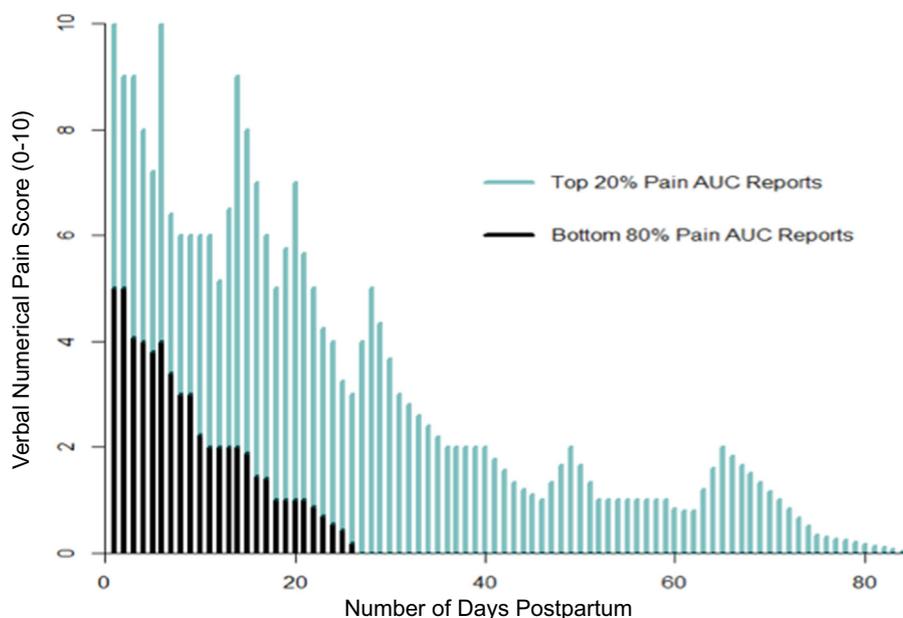


Fig. 1 Postpartum pain following cesarean and vaginal delivery. Top 20th percentile is shown in green and rest of women (bottom 80th percentile) shown in black. AUC: area-under-the-curve. Vertical axis is verbal numerical pain score 0–10 (0 = no pain and 10 = worse pain imaginable) and horizontal axis is the number of days after delivery (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

receiving intrathecal morphine and multimodal oral analgesia after cesarean delivery). These methods could be applied to those women most likely to benefit from the additional intervention.

Personalized or targeted analgesic treatment plans rely on the ability to accurately predict pre-operatively those patients at-risk of severe postoperative pain. Several studies have tried to identify patients at-risk in the pre-operative period and examined the role of genetics, psychological factors and experimental pain tests or quantitative sensory tests (QSTs).

Genetic factors

Several genes have been identified with possible links to pain after cesarean delivery and to a patient's response to analgesic drugs.^{29,30} However the ability of genetic variables to predict pain sensitivity, postoperative pain and analgesic requirements has been of limited scope to date. The phenotype of pain perception and analgesic requirements is complex, multifactorial and subjective, and the pain genotype is polygenic and complex, making this relationship difficult to elucidate.^{29,30}

Demographic and psychological factors; and QSTs

Many studies in the general surgical population have evaluated whether pre-operative psychological questionnaires and QSTs can predict the patients most likely to experience more severe pain or who are likely to have increased postoperative analgesic needs. A systematic review of demographic and pre-operative psycholog-

ical factors in the general surgical population found that anxiety, younger age, the presence of pre-operative pain and the type of surgery were significant predictors of worse postoperative pain; psychological distress, younger age and type of surgery were significant predictors of increased analgesic consumption.³¹ A review of studies investigating patients' pre-operative responses to QSTs in the general surgical population found wide variability in these tests' ability to predict postoperative pain, with 4–54% of pain variance predicted amongst the studies evaluated.³²

In the cesarean delivery setting, several studies have similarly investigated the role of pre-operative QSTs and psychological questionnaires.³³ These studies have utilized pressure, electric and thermal stimulation QSTs,^{34–38} wound hyperalgesia testing³⁹ and pain response to local anesthetic infiltration.⁴⁰ Several validated questionnaires examining various psychological states such as anxiety, depression and pain catastrophizing as predictors of pain have also been assessed.^{41–44} Two studies combined pre-operative QSTs and psychological questionnaires to determine if this approach optimized postoperative pain prediction.^{45,46} Details of these study results are presented in a systematic narrative review.³³ The association between pre-operative QSTs and postoperative pain and analgesic requirements is summarized in Table 1. Correlations of pre-operative QSTs (pressure, electric and thermal) with postoperative pain outcomes were weak to modest in most studies. The clinical role of most of these pre-operative tests is, therefore, uncertain and QSTs should currently be

Table 1 Summary of studies using quantitative sensory tests or stimulation modalities to investigate the prediction of pain following cesarean delivery

Study first author (number of patients)	Type of stimulation (modality used)	Anesthetic technique	Correlation(s) with postoperative pain scores	Correlation(s) with postoperative analgesic consumption
Wilder-Smith (120) ³⁸	<i>Electric</i> (Electric sensation threshold and electric pain tolerance threshold)	Spinal anesthesia	<ul style="list-style-type: none"> Sensation threshold correlated with pain scores 2 h after surgery ($r = -0.22$) Pain threshold correlated with pain scores 2 h after surgery ($r = -0.26$) 	<ul style="list-style-type: none"> Sensory thresholds did not correlate with time to first analgesic rescue
Nielsen (39) ³⁷	<i>Electric</i> (Electric pain threshold and electric sensory threshold)	Spinal anesthesia	<ul style="list-style-type: none"> Electric pain threshold correlated with area-under-the-curve for pain scores at rest ($r = -0.65$) and with movement ($r = -0.52$) Electric sensory threshold did not correlate with postoperative pain outcomes at rest or with movement 	<ul style="list-style-type: none"> Electric pain and sensory thresholds correlated with postoperative rescue analgesic consumption
Granot (58) ³⁶	<i>Thermal</i> (Thermal pain threshold and thermal suprathreshold pain)	Epidural anesthesia	<ul style="list-style-type: none"> Suprathreshold pain scores at 48°C correlated with postoperative pain scores at rest ($r = 0.49$) and with movement ($r = 0.53$) Pre-operative pain threshold did not correlate with postoperative pain scores 	
Pan (34) ⁴⁵	<i>Thermal</i> (Thermal pain threshold, suprathreshold thermal pain intensity and unpleasantness)	Spinal anesthesia	<ul style="list-style-type: none"> Thermal pain threshold correlated with resting pain ($r = -0.04$) and evoked pain 20–24 h after surgery ($r = -0.42$), but did not correlate with overall pain ratings or sum of pain scores Suprathreshold thermal pain intensity and unpleasantness correlated with resting pain ($r = 0.45$), and evoked pain ($r = 0.40$) at 20–24 h after surgery, but did not correlate with overall pain ratings or sum of pain scores 	<ul style="list-style-type: none"> Thermal pain threshold correlated with analgesic consumption in recovery room ($r = -0.43$) but did not correlate with intra-operative or postoperative analgesic consumption Suprathreshold thermal pain intensity and unpleasantness correlated with recovery room and total analgesic consumption ($r = 0.48$ and 0.43 respectively) but did not correlate with intra-operative or postoperative analgesic consumption
Strulov (45) ⁴⁶	<i>Thermal</i> (Tonic and phasic thermal stimulation)	Spinal anesthesia	<ul style="list-style-type: none"> Tonic heat stimulus pain scores correlated with pain scores on first ($r = 0.39$), but not second, postoperative day Phasic heat stimulus pain scores did not correlate with postoperative pain scores 	
Buhagiar (65) ³⁴	<i>Electric and Pressure</i> (Electric pain threshold, pressure pain threshold, and pressure pain tolerance)	General or spinal anesthesia	<ul style="list-style-type: none"> Electric pain threshold correlated with pain scores at 6 h ($r = -0.26$) and 24 h ($r = -0.23$) but not at 12 h Pressure pain tolerance correlated with pain scores at 6 h ($r = -0.21$), but not at 12, 24 or 48 h Pressure pain threshold did not correlate with pain scores at 6, 12, 24 or 48 h 	<ul style="list-style-type: none"> Electric pain threshold correlated with acetaminophen consumption in the first 48 h ($r = -0.33$) Pressure pain tolerance and pressure pain threshold did not correlate with 48 h acetaminophen consumption
Buhagiar (20) ³⁵	<i>Electric and Pressure</i> (Electric pain threshold, pressure pain threshold, and pressure pain tolerance)	General or spinal anesthesia	<ul style="list-style-type: none"> Electric pain threshold correlated with pain scores at 6 h ($r = -0.48$), but not at 12, 24 or 48 h Pressure pain threshold and pressure pain tolerance did not correlate with postoperative pain scores 	<ul style="list-style-type: none"> Electric pain threshold, pressure pain threshold and pressure pain tolerance correlated with 48 h morphine consumption ($r = -0.45$, -0.41 and -0.44 respectively)
Ortner (163) ³⁹	<i>Mechanical</i> (Scar hyperalgesia index)	Spinal anesthesia	<ul style="list-style-type: none"> Scar hyperalgesia index correlated with pain scores when sitting at 24 h ($r = 0.20$) and 48 h ($r = 0.25$) but not at 12 h; and not with pain scores at rest or with uterine cramping pain at 12, 24, and 48 h 	<ul style="list-style-type: none"> Scar hyperalgesia index did not correlate with analgesic consumption at 48 h
Orbach-Zinger (229) ⁴⁰	<i>Lidocaine infiltration prior to spinal anesthesia</i> (verbal pain score)	Spinal anesthesia	<ul style="list-style-type: none"> Pain score with infiltration of lidocaine correlated with average and peak pain at rest ($r = 0.47$ and 0.53 respectively), average and peak pain on movement ($r = 0.43$ and 0.48 respectively), as well as average and peak uterine cramping pain ($r = 0.18$ and 0.26 respectively) 	<ul style="list-style-type: none"> Pain score with infiltration of lidocaine correlated with first 24 h analgesic requests ($r = 0.26$)

viewed as research tools. Thermal QSTs, particularly suprathreshold heat stimuli, appear to be the most suitable QST method. A cesarean delivery scar hyperalgesia (SHA) index,³⁹ measured pre-operatively, correlated with pre-operative mechanical temporal summation (mTS) but the SHA showed inconsistent and weak to moderate correlations with post-cesarean pain outcomes.³⁹

Pain from local anesthetic infiltration prior to neuraxial anesthesia was used to predict women who would experience severe acute postoperative pain with 92% sensitivity and 93% specificity.⁴⁰ Although this modality showed the highest postoperative pain predictive value of any method published to date, these encouraging findings need confirmation. Pain reported with infiltration does not have many of the drawbacks (such as training, special equipment and time taken) of QSTs, is already part of standard clinical practice when performing neuraxial technique, and can be used at both non-urgent and urgent cesarean deliveries.

Many pre-operative questionnaires have been investigated as a means of predicting post-cesarean pain and analgesic use. These include the State Trait Anxiety Inventory (STAI), Anxiety Sensitivity Index (ASI), Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale (PCS), Fear of Pain Score (FPQ III), Eysenck Personality Questionnaire Revised-Short Scale (EPQR-S), Pittsburgh Sleep Quality Index (PSQI) and Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety Scale, Depression Scale and Posttraumatic Stress Disorder Checklist.^{10,27,33,41} Unfortunately, these detailed questionnaires appear to explain only a small percentage of postoperative pain variance, with weak to moderate correlations reported amongst the studies (Table 2).^{27,33}

Pre-operatively applied simple rating questions, asking women to rate their anxiety, anticipated pain, analgesic needs and pain thresholds, have been proposed and evaluated (Table 3).^{42,44} One study found that simply asking patients pre-operatively three questions (rating their anticipated pain, expected pain medication needs and anxiety) accounted for 20% of the variability in postcesarean pain, with modest sensitivity and specificity in predicting women in the highest 20th percentile of post-cesarean pain scores.⁴⁴ In another study, three slightly different questions about expected postoperative pain, anticipated analgesic thresholds and perceived analgesic needs predicted 45% of variance in pain and 21% of variance in opioid use and performed better than four detailed validated questionnaires examining psychological state and personality.⁴² Although promising, these simple screening questions need confirmatory investigations before being adopted into routine practice, but they emphasize the importance of asking patients about their pain and analgesic expectations prior to surgery.

Even if pre-operative screening and analgesic dose adjustments are not considered, postoperative assessment and treatment escalation for women in severe pain is essential. Women who experience severe pain on the first postoperative day are at high risk for ongoing severe pain and persistent postoperative pain.^{9,10} Screening and following-up all women undergoing cesarean delivery can help identify these outliers, enabling additional analgesic interventions such as a regional block (transversus abdominis plane or quadratus lumborum block) or analgesic adjuvants that are not routinely utilized (for example gabapentin) to be prescribed for this select group of women.⁷

Altering analgesic protocols based on pre-operative pain prediction

The ability to predict in advance which women will have more postoperative pain or higher analgesic requirements is important as pre-emptive alterations in pain management strategies in these patients may be effective. However, there are very limited data investigating the impact of altering analgesic treatment after pre-operative tests have identified women at-risk for severe postoperative pain. A study that evaluated targeted therapy for this cohort used the three simple rating questions described above in Table 3 to predict the top 20th percentile of women most likely to describe high levels of pain.⁴⁷ The authors then administered a higher dose of intrathecal morphine (300 µg versus 150 µg in the control group) plus scheduled acetaminophen to this group, in combination with scheduled nonsteroidal anti-inflammatory drugs to both groups. Although this modified analgesic protocol lead to improved pain control for this population, the study lacked a group of low-risk women randomized to the same intervention. The results may, therefore, just reflect that more analgesia was provided and not the impact of accurate pain prediction and a modified analgesic protocol for these women.

Patient-choice of analgesic drugs and dosages

Giving women a more active role in analgesic drug and dosage selection may provide useful information to guide management.^{48,22} A study randomized women to a perceived choice (low 100 µg vs high 200 µg intrathecal morphine dose) or no choice of intrathecal morphine dose after cesarean delivery.²² Women based their choice on information outlining the balance between pain relief and avoiding side effects. The study also involved deception, such that all participants were still randomly assigned to receive 100 or 200 µg of intrathecal morphine regardless of their choice. Women who requested the larger intrathecal morphine dose required more supplemental opioids and reported more pain than

Table 2 Summary of studies investigating preoperative questionnaires to predict post-cesarean delivery pain

Study first author (number of patients)	Questionnaire(s)	Anesthetic technique	Correlation(s) with postoperative pain scores	Correlation(s) with postoperative analgesic consumption
Pan (34) ⁴⁵	State Trait Anxiety Inventory	Spinal anesthesia	<ul style="list-style-type: none"> • Responses to expectation questions correlated with resting pain ($r = 0.41$) and with the sum of pain scores for resting, evoked, and overall pain ($r = 0.34$), but not with evoked pain or overall pain • State Trait Anxiety Inventory score did not correlate with any of the pain score outcomes 	<ul style="list-style-type: none"> • State Trait Anxiety Inventory score correlated with analgesic requirement in recovery room as well as total analgesic requirement ($r = 0.40$ and 0.39 respectively), but not with intraoperative analgesic consumption or patient controlled analgesia use • Expectation questions did not correlate with intra-operative, recovery room, patient-controlled analgesia or total analgesic requirement
Strulov (45) ⁴⁶	Pain catastrophizing scale	Spinal anesthesia	<ul style="list-style-type: none"> • Pain catastrophizing scale score correlated with pain scores on post-operative days 1 and 2 ($r = 0.33$ and 0.37 respectively) 	<ul style="list-style-type: none"> • Pain catastrophizing scale score did not correlate with postoperative analgesic consumption
Pan (192) ⁴⁴	Three simple questions (see Table 3).	Spinal anesthesia	<ul style="list-style-type: none"> • Individual questions significantly correlated with evoked pain scores at 24 h postoperatively ($r = 0.24$–0.33) • Response to three simple questions did not correlate with pain at rest in the multivariable model 	<ul style="list-style-type: none"> • Response to three simple questions did not correlate with analgesic consumption in the multivariable analysis
Orbach-Zinger (245) ⁴³	Pittsburgh Sleep Quality Index	Spinal anesthesia	<ul style="list-style-type: none"> • Poor sleep quality was associated with higher peak pain scores with movement compared with good sleep quality [OR (95% CI) 2.64 (1.2 to 6)] but no difference in average pain scores at rest or with movement, average uterine cramping, peak pain at rest or peak uterine cramping between good and poor sleep quality 	<ul style="list-style-type: none"> • Poor sleep quality was not different from good sleep quality with regards to requests for analgesia for breakthrough pain
Carvalho (50) ⁴²	Three simple questions (see Table 3) and four psychological questionnaires	Spinal anesthesia	<ul style="list-style-type: none"> • Anticipated analgesic threshold and anticipated analgesic needs significantly correlated with area-under-the-curve for pain scores over 48 h ($r = -0.35$ and 0.31) respectively, but there was no correlation between pain scores and any of the psychological questionnaires 	<ul style="list-style-type: none"> • Expected postoperative pain significantly correlated with opioid use ($r = 0.35$) but there was no correlation between opioid use and any of the psychological questionnaires
Borges (1062) ⁴¹	Hospital Anxiety and Depression Scale	Spinal anesthesia	<ul style="list-style-type: none"> • Pre-operative anxiety score significantly correlated with incidence of moderate to severe pain immediately postoperatively [OR (95% CI) 1.68 (1.16 to 2.20)] 	

Table 3 Proposed preoperative three simple rating questions to screen for postoperative pain and analgesic requirements

Domain assessed	Wake Forest Pan et al. ⁴⁴	Stanford Carvalho et al. ⁴²
Current anxiety	On a scale of 0–100, with 0 being not anxious at all through 100 being extremely anxious, how anxious are you about your upcoming surgery?	-
Anticipated postoperative pain	On a scale of 0–100, with 0 being no pain at all and 100 being pain as bad as you can imagine, how much pain do you anticipate experiencing after your upcoming surgery?	Anticipated Pain: How much pain do you expect to experience after your surgery on a pain scale of 0–10? (0 = no pain, 10 = worst pain imaginable)
Anticipated analgesic needs	On a scale of 0–5, with 0 being none at all, 1 being much less than average, 2 being less than average, 3 being average, 4 being more than average, and 5 being much more than average, how much pain medication do you anticipate needing after your upcoming surgery?	What do you expect your analgesic requirements will be after surgery? (0 = no analgesia, 10 = highest amount)
Anticipated analgesic threshold	-	At what point on a pain scale of 0–10 would you likely request postoperative pain relief? (0 = no pain, 10 = worst pain imaginable)

patients who chose the smaller dose regardless of the intrathecal morphine dose received. Being offered a perceived choice did not impact opioid use or pain outcomes but women who were given a choice and chose the larger dose, correctly anticipated a greater opioid requirement and more pain compared with women who chose the smaller dose.²²

In a follow-up study, women undergoing cesarean delivery with spinal anesthesia were randomly assigned a choice of postoperative pain protocols or routine care.⁴⁸ The options, which were selected by women using a standardized table that outlined expected pain relief and potential side effects, included a low-dose group (50 µg intrathecal morphine), a medium-dose group (150 µg as per routine care), and a high-dose protocol (300 µg intrathecal morphine plus a single dose of oral gabapentin 600 mg). All groups received scheduled acetaminophen and nonsteroidal anti-inflammatory drugs, with oral oxycodone available for breakthrough pain. Similarly to the previous study,²² women given a choice did not show reduced opioid use or pain scores but the study confirmed previous findings that women had insight into their pain needs. Women who chose the high-dose protocol required more postoperative rescue oxycodone despite receiving extra analgesia (six times more intrathecal morphine plus gabapentin) compared to those selecting the low-dose analgesic protocol.⁴⁸ A suggested patient choice analgesic protocol, with script and table to aid the selection, is provided in Appendix A.

Personalizing post-discharge opioid prescribing practices

Several studies from the United States report that standardized (individual physician or institutional) opioid prescription practices result in significantly more opioids being prescribed to women after cesarean delivery than are required or consumed.^{49–52} Two approaches have been proposed to better align opioid prescriptions with patients need, in an attempt to reduce the amount of opioids prescribed. One study utilized a shared decision-making approach, using a tablet computer-based decision aid, to guide opioid prescribing after cesarean delivery.⁵³ The authors were able to halve the amount of tablets prescribed from 40 to 20 oxycodone tablets, based on patients' input during shared decision sessions in which typical trajectories of pain resolution and expected opioid use after cesarean delivery were explained, before the number of oxycodone tablets prescribed was selected by each woman. Another novel approach is to base the amount of prescribed opioids on the amount of in-patient opioid used, specifically during the 24–47 h period after cesarean delivery.^{54,55} The authors of this study used a formula (predicted opioid use after discharge = $48.8 + [1.773 \times \text{in-patient } 24\text{--}47 \text{ h}]$) for opioid use

derived from their institutional analysis. They found that the individualized prescription group were prescribed significantly fewer (median [interquartile range]) oxycodone tablets (14 [12–16] vs. 30 [30–30] tablets) and consequentially also used fewer tablets (8 [4–14] vs. 15 [6–30]). This group had 50% fewer unused tablets at the end of the study period compared to the standardized prescription group.^{54,55}

Beyond pain and analgesic use metrics

The postoperative pain experience is a complex psychophysical response to a noxious stimulus that involves a cognitive evaluation and an emotional response. Women who receive good peripartum pain relief are not necessarily satisfied with their care and maternal satisfaction may be related more to coping with pain.^{56,57} Satisfaction is similarly multidimensional and is largely related to the assessed difference between actual and expected care.^{58,59} Quality of care assessment and possibly satisfaction ratings are impacted by many factors, including physician respect for the patient's values, preferences and needs; the quality of care provided; the quality of provider communication; and the patient's involvement in clinical decisions.^{60–62} A patient-centered analgesic management approach may better align patient expectations with outcomes, including satisfaction. Giving women a choice as to their analgesic protocol and drug doses increased maternal satisfaction even though pain and opioid use was not impacted.^{48,22} These results in the cesarean setting demonstrate that pain and maternal satisfaction are poorly-related constructs, as has been shown for labor pain management.^{56,57}

Most postpartum pain studies have focused on in-hospital stay, with pain and analgesic consumption being the key outcome measures. Moving away from pain and analgesic use outcomes toward a more global measure of recovery is important. A study that assesses self-reported functional recovery after delivery found that, although women took on average four weeks to achieve functional recovery after cesarean delivery, there was significant variability in their speed of recovery.² Recovery should be considered a key metric. Identifying factors that contribute towards delayed recovery and assessing interventions that accelerate recovery should be the focus of future post-cesarean delivery pain studies.¹⁰ Self-assessment of functional recovery is subjective and not a validated measure. An obstetric-specific recovery tool (ObsQoR-11) for use in patients undergoing cesarean delivery has been developed and tested.⁶³ This easy-to-use, patient-centered, recovery measure tool consists of a questionnaire that considers pain, drug side effects, comfort, control, ability to hold and feed the baby, to mobilize independently and to achieve personal hygiene. Although moderate and severe pain measure-

ments contribute to this recovery score, the ObsQoR-11 is a global and comprehensive outcome measure. Future studies that assess drug efficacy and analgesic interventions should focus beyond pain and analgesic outcomes, and consider the detailed evaluation of recovery and evaluate patient-assessed outcomes such as satisfaction. Evaluating the efficacy of implementing a personalized pain management protocol after cesarean delivery should also consider these important outcomes.

Summary

Standardized one-size-fits-all postoperative pain management protocols do not account for the significant variability in pain and analgesic requirements amongst women after cesarean delivery. A standardized approach may lead to undertreatment of women with high analgesic needs and overtreatment, with more analgesic-related side effects, of women with low analgesic needs or greater analgesic drug sensitivity. By pre-operatively identifying patients at-risk of developing severe pain, clinicians may be able to optimize care by offering personalized, stratified or targeted analgesic treatment protocols. However, such personalized plans can only be applied if women can be reliably and accurately predicted to be at-risk. Pre-operative pain prediction tools are of moderate value in this regard. Pain from local anesthetic infiltration and simple rating questions about anticipated pain and analgesic needs are the easiest to apply in the clinical setting and appear to be of some value. Patient-driven analgesic dose and protocol selection (based on individual preferences for pain relief and the avoidance of side effects) may optimally balance individual analgesic needs and side effects concerns when compared to standardized postoperative pain treatment protocols. The choice women make when given analgesic protocol options may also help identify those who will have the most postoperative pain and highest analgesic needs. This patient-driven approach, with the patient having input into analgesic protocols and doses, should be considered instead of the use of a standardized analgesic protocol. Individualized or stratified post-discharge opioid prescribing practices have been shown to reduce unnecessary opioid analgesic prescriptions and consumption, so should be implemented routinely. Future studies are required to determine if analgesic drug and dose alterations based on pre-operative predictions of women at-risk for severe postoperative pain lead to improved pain management. Outcomes beyond pain and analgesic use, including recovery measures and maternal satisfaction metrics, should be determined when evaluating personalized or patient-selected analgesic treatment protocols.

References

- Houle TT, Miller S, Lang JE, et al. Day-to-day experience in resolution of pain after surgery. *Pain* 2017;**158**:2147–54.
- Komatsu R, Carvalho B, Flood PD. Recovery after nulliparous birth: a detailed analysis of pain analgesia and recovery of function. *Anesthesiology* 2017;**127**:684–94.
- Wrench IJ, Sanghera S, Pinder A, Power L, Adams MG. Dose response to intrathecal diamorphine for elective caesarean section and compliance with a national audit standard. *Int J Obstet Anesth* 2007;**16**:17–21.
- Fassoulaki A, Gatzou V, Petropoulos G, Siafaka I. Spread of subarachnoid block, intraoperative local anaesthetic requirements and postoperative analgesic requirements in Caesarean section and total abdominal hysterectomy. *Br J Anaesth* 2004;**93**:678–82.
- Carvalho B, Cohen SE, Lipman SS, et al. Patient preferences for anesthesia outcomes associated with cesarean delivery. *Anesth Analg* 2005;**101**:1182–7.
- Carvalho B, Butwick AJ. Postcesarean delivery analgesia. *Best Pract Res Clin Anaesthesiol* 2017;**31**:69–79.
- Sutton CD, Carvalho B. Optimal pain management after cesarean delivery. *Anesthesiol Clin* 2017;**35**:107–24.
- ACOG Committee Opinion No. 742 Summary: Postpartum Pain Management. *Obstet Gynecol* 2018;**132**:252–53.
- Eisenach JC, Pan PH, Smiley R, et al. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. *Pain* 2008;**140**:87–94.
- Komatsu R, Carvalho B, Flood P. Prediction of outliers in pain, analgesia requirement, and recovery of function after childbirth: a prospective observational cohort study. *Br J Anaesth* 2018;**121**:417–26.
- 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–e18.
- Karlstrom A, Engstrom-Olofsson R, Norbergh KG, Sjoling M, Hildingsson I. Postoperative pain after cesarean birth affects breastfeeding and infant care. *J Obstet Gynecol Neonatal Nurs* 2007;**36**:430–40.
- James AH, Jamison MG, Brancazio LR, Myers ER. Venous thromboembolism during pregnancy and the postpartum period: incidence, risk factors, and mortality. *Am J Obstet Gynecol* 2006;**194**:1311–5.
- Niklasson B, Georgsson Ohman S, Segerdahl M, Blanck A. Risk factors for persistent pain and its influence on maternal wellbeing after cesarean section. *Acta Obstet Gynecol Scand* 2015;**94**:622–8.
- Kainu JP, Sarvela J, Tiippana E, Halmesmaki E, Korttila KT. Persistent pain after cesarean section and vaginal birth: a cohort study. *Int J Obstet Anesth* 2010;**19**:4–9.
- Nikolajsen L, Sorensen HC, Jensen TS, Kehlet H. Chronic pain following Caesarean section. *Acta Anaesthesiol Scand* 2004;**48**:111–6.
- Sng BL, Sia AT, Quek K, Woo D, Lim Y. Incidence and risk factors for chronic pain after caesarean section under spinal anaesthesia. *Anaesth Intensive Care* 2009;**37**:748–52.
- Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. *Ann Surg* 2008;**248**:189–98.
- Benhamou D, Kfoury T. Enhanced recovery after caesarean delivery: Potent analgesia and adequate practice patterns are at the heart of successful management. *Anaesth Crit Care Pain Med* 2016;**35**:373–5.
- Coates E, Fuller G, Hind D, et al. Enhanced recovery pathway for elective caesarean section. *Int J Obstet Anesth* 2016;**27**:94–5.
- Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: A review. *JAMA Surg* 2017;**152**:292–8.
- Carvalho B, Mirza F, Flood P. Patient choice compared with no choice of intrathecal morphine dose for caesarean analgesia: a randomised clinical trial. *Br J Anaesth* 2017;**118**:762–71.
- Whitney SN. A new model of medical decisions: exploring the limits of shared decision making. *Med Decis Making* 2003;**23**:275–80.
- Coulter A. Patient engagement-what works? *J Ambul Care Manage* 2012;**35**:80–9.
- Krones T, Keller H, Sonnichsen A, et al. Absolute cardiovascular disease risk and shared decision making in primary care: a randomized controlled trial. *Ann Fam Med* 2008;**6**:218–27.
- Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008;**16**(2) Cd000011.
- Granot M. Can we predict persistent postoperative pain by testing preoperative experimental pain? *Curr Opin Anaesthesiol* 2009;**22**:425–30.
- Carvalho B. Can We predict postoperative pain prior to undergoing surgery? *J Pain Relief* 2012;**1**:4.
- Landau R, Kraft JC. Pharmacogenetics in obstetric anesthesia. *Curr Opin Anaesthesiol* 2010;**23**:323–9.
- Landau R, Smiley R. Pharmacogenetics in obstetric anesthesia. *Best Pract Res Clin Anaesthesiol* 2017;**31**:23–34.
- Ip HY, Abrishami A, Peng PW, Wong J, Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology* 2009;**111**:657–77.
- Werner MU, Mjobo HN, Nielsen PR, Rudin A. Prediction of postoperative pain: a systematic review of predictive experimental pain studies. *Anesthesiology* 2010;**112**:1494–502.
- Gamez BH, Habib AS. Predicting severity of acute pain after cesarean delivery: a narrative review. *Anesth Analg* 2018;**126**:1606–14.
- Buhagiar L, Cassar OA, Brincat MP, et al. Predictors of post-caesarean section pain and analgesic consumption. *J Anaesthesiol Clin Pharmacol* 2011;**27**:185–91.
- Buhagiar LM, Cassar OA, Brincat MP, et al. Pre-operative pain sensitivity: a prediction of post-operative outcome in the obstetric population. *J Anaesthesiol Clin Pharmacol* 2013;**29**:465–71.
- Granot M, Lowenstein L, Yarnitsky D, Tamir A, Zimmer EZ. Postcesarean section pain prediction by preoperative experimental pain assessment. *Anesthesiology* 2003;**98**:1422–6.
- Nielsen PR, Norgaard L, Rasmussen LS, Kehlet H. Prediction of post-operative pain by an electrical pain stimulus. *Acta Anaesthesiol Scand* 2007;**51**:582–6.
- Wilder-Smith CH, Hill L, Dyer RA, Torr G, Coetzee E. Postoperative sensitization and pain after cesarean delivery and the effects of single im doses of tramadol and diclofenac alone and in combination. *Anesth Analg* 2003;**97**:526–33.
- Ortner CM, Granot M, Richebe P, et al. Preoperative scar hyperalgesia is associated with post-operative pain in women undergoing a repeat Caesarean delivery. *Eur J Pain* 2013;**17**:111–23.
- Orbach-Zinger S, Aviram A, Fireman S, et al. Severe pain during local infiltration for spinal anaesthesia predicts post-caesarean pain. *Eur J Pain* 2015;**19**:1382–8.
- Borges NC, Pereira LV, de Moura LA, Silva TC, Pedrosa CF. Predictors for moderate to severe acute postoperative pain after cesarean section. *Pain Res Manag* 2016;**2016**:5783817.
- Carvalho B, Zheng M, Harter S, Sultan P. A prospective cohort study evaluating the ability of anticipated pain, perceived analgesic needs, and psychological traits to predict pain and analgesic usage following cesarean delivery. *Anesthesiol Res Pract* 2016;**2016**:7948412.
- Orbach-Zinger S, Fireman S, Ben-Haroush A, et al. Preoperative sleep quality predicts postoperative pain after planned caesarean delivery. *Eur J Pain* 2017;**21**:787–94.
- Pan PH, Tonidandel AM, Aschenbrenner CA, et al. Predicting acute pain after cesarean delivery using three simple questions. *Anesthesiology* 2013;**118**:1170–9.

45. Pan PH, Coghill R, Houle TT, et al. Multifactorial preoperative predictors for postcesarean section pain and analgesic requirement. *Anesthesiology* 2006;**104**:417–25.
46. Strulov L, Zimmer EZ, Granot M, et al. Pain catastrophizing, response to experimental heat stimuli, and post-cesarean section pain. *J Pain* 2007;**8**:273–9.
47. Booth JL, Harris LC, Eisenach JC, Pan PH. A randomized controlled trial comparing two multimodal analgesic techniques in patients predicted to have severe pain after cesarean delivery. *Anesth Analg* 2016;**122**:1114–9.
48. Carvalho B, Sutton CD, Kowalczyk JJ, Flood P. Impact of patient choice for different postcesarean delivery analgesic protocols on opioid consumption: a randomized prospective clinical trial. *Reg Anesth Pain Med* 2019;**44**:578–85.
49. Badreldin N, Grobman WA, Chang KT, Yee LM. Opioid prescribing patterns among postpartum women. *Am J Obstet Gynecol* 2018;**219**(103):e1–8.
50. Bartels K, Mayes LM, Dingmann C, et al. Opioid use and storage patterns by patients after hospital discharge followings. *PLoS One* 2016;**11** e0147972.
51. Bateman BT, Cole NM, Maeda A, et al. Patterns of opioid prescription and use after cesarean delivery. *Obstet Gynecol* 2017;**130**:29–35.
52. Schmidt P, Berger MB, Day L, Swenson CW. Home opioid use following cesarean delivery: how many opioid tablets should obstetricians prescribe? *J Obstet Gynaecol Res* 2018;**44**:723–9.
53. 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**:42–6.
54. Osmundson SS, Raymond BL, Kook BT, et al. Individualized compared with standard postdischarge oxycodone prescribing after cesarean birth: a randomized controlled trial. *Obstet Gynecol* 2018;**132**:624–30.
55. Osmundson SS, Schornack LA, Grash JL, et al. Postdischarge opioid use after cesarean delivery. *Obstet Gynecol* 2017;**130**:36–41.
56. Duale C, Nicolas-Courbon A, Gerbaud L, et al. Maternal satisfaction as an outcome criterion in research on labor analgesia: data analysis from the recent literature. *Clin J Pain* 2015;**31**:235–46.
57. Lally JE, Murtagh MJ, Macphail S, Thomson R. More in hope than expectation: a systematic review of women's expectations and experience of pain relief in labour. *BMC Med* 2008;**6**:7.
58. Robinson PN, Salmon P, Yentis SM. Maternal satisfaction. *Int J Obstet Anesth* 1998;**7**:32–7.
59. Wu CL, Naqibuddin M, Fleisher LA. Measurement of patient satisfaction as an outcome of regional anesthesia and analgesia: a systematic review. *Reg Anesth Pain Med* 2001;**26**:196–208.
60. Heidegger T, Saal D, Nubling M. Patient satisfaction with anaesthesia - Part I: satisfaction as part of outcome – and what satisfies patients. *Anaesthesia* 2013;**68**:1165–72.
61. Hobson JA, Slade P, Wrench IJ, Power L. Preoperative anxiety and postoperative satisfaction in women undergoing elective caesarean section. *Int J Obstet Anesth* 2006;**15**:18–23.
62. Delbanco TL. Enriching the doctor-patient relationship by inviting the patient's perspective. *Ann Intern Med* 1992;**116**:414–8.
63. Ciechanowicz S, Setty T, Robson E, et al. Development and evaluation of an obstetric quality of recovery (ObsQoR-11) score after elective caesarean delivery. *Br J Anaesth* 2019;**122**:69–78.

Appendix A. Proposed patient-selected analgesic protocol with script and table to guide dose and protocol selection based on preference for pain and side effect avoidance

Proposed script and selection table:

When providing pain relief, anesthesia doctors may need to make treatment decisions that “trade off” relieving pain during and after cesarean delivery with a possible increased risk of the commonest side effects: nausea, vomiting, itching and sedation. Look at the table below and choose the analgesic protocol that best describes your preference for pain relief balanced with the possible risk of side effects during and after your surgery and anesthesia. All drugs and doses contained in the protocol are used in standard practice and have been shown in previous studies to be safe and effective for mother and baby. This information will be used to select the medication used in your current anesthetic.

Select the desired CESAREAN ANALGESIC PROTOCOL: Lower, Medium or Higher (please circle).

Risk of Possible Pain and Analgesia-related Side-effects	Cesarean Delivery Analgesic Protocol		
	Lower Dose Protocol	Medium Dose Protocol	Higher Dose and Drug Protocol
Risk of Pain	More	Average	Less
Risk of Nausea/ Vomiting	Less	Average	More
Risk of Itching	Less	Average	More
Risk of Sedation	Less	Average	More

Proposed patient-selected analgesic protocol options:

Low Dose Protocol: 50 mcg intrathecal morphine + scheduled acetaminophen + scheduled NSAIDs

Medium Dose Protocol: 100 mcg intrathecal morphine + scheduled acetaminophen + scheduled NSAIDs

High Dose and Drug Protocol: 200 mcg intrathecal morphine + scheduled acetaminophen + scheduled NSAIDs + gabapentin + local anesthetic wound infiltration/instillation or regional block (transversus abdominis plane/quadratus lumborum block)