Systematic Review

Continuation of Buprenorphine to Facilitate Postoperative Pain Management for Patients on Buprenorphine Opioid Agonist Therapy

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Background: Acute pain management in patients on buprenorphine opioid agonist therapy (BOAT) can be challenging. It is unclear whether BOAT should be continued or interrupted for optimization of postoperative pain control.

Objectives: To determine an evidence-based approach for pain management in patients on BOAT in the perioperative setting, particularly whether BOAT should be continued or interrupted with or without bridging to another mu opioid agonist and to identify benefits and harms of either perioperative strategy.

Study Design: Systematic literature review with qualitative data synthesis.

Setting: Hospital, perioperative.

Methods: The study protocol was registered on PROSPERO (Registration number 9030276355). Medline via OVID, EMBASE, CINAHL, and the Cochrane CENTRAL register of trials were searched for prospective or retrospective observational or controlled studies, case series, and case reports that described perioperative or acute pain care for patients on BOAT. References of narrative and systematic reviews addressing acute pain management in patients on BOAT and references of included articles were hand-searched to identify additional original articles for inclusion. The full text of publications were reviewed for final inclusion, and data were extracted using a standardized data extraction form. Results were summarized qualitatively. Primary outcomes were postoperative pain intensity and total opioid use and identification of benefits and harms of perioperative strategies.

Results: Eighteen publications presenting data on the perioperative management of patients on BOAT were identified: 10 case reports, 5 case series, and 3 retrospective cohort studies. Eleven articles reported continuation of BOAT, 2 concerned bridging BOAT, and 4 articles described stopping BOAT without planned bridging. In one retrospective cohort study, BOAT was continued in half and interrupted in half of patients. Patients on BOAT may have pain that is more difficult to treat than those who are not on OAT. There is no clear evidence that one particular strategy provides superior postoperative pain control, but interruption of BOAT may result in harm, including failure to return to baseline BOAT doses, continuing non-BOAT opioid use, or relapse of opioid use disorder.

Limitations: There were a limited number of articles relevant to the study question consisting of case reports and retrospective observational studies. Some omitted relevant details. No prospective studies were found.

Conclusions: There is no clear benefit to bridging or stopping BOAT but failure to restart it may pose concerns for relapse. We recommend continuing BOAT in the perioperative period when possible and incorporating an interdisciplinary approach with multimodal analgesia.

Key words: Opioid use disorder, opiate substitution treatment, buprenorphine, buprenorphine-naloxone, buprenorphine opioid agonist therapy, postoperative pain, acute pain, multimodal analgesia

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In the past several years, the prevalence and burden of opioid use disorder (OUD) have soared. Opioid agonist therapy (OAT) reduces harms from dependence by substituting the drug of dependence with safer, long-acting opioid.

Buprenorphine has been approved OAT in the United States since 2002, and in Canada since 2007. Compared with methadone, it carries a lower risk of respiratory depression, a lesser effect on QT interval, and fewer drug interactions (1,2). Because of its effectiveness and safety profile, buprenorphine opioid agonist therapy (BOAT) is becoming a preferred option in treating OUD.

Patients with OUD have higher rates of trauma and surgical disease (3). As the use of BOAT increases, physicians are more likely to encounter patients maintained on buprenorphine who present for surgery. Pain management in such patients can be challenging and fraught with concerns regarding inadequate perioperative pain control or relapse to substance use. Patients with OUD and comorbid depression and anxiety may experience higher levels of distress in response to pain (4,5).

There are also concerns about the pharmacologic nature of buprenorphine. It is often referred to as a partial agonist with a high affinity for the mu opioid receptor. The finding that binding to the mu receptor partially activates guanosine triphosphate in vitro has prompted concerns that buprenorphine has a ceiling effect, is an inadequate analgesic, and blocks the pain relieving effects of other opioids. The legitimacy of these concerns has been disputed, as clinical data indicate buprenorphine behaves as a full agonist for the endpoint of analgesia (6-8).

How to best manage a patient on BOAT perioperatively has been controversial. There have been no randomized controlled trials (RCTs), and most recommendations are based on pharmacodynamic models or expert opinion. Two strategies are often recommended: 1) discontinue BOAT preoperatively and bridge to either methadone or another full mu opioid receptor agonist, or 2) continue BOAT and use additional opioids to treat pain (9-11).

To help guide perioperative decision-making, we performed a systematic review of the literature describing patients treated with BOAT who had surgery or acute pain. Our primary outcomes were postoperative pain intensity and total opioid use. We also sought qualitative evidence of benefits and harms of each strategy. For example, failure to transition back to BOAT would be a poor outcome for someone who relies on BOAT to maintain remission in OUD.

Methods

The study protocol was registered on PROSPERO (registration number 9030276355). A medical librarian searched the following databases for articles in English published in and after 1990: Medline via OVID, EMBASE, CINAHL, and the Cochrane CENTRAL register of trials. Search concepts were mapped to Medical Subject Heading (MeSH) terms when possible and were also employed as keywords to increase sensitivity of search. The complete search strategies are included in Appendix 1. These strategies were run initially in early 2017, then repeated twice to update the review as data extraction and analyses occurred.

Two reviewers independently hand-searched resulting titles and abstracts to exclude articles that were not relevant to the study question. Differences were resolved by a third reviewer, when possible, or via discussion between the 2 reviewers. Prospective or retrospective observational or controlled studies, case series, and case reports that described perioperative or acute pain care of patients on BOAT were included. Narrative and systematic reviews, abstracts, and expert opinion reported in editorials or letters were excluded. However, the references of any narrative and systematic reviews addressing acute pain management in patients on BOAT were hand-searched by 2 independent reviewers to identify original articles missed in database searches. The references of all included articles from database searches were also hand-searched and their abstracts reviewed for inclusion.

Two authors then independently reviewed the full text of included studies for final inclusion and data extraction using a standardized data extraction form. The results were summarized qualitatively. Stated outcomes were not consistently addressed in the included articles. We included as many relevant data as possible, given the low number of relevant studies found.

Eighteen publications presenting data on the perioperative management of patients on BOAT were identified: 10 case reports, 5 case series, and 3 retrospective cohort studies. Two case reports concerning acute pain, rather than perioperative management, were included. No meta-analysis was performed, as no studies compared continuing with bridging of BOAT. Management strategies included continuing BOAT (11 studies), bridging BOAT with substitution of another opioid (2 studies), and stopping BOAT without substitution (4

studies). In one retrospective cohort study, BOAT was continued in half and interrupted in half of patients.

Results

A qualitative summary of the findings of each article is presented in Table 1. As per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a flow diagram of selection of studies is provided in Fig. 1. The included studies are summarized in Table 1 (case reports), Table 2 (case series), and Table 3 (retrospective cohort studies).

Summary of Articles in Which BOAT was Continued

In 5 case reports, BOAT was continued. Jones et al (12) reported good pain control after caesarean section using patient-controlled analgesia (PCA) and then oral oxycodone. Pain control outcomes for outpatient breast surgery using additional doses of buprenorphine-naloxone (13), and total knee arthroplasty (TKA) using hydromorphone PCA (14) were adequate. For a Clagett window procedure, Huang et al (15) reported initial pain control with epidural analgesia, but refractory pain when it was discontinued. Gilmore et al (16) reported a lack of response to morphine and remifentanil for reduction of traumatic fracture, followed by success with regional anesthesia.

One case series reported experiences with posterior tibial tendon repair, wrist injury repair, and cervical spine fusion (17). Pain was managed with an increase in BOAT and fentanyl PCA, an increase in BOAT, and the addition of fentanyl PCA to the usual dose of BOAT, respectively. The quality of analgesia was not reported. All patients returned to their home BOAT doses, as verified by postdischarge follow-up.

A case series of 7 patients demonstrated adequate to excellent pain control and continuation of home doses of BOAT on discharge (18). In 2 patients, BOAT was stopped in the hospital, and 3 received lower doses. Four patients had epidurals, and 2 had local anesthetic infusion pumps, for postoperative analgesia.

Leighton and Crock (19) reported 4 patients on buprenorphine, but we excluded 3 who obtained it illicitly. The remaining patient experienced good pain control for caesarean section with plain bupivacaine patient-controlled epidural analgesia and adjuvant nonsteroidal antiinflammatory drugs (NSAIDs). Her pain scores remained low 2 hours after her epidural was discontinued.

Another case series of 8 peripartum women demonstrated variable pain control and opioid requirements on discharge (20). Of the 5 who delivered by caesarean section, 3 had epidural infusions postoperatively for adequate pain control, and all transitioned to oral analgesics, although sometimes with difficulty. One patient received a fentanyl PCA and ketamine infusion, rather than epidural infusion, with good pain control. In postdischarge follow-up, 3 women were found to have relapsed into opioid use, and one overdosed.

Of the 3 retrospective cohort studies in which BOAT was continued, 2 focused on parturients. Meyer et al (21) found that in 61 patients, overall pain scores and opioid use were modestly higher than in matched controls. Vilkins et al (22) compared BOAT to methadone in caesarean section and found no difference in postoperative opioid use, complications, or length of hospital stay.

The third cohort study compared 22 patients on BOAT with 29 patients on methadone opioid agonist therapy (OAT) in the setting of a variety of surgeries (23). The authors found no differences in the efficacy or side effect profile of postoperative opioids. Eleven patients had their BOAT continued, and 11 did not receive their dose on the first day after surgery. Those who continued their BOAT used less PCA, ketamine, and NSAIDs.

Summary of Articles in Which BOAT was Bridged

Buprenorphine was bridged to another mu agonist in 2 case reports. A woman was switched to fentanyl patch 3 days before bilateral mastectomies (24). Her pain was initially poorly controlled with the fentanyl patch, ketorolac, and a fentanyl PCA. The acute pain service stopped her PCA, continued the fentanyl patch, and added oxycodone 10 to 30 mg q3h, resulting in adequate pain control and discharge on postoperative day 2.

The second case report concerned a woman on BOAT 24 mg daily presenting for a vaginal mesh removal and cystoscopy (25). As she had a history of poor pain control with BOAT continuation for a previous procedure, she was switched to hydromorphone before surgery. Her opioid tolerance was noted to be very high both pre- and post-operatively. She transitioned to oral hydromorphone on postoperative day 1, and was discharged with instructions to follow-up with her usual BOAT provider.

Table 1. *Summary of case reports.*

Article (authors and year)	Patient Age and Gender	Daily BOAT Dose	Perioperative BOAT Management Strategy	Procedure or Injury	Pain Management Strategy	Pain Scores or Quality of Pain Control	Other Postoperative Outcomes and Additional Notes
Jones et al 2006* (12)	32y F	18 mg	BOAT continued without interruption	C-section	Intraoperative epidural anesthesia with fentanyl and postoperative morphine PCA 180 mg/day.	POD 1 pain scores 0/10	Discharged on POD 3 with acetaminophen and 60 mg/day oxycodone. Pain scores 0-5 up to POD 9.
Book et al 2007 (13)	27y F	24 mg	BOAT continued without interruption	Day-case breast implant removal	Additional doses of buprenorphine-naloxone.	Adequate postoperative pain control	Tapered back to baseline BOAT dose over 10 days.
Gilmore et al 2012 (16)	22y M	Not reported	BOAT continued without interruption	Closed reduction of forearm fracture	SQ morphine, then IV remifentanil (for sedation).	Not responsive	Required IV regional anesthesia for fracture reduction.
Huang et al 2014 (15)	47y F	32 mg	BOAT continued, disrupted on POD 16	Clagett window closure	Postoperative epidural and hydromorphone PCA.	Good pain control until POD 5-7 when epidural discontinued. Inadequate pain control until POD 16 when BOAT taper started.	BOAT tapered off by discharge on POD 36 with hydromorphone 27 mg daily. Tapered off hydromorphone over next 6 months. BOAT not reinitiated.
Leighton and Crock 2017* (19)	22y F	16 mg	BOAT continued without interruption	C-section	Epidural PCEA for 48 hours with 0.0625% plain bupivacaine with ketorolac 30 mg for first 24 hours, then ibuprofen 800 q8h.	Pain score 1/10 on POD 1, 0/1 on POD 2, and 0/10 2 hours postepidural discontinuation.	
Silva and Rubinstein 2016 (14)	53y M	Not reported	BOAT continued without interruption	TKA	Hydromorphone PCA and femoral nerve block.	Good pain control and discharged with hydrocodone.	Tapered off additional opioids by 16 weeks, but self-initiated transition off BOAT to hydrocodone. Remained on hydrocodone for contralateral TKA 2 years later with poor postoperative pain control despite similar analgesic strategy.
Israel and Poore 2013 (24)	37y F	Not reported	BOAT bridged to fentanyl patch 3 days preoperatively	Bilateral mastectomy	Fentanyl PCA.	Poor pain control initially, improved with discontinuation of PCA and initiation of oral oxycodone 10-30 mg 13 h and acetaminophen.	Discharged on POD 1 on oral hydromorphone with outpatient follow-up with usual BOAT provider. Had multiple previous procedures with BOAT continued and poor postoperative pain control.

Table 1 (cont.). *Summary of case reports*.

Article (authors and year)	Patient Age and Gender	Daily BOAT Dose	Perioperative BOAT Management Strategy	Procedure or Injury	Pain Management Strategy	Pain Scores or Quality of Pain Control	Other Postoperative Outcomes and Additional Notes
Chern et al 2013 (25)	37y F	24 mg	BOAT bridged to hydromorphone	Vaginal mesh removal and cystoscopy	Noted to have opioid tolerance and high doses of opioids used for pain management.	Not stated.	Transitioned to oral. Hydromorphone and discharged with instructions to follow-up with her BOAT provider.
Brummett et al 2009 (26)	41y M	16 mg	BOAT interrupted; timing not stated	Spinal surgery	High doses of opioids with intensive care unit admission for 2-day dexmedetomidine infusion for rescue.	Uncontrolled postoperative pain.	Discharged off OAT and on morphine and oxycodone.
Harrington and Zaydfudim 2010 (27)	20y M	2 mg	BOAT interrupted	Multitrauma with TBI and associated agitation	High opioid requirements postinjury with analgesic requirements declining on POD 4.	Not stated.	BOAT reinitiated on POD 4 with subsequent escalation of opioid requirements. Discharged on POD 6 with 120 mg daily oxycodone.
McCormick et al 2013 (28)	50y M	Not reported	BOAT interrupted	Acute pain crisis secondary to compartment syndrome related to McArdle disease requiring fasciotomies	High doses of IV hydromorphone (8 mg) for first 8 hours, then IV PCA 0.5 mg bolus with 15-minute lockout. Postoperative basal requirements of 0.5-0.8 mg per hour. Transitioned to oxycodone, oral hydromorphone, and acetaminophen on POD2.	POD 2 pain scores of 3/10.	Discharged off BOAT and transitioned back to BOAT 2 months postoperative.
Rodgman and Pletsch 2012 (29)	29y F	Not reported	BOAT interrupted 12 hours preoperatively	Heart transplant (for familial cardiomyopathy)	Opioids, total doses not reported.	Pain scored not reported.	BOAT reinitiated on POD 7 with transient increase in pain scores. Discharged on double preoperative BOAT dose and gabapentin.

Abbreviations: F, female; IV, intravenous; M, male; PCEA, Patient-controlled epidural analgesia; POD #, postoperative day #; SQ, subcutaneous; TBI, traumatic brain injury.
*These were case series but only one case met inclusion criteria.

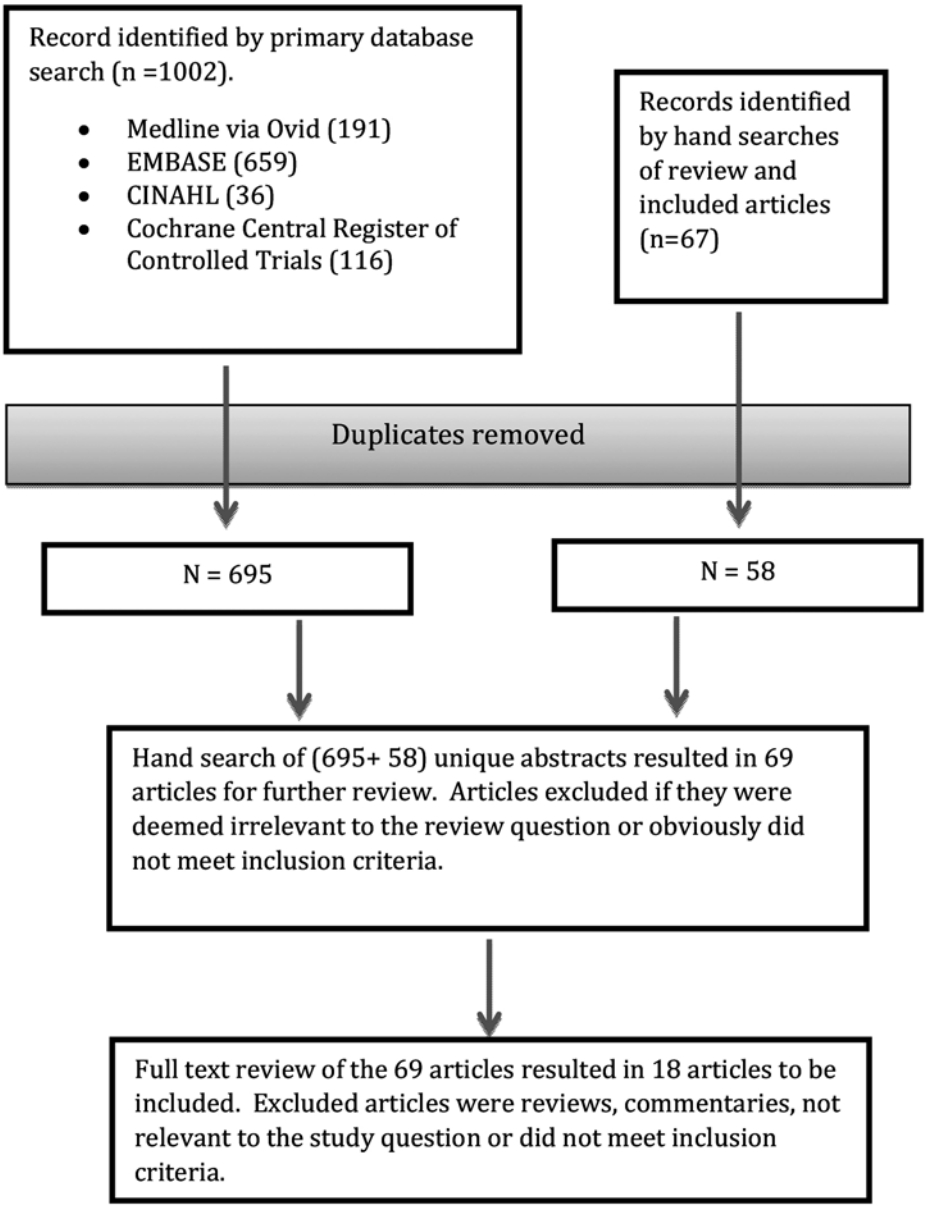

Fig. 1. *PRISMA diagram of selection of studies.*

Summary of Articles in Which BOAT was Interrupted

In 4 case reports, BOAT was interrupted with the attempt of using other strategies to manage pain. Brummett et al (26) reported use of dexmedetomidine infusion for a patient who experienced uncontrolled postoperative pain, despite high doses of opioids, after spinal surgery. This patient was discharged on morphine and oxycodone; no follow-up regarding BOAT was mentioned.

Harrington and Zaydfudim (27) reported a 30-year-old man who presented with polytrauma after a motorcycle accident. His pain was initially difficult to treat, but responded to higher doses of opioids. On postadmission day 3, his BOAT was restarted, and he experienced unpleasant symptoms and increased opioid use.

Table 2. *Summary of case series.*

Article (authors and year)	Patient Age and Gender	Daily BOAT Dose	Perioperative BOAT Management Strategy	Procedure or Injury	Pain Management Strategy	Pain Scores or Quality of Pain Control	Other Postoperative Outcomes and Additional Notes
Heit and Gourlay 2008 (17)	24y F	16 mg	BOAT continued	Posterior tibial tendon repair	Fentanyl PCA and BOAT increased to 24 mg daily.	Not reported.	Discharged on hydromorphone 8 mg daily for 6 weeks, with subsequent resumption of baseline BOAT. No relapse of OUD.
	42y M	4 mg	BOAT continued	Wrist injury and laceration	BOAT increased to 8 mg daily.	Not reported.	No relapse of OUD.
	59y F	16 mg	BOAT continued	Cervical spine fusion	Fentanyl PCA.	Not reported.	Discharged on hydromorphone 8 mg daily for 4 weeks, with subsequent resumption of baseline BOAT. No relapse of OUD.
Kornfeld and Manfredi 2010 (18)	60y M	24 mg	BOAT continued	Right colectomy	Epidural containing morphine and morphine IV PCA with doses up to 27 mg/day tapered to 6 mg/day predischarge. BOAT increased to 32 mg/day.	Pain control outcomes positive, "pain free."	Discharged on POD 9 on 32 mg BOAT and PO hydrocodone 10 mg for breakthrough pain.
	43y M	12 mg	BOAT continued	R knee replacement	Epidural with bupivacaine and single dose morphine (0.2 mg) for 48 hours, IV hydromorphone until POD 3, then PO hydromorphone and oxycodone, and ketamine.	"Excellent pain management."	Discharged on POD 4 with increased dose of BOAT (16 mg) and hydromorphone for breakthrough pain.
	43y M (same patient as previous)	12 mg	BOAT interrupted	L knee replacement (2 years post-R knee replacement)	Epidural bupivacaine and opioids (hydromorphone averaging 7 mg/day and fentanyl 70 mcg/day for 48 hours), IV and PO opioids, and IV and PO ketamine.	"Excellent analgesia."	Discharged on POD 3 with BOAT restarted.
	60y M	2 mg	BOAT interrupted	Small bowel resection	Hydromorphone 1 mg in recovery room, Epidural bupivacaine and average of 0.2 mg/hour epidural hydromorphone until POD 3, IV PCA hydromorphone averaging 5-10 mg daily until POD 4.	Good pain control from POD 1 to 4, "good analgesia."	IV BOAT restarted on POD 3. Discharge on POD 5 with home dose sublingual BOAT.
	42y F	8 mg	BOAT interrupted (dose reduced to 2 mg daily)	Bilateral mastectomy with reconstruction	Accufuser local anesthetic pump with bupivacaine and PCA-like push button, IV PCA hydromorphone averaging 26 mg/day until POD 2, PO hydromorphone up to 96 mg and additional IV hydromorphone up to 16 mg.	Higher pain scores but responded to hydromorphone, "Pain fluctuates…responds to hydromorphone."	Discharged on POD 4 with home dose of BOAT and PO hydromorphone for breakthrough pain.
	42y F (same patient as previous)	6 mg	BOAT continued	Removal bilateral breast tissue expanders and reconstruction (8 months postmastectomy)	Accufuser local anesthetic pump with bupivacaine and PCA-like push button, IV hydromorphone (5.4 mg on POD 1) and PO hydromorphone (16 mg on POD 1).	"Good pain control."	Discharged on POD 2 with PO hydromorphone for breakthrough pain.
	58y M	16 mg	BOAT interrupted (dose reduced to 3 mg on POD 1)	X-STOP removal from lumbar spine and lumbar decompression at 2 levels	200 mcg IV fentanyl and 4 mg IV hydromorphone in recovery room, then IV PCA with hydromorphone on (20 mg total on POD 1).	"Excellent pain control."	Discharged on POD 2 on home dose of BOAT with hydromorphone for breakthrough pain.

Table 2 (cont). *Summary of case series.*

Article (authors and year)	Patient Age and Gender	Daily BOAT Dose	Perioperative BOAT Management Strategy	Procedure or Injury	Pain Management Strategy	Pain Scores or Quality of Pain Control	Other Postoperative Outcomes and Additional Notes
Tith et al 2018* (20)	37y F	8 mg	BOAT continued	C-section	Labor epidural analgesia, postoperative IV hydromorphone, PO oxycodone, hydromorphone, acetaminophen, and ibuprofen.	Inadequate, VAS scored 0 to 5 on PP 1.	Discharged on POD 6 with 10-day supply of hydromorphone 2-4 mg PO q4h.
	27y F	8 mg	BOAT continued	C-section	Hydromorphone PCA with PO oxycodone, acetaminophen, and ibuprofen.	Satisfactory, VAS scored 0 to 8 on PP 1.	Discharged POD 1 with 7-day supply of oxycodone 5-15 mg q3h.
	34y F	8 mg	BOAT continued	Vaginal delivery	PO hydromorphone, acetaminophen, and ibuprofen.	Quality not reported, VAS scores 0 to 7 on PP 1.	Discharge PP1 with no opioids. Had postdural puncture headache treated with epidural blood patch.
	28y F	24 mg	BOAT continued	C-section	IV fentanyl PCA, IV ketamine, IV benzodiazepines PO hydromorphone, acetaminophen, and ibuprofen.	Satisfactory, VAS scores 6 to 8 on POD 1.	Discharged on POD 2 with 10-day supply of hydromorphone 4 mg q6h.
	21y F	4 mg	BOAT continued	Vaginal delivery	Labor epidural analgesia, postpartum hydromorphone PCA, PO oxycodone, acetaminophen, and ibuprofen.	Satisfactory, VAS scores – 0 to 4 on PP 1.	Discharged on PP 3 with no opioids.
	22y F	16 mg	BOAT continued	C-section	Labor epidural analgesia, postoperative hydromorphone PCA, PO hydromorphone, acetaminophen, and ibuprofen.	Satisfactory, VAS scores 2 to 8 on POD 1.	Discharged on POD 2 with 36 tablets of 2 mg hydromorphone.
	35y F	16 mg	BOAT continued	Vaginal delivery	Acetaminophen and ibuprofen.	Satisfactory, VAS pain scores 2 to 7 on PP 1.	Discharged on POD 2 with no opioids.
	34y F	2 mg	BOAT continued	C-section	Labor epidural analgesia, postoperative hydromorphone PCA, PO oxycodone, acetaminophen, and ibuprofen.	Quality not reported, VAS scores 2 to 9 on POD 1.	Discharged on POD 5 with 30 tablets of 5 mg oxycodone.

Abbreviations: F, female; IV, intravenous; L, left; M, male; PO, oral; POD #, postoperative day #; PP #, postpartum day #; R, right; VAS, Visual Analog Scale.
*These were case series but only one case met inclusion criteria.

Table 3. *Summary of retrospective cohort studies*.

Article (authors and year)	Average Daily BOAT Dose	Perioperative BOAT Management Strategy and Number of Patients	Procedure or Injury	Summary and Reported Outcomes
Meyer et al 2010 (21)	13.7 mg	BOAT continued in 63 patients.	Parturient with either C-section or vaginal delivery.	This study of 63 parturient on BOAT compared outcomes to matched controls. A total of 88% of included patients had neuraxial techniques prior to delivery. Opioid use was higher in C-section group on BOAT.
MacIntyre et al 2013 (23)	13.7 mg (range 4-32 mg)	BOAT continued in 11 patients; BOAT disrupted in 11 patients.	7 orthopedic, 5 abdominal, 4 orofacial, 4 thoracic, and 2 other procedures.	This retrospective study compared patients on MOAT and BOAT. For the 22 patients in the BOAT group, 11 were continued on their usual BOAT. Of the 11 who did not receive their BOAT on the first day after surgery, 8 also did not receive on the day of surgery. The only statistically significant finding was that patients who had BOAT continued had less PCA use and were also receiving less adjuvants including NSAIDs and ketamine.
Vilkins et al 2017 (22)	16.1 mg	BOAT continued in 88 patients.	Parturient with either C-section or vaginal delivery.	This study focused on postoperative opioid requirements comparing a group of BOAT maintained parturients to those on MOAT. They noted a higher use of ketorolac but less spinal analgesia in the BOAT group.

Abbreviation: MOAT, methadone opioid agonist therapy.

His opioid use decreased on stopping BOAT, and he was discharged on oxycodone 120 mg daily.

McCormick et al (28) described a 50-year-old patient with McArdle disease who presented in acute pain crisis due to compartment syndrome. His BOAT was not continued in the hospital. He initially received 12 mg hydromorphone intravenously over 8 hours, with minimal pain relief. He then underwent emergent bilateral fasciotomies, and postoperative pain was treated with a hydromorphone PCA at 0.8 mg as needed with a 15-minute lockout and basal rate of 0.5 mg/hr. He was discharged on postoperative day 2 with a pain score of 3out of 10 after transitioning to oral oxycodone and hydromorphone-acetaminophen. His BOAT was restarted 2 months later.

Finally, a complex patient with familial cardiomyopathy and iatrogenic opioid dependence had BOAT interrupted 12 hours before heart transplant (29). Her postoperative pain was treated with opioids. Restarting her BOAT 1 week later was associated with a transient increase in pain scores. She was discharged on twice her usual dose of BOAT, as well as gabapentin.

Discussion

How to best treat pain in a patient on BOAT has been controversial. The main strategies of either continuing or stopping BOAT before an operation have been largely based on anecdote and theory. We sought to review all published literature on patients taking BOAT who presented for surgery or in acute pain, thus providing a more evidence-based rationale to managing patients on BOAT.

As there are no RCTs to settle this issue, we must work with case reports, case series, and retrospective cohort studies. These studies do not consistently support the concern that continuing buprenorphine interferes with the ability to treat surgical or nonsurgical acute pain. Of the 5 case reports in which BOAT was continued before surgery, 3 reported at least adequate pain control (12-14). Two case series reported no special difficulty in acute pain management (17,18). Such findings are consistent with in vivo data that suggest buprenorphine does not block other opioids and is a good analgesic (8).

The evidence for continuing BOAT in parturients seems compelling, as 2 retrospective cohort studies concluded that adequate pain management is possible in vaginal or operative delivery (21,22). Meyer et al (21) noted that overall pain scores and opioid use were modestly higher than in matched controls not taking OAT. This heightened pain response is expected and has been demonstrated in OAT (30). Vilkins et al (22) found

that pain control in BOAT is noninferior to methadone. A multicenter RCT found that neonates of mothers on BOAT had better outcomes than those of mothers on methadone (31). Therefore continuing BOAT through the peripartum period seems appropriate.

Patients taking BOAT may have refractory pain and may require extremely high doses of opioids. McCormick et al (28) reported difficulty treating pain after fasciotomies for compartment syndrome in a patient with McArdle disease, citing inadequate dosing of hydromorphone PCA. Increasing the dose to 0.8 mg as needed with a 15-minute lockout and a basal rate of 0.5 mg/h decreased pain intensity to 3 out of 10. Brummett et al (26) reported decreasing pain scores to 4 out of 10 after spine surgery with multimodal analgesia and high doses of opioids, but on transfer to the ward pain became unmanageable despite 167 mg morphine by PCA over 13 hours. In this case, transfer to the intensive care unit for combination of dexmedetomidine infusion and hydromorphone PCA 0.5 mg with a 6-minute lockout and 0.5 mg/hr basal rate improved pain to "acceptable."

The potential blocking effect of buprenorphine has been cited as contributing to such difficulty treating acute pain. However, refractory pain could be associated with opioid tolerance, which is not specific to buprenorphine. As mentioned, Vilkins et al (22) found no difference in analgesic requirements between buprenorphine and methadone maintenance in women having caesarean sections. Methadone and other opioids have also been implicated in refractory pain, and dexmedetomidine used as a rescue (32).

Interestingly, bridging BOAT preoperatively was only described in 2 case reports (24,25). Israel and Poore (24) reported switching to fentanyl patch 3 days before bilateral mastectomies. Pain control with fentanyl patch and PCA was initially poor, but improved after discontinuing PCA and adding oxycodone 30 mg q3h and acetaminophen. Chern et al (25) described a 37-year-old woman who had urogynecologic procedures on separate occasions. For the first procedure she continued buprenorphine up to the day of surgery, and for the second she switched to hydromorphone 5 days before surgery. Her pain was poorly controlled in both situations; bridging BOAT offered no advantage.

Silva and Rubinstein (14) also reported a patient undergoing 2 separate but similar operations. A 53-year-old man continued buprenorphine 8 mg 3 times a day throughout a TKA. Pain was treated with femoral nerve block and hydromorphone PCA, and he tapered off additional opioids over 16 weeks with good pain control throughout, using 6,500 mg morphine equivalents. He then transitioned from BOAT to hydrocodone in hopes of tapering off all opioids. Two years later, he had a contralateral TKA while taking hydrocodone 80 mg daily. His pain was poorly controlled despite a similar analgesic strategy, and he could not participate in physical therapy because of pain, required manipulation under anesthesia, and used a total of 25,200 mg morphine equivalents.

Rodgman and Pletsch (29) reported stopping BOAT 12 hours before successful perioperative management of a heart transplant. The 31- to 42-hour elimination half-life of buprenorphine in plasma may suggest it was still in the patient's system, although the effective half-life may be shorter (33). Pain was initially controlled with opioids, but increased to 8 out of 10 on reinitiating BOAT 1 week later, suggesting the phenomenon of precipitated withdrawal.

Precipitated withdrawal, rather than maintenance therapy itself, may have also been implicated in the case of a 30-year-old man posttrauma from a motorcycle collision and requiring high doses of opioids for pain control. His clinical picture was confounded by traumatic brain injury and agitation. His agitation and analgesic needs declined 4 days after injury, and restarting his BOAT was associated with increasing agitation and analgesic requirements.

The case of a 37-year-old woman continuing BOAT 24 mg daily throughout removal of breast implants was particularly interesting, as buprenorphine-naloxone itself was used as the postoperative analgesic (13). She was prescribed 2 to 4 mg q4h as needed in addition to her baseline dose, using 72 mg total on each of the first 2 days postoperatively. By day 11, she had tapered back to her baseline dose. Her high but effective use of buprenorphine-naloxone offers evidence against a ceiling effect or concerns that naloxone component interferes with analgesia. Heit and Gourlay (17) also described using increased dose of BOAT as the sole analgesic, from 4 to 8 mg for 1 week, following a deep laceration to the wrist.

Strategies of multimodal analgesia, maximizing nonopioids analgesics, and using regional anesthetic techniques have been promoted in the setting of opioid tolerance. The effectiveness of intravenous regional anesthesia, epidural anesthesia, and peripheral nerve block for patients on BOAT was demonstrated in our

review (14-16). Thus we echo recommendations to use regional anesthetic techniques when possible in the setting of BOAT.

The studies reviewed variably reported difficulties in treating pain in patients taking BOAT; however, no clear link emerged between continuing BOAT and these challenges. It remains possible that the challenges encountered are related to opioid tolerance in general and the nature of OUD, rather than the pharmacodynamic properties of buprenorphine. These observations agree with recent guidelines recommending continuing BOAT perioperatively when possible (34).

The strategies of stopping or bridging BOAT to another opioid may be associated with harm, as only McCormick et al (28) reported the patient returning to his maintenance dose after disruption of BOAT. If patients discontinue their BOAT, regardless of cause, most will relapse to opioid use within 1 month (35). Furthermore, bridging to another opioid requires extra coordination from the patient and medical team, which does not seem justified by a clear benefit.

To help meet the complex needs of patients with OUD, many hospitals now incorporate addiction medicine consult teams (AMCT). An AMCT may integrate the expertise of physicians, nurses, pharmacists, counsellors, and peer support workers, improving the care and hospital experience of the patient with OUD (36). An interdisciplinary approach can also be helpful for discharge planning, community support, and ongoing follow-up.

Our study clearly has limitations. Conclusions drawn from heterogeneous, observational studies are inherently limited, and we found no prospective studies. Some studies omitted relevant details, such as the quality of pain postoperatively. Nevertheless, we hope that a systematic approach has identified trends that may better influence decision-making in this area, as well as areas for further research to better support this patient group in their perioperative course.

Conclusions

Indeed, pain was often difficult to treat whether BOAT was continued or stopped. There was no clear advantage to discontinuing buprenorphine; however, there is potential for harm with this strategy, as some patients many not be transitioned back to maintenance therapy and risk relapse of OUD. Many patients maintained on BOAT obtained acceptable analgesia. We recommend continuing BOAT throughout the operative period in most cases, with an interdisciplinary approach incorporating multimodal analgesia.

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Author contributions: Dr. Mehta had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses. Dr Mehta, Mr. Thomas, and Dr. Johnson designed the study protocol. Ms. Scott designed and implemented the systematic search protocol. Dr. Mehta managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Dr. Mehta and Mr. Thomas acted as primary and secondary reviewers for included studies and data extraction. Drs. Berger, Cortina, and Johnson acted as additional reviewers, conducting initial screens of search results and hand searches of article references. Ms. Scott specifically provided review of methods and literature search design. Drs. Berger, Cortina, and Johnson, and Mr. Thomas provided revision for intellectual content and final approval of the manuscript.

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