

A Retrospective Study of Liposomal Bupivacaine Versus Conventional Bupivacaine on Opioid Use and Healthcare Resource Utilization Following DIEP Flap Breast Reconstruction

Rebecca Knackstedt,¹ Jennifer H. Lin,² Swapnabir Kakoty²

¹Division of Plastic, Maxillofacial and Oral Surgery, Duke University Medical Center, Durham, NC;

²Pacira BioSciences, Inc., Parsippany, NJ

Presented at: 68th Annual Meeting of the Plastic Surgery Research Council; April 13-16, 2023; Cleveland, OH

Disclosures

RK has received travel funds from Pacira BioSciences, Inc.

JHL and SK are employees of Pacira BioSciences, Inc., and may own stock or stock options in the company

Patients Undergoing Breast Reconstruction Can Experience Significant Postoperative Pain and Can Develop Persistent Pain^{1,2}



Local anesthetics, including ConvB, are often used in enhanced recovery pathway protocols and have been explored to treat pain in patients undergoing DIEP flap procedures³⁻⁶



LB uses proprietary multivesicular liposome technology to safely deliver bupivacaine over time for extended analgesia³



Although previous studies of breast reconstruction, including DIEP flap procedures, have suggested LB is associated with reduced postsurgical opioid consumption, postdischarge outcomes have not been previously evaluated³⁻⁶

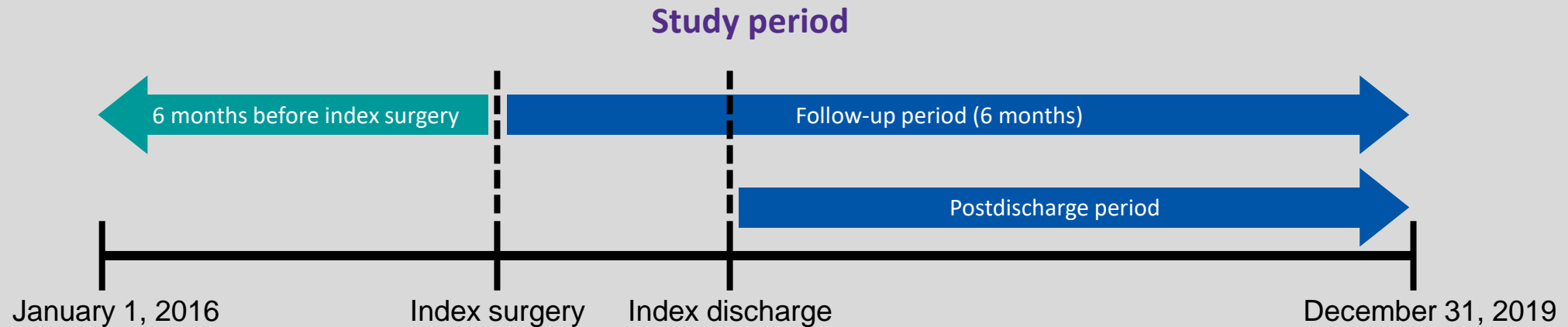
- **This study examined real-world clinical and economic benefits of LB after breast reconstruction**

ConvB, conventional bupivacaine; DIEP, deep inferior epigastric perforator; LB, liposomal bupivacaine.

1. De Oliveira et al. *Breast*. 2014;23(4):329-333. 2. Roth et al. *Breast*. 2018;37:119-125. 3. Haddock et al. *Plast Reconstr Surg*. 2021;148:948-957. 4. Rendon et al. *Plast Reconstr Surg Glob Open*. 2022;10:e4010. 5. Afonso et al. *Plast Reconstr Surg*. 2017;139:1053-1061. 6. Gatherwright et al. *Plast Reconstr Surg*. 2018;141:1327-1330.

Methods: Study Period and Patient Eligibility

- Retrospective study using deidentified patient records from the IQVIA linkage claims databases who underwent inpatient DIEP flap reconstruction between 2016 and 2019*



Inclusion criteria

- Women undergoing primary open breast reconstruction*
- Received LB (treatment cohort) or ConvB (comparator cohort) for postsurgical analgesia
- ≥ 18 years of age
- ≥ 6 months of continuous enrollment before and after surgery

Exclusion criteria

- Hospital LOS was >95 th percentile of the respective distribution
- MMEs were >95 th percentile of the respective distribution

*DIEP flap reconstruction defined by the International Classification of Diseases, 10th Revision procedure codes 0HRT077, 0HRU077, and 0HRV077.
ConvB, conventional bupivacaine; DIEP, deep inferior epigastric perforator; LB, liposomal bupivacaine; LOS, length of stay; MME, morphine milligram equivalent.

Methods: Outcomes and Statistical Analysis

Outcomes

Opioid use in MMEs	HRU
<ul style="list-style-type: none">• Perioperative period (2 wk before to 2 wk after surgery; opioid intake)<ul style="list-style-type: none">• 72-h postsurgical period• In-hospital period• Postoperative period (filled prescriptions)<ul style="list-style-type: none">• Continued (>2 wk to 3 mo)• Persistent (>3 mo to 6 mo)	<ul style="list-style-type: none">• In-hospital<ul style="list-style-type: none">• LOS• Postdischarge<ul style="list-style-type: none">• Inpatient admissions• ED visit• Outpatient clinic/office visit

Statistical Analysis



Age



Rural or urban location



Breast laterality



Surgery year



Insurance type



Provider region



Teaching hospital status



Quan-Charlson Comorbidity Index



History of cancer or metastatic cancer








Prior opioid exposure

Treatment (LB) and comparator (ConvB) groups were weighted by the above baseline characteristics using the IPTW method and compared using generalized linearized modeling

Results: Patient Characteristics

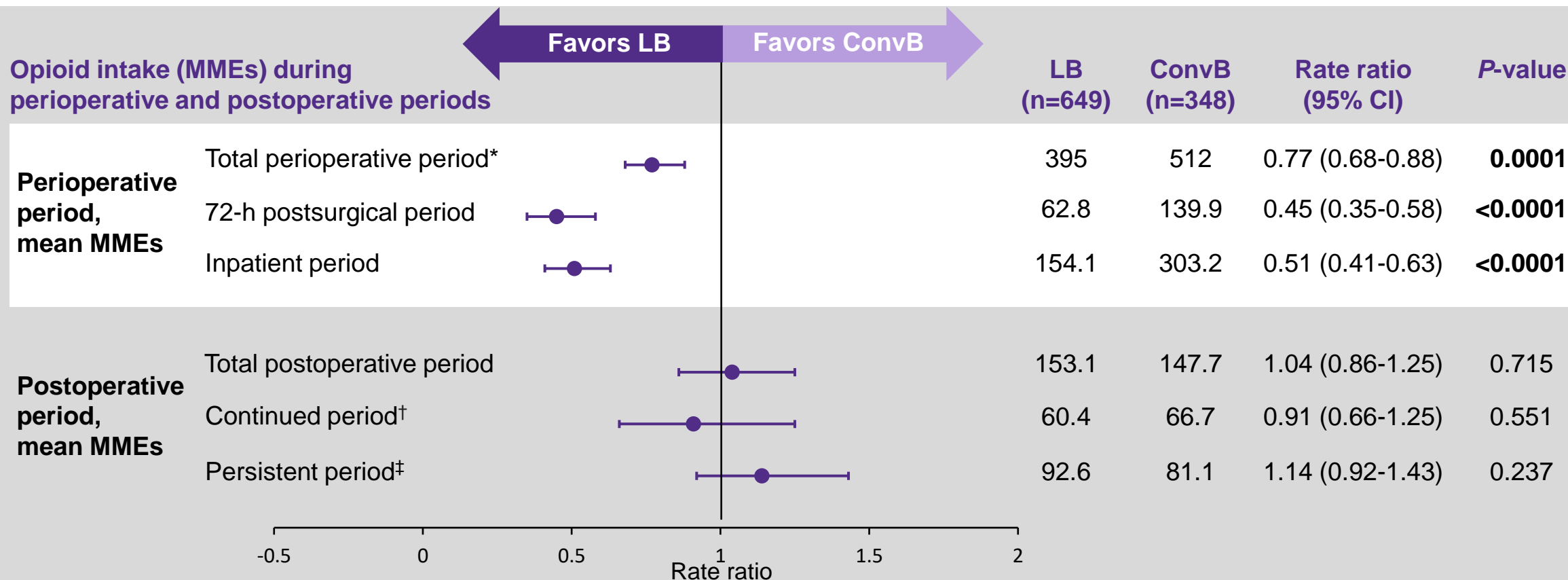
- In total, 1017 women (669 LB and 348 ConvB) were included in the analysis

Baseline patient characteristics	Unweighted		Weighted		
	LB (n=669)*	ConvB (n=348)*	LB (n=669)*	ConvB (n=348)*	Standardized difference
 Age, y	51.7 (9.8)	50.4 (9.2)	51.5	51.2	-3.0%
 Quan-Charlson Comorbidity Index	2.4 (2.5)	2.8 (2.71)	2.7	2.5	-6.2%
 Unilateral Bilateral	295 (44.1)	93 (26.7)	39.4	45.3	12.1%
	374 (55.9)	255 (73.3)	60.6	54.7	-12.1%
 Opioid Naive	408 (61.0)	152 (43.7)	56.7	56.9	0.4%
 Cancer History	459 (68.6)	270 (77.6)	72.6	66.9	-12.4%

All baseline characteristics, including age, comorbidities, and proportion of opioid-naive participants, were balanced between groups after weighting, with a standardized difference <20% across variables

*Values are the mean (standard deviation) for age and Quan-Charlson Comorbidity Index, and n (%) in unweighted and % in weighted for all others.
ConvB, conventional bupivacaine; LB, liposomal bupivacaine.

Results: Perioperative and Postoperative Opioid Use

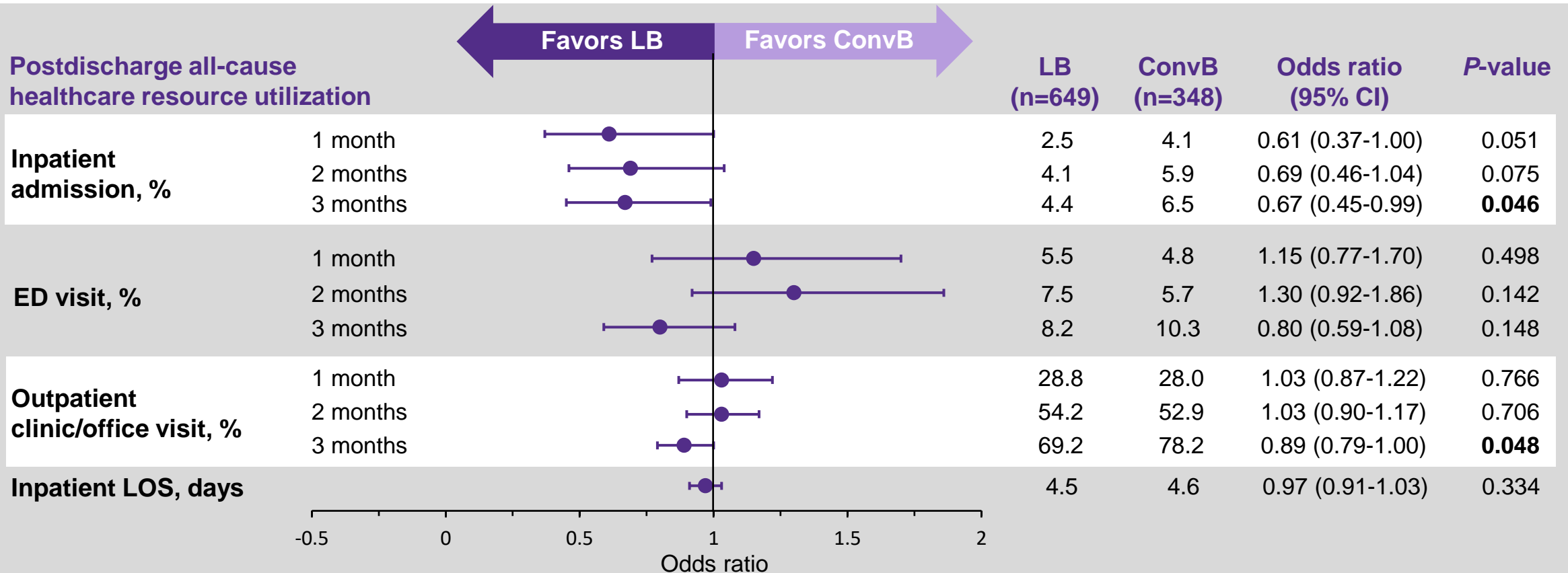


Total inpatient opioid intake during the perioperative period was significantly less in the LB cohort compared with the ConvB cohort
No patients in either group developed opioid use disorder after discharge

*Perioperative period includes 2 weeks before surgery to 2 weeks after discharge. [†]Continued period includes >2 weeks to 3 months after discharge. [‡]Persistent period includes >3 months to 6 months after discharge.

CI, confidence interval; ConvB, conventional bupivacaine; LB, liposomal bupivacaine; MME, morphine milligram equivalent.

Results: Healthcare Resource Utilization



At 3 months after discharge, the LB cohort was 33% less likely to be admitted to the hospital and 11% less likely to have outpatient visits compared with the ConvB cohort

Study Limitations and Conclusions



Limitations

- Patients may have received additional pain management regimens other than LB or ConvB, which could confound comparisons
- Filled opioid prescriptions after discharge may not indicate opioid consumption
- Pain scores were unavailable and prevented direct comparison of perioperative and postoperative pain control to complement opioid intake observations
- Some surgical details (eg, immediate or delayed mastectomy) were unavailable for analysis



Conclusions

- In this real-world analysis, pain management with LB for DIEP flap breast reconstruction was associated with reduced in-hospital opioid intake
- Marginal significant improvements in some postdischarge HRU measures in favor of LB are of interest; however, the underlying reason is unclear and further research is needed
- Prolonged opioid use in both cohorts after discharge underscores the need for judicious opioid practices

Appendix

Appendix: Opioid Intake by Laterality of Surgery

	LB (N=669)	ConvB (N=348)	MME Ratio (95% CI)	P-value
Unilateral surgery, n	295	93		
Perioperative opioid, MME	364.85	448.67	0.81 (0.65, 1.02)	0.08
72 hours postsurgery, MME	69.57	76.62	0.91 (0.58, 1.43)	0.68
Total inpatient opioid intake, MME	158.53	272.33	0.58 (0.40, 0.84)	0.00
Post perioperative filled opioid prescription, MME	116.01	127.91	0.91 (0.66, 1.25)	0.55
Continued opioid use,* MME	37.31	33.83	1.10 (0.65, 1.87)	0.72
Persistent opioid use, [†] MME	78.70	94.08	0.84 (0.57, 1.23)	0.36
Bilateral surgery, n	374	255		
Perioperative opioid, MME	414.51	564.48	0.73 (0.63, 0.86)	0.00
72 hours postsurgery, MME	58.34	192.27	0.30 (0.22, 0.41)	0.00
Total inpatient opioid intake, MME	151.17	328.75	0.46 (0.35, 0.60)	0.00
Post perioperative filled opioid prescription, MME	177.11	164.14	1.08 (0.85, 1.37)	0.53
Continued opioid use,* MME	75.44	93.87	0.80 (0.55, 1.19)	0.27
Persistent opioid use, [†] MME	101.67	70.27	1.45 (1.10, 1.91)	0.01

ConvB, conventional bupivacaine; LB, liposomal bupivacaine; MME, morphine milligram equivalent. *Continued period includes >2 weeks to 3 months after discharge.

[†]Persistent period includes >3 months to 6 months after discharge.

Appendix: Opioid Intake by Opioid Experience

	LB (N=669)	ConvB (N=348)	MME Ratio (95% CI)	P-value
Opioid-naive, n	408	152		
Perioperative opioid, MME	308.37	359.50	0.86 (0.69, 1.06)	0.15
72 hours postsurgery, MME	63.73	70.97	0.90 (0.62, 1.31)	0.57
Total inpatient opioid intake, MME	136.29	232.69	0.59 (0.43, 0.81)	0.00
Post perioperative filled opioid prescription, MME	97.12	78.96	1.23 (0.89, 1.71)	0.21
Continued opioid use,* MME	37.17	19.51	1.91 (1.11, 3.28)	0.02
Persistent opioid use, [†] MME	59.95	59.45	1.01 (0.69, 1.48)	0.96
Opioid-experienced, n	261	196		
Perioperative opioid, MME	508.37	713.17	0.71 (0.62, 0.83)	0.00
72 hours postsurgery, MME	61.48	230.72	0.27 (0.19, 0.38)	0.00
Total inpatient opioid intake, MME	177.35	396.18	0.45 (0.34, 0.60)	0.00
Post perioperative filled opioid prescription, MME	226.30	238.43	0.95 (0.76, 1.18)	0.64
Continued opioid use,* MME	90.89	128.86	0.71 (0.48, 1.03)	0.07
Persistent opioid use, [†] MME	135.42	109.57	1.24 (0.95, 1.61)	0.11

ConvB, conventional bupivacaine; LB, liposomal bupivacaine; MME, morphine milligram equivalent. *Continued period includes >2 weeks to 3 months after discharge.

[†]Persistent period includes >3 months to 6 months after discharge.

Appendix: Additional Baseline Patient Characteristics

	Unweighted			Weighted		
	LB (n=669)*	ConvB (n=348)*	Standardized difference, %	LB, %	ConvB, %	Standardized difference, %
Index surgery year						
2016	199 (29.8)	84 (24.1)	-12.7	28.1	31.1	6.4
2017	192 (28.7)	89 (25.6)	-7	26.6	23.8	-6.3
2018	219 (32.7)	147 (42.2)	19.7	35.5	36	1.1
2019	59 (8.8)	28 (8.1)	-2.8	9.8	9.1	-2.4
History of metastatic cancer	77 (11.5)	52 (14.9)	10.1	13.4	12.9	-1.7
Payer						
Medicaid	3 (0.5)	4 (1.2)	7.9	0.6	0.5	-0.2
Medicare	34 (5.1)	14 (4.0)	-5.1	4.6	3.2	-7.3
Third party	327 (48.9)	266 (76.4)	59.4	58.4	50.6	-15.8
Unknown	305 (45.6)	64 (18.4)	-61.0	36.4	45.6	18.9

After inverse treatment probability weighting, the 2 cohorts were balanced in all characteristics with a standardized difference <20%

*Values are the n (%).

ConvB, conventional bupivacaine; LB, liposomal bupivacaine.

Appendix: Additional Hospital Characteristics

	Unweighted			Weighted		
	LB (n=669)*	ConvB (n=348)*	Standardized difference, %	LB, %	ConvB, %	Standardized difference, %
Hospital location						
Rural	0 (0.0)	1 (0.3)	NA	NA	NA	NA
Urban	669 (100.0)	347 (99.7)	NA	NA	NA	NA
Teaching hospital						
Yes	383 (57.3)	88 (25.3)	-68.6	47.2	54.6	14.9
No	259 (38.7)	166 (47.7)	14.6	40.6	34.5	-12.6
Unknown	27 (4.0)	94 (27.0)	66.9	12.3	10.9	-4.2
Provider region						
Midwest	3 (0.5)	3 (0.9)	5.1	0.8	0.9	1.3
Northeast	69 (10.3)	38 (10.9)	2	10.8	11	0.7
South	459 (68.6)	277 (79.6)	25.3	72.2	78.4	14.4
West	138 (20.6)	30 (8.6)	-34.5	16.3	9.7	-19.6

After inverse treatment probability weighting, the 2 cohorts were balanced in all characteristics with a standardized difference <20%

*Values are the mean (standard deviation) for age and Quan-Charlson Comorbidity Index, and n (%) in unweighted and % in weighted for all others.
ConvB, conventional bupivacaine; LB, liposomal bupivacaine; NA, not applicable.