EXPAREL®

(bupivacaine liposome injectable suspension)

Dossier

TABLE OF CONTENTS

Contents

THE DISEASE OF PAIN

Surgical procedures can produce tissue damage and pain from 3 separate quarters: somatic tissue (bone, joint, muscle, skin, or connective tissue), visceral (caused by damage to/manipulation of the viscera or chest cavity), and the nervous system.[1] Somatic or visceral pain is evoked when noxious thermal, mechanical, and/or chemical (e.g., release of potent inflammatory mediators) stimuli are detected by peripheral nerve fiber nociceptors. Nociceptors in visceral structures are highly sensitive to stretch, ischemia, and inflammatory mediators, while somatic tissue contains nociceptors of both deep (tendons, bones, blood vessels, muscles, etc.) and superficial (skin) origin. Neuropathic pain occurs when neurons are directly impaired or damaged as a result of the procedure.[1] The degree to which a patient experiences one or more of these types of pain is determined by the type and duration of the surgery they undergo.[1] Beyond the initial assault (surgery), pain also arises from ongoing stimuli during the recovery phase when inflammatory mediators released around the incision site sensitize nociceptors in the normally silent primary afferent neurons (Aδ- and C-fibers).[1,2] No single anesthetic/analgesic is able to target all 3 types of pain (e.g., local anesthetics target only somatic pain), prompting physicians to explore a multimodal approach that utilizes different combinations of agents in the pursuit of effective postsurgical pain relief. Most patients who undergo surgery of any kind experience pain that persists for at least several days, or longer if they have undergone more extensive surgery.[3-7] Appropriate postsurgical pain management is therefore important to improve healing, fast-track patient mobilization, shorten hospital stays (in relation to extensive surgery), and reduce costs.[8-10]

DIESEASE EPIDEMIOLOGY

Ambulatory surgical centers (ASC) continue to perform more than half of all U.S. outpatient surgical procedures. ASC patient volumes increased 13% from pre-pandemic levels and exceeded 1.2 billion in June 2023. In the next ten years, ASCs are projected to experience 22% growth in procedure volumes.[11] Other national surveys have found that, among patients undergoing surgery, approximately 80% report pain that is moderate, severe, or extreme in intensity during the 2 weeks immediately following the procedure.[3,4] The most intense pain occurs on days 1 and 2 post- procedure with VAS indicating pain of moderate (score of 4-6) or severe (7-10) intensity particularly during the first 24 hours.[12-15] Unrelieved acute pain not only causes unnecessary patient suffering, it can also lead to other health problems, thus delaying recovery from surgery and hospital discharge, and resulting in higher healthcare costs.[16,17] Controlling acute postsurgical pain is also important because the intensity of acute pain is a predictor of ongoing chronic pain postsurgery.[5,18]

The incidence and severity of postsurgical pain can vary significantly from patient to patient, but is primarily determined by the type and duration of the surgery and the type of pain relief given intra- and postoperatively.[5-7,12,14,15,18,19] Approximately 25% to 40% of patients will experience moderate to severe pain within 24 hours of “minor” types of surgery (i.e., procedures that can be accomplished in the ambulatory setting),[12,14,15] while approximately 80% to 90% of inpatients experience moderate to extreme pain for up to 2 weeks following surgery.[3,4] After discharge, pain may continue to interfere with daily activities (e.g., sleep, work) for several days,[14,02] and the occurrence of severe pain at home may reflect inadequate pain control during the first few hours after surgery.[14]

OPIOID EPIDEMIC

Opioids are a mainstay of postsurgical pain control,[21] but are associated with a variety of unwanted and potentially severe side effects such as respiratory depression, drowsiness and sedation, postsurgical nausea and vomiting, pruritus, urinary retention, and ileus. ORADEs tend to increase in frequency with higher dosages,[22] and significantly increase LOS and the cost of care in postsurgical patients.[21-25] Increased costs are often related to the greater nursing time and monitoring associated with the risk and/or occurrence of delirium[26] or respiratory depression,[27] or the prolonged LOS caused by infection,[28] noninfectious complications (e.g., falls),[29] and delayed ambulation[28] associated with urinary catheterization. Opioids have been shown to be problematic in key patient populations, including:

- Elderly
- Comorbid airway disease (asthma, chronic obstructive pulmonary disease, obstructive sleep apnea)
- Chronic opioid users

In addition to these issues, opioids are highly addictive.[30] Their dependence and abuse has created an ongoing opioid crisis which has become a major public health problem in the United States, with half a million opioid overdose deaths in the last 20 years[31]. Deaths have risen rapidly since 2014, with nearly 70,000 in 2020 alone[31], driven in part by the continuing spread of illicit fentanyl and other deadly synthetic opioids.[31] Millions of people now suffer from opioid use disorder, with severe health, social, and economic consequences.[31] Opioids (including prescription opioids, heroin, and synthetic opioids such as fentanyl and its chemical analogs) are the leading cause of overdose deaths.[32]

MULTI-MODAL Treatment

Postsurgical pain management is challenging and complex because the pathophysiology of postsurgical pain is multifaceted. The current approach to treatment is therefore to employ a multimodal or "balanced" treatment approach using a variety of analgesic modalities, preventing postsurgical pain by combining opioid and non-opioid agents that act at different sites within the central and peripheral nervous systems to provide a broad spectrum of pain relief. While the main aim is to effectively reduce pain using all the pharmacological tools currently available, there is an increasing secondary drive toward minimizing opioid use and thus opioid-related side effects (approximately 98% of patients currently receive opioids for postsurgical pain relief in the United States).[19,33] This in turn hastens the recovery process, allows "fast-tracking" of patient ambulation and return to normal activities, and so reduces hospital stays and their associated costs.

Typically, surgeons initiate postsurgical pain relief intra-operatively or at the end of surgery with the administration of local anesthetics/analgesics such as bupivacaine HCl at the surgical site. Local agents are very effective, but relatively short acting (bupivacaine HCl is one of the longest-acting agents with a duration of approximately 7 hours).[34]

A medical need still exists to extend the pain relief supplied by bupivacaine HCl, thereby delaying, decreasing, and/or eliminating the need for opioids. In clinical studies, EXPAREL has been shown to extend pain relief up to 72 hours.[35] The 3-day pain relief provided by EXPAREL should simplify postsurgical pain management, minimize breakthrough pain episodes, and reduce opioid-specific side effects by reducing the need for supplemental opioid medications.[36]

Product Information

EXPAREL

EXPAREL® (bupivacaine liposome injectable suspension) is a liposomal injection of bupivacaine, an amide-type local anesthetic, indicated for single-dose local administration into the surgical site to produce postsurgical analgesia. After injection of EXPAREL into soft tissue, bupivacaine is released from the multivesicular liposomes providing effective local analgesia for up to 72 hours.

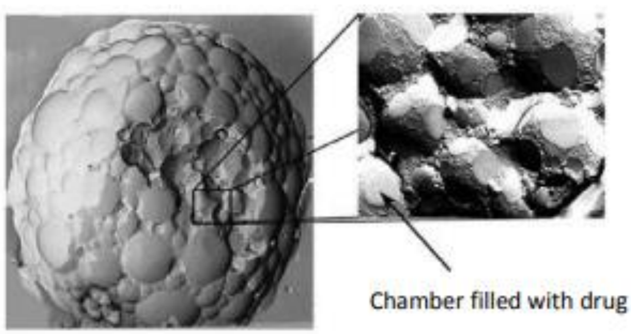
EXPAREL is indicated to produce postsurgical local analgesia via infiltration in patients aged 6 years and older and regional analgesia in adults via an interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and an adductor canal block. Safety and efficacy have not been established in other nerve blocks

EXPAREL utilizes a drug delivery technology called pMVL (proprietary multivesicular liposome) which allows the active drug to be released over a desired period without any alteration to the molecular structure.[35]

The multivesicular liposomal formulation of bupivacaine slowly releases bupivacaine over time and provides long-lasting analgesia in the first few days after surgery for postsurgical pain. [37,38]

pMVL (proprietary multivesicular liposome) technology

Figure 1: multivesicular liposome



pMVL (proprietary multivesicular liposome) is an advanced drug-delivery platform that encapsulates drugs without altering their molecular structure and then releases them over a desired period.[35]

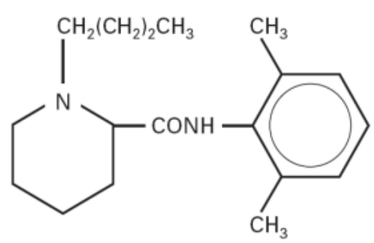
The drug delivery system consists of microscopic, polyhedral, lipid-based particles composed of a honeycomb-like structure of numerous, nonconcentric, internal aqueous chambers containing the encapsulated drug.[36] Each chamber is separated from adjacent chambers by lipid membranes. In vivo, the particles release the drug over an extended period by erosion and/or reorganization of the particles' lipid membranes. Release rates are determined by the choice and relative amounts of the lipids in the formulation. The lipids (i.e., phospholipids, cholesterol, and triglycerides) are naturally occurring or close analogues of endogenous lipids so they are well tolerated and cleared by normal metabolic pathways.[36]

pMVL technology achieves targeted analgesia at the surgical site, providing safe and consistent levels of bupivacaine.[35]

Pharmacology

The pharmacology of local anesthetics such as bupivacaine is well documented. Local anesthetics block nerve impulses by binding to sodium channels on the neuronal cell wall, preventing sodium influx, and therefore, preventing cell depolarization. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of effected nerve fibers. Nerve conduction is more readily hindered by anesthetics in sensory nerve fibers because these fibers have longer action potentials, allowing more anesthetic to bind. This means that small, unmyelinated C-fibers (which mediate pain) and small myelinated Aδ-fibers (which mediate pain and temperature sensation) are blocked more readily than larger myelinated Aγ-, Aβ-, and Aα-fibers (which mediate touch, pressure, muscle and postural sensations).[39] The potency of any given local anesthetic is governed by its lipid solubility. Agents that are highly lipid soluble are more able to penetrate connective tissue and cell membrane walls than those that are less soluble. The duration of action of local anesthetics is determined by the degree to which they bind proteins. Those with a high affinity for protein binding remain bound to nerve cells for longer, thus increasing their duration of action. Binding to serum proteins also reduces the potential for toxicity in primary organs by decreasing the drug availability in the blood.[40] Structurally, local anesthetics are characterized by a lipophilic aromatic ring and a hydrophilic molecule joined by a hydrocarbon chain. The molecule that links the aromatic ring to the hydrocarbon chain is what classifies local anesthetics as either ester (-CO-) or amide (-NHC-) anesthetics. Bupivacaine is an amide- type local anesthetic. It is a homologue of mepivacaine and is chemically related to lidocaine. Chemically, bupivacaine is 1-butyl-N-(2,6- dimethylphenyl)-2-piperidinecarboxamide and has a molecular weight of 288.4. The structural formula for bupivacaine is shown in **Figure 2** below:[41]

Figure 2: Structural formula of bupivacaine



EXPAREL is a sterile, nonpyrogenic, preservative-free aqueous suspension of multivesicular liposomes containing bupivacaine. Bupivacaine is present at a concentration of 13.3 mg/mL. Almost all of the bupivacaine in EXPAREL is encapsulated in the multivesicular liposomes, but a small amount (3%) is present as free bupivacaine. After injection of EXPAREL into soft tissue, the free bupivacaine is released immediately and the rest is released from the multivesicular liposomes over a period of time.[41]

EXPAREL Dosing

EXPAREL is available in the following single-dose vial sizes:

266 mg (20 ml) 13.3 mg/ml

133 mg (10 ml) 13.3 mg/ml

The **266 mg (20 mL) dose**
is appropriate for procedures such as*:

Abdominal/colorectal/general/urologic: abdominal wall reconstruction, bariatric, colectomy, hernia, TAP–block-based procedures, nephrectomy

Breast: mastectomy, reconstruction

OB/GYN: C-section, hysterectomy, myomectomy

Orthopedic: TKA, THA, fusions/fractures

Spinal: fusions, discectomy, laminectomy

Fascial plane blocks: TAP, ESP, rectus sheath, PECS I and II, QL

The **133 mg (10 mL) dose**
should be used for procedures that are limited to a small anatomical area, such as*:

Facial/plastic

Oral/maxillofacial

Upper extremity: interscalene brachial

Lower extremity: adductor canal block or sciatic nerve block in the popliteal fossa

EXPAREL Infiltration/Fascial Plane/Field Block

EXPAREL is administered via single-dose infiltration. When infiltrated into the surgical site, it produces local analgesia. [41]

It may also be infiltrated in the fascial plane to produce regional analgesia as a regional field block. A regional field block is accomplished by infiltrating a local anesthetic into a defined plane or compartment.[41]

Regional anesthetic techniques to produce regional analgesia include, but are not limited to, transversus abdominis plane (TAP) block, pectoralis (PEC) and serratus plane blocks, erector spinae plane (ESP) block and quadratus lumborum (QL) block.[42,43]

On December 14, 2015 the US Food and Drug Administration (FDA) provided clarification regarding the use of EXPAREL in a fascial plane or regional field block. It was the position of Janet Woodcock, MD Director Center for Drug Evaluation and Research FDA that “In a field block, local anesthetic is infiltrated around the border of the surgical field, leaving the operative area undisturbed. A field block is consistent with the procedure described in your hemorrhoidectomy trial submitted in support of EXPAREL's approval...Therefore, TAP blocks are covered by EXPAREL's labeling."[44]

References:

1. De Andres J, Fischer HBJ, Ivani G, et al. Postoperative pain management - good clinical practice. General recommendations and principles for successful pain management. Sodertalje, Sweden: European Society of Regional Anaesthesia and Pain Therapy; 2009.
2. Wu CL, Raja SN. Treatment of acute postoperative pain. Lancet. 2011;377(9784):2215-2225.
3. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg. 2003;97(2):534-540.
4. Warfield CA, Kahn CH. Acute pain management. Programs in U.S. hospitals and experiences and attitudes among U.S. adults. Anesthesiology. 1995;83(5):1090-1094
5. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. Anesthesiology. 2000;93(4):1123-1133.
6. Macrae WA. Chronic pain after surgery. Br J Anaesth. 2001;87(1):88-98.
7. Taillefer MC, Carrier M, Belisle S, et al. Prevalence, characteristics, and predictors of chronic nonanginal postoperative pain after a cardiac operation: a cross-sectional study. J Thorac Cardiovasc Surg. 2006;131(6):1274-1280
8. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology. 2012;116(2):248-273.
9. Coley KC, Williams BA, DaPos SV, Chen C, Smith RB. Retrospective evaluation of unanticipated admissions and readmissions after same day surgery and associated costs. J Clin Anesth. 2002;14(5):349-353.
10. Brooks JM, Titler MG, Ardery G, Herr K. Effect of evidence-based acute pain management practices on inpatient costs. Health Serv Res. 2009;44(1):245-263.
11. Accessed at: https://www.hida.org/uploadedfiles/research/market-reports/2023/samples/ambulatory-surgery-center-sample-market-report-dec23.pdf
12. McGrath B, Elgendy H, Chung F, Kamming D, Curti B, King S. Thirty percent of patients have moderate to severe pain 24 hr after ambulatory surgery: a survey of 5,703 patients. Can J Anaesth. 2004;51(9):886-891.
13. Lynch EP, Lazor MA, Gellis JE, Orav J, Goldman L, Marcantonio ER. Patient experience of pain after elective noncardiac surgery. Anesth Analg. 1997;85(1):117-123.
14. Beauregard L, Pomp A, Choiniere M. Severity and impact of pain after day-surgery. Can J Anaesth. 1998;45(4):304-311.
15. Gramke HF, de Rijke JM, Van Kleef M, et al. The prevalence of postoperative pain in a cross-sectional group of patients after day-case surgery in a university hospital. Clin J Pain. 2007;23(6):543-548.
16. Carr DB, Jacox A. Acute pain management: operative or medical procedures and trauma. U. S. Department of Health and Human Services, Agency for Healthcare Research and Quality http://www.ahrq.gov/clinic/medtep/acute.htm. Accessed September 22, 2014.
17. Pavlin DJ, Chen C, Penaloza DA, Polissar NL, Buckley FP. Pain as a factor complicating recovery and discharge after ambulatory surgery. Anesth Analg. 2002;95(3):627-634.
18. Gottschalk A, Ochroch EA. Clinical and demographic characteristics of patients with chronic pain after major thoracotomy. Clin J Pain. 2008;24(8):708-716.
19. Cost and quality imPlications of opioid-based post suRgical pain cOntrol in a large US integrated DeliVEry network: a study of cost outliers and opIoid relaTed adverse events (PROVE-IT-VHA). Chesterbrook, PA: AmerisourceBergen Consulting Services; 2011.
20. Watt-Watson J, Chung F, Chan VW, McGillion M. Pain management following discharge after ambulatory sameday surgery. J Nurs Manag. 2004;12(3):153-161.
21. Veterans Health Administration DoD, The Management of Postoperative Pain Working Group. VHA/DoD clinical practice guideline for the management of postoperative pain, 2002. US Department of Veterans Affairs http://www.healthquality.va.gov/guidelines/Pain/pop/pop_fulltext.pdf. Accessed: January 09, 2023.
22. Oderda GM, Evans RS, Lloyd J, et al. Cost of opioid-related adverse drug events in surgical patients. J Pain Symptom Manage. 2003;25(3):276-283.
23. Oderda GM, Said Q, Evans RS, et al. Opioid-related adverse drug events in surgical hospitalizations: impact on costs and length of stay. Ann Pharmacother. 2007;41(3):400-407.
24. Simons JW, Kim R, Chow W. Retrospective analysis of adverse events and economic costs [abstract]. Reg Anesth Pain Med. 2009;PS3:17.
25. Suh DC, Kim MS, Chow W, Jang EJ. Use of medications and resources for treatment of nausea, vomiting, or constipation in hospitalized patients treated with analgesics. Clin J Pain. 2011;27(6):508-517.
26. Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. Arch Intern Med. 2008;168(1):27-32.
27. Overdyk FJ. Postoperative respiratory depression and opioids. Initiatives in Safe Patient Care 2009. pp1-7. http://www.initiatives-patientsafety.org/assets/initiatives1.pdf. Accessed: March 18, 2016.
28. Wald HL, Ma A, Bratzler DW, Kramer AM. Indwelling urinary catheter use in the postoperative period: analysis of the national surgical infection prevention project data. Arch Surg. 2008;143(6):551-557.
29. Aaronson DS, Wu AK, Blaschko SD, McAninch JW, Garcia M. National incidence and impact of noninfectious urethral catheter related complications on the Surgical Care Improvement Project. J Urol. 2011;185(5):1756-1760.
30. Mayo Foundation for Medical Education and Research. (2022, April 12). Am I vulnerable to opioid addiction? Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/prescription-drug-abuse/in-depth/how-opioid-addiction-occurs/art20360372#:~:text=Opioids%20are%20highly%20addictive%2C%20in,powerful%20sense%20of%20well%2Dbeing. Accessed January 9, 2023.
31. Tse Yang Lim, Erin J. Stringfellow, Celia A. Stafford, Catherine DiGennaro, Jack B. Homer, Wayne Wakeland, Sara L. Eggers, Reza Kazemi, Lukas Glos, Emily G. Ewing, Calvin B. Bannister, Keith Humphreys, Douglas C. Throckmorton, and Mohammad S. Jalali. Modeling the evolution of the US opioid crisis for national policy development. *PNAS*. May 31, 2022. 119 (23) e2115714119. https://doi.org/10.1073/pnas.2115714119.
32. Jalal H, Buchanich JM, Roberts MS, Balmert LC, Zhang K, Burke DS. 2018. Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. Science 361(6408):eaau1184.

33. Awad IT, Moore M, Rushe C, Elburki A, O'Brien K, Warde D. Unplanned hospital admission in children undergoing day-case surgery. Eur J Anaesthesiol. 2004;21(5):379-383.
34. Marcaine [package insert]. Lake Forest, IL: Hospira, Inc.; 2013.
35. Bramlett K, Onel E, Viscusi ER, Jones K. A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCl for postsurgical analgesia in total knee arthroplasty. Knee. 2012;19(5):530-536.
36. Lambert WJ, Los K. DepoFoam multivesicular liposomes for the sustained release of macromolecules. In: Rathbone MJ, Hadgraft J, Roberts MS, Lane ME, eds. Modified-Release Drug Delivery Technology. Vol 2. 2nd ed. New York, NY: Informa Healthcare; 2008:207-214.
37. M. A. Mont, W. B. Beaver, S. H. Dysart, J. W. Barrington and D. J. Del Gaizo. Local Infiltration Analgesia With Liposomal Bupivacaine Improves Pain Scores and Reduces Opioid Use After Total Knee Arthroplasty: Results of a Randomized Controlled Trial. *The Journal of Arthroplasty*. 2018 Vol. 33 Issue 1 Pages 90-96. DOI: 10.1016/j.arth.2017.07.024
38. M. A. Patel, J. C. Gadsden, S. S. Nedeljkovic, X. Bao, J. L. Zeballos, V. Yu, et al. Brachial Plexus Block with Liposomal Bupivacaine for Shoulder Surgery Improves Analgesia and Reduces Opioid Consumption: Results from a Multicenter, Randomized, Double-Blind, Controlled Trial. *Pain Med*. 2020 Vol. 21 Issue 2 Pages 387-400. DOI: 10.1093/pm/pnz103.
39. Buttersworth J. Local anesthetics: clinical pharmacology and rational selection. The New York School of Regional Anesthesia https://www.nysora.com/topics/pharmacology/clinical-pharmacology-local-anesthetics. Accessed January 12, 2023.
40. Buckenmaier CC, III, Bleckner LL. Anaesthetic agents for advanced regional anaesthesia: a North American perspective. Drugs. 2005;65(6):745-759
41. Exparel [prescribing information]. Parsippany, NJ: Pacira Pharmaceuticals, Inc.; 2023.
42. Young MJ, Gorlin AW, Modest VE, Quraishi SA. Clinical implications of the transversus abdominis plane block in adults. Anesthesiol Res Pract. 2012;2012:731645.
43. Børglum J, Jensen K. Abdominal surgery: advances in the use of ultrasound-guided truncal blocks for perioperative pain management. In: Derbel F, ed. Abdominal Surgery. Rijeka,Croatia: InTech; 2012:69-94.
44. United States Food and Drug Administration. (2015, December 14) Pacira Letter- US Food and Drug Administration. https://www.fda.gov/media/95042/download

CLINICAL GUIDELINES

	SOCIETY	RECOMMENDATION
ANESTHESIOLOGY 2016	ASRA and ASA[1]	Recommendation for site-specific local anesthetic infiltration for surgical procedures, noting that "**clinicians should be knowledgeable regarding specific local anesthetic infiltration techniques, including the use of extended-release formulations of local anesthetics, such as liposomal bupivacaine (EXPAREL).**"[1]
COLORECTAL SURGERY 2016	ASCRS and SAGES[2]	Strong recommendation for the use of a perisurgical multimodal, opioid-sparing, pain management plan, noting that **liposomal bupivacaine wound infiltration and TAP blocks "have shown promising results in patients undergoing open and laparoscopic colorectal surgery."**[2]
BREAST RECONSTRUCTION 2017	ERAS® Society[3]	Strong recommendation for the use of multimodal opioid-sparing postsurgical pain management regimens, noting that **"a single injection of liposomal bupivacaine lasts for several days, potentially avoiding the need for catheter-based infusions."**[3]
COLORECTAL SURGERY 2018	ERAS® Society[4]	Strong recommendation for the use of TAP blocks for minimally invasive colorectal surgery, noting that shorter acting local anesthetics have limited duration. **Liposomal bupivacaine is included as an alternative to extend the duration.**[4]
GYNECOLOGIC ONCOLOGY 2019	ERAS® Society[5]	Strong recommendation for a multimodal postsurgical analgesic protocol using non-opioid oral medications and incisional injection of local anesthetic to decrease the need for systemic medications, stating that **"incisional infiltration with either bupivacaine or liposomal bupivacaine has no systemic side effects when used appropriately and should be incorporated into all ERAS protocols as a component of multimodal analgesia."**[5]
THORACIC SURGERY 2019	ERAS® Society[6] and ESTS	Recommendation for peripheral nerve blocks over thoracic epidural, noting that **liposomal bupivacaine also shows promise when delivered as multilevel intercostal injections potentially providing blockade of intercostal nerves for up to 96 hours.**[6]
LUMBAR FUSION 2021	ERAS® Society[7]	Strong recommendation for a **multimodal using local and regional anesthesia techniques, such as spinal or epidural analgesia, regional blocks, or wound infiltration, could reduce opioid consumption.**[7]

ASA=American Society of Anesthesiologists; ASRA=American Society of Regional Anesthesia and Pain Medicine; ERAS=Enhanced Recovery After Surgery; ESTS=European Society of Thoracic Surgeons; SAGES=Society of American Gastrointestinal and Endoscopic Surgeons; TAP=transversus abdominis plane.

1. Chou R, et al. *J Pain*. 2016;17(2):131-157; **2.** Carmichael JC, et al. *Dis Colon Rectum*. 2017;60(8):761-784; **3.** Temple-Oberle C, et al. *Plast Reconstr Surg*. 2017;139(5):1056e-1071e; **4.** Gustafsson UO, et al. *World J Surg*. 2019;43(3):659-695; **5.** Nelson G, et al. *Int J Gynecol Cancer*. 2019;29(4):651-668; **6.** Batchelor TJP, et al. *Eur J Cardiothorac Surg*. 2019;55(1):91-115; **7.** Debono B, et al. *Spine J*. 2021;21(5):729-752.

CLINICAL EVIDENCE

ORTHOPEDICS

TOTAL KNEE ARTHOPLASTY - INFILTRATION	
Study	**Results**
Hamilton et al (SPAARK) 2022[1] Multicenter, patient-blinded, RCT LB + Bupivacaine (N=267) vs Bupivacaine (N=266)	• Lower mean VAS pain scores the evening of surgery, P=0.02

Dysart et al 2019[2]
Multi-Center
Double-blinded RCT:
LB (N=69) vs. Bupivacaine (N=70)
	• Within 24-hour post-op
	  ◦ 19% reduction in pain (98.5 vs 121.6 AUC of VAS; P=0.0142)
	  ◦ 91% reduction in opioid use (3.5 vs 38.5; P=0.0009)
	  ◦ 17% vs 1% opioid free (P<0.01)
	  ◦ Higher patient satisfaction (84.6% vs 69.2%; P=0.0306)
	• More patients discharge ready within 12 hours (43% vs 27.5%; P=0.0499**)**

Lakra et al 2019[3]
Retrospective Cohort
Bupivacaine ACB + LB local infiltration (N=75) vs Bupivacaine ACB + Bupivacaine local infiltration (N=75)
	• Less pain (VAS)
	  ◦ POD 0: 2.1±1.6 vs. 2.8± 2.8, P=0.046
	  ◦ POD 1: 2.2±1.3 vs. 3.3± 2.1, P<0.001
	  ◦ POD 2: 2.1 ± 1.5 vs. 3.7 ±2.4,P<0.001
	• Less opioids (MME)
	  ◦ POD 0: 18.7±14.5 vs. 25.2±19.1, P=0.02
	  ◦ POD 1: 23.4±18.5 vs. 37.8±37.7, P=0.003
	• Less MME/day
	  ◦ 24.6±14.4 vs. 41.7±37.3, P=<0.001
	• Better ambulation (feet walked)
	  ◦ POD 0: 261.6 vs. 108.2, P<0.001
	• POD 1: 761.5 vs. 372.0, P<0.001

Asche et al 2019[4] Retrospective Observational LB vs Alternate SOC (N=33,412)	• 22% and 19% less inpatient opioid use (Medicare: 260.5 vs 332.1 MME, P<0.001; Commercial: 317.4 vs 393.7 MME, P<0.001) • 0.6 day shorter hospital stay (P<0.0001) • 1.6x more likely to be discharged to home (P<0.001) • Similar readmissions • Greater total hospital cost savings (Medicare: $616, P<0.0001; Commercial $775, P<0.0001)

Sandhu et al 2019[5]
Retrospective Observational
LB + ACB (N=209) vs FNB (N=181)
	• Less opioids (MME)
	    • 48-72h: 4.2 (3.3–5.2) vs 9.6 (8.3–11.0), P<0.001
	• Shorter length of stay (days)
	    • 2.22 (1.19) vs 4.13 (1.32), P<0.001
	• Less ORAEs (mean #): 0.91 vs 1.43, P<0.001
	• Fewer 90 day readmissions: 8 (3.83) vs 19 (10.5), P=0.017
	• Fewer 90 day re-operations: 3 (1.44) vs 11 (6.08), P= 0.025
	• Lower percent total costs: 91.56 (15.51) vs 101.87 (17.33), P<0.001

Mont et al 2018[6]
Multi-Center
Double-blinded RCT:
LB infiltration +(N=69) vs. Bupivacaine (N=70)
	• Pain – measured as $AUC_{12\text{-}48}$ of VAS *(Primary Endpoint)*
	    • 14% decrease in pain (180.8 vs. 209.3, respectively; *P*=0.0381)
	• Opioid Consumption in morphine equivalents (mg) *(Primary Endpoint)*
	    • 0-48 hours post-op: 78% decrease (18.7mg vs. 84.9mg, respectively; *P*=0.0048).
	    • 0-72 hours post-op: 78% decrease (20.9 vs. 93.6, respectively; *P*=0.0108)
	• 10% of LB patients were opioid free (0-72hrs) vs. 0% with bupivacaine (*P*<0.01)
	• 29% increase in the time for 50% of patients in the LB group to first opioid rescue vs. with bupivacaine (4.1hrs vs. 2.9hrs, respectively; *P*=0.0230)
	• Safety: No difference in AEs

Zlotnicki et al 2018[7]
Double-blind RCT
LB (N=38) vs Bupivacaine (N=40) vs SOC (N=40)
	• Lower physical therapy pain scores
	    • At 24 hours: LB-5.4 vs SOC-7.3; P=0.005
	    • At 24 hours: LB-5.4 vs bupivacaine-6.9; P=0.03
	• Fewer opioids compared to bupivacaine or SOC at 24 hours, results not reported
	• Increased ROM
	    • POD1 Flexion: LB-82.7 vs bupivacaine-66.4; P<0.0001
	• Discharge Extension: LB—5.8 vs SOC:-4.9, P=0.01

Yu et al 2018[8]
Retrospective obs:
LB (N=527)
vs Single Shot FNB (N=583)
	• Pain measured via VAS pain scores *(Primary Endpoint)*
	    • Less pain at 8, 64, 72hrs 8hrs: 3.2 vs. 4, (*P*=0.012)
	        • 64hrs: 4 vs. 4, (*P*=0.049)
	        • 72hrs: 4 vs. 4, (*P*=0.018)
	    • No differences were observed at any other time points (hours 16–48, 80, and beyond)
	• Less overall opioid use (MME, mg) with LB *(Primary Endpoint)*
	    • 84 vs. 96, (*P*=0.004)
	• Fewer inpatient falls with LB
	• 0.6% (3) vs. 2% (12); (OR = 3.67, *P*=0.030)

<table>
<tr><td>Kim et al 2018[9]
Retrospective Observational
LB (N=685) vs LB+PCA (N=540) vs FNB+PCA (N=583)</td><td>Lower opioid use (MME)
66 vs 82 vs 96, P<0.001
Shorter length of stay (days)
2.7 vs 3.1 vs 3.2, P<0.001
Higher prevalence of achieving physiotherapy milestones of both stair-climbing and walking for 100 feet:
POD1: 47% vs 30% vs 16%, P<0.001
Remainder of stay (%): 90% vs 93% vs 73%, P<0.001 (vs FNB)
Lower cost: Mean saving of 2.63% for hospitalization of the LB group compared with FNB + PCA and 4.81% compared with LB + PCA</td></tr>
<tr><td>Wang et al 2017[10]
Meta-analysis:
(3 RCTs and 2 non-RCTs)
LB infiltration (N=481) vs PAI w/ standard bupivacaine (N=733)</td><td>Significantly less pain at 24 and 48 hours with LB infiltration:
24hr: SMD=-0.241; (P=0.000) and 48hr: SMD=-0.124; (P=0.0068)
No statistical difference at 72hr
Significantly fewer opioid consumption with LB infiltration at POD1 (MME):
POD1: SMD= -0.275; (P=0.0001)</td></tr>
<tr><td>Phillips et al 2016[11]
Retrospective
LB cocktail + ACB (N=86)
vs. Bupivacaine with epinephrine cocktail + FNB (N=86)</td><td>Less total opioid consumption (MME, mg) with LB
64.6 vs. 83.7, (P=0.0016)
1 case of postoperative ileus in the bupivacaine group</td></tr>
<tr><td>Sporer et al 2016[12]
Retropspective Obsrervational
LB + bupivacaine (n=272) vs single shot FNB + bupivacaine PAI (n=325)</td><td>Less pain at 12 hrs PO (NRS): 12hr: 3.2 vs 3.6, P<.003
Fewer patients used opioids for breakthrough pain: 16.9% vs 36.3%, P<.001
Earlier time to ambulation (hrs) : 29.5 vs 32.2, P<.017</td></tr>
<tr><td>Kirkness et al 2016[13]
Retrospective
TKA
LB vs Cocktails + Continuous FNB; (N=268)</td><td>Lower total direct hospital cost: $8757.95 vs $9213.23, (P=0.033)
Cost-benefit:
$285 LB investment:
Savings of $624 vs conventional treatment
$742 savings in net direct hospital cost</td></tr>
<tr><td>Emerson et al 2016[14]
Retrospective
LB (N=36) vs. Continuous FNB (N=36)</td><td>Statistically significant lower opioid use (hydrocodone equivalents, mg) with LB
90 vs. 162, (P<0.001, adj. P=0.0188)
Statistically significant fewer rescue opioid doses with LB
7.5 vs. 15, (P<0.001, adj. P=0.0018)</td></tr>
</table>

Snyder et al 2016[15]
RCT
Total Knee Arthroplasty (N=70)
LB vs Ropivacaine cocktail
	• Less pain in the PACU, POD1 and POD2
	  • 2.11 vs 3.49, P=0.033; 2.57 vs 3.31, P=0.023; 2.4 vs 3.51, *P*=0.002; respectively
	• Greater satisfaction with pain control, 5 point scale
	  • Hospital: 4.91 vs 4.11, *P*=0.0001; Overall: 4.57 vs 3.97; *P*=0.001
	• Less opioid use PACU, POD 1 and POD2 (MME: 2.99 vs 6.85, *P*=0.002; 10.91 vs 15.57, *P*=0.079; 6.89 vs 13.11, *P*=0.005 respectively)
	• 53% reduction in nausea (25.71% vs 54.29%, *P*=0.011)

Cien et al 2015[16]
Retrospective
LB cocktail (N=59) vs. Single Shot FNB + PCA (N=66)
	• Trending toward less opioid use overall (mg) *(Primary Endpoint)*
	  • 121 vs. 199, (*P*=0.075) *[not statistically significant]*
	• Statistically significant lower peak postoperative pain score (VAS) with LB
	  • 4.4 vs. 7.5, *(P<0.*001)

Barrington et al 2015[17] *Retrospective* TKA and THA cases LB vs Bupivacaine cocktail with or w/o ketorolac and morphine + FNB; (N=2248)	• Lower cost of supplies and pharmaceuticals: • Total saved (aggregate): $1,246,113 • Per patient average saved: $1246

References: TKA - INFILTRATION

1. Hamilton TW, Knight R, Stokes JR, Rombach I, Cooper C, Davies L, Dutton SJ, Barker KL, Cook J, Lamb SE, Murray DW, Poulton L, Wang A, Strickland LH, Van Duren BH, Leal J, Beard D, Pandit HG; Study of Peri-Articular Anaesthetic for Replacement of the Knee (SPAARK) Study Group. Efficacy of Liposomal Bupivacaine and Bupivacaine Hydrochloride vs Bupivacaine Hydrochloride Alone as a Periarticular Anesthetic for Patients Undergoing Knee Replacement: A Randomized Clinical Trial. JAMA Surg. 2022 Jun 1;157(6):481-489. doi: 10.1001/jamasurg.2022.0713. PMID: 35385072; PMCID: PMC8988023. https://pubmed.ncbi.nlm.nih.gov/35385072/
2. Dysart SH, Barrington JW, Del Gaizo DJ, Sodhi N, Mont MA. Local Infiltration Analgesia With Liposomal Bupivacaine Improves Early Outcomes After Total Knee Arthroplasty: 24-Hour Data From the PILLAR Study. J Arthroplasty. May 2019;34(5):882-886 e1. doi:10.1016/j.arth.2018.12.026 https://www.ncbi.nlm.nih.gov/pubmed/30799269
3. Lakra A, Grosso M, Jennings EL, Cooper HJ, Shah RP, Geller JA. Improved pain control with adductor canal block using liposomal bupivacaine after total knee replacement: a retrospective cohort study. Arthroplast Today. Sep 2019;5(3):325-328. doi:10.1016/j.artd.2019.04.008 https://www.ncbi.nlm.nih.gov/pubmed/31516976.
4. Asche CV, Dagenais S, Kang A, Ren J, Maurer BT. Impact of treatment with liposomal bupivacaine on hospital costs, length of stay, and discharge status in patients undergoing total knee arthroplasty at high-use institutions. J Med Econ. 2019 Dec;22(12):1253-1260. doi: 10.1080/13696998.2019.1627363.
5. Sandhu S, Zadzilka JD, Nageeb E, Siqueira M, Klika AK, Molloy RM, Higuera CA. A Comparison of Pain Management Protocols Following Total Knee Arthroplasty: Femoral Nerve Block versus Periarticular Injection of Liposomal Bupivacaine with an Adductor Canal Block. Surg Technol Int. 2019 May 15;34:403-408. PMID: 30388725. https://pubmed.ncbi.nlm.nih.gov/30388725/
6. Mont MA, Beaver WB, Dysart SH, Barrington JW, Del Gaizo DJ. Local Infiltration Analgesia With Liposomal Bupivacaine Improves Pain Scores and Reduces Opioid Use After Total Knee Arthroplasty: Results of a Randomized Controlled Trial. The Journal of Arthroplasty. 2018;33(1):90-96. doi:10.1016/j.arth.2017.07.024 https://www.ncbi.nlm.nih.gov/pubmed/28802777
7. Zlotnicki JP, Hamlin BR, Plakseychuk AY, Levison TJ, Rothenberger SD, Urish KL. Liposomal Bupivacaine vs Plain Bupivacaine in Periarticular Injection for Control of Pain and Early Motion in Total Knee Arthroplasty: A Randomized, Prospective Study. J Arthroplasty. Aug 2018;33(8):2460-2464. doi:10.1016/j.arth.2018.03.014 https://www.ncbi.nlm.nih.gov/pubmed/29656977
8. Yu S, Dundon J, Solovyova O, Bosco J, Iorio R. Can Multimodal Pain Management in TKA Eliminate Patient-controlled Analgesia and Femoral Nerve Blocks? Clin Orthop Relat Res. Jan 2018;476(1):101-109. doi:10.1007/s11999.0000000000000018 https://www.ncbi.nlm.nih.gov/pubmed/29529623
9. Kim K, Elbuluk A, Yu S, Iorio R. Cost-effective peri-operative pain management: assuring a happy patient after total knee arthroplasty. Bone Joint J. Jan 2018;100-b(1 Supple A):55-61. doi:10.1302/0301-620x.100b1.bjj-2017-0549.r1 https://www.ncbi.nlm.nih.gov/pubmed/29292341
10. Wang X, Xiao L, Wang Z, Zhao G, Ma J. Comparison of peri-articular liposomal bupivacaine and standard bupivacaine for postsurgical analgesia in total knee arthroplasty: a systematic review and meta-analysis. Int J Surg. Feb 10 2017;39:238-248. doi:10.1016/j.ijsu.2017.02.011 https://www.ncbi.nlm.nih.gov/pubmed/28192247
11. Phillips J, Doshi A. The Effects of Liposomal Bupivacaine With Adductor Canal Block on Pain and Functional Outcomes in Patients Undergoing Total Knee Arthroplasty. Ann Pharmacother. 2016;50(9):706-711. https://www.ncbi.nlm.nih.gov/pubmed/27289131
12. Sporer SM, Rogers T. Postoperative Pain Management Following Primary Total Knee Arthroplasty: The Value of Liposomal Bupivacaine. The Journal of Arthroplasty. 2016;31(11):2603-2607. https://www.ncbi.nlm.nih.gov/pubmed/27259389
13. Kirkness CS, Asche CV, Ren J, Kim M, Rainville EC. Cost-benefit evaluation of liposomal bupivacaine in the management of patients undergoing total knee arthroplasty. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2016;73(9):e247-254. https://www.ncbi.nlm.nih.gov/pubmed/27099332
14. Emerson RH, Barrington JW, Olugbode O, Lovald S, Watson H, Ong K. Femoral nerve block versus long-acting wound infiltration in total knee arthroplasty. Orthopedics. 2016;39(3):e449-e455. http://www.ncbi.nlm.nih.gov/pubmed/27018607.
15. Snyder MA, Scheuerman CM, Gregg JL, Ruhnke CJ, Eten K. Improving total knee arthroplasty perioperative pain management using a periarticular injection with bupivacaine liposomal suspension. Arthroplast Today. 2016 Jan 11;2(1):37-42. doi: 10.1016/j.artd.2015.05.005. PMID: 28326395; PMCID: PMC4957154. https://pubmed.ncbi.nlm.nih.gov/28326395/
16. Cien AJ, Penny PC, Horn BJ, Popovich JM, Taunt CJ. Comparison Between Liposomal Bupivacaine and Femoral Nerve Block in Patients Undergoing Primary Total Knee Arthroplasty. J Surg Orthop Adv. 2015;24(4):225-229. http://www.ncbi.nlm.nih.gov/pubmed/26731385
17. Barrington JW, Olugbode O, Lovald S, Ong K, Watson H, Emerson RH Jr. Liposomal Bupivacaine: A Comparative Study of More Than 1000 Total Joint Arthroplasty Cases. Orthop Clin North Am. 2015 Oct;46(4):469-77. doi: 10.1016/j.ocl.2015.06.003. Epub 2015 Aug 6. PMID: 26410636. https://pubmed.ncbi.nlm.nih.gov/26410636/

ADDUCTOR CANAL BLOCK (ACB)	
Study	**Results**

Quaye et al. 2024[1]
RCT
Targeting saphenous nerve
LB ACB 133 mg/10 mL + 0.25% bupivacaine HCl (10 mL) (N=40)
vs. 0.5% bupivacaine HCl ACB (20 mL).
	• Reduced Opioid Use
	  ○ Total MME POD 0: (26.2 vs. 37.5, P=0.016)
	  ○ Total MME POD 1: (27.5 vs. 36, P=0.016)
	  ○ Received opioids POD 2: (66.7% vs. 89.5%, P=0.024)
	• Total MME POD 2: (28.8 vs. 30.0, P=0.016)

Gadsden et al 2023[2]
RCT
Primary Unilateral Total Knee Arthroplasty (N=166)
ACB with LB 133 mg + 10 mL (50 mg) 0.5% Bupivacaine
vs. ACB with 10 mL (50 mg) 0.5% Bupivacaine + 10 mL normal saline
	• AUC of NRS Pain Intensity Scores 0-96 hrs post surgery (*Primary Endpoint*)
	  ○ Lower pain scores in LB ACB group through 4 days post-surgery (P=0.0074)
	  ○ Current NRS pain scores lower in LB ACB group particularly 30 to 96 hrs
	• Total opioid consumption 0-96 hrs post surgery (*Secondary Endpoint*)
	  ○ 23% difference in total opioid consumption with LB ACB (132.8 vs 101.8 MMEs, P=0.0071)
	  ○ Total opioid consumption consistently lower in LB ACB group in 24-hr increments

Walls et al 2023[3]
Retrospective study
ACL reconstruction
LB + 0.25% bupivacaine ACB (N=26) vs. 0.25% bupivacaine ACB (N=32)
	• Lower Opioid MME
	  ○ POD 1 (0 vs 1.1, P=0.037)
	  ○ POD 2 (0.095 vs 1.3, P=0.023)
	• MME Total (0.29 vs 3.52, P=0.033)

Lonza et al 2022[4] Retrospective chart review LB 10 mL (133mg) + 0.5% bupivacaine injected ACB (N=1640) vs. On-Q group 0.125% bupivacaine at 6 mL/hr ACB for 36 hours (N=738)	• LB non-inferior in average daily pain through POD3, readmissions, ED visits related to pain, opioid MME usage, and length of stay • Lower cost than On-Q pump ($180 vs $275) per treatment • Total potential cost savings of whole EXPAREL group was $155,800 for the study period

Malige et al 2022[5]
RCT
LB 266mg ACB + 5mL Bupivacaine 0.5% (N=50)
vs. ACB with 25mL Ropivacaine 0.2% (N=50)
	• 27% shorter length of stay [36.3 vs 49.7 h, p<0.01]
	• Increased NRS pain score improvement *(negative score denotes a pain score increase)*
	    ○ POD 0 [1.8 vs -0.2, p<0.01]; POD 1 [1.0 vs -1.3, p<0.01]; POD 2 [2.3 vs -0.1, p=0.03]
	    ○ 1 week [1.8 vs 0.2, p=0.04]
	    ○ 2 week [3.2 vs 1.3, p=0.01]
	    ○ 4 week [3.9 vs 2.2, p=0.02]
	    ○ 6 week [5.2 vs 3.0, p=<0.01]
	• 13.5% reduction in daily inpatient opioid use [40.9 vs 47.3, p=0.038]
	• Improvement in WOMAC score
	    ○ 1 week [20.3 vs 6.0, p<0.01]
	    ○ 2 week [31.1 vs 19.6, p=0.02]
	• 6 week [48.2 vs 35.7, p<0.01]

Chen et al 2021[6] Retrospective ACB with LB 133mg + 22.5-47.5 mg Bupivacaine HCl vs. PAI with 100mg bupivacaine HCl (N=146) and EITHER ACB with Bupivacaine 65-80mg bolus + 0.2% ropivacaine continuous infusion or ACB with Ropivacaine 65-105mg bolus + 0.2% ropivacaine continuous infusion (N=106)	• 22% of patients in the continuous catheter group reported problems with their catheters ranging from mild leakage to possible infection requiring antibiotics
Hubler et al 2021[7] RCT ACB with LB 266mg + PAI of 0.25% Bupivacaine HCl (N=31) vs. ACB with Bupivacaine HCl 100mg + PAI of 0.25% Bupivacaine HCl (N=32)	• 26% reduction in pain with activity on POD2 [4.4 vs 5.9, p=0.009]. NSD at any other time point • 23% reduction in Opioids on POD1 [51.2 vs 66.1 MME, p=0.020] • 28% reduction in Opioids on POD2 [39.5 vs 54.8 MME, p=0.016], NSD at any other time point
Meftah et al 2020[8] RCT LB 266mg infiltration + 100mg of Bupivacaine HCl + 80mL NS (N=35) vs. ACB with LB 266mg (N=35)	• PAI with less pain vs ACB on POD3 [1.83 vs 4.83, p=0.037]

Chen et al 2020[9] Retrospective ACB with LB 133mg + PAI with LB 133mg & 30mg of Bupivacaine HCl +NS (N=142) vs. ACB with Ropivacaine 100mg + PAI with LB 266mg & NS (N=91)	• LB ACB with more patients opioid free at 8 hours [33% vs 21%, p=0.026] • LB ACB with less mean opioids used at 8 hr + PACU [11 vs 16 MME, p=0.022] • LB ACB with shorter LOS in days [1 vs 2, p<0.0001]
Lakra et al 2019[10] Retrospective 66.5mg ACB & 37.5mg Bupivacaine HCl + PAI with LB 199.5mg & 50mg Bupivacaine HCl & NS (N=75) vs. ACB with Bupivacaine HCl 75mg + PAI with Bupivacaine HCl 125mg (N=75)	• LB ACB with lower pain at POD0 [2.1 vs 2.8, p<=0.046] • LB ACB with lower pain at POD1 [2.2 vs 3.3, p<0.001] • LB ACB with lower pain at POD2 [2.1 vs 3.7, p<0.001] • LB ACB with less opioid usage at POD0 [18.7 vs25.2 MME, p=0.02] • LB ACB with less opioid usage at POD1 [23.4 vs 37.8 MME, p=0.003] • LB ACB with less MME/day [24.6 vs 41.7 MME, p<0.001] • LB ACB with improved feet walked on POD0 and POD1 [261.6 vs 108.2, p<0.001; 761.5 vs 372, p<0.001}
Wang et al 2016[11] Retrospective ACB with LB 266mg (N=111) vs. Ropivacaine 0.1% continuous infusion via Pain Ball (N=111)	• LB ACB with lower pain at 0-36h [3.1 vs 4, p<0.001] • LB ACB with lower pain at 0-72h [3.24 vs 3.83, p<0.001] • LB ACB with lower pain at 0-6h, 7-12h, 13-24h, 25-36h [All p values <0.001] • Less IV opioid usage [Fentanyl 80.1% vs 93.7%, p=0.005; Hydromorphone 38.7% vs 58.6%, p=0.005] • Lower Direct Costs for LB ACB [$14,151.10 vs $15,465.50, p=0.04] • Lower Total Costs for LB ACB [$20,919.53 vs $22,574.17, p=0.03}

References: ADDUCTOR CANAL BLOCK (ACB)

1. Quaye A, McAllister B, Garcia JR, et al. A prospective, randomized trial of liposomal bupivacaine compared to conventional bupivacaine on pain control and postoperative opioid use in adults receiving adductor canal blocks for total knee arthroplasty. Arthroplasty. Feb 1 2024;6(1):6. doi:10.1186/s42836- 023-00226-y. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10832097/
2. Gadsden J, Hamilton M, Schwartz G, et al. Liposomal Bupivacaine via Adductor Canal Block After Total Knee Arthroplasty: a Randomized, Double-blind, Phase 3 Trial. presented at: Annual Regional Anesthesiology and Acute Pain Medicine Meeting ASRA; 2023.
3. Walls HR, Thomas ES, Kain ZN, Schlechter JA. Does Liposomal Bupivacaine Injectable Suspension Peripheral Nerve Block Further Aid in Decreasing At-home Narcotic Utilization in Children and Adolescents After Anterior Cruciate Ligament Reconstruction. J Pediatr Orthop. Jul 3 2023;doi:10.1097/bpo.0000000000002466. https://pubmed.ncbi.nlm.nih.gov/37400092/
4. Lonza GC, Yuan F, Pham FM, Wright CT, Arellano-Kruse A, Andrawis J. Liposomal Bupivacaine Vs. Continuous Nerve Block: Liposomal Bupivacaine may be non-inferior and more cost effective. J Arthroplasty. Dec 15 2022;doi:10.1016/j.arth.2022.12.014. https://pubmed.ncbi.nlm.nih.gov/36529199/
5. Malige A, Pellegrino AN, Kunkle K, Konopitski A, Brogle P, Nwachuku C. Liposomal Bupivacaine in Adductor Canal Blocks Before Total Knee Arthroplasty Leads to Improved Post-Operative Outcomes: A Randomized Controlled Trial. The Journal of Arthroplasty. 2022;doi:10.1016/j.arth.2022.03.073. https://pubmed.ncbi.nlm.nih.gov/35351553/
6. Chen CM, Yun AG, Fan T. Continuous Bupivacaine Infusion versus Liposomal Bupivacaine in Adductor Canal Block for Total Knee Arthroplasty. J Knee Surg. Feb 15 2021;(EFirst)doi:10.1055/s-0040- 1722661. https://pubmed.ncbi.nlm.nih.gov/33588474/
7. Hubler CP, Bevil KM, Greiner JJ, Hetzel SJ, Borden SB, Cios HA. Liposomal Bupivacaine Versus Standard Bupivacaine in the Adductor Canal for Total Knee Arthroplasty: A Randomized, Controlled Trial. Orthopedics. Jul-Aug 2021;44(4):249-255. doi:10.3928/01477447-20210621-01. https://pubmed.ncbi.nlm.nih.gov/34292820/
8. Meftah M, Boenerjous-Abel S, Siddappa VH, Kirschenbaum IH. Efficacy of Adductor Canal Block With Liposomal Bupivacaine: A Randomized Prospective Clinical Trial. Orthopedics. Nov 26 2019:1-7. doi:10.3928/01477447-20191122-05. https://pubmed.ncbi.nlm.nih.gov/31770446/
9. Chen CM, Yun AG, Fan T. Efficacy of Liposomal Bupivacaine versus Ropivacaine in Adductor Canal Block for Total Knee Arthroplasty. J Knee Surg. Jun 24 2020;doi:10.1055/s-0040-1713114. https://pubmed.ncbi.nlm.nih.gov/32583397/
10. Lakra A, Grosso M, Jennings EL, Cooper HJ, Shah RP, Geller JA. Improved pain control with adductor canal block using liposomal bupivacaine after total knee replacement: a retrospective cohort study. Arthroplast Today. Sep 2019;5(3):325-328. doi:10.1016/j.artd.2019.04.008 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6728435/
11. Wang Y, Klein MS, Mathis S, Fahim G. Adductor Canal Block With Bupivacaine Liposome Versus Ropivacaine Pain Ball for Pain Control in Total Knee Arthroplasty: A Retrospective Cohort Study. Annals of Pharmacotherapy. 2016;50(3):194-202. https://pubmed.ncbi.nlm.nih.gov/26783357/

TOTAL HIP ARTHOPLASTY	
Study	**Results**
Chintalapudi et al 2022[1] Intertrochanteric hip fracture Retrospective Cost Benefit Analysis LB (N=46) vs no LB (N=56)	• Greater cost savings ($1323) • Lower likelihood of requiring discharge to skilled nursing facility (84.8% vs 96.4%; P=0.002)

Basmajian et al 2020[2]
Retrospective Observational:
Intertrochanteric hip fracture
LB (N=46) vs no LB (n=56)
	• Less pain (NRS):
	  • PACU: 2.57 vs 4.76; P=0.02
	  • 24 hr: 3.29vs 5.13; P=0.04
	• Less opioid use (MME): 24 hr.: 0.34 vs 0.92; P=.04

Rainville et al 2020[3]
Retrospective Observational
LB (N=70) vs Control (103)
	• Less frequent use of single pre-operative oral opioid dose (mg ME): 0.4 vs 3.9, P=0.006
	• Lesser PCA use (%):0 vs 12.6, P=0.002
	• Shorter length of stay (days): 2.5 vs 3.0, P=0.010
	• Greater walking distance (feet):
	  • POD0: 27.6 vs 12.5, P=0.001
	  • POD1: 186.8 vs 155.2, P=0.039
	• Less costs (USD): Indirect costs:$6,098 vs $6,753, P<0.001
	• Total costs (w/o medical supply cost): $10,670 vs $11,351, P=0.022

VanWagner et al 2019[4]
Retrospective Observational:
LB (N=85) vs Cocktail (N=85)
	• Less opioid use (hydrocodone equivalent, mg):
	  • Total: 51.36 vs 131.27, P<0.001
	  • POD0: 4.71 vs 8.94, P=0.039
	  • POD1: 22.58 vs 61.03, P<0.001
	  • POD2: 8.9 vs 32.88, P<0.001
	  • POD3: 1.71 vs 8, P=0.006
	• Shorter LOS (days): 1.89 vs 2.48, P=0.001

Asche et al 2018[5] Retrospective Observational LB (N=6270) vs Alternate SOC (N=6319)	• 24% and 28% less inpatient opioid use (Medicare: 244.2 vs 319.9 MME, P<0.001; Commercial: 255.0 vs 355.2 MME, P<0.001) • 0.7 day shorter hospital stay (P<0.0001) • 1.6 – 1.7x more likely to be discharged to home (P<0.001) • Similar readmissions • Greater total hospital cost savings for Medicare: $561, P<0.0001 • Similar hospital cost for Commercial pay (P=0.7697)

Asche et al 2018[6]
Retrospective Observational:
LB + bupivacaine w/ epinephrine + ketorolac (n=64) vs. Bupivacaine w/epinephrine + ketorolac (n=66)
	• Less cumulative AUC pain (NRS):
	  • POD0: 127.6 vs 292.5; P<0.001
	  • POD1 92.9 vs 185.0; P<0.001
	  • POD2 93.8 vs 213.8; P=0.006
	• Less proportion of patients who used opioid rescue medication:
	  • POD1 29.7% vs 56.1%; P=0.002, adj P=0.003
	  • POD2 7.8% vs 30.3%; P=0.001, adj P=0.003
	• Lower opioid use (mg):
	  • POD1: 9.6 vs 14.5, P=0.008
	  • POD2: 2.0 vs 7.5, P<0.001
	• Shorter LOS (days): 2.0 vs 2.7, P<0.001, adj P=0.002
	• Greater distance walked at discharge (feet): 249.2 vs 180.0, P=0.025, adj P=0.070
	• Lower hospital charges (USD): $43,794 vs $48,010, P<0.001

Ma et al 2017[7] Meta-analysis LB (n=6009) vs Bupivacaine (n=50195)	• Less pain at 24h (VAS) Mean difference=-3.98, P=0.018 • Shorter LOS (mean difference=-0.46; 95% CI, -0.58 to -0.35) (P=0.000) • Mean difference=-0.46, P=0.0001
Beachler et al 2017[8] Retrosepctive Observational LB (n=29) vs bupivacaine + morphine + ketorolac (n=40)	• Less opioid use (MME, mg): 64.7 vs 96.6, P=.036 • Less mean opioid use per day 22.59 vs 29.01, P=.045
Johnson et al 2017[9] *RCT* Total Hip Arthroplasty (N=159) LB cocktail vs continuous lumbar plexus block (PNB) vs ropivacaine cocktail	• Less pain compared to ropivacaine cocktail on POD1 and POD 2 (4.0 vs 5.5, *P*=0.006; 3.5 vs 5.0, *P*=0.016 respectively) • Comparable pain scores to continuous PNB • Comparable opioid use • Comparable hospital stay
Yu et al 2016[10] Retrospective Observational: LB+ bupivacaine cocktail (n=586) vs bupivacaine cocktail alone (n=686) Bupivacaine cocktail= bupivacaine, ketorolac, morphine	• Less pain at 8hrs post op, P=0.03 • Less overall opioid use (MME): 15.5mg reduction, P<.001 POD0-1: "significant reduction" P<.001 (no value provided) • Shorter LOS (days): 2.62 vs 2.93, P=<0.001 • 5.19% more discharged to home (vs. rehab or nursing), P<.02 (values not provided) • More patients achieved gait milestone (>100ft): 82% vs 64%, P<.001 • More patients completed stair climb: 93% vs 76%, P<.001

Emerson et al 2015[11] Retrospective Observational: LB + bupivacaine + ketorolac (n=36) vs. bupivacaine + ketorolac (n=36)	• Less pain (VAS): Overall: 1.34 vs 2.2,P=.0013; adj P=.003 • More patients reporting no pain: 56.70% vs 44.41%, P=.024; adj P<.0001 • Less overall consumption (Hydrocodone equivalents, mg): 72.3 vs 105.4 P=.071; adj P=.0075 • Fewer rescue med doses scheduled/requested (#): 4.97 vs 13.14, P<.0001

References: TOTAL HIP ARTHROPLASTY

1. Chintalapudi N, Agarwalla A, Bortman J, et al. Liposomal Bupivacaine Associated with Cost Savings during Postoperative Pain Management in Fragility Intertrochanteric Hip Fractures. Clinics in Orthopedic Surgery. 2022. https://pubmed.ncbi.nlm.nih.gov/35685981/
2. Basmajian, Hrayr G. MD; Liu, Joseph N. MD; Farmer, Travis D. MD, PharmD; Agarwalla, Avinesh MD; Lu, Joana PA; Amin, Nirav H. MD. Liposomial Bupivacaine for Postoperative Pain Control in Fragility Intertrochanteric Hip Fractures. Journal of Orthopaedic Trauma 34(3):p 139-144, March 2020. | DOI: 10.1097/BOT.0000000000001665. https://pubmed.ncbi.nlm.nih.gov/31634285/
3. Rainville EC, Asche C, Ren J, et al. Evaluation of Intraoperative, Local Site Injections of Liposomal Bupivacaine as an Alternative to Standard Local Anesthetics in Patients Undergoing Total Hip Arthroplasty. Hosp Pharm. Aug 2020;55(4):273-278. doi:10.1177/0018578719844702. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7370345/
4. VanWagner MJ, Krebs NM, Corser W, Johnson CN. Liposomal bupivacaine reduces opioid consumption and length of stay in patients undergoing primary total hip arthroplasty. Hip international : the journal of clinical and experimental research on hip pathology and therapy. May 2019;29(3):276-281. doi:10.1177/1120700018778240. https://pubmed.ncbi.nlm.nih.gov/29808726/
5. Asche CV, Dagenais S, Kang A, Ren J, Maurer BT. Impact of treatment with liposomal bupivacaine on hospital costs, length of stay, and discharge status in patients undergoing total hip arthroplasty at high-use institutions. J Med Econ. Oct 31 2018;22(1):1-10. doi:10.1080/13696998.2018.1543190. https://pubmed.ncbi.nlm.nih.gov/30378454/
6. Asche CV, Ren J, Kim M, et al. Local infiltration for postsurgical analgesia following total hip arthroplasty: a comparison of liposomal bupivacaine to traditional bupivacaine. Curr Med Res Opin. Apr 04 2017;33(7):1283-1290. doi:10.1080/03007995.2017.1314262. https://pubmed.ncbi.nlm.nih.gov/28375752/
7. Ma TT, Wang YH, Jiang YF, Peng CB, Yan C, Liu ZG, Xu WX. Liposomal bupivacaine versus traditional bupivacaine for pain control after total hip arthroplasty: A meta-analysis. Medicine (Baltimore). 2017 Jun;96(25):e7190. doi: 10.1097/MD.0000000000007190. PMID: 28640101; PMCID: PMC5484209. https://pubmed.ncbi.nlm.nih.gov/28640101/
8. Beachler JA, Kopolovich DM, Tubb CC, Sayeed SA. Liposomal bupivacaine in total hip arthroplasty: Do the results justify the cost?. J Orthop. 2017;14(1):161-165. Published 2017 Jan 3. doi:10.1016/j.jor.2016.12.008. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5219621/
9. Johnson RL, Amundson AW, Abdel MP, Sviggum HP, Mabry TM, Mantilla CB, Schroeder DR, Pagnano MW, Kopp SL. Continuous Posterior Lumbar Plexus Nerve Block Versus Periarticular Injection with Ropivacaine or Liposomal Bupivacaine for Total Hip Arthroplasty: A Three-Arm Randomized Clinical Trial. J Bone Joint Surg Am. 2017 Nov 1;99(21):1836-1845. doi: 10.2106/JBJS.16.01305. PMID: 29088038. https://pubmed.ncbi.nlm.nih.gov/29088038/
10. Yu SW, Szulc AL, Walton SL, Davidovitch RI, Bosco JA, Iorio R. Liposomal Bupivacaine as an Adjunct to Postoperative Pain Control in Total Hip Arthroplasty. Journal of Arthroplasty. 2016. https://pubmed.ncbi.nlm.nih.gov/26872584/
11. Emerson RH, Barrington JW, Olugbode O, Lovald S, Watson H, Ong K. Comparison of Local Infiltration Analgesia to Bupivacaine Wound Infiltration as Part of a Multimodal Pain Program in Total Hip Replacement. J Surg Orthop Adv. 2015;24(4):235-41. https://pubmed.ncbi.nlm.nih.gov/26731387/

SHOULDER SURGERY (INTERSCALENE BRACHIAL PLEXUS)	
Study	**Results**
Finkel et al. 2023[1] RCT Anatomic or Reverse Total Shoulder Arthroplasty LB + 0.5% bupi ISBPB (n=45) vs 0.5% bupi + dexamethasone + epinephrine (n=45)	• Lower post operative average pain scores at 24-48 hours (2.0 vs 4.0; p<0.001), 48-72 hours (2.0 vs 3.0; p=0.003), and 72-96 hours (2.0 vs 3.0; p=0.011) • Lower post operative maximum pain scores at 24-48 hours (4.5 vs 7.0; p<0.001), 48-72 hours (4.0 vs 6.0; p=0.001), and 72-96 hours (4.0 vs 5.0; p=0.007) • Lower maximum pain score on Day 60 (5.0 vs 6.0; p=0.001) • The LBB group resulted in higher reports of 10/10 pain control satisfaction on POD 4 (32/41 vs 24/41; p=0.048)
Lee et al 2023[2] Quality Improvement Study Total or Reverse Shoulder Arthroplasty LB ISBPB (n=285) vs Other block with bupi-, ropi-, or mepivacaine (n=178) vs No block (n=28)	• Greater proportion of patients with clinically tolerable pain of VAS<4 (0.69 vs 0.53 vs 0.38; P<0.001, P<0.001) • Less average pain (3.35 vs 4.26 vs 4.86; P<0.001, P<0.001) • Less opioid use (61.61 vs 83.33 vs 106.18 MME; P<0.001, P<0.001)

Pickle et al 2023[3]
Quality Improvement Study
Ambulatory Rotator Cuff Repair
LB + 0.5% bupi (n=26) ISBPB
vs 0.5% bupi (n=27)
	• Less median pain (NRS)
	    • POD 1 (3 vs 6.2; P<0.001)
	    • POD 2 (3 vs 6.6; P<0.001)
	    • POD 3 (3.1 vs 6; P<0.001)
	    • Combined pain days 1-3 (3 vs 6.2; P<0.001)
	• Less median opioid use (OME)
	    • POD 1 (7.5 vs 37.5; P<0.001)
	    • POD 2 (5 vs 37.5; P<0.001)
	    • POD 3 (0 vs 32.5; P<0.001)
	    • Combined opioid use days 1-3 (7.5 vs 37.5; P<0.001)

Simovitch et al 2022[4]
RCT
Arthroscopic rotator cuff repair
LB + bupi ISBPB (N=45) vs ropivacaine + dexamethasone ISBPB (N=44)
	• 68% average lower daily “worst pain” level POD 0-5 [≤0.002]
	    • POD 0 [0.7 vs 2.9, P<0.001]
	    • POD 1 [1.2 vs 5.2, P<0.001]
	    • POD 2 [1.4 vs 4.5, P<0.001]
	    • POD 3 [1.5 vs 3.9, P<0.001]
	    • POD 4 [1.3 vs 3.7, P<0.001]
	    • POD 5 [1.1 vs 2.2, P=0.002]

	• -2.4 average reduction in "worse pain" from baseline POD 0-5 [P<0.001]
	  ◦ POD 0 [-5.0 vs -2.5, P<0.001]
	  ◦ POD 1 [-4.6 vs -1.4, P<0.001]
	  ◦ POD 2 [-4.4 vs -1.0, P<0.001]
	  ◦ POD 3 [-4.3 vs -1.4, P<0.001]
	  ◦ POD 4 [-4.4 vs -2.5, P<0.001]
	  ◦ POD 5 [-4.6 vs -3.6, P=0.005]
	• 74% reduction in cumulative opioid consumption [48.5 vs 190.1, P<0.001]
	  ◦ Significantly lower daily opioid use POD 0-7
	• Greater percentage of opioid-free patients on POD 0-2

Kenny et al 2021[5] Retrospective chart review Total Shoulder Arthroplasty LB + bupi ISBPB (N=207) vs ropivacaine continous catheter (N=126)	• Lower cost [$1115.29 vs $1878.22] • Pain scores non-inferior to continuous catheter POD 0-2

Krupp et al[6]
Prospective RCT
Total shoulder arthroplasty
LB ISBNB (N=19) vs indwelling interscalene catheter (N=35)
	• Less pain (NRS):
	  ◦ 77% reduction in pain at 24 hours (0.76 vs 3.29) (P<0.000)
	  ◦ 46% reduction in pain at 48 hours (2.53 vs 4.70) (P=0.005)
	• Opioid consumption:
	  ◦ Lower opioid consumption at 48 hours (0.00 vs 0.62) (P=0.001)
	• Similar in operative time or time to discharge
	• Shorter administration time (4.84 min vs 10 min) (P<0.0001)
	• Cost:
	  ◦ Lower cost of administration ($190.17 vs $357.12)
	  ◦

Patel et al[7]
RCT
Total Shoulder or Rotator Cuff Repair
LB ISBPB (N=69) vs Placebo (N=71)
	• Less pain at 48 hours (AUC of VAS scores, 136.4 vs 254.1; P<0.0001)
	• Less opioid use at 48 hours (12.0 mg vs 54.3 mg; P<0.0001)
	• Greater percentage of patients opioid-free at 48 hours (9% vs 1%; P=0.008)
	• Less opioid use at 24 hours (4.69 vs 34.45; P<0.001)
	• Less opioid use from 24 to 48 hours (3.84 vs 14.18; P=0.0001)
	• Less opioid use from 48-72 hours (3.99 vs 11.62; P=0.002)
	• Less opioid use from 0-72 hours (22.97 vs 70.38; P<0.0001)
	• Greater proportion of discharge ready patients
	    • 51 vs 32 at 12 hours (P=0.02)
	    • 78 vs 52 at 24 h hours (P=0.0004)
	    • 86 vs 68 at 48 hours (P=0.0004)
	• Greater overall satisfaction with analgesia

Vandepitte et al[8]
RCT
Major shoulder surgery (rotator cuff repair or total shoulder replacement)
LB + bupivacaine ISPBP (N=26) vs bupivacaine ISPBPB (N=26)
	• Greater satisfaction with pain management (OBAS)
	    • POD1 (1.4 vs 2.8; P=0.05)
	    • POD2 (1.8 vs 3.3; P=0.03)
	    • POD4 (2.2 vs 3.6; P=0.05)

Weir et al[9] Retrospective observational Total Shoulder arthroplasty LB ISBPB (N=34)vs continuous ISBPB (N=70)	• Less pain 0-4 hours (0.6±1.1 vs 1.5±2.0±; P=0.034) • Less opioid use 0-4 hours (2.2±5.1 vs 6±12.7; P=0.014) • Less opioid use 9-12 hours (4.9±7.4 vs 8.3±8.7; P=0.026) • Less opioid use in 24 hours (32.3±38.2 vs 45.7±54.5; P=0.039) • Less opioid use for total length of stay (40.1±50.6 vs 54.1±51.0; P=0.028) • Morphine equivalents per hour: 91.5±1.6 vs 2.0±2.0; P=0.035)

Baessler et al[10]
RCT
Arthroscopic rotator cuff repair
ISBPB with LB + Bupi (N=24) vs LB+ Bupi+ Steroid ([LBD]N=26) vs Control with Bupi (N=26)
	• POD 3: LBD had significantly lower VAS than LB group (mean difference, -1.0; 95% CI, -1.9 to -0.08; P=0.03
	• LB vs Control: Less MME over time; (mean difference, -8.5 MME; 95% CI, -15.4 to -1.6; P = 0.015)
	• Control vs LB: Less opioid use (MME):
	    • POD2: mean difference, 16.6 MME; 95% CI, 5.3 to 28.0; P = 0.004
	    • POD3: mean difference, 13.8 MME; 95% CI, 2.3 to 25.4; P = 0.02)
	• Control vs LBD: Less opioid use (MME):
	    • POD2: mean difference, 14.0 MME; 95% CI, 3.3 to 24.6; p = 0.01

	• POD3: mean difference, 16.3 MME; 95% CI, 5.5 to 27.0; p = 0.003) • LBD group: decrease in narcotic consumption from POD 2 to 3 (mean difference,28.5 MME; 95% CI, 214.1 to 22.9; p = 0.003)

Mandava et al[11]
RCT
Arthroscopic rotator cuff repair
LB ISBPB (N=52) vs bupivacaine ISBPB (N=55)
	• Less average daily pain (NRS):
	  • POD 1: 2 vs 3.3, P=0.01
	  • POD2: 2.2 vs 3.5, P=0.006
	• Average Cumulative NRS:
	  • POD1: 2.9 vs 4.3, P=0.045
	  • POD2: 5.0 vs 7.8, P=0.013
	  • POD3: 7.3 vs 10.8, P=0.016
	  • POD4: 9.4 vs 13.6, P=0.019
	  • POD5: 11.5 vs 16.2, P=0.034
	• Average daily opioid consumption difference (%): POD2: -64.7%, P=.019
	• Average cumulative opioid (MME) difference (%):
	  • POD1: -59.5%, P=.02
	  • POD 2: -54.4%, P=.03
	• No opioids consumption (%): 44 vs 15 P=.03

Budge et al[12]
Retrosepective, observational
Total Shoulder Arthroplasty
LB ISBPB (N=50) vs bupivacaine continous catheter (N=50)
	• Less pain (NRS):
	  • POD0: 1.2 ± 1.5 vs 2.5 ± 1.9; P=0.0001
	  • POD1: 1.2 ± 1.5 vs 2.5 ± 1.9; P=0.0001
	• Cost for anesthesia professional fees, equipment and meds associated with the nerve block per case: $373 vs $706 (p value not provided)

Levin 2022[13]
Retrospective cohort
Total Shoulder arthroplasty
LB ISBPB (N=323) vs continuous catheter (N=242)
	• Less pain
	  • Less mean pain at 24 hr (2.2 vs 3.3, P<0.001)
	  • Less mean pain at 36 hr (2.8 vs 3.4, P<0.001)
	  • Less patients experiencing severe pain (17% vs 29%, P=0.001)
	  • Less mean maximum pain (5.4 vs 6.9, P<0.001)
	• Greater proportion of opioid-free patients (32% vs 10%, P<0.001)
	• Less patients required PCA (2% vs 7%, P=0.002)
	• Less 30-day ED visits (2% vs 5%, P=0.038)
	• Shorter length of stay (2.1 vs 2.3 d, P=0.01)

Jindia 2022[14] Randomized clinical trial Total Shoulder Arthroplasty LB ISBPB (N=30) vs ropivacaine block + continous catheter (N=30)	• Shorter administration time (5 vs 15 min, P<0.02) • Less opioid use at 24 hr (24.8 vs 41.1 MME, P=0.045)
Weller 2017[15] Retrospective chart review Total Shoulder Arthroplasty LB ISBPB (N=58) vs bupivacaine continous catheter (N=156)	• Less major complications (3% vs 13%, P=0.045) • Major complications: significant additional intervention and/or hospitalization • LB associated with lower cost ($289.04 vs $1559.42)

Flaherty et al 2022[16]
Prospective RCT
Rotator cuff repair
LB ISBNB + 0.5% bupi vs 0.5% bupi; N=80
	• Quality of Recovery 15 (QoR-15)
	  • 11.5 point improvement in QoR score after 72 hours (114.3 (19.0) vs 125.8 (15.9))
	• Lower worst pain score
	  • At 24 hours (1.0 vs 3.0; P=0.02)
	  • At 72 hours (3.0 vs 4.0; P=0.03)

Hutchins et al 2020[17] Retrospective Comparison LB ISBPB + various meds vs non-LB + various meds; N=1518	• Call for pain within 3 days • 25 (3.2%) vs 41 (5.6%); P=0.036

Wall et al 2022[18]
Prospective RCT
Outpatient arthroscopic rotator cuff repair
LB ISBNB vs ropicaine continous catheter; N=63
	• Fewer overall complications
	  • 22 (13.1%) vs 59 (29.8%); P<0.001
	• Anesthetic site complications
	  • Discomfort: 2 (7.1%) vs 12 (36.4%); P=0.007
	  • Leakage: 2 (7.1%) vs 10 (30.3%); P=0.023

Schoenherr et al 2022[19] Prospective Quality Improvement Rotator Cuff Repair LB ISBPB vs ropivacaine On-Q catheter; N=80	• Improved quality of recovery per smaller change in QOR-15 score at 48 hours (-3.9 vs -25.1; P<0.001) • Lower worst pain score on POD2 (5.28 vs 6.72; P=0.048) • Better quality of sleep (3.0 vs 4.5; P=0.038) • Higher patient satisfaction on POD1 (P=0.046) and POD2 (P=0.035)

References: SHOULDER SURGERY (INTERSCALENE BRACHIAL PLEXUS)

1. Finkel KJ, Walker A, Maffeo-Mitchell CL, et al. Liposomal Bupivacaine Provides Superior Pain Control Compared To Bupivacaine With Adjuvants In Interscalene Block For Total Shoulder Replacement: A Prospective Double-Blinded, Randomized Controlled Trial. J Shoulder Elbow Surg. Feb 2 2024;doi:10.1016/j.jse.2023.12.014. https://pubmed.ncbi.nlm.nih.gov/38311100/
2. Lee KJ, Greenberg S, Wixson RM, et al. The Effects of Liposomal Bupivacaine in Interscalene Blocks on Clinically Tolerable Pain in Total Shoulder Arthroplasty Patients - A Retrospective Quality Improvement Study of 491 Patients. Journal of Biomedical Research & Environmental Sciences. 2023; https://pubmed.ncbi.nlm.nih.gov/37866512/
3. Pickle E, Nerdecchia N, Pearce-Smith BA, et al. Liposomal Bupivacaine for Interscalene Block in Ambulatory Rotator Cuff Repair. Ambulatory Surgery. 2023; https://ambulatorysurgery.org/wp-content/uploads/2023/06/AMB-SURG-29.2_PICKLE.pdf
4. Simovitch RW, Pociask C, Matz JD, Deziel LP, Thomas HM. Efficacy of Brachial Plexus Blockade with Liposomal Bupivacaine and Bupivacaine Compared to Ropivacaine combined with Dexamethasone for Arthroscopic Rotator Cuff Repair. presented at: AAOS-American Academy of Orthopaedic Surgeons; 2021; San Diego. https://pubmed.ncbi.nlm.nih.gov/36147653/
5. Kenny, B. , Schmidt, E. , Wozniak, A. and Byram, S. (2021) A Retrospective Comparison of Interscalene Continuous Catheter Verse Single-Injection with Liposomal Bupivacaine in Total Shoulder Arthroplasty. Open Journal of Anesthesiology, 11, 269-278. doi: 10.4236/ojanes.2021.119026. https://www.scirp.org/journal/paperinformation?paperid=111746
6. Krupp R, Smith A, Nyland J, Mojesky C, Perkins D, Carreon LY. Liposomal bupivacaine nerve block provides better pain control post-total shoulder arthroplasty than continuous indwelling catheter. Arch Orthop Trauma Surg. Mar 2 2022;doi:10.1007/s00402-022-04386-5. https://pubmed.ncbi.nlm.nih.gov/35235030/
7. Patel MA, Gadsden JC, Nedeljkovic SS, et al. Brachial Plexus Block with Liposomal Bupivacaine for Shoulder Surgery Improves Analgesia and Reduces Opioid Consumption: Results from a Multicenter, Randomized, Double-Blind, Controlled Trial. Pain Med. May 31 2020;21(2):387-400. doi:10.1093/pm/pnz103. https://pubmed.ncbi.nlm.nih.gov/31150095/
8. Vandepitte C, Kuroda M, Witvrouw R, et al. Addition of Liposome Bupivacaine to Bupivacaine HCl Versus Bupivacaine HCl Alone for Interscalene Brachial Plexus Block in Patients Having Major Shoulder Surgery. Regional anesthesia and pain medicine. Feb 03 2017;42(3):334-341. doi:10.1097/aap.0000000000000560. https://pubmed.ncbi.nlm.nih.gov/28157791/
9. Weir TB, Simpson N, Aneizi A, et al. Single-shot liposomal bupivacaine interscalene block versus continuous interscalene catheter in total shoulder arthroplasty: Opioid administration, pain scores, and complications. J Orthop. Nov-Dec 2020;22:261-267. doi:10.1016/j.jor.2020.05.006. https://pubmed.ncbi.nlm.nih.gov/32435107/
10. Baessler AM, Moor M, Conrad DJ, Creighton J, Badman BL. Single-Shot Liposomal Bupivacaine Reduces Postoperative Narcotic Use Following Outpatient Rotator Cuff Repair: A Prospective, Double-Blinded, Randomized Controlled Trial. JBJS. 2020;Latest Articles:10.2106/JBJS.20.00225. doi:10.2106/jbjs.20.00225. https://pubmed.ncbi.nlm.nih.gov/33208641/
11. Mandava NK, Sethi PM, Routman HD, Liddy N, Haidamous G, Denard PJ. Opioid requirement after rotator cuff repair is low with a multimodal approach to pain. J Shoulder Elbow Surg. Jul 2021;30(7):e399-e408. doi:10.1016/j.jse.2020.09.032. https://pubmed.ncbi.nlm.nih.gov/33144226/
12. Budge M, Orvets N, Shields E. Single-shot liposomal bupivacaine interscalene nerve block provides equivalent pain relief compared to continuous catheter interscalene nerve block in total shoulder arthroplasty. Seminars in Arthroplasty: JSES. 2020/10/10/ 2020;30(4):285-290. doi:10.1053/j.sart.2020.09.003. https://www.sciencedirect.com/science/article/abs/pii/S1045452720300419
13. Levin JM, Charalambous LT, Girden A, Twomey-Kozak J, Goltz D, Wickman J, Bullock WM, Gadsden JC, Klifto CS, Anakwenze OA. Interscalene block with liposomal bupivacaine versus continuous interscalene catheter in primary total shoulder arthroplasty. J Shoulder Elbow Surg. 2022 Oct;31(10):e473-e479. doi: 10.1016/j.jse.2022.03.013. Epub 2022 Apr 25. PMID: 35472576. https://pubmed.ncbi.nlm.nih.gov/35472576/
14. Jindia, L.; Christensen, J.; Deng, J.; Puri, S.; Balouch, M.; Haidamous, G.; Frankle, M.; Camporesi, E.M. Opioid Sparing at 24 h after Total Shoulder Arthroplasty by Undiluted Liposomal Bupivacaine Single Shot Interscalene Block: A Randomized Clinical Trial, First Results. Surgeries 2022, 3, 64-70. https://doi.org/10.3390/surgeries3010008. https://www.mdpi.com/2673-4095/3/1/8
15. Weller WJ, Azzam MG, Smith RA, Azar FM, Throckmorton TW. Liposomal Bupivacaine Mixture Has Similar Pain Relief and Significantly Fewer Complications at Less Cost Compared to Indwelling Interscalene Catheter in Total Shoulder Arthroplasty. J Arthroplasty. 2017 Nov;32(11):3557-3562. doi: 10.1016/j.arth.2017.03.017. Epub 2017 Mar 16. PMID: 28390888. https://pubmed.ncbi.nlm.nih.gov/28390888/
16. Flaherty JM, Berg AA, Harrison A, Braman J, Pearson JM, Matelich B, Kaizer AM, Hutchins JL. Comparing liposomal bupivacaine plus bupivacaine to bupivacaine alone in interscalene blocks for rotator cuff repair surgery: a randomized clinical trial. Reg Anesth Pain Med. 2022 May;47(5):309-312. doi: 10.1136/rapm-2021-103349. Epub 2022 Feb 21. PMID: 35190468. https://pubmed.ncbi.nlm.nih.gov/35190468/
17. Hutchins JL, Habeck J, Novaczyk Z, et al. Patient Complications after Interscalene Block: A Retrospective Comparison of Liposomal Bupivacaine to Nonliposomal Bupivacaine. Anesthesiology research and practice. 2020;2020:6704303. doi:10.1155/2020/6704303. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7139877/
18. Wall KC, Elphingstone J, Paul KD, et al. Nerve Block with Liposomal Bupivacaine Yields Fewer Complications and Similar Pain Relief When Compared to an Interscalene Catheter for Arthroscopic Shoulder Surgery: A Randomized Controlled Trial. J Shoulder Elbow Surg. Sep 14 2022;doi:10.1016/j.jse.2022.07.030. https://pubmed.ncbi.nlm.nih.gov/36115616/
19. Schoenherr J, Gonzalez M, Serrano R, et al. Interscalene Liposomal Bupivacaine Vs. Interscalene Catheter for Arthrosocopic Rotator Cuff repair. presented at: ASRA- American Society of Regional Anesthesia and Pain Medicine Annual Meeting; 2022; Las Vegas, NV. https://pubmed.ncbi.nlm.nih.gov/36458106/

SHOULDER SURGERY (INFILTRATION)	
Study	**Results**
Sethi et al 2019[1] *RCT* Arthroscopic Rotator Cuff Repair LB + bupivacaine ISBPB (N=25) vs Bupivacaine ISBPB alone (N=25)	• Less pain at POD1 (2.58 vs 5.74; P=0.001) • Less pain at POD2 (3.63 vs 5.13; P=0.029) • Less opioid use POD0 (4 vs 15.5; P=0.001) • Less opioid use POD1 (24.4 vs 62; P=0.002) • Less opioid use POD2 (28.3 vs 57.0; P=0.006) • Less opioid use POD3 (10.6 vs 38.6; P=0.01) • Less opioid use POD4 (7.0 vs 28.5; P=0.009) • Less opioid use POD5 (3.4 vs 18.9; P= 0.01) • Lower average opioid use (12.4 vs 34.1; P=0.003) • Lower cumulative opioid use (73.8 vs 204.9 (P=0.003)

Routman et al 2017[2]
Retrospective, observational
Shoulder arthroplasty
(primary total, reverse, or hemi)
LB + ISBPB vs ISBPB alone; N=55
	• Less pain at POD0 (3.5 vs 6.5; P<0.001)
	• Less pain at POD1 (3.5 vs 7.5; P<0.001)
	• Less pain in opioid naïve patients
	    • POD0 (4.0 vs 6.0, P=0.02)
	    • POD1 (3.5 vs 7.0; P<0.001)
	• Less pain in chronic opioid users (POD1 3.5 vs 7.0; P=0.006)
	• Less opioid use POD1 (10.0 vs 21.0; P<0.001)
	• Less opioid use POD0+1 (17.5 vs 30.5; P=0.001)
	• Less opioid us in opioid naïve patients
	    • POD1 (2.5 vs 15.0; P=.005)
	    • POD0+1 (5.0 vs 26.0; P=0.009)
	    • All days (5.0 vs 29.5; P=0.005)
	• Less opioid us in chronic opioid useres
	    • POD1 (11.0 vs 34.0; P=.004)
	    • POD0+1 (20.0 vs 58.5, P=0.03)
	    • All days (23.0 vs 61.0, P=.01)
	• Shorter length of stay (1.0 vs 2.0 days; P<0.001)
	• Shorter length of stay in opioid naïve patients (1.0 vs 2.0 days; P=0.002)

Hannan et al 2016[3]
Retrospective, observational
Shoulder arthroplasty
(primary total, reverse, or hemi)
LB local infiltration vs ropivacaine ISNB
N=58
	• Less pain
	    • 38% reduction in pain NRS (4 vs 6.5) (P=0.001)
	    • 29% reduction in pain NRS (5 vs 7) (P=0.029)
	• Less opioid consumption MME
	    • 67% reduction in opioid consumption POD2 (37 mg vs 112 mg) (P=0.001)
	    • 80% reduction in opioid consumption POD3 (5 mg vs 25 mg) (P=0.002)
	• Shorter LOS (46 hours vs 57 hours) (P=0.012)
	    • More patients discharged on POD 1 (16 vs 2) (P=0.010)

References: SHOULDER SURGERY (INFILTRATION)

1. Sethi PM, Brameier DT, Mandava NK, Miller SR. Liposomal bupivacaine reduces opiate consumption after rotator cuff repair in a randomized controlled trial. J Shoulder Elbow Surg. May 2019;28(5):819-827. doi:10.1016/j.jse.2019.01.008
2. Routman HD, Israel LR, Moor MA, Boltuch AD. Local injection of liposomal bupivacaine combined with intravenous dexamethasone reduces postoperative pain and hospital stay after shoulder arthroplasty. J Shoulder Elbow Surg. Nov 15 2017;26(4):641-647. doi:10.1016/j.jse.2016.09.033.
3. Hannan CV, Albrecht MJ, Petersen SA, Srikumaran U. Liposomal Bupivacaine vs Interscalene Nerve Block for Pain Control After Shoulder Arthroplasty: A Retrospective Cohort Analysis. Am J Orthop. 2016;45(7):424-430.

SPINE SURGERY	
Study	**Results**

McClure et al 2024[1]
Retrospective review
Open Lumbar Spinal Fusion
LB 266 mg (20 ml) + 100 mg 0.5% bupi + NS (N=99) vs. 400 ml 0.5% bupi pain pump (5 ml/hr continuous infusion) N(=99)
	• Reduced postoperative opioids by 43% in terms of mean MME/minute
	  • (0.024 vs 0.042 MME/min, P<0.0001)
	• Reduced total postoperative opioids by 31%
	  • (48.9 vs 70.9 MME; P=0.0001)

Berven et al. 2024[2]
Retrospective cohort study
Outpatient discectomy, laminectomy, and lumbar fusion procedures
LB (n=381) vs non-LB (n=1143)
	• ~39% reduction in opioid use before hospital outpatient discharge
	  • 80 vs 132 MMEs (mean difference, -52; p=0.0041).
	• ~63% reduction in opioid use for laminectomy surgery during the hospital outpatient stay
	  • 54.2 vs 146.2 MMEs (mean difference, -92; p=0.0107)
	• ~30% reduction in opioid use in discectomy surgery subtype at 3 months
	  • 298 vs 425 MMEs (mean difference, -127; p=0.0354)
	• Lower rate of ED visits at 2 months after discharge
	  • 3.9% vs 7.6% (p=0.015)

Stewart et al. 2023[3] Observational, retrospective study One or two level lumbar laminectomy (N=50) LB ESPB vs. Multimodal analgesia alone (Control)	• No PACU median hydromorphone consumption (0 vs 0.8 mg; P=0.001) • 48% reduction in mean morphine equivalents 0-24 h (31.9 mg vs 61.2 mg; P=0.001) • 27% reduction in mean morphine equivalents 24-48 h (31.9 mg vs 43.6 mg; P=0.04) • 45% reduction in mean PACU NRS pains scores (2.8 vs 5.1; P=0.01) • 45% reduction in mean POD1 pain scores (3.0 vs 5.5; P<0.001) • 27% reduction in mean POD2 pain scores (3.5 vs 4.8; P=0.01) • Lower antiemetic use (12% vs 48%; P<0.005)
Forrester et al 2022[4] Retrospective analysis Posterior cervical or lumbar surgery VA Health System LB infiltration vs control; N=104	• 19% reduction in pain at 24 hours (5.2 vs 6.4; P=0.042) • 26% reduction in pain at 48-72 hours (4.9 vs 6.6; P=0.007)
Alhammoud et al 2022[5] Retrospective cohort Multilevel Lumbar Decompression (2-4 levels) LB infiltration vs control; N=86	• 48% reduction in pain before discharge (1.6 vs 3.1; P<0.001) • Shorter length of stay in patients without complications (26.7 vs 41.1 h; P=0.029) • Trend toward shorter LOS when include patients with complications (32.4 vs 47.5 h; P=0.069)

Dincer et al 2022[6] Retrospective analysis TLIF LB Erector Spinae Plane plus infiltration vs LB infiltration alone; N=50	• 24% shorter length of stay (2.56 vs 3.36 days; P=0.007) • 26% Shorter time to ambulation (0.96 vs 1.29 days; P=0.026) • 26% reduction in pain AUC at 12-24 hours (39.4 vs 53.4; P=0.03) • 12% reduction in pain AUC total hospital stay (44.5 vs 50.5; P=0.025) • 20% less in opioid use at 12-24 hours (50.1 vs 62.3 MME; P<0.001) • 29% less in opioid use total hospital stay (137.3 vs 194.7 MME; P=0.04)
Gannon et al 2022[7] Retrospective observational study One-level and two-level posterior lumbar fusion LB local infiltration vs historical controls; N=84	• 34% reduction in mean opioid use (153.5 vs 233.1, P=0.001)

Kurnutala et al 2021[8]
ERAS + mTLIP block with LB vs No ERAS/mTLIP
Lumber Laminectomy N = 24;
Lumbar Spinal Fusion N =41
	• Reduced length of stay and opioid use in lumbar laminectomy
	  • 73% reduction in length of stay (0.75 vs 2.79; P=0.01)
	  • 51% difference in opioid use (39.68 vs 81.68; P=0.03)
	• Reduced opioid use in spinal fusion
	• 38% difference in opioid use (97.12 vs 157.48; P=0.04)

Nguyen et al 2021[9]
Systemic review, meta-analysis
Cervical spine, lumbar, and spinal deformity
Meta-analysis of LB 10 studies; N=1112
	• LB was associated with significantly lower:
	  • MME of postoperative opioids, especially in opiate-tolerant patients
	  • VAS scores
	  • AUC of cumulative pain scores and numeric pain scale scores
	  • Hospital length of stay
	  • Comparable or lower odds of adverse effects relative to controls
	• Decreased time spent receiving IV opioids (13.0 vs 23.3 hr; p<0.001) in lumbar surgeries

Roh et al 2020[10]
Lumbar spinal fusion
LB local infiltration vs non-liposomal bupivacaine local infiltration; N=210
	• Less opioid use (geometric mean)
	  • Day of surgery: 32% difference (102.7 vs 152.1; P<0.001)
	  • POD1: 40% difference (49.0 vs 81.4; P<0.001)
	  • POD2: 39% difference (29.6 vs 48.7; P<0.001)
	• Higher percentage of patients ambulated ≤12 hrs (61.2% vs 3.0%; P<0.001)
	• More patients discharged
	  • POD1: 32.4% vs 1.0%; P<0.001
	  • POD2:56.2% vs 37.1%; P=0.006
	• Less total direct cost ($15,528.74 vs $18,564.67; P<0.001)

Katsevman et al 2020[11] Lumbar fusion (PLIF or TLIF) LB local infiltration vs control; N=122	• 75% reduction in IV opioid use at 48-60 hrs (0.3 mg vs 1.2 mg; P=0.049) • 61% reduction in length of stay (1.94 days vs 3.08 days; P=0.0043) • Greater percentage of patients discharged home at 36-48 hrs (19 vs 0; P=0.0226)

Brusko et al 2019[12]
Lumbar fusion surgery
LB ERAS vs Control/ Pre-ERAS; (N=97)
	• Lower pain scores (1-10 scale):
	    • 30% reduction on POD1: 4.2±3.2 vs 6.0±3.2, (P=0.006)
	• Lower opioid use (mg):
	    • 63% difference on POD0: 408.0±527.2 vs 1094.7±847.6, (P=0.0004)
	    • 23% difference on POD1: 1320.0±1026.4 vs 1708.4±819.6, (P=0.04)
	    • 29% difference on POD3: 1500.1±778.5 vs 2105.4±1090.6 (P=0.03)
	    • Entire LOS: 2729.5±4594.3 vs 5230.3±3920.3, (P=0.003)
	• Shorter LOS (days): 2.9±1.9 vs 3.8±1.8, (P=0.01)
	• Less ondansetron (mg) 2.81±4.3 vs 6.0±10.5, (P=0.02)

Brown et al 2018[13] Lumbar decompression & fusion LB local infiltration vs. placebo;N=50	• 35% reduction in opioids in narcotic tolerant patients (13.3 mg vs 20.6 mg; P=0.048)
Gannon et al 2018[14] Lumbar procedures LB local infiltration vs. control (no local anesthetic); N=104	• 25% decrease in length of stay (2.04 days vs 2.73 days; P=0.0071) • Lower average VAS pain score (P=0.016) • Lower opioid consumption (P=0.048)

Tomov et al 2017[15]
Single level TLIF
LB local infiltration vs control;N=30
	• Less IV opioid use on POD0-3
	    • POD0: 78% reduction (5.2 vs 23.7; P=0.0051)
	    • POD1: 66% reduction (20.1 vs 58.4; P=0.0175)
	    • POD2: 78% reduction (9.7 vs 44.9; P=0.001)
	    • POD3:26% reduction (3.9 vs 21.4; P=0.0002)

Wang et al 2017[16] Minimally invasive TLIF LB local infiltration + ERAS vs no infiltration + ERAS; N=53	• 68% reduction in length of stay (1.23 days vs 3.9 days; P=0.009) • 15% reduction in total acute costs ($19,212 vs $22,656; P<0.001)
Puffer et al 2016[17] Single level lumbar microdiskectomy LB local infiltration @ closure vs no infiltration @ closure;N=80 (all arms received bupivacaine prior to incision)	• 43% reduction in time on IV narcotics (13.0 hrs vs 23.3 hrs; P<0.001) • 35% reduction in pain scores measured in PACU for non-chronic pain patients (2.4 vs 3.7;P<0.04)

Kim et al 2016[18] Unilateral single level TLIF LB local infiltration vs bupivacaine local infiltration; N=74	• 67% reduction in pain scores between 0-12 hours (15 vs 45.6;P=0.003) • 22% reduction in pain scores between 12-24 hours (37.6 vs 48.4; P=0.05) • 34% reduction in opioid use between 12-24 hours (16.0 vs 24.1; P=0.04) • 28% reduction in length of stay (3.1 days vs 4.3 days; P<0.001) • Lower mean total cost per patient ($14,536 vs $15,406; no p-value provided)

References: SPINE SURGERY

1. McClure A, Silveri OC, Foddrell M, Duteil K, Madarász LE, Silveri CP. Efficacy of Liposomal Bupivacaine in Reducing Opioid Use After Posterior Lumbar Spinal Decompression and Fusion. Orthopedics. Apr 4 2024:1-5. doi:10.3928/01477447-20240325-07. https://pubmed.ncbi.nlm.nih.gov/38568003/
2. Berven S, Wang MY, Lin JH, Kakoty S, Lavelle W. Effects of Liposomal Bupivacaine on Opioid Use and Healthcare Resource Utilization After Outpatient Spine Surgery: a Real-world Assessment. Spine J. Jun 4 2024;doi:10.1016/j.spinee.2024.05.005. https://pubmed.ncbi.nlm.nih.gov/38843956/
3. Stewart JW, Dickson D, Van Hal M, et al. Ultrasound-guided erector spinae plane blocks for pain management after open lumbar laminectomy. European Spine Journal. 2023/08/12 2023;doi:10.1007/s00586-023-07881-4. https://pubmed.ncbi.nlm.nih.gov/37572144/
4. Forrester DA, Miner H, Shirazi C, Kavadi N. Liposomal bupivacaine in posterior spine surgery: A piece of the puzzle for postoperative pain. Journal of Orthopaedics. 2022/09/01/ 2022;33:55-59. doi:https://doi.org/10.1016/j.jor.2022.07.004. https://pubmed.ncbi.nlm.nih.gov/35864926/
5. Alhammoud A, Bouloussa H, Oganesian A, et al. Does liposomal bupivacaine reduce hospital length of stay for multilevel lumbar decompressions? A retrospective matched cohort study. Journal of Musculoskeletal Surgery and Research. 2022;6doi:10.25259/JMSR_108_2022. https://journalmsr.com/does-liposomal-bupivacaine-reduce-hospital-length-of-stay-for-multilevel-lumbar-decompressions-a-retrospective-matched-cohort-study/
6. Dincer A, Wang A, Kanter MJ, Olmos M, Yang M, Riesenburger RI, Kryzanski JT. Clinical Outcomes of Liposomal Bupivacaine Erector Spinae Block in Minimally Invasive Transforaminal Lumbar Interbody Fusion Surgery. Neurosurgery. 2022 Dec 5. doi: 10.1227/neu.0000000000002249. Epub ahead of print. PMID: 36512838. https://pubmed.ncbi.nlm.nih.gov/36512838/
7. Gannon E, Freeman M, Cornett C, Vincent S, Powers S, Lyden E. The Effects of Liposomal Bupivacaine on Long-term Outcomes and Decreasing Immediate Postoperative Opioid Use Following One-level and Two-level Posterior Lumbar Fusions. Clinical spine surgery. Jun 16 2022;doi:10.1097/bsd.0000000000001354. https://pubmed.ncbi.nlm.nih.gov/35706091/
8. Kurnutala LN, Dibble JE, Kinthala S, Tucci MA. Enhanced Recovery After Surgery Protocol for Lumbar Spinal Surgery With Regional Anesthesia: A Retrospective Review. Cureus. Sep 2021;13(9):e18016. doi:10.7759/cureus.18016. https://pubmed.ncbi.nlm.nih.gov/34667691/
9. Nguyen TH, Iturriaga C, Verma R. Efficacy of liposomal bupivacaine in spine surgery: a systematic review. Spine J. Sep 2021;21(9):1450-1459. doi:10.1016/j.spinee.2021.02.014. https://pubmed.ncbi.nlm.nih.gov/33618032/
10. Roh MS, Kucher OA, Shick KM, Knolhoff DR, McGarvey JS, Peterson SC. Intramuscular Liposomal Bupivacaine Decreases Length of Stay and Opioid Usage Following Lumbar Spinal Fusion. Clinical spine surgery. Oct 2020;33(8):E359-E363. doi:10.1097/BSD.0000000000001006. https://pubmed.ncbi.nlm.nih.gov/32427717/
11. Katsevman GA, Allison AA, Fang W, et al. Retrospective Assessment of the Use of Liposomal Bupivacaine in Lumbar Fusions in Immediate Postoperative Hospital Care. World Neurosurg. Sep 2020;141:e820-e828. doi:10.1016/j.wneu.2020.06.049. https://pubmed.ncbi.nlm.nih.gov/32540284/
12. Brusko GD, Kolcun JPG, Heger JA, et al. Reductions in length of stay, narcotics use, and pain following implementation of an enhanced recovery after surgery program for 1- to 3-level lumbar fusion surgery. Neurosurg Focus. Apr 1 2019;46(4):E4. doi:10.3171/2019.1.FOCUS18692. https://pubmed.ncbi.nlm.nih.gov/30933921/
13. Brown L, Weir T, Shasti M, et al. The Efficacy of Liposomal Bupivacaine in Lumbar Spine Surgery. 10.14444/5052. International journal of spine surgery. Aug 2018;12(4):434-440. doi:10.14444/5052. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6159630/
14. Gannon EJ, Cornett CA, Larson EP, Lyden ER. The Efficacy of Liposomal Bupivacaine in Lumbar Spine Surgery. J Surg Curr Trend Innov. 2018;2(005). https://www.heraldopenaccess.us/openaccess/the-efficacy-of-liposomal-bupivacaine-in-lumbar-spine-surgery
15. Tomov M, Tou K, Winkel R, et al. Does Subcutaneous Infiltration of Liposomal Bupivacaine Following Single-Level Transforaminal Lumbar Interbody Fusion Surgery Improve Immediate Postoperative Pain Control? Asian spine journal. Feb 2018;12(1):85-93. doi:10.4184/asj.2018.12.1.85. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5821938/
16. Wang MY, Chang HK, Grossman J. Reduced Acute Care Costs With the ERAS(R) Minimally Invasive Transforaminal Lumbar Interbody Fusion Compared With Conventional Minimally Invasive Transforaminal Lumbar Interbody Fusion. Neurosurgery. Oct 1 2018;83(4):827-834. doi:10.1093/neuros/nyx400. https://pubmed.ncbi.nlm.nih.gov/28945854/
17. Puffer RC, Tou K, Bydon M, Currier B, Freedman BA. Liposomal bupivacaine incisional injection in single-level lumbar spine surgery. Spine J. 2016;16(11):1305–1308. doi:10.1016/j.spinee.2016.06.013. https://pubmed.ncbi.nlm.nih.gov/27349628/
18. Kim J, Burke SM, Kryzanski JT, et al. The Role of Liposomal Bupivacaine in Reduction of Postoperative Pain after Transforaminal Lumbar Interbody Fusion: A Clinical Study. World Neurosurgery. 1 2016;91:460-467. https://pubmed.ncbi.nlm.nih.gov/27113396/

FOOT AND ANKLE SURGERY	
Study	**Results**

Schwartz et al 2024[1]
RCT
Sciatic Nerve Block in the Popliteal Fossa in bunionectomy (N=185)
SNB LB 133 mg + 20 mL normal saline vs.
SNB 20 mL (50 mg) 0.25% bupivacaine + 10 mL normal saline
After: All patients received Mayo field block with 20 mL 0.5% bupivacaine
	• AUC of NRS Pain Intensity Score 0-96 hrs post-surgery (Primary Endpoint)
	  ◦ 44% difference in AUC of NRS pain intensity scores through 4 days (P<0.00001)
	  ◦ After 24 hrs, pain scores were significantly lower with LB SNB at every time point through 4 days
	• Total Opioid Consumption 0-96 hrs post-surgery (Secondary Endpoint)
	  ◦ 61% fewer opioids consumed in first 4 days after surgery (P<0.00001)
	  ◦ 5 times higher odds of being opioid free through 4 days after surgery (P=0.003)

Robbins et al. 2015[2]
Prospective study
Infiltration forefoot (N=20)
LB 266 mg (20 ml) vs. Pain protocol no LB
All patients received ankle block of 10 ml 1% lidocaine + 0.5% bupivacaine HCL
LB: 20 ml of 0.5% Bupi HCL for ankle block
Control: 15 ml of 0.5% Bupi HCL for ankle bloc*k*
	• Mean narcotic pills consumed
	  ◦ POD 1 (1.4 vs 3.6, P=0.002)
	  ◦ POD 2 (1.8 vs 3.6, P=0.021)
	• Wound complications (1 vs 4)

Golf et al. 2011[3]
RCT
Infiltration in Bunionectomy (N=185)
LB 120 mg (8 ml) vs placebo
	• Mean AUC of NRS Pain Score 0-24 hrs post-surgery
	  ◦ 0-24 hrs (123.9 vs 146.2, P=0.0005)
	  ◦ 0-36 hrs (196.9 vs 220.3, P=0.0229)
	• Pain Free
	  ◦ 2 hrs (68% vs 45.8%, P=0.0019)
	  ◦ 4 hrs (38.1% vs14.6%, P=0.0002)
	  ◦ 8 hrs (13.4% vs 3.1%, P=0.0078)
	  ◦ 48 hrs (35.1% vs 19.1%, P=0.0153)
	• Time to first opioid (7.2 hrs vs 4.3 hrs, P<0.0001)
	• Opioid free
	  ◦ 8 hrs (41.2% vs 9.4%, P<0.0001)
	  ◦ 12 hrs (20.6% vs 3.1%, P=0.0003)
	  ◦ 20 hrs (7.2% vs 1.0%, P=0.0404)
	• Opioid consumption 0-24 hrs (3.8 tabs vs 4.7 tabs, P=0.0077)

References: FOOT AND ANKLE SUREGRY

1. Schwartz G, Gadsden JC, Gonzales J, Hutchins J, Song J, Brady O, DiGiorgi M, Winston R. A phase 3 active-controlled trial of liposomal bupivacaine via sciatic nerve block in the popliteal fossa after bunionectomy. J Clin Anesth. 2024 Jun;94:111402. doi: 10.1016/j.jclinane.2024.111402. Epub 2024 Feb 9. PMID: 38340677. https://pubmed.ncbi.nlm.nih.gov/38340677/
2. Robbins J, Green CL, Parekh SG. Liposomal bupivacaine in forefoot surgery. Foot Ankle Int. 2015 May;36(5):503-7. doi: 10.1177/1071100714568664. Epub 2015 Jan 22. PMID: 25614060. https://pubmed.ncbi.nlm.nih.gov/25614060/
3. Golf M, Daniels SE, Onel E. A phase 3, randomized, placebo-controlled trial of DepoFoam® bupivacaine (extended-release bupivacaine local analgesic) in bunionectomy. Adv Ther. 2011 Sep;28(9):776-88. doi: 10.1007/s12325-011-0052-y. Epub 2011 Aug 12. PMID: 21842428. https://pubmed.ncbi.nlm.nih.gov/21842428/

General Surgery

COLORECTAL	
Study	**Results**

Schwartz et al 2024[1]
Real World Study IQVIA
Healthcare Resource Utilization
LB vs non-LB (N=4397 each)
	• Inpatient readmission
	    • Month 1: 6% vs 8.5%, mean difference 0.69, (P<0.0001)
	    • Month 2: 8.3% vs 12.1%, mean difference 0.66, (P<0.0001)
	    • Month 3: 11.0% vs 14.8%, mean difference 0.71, (P<0.0001)
	• Emergency department visit
	    • Month 1: 8.7% vs 10.0%, mean difference 0.85, (P=0.023)
	    • Month 2: 11.2% vs 13.4%, mean difference 0.80, (P<0.001)
	    • Month 3: 13.7% vs 17.0%, mean difference 0.78, (P<0.0001)
	• Outpatient visit
	    • Month 1: 34.1% vs 38.5%, mean difference 0.83, (P<0.0001)
	    • Month 2: 47.7% vs 51.2%, mean difference 0.87, (P=0.001)
	    • Month 3: 54.9% vs 57.2%, mean difference 0.91, (P<0.028)
	• Length of stay: 5.2 vs 5.7 days, (P<0.0001)

Holtz et al 2022[2]
Retrospective
Abdominal or colorectal resection
LB vs epidural; (N=5799)
	• Lower hospital cost
	    • $6,304 less hospital cost with EXPAREL vs epidural group ($27,315 vs. $33,619; P<0.0001)
	• Hospital Stay
	    • Mean LOS was 6.9 days and 8.5 days in patients receiving EXPAREL vs epidural analgesia
	    • Patients receiving EXPAREL were more likely to be discharged directly to home than epidural (87% vs. 75% ; P<0.0001)
	    • 30-day readmissions rate lower in EXPAREL group 11% vs. epidural group 15% (P=0.0073)
	• Incidence of hypotension
	    • Postoperative hypotension lower in EXPAREL group 11% vs. epidural group 30% (P<0.0001)
	• Vasopressor use lower in EXPAREL group 7% vs. epidural group 22% (P<0.0001)

Tran et al 2021[3]
Pharmacoeconomic evaluation
Colorectal resection
LB via TAP or local infiltration vs non-LB (N=486)
	• Average LOS 3.4 vs 5.9 days
	• Lower cost of care
	  • -23% (-$1435) in primary analysis of public costs (P=0.004)
	  • -25% (-$1345) in sensitivity analysis of internal costs (P=0.002)
	• -27% in open surgery (P=0.002) and -23% in laparoscopic surgery (P=0.046) subgroup analysis

Rizk et al 2020[4] Retrospective Open or minimally invasive colorectal resection LB vs IV APAP	• Reduction in hospital length of stay after surgery (adjusted change=-1.2 d, 95%CI -2.1 to -0.3) vs IV APAP (adjusted change= 1.5 d, 95%CI 0.7 to 2.2)
Guerra et al 2019[5] Prospective, observational Laparoscopic colorectal surgery LB TAP vs bupivacaine TAP (N=100)	• 73% reduction in overall opioid use (P=0.0002) • More patients required no narcotics during hospital stay (32% vs 8%; P=0.005) • Shorter length of stay (2.7 vs 3.4 days; P=0.0146) • Quicker return to bowel function (1.7 vs 2.4 days; P=0.0002)
Torgeson et al 2019[6] RCT Colorectal Surgery ERP with LB TAP (n=44) vs ERP with Epidural (n=39)	• 13% reduction in length of stay (P=0.045)
Fields et al 2019[7] Retrospective, observational Laparoscopic colorectal surgery LB TAP vs bupivacaine infiltration (N=940)	• Decreased opioid use (-15.9 mg; P=0.04) • Decreased length of stay (-0.8 days; P<0.001)
Pricolo et al 2018[8] Retrospective Cohort Colectomy ERP with LB (n=39) vs Opioid + routine mech. bowel prep (n=34) vs Opioid + selective bowel prep (n=36)	• 84% reduction in opioid use vs opioid + routine mech bowel prep (P<0.0001) • 74% reduction in opioid use vs opioid + selective bowel prep (P=0.0017) • 65% reduction in overnight opioid use vs opioid + routine mech bowel prep (P<0.0001) • 59% reduction in overnight opioid use vs opioid + selective bowel prep (P=0.0006) • 63% reduction in length of stay vs opioid + routine mech bowel prep (P<0.0001) • 43% reduction in length of stay vs opioid + selective bowel prep (P<0.0001)
Burnett et al 2018[9] Retrospective cohort Laparotomy LB + multimodal (n=31) vs Multimodal (n=30	• 46% reduction in opioid use @ 24-48 hrs (P=0.04) • 55% reduction in opioid us @ 48-72 hrs (P=0.02) • 30% reduction in opioid use @ 0-72 hrs (P=0.04) • 25% reduction in time to flatus (P=0.0054)

Felling et al 2018[10] RCT Colon and rectal surgery ERP with LB TAP vs ERP with Epidural	• 52% reduction in opioid consumption (P<0.001)-includes fentanyl from epidural
Stokes et al 2017[11] Retrospective Observation Abdominopelvic Colrectal Surgery LB TAP vs Bupivacaine TAP (N=407)	• Significantly less reported pain 1st 24-36 hours post-op • 35% reduction in opioid consumption (P=0.040)
Keller et al 2017[12] Retrospective, observational Laparoscopic colon surgery ERP with LB vs ERP without LB (N=140)	• 59% reduction in pain in the PACU (P=0.001) • 67% reduction in opioid use on POD0 (P<0.01) • 54% reduction in opioid use on POD1 (P=0.03) • 74% reduction in opioid use on POD2 (P=0.02) • 58% reduction in opioid use on POD3 (P<0.001) • Shorter length of stay (2.96 vs 3.93 days; P=0.003) • Less indirect costs ($7,298.68 vs $9,449.27; P=0.02)
Keller et al 2016[13] Retrospective Observational Laparoscopic colon resection LB TAP vs No TAP (N=50)	• 100% reduction pain on initial PACU survey (P<0.01) • 67% reduction in pain on final PACU survey (P=0.03) • 100% reduction in pain on POD2 (P=0.002) • 65% reduction in opioid consumption POD0 (P<0.01) • 25% reduction in length of stay (P=0.04)
Beck et al 2015[14] Retrospective Observational Open and lap colon resection Multimodal with LB (n=66) vs Traditional regimen (n=167)	• 17% reduction in pain scores (P<0.05) • 43% reduction in cumulative opioids through 72 hours (P=0.03) • Longer time to first opioid use (5.2 hrs vs. 2.9 hrs; P<0.05) • 20% decrease in length of stay (P=0.04) • Fewer opioid related adverse event medications (antipruritic, antiemetic, laxative)
Cohen et al 2014[15] Pooled Analysis Laparoscopic and open colon resection and ileostomy reversal LB (N=86) vs IV PCA (N=105)	• 60% reduction in overall opioid use (P<0.0001) • Longer time to first opioid consumption (1.2 hrs vs 0.6 hrs; P<0.0001) • 33% reduction in length of stay (P<0.0001) • 23% reduction in hospital costs (P=0.0109)

Marcet et al 2013[16] Ileostomy reversal LB vs opioid; N=27	• Mean Hospital Costs: • $6,482 vs. $9,282, (P=0.01) • Median LOS: • 3 days vs. 5.1 days; (P<0.001)
Cohen et al 2012[17] Prospective Cohort Open colectomy Multimodal with LB vs Opioid PCA (N=39)	• 60% reduction in overall opioid use (P<0.0001) • Longer time to first opioid consumption (1.2 hrs vs 0.6 hrs; P<0.0001) • 33% reduction in length of stay (P<0.0001) • 23% reduction in hospital costs (P=0.0109)

References: COLORECTAL

1. Schwartz G, Lin JH, Kakoty S. Real-world assessment of longitudinal opioid use and healthcare resource utilization in patients undergoing colorectal resection. Surg Open Sci. 2024 May 31;20:94-97. doi: 10.1016/j.sopen.2024.05.022. PMID: 38973811; PMCID: PMC11226975. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11226975/
2. Holtz M, Liao N, Lin JH, Asche CV. Economic Outcomes and Incidence of Postsurgical Hypotension With Liposomal Bupivacaine vs Epidural Analgesia in Abdominal Surgeries. Journal of Health Economics and Outcomes Research. 2022. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9473799/
3. Tran AT, Rizk E, Haas EM, Naufal G, Zhong L, Swan JT. Real-World Data on Liposomal Bupivacaine and Inpatient Hospital Costs After Colorectal Surgery. J Surg Res. Jan 6 2022;272:175-183. doi:10.1016/j.jss.2021.12.002. https://pubmed.ncbi.nlm.nih.gov/34999518/
4. Rizk E, Haas EM, Swan JT. Opioid-Sparing Effect of Liposomal Bupivacaine and Intravenous Acetaminophen in Colorectal Surgery. J Surg Res. Mar 2021;259:230-241. doi:10.1016/j.jss.2020.09.002. https://pubmed.ncbi.nlm.nih.gov/33051063/
5. Guerra L, Philip S, Lax EA, Smithson L, Pearlman R, Damadi A. Transversus Abdominis Plane Blocks in Laparoscopic Colorectal Surgery: Better Pain Control and Patient Outcomes with Liposomal Bupivacaine than Bupivacaine. The American Surgeon. // 2019;85(9):1013-1016. https://pubmed.ncbi.nlm.nih.gov/31638516/
6. Torgeson M, Kileny J, Pfeifer C, Narkiewicz L, Obi S. Conventional Epidural vs Transversus Abdominis Plane Block with Liposomal Bupivacaine: A Randomized Trial in Colorectal Surgery. J Am Coll Surg. Jul 2018;227(1):78-83. doi:10.1016/j.jamcollsurg.2018.04.021. https://pubmed.ncbi.nlm.nih.gov/29723578/
7. Fields AC, Weiner SG, Maldonado LJ, et al. Implementation of liposomal bupivacaine transversus abdominis plane blocks into the colorectal enhanced recovery after surgery protocol: a natural experiment. Int J Colorectal Dis. Jan 2020;35(1):133-138. doi:10.1007/s00384-019-03457-1. https://pubmed.ncbi.nlm.nih.gov/31797098/
8. Pricolo VE, Fei P, Crowley S, Camisa V, Bonvini M. A novel enhanced recovery protocol, combining multimodal analgesia with liposomal bupivacaine and pharmacologic intervention, reduces parenteral opioid use and hospital length of stay after colectomy – A cohort study. International Journal of Surgery Open. 2018;13:24-28. doi:10.1016/j.ijso.2018.07.007. https://www.sciencedirect.com/science/article/pii/S2405857218300433
9. Burnett A, Faley B, Nyirenda T, Bamboat ZM. Liposomal bupivacaine reduces narcotic use and time to flatus in a retrospective cohort of patients who underwent laparotomy. Int J Surg. 2018 Nov;59:55-60. doi: 10.1016/j.ijsu.2018.09.018. Epub 2018 Oct 5. PMID: 30292778. https://pubmed.ncbi.nlm.nih.gov/30292778/
10. Felling DR, Jackson MW, Ferraro J, et al. Liposomal Bupivacaine Transversus Abdominis Plane Block Versus Epidural Analgesia in a Colon and Rectal Surgery Enhanced Recovery Pathway: A Randomized Clinical Trial. Dis Colon Rectum. Oct 2018;61(10):1196-1204. doi:10.1097/dcr.0000000000001211. https://pubmed.ncbi.nlm.nih.gov/30192328/
11. Stokes AL, Adhikary SD, Quintili A, et al. Liposomal Bupivacaine Use in Transversus Abdominis Plane Blocks Reduces Pain and Postoperative Intravenous Opioid Requirement After Colorectal Surgery. Dis Colon Rectum. Feb 2017;60(2):170-177. doi:10.1097/dcr.0000000000000747. https://pubmed.ncbi.nlm.nih.gov/28059913/
12. Keller DS, Pedraza R, Tahilramani RN, Flores-Gonzalez JR, Ibarra S, Haas EM. Impact of long-acting local anesthesia on clinical and financial outcomes in laparoscopic colorectal surgery. American Journal of Surgery. 2017;214(1):53-58. doi:10.1016/j.amjsurg.2015.10.035. https://pubmed.ncbi.nlm.nih.gov/28624028/
13. Keller DS, Tahilramani RN, Flores-Gonzalez JR, Ibarra S, Haas EM. Pilot study of a novel pain management strategy: evaluating the impact on patient outcomes. Surg Endosc. 2016 Jun;30(6):2192-8. doi: 10.1007/s00464-015-4459-4. Epub 2015 Aug 15. PMID: 26275549. https://pubmed.ncbi.nlm.nih.gov/26275549/
14. Beck DE, Margolin DA, Babin SF, Russo CT. Benefits of a Multimodal Regimen for Postsurgical Pain Management in Colorectal Surgery. Ochsner J. 2015;15(4):408-12. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4679301/
15. Cohen SM, Vogel JD, Marcet JE, Candiotti KA. Liposome bupivacaine for improvement in economic outcomes and opioid burden in GI surgery: IMPROVE Study pooled analysis. J Pain Res. 2014 Jun 24;7:359-66. doi: 10.2147/JPR.S63764. PMID: 25018650; PMCID: PMC4075953. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4075953/
16. Marcet JE, Nfonsam VN, Larach S. An extended paIn relief trial utilizing the infiltration of a long-acting Multivesicular liPosome foRmulation Of bupiVacaine, EXPAREL (IMPROVE): a Phase IV health economic trial in adult patients undergoing ileostomy reversal. J Pain Res. 2013 Jul 18;6:549-55. doi: 10.2147/JPR.S46467. PMID: 23901290; PMCID: PMC3720574. https://pubmed.ncbi.nlm.nih.gov/23901290/
17. Cohen SM. Extended pain relief trial utilizing infiltration of Exparel((R)), a long-acting multivesicular liposome formulation of bupivacaine: a Phase IV health economic trial in adult patients undergoing open colectomy. J Pain Res. 2012;5:567-72. doi:10.2147/JPR.S38621. https://pubmed.ncbi.nlm.nih.gov/23204866/

ABDOMINAL	
Study	**Results**

Holtz et al 2022[1]
Retrospective
Abdominal or colorectal resection
LB vs epidural; (N=5799)
	• Lower hospital cost
	    • $6,304 less hospital cost with EXPAREL vs epidural group ($27,315 vs. $33,619; P<0.0001)
	• Hospital Stay
	    • Mean LOS was 6.9 days and 8.5 days in patients receiving EXPAREL vs epidural analgesia
	    • Patients receiving EXPAREL were more likely to be discharged directly to home than epidural (87% vs. 75% ; P<0.0001)
	    • 30-day readmissions rate lower in EXPAREL group 11% vs. epidural group 15% (P=0.0073)
	• Incidence of hypotension
	    • Postoperative hypotension lower in EXPAREL group 11% vs. epidural group 30% (P<0.0001)
	• Vasopressor use lower in EXPAREL group 7% vs. epidural group 22% (P<0.0001)

Rendon et al 2022[2] Retrospective cohort study Autologous breast reconstruction Historical control (before ERAS) vs ERAS with catheter vs ERAS with LB TAP block; N=145	• Lower length of stay (3.0 (LB) vs 3.0 (ERAS cont. catheter) vs 4.0 (pre-ERAS), P<0.001) • Lower opioid use (211.0 (LB) vs 215.9 (ERAS cont. catheter) vs 518.4 (pre-ERAS), P<0.001) • Less patients on PCA opioid pump (1 (LB) vs 1 (ERAS cont. catheter) vs All (pre-ERAS))

Yip et al 2022[3]
Robot assisted laparoscopic nephrectomy
ERAS with LB quadratus lumborum (QL) vs non-ERAS; N=614
	• Less opioid use in LB group
	    • 21% less on POD 0 (P<0.001)
	    • 31% less on POD 1 (P<0.001)
	    • 34% less on POD 2 (P<0.001)
	    • 19% less throughout total admission (P=0.03)

Greenbaum et al 2021[4] Hepatopancreaticobiliary Erector spinae plane (ESP) Block with LB vs thoracic epidural analgesia (TEA); N=67	• 0% LB patients required opioid IV PCA vs 32.5% TEA (P<0.001) • Lower postoperative hypotension (22% vs 55%; P=0.03) • LB opioid MME requirement decreased over 72 h, while TEA MME increased (P=0.019) • Lower postoperative colloid received (142 mL vs 340 mL; P=0.01) • Earlier removal of indwelling urinary catheters (1.6 vs 2.4 days; P=0.002)

Haddock et al 2021[5]
DIEP flaps for breast reconstruction
Retrospective Review
Pre-ERAS vs ERAS vs ERAS w/LB TAP N=216
	• Lower opioid use:
	  • 21% reduction in opioid use compared to ERAS [115.5 ± 54.6 vs 146.8 ± 93.9 (ERAS) vs 275.7 ± 151.1 (Pre-ERAS), P<0.0001]
	  • 58% reduction in opioid use compared to Pre-ERAS [115.5 ± 54.6 vs 146.8 ± 93.9 (ERAS) vs 275.7 ± 151.1 (Pre-ERAS), P<0.0001]
	• Lower LOS:
	  • 21% reduction in LOS compared to ERAS [2.550 ± 0.840 vs 3.217 ± 0.802 (ERAS) vs 3.642 ± 0.829 (Pre-ERAS), P<0.001]
	  • 30% reduction in LOS compared to Pre-ERAS [2.550 ± 0.840 vs 3.217 ± 0.802 (ERAS) vs 3.642 ± 0.829 (Pre-ERAS), P<0.001]
	• Lower mean surgery time, hours:
	  • 5% reduction in mean surgery time compared to ERAS [7.693 ±1.681 vs 8.134 ± 1.792 (ERAS) vs 9.272 ± 2.119 (Pre-ERAS), P<0.001]
	  • 17 % reduction in mean surgery time compared to Pre-ERAS [7.693 ±1.681 vs 8.134 ± 1.792 (ERAS) vs 9.272 ± 2.119 (Pre-ERAS), P<0.001]

Roebuck et al 2021[6]
Radical cystectomy
Laparoscopic TAP with LB vs No TAP; N=178
	• Improved time to pain control (1 day vs 3 days) (P<0.001)
	• Less opioid use (MME):
	  • 44% reduction in total opioid use on POD 0-3 (72.5 vs 130.3; P=0.003)
	  • Less total opioids on POD 1-3 (43.3 vs 73.5; P=0.019)
	  • 55% reduction on POD 0 (25 vs 55.8; P=0.007)
	  • 65% reduction on POD 1 (12.5 vs 35.8; P<0.001)
	• Reduced length of stay when adjusted for ERAS compliance:
	  • (5.9 days vs 7.8 days; P=0.002)

Waddimba et al 2021[7] Laparascopic appendectomy Bupi+epi vs LB undiluted vs LB diluted vs LB+bupi; N=155	• Less opioid MME use in LB groups • (60.4 vs 46.0 vs 35.5 vs 30.4; P<0.001)
Turan et al 2021[8] Major abdominal surgery LB TAP w/ Bupi vs Thoracic Epidural; N=498	• Lower incidence of hypotension (31% vs 48%) (P=0.006)
Fafaj et al 2020[9] Abdominal wall reconstruction LB TAP vs Bupi TAP vs placebo TAP; N=164	• Lower rate of urinary tract infections (7.84 vs 1.82) (P-0.02)

Babazade et al 2019[10] Retrospective cost effectiveness analysis Major lower abdominal surgery LB vs PCA IV vs Epidural	• With a willingness-to-pay (WTP) of $150: IV PCA and TAP infiltration were each the optimal strategy for approximately 50% of iterations • Little differentiation in cost-effectiveness between IV PCA and TAP infiltration with LB
Shaker et al 2018[11] Abdominal oncologic surgery LB TAP vs. Thoracic epidural anesthesia (N=67)	• 68% reduction in pain on POD0 (*P*<0.001) • 73% reduction in pain on POD1 (*P*<0.001) • 71% reduction in pain on POD2(*P*=0.001) • 66% reduction in pain on POD3(*P*=0.001) • 80% reduction in hypotension on POD1 (*P*=0.02)
Torgeson et al 2018[12] Colorectal surgery LB TAP vs Epidural (N=83)	• 13% reduction (hours) in length of stay (P=0.045) • Earlier discharge (days) (P=0.023)
Ramshaw et al 2016[13] Laparoscopic Ventral Hernia Repair LB TAP + low pressure pneumoperitoneum (LPP) vs LB TAP Only vs No TAP-No LPP	• 56% reduction in overall opioid consumption (LB TAP+LPP vs LB TAP only;P=0.004) • 74% reduction in overall opioid consumption (LB TAP+LPP vs No TAP-No-LPP;P=0.002) • 38% reduction in PACU opioid consumption (LB TAP+ LPP vs LB TAP only;P=0.02) • 50% reduction in PACU opioid consumption (LB TAP+LPP vs No TAP-No-LPP;P=0.001) • 50% reduction in total length of stay (LB TAP+ LPP vs LB TAP only;P=0.02) • 63%% reduction in total length of stay (LB TAP+LPP vs No TAP-No-LPP;P<0.001) • 25% reduction in PACU stay (LB TAP+ LPP vs LB TAP only;P=0.02) • 34%% reduction in PACU stay (LB TAP+LPP vs No TAP-No-LPP;P<0.001)
Ayad et al 2016[14] Major lower abdominal surgery LB TAP vs Continuous epidural vs IV PCA (N=318)	• 36% reduction in length of stay (LB TAP vs Epidural; (P=0.005) • Pain scores were non-inferior to epidural and PCA • Opioid consumption was non-inferior to epidural and PCA
Fayezizadeh et al 2016[15] Abdominal wall reconstruction LB TAP vs. No TAP;N=100	• 29% reduction in pain on POD0 (*P*<0.001) • 24% reduction in pain on POD1 (*P*=0.002) • 19% reduction in pain on POD2(*P*=0.0.048) • 42 % reduction in opioid consumption on POD0 (P=0.005) • 32 % reduction in opioid consumption on POD1(P=0.01) • 27 % reduction in opioid consumption on POD2 (P=0.047) • 24% reduction in length of stay (P=0.006)

Redan et al 2016[16] Laparoscopic colon resection and open hernia repair LB TAP + low pressure pneumoperitoneum LB TAP + local infiltration vs. IV Opioids ; N=82	• No incidences of urinary retention (P=0.038) • Less incidences of respiratory depression (2.2% vs 21.6%; P=0.009)
Majumder et al 2016[17] Open ventral hernia repair ERP with LB TAP vs Pre-ERP, no TAP;N=200	• 39% reduction in time to transition from IV to oral opioids (P<0.001) • 34% reduction in length of stay (P<0.001) • More patients discharged within 3 days (18% vs 2%; P=0.002) • 21% reduction in time to 1st flatus (P<0.001) • 31% reduction in time to BM (P<0.001) • 38% reduction in time to regular diet (P<0.001) • Fewer 90-day readmissions (4% vs 16%;P=0.008)

References: ABDOMINAL

1. Holtz M, Liao N, Lin JH, Asche CV. Economic Outcomes and Incidence of Postsurgical Hypotension With Liposomal Bupivacaine vs Epidural Analgesia in Abdominal Surgeries. Journal of Health Economics and Outcomes Research. 2022. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9473799/
2. Rendon JL, Borrell-Vega J, Reyes JC, Wang DM, Roeth C, Abdel-Rasoul M, Skoracki RJ, Harter RL, Moffatt-Bruce SD, Humeidan ML. Evaluating the Efficacy of Two Regional Pain Management Modalities in Autologous Breast Reconstruction. Plast Reconstr Surg Glob Open. 2022 Jan 19;10(1):e4010. doi: 10.1097/GOX.0000000000004010. PMID: 35070591; PMCID: PMC8769083. https://pubmed.ncbi.nlm.nih.gov/35070591/
3. Yip W, Chen AB, Malekyan C, Widjaja W, Yan K, Stankey M, Sun X, Ashrafi AN, Graham JN, Dickerson SC, Eloustaz MH, Desai MM, Gill IS, Aron M, Kim MP. An Enhanced Recovery After Surgery protocol for robotic-assisted laparoscopic nephrectomies utilizing a quadratus lumborum block. J Robot Surg. 2022 Dec;16(6):1383-1389. doi: 10.1007/s11701-022-01379-9. Epub 2022 Feb 10. PMID: 35142979. https://europepmc.org/article/med/35142979
4. Greenbaum A, Wilcox H, Teng CH, Petersen T, Billstrand M, Campbell R, Bordegaray N, Nir I. Use of Erector Spinae Fascial Plane Blocks in Enhanced Recovery for Open Abdominal Surgery. J Surg Res. 2021 Dec;268:673-680. doi: 10.1016/j.jss.2021.08.008. Epub 2021 Sep 3. PMID: 34482007. https://pubmed.ncbi.nlm.nih.gov/34482007/
5. Haddock NT, Garza R, Boyle CE, Liu Y, Teotia SS. Defining Enhanced Recovery Pathway with or without Liposomal Bupivacaine in DIEP Flap Breast Reconstruction. Plast Reconstr Surg. 2021 Nov 1;148(5):948-957. doi: 10.1097/PRS.0000000000008409. PMID: 34705768. https://pubmed.ncbi.nlm.nih.gov/34705768/
6. Roebuck E, Beano H, Robinson M, Edwards D, Worrilow WM, Sinks A, Gaston KE, Clark PE, Riggs SB. Surgeon-administered Transversus Abdominis Plane (TAP) Block is Associated With Decreased Opioid Usage and Length of Stay Following Radical Cystectomy. Urology. 2022 Mar;161:135-141. doi: 10.1016/j.urology.2021.11.023. Epub 2021 Dec 3. PMID: 34864053. https://pubmed.ncbi.nlm.nih.gov/34864053/
7. Waddimba AC, Newman P, Shelley JK, McShan EE, Cheung ZO, Gibson JN, Bennett MM, Petrey LB. Pain management after laparoscopic appendectomy: Comparative effectiveness of innovative pre-emptive analgesia using liposomal bupivacaine. Am J Surg. 2022 May;223(5):832-838. doi: 10.1016/j.amjsurg.2021.09.019. Epub 2021 Sep 24. PMID: 34610868. https://pubmed.ncbi.nlm.nih.gov/34610868/
8. Turan A, Cohen B, Elsharkawy H, Maheshwari K, Soliman LM, Babazade R, Ayad S, Hassan M, Elkassabany N, Essber HA, Kessler H, Mao G, Esa WAS, Sessler DI; EXPLANE Study Group. Transversus abdominis plane block with liposomal bupivacaine versus continuous epidural analgesia for major abdominal surgery: The EXPLANE randomized trial. J Clin Anesth. 2022 May;77:110640. doi: 10.1016/j.jclinane.2021.110640. Epub 2021 Dec 27. PMID: 34969004. https://pubmed.ncbi.nlm.nih.gov/34969004/
9. Fafaj A, Krpata DM, Petro CC, Prabhu AS, Rosenblatt S, Tastaldi L, Alkhatib H, Tu C, Zolin SJ, Thomas JD, Costanzo AM, Rosen MJ. The Efficacy of Liposomal Bupivacaine on Postoperative Pain Following Abdominal Wall Reconstruction: A Randomized, Double-blind, Placebo-controlled Trial. Ann Surg. 2022 Aug 1;276(2):224-232. doi: 10.1097/SLA.0000000000004424. Epub 2020 Dec 2. PMID: 33273351. https://pubmed.ncbi.nlm.nih.gov/33273351/
10. Babazade R, Saasouh W, Naylor AJ, Makarova N, Udeh CI, Turan A, Udeh BL. The cost-effectiveness of epidural, patient-controlled intravenous opioid analgesia, or transversus abdominis plane infiltration with liposomal bupivacaine for postoperative pain management. J Clin Anesth. 2019 Mar;53:56-63. doi: 10.1016/j.jclinane.2018.10.003. Epub 2018 Oct 13. PMID: 30326379. https://pubmed.ncbi.nlm.nih.gov/30326379/
11. Shaker TM, Carroll JT, Chung MH, et al. Efficacy and safety of transversus abdominis plane blocks versus thoracic epidural anesthesia in patients undergoing major abdominal oncologic resections: A prospective, randomized controlled trial. Article. American Journal of Surgery. 2018;215(3):498-501. doi:10.1016/j.amjsurg.2017.10.055. https://pubmed.ncbi.nlm.nih.gov/29198854/

12. Torgeson M, Kileny J, Pfeifer C, Narkiewicz L, Obi S. Conventional Epidural vs Transversus Abdominis Plane Block with Liposomal Bupivacaine: A Randomized Trial in Colorectal Surgery. J Am Coll Surg. 2018 Jul;227(1):78-83. doi: 10.1016/j.jamcollsurg.2018.04.021. Epub 2018 May 1. PMID: 29723578. https://pubmed.ncbi.nlm.nih.gov/29723578/
13. Ramshaw B, Forman B, Heidel E, Dean J, Gamenthaler A, Fabian M. A Clinical Quality Improvement (CQI) Project to Improve Pain After Laparoscopic Ventral Hernia Repair. Surg Technol Int. Oct 26 2016;Xxix:125-130. https://pubmed.ncbi.nlm.nih.gov/27728945/
14. Ayad S, Babazade R, Elsharkawy H, et al. Comparison of Transversus Abdominis Plane Infiltration with Liposomal Bupivacaine versus Continuous Epidural Analgesia versus Intravenous Opioid Analgesia. *PLoS One*. 2016;11(4):e0153675. doi:10.1371/journal.pone.0153675. https://pubmed.ncbi.nlm.nih.gov/27082959/
15. Fayezizadeh M, Majumder A, Neupane R, et al. Efficacy of transversus abdominis plane block with liposomal bupivacaine during open abdominal wall reconstruction. *American Journal of Surgery*. 2016;212(3):399-405. https://pubmed.ncbi.nlm.nih.gov/27156796/
16. Redan JA, Wells T, Reeder S, McCarus SD. Reducing Opioid Adverse Events: A Safe Way to Improve Outcomes. *Surg Technol Int*. Apr 4 2016;28:101-9. https://pubmed.ncbi.nlm.nih.gov/27042786/
17. Majumder A, Fayezizadeh M, Neupane R, et al. Benefits of multimodal enhanced recovery pathway in patients undergoing open ventral hernia repair. *Journal of the American College of Surgeons*. 1 2016;222(6):1106-1115. https://pubmed.ncbi.nlm.nih.gov/27049780/

Transversus abdominis plane (TAP)	
Study	**Results**

Peebles et al 2023[1]
Retrospective chart review
Cesarean section
LB TAP (N=107) vs LB infiltration (N=185) vs Standard of Care (spinal anesthesia) (N=110)
	• Opioid use:
	  ◦ Less total opioid use: 24.9 vs 25.2 vs 64.4 MME; P<0.001
	  ◦ Less average daily opioid use: 9.9 vs 9.7 vs 25.8 MME; P<0.001
	  ◦ More opioid free patients: 42.1% vs 55.1% vs 0%; P<0.001
	• Pain:
	  ◦ POD 0: 5.5 vs 4.6 vs 5.9; P<0.001
	  ◦ POD 1: 5.6 vs 5.3 vs 6.3; P=0.003
	  ◦ POD 2: 5.7 vs 5.5 vs 6.3; P=0.29
	• Length of stay: 2.3 vs 2.4 vs 2.5 days; P=0.01

Heffern et al 2023[2]
Retrospective chart review
Abdominoplasty
LB (N=60): 4 injections 266mg/20 mL + 50 mL 0.25% bupivacaine + 30 mL NS + 0.5 mL of 1:1000 epinephrine with remaining 20 mL infiltrated into incision area
VS Local infiltration (10 mL of 0.25% bupivacaine + epinephrine) with or without blind rectus sheath block (4 injections of 10 mL of 0.25% bupivacaine with epinephrine)
	• PACU Opioid Utilization
	  ◦ TAP block LB: lower opioid requirements (3.07 vs 8.93 MMEs; P=0.0001)
	• Time in PACU
	  ◦ TAP block LB: shorter stay (95.7 vs 117.18 minutes; P=0.0001)

Chevrollier et al 2022[3] RCT Laparoscopic colorectal resection LB TAP block (n=38) vs bupivacaine HCl TAP blocks (n=38)	• LB group experienced significantly lower maximum pain scores on the day of surgery (6.5 vs 7.7; P=0.008)
Rendon et al 2022[4] Retrospective cohort study Autologous breast reconstruction Historical control (before ERAS) vs ERAS with catheter vs ERAS with LB TAP block; N=145	• Lower length of stay (3.0 (LB) vs 3.0 (ERAS cont. catheter) vs 4.0 (pre-ERAS), P<0.001) • Lower opioid use (211.0 (LB) vs 215.9 (ERAS cont. catheter) vs 518.4 (pre-ERAS), P<0.001) • Less patients on PCA opioid pump (1 (LB) vs 1 (ERAS cont. catheter) vs All (pre-ERAS))

Roebuck et al 2022[5]
Radical cystectomy
Laparoscopic TAP with LB vs No TAP; N=178
	• Improved time to pain control (1 day vs 3 days) (P<0.001)
	• Less opioid use (MME):
	    • 44% reduction in total opioid use on POD 0-3 (72.5 vs 130.3; P=0.003)
	    • Less total opioids on POD 1-3 (43.3 vs 73.5; P=0.019)
	    • 55% reduction on POD 0 (25 vs 55.8; P=0.007)
	    • 65% reduction on POD 1 (12.5 vs 35.8; P<0.001)
	• Reduced length of stay when adjusted for ERAS compliance:
	• (5.9 days vs 7.8 days; P=0.002)

Haddock et al 2021[6]
DIEP flaps for breast reconstruction
Retrospective Review
Pre-ERAS vs ERAS vs ERAS w/LB TAP N=216
	• Lower opioid use:
	    • 21% reduction in opioid use compared to ERAS [115.5 ± 54.6 vs 146.8 ± 93.9 (ERAS) vs 275.7 ± 151.1 (Pre-ERAS), P<0.0001]
	    • 58% reduction in opioid use compared to Pre-ERAS [115.5 ± 54.6 vs 146.8 ± 93.9 (ERAS) vs 275.7 ± 151.1 (Pre-ERAS), P<0.0001]
	• Lower LOS:
	    • 21% reduction in LOS compared to ERAS [2.550 ± 0.840 vs 3.217 ± 0.802 (ERAS) vs 3.642 ± 0.829 (Pre-ERAS), P<0.001]
	    • 30% reduction in LOS compared to Pre-ERAS [2.550 ± 0.840 vs 3.217 ± 0.802 (ERAS) vs 3.642 ± 0.829 (Pre-ERAS), P<0.001]
	• Lower mean surgery time, hours:
	    • 5% reduction in mean surgery time compared to ERAS [7.693 ±1.681 vs 8.134 ± 1.792 (ERAS) vs 9.272 ± 2.119 (Pre-ERAS), P<0.001]
	• 17 % reduction in mean surgery time compared to Pre-ERAS [7.693 ±1.681 vs 8.134 ± 1.792 (ERAS) vs 9.272 ± 2.119 (Pre-ERAS), P<0.001]

Turan et al 2021[7] Major abdominal surgery LB TAP w/ Bupi vs Thoracic Epidural; N=498	• Lower incidence of hypotension (31% vs 48%) (P=0.006)
Colonna et al 2020[8] Cost-effectiveness analysis Laparoscopic ventral hernia repair LB TAP vs no TAP	• $456.75 decrease in cost and an 0.1 increase in QALY relative to the no TAP block treatment strategy. • In probabilistic sensitivity analyses (PSA), EXPAREL TAP strategy was cost-effective at a willingness-to-pay threshold of $50,000/QALY in 94.5% of iterations and pay threshold of $100,000/QALY in 97.1% of iterations
Fafaj et al 2020[9] Abdominal wall reconstruction LB TAP vs Bupi TAP vs placebo TAP; N=164	• Lower rate of urinary tract infections (7.84 vs 1.82) (P=0.02)

Shaker et al 2018[10] Abdominal oncologic surgery LB TAP vs. Thoracic epidural anesthesia ;N=67	• 68% reduction in pain on POD0 (*P*<0.001) • 73% reduction in pain on POD1 (*P*<0.001) • 71% reduction in pain on POD2(*P*=0.001) • 66% reduction in pain on POD3(*P*=0.001) • 80% reduction in hypotension on POD1 (*P*=0.02)
Torgeson et al 2018[11] Colorectal surgery LB TAP vs Epidural (N=83)	• 13% reduction (hours) in length of stay (P=0.045) • Earlier discharge (days) (P=0.023)
Ramshaw et al 2016[12] Laparoscopic Ventral Hernia Repair LB TAP + low pressure pneumoperitoneum (LPP) vs LB TAP Only vs No TAP-No LPP	• 56% reduction in overall opioid consumption (LB TAP+LPP vs LB TAP only;P=0.004) • 74% reduction in overall opioid consumption (LB TAP+LPP vs No TAP-No-LPP;P=0.002) • 38% reduction in PACU opioid consumption (LB TAP+ LPP vs LB TAP only;P=0.02) • 50% reduction in PACU opioid consumption (LB TAP+LPP vs No TAP-No-LPP;P=0.001) • 50% reduction in total length of stay (LB TAP+ LPP vs LB TAP only;P=0.02) • 63%% reduction in total length of stay (LB TAP+LPP vs No TAP-No-LPP;P<0.001) • 25% reduction in PACU stay (LB TAP+ LPP vs LB TAP only;P=0.02) • 34%% reduction in PACU stay (LB TAP+LPP vs No TAP-No-LPP;P<0.001)
Oh et al 2018[13] Cost-effectiveness study LB TAP vs TRAS; N=200	• Adjusted mean cost: $4,576 lower than those of the TRAS control group ($38,688 versus $43,264) • Lower costs than controls in all categories, with the greatest difference associated with the room and board ($12,266 vs. $8,395)

Gatherwright et al 2018[14]
Prospective
DIEP free flap reconstruction
LB + NS + 0.25% bupi vs 0.25% bupi vs OnQ 0.25% bupi vs historical control
	• Lower average IV opioids MME (19.3 vs 29.6 vs 37.9 vs 61.4)
	    • 19.3 LB vs 29.6 OnQ (P=0.005) vs 37.9 bupi (P=0.004) vs 61.4 control (P=0.002)
	• Lower average IV opioid mg/kg/day
	    • 0.08 LB vs 0.1 OnQ (P=0.004) vs 0.16 bupi (P=0.02) vs 0.29 (P=0.012)
	• Lower average total MME
	    • 40.9 LB vs 53.2 OnQ (P<0.001) vs 79.9 bupi (P=0.002) vs 97.6 control (P=0.006)
	• Lower average total opioid use mg/kg/day
	    • 0.08 LB vs 0.1 OnQ (P<0.001) vs 0.18 bupi (P=0.001) vs 0.31 control (P=0.002)
	• Lower length of stay (days)
	• 3.38 LB vs 3.8 OnQ vs 3.63 bupi vs 3.83 control (P=0.08)

Ayad et al 2016[15] Major lower abdominal surgery LB TAP vs Continuous epidural vs IV PCA (N=318)	• 36% reduction in length of stay (LB TAP vs Epidural; (P=0.005) • Pain scores were non-inferior to epidural and PCA • Opioid consumption was non-inferior to epidural and PCA

Fayezizadeh et al 2016[16] Abdominal wall reconstruction LB TAP vs. No TAP;N=100	• 29% reduction in pain on POD0 (*P*<0.001) • 24% reduction in pain on POD1 (*P*=0.002) • 19% reduction in pain on POD2(*P*=0.0.048) • 42 % reduction in opioid consumption on POD0 (P=0.005) • 32 % reduction in opioid consumption on POD1(P=0.01) • 27 % reduction in opioid consumption on POD2 (P=0.047) • 24% reduction in length of stay (P=0.006)
Redan et al 2016[17] Laparoscopic colon resection and open hernia repair LB TAP + low pressure pneumoperitoneum LB TAP + local infiltration vs. IV Opioids ; N=82	• No incidences of urinary retention (P=0.038) • Less incidences of respiratory depression (2.2% vs 21.6%; P=0.009)
Majumder et al 2016[18] Open ventral hernia repair ERP with LB TAP vs Pre-ERP, no TAP;N=200	• 39% reduction in time to transition from IV to oral opioids (P<0.001) • 34% reduction in length of stay (P<0.001) • More patients discharged within 3 days (18% vs 2%; P=0.002) • 21% reduction in time to 1st flatus (P<0.001) • 31% reduction in time to BM (P<0.001) • 38% reduction in time to regular diet (P<0.001) • Fewer 90-day readmissions (4% vs 16%;P=0.008)

References: TRANSVERSUS ABDOMINIS PLANE BLOACK

1. Peebles AF, Mouch A, Maxwell RA, Ruby T, Kindig MJ. Long-Acting Bupivacaine for Pain Control After Cesarean Birth. Nurs Womens Health. Jun 26 2023;doi:10.1016/j.nwh.2023.03.003. https://pubmed.ncbi.nlm.nih.gov/37385592/
2. Heffern JN, Puyana S, Hajebian HH, Kresofsky K, Chaffin AE, Lindsey JTS. Ultrasound-Guided Transversus Abdominis Plane Blocks Versus Local Infiltration Anesthesia on Postanesthesia Care Unit Pain Control in Patients Undergoing Abdominoplasty. Annals of Plastic Surgery. 2023:10.1097/SAP.0000000000003726. doi:10.1097/sap.0000000000003726. https://pubmed.ncbi.nlm.nih.gov/37962248/
3. Chevrollier GS, Klinger AL, Green HJ, Gastanaduy MM, Johnston WF, Vargas HD, Kann BR, Whitlow CB, Paruch JL. Liposomal Bupivacaine Transversus Abdominis Plane Blocks in Laparoscopic Colorectal Resections: A Single-Institution Randomized Controlled Trial. Dis Colon Rectum. 2023 Feb 1;66(2):322-330. doi: 10.1097/DCR.0000000000002346. Epub 2022 May 24. PMID: 35849756. https://pubmed.ncbi.nlm.nih.gov/35849756/
4. Rendon JL, Borrell-Vega J, Reyes JC, Wang DM, Roeth C, Abdel-Rasoul M, Skoracki RJ, Harter RL, Moffatt-Bruce SD, Humeidan ML. Evaluating the Efficacy of Two Regional Pain Management Modalities in Autologous Breast Reconstruction. Plast Reconstr Surg Glob Open. 2022 Jan 19;10(1):e4010. doi: 10.1097/GOX.0000000000004010. PMID: 35070591; PMCID: PMC8769083. https://pubmed.ncbi.nlm.nih.gov/35070591/
5. Roebuck E, Beano H, Robinson M, Edwards D, Worrilow WM, Sinks A, Gaston KE, Clark PE, Riggs SB. Surgeon-administered Transversus Abdominis Plane (TAP) Block is Associated With Decreased Opioid Usage and Length of Stay Following Radical Cystectomy. Urology. 2022 Mar;161:135-141. doi: 10.1016/j.urology.2021.11.023. Epub 2021 Dec 3. PMID: 34864053. https://pubmed.ncbi.nlm.nih.gov/34864053/
6. Haddock NT, Garza R, Boyle CE, Liu Y, Teotia SS. Defining Enhanced Recovery Pathway with or without Liposomal Bupivacaine in DIEP Flap Breast Reconstruction. Plast Reconstr Surg. 2021 Nov 1;148(5):948-957. doi: 10.1097/PRS.0000000000008409. PMID: 34705768. https://pubmed.ncbi.nlm.nih.gov/34705768/
7. Turan A, Cohen B, Elsharkawy H, Maheshwari K, Soliman LM, Babazade R, Ayad S, Hassan M, Elkassabany N, Essber HA, Kessler H, Mao G, Esa WAS, Sessler DI; EXPLANE Study Group. Transversus abdominis plane block with liposomal bupivacaine versus continuous epidural analgesia for major abdominal surgery: The EXPLANE randomized trial. J Clin Anesth. 2022 May;77:110640. doi: 10.1016/j.jclinane.2021.110640. Epub 2021 Dec 27. PMID: 34969004. https://pubmed.ncbi.nlm.nih.gov/34969004/
8. Colonna AL, Bellows BK, Enniss TM, et al. Reducing the pain: A cost-effectiveness analysis of transversus abdominis plane block using liposomal bupivacaine for outpatient laparoscopic ventral hernia repair. Surgery Open Science. 2020/01/23/ 2020;2(2):75-80. doi:10.1016/j.sopen.2019.12.003. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8097728/
9. Fafaj A, Krpata DM, Petro CC, Prabhu AS, Rosenblatt S, Tastaldi L, Alkhatib H, Tu C, Zolin SJ, Thomas JD, Costanzo AM, Rosen MJ. The Efficacy of Liposomal Bupivacaine on Postoperative Pain Following Abdominal Wall Reconstruction: A Randomized, Double-blind, Placebo-controlled Trial. Ann Surg. 2022 Aug 1;276(2):224-232. doi: 10.1097/SLA.0000000000004424. Epub 2020 Dec 2. PMID: 33273351. https://pubmed.ncbi.nlm.nih.gov/33273351/
10. Shaker TM, Carroll JT, Chung MH, et al. Efficacy and safety of transversus abdominis plane blocks versus thoracic epidural anesthesia in patients undergoing major abdominal oncologic resections: A prospective, randomized controlled trial. Article. American Journal of Surgery. 2018;215(3):498-501. doi:10.1016/j.amjsurg.2017.10.055. https://pubmed.ncbi.nlm.nih.gov/29198854/
11. Torgeson M, Kileny J, Pfeifer C, Narkiewicz L, Obi S. Conventional Epidural vs Transversus Abdominis Plane Block with Liposomal Bupivacaine: A Randomized Trial in Colorectal Surgery. J Am Coll Surg. 2018 Jul;227(1):78-83. doi: 10.1016/j.jamcollsurg.2018.04.021. Epub 2018 May 1. PMID: 29723578. https://pubmed.ncbi.nlm.nih.gov/29723578/
12. Ramshaw B, Forman B, Heidel E, Dean J, Gamenthaler A, Fabian M. A Clinical Quality Improvement (CQI) Project to Improve Pain After Laparoscopic Ventral Hernia Repair. Surg Technol Int. Oct 26 2016;Xxix:125-130. https://pubmed.ncbi.nlm.nih.gov/27728945/
13. Oh C, Moriarty J, Borah BJ, et al. Cost analysis of enhanced recovery after surgery in microvascular breast reconstruction. J Plast Reconstr Aesthet Surg. Mar 2 2018;doi:10.1016/j.bjps.2018.02.018. https://pubmed.ncbi.nlm.nih.gov/29606583/
14. Gatherwright J, Knackstedt RW, Ghaznavi AM, et al. Prospective, Randomized, Controlled Comparison of Bupivacaine versus Liposomal Bupivacaine for Pain Management after Unilateral Delayed Deep Inferior Epigastric Perforator Free Flap Reconstruction. Plast Reconstr Surg. Jun 2018;141(6):1327-1330. doi:10.1097/PRS.0000000000004360. https://pubmed.ncbi.nlm.nih.gov/29750760/
15. Ayad S, Babazade R, Elsharkawy H, et al. Comparison of Transversus Abdominis Plane Infiltration with Liposomal Bupivacaine versus Continuous Epidural Analgesia versus Intravenous Opioid Analgesia. PLoS One. 2016;11(4):e0153675. doi:10.1371/journal.pone.0153675. https://pubmed.ncbi.nlm.nih.gov/27082959/
16. Fayezizadeh M, Majumder A, Neupane R, et al. Efficacy of transversus abdominis plane block with liposomal bupivacaine during open abdominal wall reconstruction. American Journal of Surgery. 2016;212(3):399-405. https://pubmed.ncbi.nlm.nih.gov/27156796/
17. Redan JA, Wells T, Reeder S, McCarus SD. Reducing Opioid Adverse Events: A Safe Way to Improve Outcomes. Surg Technol Int. Apr 4 2016;28:101-9. https://pubmed.ncbi.nlm.nih.gov/27042786/
18. Majumder A, Fayezizadeh M, Neupane R, et al. Benefits of multimodal enhanced recovery pathway in patients undergoing open ventral hernia repair. Journal of the American College of Surgeons. 1 2016;222(6):1106-1115. https://pubmed.ncbi.nlm.nih.gov/27049780/

BARIATRIC	
Study	**Results**
Wong et al 2020[1] Lap Roux-en-Y gastric bypass, sleeve gastrectomy, sleeve to bypass conversion TAP block with LB vs TAP block With Bupi and no TAP block; N=219	• Patients experienced less nausea (35.7 % vs 57.8 % vs 46.5) (P=0.03)

Ma et al 2019[2]
Lap Roux-en-Y gastric bypass and Vertical sleeve gastrectomy
ERABS + LB vs LB vs Pre-LB
	• Experienced less pain
	  • Average pain entering PACU (2.6 vs 4.9) (P<0.001, between LB and ERABS+LB)
	  • Average pain entering PACU (4.9 vs 6.3) (P=0.04, between LB and Pre-LB)
	  • Average pain entering PACU (2.6 vs 6.3) (P<0.001, between ERABS+LB and Pre-LB)
	  • Average pain exiting PACU (4.4 vs 3.0) (P<0.001, between LB and ERABS+LB)
	  • Average pain exiting PACU (3.0 vs 4.3) (P=0.01, between ERABS+LB and Pre-LB)
	  • Average pain in POD 1 (2.7 vs 1.4) (P<0.01, between LB and ERABS+LB)
	  • Average pain in POD 1 (1.4 vs 2.7) (P=0.002, between ERABS+LB and Pre-LB)
	• Less opioids used in ERABS+LB vs LB and Pre-LB
	  • Total hospital opioid use in MEU (23.8 vs 40.8 vs 58.6) (P=0.01)
	  • 59% reduction in opioid requirements vs Pre-LB (P<0.001)
	  • Did not require additional narcotics on the floor (44.9% ERABS+LB vs 0% in Pre-LB) (P<0.001)
	• Shorter LOS (1.48 days vs 1.54 days) (P=0.03)
	• Overall decrease in readmission rate, ERABS+LB (3.74%) (P=0.03)

Moon et al 2019[3] Sleeve gastrectomy, Roux-en-Y gastric bypass, duodenal switch, and revisional procedures LB TAP vs no TAP; N=191	• 28% reduction in IV hydromorphone or morphine (69.2% vs 95.9%) (P<0.0001) • 38% reduction in oral acetaminophen or codeine (46.8% vs 75.3 %) (P<0.0001)
Bhakta et al 2018[4] Sleeve Gastrectomy or Roux-En-Y gastric bypass Laparoscopic-guided LB TAP /no PCA vs bupivacaine HCl+PCA ;N=476	• 43% reduction in opioid consumption across all procedures (P<0.0001) • 41 % reduction in opioid consumption in sleeve arm (P<0.0001) • 34 % reduction in opioid consumption in Roux –En-Y (P<0.0001)

Robertson et al 2018[5] Laparoscopic Roux-En-Y or laparoscopic sleeve gastrectomy Ultrasound guided LB TAP + PCA vs PCA only; N=440	• 62% reduction in opioid consumption in LRYGB (P≤0.0001) • 60% reduction in opioid consumption in LSG (P≤0.0001) • 50% reduction in length of stay in LRYGB (**1.1 vs 2.2** days; P<0.0001) • 39% reduction in length of stay in LSG (**1.1 vs 1.8** days; P<0.0001)

References: BARIATRIC

1. Wong KA, Cabrera AG, Argiroff AL, Pechman DM, Parides MK, Vazzana JT, Moran-Atkin EM, Choi JJ, Camacho DR. Transversus abdominis plane block with liposomal bupivacaine and its effect on opiate use after weight loss surgery: a randomized controlled trial. Surg Obes Relat Dis. 2020 Jul;16(7):886-893. doi: 10.1016/j.soard.2020.03.031. Epub 2020 Apr 10. PMID: 32402732. https://pubmed.ncbi.nlm.nih.gov/32402732/
2. Ma P, Lloyd A, McGrath M, Moore R, Jackson A, Boone K, Higa K. Reduction of opioid use after implementation of enhanced recovery after bariatric surgery (ERABS). Surg Endosc. 2020 May;34(5):2184-2190. doi: 10.1007/s00464-019-07006-3. Epub 2019 Jul 24. PMID: 31342260. https://pubmed.ncbi.nlm.nih.gov/31342260/
3. Moon RC, Lastrapes L, Wier J, et al. Preoperative Transversus Abdominis Plane (TAP) Block with Liposomal Bupivacaine for Bariatric Patients to Reduce the Use of Opioid Analgesics. Obes Surg. 2019. https://www.ncbi.nlm.nih.gov/pubmed/30661208.
4. Bhakta A, Glotzer O, Ata A, Tafen M, Stain SC, Singh PT. Analgesic efficacy of laparoscopic-guided transverse abdominis plane block using liposomal bupivacaine in bariatric surgery. *Am J Surg.* 2018;215(4):643-646.https://www.ncbi.nlm.nih.gov/pubmed/29061282.
5. Robertson TC, Hall K, Bear S, Thompson KJ, Kuwada T, Gersin KS. Transversus abdominis block utilizing liposomal bupivacaine as a non-opioid analgesic for postoperative pain management. *Surg Endosc.* 2018.https://www.ncbi.nlm.nih.gov/pubmed/30390161.

<table>
<tr><th colspan="2"><u>HEMORRHOIDECTOMY</u></th></tr>
<tr><th>Study</th><th>Results</th></tr>
<tr><td>Chitty et al 2022[1]
Hemorrhoidectomy
LB (post-intervention) vs 0.25% bupi (pre-intervention); N=94</td><td>• Lower recovery time (67 min vs 80 min; P=0.01)
• Lower pain score (NRS), median IQR:
    • First PACU pain score (0 (0-0) vs 0 (0-4); P=0.02)
• Peak PACU pain score (0 (0-4) vs 3 (0-6); P=0.03)</td></tr>
<tr><td>Haas et al 2012[2]
Excisional hemorrhoidectomy
Dose range LB vs 0.25% bupi with Epi; N=100</td><td>• Cumulative pain scores (NRS):
    • Lower pain scores with 199 mg and 266 mg from 0-72 hours (199 mg and 266 mg vs 75 mg, P=0.002)
    • Lower pain scores with 199 mg and 266 mg from 0-96 hours (199 mg, 95% CI for difference, –363,
    • –52, P=0.001; 266 mg, 95% CI for difference, –373, –60, P<0.001)
    • Lower pain scores at first BM (NRS-BM): LB 199-mg [4.5 (3.0),P=0.01] and 266-mg [4.1 (2.1), P=0.003] vs bupi [6.7 (2.7)]
• More patients opioid free: 266-mg group (32% vs 8%, P=0.074)
• Lower median time to first post surgical rescue opioid medication [8 hrs (0.3-96.0) vs 19 hrs (0.1-96.0), P=0.005]
• Lower total amount of rescue opioid medication (96 hrs, P=0.004)
• Higher blinded care provider's satisfaction (P=0.03)
• Improvement in EQ-5D QOL score (P=0.006 and P<0.001 at 48 hrs and 72 hrs, respectively)</td></tr>
<tr><td>Gorfine et al 2011[3]
2- or 3-column excisional hemorrhoidectomy
LB vs placebo; N=189</td><td>• Less pain through 72 hours after surgery:
    • AUC_{0-72} (141.8 (10.7) vs 202.5 (10.7), P<0.0001)
• Opioids
    • Greater proportion of patients received no opioid rescue medication from 12 to 72 hours, (P<0.0008)
    • Lower total opioid rescue medication consumed through 72 hours, (P≤0.0006)
    • Lower median time to first use of opioid rescue medication (14 hours 20 min vs 1 hour 10 min, P<0.0001)
• Higher postsurgical analgesia satisfaction at 72 hours (94.7% vs 73.1%, P=0.0007)</td></tr>
</table>

References: HEMORROIDECTOMY

1. Chitty L, Ridley B, Johnson B, Ibrahim M, Mongan PD, Hoefnagel AL. Liposomal compared to 0.25% bupivacaine in patients undergoing hemorrhoidectomy: A pre- and post-implementation quality improvement evaluation. J Clin Anesth. 2022 Sep;80:110868. doi: 10.1016/j.jclinane.2022.110868. Epub 2022 Apr 29. PMID: 35500430. https://pubmed.ncbi.nlm.nih.gov/35500430/
2. Haas E, Onel E, Miller H, Ragupathi M, White PF. A double-blind, randomized, active-controlled study for post-hemorrhoidectomy pain management with liposome bupivacaine, a novel local analgesic formulation. The American surgeon. 2012;78(5):574-581.http://www.ncbi.nlm.nih.gov/pubmed/22546131. https://pubmed.ncbi.nlm.nih.gov/22546131/
3. Gorfine SR, Onel E, Patou G, Krivokapic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. Diseases of the colon and rectum. 2011;54(12):1552-1559.http://www.ncbi.nlm.nih.gov/pubmed/22067185. https://pubmed.ncbi.nlm.nih.gov/22067185/

ERECTOR SPINAE PLANE BLOCK (ESP)

ERECTOR SPINAE PLANE BLOCK (ESP)	
Study	**Results**

Changoor et al 2023[1]
Retrospective pediatric study
Adolescent idiopathic scoliosis
LB 4 mg/kg Erector
Spinae Plane (ESP) block (N=53) vs multimodal pain protocol alone (N=66)
	• Opioid use
	    • Total opioid use (44.5 vs 70.2, P<0.001)
	    • Oral opioid use only (81.1% vs 40.9, P=0.001)
	    • Morphine POD 0 (0.30 mg vs 1.44 mg, P<0.001)
	    • Oxycodone POD 1 (11.9 vs 15.8, P=0.004)
	    • Oxycodone POD 2 (10.2 vs 16.4, P=0.002)
	• Ambulation
	    • Ambulation POD 1 (47.8 ft vs 18.7 ft, P=0.038)
	    • Ambulation POD 2 (888.7 ft vs 553.4 ft, P=0.002)
	• Length of stay (2.42 days vs 2.74 days, P=0.005)
	• Percentage discharged on POD 2 (54.7% vs 27.3%, P=0.002)

Stewart et al 2023[2] Observational, retrospective study One or two level lumbar laminectomy (N=50) LB ESPB vs Multimodal analgesia alone (Control)	• No PACU median hydromorphone consumption (0 vs 0.8 mg; P=0.001) • 48% reduction in mean morphine equivalents 0-24 h (31.9 mg vs 61.2 mg; P=0.001) • 27% reduction in mean morphine equivalents 24-48 h (31.9 mg vs 43.6 mg; P=0.04) • 45% reduction in mean PACU NRS pains scores (2.8 vs 5.1; P=0.01) • 45% reduction in mean POD1 pain scores (3.0 vs 5.5; P<0.001) • 27% reduction in mean POD2 pain scores (3.5 vs 4.8; P=0.01) • Lower antiemetic use (12% vs 48%; P<0.005)

Dahl et al 2022[3]
Cardiac
ERAS plus LB via ESP for patients with severe pulmonary disease or opioid dependence vs pre-ERAS;
CABG and/or aortic or mitral intervention via median sternotomy; N=236
	• Less opioid use (MME):
	    • Pre/Intra-op (19.2 vs 250.0; P<0.001)
	    • Post-op POD0 (13.8 vs 40.0; P<0.001)
	    • POD0 (41.5 vs 277.3; P<0.001)
	    • POD1 (30.0 vs 75.0; P<0.001)
	    • Prescribed at discharge (30.0 vs 75.0; P<0.001)
	• Less pain POD1 (4.15 vs 4.82 NRS; P=0.011)
	• Less nausea/vomiting (42.4% vs 71.2%; P<0.001)

Dincer et al 2022[4] Spine Transforaminal lumbar interbody fusion (TLIF) LB Erector Spinae Plane plus infiltration vs LB infiltration alone; N=50	• 24% shorter length of stay (2.56 vs 3.36 days; P=0.007) • 26% Shorter time to ambulation (0.96 vs 1.29 days; P=0.026) • 26% reduction in pain AUC at 12-24 hours (39.4 vs 53.4; P=0.03) • 12% reduction in pain AUC total hospital stay (44.5 vs 50.5; P=0.025) • 20% less in opioid use at 12-24 hours (50.1 vs 62.3 MME; P<0.001) • 29% less in opioid use total hospital stay (137.3 vs 194.7 MME; P=0.04)
Song et al 2020[5] Letter to editor Retrospecitve pilot study Cardiac surgery via median sternotomy and cardiopulmonary bypass LB ESP vs matched control; N=24	• Less opioid consumption • Lower intraoperatively opioid consumption (4.25mcg/kg and 11.25mcg/kg fentanyl, respectively; P<0.05) • Lower total opioid consumption at 4 and 12 hours (0.064mg/kg vs. 0.349mg/kg and 0.203mg/kg vs. 0.334mg/kg, respectively; P<0.05).
Greenbaum et al 2019[6] *Retrospective* open hepatopancreaticobiliary (HPB) surgery LB bilateral ESP vs ropivacaine thoracic epidural anesthesia; N=67	• Opioid consumption • Higher percentage did not require any opioids in the postoperative period (33% vs 10%; P=0.03). • Less intraoperative colloid administration (142 vs. 340 mL; P=0.01) • less post-operative hypotension (22% vs. 55%; P=0.03)

References: ERECTOR SPINAE PLANE BLOCK (ESP)

1. Changoor S, Giakas A, Sacks K, et al. The Role of Liposomal Bupivacaine in Multimodal Pain Management following Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis: Faster and Farther with Less Opioids. Spine (Phila Pa 1976). May 1 2023;doi:10.1097/brs.0000000000004702. https://pubmed.ncbi.nlm.nih.gov/37159268/
2. Stewart JW, Dickson D, Van Hal M, et al. Ultrasound-guided erector spinae plane blocks for pain management after open lumbar laminectomy. European Spine Journal. 2023/08/12 2023;doi:10.1007/s00586-023-07881-4. https://pubmed.ncbi.nlm.nih.gov/37572144/
3. Dahl JJ, Krebs ED, Teman NR, Hulse M, Thiele RH, Singh K, Yount KW; UVA Cardiac ERAS group. Cardiac Enhanced Recovery Program Implementation and Its Effect on Opioid Administration in Adult Cardiac Surgery. Semin Thorac Cardiovasc Surg. 2022 Aug 17:S1043-0679(22)00186-1. doi: 10.1053/j.semtcvs.2022.06.020. Epub ahead of print. PMID: 35985451. https://pubmed.ncbi.nlm.nih.gov/35985451/
4. Dincer A, Wang A, Kanter MJ, et al. Clinical Outcomes of Liposomal Bupivacaine Erector Spinae Block in Minimally Invasive Transforaminal Lumbar Interbody Fusion Surgery. Neurosurgery. Dec 5 2022;doi:10.1227/neu.0000000000002249. https://pubmed.ncbi.nlm.nih.gov/36512838/
5. Song K, Xu Q, Knott VH, et al. Liposomal Bupivacaine-Based Erector Spinae Block for Cardiac Surgery. Journal of cardiothoracic and vascular anesthesia. Sep 20 2020;doi:10.1053/j.jvca.2020.09.115. https://pubmed.ncbi.nlm.nih.gov/33046362/
6. Greenbaum A, Bordegaray N, Nir I. Erector Spinae Fascial Plane Blocks with Liposomal Bupivacaine Improve Enhanced Recovery Parameters Compared with Thoracic Epidural Anesthesia. Conference Abstract. Journal of the American College of Surgeons. 2019;229(4):S173. doi:10.1016/j.jamcollsurg.2019.08.381. https://pubmed.ncbi.nlm.nih.gov/34482007/

PEDIATRICS

<table>
<tr><th colspan="2">PEDIATRICS</th></tr>
<tr><th colspan="2">SAFETY</th></tr>
<tr><th>Study</th><th>Results</th></tr>
<tr><td>Tirotta et al (PLAY) 2021[1]
Pharmacokinetic Study
Spine and Cardiac Surgery
Group 1: LB infiltration vs Bupi HCL infiltration
Spine Surgery Only
Group 2: LB Spine or Cardiac Surgery
;N=98</td><td>• Group 1 LB vs Bupi HCL (12 to <17, Spine Surgery)
  ◦ Lower mean C_{max} (357 ng/ml vs 564 ng/ml)
  ◦ Greater mean $AUC_{0\text{-}inf}$ (14,246 ngh/ml vs 5709 ngh/ml)
  ◦ Similar median t_{max} (1.1 vs 0.9 hours)
  ◦ TEAEs were comparable (61.3% LB and 73.3 % Bupi HCL)
• Group 2
  ◦ Lower mean C_{max} in spine (320 ng/ml vs 447 ng/ml)
  ◦ Greater mean $AUC_{0\text{-}inf}$ in cardiac (11,570 ngh/ml vs 26,164 ngh/ml)
  ◦ Median t_{max} observed (15.3 h vs 30.1 h)
  ◦ TEAEs experienced (100% spine and 31% in cardiac)
• Both Groups
  ◦ TEAEs were mild or moderate
  ◦ 1 severe TEAE with Bupi HCl (constipation)
  ◦ There were no discontinuations due to TEAEs or deaths</td></tr>
<tr><td>Cohen et al 2019[2]
Retrospective
Laparoscopic or orthopedic surgery
LB vs Bupi HCL
;N=924</td><td>• Groups were matched based on age, ASA score, and surgical procedure
• Endpoint was the incidence of LAST in patient receiving LB or Bupi HCL:
  ◦ LAST was defined as having 2 or more sign/symptoms of LAST out of 13 or 6 other major complications that occurred with 48 hours
  ◦ LAST: Dizziness, bradycardia requiring treatment, blurred vision, tinnitus, desaturation/hypoventilation, loss of consciousness, seizure, drowsiness, dysarthria, confusion, malignant ventricular arrythmias, hypotension, perioral numbness
  ◦ Other Major Complications: Agitation, tachycardia requiring treatment, new onset atrial arrythmias, new onset atrial arrythmias, mortality, cardiac arrest, CPR
• LAST was not identified in any patient (P > 0.99)
• Sensitivity analysis showed a low incidence of complications judged as potentially related to LAST (3 LB and 2 Bupi HCL) (RR=2.4, 95% CI 0.4-14.0, P=0.38)
• Clinical descriptions of patients with LAST symptoms:</td></tr>
</table>

	• Agitation: Patient with baseline developmental delay reported agitated and crying in PACU, necessitated sedation with dexmedetomidine • Drowsiness: Patient reported drowsy but easily aroused in PACU 2 hours after surgery. Resolved spontaneously • Tachycardia: Intermittent tachycardia from 5 until 48 hours after surgery conclusion, to a maximum of 130 bpm. Not associated with hemodynamic compromise, sometimes related to pain and to fever. Finally resolved without specific medical treatment • Blurred vision: Mild blurred vision immediately after surgery, accompanied by pain and "clouding of the ears". Resolved within minutes without intervention other than analgesia • Desaturation/Hypoventilation: Desaturation to 80% for several minutes during stay in PACU, accompanied by shallow breathing pattern. Resolved promptly with oxygen enrichment and position change
CARDIOTHORACIC	
Tirotta et al 2021[1] *Retrospective, cohort* VATS CT Surgery LB (n=90) vs non-LB (n=1480)	• 36% reduction in postsurgical opioids (632 MME vs 991 MME; P<0.0001) • 22% lower intraoperative opioid use (300 MME vs 383 MME; P<0.0001) • 9% reduction in length of stay (5.1 days vs 5.6 days; P=0.0023) • 18% reduction in total hospital costs ($18,084 vs $21,962;P<0.0001)
Tirotta et al 2021[2] *Retrospective, cohort* Elective cardiac surgery, median sternotomy LB (n=111) vs OnQ 0.25% bupi HCL (n=111)	• 5% lower morphine administration incidence (95% vs 100%, P<0.05)
Jeziorczak et al 2021[3] *Retrospective review* Nuss procedure LB (n=10) vs non-LB (n=9)	• 73% lower opioid use (76.8 MME vs 282 MME; P=.004) • 40% reduction in length of stay (3 days vs 5 days; P=0.003) • 80% less Foley catheter usage (20% vs 100%; P=0.001) • 0% patients in LB group on epidural vs 100% patients in control group on epidural (P<0.001) • 78% reduction in total hospital costs ($13,289 vs $60,746; P=0.001)
Eubanks et al 2021[4] *Retrospective review* Nuss Procedure	• 71% lower opioid use intra-op (0.4 vs 1.1 vs 1.4 MME/kg; P=0.022) • 90% lower opioid use post-op (0.8 vs 1.2 vs 8.2 MME/kg; P<0.0001) • 25% reduction in length of stay (3 vs 3 vs 5 days; P=0.002) • No Foley catheter usage in the ERB with LB and transition cohorts

ERP with LB (n=13) vs transition cohort (n=4) vs pre-ERP cohort (n=15)	
SPINE	

Changoor et al 2023[1]
Retrospective pediatric study
Adolescent idiopathic scoliosis
LB 4 mg/kg Erector
Spinae Plane (ESP) block (N=53) vs multimodal pain protocol alone (N=66)
	• Opioid use
	  • Total opioid use (44.5 vs 70.2, P<0.001)
	  • Oral opioid use only (81.1% vs 40.9, P=0.001)
	  • Morphine POD 0 (0.30 mg vs 1.44 mg, P<0.001)
	  • Oxycodone POD 1 (11.9 vs 15.8, P=0.004)
	  • Oxycodone POD 2 (10.2 vs 16.4, P=0.002)
	• Ambulation
	  • Ambulation POD 1 (47.8 ft vs 18.7 ft, P=0.038)
	  • Ambulation POD 2 (888.7 ft vs 553.4 ft, P=0.002)
	• Length of stay (2.42 days vs 2.74 days, P=0.005)
	• Percentage discharged on POD 2 (54.7% vs 27.3%, P=0.002)

Collis et al 2023[2]
Retrospective chart review
Posterior spinal fusion for adolescent idiopathic scoliosis
Regional tertiary referral center (TRC) with EXPAREL (N=88) vs dedicated children's hospital without EXPAREL (CH) (N=49)
	• Less opioid use MME (56.09 vs 70.14, P=0.009)
	• Length of stay (35.05 hrs vs 58.29 hrs, P<0.0001)
	• Time to ambulation (19.30 hrs vs 22.33 hrs, P<0.001)
	• Discharge Date
	  • POD 1 (54% vs 0%, P<0.0001)
	  • POD 2 (34% vs 35%, P<0.0001)
	  • POD 3 (0% vs 10%, P<0.0001)
	  • POD 4 (0% vs 4%, P<0.0001)

McIntosh et al 2022[3] *Prospective* Adolescent idiopathic scoliosis undergoing posterior spinal fusion LB vs continuous ropivacaine epidural ; N=159	• 9% reduction in oral MME from 24-48 hours (37.2 vs 41.0) (P=0.031) • 21% reduction in oral MME from 48-72 hours (23.3 vs 29.6) (P=0.015) • 28% reduction in time to ambulation (17.1 hours vs 23.9 hours) (P=0.0001)

Chughtai et al 2020[4]
Retrospective review
LB vs standard pain management
Spinal deformity surgery
	• Average pain score:
	  • 60% reduction in pain score on POD 1 (2 (0,5) vs 5 (2.5,7) (P<0.001)
	  • 25% reduction in pain score on POD 2 (3 (0,5) vs 4 (3,6) (P<0.001)
	  • Opioid Consumption in MME

	• 33% reduction in MME POD 0 (14.85 vs 22.27) (P=0.0001) • 19% reduction in MME POD 1 (33.41 vs 42.45) (P=0.007) • 46% reduction in MME POD 2 (19.97 vs 37.17) (P=0.0001) • 63% reduction in MME POD 3 (10.03 vs 27.33) (P=0.0001) • Overall (POD 0 through POD 3) (78.2 vs 129) (P=0.0001) • Median LOS: • 25% reduction in days to discharge (3 IQR=3 to 4 vs 4 IQR=4 to 6) (P<0.001) • Similar complications rates (13 out of 15, P<0.05) • Lower odds for complications ([OR]; 95% CI = 0.77; 95% CI=0.64-0.93, P=0.009 and P=0.67; 95 % CI= 0.50 – 0.90, P=0.008)
Ballock et al 2021[5] *Retrospective, cohort* discectomy, lumbosacral fusion, other fusion, laminectomy, or other LB (n=373) vs non-LB (n=9816)	• 47% reduction in postsurgical opioids (1288 MME vs 2437 MME; P<0.0001) • 14% reduction in length of stay (3.5 days vs 4.0 days; P=0.0003) • 8% reduction in total hospital costs ($29,790 vs $32,284;P<0.0227)

References: PEDIATRICS SAFETY

1. Tirotta CF, de Armendi AJ, Horn ND, et al. A multicenter study to evaluate the pharmacokinetics and safety of liposomal bupivacaine for postsurgical analgesia in pediatric patients aged 6 to less than 17 years (PLAY). *J Clin Anesth*. Sep 14 2021;75:110503. doi:10.1016/j.jclinane.2021.110503. https://pubmed.ncbi.nlm.nih.gov/34534923/
2. Cohen B, Glosser L, Saab R, et al. Incidence of adverse events attributable to bupivacaine liposome injectable suspension or plain bupivacaine for postoperative pain in pediatric surgical patients: A retrospective matched cohort analysis. *Paediatr Anaesth*. Feb 2019;29(2):169-174. doi:10.1111/pan.13561. https://pubmed.ncbi.nlm.nih.gov/30521078/

References: PEDIATRICS CARDIOTHORACIC

1. Tirotta CF, Lin JH, Tran MH. Effectiveness of Liposomal Bupivacaine Compared With Standard-of-Care Measures in Pediatric Cardiothoracic Surgery: A Retrospective Cohort Study. J Cardiothorac Vasc Anesth. 2021 Dec;35(12):3681-3687. doi: 10.1053/j.jvca.2021.04.003. Epub 2021 Apr 14. PMID: 33975790. https://pubmed.ncbi.nlm.nih.gov/33975790/
2. Tirotta CF, Lagueruela RG, Salyakina D, Gupta A, Alonso F, Inoa J, Hughes J, Pappas J, Burke R. Liposomal Bupivacaine Infiltration After Median Sternotomy in Pediatric Cardiac Surgery. J Cardiothorac Vasc Anesth. 2021 Jun;35(6):1715-1721. doi: 10.1053/j.jvca.2021.01.053. Epub 2021 Feb 6. PMID: 33663978. https://pubmed.ncbi.nlm.nih.gov/33663978/
3. Jeziorczak PM, Frenette RS, Aprahamian CJ. Liposomal Bupivacaine Injection in Nuss Procedure Allows Narcotic Avoidance and Improved Outcomes. J Laparoendosc Adv Surg Tech A. Nov 5 2021;doi:10.1089/lap.2021.0357. https://pubmed.ncbi.nlm.nih.gov/34748425/
4. Eubanks AL, Grabski DF, Pollack J, Levin DE, McGahren E, Martin LW, Gander J. A multimodal protocol utilizing liposomal bupivacaine rib blocks leads to opioid reduction in patients undergoing the Nuss procedure. J Thorac Dis. 2021 Nov;13(11):6363-6372. doi: 10.21037/jtd-21-1314. PMID: 34992816; PMCID: PMC8662494. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8662494/

References: PEDIATRICS CARDIOTHORACIC

1. Changoor S, Giakas A, Sacks K, et al. The Role of Liposomal Bupivacaine in Multimodal Pain Management following Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis: Faster and Farther with Less Opioids. Spine (Phila Pa 1976). May 1 2023;doi:10.1097/brs.0000000000004702. https://pubmed.ncbi.nlm.nih.gov/37159268/
2. Collis RW, Dry T, Ray HE, Grundlingh N, Chan G, Oswald T. Evidence for a Multimodal Pain Management Regimen in Reduction of Postoperative Opioid Use in Pediatric Patients Receiving Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis. Spine (Phila Pa 1976). Jun 9 2023;doi:10.1097/brs.0000000000004747. https://pubmed.ncbi.nlm.nih.gov/37294836/
3. McIntosh AL, McLeod C. Local Infiltration Anesthesia with Liposomal Bupivacaine Decreases Postoperative Narcotic Consumption in AIS. The Journal of the Pediatric Orthopaedic Society of North America (JPOSNA). 2022. https://www.researchgate.net/publication/363001393_Local_Infiltration_Anesthesia_with_Liposomal_Bupivacaine_Decreases_Postoperative_Narcotic_Consumption_in_AIS
4. Chughtai M, Sultan A, Hudson B, et al. Liposomal Bupivacaine is Both Safe and Effective in Controlling Post-Operative 1 Pain Following Spinal Surgery in Children: A Controlled Cohort Study. Clinical spine surgery. 2020. https://pubmed.ncbi.nlm.nih.gov/32324672/
5. Ballock RT, Seif J, Goodwin R, Lin JH, Cirillo J. Clinical and Economic Outcomes Associated With Use of Liposomal Bupivacaine Versus Standard of Care for Management of Postsurgical Pain in Pediatric Patients Undergoing Spine Surgery. J Health Econ Outcomes Res. Apr 14 2021;8(1):29-35. doi:10.36469/jheor.2021.21967. https://pubmed.ncbi.nlm.nih.gov/33880386/

CARDIOTHORACIC

CARDIOTHORACIC	
CARDIAC	
Study	**Results**

Sharma et al 2020[1]
Epicardial ventricular tachycardia (VT) ablation and Lariat left atrial appendage ligation (LAA)
LB vs non LB; (N=104)
	• Less pain:
	  ◦ LARIAT procedure (n=28 in LB group, n=27 in non-LB group)
	    ▪ 6h: 1.0 (1-2) vs. 8.0 (6-8), (P<0.001)
	    ▪ 12h: 2.0 (1-3) vs. 6.0 (5-6), (P<0.001)
	    ▪ 18h: 2.0 (1.5-3.5) vs. 5.0 (5-7), (P<0.001)
	    ▪ 24h: 3.0 (2-3) vs. 5.0(4-5), (P<0.001)
	    ▪ 48h: 1.0 (1-2) vs. 5.0(4-5), (P<0.001)
	• Epicardial VT ablation (n=25 in LB group, n=24 in non-LB group)
	  ◦ 6h: 1.0 (1-2) vs. 8.0 (6-8), (P<0.001)
	  ◦ 12h: 1.0 (1-1) vs. 5.5(5-6), (P<0.001)
	  ◦ 18h: 2.0 (1-2) vs. 5.0 (4-6.5), (P<0.001)
	  ◦ 24h: 2.0 (2-3) vs. 4.0(3-4), (P<0.001)
	  ◦ 48h: 1.0 (1-1) vs. 5.0(4-5), (P<0.001)
	• Shorter LOS: Median number days (IQR) 2 (2-2) vs 3 (3-3), (P<0.001)

Tirotta et al (PLAY) 2021[2]
Pharmacokinetic Study
Spine and Cardiac Surgery
Group 1: LB infiltration vs Bupi HCL infiltration Spine Surgery Only
Group 2: LB Spine or Cardiac Surgery
;N=98
	• Group 1 LB vs Bupi HCL (12 to <17, Spine Surgery)
	  ◦ Lower mean C_{max} (357 ng/ml vs 564 ng/ml)
	  ◦ Greater mean $AUC_{0\text{-}inf}$ (14,246 ngh/ml vs 5709 ngh/ml)
	  ◦ Similar median t_{max} (1.1 vs 0.9 hours)
	  ◦ TEAEs were comparable (61.3% LB and 73.3 % Bupi HCL)
	• Group 2
	  ◦ Lower mean C_{max} in spine (320 ng/ml vs 447 ng/ml)
	  ◦ Greater mean $AUC_{0\text{-}inf}$ in cardiac (11,570 ngh/ml vs 26,164 ngh/ml)
	  ◦ Median t_{max} observed (15.3 h vs 30.1 h)
	  ◦ TEAEs experienced (100% spine and 31% in cardiac)
	• Both Groups
	  ◦ TEAEs were mild or moderate
	    ▪ 1 severe TEAE with Bupi HCl (constipation)
	  ◦ There were no discontinuations due to TEAEs or deaths

References: CARDIOTHORACIC - CARDIAC

1. Sharma SP, Turagam MK, Mohanty S, Di Biase L, Burkhardt D, Horton R, Natale A, Lakkireddy D. Epicardial Interventions: Impact of Liposomal Bupivacaine on Postprocedural Management (The EPI-LIBRE Study). Circ Arrhythm Electrophysiol. 2020 Jul;13(7):e007425. doi: 10.1161/CIRCEP.119.007425. Epub 2020 Jun 4. PMID: 32496820. https://pubmed.ncbi.nlm.nih.gov/32496820/
2. Tirotta CF, de Armendi AJ, Horn ND, et al. A multicenter study to evaluate the pharmacokinetics and safety of liposomal bupivacaine for postsurgical analgesia in pediatric patients aged 6 to less than 17 years (PLAY). J Clin Anesth. Sep 14 2021;75:110503. doi:10.1016/j.jclinane.2021.110503. https://pubmed.ncbi.nlm.nih.gov/34534923/

BREAST AND PLASTICS

<table>
<tr><th colspan="2">BREAST and PLASTICS</th></tr>
<tr><td colspan="2"><u>BREAST RECONSTRUCTION</u></td></tr>
<tr><td>Study</td><td>Results</td></tr>
<tr><td>Park et al 2024[1]
RCT
(DIEP) flap breast reconstruction
(N=58) LB 266 mg+ 30 mL 0.25% bupivacaine HCl + 0.15 mL of 1:1000 epinephrine + 50 mL of NS vs Control group (n=59): 30 mL 0.25% bupivacaine HCl + 0.15 mL of 1:1000 Epinephrine + 50 mL NS</td><td>• Lower pain scores in the EXPAREL group:
  • 24 hours (3.3 vs 4.3; p=0.02)
  • 48 hours (3.3 vs 4.3; p=0.004)</td></tr>
<tr><td>Knackstedt et al 2024[2]
RWE IQVIA
unilateral or bilateral deep inferior epigastric perforator (DIEP) flap breast reconstruction
LB (N=669) vs Bupivacaine HCL (N=348)</td><td>• Lower mean MME:
  • Total perioperative period (395 vs 512, P=0.0001)
  • 72 hrs (62.8 vs 139.9, P<0.0001)
  • Inpatient period (154.1 vs 303.2, P<0.0001)
• Less acetaminophen received (75% vs 84%; P<0.01)
• Lower inpatient readmission rates:
  • 1 month (2.5% vs 4.1%; p=0.051)
  • 3 months (4.4% vs 6.5%; p=0.046) compared to bupivacaine HCl group
• Lower rate of outpatient office visits (69.2% vs 78.2%; p=0.048) and pain related ED visits (2.6% vs 4.8%; p=0.014) at 3 months</td></tr>
<tr><td>Rendon et al 2022[3]
Retrospective cohort study
Autologous breast reconstruction
ERAS (LB) vs ERAS (catheter) vs control
; N= 145</td><td>• Lower oral morphine equivalents (OME):
  • 211.0 (95% CI, 154.8–267.2) LB group vs 518.4 (95% CI, 454.2–582.7) for the control group vs catheter 215.9 (95% CI, 165.4–266.3), (P<0.001).
  • Less OME during perioperative and intraoperative care, P=0.001. As well as postoperative care, P<0.001
• Shorter length of stay (LOS):
  • 3.0 days [3.0, 4.0] LB and catheter group vs 4.0 days [4.0, 5.0] control group, P<0.001
  • Lower predictive probability of prolonged LOS to POD5 or later vs POD 4 or earlier</td></tr>
</table>

	• LB group (0.18 [95% CI, 0.03–0.24];OR 7.54 [95% CI, 1.77–32.06], P = 0.006) • (0.62 [95% CI, 0.36–0.83] vs 0.08 [95% CI, 0.03–0.24] OR 17.51 [95% CI, 3.60–85.23], P < 0.001)
Haddock et al 2021[4] Retrospective review DIEP flaps for breast reconstruction Historical controls (before ERAS) vs ERAS, ERAS with LB TAP block; N=216	• Lower length of stay (2.550± 0.840 (LB) vs 3.642 ± 0.829 (pre-ERAS) vs 3.217 ± 0.802 (ERAS), P<0.001) • Lower opioid use (115.5 ± 54.6 (LB) vs 275.7 ± 151.1 (pre-ERAS) vs 146.8 ± 93.9 (ERAS), P<0.001) • Lower mean surgery time (7.693 ± 1.681 (LB) vs 9.272 ± 2.119 (pre-ERAS) vs 8.134 ± 1.792 (ERAS), P<.0.001)
Clary et al 2020[5] Autologous breast reconstruction LB TAP vs Thoracic epidural;N=30	• 59% reduction in opioid use POD3 (24.5 MME vs 59.6 MME; P=0.005) • 18% reduction in length of stay (3.53 days vs 4.33 days; P=0.0002) • Shorter time to foley catheter removal (2.1 days vs 2.7 days; P=0.0056)
Jogerst et al 2020[6] Mastectomy LB local infiltration with ERAS vs Pre-ERAS without LB	• More same day discharges (58.6% vs 7.2%; P<0.001) • 25% reduction in length of stay (1.2 days vs 1.6 days; P<0.001) • Less overall complications (32.9% vs 52.4%; P<0.001) • Less hematoma (4.1% vs 10.7%; P=0.03) • Lower rate of implant or expander removal (7.1% vs 14.4%; P=0.03)
Sharif-Askary et al 2019[7] Retrospective chart review Abdominal-based free flap breast reconstruction (muscle-sparing TRAM or DIEP) LB TAP block (post ERAS) vs non-standard treatment (pre-ERAS); N=276	• Shorter length of surgery (502.5 vs 592.5 min; P<0.001) • Lower postoperative opioid consumption (57.3 vs. 297.3 MME; P<0.0001). • Decreased PCA use [4 (2.9%) vs. 129 (93.5%); P<0.0001] • Lower highest pain scores during the time interval of 0-4hr [4.0 (IQR 0.0-5.0) vs.4.0 (IQR 1.5-6.0), respectively; P = 0.05]
Gatherwright et al 2018[8] Blinded RCT LB TAP vs Bupivacaine TAP vs Bupivacaine On-Q vs Control; N=27	• 58% reduction in opioid use versus control (19.3 MME vs 61.4 MME; P=0.006) • 49% reduction in opioid use versus bupivacaine TAP (19.3 MME vs 37.9 MME; P=0.002) • 23% reduction in opioid use versus On-Q pump (19.3 MME vs 29.6; P<0.001) • 40% reduction in time to first ambulation versus bupivacaine TAP (21.43 hours vs 36 hours; P=0.05)
Salibian et al 2018[9] Retrospective Observational LB TAP vs Bupivacaine TAP; N=114	• 23% reduction in pain scores (3.3 vs 4.3; P<0.0001) • 42% reduction in overall opioid use (25.9 mg vs 44.4mg; P<0.0001) • Lower rate of flap necrosis (7.4% vs. 17.5%; P=0.0493)

Oh et al 2018[10] Retrospective Observational LB TAP + ERP vs. SOC; N=118	• 11% reduction in hospital cost ($38,688 vs $43.264)
Rojas et al 2018[11] Prospective observational study ERP w/LB vs control; N=157	• Less patients discharged with opioids (MME) (0 vs 54.5) (P<0.001)
Motakef et al 2017[12] RCT LB local infiltration vs Bupivacaine local infiltration; N=24	• 47% reduction in hourly opioid use (0.76 MED vs 1.43 MED; P=0.017) • 37% reduction in length of stay (29.8 hours vs 46.7 hours; P=0.035) • 42% reduction in hospital charges ($10,828 vs $18,632; P=0.039)
Jablonka et al 2017[13] Breast reconstruction (TRAM/DIEP/SIEA) LB TAP + LB local infiltration vs continuous bupivacaine TAP vs PCA opioids (N=128)	• 74% & 96% reduction in opioid use on POD0-1 compared to continuous bupivacaine & PCA, respectively (1.88 mg vs 7.25 mg vs 52.86 mg; *P*<0.0001) • 59% & 93% reduction in opioid use on POD2 compared to continuous bupivacaine & PCA, respectively (2.12 mg vs 5.17 mg vs 29.9 mg; *P*<0.0001) • 38% & 86% reduction in opioid use on POD3 compared to continuous bupivacaine & PCA, respectively (2.23 mg vs 3.6 mg vs 16.0 mg; *P*<0.0001) • 25% & 35% reduction in length of stay compared to continuous bupivacaine & PCA, respectively (2.65 days vs 3.52 days vs 4.05 days; *P*<0.0001)
Afonso et al 2017[14] Microsurgical breast reconstruction ERP + LB TAP vs pre-ERP; N=91	• 35% reduction in total IV morphine use (46.0 mg vs 70.5 mg; P=0.003) • 40% reduction in IV morphine use POD1 (18.0 mg vs 30.0 mg; P=0.03) • 38% reduction in IV morphine use POD2 (12.5 mg vs 20.0 mg; P=0.004) • Less PCA use (21% vs 98%; P<0.0001) • Shorter PCA duration (24.9 hours vs 41.0 hours; P=0.011) • 20% reduction in length of stay (4.0 days vs 5.0 days; P<0.0001)
Abdelsattar et al 2016[15] Mastectomy with tissue expander reconstruction LB local infiltration vs paravertebral block; N=97	• 24% reduction in pain scores POD0 (3.2 vs 4.2; P=0.008) • 62% reduction in opioid use in the PACU (9.4 MME vs 24.8 MME; P<0.001)
Butz et al 2015[16] Retrospective Observational LB local infiltration vs Bupivacaine pump, vs opioids; N=90	• Less pain at 4, 8, 12, 16 and 24 hours post-operatively (P<0.01) • 25% reduction in length of stay versus opioids (1.5 days vs 2.0 days; P=0.016) • More patients discharged within 1 day compared to pump or opioids (20% vs 13%; P=0.016)
Batdorf et al 2015[17] Free-flap reconstruction ERP + LB TAP vs traditional recovery; N=100	• 20% reduction in pain scores at 24 hours (3.3 vs 4.1; P=0.02) • 71% reduction in total opioid use (167.43 MME vs 574.3 MME; P<0.001) • 74% reduction in opioid use on POD1 (67.3 MME vs 260.0 MME; *P*<0.001)

	• 72% reduction in opioid use on POD2(53.5 MME vs 192.2 MME; *P*<0.001) • 66% reduction in opioid use on POD3 (39.0 MME vs 113.1 MME; *P*<0.001) • 76% less PCA use (20% vs 96%; P<0.001) • 29% reduction in length of stay (3.9 days vs 5.5 days; P<0.001)
<u>AESTHETIC BREAST</u>	

Nadeau et al 2016[1]
RCT
Primary Submuscular Augmentation Mammaplasty
LB vs bupivacaine; N=34
	• Lower pain scores:
	  • Worst Pain Category: 12, 36, and 48 h time points
	  • Least Pain Category: 24, 36, 48, and 60 h time points
	  • Average Pain Category: 12, 24, 36, 48, 60, and 72 h time points
	  • Pain at Time of Survey: 24, 48, and 72 h time points

<u>ABDOMINOPLASTY</u>	

Little et al 2019[1]
Retrospective claims analysis
Includes; Abdominoplasty, abdominal wall reconstruction, mastectomy with immediate tissue expander placement, mastectomy with direct-to-implant reconstruction, autologous breast reconstruction, and augmentation mammoplasty
LB vs control; N=958
	• Shorter length of stay (5.8 days vs 0.2 days, P=0.004)
	• No 30 day readmission rate (0% vs 4%, P=0.043)
	• Lower mean costs
	  • Total cost: $28,021 vs $39,531, P=0.020
	  • Direct cost: $17,561 vs $23,960, P=0.047

<u>OTHER AESTHETIC SURGERY</u>	
Boyd et al 2020[1] Burn patients: Autograft harvesting Prospective observational LB infiltration vs matched historical control with no LB; N=42	• 15% reduction in median AUC_{0-24} (IQR): (577.5 (407.9, 739.8) vs 680.3 (543.6, 802.8)) (P=0.05) • 33% reduction in median LOS (IQR): (4 (1,9.5) vs 6 (318)) (P=0.01) • Less nausea/vomiting documented, n%: (14 (67) vs 20 (95)) (P=0.05)
Artz et al 2020[2] Burn Patients (skin graft donor site analgesia) Retrospective study	• Less donor site pain: (25 (86%) vs 1(3.4%)) (P<0.0001) • Less donor site pain than graft site pain: (22 (76%) vs 1(3.4%)) (P<0.0001)

Intraoperative donor site LB infiltration vs. control with no intraoperative donor site infiltration; N=58	

References: BREAST RECONSTRUCTION

1. Park RH, Chou J, DeVito RG, et al. Effectiveness of Liposomal Bupivacaine Transversus Abdominis Plane Block in DIEP Flap Breast Reconstruction: Randomized Controlled Trial. Plast Reconstr Surg. Feb 2 2024;doi:10.1097/prs.0000000000011326. https://pubmed.ncbi.nlm.nih.gov/38315156/
2. Knackstedt RW, Lin JH, Kakoty S. Liposomal Bupivacaine Analgesia in Deep Inferior Epigastric Perforator Flap Breast Reconstruction: A Retrospective Cohort Study. Plastic and Reconstructive Surgery – Global Open. 2024;12(6):e5874. doi:10.1097/gox.0000000000005874. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11161287/
3. Rendon JL, Borrell-Vega J, Reyes JC, Wang DM, Roeth C, Abdel-Rasoul M, Skoracki RJ, Harter RL, Moffatt-Bruce SD, Humeidan ML. Evaluating the Efficacy of Two Regional Pain Management Modalities in Autologous Breast Reconstruction. Plast Reconstr Surg Glob Open. 2022 Jan 19;10(1):e4010. doi: 10.1097/GOX.0000000000004010. PMID: 35070591; PMCID: PMC8769083. https://pubmed.ncbi.nlm.nih.gov/35070591/
4. Haddock NT, Garza R, Boyle CE, Liu Y, Teotia SS. Defining Enhanced Recovery Pathway with or without Liposomal Bupivacaine in DIEP Flap Breast Reconstruction. Plast Reconstr Surg. Nov 1 2021;148(5):948-957. doi:10.1097/PRS.0000000000008409 https://www.ncbi.nlm.nih.gov/pubmed/34705768.
5. Clary Z, Nazir N, Butterworth J. Transversus Abdominis Plane Block With Liposomal Bupivacaine Versus Thoracic Epidural for Postoperative Analgesia After Deep Inferior Epigastric Artery Perforator Flap–Based Breast Reconstruction. Annals of Plastic Surgery. 2020;Publish Ahead of Printdoi:10.1097/sap.0000000000002423 https://journals.lww.com/annalsplasticsurgery/Fulltext/9000/Transversus_Abdominis_Plane_Block_With_Liposomal.96541.aspx.
6. Jogerst K, Thomas O, Kosiorek HE, et al. Same-Day Discharge After Mastectomy: Breast Cancer Surgery in the Era of ERAS((R)). Ann Surg Oncol. Sep 2020;27(9):3436-3445. doi:10.1245/s10434-020-08386-w https://www.ncbi.nlm.nih.gov/pubmed/32221736.
7. Sharif-Askary B, Hompe E, Broadwater G, Anolik R, Hollenbeck ST. The Effect of Enhanced Recovery after Surgery Pathway Implementation on Abdominal-Based Microvascular Breast Reconstruction. J Surg Res. Oct 2019;242:276-285. doi:10.1016/j.jss.2019.04.062 https://www.ncbi.nlm.nih.gov/pubmed/31125841.
8. Gatherwright J, Knackstedt RW, Ghaznavi AM, Bernard S, Schwarz G, Moreira A, Gurunluoglu R, Djohan R. Prospective, Randomized, Controlled Comparison of Bupivacaine versus Liposomal Bupivacaine for Pain Management after Unilateral Delayed Deep Inferior Epigastric Perforator Free Flap Reconstruction. Plast Reconstr Surg. 2018 Jun;141(6):1327-1330. doi: 10.1097/PRS.0000000000004360. PMID: 29750760. https://pubmed.ncbi.nlm.nih.gov/29750760/
9. Salibian AA, Frey JD, Thanik VD, Karp NS, Choi M. Transversus Abdominis Plane Blocks in Microsurgical Breast Reconstruction: Analysis of Pain, Narcotic Consumption, Length of Stay, and Cost. Plast Reconstr Surg. 2018 Sep;142(3):252e-263e. doi: 10.1097/PRS.0000000000004632. PMID: 29879000. https://pubmed.ncbi.nlm.nih.gov/29879000/
10. Oh C, Moriarty J, Borah BJ, et al. Cost analysis of enhanced recovery after surgery in microvascular breast reconstruction. J Plast Reconstr Aesthet Surg. Mar 2 2018;doi:10.1016/j.bjps.2018.02.018. https://pubmed.ncbi.nlm.nih.gov/29606583/
11. Rojas KE, Manasseh DM, Flom PL, et al. A pilot study of a breast surgery Enhanced Recovery After Surgery (ERAS) protocol to eliminate narcotic prescription at discharge. Breast cancer research and treatment. Oct 2018;171(3):621-626. doi:10.1007/s10549-018-4859-y https://www.ncbi.nlm.nih.gov/pubmed/29915947.
12. Motakef S, Wong WW, Ingargiola MJ, et al. Liposomal Bupivacaine in Implant-Based Breast Reconstruction. Plast Reconstr Surg Glob Open. Nov 2017;5(11):e1559. doi:10.1097/GOX.0000000000001559 https://www.ncbi.nlm.nih.gov/pubmed/29263963.
13. Jablonka EM, Lamelas AM, Kim JN, et al. Transversus Abdominis Plane Blocks with Single-Dose Liposomal Bupivacaine in Conjunction with a Nonnarcotic Pain Regimen Help Reduce Length of Stay following Abdominally Based Microsurgical Breast Reconstruction. Plast Reconstr Surg. Aug 2017;140(2):240-251. doi:10.1097/prs.0000000000003508 https://www.ncbi.nlm.nih.gov/pubmed/28746269.
14. Afonso A, Oskar S, Tan KS, et al. Is Enhanced Recovery the New Standard of Care in Microsurgical Breast Reconstruction? Plast Reconstr Surg. May 2017;139(5):1053-1061. doi:10.1097/PRS.0000000000003235 https://www.ncbi.nlm.nih.gov/pubmed/28092334.
15. Abdelsattar JM, Boughey JC, Fahy AS, et al. Comparative Study of Liposomal Bupivacaine Versus Paravertebral Block for Pain Control Following Mastectomy with Immediate Tissue Expander Reconstruction. Annals of Surgical Oncology. 2016;23(2):465-470. https://www.ncbi.nlm.nih.gov/pubmed/26307232.
16. Butz DR, Shenaq DS, Rundell VLM, et al. Postoperative Pain and Length of Stay Lowered by Use of Exparel in Immediate, Implant-Based Breast Reconstruction. Plast Reconstr Surg Glob Open. 2015;3(e391)doi:10.1097/GOX.0000000000000355 https://www.ncbi.nlm.nih.gov/pubmed/26090281.
17. Batdorf NJ, Lemaine V, Lovely JK, et al. Enhanced recovery after surgery in Microvascular Breast Reconstruction. J Plast Reconstr Aesthet Surg. 2015;68(3):395-402. https://www.ncbi.nlm.nih.gov/pubmed/25488326.

References: AESTHETIC BREAST

1. Nadeau MH, Saraswat A, Vasko A, Elliott JO, Vasko SD. Bupivacaine Versus Liposomal Bupivacaine for Postoperative Pain Control after Augmentation Mammaplasty: A Prospective, Randomized, Double-Blind Trial. Aesthet Surg J. Feb 2016;36(2):NP47-52. doi:10.1093/asj/sjv149 http://www.ncbi.nlm.nih.gov/pubmed/26704270.

References: ABDOMINOPLASTY

1. Little A, Brower K, Keller D, Ramshaw B, Janis JE. A Cost-Minimization Analysis Evaluating the Use of Liposomal Bupivacaine in Reconstructive Plastic Surgery Procedures. Plast Reconstr Surg. 2019 Apr;143(4):1269-1274. doi: 10.1097/PRS.0000000000005435. PMID: 30730499. https://pubmed.ncbi.nlm.nih.gov/30730499/

References: OTHER AESTHETIC SURGERY

1 Boyd AN, Blair ME, Degenkolb KE, Foster DR, Hartman BC, Sood R, Walroth TA. A prospective analysis describing the innovative use of liposomal bupivacaine in burn patients. Burns. 2020 Mar;46(2):370-376. doi: 10.1016/j.burns.2019.07.031. Epub 2019 Aug 14. PMID: 31420265. https://pubmed.ncbi.nlm.nih.gov/31420265/

2. Artz C, Ward MA Jr, Miles MVP, Brennan P, Alexander KM, Lintner A, Bright A, Kahn SA. Intraoperative liposomal bupivacaine for skin graft donor site analgesia: A retrospective cohort study. Burns. 2021 Aug;47(5):1045-1052. doi: 10.1016/j.burns.2020.06.011. Epub 2020 Jun 20. PMID: 34034954. https://pubmed.ncbi.nlm.nih.gov/34034954/

CESAREAN SECTION

CESAREAN SECTION	
Study	**Results**

Grasch et al 2023[1]
Prospective trial
C-Section
ERAS (N=72) + LB vs pre-ERAS (N=56)
	• Lower opioid use in the first 48 hrs postoperatively:
	  • 0-24 hrs postpartum (9.4±12.7 vs. 21.3±14.1 MME, P<0.001)
	  • 24-48 hrs postpartum (14.1±14.9 vs. 25.7±14.9 MME, P<0.001)
	• Fewer opioid pills after discharge (10 (IQR 3-16) vs. 20 (IQR 15-23) pills, P<0.001) Decreased mean length of initial perioperative bladder catheterization (8.4±9.1 vs 14.1±4.7 hours, P<0.001; median (IQR) 3.5 (2.9-14.5) vs 12.6 (12.2-13.6) hours, respectively

Peebles et al 2023[2]
Retrospective chart review
C-Section
LB TAP (N=107) vs LB wound infiltration (N=185) vs SOC (N=110)
	• Lower total opioids MME (24.9 vs 25.2 vs 64.4, P<0.001)
	• Lower average daily opioids (9.9 vs 9.7 vs 25.8, P<0.001)
	• Higher opioid free percentage (42.1% vs 55.1% vs 0%, P<0.001)
	  • POD 0 (5.5 vs 4.6 vs 5.9, P<0.001)
	  • POD 1 (5.6 vs 5.3 vs 6.3, P=0.003)
	• Lower length of stay (2.3 vs 2.4 vs 2.5, P=0.01)

Habib et al 2021[3] C-Section *Multi-Center RCT* *LB TAP vs LB TAP + ITM 50mcg vs ITM 150mcg (N=153)*	• Noninferior overall pain scores at 24, 48, and 72 hours for both LB groups vs ITM • Reduced opioid exposure from 0-72 hours in both for LB TAP alone and LB TAP + ITM vs ITM (81.3mg vs 120.2mg, p<0.0001) (87.2mg vs 120.2mg, p=0.0005) • Reduced Opioid Related Symptom Distress Scale (ORSDS) scores at 24h for both LB groups (0.51 vs 0.56 vs 0.84) (p: 0.0006-0.0036) • Reduced pruritis severity at all time points (12h, 24h, 48h, 72h) for both LB groups
Feierman et al 2021[4] C-section LB TAP vs Bupivacaine TAP (2020 and historic 2012) vs Neuraxial morphine (2012) (N=288)	• Reduction in patients using opioids in any time during hospital stay vs ITM and Bupivacaine TAP (18% vs 60% vs 54%) (p<0.0001) • Reduction in LOS vs Bupivacaine TAP during pandemic (2.29 days vs 3.22 days, p<0.001) • Reduction in LOS vs historical neuraxial morphine (2.29 days vs 3.16 days, p<0.001)
Nedeljkovic et al 2020[5] C-section *Multi-Center RCT* LB TAP vs Bupivacaine TAP (N=136)	• 52% reduction in opioid consumption through 72 hours (15.5 mg vs 32.0 mg, P=0.012) • 56% reduction in opioid consumption at 48 hours (9.1 mg vs 20.5 mg, P=0.010) • 49% reduction in opioid consumption at 7 days (23.3 mg vs 45.8 mg, P=0.018) • >2x more patients opioid spared (defined as taking ≤15 mg of oxycodone with no opioid related side effects reported: 53.5% vs 25%, P=0.0012)

Fiol et al 2020[6] C-section LB TAP vs no TAP (N=222)	• 56% reduction in incisional pain (1.8 vs 2.8, P=0.003) • 50% reduction in time to first opioid (30 hours vs 15 hours, P<0.001) • 58% reduction in opioid use in the first 24 hours (41.5 vs 99.3, P<0.001) • 50% reduction in opioid use in the first 48 hours (64.4 vs 129.8, P<0.001) • 46% reduction in opioid use in the first 72 hours (82.5 vs 152.7, P<0.001)
Hutchins et al 2019[7] C-section *Retrospective review* LB TAP + intrathecal morphine (ITM) vs LB TAP (N=358)	• 67% reduction in opioid use in the first 24 hours (5mg vs 15 mg, P<0.001) • 26% reduction in opioid use in the 0-72 hours range (35 mg vs 47.5, P=0.041) • 9% reduction in LOS (78.9 hours vs 87 hours, P=0.046)
Baker et al 2018[8] C-section LB TAP vs Control (N=186)	• 47% decrease in opioid use (41.9 vs 79.6, P<0.001) • 46% reduction in total pain scores (132.8 vs 246.3, P<0.001) • 15% reduction in time to discharge readiness from PACU (138 min vs 163 min, P=0.028) • 39% reduction in time to ambulation (18.7 vs 30.7, P<0.001) • 31% reduction in time to solid food (22.3 vs 32.1, P=0.008) • 26% reduction in time to bowel movement (21.6 vs 29.1, P=0.05) • 26% reduction in length of stay (2.9 days vs 3.9 days, P<0.001)
Parikh et al 2017[9] C-section LB local infiltration vs Control (N=80)	• 41% decrease in opioid use (41.51 vs 69.9, P<0.001)

References: CESAERAN SECTION

1. Grasch JL, Rojas JC, Sharifi MM, McLaughlin MMM, Bhamidipalli SS, Haas DM. Impact of enhanced recovery after surgery pathway for cesarean delivery on postoperative pain. AJOG Global Reports. 2023/01/29/ 2023:100169. doi:https://doi.org/10.1016/j.xagr.2023.100169. https://pubmed.ncbi.nlm.nih.gov/36876160/
2. Peebles AF, Mouch A, Maxwell RA, Ruby T, Kindig MJ. Long-Acting Bupivacaine for Pain Control After Cesarean Birth. Nurs Womens Health. Jun 26 2023;doi:10.1016/j.nwh.2023.03.003. https://pubmed.ncbi.nlm.nih.gov/37385592/
3. Habib AS, Nedeljkovic SS, Horn JL, et al. Randomized trial of transversus abdominis plane block with liposomal bupivacaine after cesarean delivery with or without intrathecal morphine. J Clin Anesth. Oct 6 2021;75:110527. doi:10.1016/j.jclinane.2021.110527 https://www.ncbi.nlm.nih.gov/pubmed/34626927.
4. Feierman DE, Kim J, Bronstein A, et al. The use of bilateral transversus abdominis plane blocks with liposomal bupivacaine on postoperative cesarean delivery patients during COVID-19 pandemic is associated with reduced narcotics use and reduced length of stay. Womens Health (Lond). Jan-Dec 2021;17:17455065211058046. doi:10.1177/17455065211058046 https://www.ncbi.nlm.nih.gov/pubmed/34775851.
5. Nedeljkovic SS, Kett A, Vallejo MC, et al. Transversus Abdominis Plane Block With Liposomal Bupivacaine for Pain After Cesarean Delivery in a Multicenter, Randomized, Double-Blind, Controlled Trial. Anesth Analg. Dec 2020;131(6):1830-1839. doi:10.1213/ANE.0000000000005075 https://www.ncbi.nlm.nih.gov/pubmed/32739962
6. Fiol AG, Eid A, Elgamal MY, et al. Is There A Role for Liposomal Bupivacaine as Part of a Multimodal Strategy Inclusive of Intrathecal Morphine for Post-Cesarean Analgesia? A Retrospective Chart Review Study. Anesth Pain Res. 2020;4(2):1-4. https://www.researchgate.net/publication/348596565_Is_There_A_Role_for_Liposomal_Bupivacaine_as_Part_of_a_Multimodal_Strategy_Inclusive_of_Intrathecal_Morphine_for_Post-Cesarean_Analgesia_A_Retrospective_Chart_Review_Study
7. Hutchins JL, Renfro L, Orza F, Honl C, Navare S, Berg AA. The addition of intrathecal morphine to a transversus abdominis plane block with liposome bupivacaine provides more effective analgesia than transversus abdominis plane block with liposome bupivacaine alone: a retrospective study. Local and Regional Anesthesia. 2019;12:7-13. https://www.ncbi.nlm.nih.gov/pubmed/30863147.
8. Baker BW, Villadiego LG, Lake YN, et al. Transversus abdominis plane block with liposomal bupivacaine for pain control after cesarean delivery: a retrospective chart review. J Pain Res. 2018;11:3109-3116. doi:10.2147/JPR.S184279 https://www.ncbi.nlm.nih.gov/pubmed/30573987.
9. Parikh P, Sunesara I, Singh Multani S, Patterson B, Lutz E, Martin JN Jr. Intra-incisional liposomal bupivacaine and its impact on postcesarean analgesia: a retrospective study. J Matern Fetal Neonatal Med. 2019 Mar;32(6):966-970. doi: 10.1080/14767058.2017.1397118. Epub 2017 Nov 7. PMID: 29065741. https://pubmed.ncbi.nlm.nih.gov/29065741/

GYNECOLOGY

GYNECOLOGY	
Study	**Results**

Trad et al 2022[1]
Retrospective cohort study
Abdominal sacrocolpopexy
LB local infiltration Post-ERAS vs Post-ERAS alone vs Pre-ERAS
N=302
	• 38% reduction in cost compared to Pre-ERAS ($2391 vs $3844; P<0.001)
	• 20% reduction in cost compared to Post-ERAS alone ($2391 vs $2975; P<0.001)
	• Less opioid use compared to both Pre-ERAS and Post-ERAS alone
	    • Lower median intraoperative (67.5 vs 76.3 vs 86; P<0.001)
	    • Lower median PACU (35 vs 51 vs 93; P<0.001)
	    • Lower median POD0 (48 vs 60 vs 114; P<0.001)
	    • Lower median POD1 (62 vs 74 vs 120; P<0.001)
	    • Lower mean daily POD0-3 opioid use (18.8 vs 26 vs 41.3; P<0.001)
	    • Lower POD0-3 any opioid use (75.8% vs 92.8% vs 97.7%; P<0.001)
	• Shorter length of stay compared to both Pre-ERAS and Post-ERAS alone
	    • Lower mean LOS (1.8 vs 2.3 vs 2.9 days; P<0.001)
	    • Lower LOS >1day (51.6% vs 91.6% vs 98.4%; P<0.001)
	• Less complications compared to both Pre-ERAS and Post-ERAS alone
	    • Lower PACU complications (7 vs 17 vs 47; P<0.001)
	• Lower clinical visit within 30 days (18 vs 41 vs 46; P<0.001)

Hutchins et al 2019[2] Robot-assisted & laparoscopic hysterectomy LB TAP vs. Bupivacaine port site infiltration; N=62	• 40% reduction in max pain score 0-24 hours (3.0 vs 5.0 ; P=0.018) • 33% reduction in max pain score 48-72 hours (2.0 vs 3.0; P=0.009) • 38% reduction in max pain score 0-72 hours (8.0 vs 13.0; P=0.022) • 17% less opioid use 0-72 hours (20.8 vs 25.0; P=0.034) • Better quality of recovery (126 vs 115; P=0.021)
Barron et al 2017[3] Laparoscopic or robotic-assisted total hysterectomy LB local infiltration vs bupivacaine local infiltration; N=64	• 31% reduction in mean pain scores POD3 (2.79 vs 4.07; P=0.02) • 26% reduction in worst pain scores POD2 (4.14 vs 5.58; P=0.03) • 36% reduction in worst pain scores POD3 (3.72 vs 5.60; P=0.01)
Seagle et al 2017[4] Laparoscopic hysterectomy LB TAP vs oral opioids	• LB TAP was associated with decreased healthcare costs and increased effectiveness

Kalogera et al 2016[5] Complex cytoreductive surgery LB local infiltration vs Bupivacaine local infiltration; N=202	• 44% reduction in opioid use through 24 hours (30 MME vs 53.5 MME; P=0.02) • 55% reduction in opioid use through 48 hours (37.5 MME vs 82.5 MME; P=0.005) • 38% reduction in opioid use for remainder of hospitalization (62 MME vs 100.5 MME; P=0.006) • Less IV opioid rescue required (LB 28.95% vs bupivacaine 55.6%; P<0.001) • Fewer patients required IV opioid rescue (LB 11.4% vs bupivacaine 46.7%; P<0.001) • Fewer patients required PCA (LB 4.1% vs bupivacaine 33.3%; P<0.001) • Fewer patients experienced nausea through 24 hours (24.8% vs 60.5%; P<0.001) • Fewer patients experience nausea through 48 hours (30% vs 55.6%; P<0.001)
Hutchins et al 2015[6] Robot-assisted hysterectomy LB TAP vs. Bupivacaine TAP; N=58	• 67% and 17% reduction in minimum (1.5 vs 3.0; P=0.01) and maximum pain scores (5.0 vs 6.0; P=0.002), respectively, PACU • 67% and 21% reduction in minimum (1.5 vs 3.0; P=0.003) and maximum pain scores (5.5 vs 7; P=0.006), respectively, 0-24 hrs post-op • 20% reduction maximum pain scores (4 vs 5; P=0.044), 24-48 hrs post-op • 40% reduction maximum pain scores (3 vs 5; P=0.047), 48-72 hrs post-op • 52% reduction in opioid consumption (24.9 MME vs 51.7 MME; P=0.002), 0-72 hrs post-op • 47% reduction in opioid consumption (13.3 MME vs 25 MME; P=0.023), 0-24 hrs post-op • 61% reduction in opioid consumption (2.9 MME vs 7.5 MME; P=0.015), 24-48 hrs post-op • Lower incidences of nausea (25% vs 57%; P=0.014)
Hutchins et al 2015[7] Robot-assisted hysterectomy LB TAP vs. No TAP; N=60	• 40% reduction in maximum pain scores (5 vs 7; P=0.05) • 58% reduction in length of stay (12 hours vs. 28 hours; P<0.0001) • Lower incidences of nausea/vomiting (20% vs 54%; P=0.02
Gasanova et al 2015[8] Open total hysterectomy LB local infiltration vs Bupivacaine TAP; N=58	• Less pain through 48 hours (P<0.001) • 30% reduction in morphine use in the 1st 24 hours (34 mg vs 48 mg; P=0.05) • 47% reduction in hydrocodone use at 24-48 hours (1.9 tabs vs 3.6 tabs; P=0.009)

References: GYNECOLOGY

1. Teles Abrao Trad A, Tamhane P, Weaver AL, et al. Impact of Enhanced Recovery Implementation in Women Undergoing Abdominal Sacrocolpopexy. Int J Gynaecol Obstet. May 22 2022;doi:10.1002/ijgo.14279. https://pubmed.ncbi.nlm.nih.gov/35598156/
2. Hutchins J, Argenta P, Berg A, Habeck J, Kaizer A, Geller MA. Ultrasound-guided subcostal transversus abdominis plane block with liposomal bupivacaine compared to bupivacaine infiltration for patients undergoing robotic-assisted and laparoscopic hysterectomy: a prospective randomized study. J Pain Res. 2019;12:2087-2094. doi:10.2147/JPR.S193872. https://pubmed.ncbi.nlm.nih.gov/31308734/
3. Barron KI, Lamvu GM, Schmidt RC, Fisk M, Blanton E, Patanwala I. Wound infiltration with extended-release versus short-acting bupivacaine before laparoscopic hysterectomy: a randomized controlled trial. J Minim Invasive Gynecol. Nov 14 2017;24(2):286-292. doi:10.1016/j.jmig.2016.11.002. https://pubmed.ncbi.nlm.nih.gov/27856385/
4. Seagle BL, Miller ES, Strohl AE, Hoekstra A, Shahabi S. Transversus abdominis plane block with liposomal bupivacaine compared to oral opioids alone for acute postoperative pain after laparoscopic hysterectomy for early endometrial cancer: a cost-effectiveness analysis. Gynecol Oncol Res Pract. 2017;4(1):12. doi:10.1186/s40661-017-0048-7. https://pubmed.ncbi.nlm.nih.gov/28852531/
5. Kalogera E, Bakkum-Gamez JN, Weaver AL, et al. Abdominal Incision Injection of Liposomal Bupivacaine and Opioid Use After Laparotomy for Gynecologic Malignancies. Obstet Gynecol. Oct 06 2016;128(5):1009-1017. doi:10.1097/aog.0000000000001719. https://pubmed.ncbi.nlm.nih.gov/27741199/
6. Hutchins J, Delaney D, Vogel RI, et al. Ultrasound guided subcostal transversus abdominis plane (TAP) infiltration with liposomal bupivacaine for patients undergoing robotic assisted hysterectomy: A prospective randomized controlled study. Gynecol Oncol. 2015;138(3):609-13. doi:10.1016/j.ygyno.2015.06.008. https://pubmed.ncbi.nlm.nih.gov/26056753/
7. Hutchins J, Vogel RI, Ghebre R, et al. Ultrasound-Guided Subcostal Transversus Abdominis Plane Infiltration With Liposomal Bupivacaine for Patients Undergoing Robotic-Assisted Hysterectomy: A Retrospective Study. Int J Gynecol Cancer. 2015;25(5):937-941. doi:10.1097/igc.0000000000000429. https://pubmed.ncbi.nlm.nih.gov/25790044/
8. Gasanova I, Alexander J, Ogunnaike B, et al. Transversus abdominis plane block versus surgical site infiltration for pain management after open total abdominal hysterectomy. Anesth Analg. 2015;121(5):1383-1388. doi:10.1213/ane.0000000000000909. https://pubmed.ncbi.nlm.nih.gov/26252171/

UROGYNECOLOGY

UROGYNECOLOGY	
Study	**Results**
Propst et al 2018[1] Sacrospinous ligament fixation LB local infiltration vs lidocaine local infiltration; N=33	• 100% reduction in global pain at 36 hours (P=0.04)
Iwanoff et al 2017[2] Midurethral sling placement LB local infiltration vs bupivacaine + lidocaine local infiltration; N=57	• 33% reduction in pain scores POD1 (P=0.0459)
Mazloomdoost et al 2017[3] Retropubic sling placement for stress urinary incontinence LB local infiltration vs placebo; N=109	• 73% reduction in pain scores 4 hours after discharge (P=0.014) • 65% reduction in pain scores POD1 morning (P=0.014) • 45% reduction in pain scores POD2 bedtime (P=0.027) • 40% reduction in pain scores POD3 morning (P=0.011) • 43% reduction in pain scores POD3 bedtime (P=0.043) • 22% of patients in the LB arm required narcotics vs 49% in the placebo arm (P=0.006)

References: UROGYNECOLOGY

1. Propst K, O'Sullivan DM, Steinberg AC. Randomized double-blind trial of short- versus long-acting analgesia at the sacrospinous ligament. Int Urogynecol J. 2019 Jan;30(1):123-130. doi: 10.1007/s00192-018-3758-4. Epub 2018 Sep 6. PMID: 30191249. https://pubmed.ncbi.nlm.nih.gov/30191249/
2. Iwanoff C, Salamon C. Liposomal Bupivacaine Versus Bupivacaine Hydrochloride with Lidocaine during Midurethral Sling Placement: A Randomized Controlled Trial. J Minim Invasive Gynecol. 2019 Sep-Oct;26(6):1133-1138. doi: 10.1016/j.jmig.2018.11.005. Epub 2018 Nov 22. PMID: 30472302. https://pubmed.ncbi.nlm.nih.gov/30472302/
3. Mazloomdoost D, Pauls RN, Hennen EN, Yeung JY, Smith BC, Kleeman SD, Crisp CC. Liposomal bupivacaine decreases pain following retropubic sling placement: a randomized placebo-controlled trial. Am J Obstet Gynecol. 2017 Nov;217(5):598.e1-598.e11. doi: 10.1016/j.ajog.2017.07.001. Epub 2017 Jul 8. PMID: 28694151. https://pubmed.ncbi.nlm.nih.gov/28694151/

ORAL MAXILLOFACIAL SURGERY (OMFS)

OMFS	
Study	**Results**
Layon et al 2024[1] Retrospective chart review Orthognathic surgery LB (N=10) vs standard of care (SOC) (N=12)	• Lower total breakthrough opioid use MME (8.60 vs 35.10, P=0.0037) • Lower breakthrough opioid use MME (5.75 vs 14.70, P=0.026) • Lower opioids prescribed at discharge (60% vs 100%, P=0.029)
Lieblich et al 2021[2] Retrospective cross-sectional Mandibular Third Molar Extraction LB (n=300) vs no LB (n=300)	• 59% less total opioids (MME) prescribed (P<0.0001) • 57% Less patients needing opioid refill (P=0.028)

Jacobus et al 2021[3]
Retrospective
Outpatient lingual nerve microsurgery
LB (N=9) vs bupivacaine HCl (N=11)
	• Less mean pain (NRS) in LB group vs Bupivacaine HCl
	    • 55% less pain day 2 (P=0.001)
	    • 63% less pain day 3 (P=0.006)
	    • 50% less total pain over 3 days (P=0.002)
	• Less opioids used in LB group vs Bupivacaine HCl
	    • 52.1% reduction among patients that required opioids (P<0.001)
	    • 33.3% of LB group required opioids vs 100% of Bupivacaine HCl group(P=0.002)

Crowley et al 2020[4] Retrospective Pediatric alveolar bone grafting LB (N=25) vs bupivacaine or lidocaine (N=19)	• 83% less opioid use (OME) first 24 hours post-surgery (P=0.0006) • 2.51 lower median pain NRS score
Patel et al 2019[5] Retrospective Donor site iliac crest analgesia during alveolar bone grafting LB (N=17) vs bupivacaine (N=21)	• 67% less opioid use (OME) (P=0.002) • 68% less opioid use (OME) by patient weight (mg/kg) (P<0.001) • Reduced mean pain (NRS) • 59% less pain 24 hours post-surgery (P=0.009) • Statistically significant at 4-h (P<0.001), 12-h (P=0.010), 16-h (P=0.002), 20-h (p=0.006) • Increased steps walked Days 1-3 (p<0.001) and Day 5 (P=0.032)
Iero et al 2018[6] Open label RCT Full Arch Implant to Mandible/Maxilla LB local infiltration (n=34) vs. no LB (n=35)	• Less cumulative pain (NRS) • At all-time points 33% less at 7 days (mandible: P ≤ .0112; maxilla P ≤ .0083) • Greater satisfaction with pain control on POD 0-1

Lieblich et al 2017[7]
Multi-center RCT
Bilateral Third Molar Extraction
ITT population:
LB (n=99) vs placebo (n=51)
Per-protocol population:
LB (n=59) vs placebo (n=30)
	• Less pain in the per protocol group
	    • 28% reduction 0-24 hours (P<0.05)
	    • 34% reduction 0-48 hours (P=0.023)
	    • 34% reduction 0-72 hours (P<0.05)
	    • 36% reduction 0-96 hours (P<0.05)
	• No difference in pains score scores for the ITT group

Bultema et al 2016[8] Open label RCT Pre-endodontic treatment due to symptomatic irreversible pulpitis LB (n=47) vs bupivacaine (n=48)	• LB patients reported more numbness through POD3 (P<0.05)

Glenn et al 2016[9]
Open label RCT
Endodontic debridement for pulpal necrosis
LB (n=52) vs bupivacaine (n=48)
	• Significantly less pain overall days 1-5 (P=0.0001)
	• LB patients reported more numbness
	    • Day 1 (P=0.003)
	    • Day 2 (P=0.0007)

References: ORAL MAXILLOFACIAL SURGERY (OMFS)

1. Layon SA, Burns HR, Williams AD, Ding Y, Mohammad S, Buchanan EP. Liposomal Bupivacaine Use During Orthognathic Surgery in Cleft Lip and Palate Patients. The Journal of craniofacial surgery. Jan 15 2024;doi:10.1097/scs.0000000000009966. https://pubmed.ncbi.nlm.nih.gov/38227634/
2. Lieblich SE, Misiek D, Olczak J, Fleck H, Waterman F. A Retrospective Cross-Sectional Study of the Effect of Liposomal Bupivacaine on Postoperative Opioid Prescribing After Third Molar Extraction. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. Jul 2021;79(7):1401-1408 e1. doi:10.1016/j.joms.2021.02.012 https://www.ncbi.nlm.nih.gov/pubmed/33744242.
3. Jacobus D, Mehr S, Ziccardi V. Liposomal bupivacaine use in exploratory lingual nerve microsurgery: does liposomal bupivacaine use decrease postoperative pain and opioid consumption compared to bupivacaine hydrochloride? A pilot study. Quintessence Int. Sep 9 2021;52(9):812-818. doi:10.3290/j.qi.b1763651 https://www.ncbi.nlm.nih.gov/pubmed/34269041
4. Crowley JS, McLean P, Gabriel RA, et al. The Association of Liposomal Bupivacaine on Opioid Consumption in the Pediatric Alveolar Cleft Population. The Journal of craniofacial surgery. Jun 2020;31(4):1078-1081. doi:10.1097/SCS.0000000000006310 https://www.ncbi.nlm.nih.gov/pubmed/32195834.
5. Patel RA, Jablonka EM, Rustad KC, et al. Retrospective cohort-based comparison of intraoperative liposomal bupivacaine versus bupivacaine for donor site iliac crest analgesia during alveolar bone grafting. J Plast Reconstr Aesthet Surg. Dec 2019;72(12):2056-2063. doi:10.1016/j.bjps.2019.09.026 https://www.ncbi.nlm.nih.gov/pubmed/31648962.
6. Iero PT, Mulherin DR, Jensen O, Berry T, Danesi H, Razook SJ. A Prospective, Randomized, Open-Label Study Comparing an Opioid-Sparing Postsurgical Pain Management Protocol With and Without Liposomal Bupivacaine for Full-Arch Implant Surgery. Journal. The Intl J Oral Maxillofac Implants. September 19, 2018 2018;33((5)):1155-64. https://www.ncbi.nlm.nih.gov/pubmed/30231106.
7. Lieblich SE, Danesi H. Liposomal Bupivacaine Use in Third Molar Impaction Surgery: INNOVATE Study. Anesthesia progress. Fall 2017;64(3):127-135. doi:10.2344/anpr-64-02-03 https://www.ncbi.nlm.nih.gov/pubmed/28858553.
8. Bultema K, Fowler S, Drum M, Reader A, Nusstein J, Beck M. Pain Reduction in Untreated Symptomatic Irreversible Pulpitis Using Liposomal Bupivacaine (Exparel): A Prospective, Randomized, Double-blind Trial. Journal of endodontics. Oct 18 2016;42(12):1707-1712. doi:10.1016/j.joen.2016.08.018 https://www.ncbi.nlm.nih.gov/pubmed/27769675.
9. Glenn B, Drum M, Reader A, Fowler S, Nusstein J, Beck M. Does Liposomal Bupivacaine (Exparel) Significantly Reduce Postoperative Pain/Numbness in Symptomatic Teeth with a Diagnosis of Necrosis? A Prospective, Randomized, Double-blind Trial. Journal of endodontics. 2016;42(9):1301-1306. doi:10.1016/j.joen.2016.05.018 https://www.ncbi.nlm.nih.gov/pubmed/27461787.

IMPORTANT SAFETY INFORMATION

Indication

EXPAREL® (bupivacaine liposome injectable suspension) is indicated to produce postsurgical local analgesia via infiltration in patients aged 6 years and older and regional analgesia in adults via an interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and an adductor canal block. Safety and efficacy have not been established in other nerve blocks.

Important Safety Information

- EXPAREL is contraindicated in obstetrical paracervical block anesthesia.
- Adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported in adults with an incidence greater than or equal to 10% following EXPAREL administration via nerve block were nausea, pyrexia, headache, and constipation.
- Adverse reactions with an incidence greater than or equal to 10% following EXPAREL administration via infiltration in pediatric patients six to less than 17 years of age were nausea, vomiting, constipation, hypotension, anemia, muscle twitching, vision blurred, pruritus, and tachycardia.
- Do not admix lidocaine or other non-bupivacaine local anesthetics with EXPAREL. EXPAREL may be administered at least 20 minutes or more following local administration of lidocaine.
- EXPAREL is not recommended to be used in the following patient populations: patients <6 years old for infiltration, patients younger than 18 years old for nerve blocks, and/or pregnant patients.
- Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease.

Warnings and Precautions Specific to EXPAREL

- Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL.
- EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks **other than interscalene brachial plexus nerve block, sciatic nerve block in the popliteal fossa, and adductor canal block,** or intravascular or intra-articular use.
- The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days, as seen in clinical trials.

Warnings and Precautions for Bupivacaine-Containing Products

- **Central Nervous System (CNS) Reactions:** There have been reports of adverse neurologic reactions with the use of local anesthetics. These include persistent anesthesia and paresthesia. CNS reactions are characterized by excitation and/or depression.
- **Cardiovascular System Reactions:** Toxic blood concentrations depress cardiac conductivity and excitability, which may lead to dysrhythmias, sometimes leading to death.
- **Allergic Reactions:** Allergic-type reactions (eg, anaphylaxis and angioedema) are rare and may occur as a result of hypersensitivity to the local anesthetic or to other formulation ingredients.
- **Chondrolysis:** There have been reports of chondrolysis (mostly in the shoulder joint) following intra-articular infusion of local anesthetics, which is an unapproved use.
- **Methemoglobinemia:** Cases of methemoglobinemia have been reported with local anesthetic use.

Please refer to full **Prescribing Information**.