Multimodal Pain Management – Do Good *versus* Do No Harm

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Conflicts of Interest

None

August Bier 1861-1946

XVI.

Aus der Königlichen chirurgischen Klinik zu Kiel.

Versuche über Cocainisirung des Rückenmarkes.

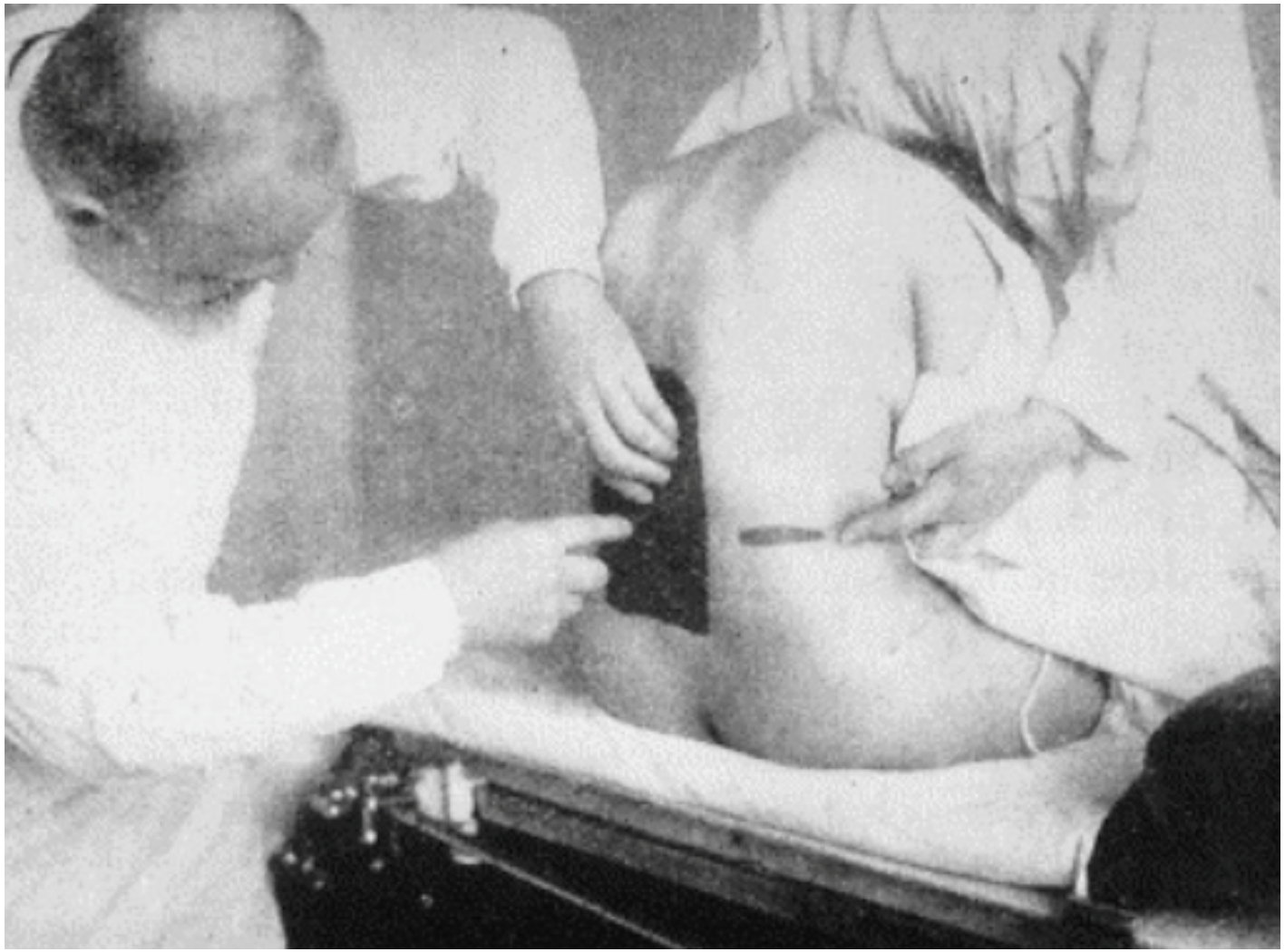
Von

Prof. Dr. August Bier.

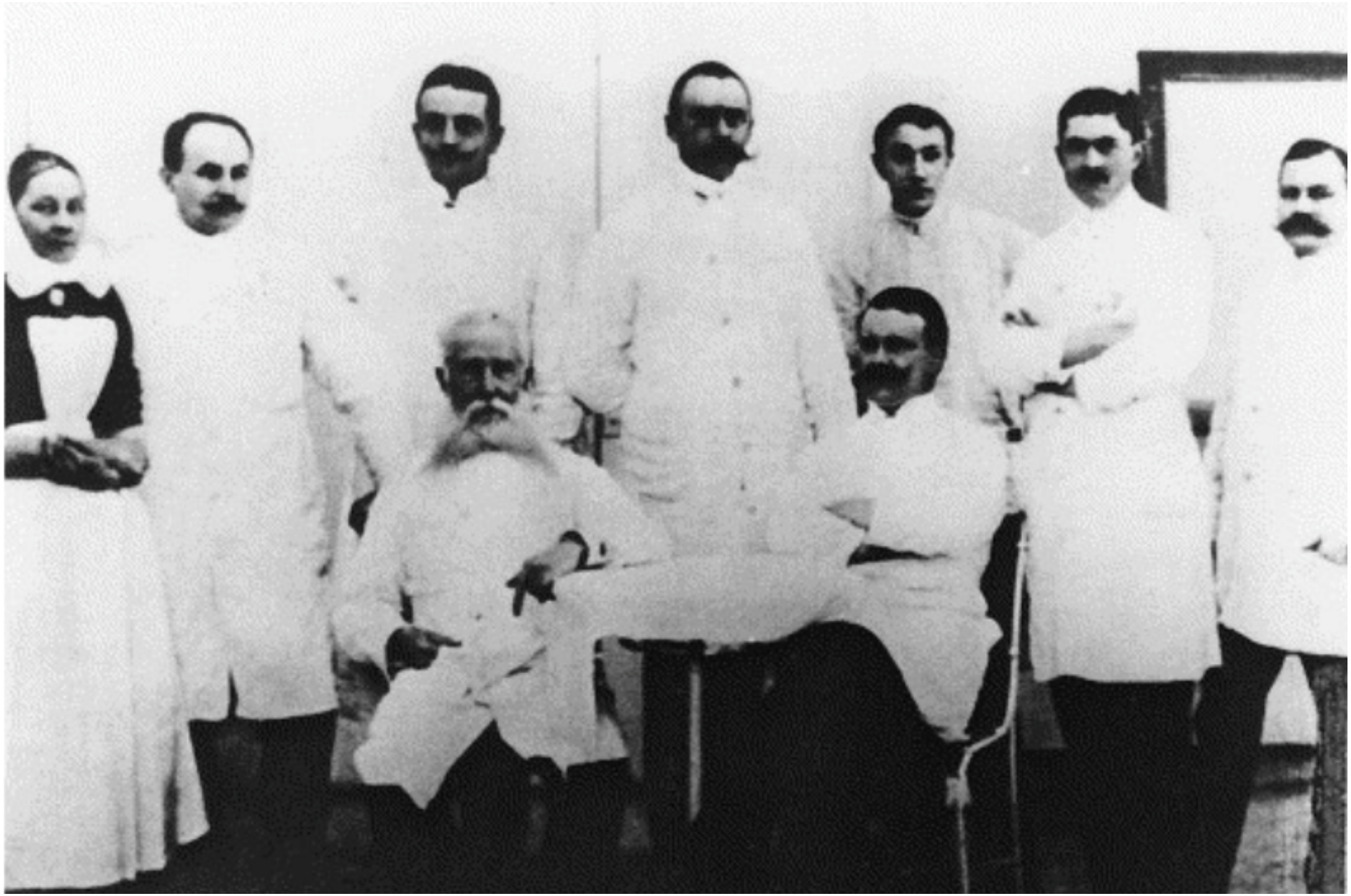
Die Schleich'sche Infiltrations- und die Oberst'sche regionäre Cocainanästhesie haben die gefährliche allgemeine Narkose in sehr wesentlicher und erfreulicher Weise beschränkt. Aber für „grosse" Operationen sind beide Verfahren doch nur im geringen Grade verwendbar. Ich habe den Versuch gemacht, durch Cocainisirung des Rückenmarkes grosse Strecken des Körpers unempfindlich gegen Schmerz zu machen. Dies wurde in folgender Weise ausgeführt:

Bei dem in Seitenlage befindlichen Kranken wird die Quincke'sche Lumbalpunktion in bekannter Weise vorgenommen. Die Hohlnadel wählt man sehr dünn. Nachdem sie in den Sack der Rückenmarkshäute eingedrungen ist, entfernt man den Stöpsel, welcher die Lichtung der Nadel verschliesst, und setzt sofort den Finger auf die Mündung, damit möglichst wenig Liquor cerebrospinalis ausfliesst. Mit einer Pravaz'schen Spritze, welche genau auf die Punktionsnadel passt, wird die gewünschte Menge Cocain eingespritzt. Dabei muss man natürlich bei der Länge der Nadel so viel Cocainlösung mehr nehmen, als die Lichtung derselben fasst. (Bei unserer Nadel 1½ Theilstriche der Pravaz'schen Spritze.) Damit das Cocain nicht aus dem Stichkanale der Rückenmarkshäute in die Gewebe sickert, lässt man die Nadel mit der daraufsitzenden Spritze 2 Minuten stecken und entfernt sie dann. Die Stichöffnung in der Haut wird mit Collodium verklebt.

Die Lumbalpunktion wird unter Schleich's Infiltrationsanästhesie schmerzlos ausgeführt. Zuerst wird die Haut, dann werden mit einer langen Nadel die übrigen Weichtheile bis auf die Wirbelsäule infiltrirt.



Bier A: Bemerkungen zur Cocanisierung des Rückenmarkes. Münchner Medizinische Wochenschrift 1900; 47:1226



Anaesthesia, surgery, and challenges in postoperative recovery

Henrik Kehlet, Jørgen B Dahl

Panel 1: **The process of postoperative recovery**

Preoperative period
Preoperative assessment
Preoperative optimisation

Perioperative period
Anaesthesia
Surgery
Organ dysfunction

Early postoperative period
Surgical stress response
Pain
Nausea, vomiting, ileus
Fluid management
Mobilisation
Nutrition
Fatigue and sleep disturbances

Late postoperative period
Pain
Fatigue and sleep disturbances
Convalescence

All stages can be improved by interventions from the anaesthetist (except surgery) and the surgeon (except anaesthesia).

Side Effects of
PAIN Management
PAIN Management

Lancet. 2003 Dec 6;362(9399):1921-8. doi: 10.1016/S0140-6736(03)14966-5.
Anaesthesia, surgery, and challenges in postoperative recovery
Henrik Kehlet, Jørgen B Dahl

ERAS experience at MSQC

"We applied a strict definition of ERP that included, at a minimum,
preoperative education
carbohydrate loading
multimodal analgesia
intravenous fluid limitation
early enteral nutrition and ambulation"

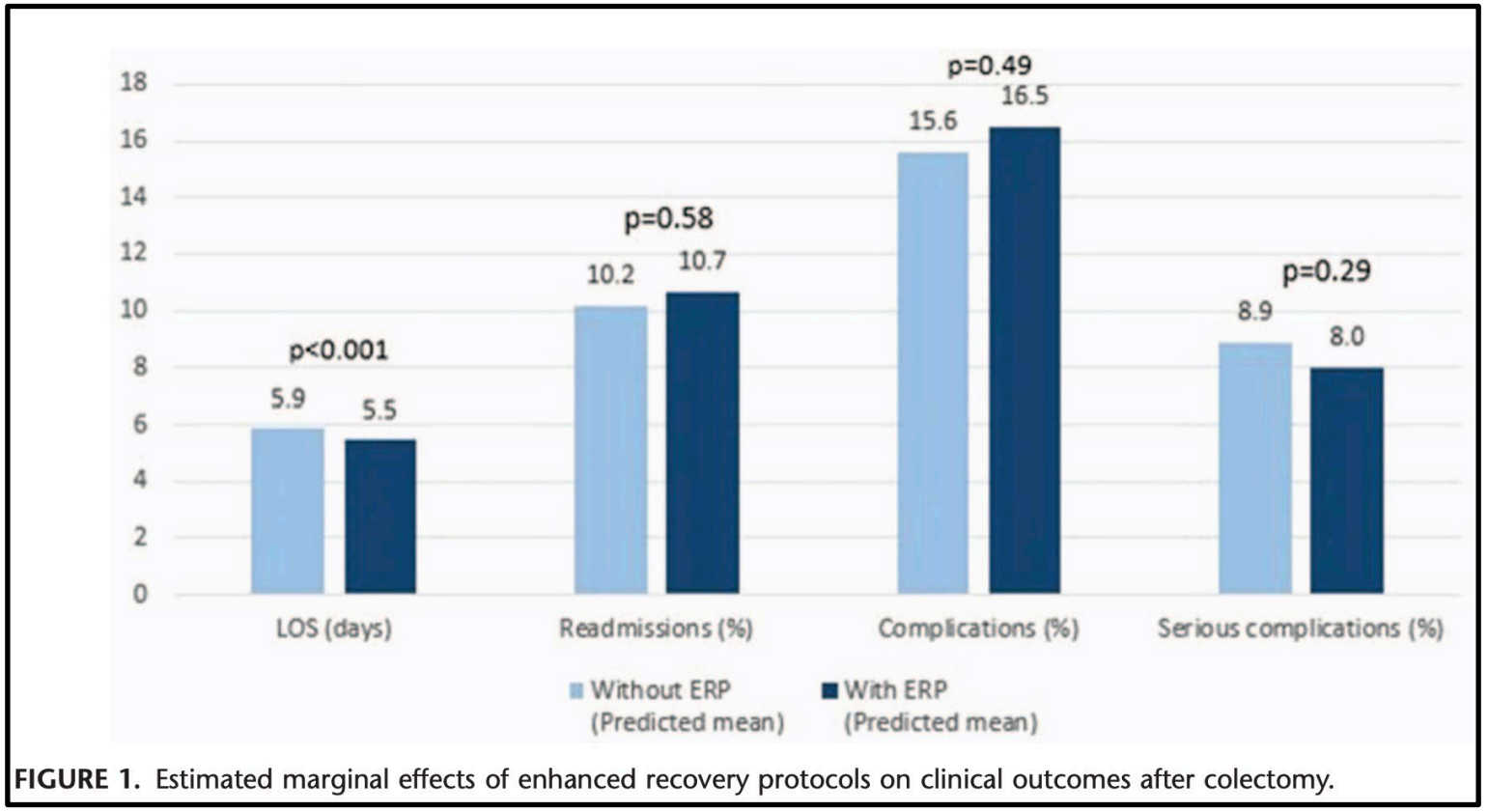


FIGURE 1. Estimated marginal effects of enhanced recovery protocols on clinical outcomes after colectomy.

Ann Surg. 2021 Aug 1;274(2):199-205. doi: 10.1097/SLA.0000000000004726. Clinical and Economic Outcomes of Enhanced Recovery Dissemination in Michigan Hospitals
Scott E Regenbogen, Anne H Cain-Nielsen, John D Syrjamaki, Edward C Norton

ERAS experience at MSQC

TABLE 3. Unadjusted Outcomes by Enhanced Recovery Protocol Adoption Status

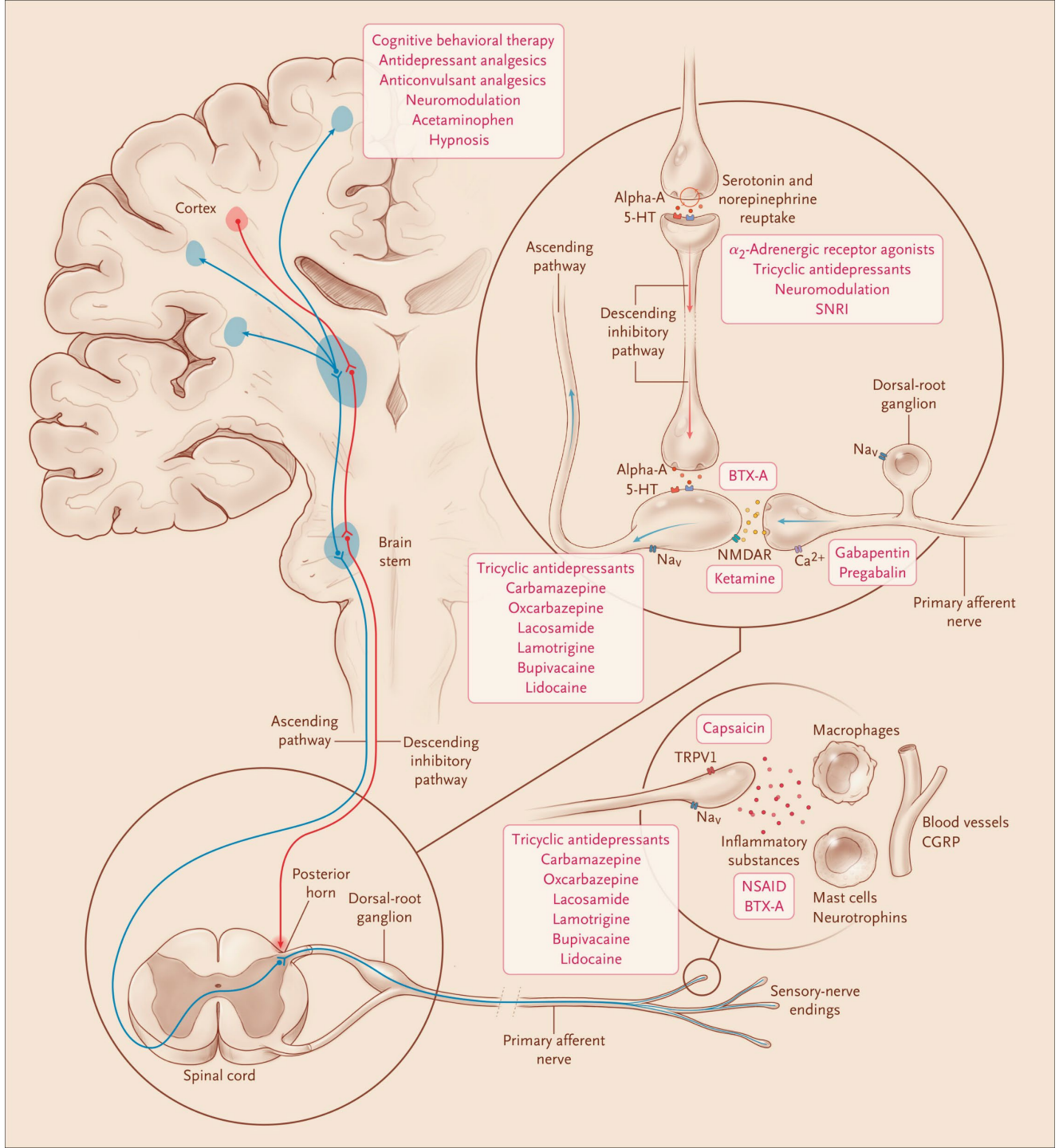
Clinical Registry (MSQC)	Never-ERP N = 6071	Pre-ERP N = 3633	Post-ERP N = 3907	*P* value
Length of stay, mean (standard deviation)	5.6 (4.2)	6.5 (5.1)	5.1 (4.3)	<0.001
Complications, N (%)	948 (15.6%)	615 (16.9%)	571 (14.6%)	<0.001
Serious complications, N (%)	543 (8.9%)	355 (9.8%)	281 (7.2%)	<0.001
Readmission within 30 d, N (%)	571 (9.5%)	402 (11.3%)	407 (10.4%)	0.02
Claims Registry (MVC)	**Never-ERP n = 5706**	**Pre-ERP n = 4037**	**Post-ERP n = 5057**	***P* value**
Total episode payment, mean (standard deviation)	$29,228 ($23,948)	$31,192 ($30,814)	$28,550 ($29,799)	<0.001
Index Payment, mean (standard deviation)	$18,142 ($12,324)	$19,472 ($21,872)	$17,872 ($20,315)	<0.001
Post-Acute Care Payment, mean (standard deviation)	$3907 ($7278)	$3,909 ($7173)	$3384 ($8612)	<0.001
Readmission Payment, mean (standard deviation)	$3156 ($11,054)	$3,208 ($9363)	$3150 ($11,208)	0.96

Ann Surg. 2021 Aug 1;274(2):199-205. doi: 10.1097/SLA.0000000000004726. Clinical and Economic Outcomes of Enhanced Recovery Dissemination in Michigan Hospitals
Scott E Regenbogen, Anne H Cain-Nielsen, John D Syrjamaki, Edward C Norton

Rationale for Multimodal Pain Management

“Combine different treatment modalities to, working at different pain mechanisms, in order to improve analgesia and reduce side effects”

Lancet. 2003 Dec 6;362(9399):1921-8. doi: 10.1016/S0140-6736(03)14966-5. Anaesthesia, surgery, and challenges in postoperative recovery. Henrik Kehlet, Jørgen B Dahl



Nonnarcotic Methods of Pain Management
Nanna B. Finnerup, M.D. N Engl J Med 2019;380:2440-2448

Special article

A multisociety organizational consensus process to define guiding principles for acute perioperative pain management

Reg Anesth Pain Med. 2022 Feb;47(2):118-127. doi: 10.1136/rapm-2021-103083.

Organization
1. American Hospital Association
2. American Medical Association
3. American College of Surgeons
4. American Academy of Orthopaedic Surgeons
5. American Academy of Otolaryngology-Head and Neck Surgery
6. American Association of Neurological Surgeons and the Congress of Neurological Surgeons
7. American College of Obstetricians and Gynecologists
8. American Association of Oral and Maxillofacial Surgeons
9. American Society of Breast Surgeons
10.American Society of Plastic Surgeons
11.American Society of Regional Anesthesia and Pain Medicine
12.American Urological Association
13.Society of Thoracic Surgeons
14.American Society of Anesthesiologists

Conduct a preoperative evaluation including assessment of medical and psychological conditions, concomitant medications, history of chronic pain, substance abuse disorder, and previous postoperative treatment regimens and responses, to guide the perioperative pain management plan

Use a validated pain assessment tool to track responses to postoperative pain treatments and adjust treatment plans accordingly

Offer multimodal analgesia, or the use of a variety of analgesic medications and techniques combined with nonpharmacological interventions, for the treatment of postoperative pain in adults

Provide patient and family-centered, individually tailored education to the patient (and/or responsible caregiver), including information on treatment options for managing postoperative pain, and document the plan and goals for postoperative pain management.

Provide education to all patients (adult) and primary caregivers on the pain treatment plan, including proper storage and disposal of opioids and tapering of analgesics after hospital discharge

Adjust the pain management plan based on adequacy of pain relief and presence of adverse events

Have access to consultation with a pain specialist for patients who have inadequately controlled postoperative pain or are at high risk of inadequately controlled postoperative pain at their facilities (e.g., long-term opioid therapy, history of substance use disorder)

Reg Anesth Pain Med. 2022 Feb;47(2):118-127. doi: 10.1136/rapm-2021-103083.

Multimodal Analgesia

MPOG
MULTICENTER PERIOPERATIVE OUTCOMES GROUP

Success Criteria

At least one non-opioid adjunct (medication, regional block, neuraxial block, or local injection) was administered to the patient during the measure time period.

Spinal Anesthesia

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 25, 2021 VOL. 385 NO. 22

Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults

M.D. Neuman, R. Feng, J.L. Carson, L.J. Gaskins, D. Dillane, D.I. Sessler, F. Sieber, J. Magaziner, E.R. Marcantonio, S. Mehta, D. Menio, S. Ayad, T. Stone, S. Papp, E.S. Schwenk, N. Elkassabany, M. Marshall, J.D. Jaffe, C. Luke, B. Sharma, S. Azim, R.A. Hymes, K.-J. Chin, R. Sheppard, B. Perlman, J. Sappenfield, E. Hauck, M.A. Hoeft, M. Giska, Y. Ranganath, T. Tedore, S. Choi, J. Li, M.K. Kwofie, A. Nader, R.D. Sanders, B.F.S. Allen, K. Vlassakov, S. Kates, L.A. Fleisher, J. Dattilo, A. Tierney, A.J. Stephens-Shields, and S.S. Ellenberg, for the REGAIN Investigators*

N=1,600

"Spinal anesthesia for hip-fracture surgery in older adults was not superior to general anesthesia with respect to survival and recovery of ambulation at 60 days. The incidence of postoperative delirium was similar with the two types of anesthesia."

ORIGINAL RESEARCH

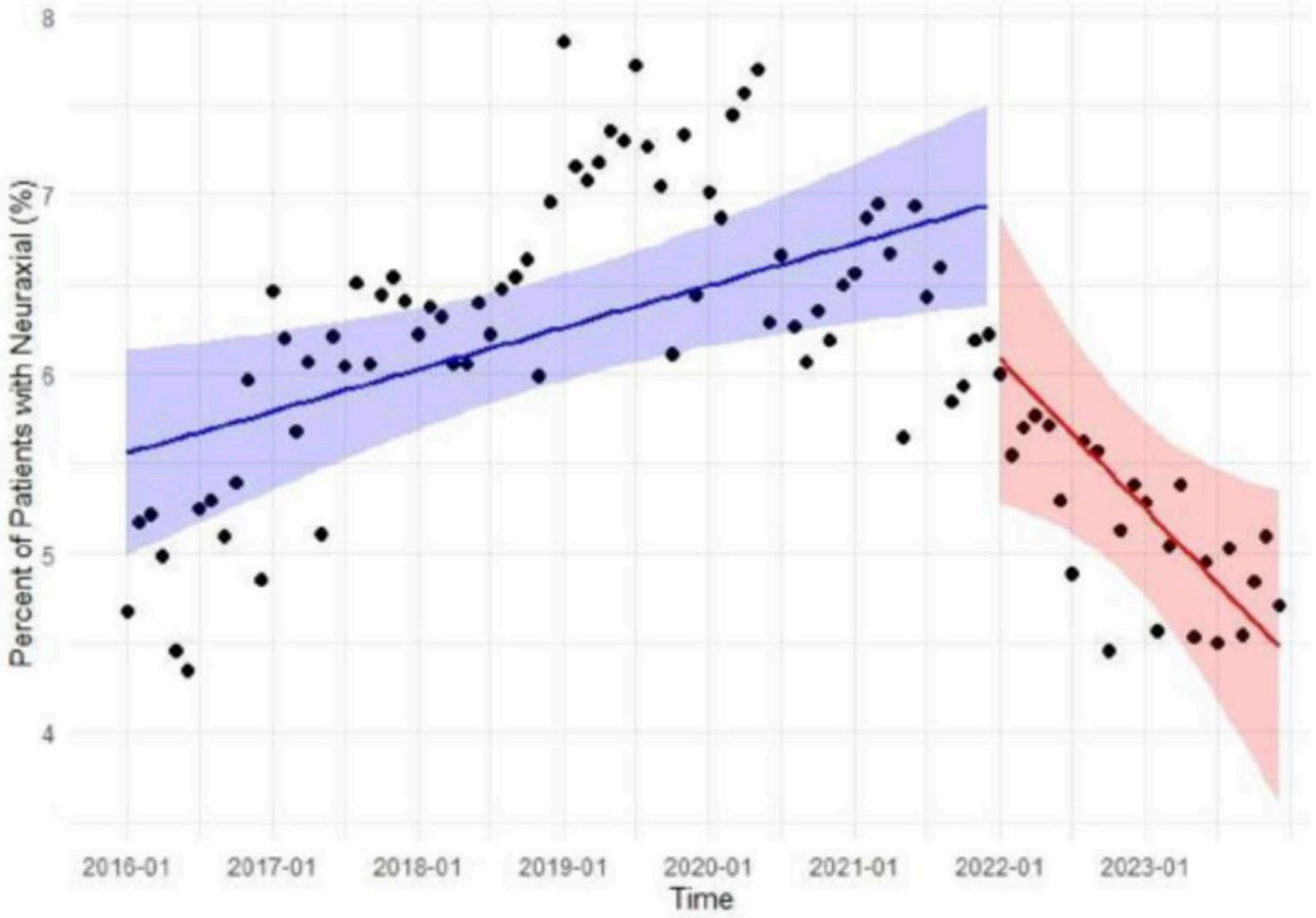
Annals of Internal Medicine

Pain, Analgesic Use, and Patient Satisfaction With Spinal Versus General Anesthesia for Hip Fracture Surgery

A Randomized Clinical Trial

Ann Intern Med. 2022;175:952-960. doi:10.7326/M22-0320

"Severe pain is common after hip fracture. **Spinal anesthesia was associated with more pain in the first 24 hours after surgery and more prescription analgesic use at 60 days compared with general anesthesia.**"



Did the REGAIN and RAGA trials impact use of neuraxial anesthesia among surgical hip fracture patients? -An observational study using US claims data
Jashvant Poeran, Periklis Giannakis, Junying Wang, Crispiana Cozowicz, Alexander Stone, Philipp Gerner, Jiabin Liu, and Stavros G Memtsoudis. RAPM

Multimodal Analgesia / Medications

MPOG
MULTICENTER PERIOPERATIVE OUTCOMES GROUP

OPIOID SPARING MEDICATION

10007 Acetaminophen
10222 Ibuprofen
10747 Naproxen
10116 Celecoxib
10765 Meloxicam
10239 Ketorolac
10132 Clonidine
10149 Dexmedetomidine
10238 Ketamine
10453 Propofol w/Ketamine 10 mg/ml + 1 mg/mL
10572 Propofol w/Ketamine 10 mg/ml + Unspecified Ketamine
10577 Propofol w/Ketamine 10 mg/ml + 0.5 mg/mL
10578 Propofol w/Ketamine 10 mg/ml + 1.5 mg/mL
10579 Propofol w/Ketamine 10 mg/ml + 2 mg/mL

Acetaminophen
NSAIDs
Alpha-2 agonists
Ketamine

Multimodal Analgesia / Medications

Variable Options:

Multimodal Pain Management ordered Preop/Intraop? Indicate whether there were at least two medications or pharmacologic strategies ordered within the designated timeframe.

1. **No:** Multimodal approach to pain management was not ordered.

2. **Yes:** Two or more non-opioid analgesic agents with different mechanisms of action were ordered

Multimodal Analgesia / Medications

1. **Non-steroidal anti-inflammatory drugs (NSAIDs)** (e.g., ibuprofen, ketorolac/
   [1], cyclooxygenase-2 inhibitors- Celebrex, meloxicam/Mobic)
2. **Acetaminophen PO** (do not select this option if the only acetaminophen admi
   a component of a combination medication also containing an opioid (e.g., Nor
   Percocet))
3. **Acetaminophen IV** (Ofirmev)
4. **Gabapentinoids** (Neurontin/gabapentin, Lyrica/pregabalin)
5. **Ketamine**
6. **Intravenous lidocaine** (infusion -normally administered at 1.5-3mg/kg/hr). Bo
   doses are not included as multimodal analgesia

11. **Decadron/dexamethasone**
12. **Precedex/dexmedetomidine**
13. **Clonidine**
14. **Cymbalta/duloxetine**
15. **Robaxin/methocarbamol**
16. **Other non-opioid analgesic** (not listed above). If selected enter the name of t
    opioid in the text box. Please contact msqc-info@med.umich.edu before sele
    option if a medication administered is not in this list. Do not include non- phar
    strategies in this category. See Note 2

Acetaminophen
NSAIDs
Alpha-2 agonists
Ketamine
Gabapentinoid
Lidocaine infusion
Dexamethasone
SNRI (duloxetine)
Methocarbamol

Acetaminophen FACTOR TRIAL

JAMA Network™

QUESTION What is the effect of postoperative administration of intravenous (IV) acetaminophen, which is hypothesized to reduce opioid consumption, on hypoxemia following abdominal surgery?

CONCLUSION This clinical trial found that IV acetaminophen did not significantly reduce the duration of postoperative hypoxemia over 48 hours following abdominal surgery.

POPULATION

294 Men
276 Women

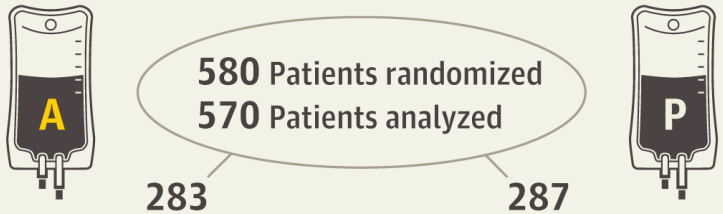
Adults undergoing elective abdominal surgery (open or laparoscopic)

Mean age: 49 years

LOCATIONS

2
Academic hospitals in the US

INTERVENTION



283

Acetaminophen
1 g of IV acetaminophen (paracetamol) every 6 hours

287

Placebo
IV saline placebo every 6 hours

PRIMARY OUTCOME

Duration of hypoxemia (Spo_2 <90%) measured over initial 48 postoperative hours

FINDINGS

Median minutes of hypoxemia per hour

Acetaminophen	Placebo
0.7 minutes (IQR, 0.1 to 5.1)	1.1 minutes (IQR, 0.1 to 6.6)

The between-group difference was not significant:
median, **-0.04** (IQR, -0.18 to 0.11) minutes of hypoxemia per hour (P = .29)

Turan A, Essber H, Saasouh W, et al; for the FACTOR Study Group. Effect of intravenous acetaminophen on postoperative hypoxemia after abdominal surgery: the FACTOR randomized clinical trial. *JAMA*. Published July 28, 2020. doi:10.1001/jama.2020.10009

Acetaminophen FACTOR TRIAL

Table 3. Effect of Acetaminophen on Secondary Outcomes

Secondary outcomes	Intravenous acetaminophen (n = 283)	Placebo (n = 287)	Treatment effect, acetaminophen vs placebo (99.4% CI)[a]	*P* value
Time-weighted pain score during initial 48 postoperative hours, mean (SD)[b,c]	4.2 (1.8) [n = 276]	4.4 (1.8) [n = 282]	−0.28 (−0.71 to 0.15)	.17
Time-weighted pain score in postanesthesia care unit, mean (SD)[b,c]	4.3 (1.7) [n = 281]	4.4 (1.8) [n = 281]		
Fatigue score on morning of postoperative day 1, mean (SD)[b,d]	5.0 (2.6) [n = 271]			
Lowest RASS score during initial 48 postoperative hours, mean (SD)[b,e]			0.29 to 0.13)	.30
Opioid consumption during initial 48 postoperative ho… morphine equivalents, median (IQR), mg[f]			0.86 (0.61 to 1.21)	.22
Time spend in sitting… hours, me…	(0.8-4.1) [n = 252]	2.2 (0.9-4.2) [n = 248]	0.94 (0.63 to 1.39)	.65
Total moni… (IQR), h	28 (19-39) [n = 252]	28 (21-38) [n = 248]		
Nausea and … initial 48 postoperative hours, No./total (%)[g]	140/280 (50)	124/280 (44)	1.13 (0.88 to 1.45)	.18
Low respiratory function event during initial 48 postoperative hours, No./total (%)[g,h]	52/188 (28)	50/163 (31)	0.90 (0.57 to 1.43)	.53
Total respiratory function monitoring time, median (IQR), h	45 (44-47) [n = 188]	47 (46-47) [n = 163]		
Total anesthetic dose from induction to extubation, median (IQR)[i]	2.9 (2.6-3.0) [n = 282]	2.9 (2.7-3.0) [n = 287]	0.0 (−0.39 to 0.36)	.99

All secondary outcomes – no difference

Acetaminophen – IV vs PO

Impact of Intravenous Acetaminophen on Perioperative Opioid Utilization and Outcomes in Open Colectomies

A Claims Database Analysis

Isaac Wasserman, M.P.H., Jashvant Poeran, M.D., Ph.D., Nicole Zubizarreta, M.P.H., Jason Babby, Pharm.D., B.C.P.S., Stelian Serban, M.D., Andrew T. Goldberg, M.D., Alexander J. Greenstein, M.D., Stavros G. Memtsoudis, M.D., Ph.D., Madhu Mazumdar, Ph.D., Andrew B. Leibowitz, M.D.

"Our data from 181,640 patients undergoing open colectomies revealed that IV acetaminophen was used in a minority (25.1%) of patients, of which nearly half (48.0%, n = 21,878) received only 1 dose on the day of surgery.

In addition, IV acetaminophen use was not associated with clinically significant reductions in opioid utilization, prespecified as a minimum reduction of 25%.

However, IV acetaminophen did coincide with reductions in length and cost of hospitalization along with some reduction in opioid-related adverse effects. **Crucially, oral acetaminophen demonstrated more pronounced reductions in opioid utilization than IV acetaminophen in those using more than 1 dose of acetaminophen on postoperative day 1. Oral acetaminophen was associated with a 22.6% decrease while IV acetaminophen only demonstrated a 12.4% decrease."**

Anesthesiology, 2018 Jul;129(1):77-88.

Of the non-opioid analgesics, acetaminophen has the most favorable side effect profile.

If you want to save $, limit IV acetaminophen to patients who are unable to take PO.

NSAIDs

72 studies compared ibuprofen and placebo (9,186 participants). Studies were predominantly of high reporting quality.

For at least 50% pain relief compared with placebo the NNT for ibuprofen 200 mg (2690 participants) was 2.7 (2.5 to 3.0)

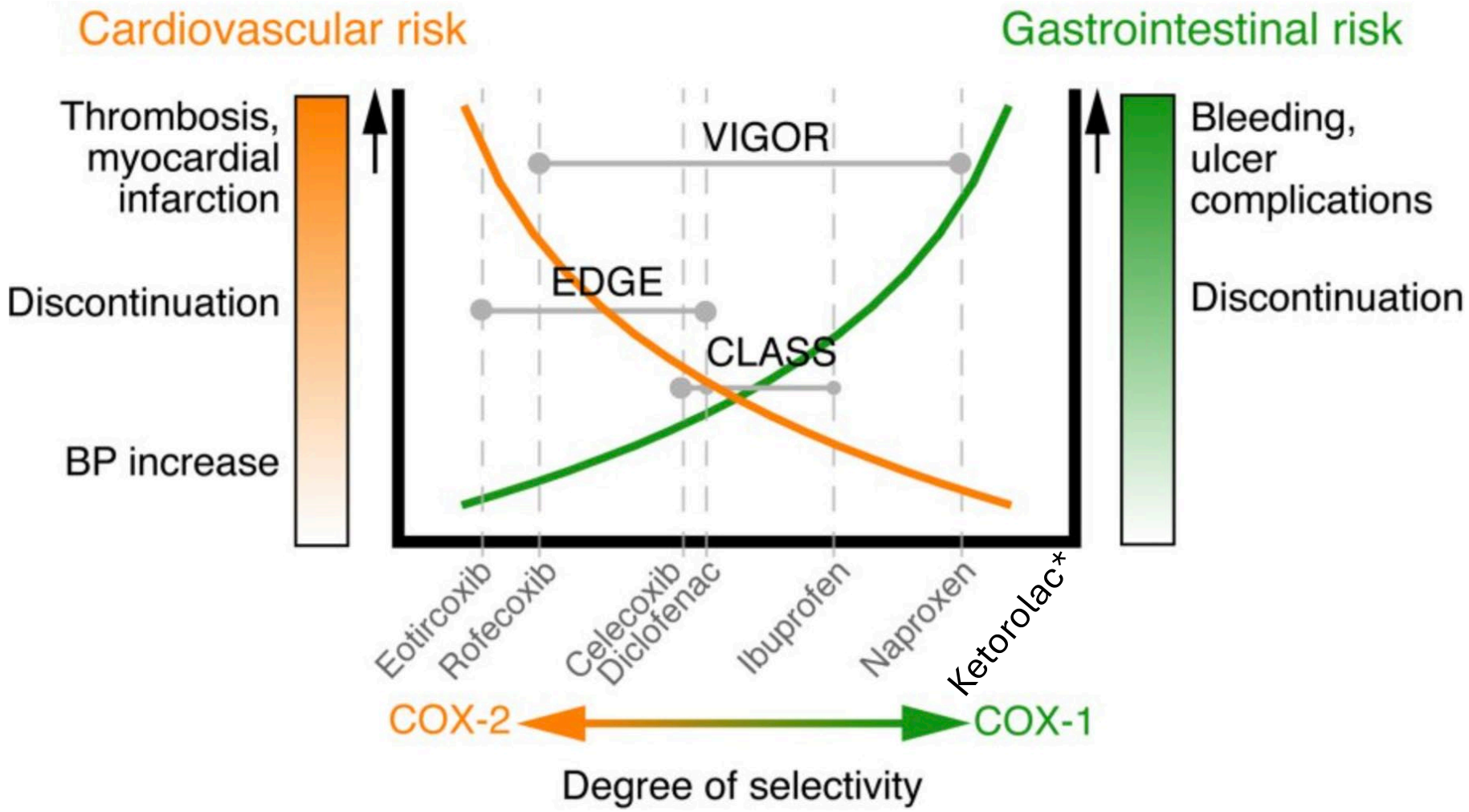
Cochrane Database of Systematic reviews | Review - Intervention

Full access

Single dose oral ibuprofen for acute postoperative pain in adults

Christopher J Derry, Sheena Derry, R Andrew Moore, Henry J McQuay Authors' declarations of interest

Version published: 08 July 2009 Version history



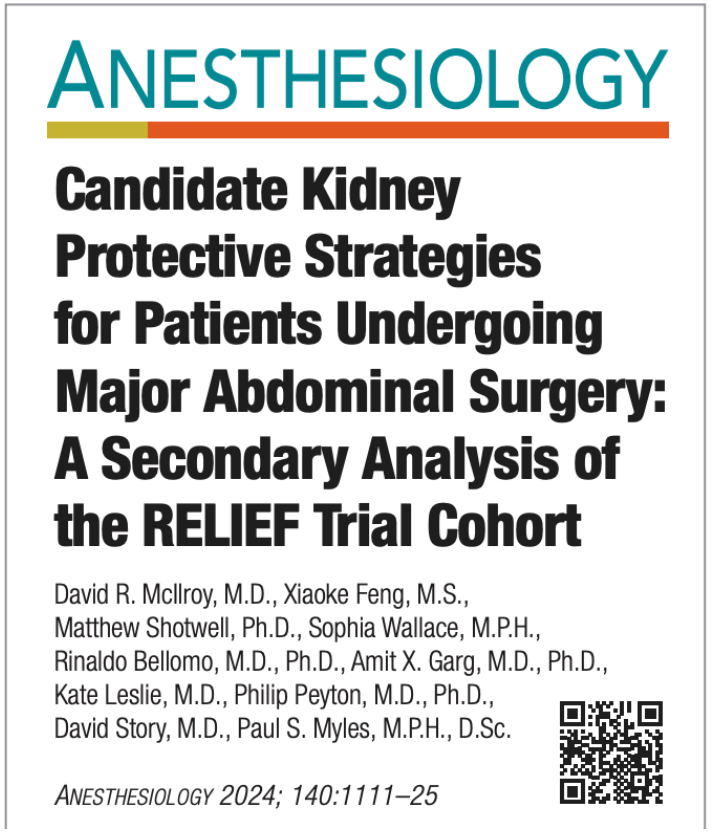
*Adapted. From: J Clin Invest. 2006 Jan;116(1):4-15. doi: 10.1172/JCI27291. Biological basis for the cardiovascular consequences of COX-2 inhibition: therapeutic challenges and opportunities. Tilo Grosser, Susanne Fries, Garret A FitzGerald

NSAIDs

Of 2,444 patients analyzed, stage 1, 2, and 3 AKI occurred in 9.1%, 2.4%, and 1.5% patients, respectively.

In multivariable modeling, administration of a nonsteroidal anti-inflammatory drug or cyclooxygenase-2 inhibitor, intraoperatively only (odds ratio, 1.77 [99% CI, 1.11 to 2.82]) was associated with increased odds for greater maximum stage AKI

Preoperative day-of-surgery administration of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker compared to no regular use (odds ratio, 1.84 [99% CI, 1.15 to 2.94]) was associated with increased odds for greater maximum stage AKI.

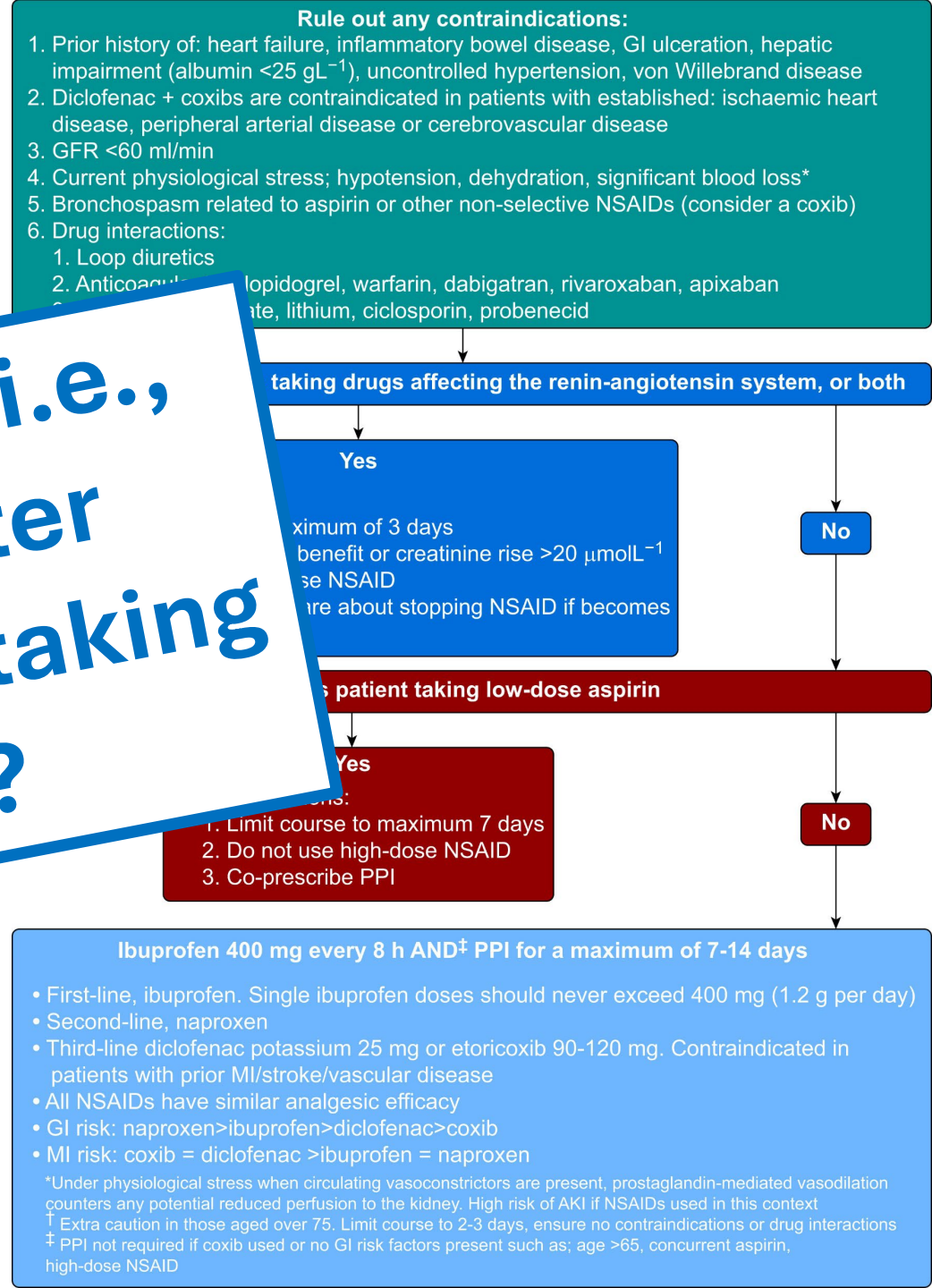


NNT to reduce acute pain by 50%

Vs.

N

Should we pre-emptively, i.e., intraoperatively, administer NSAIDs, to frail patients taking and ACE-I and a diuretic?

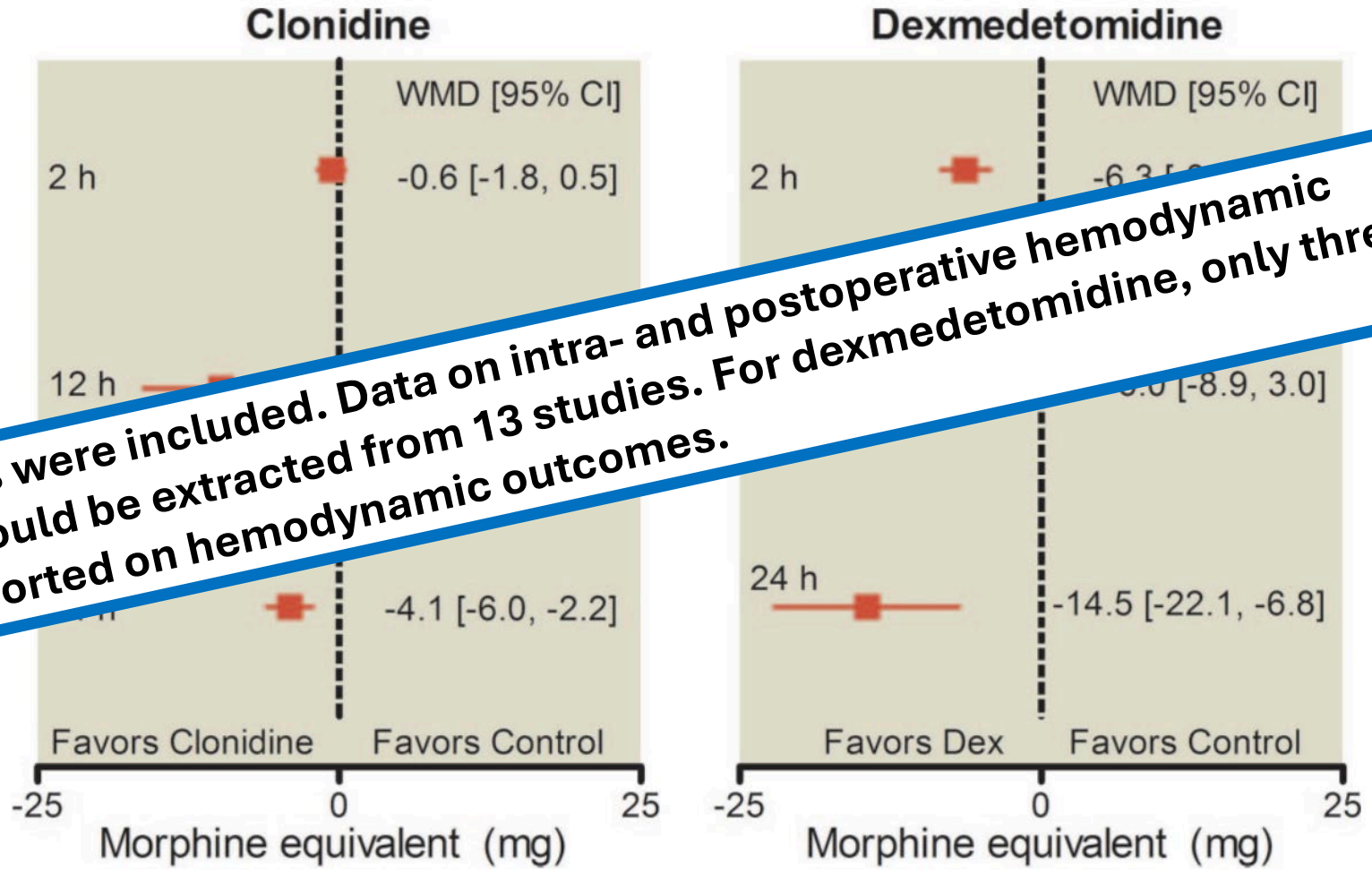


BJA Educ. 2023 Sep 9;23(11):440–447. doi: 10.1016/j.bjae.2023.08.001
Non-steroidal anti-inflammatory drugs in the perioperative period
EJ Halvey, N Haslam, ER Mariano

NSAIDs have high clinical efficacy.

Side effects can be significant, and administration needs to account for procedure- and patient-specific risks.

Alpha-2 agonists

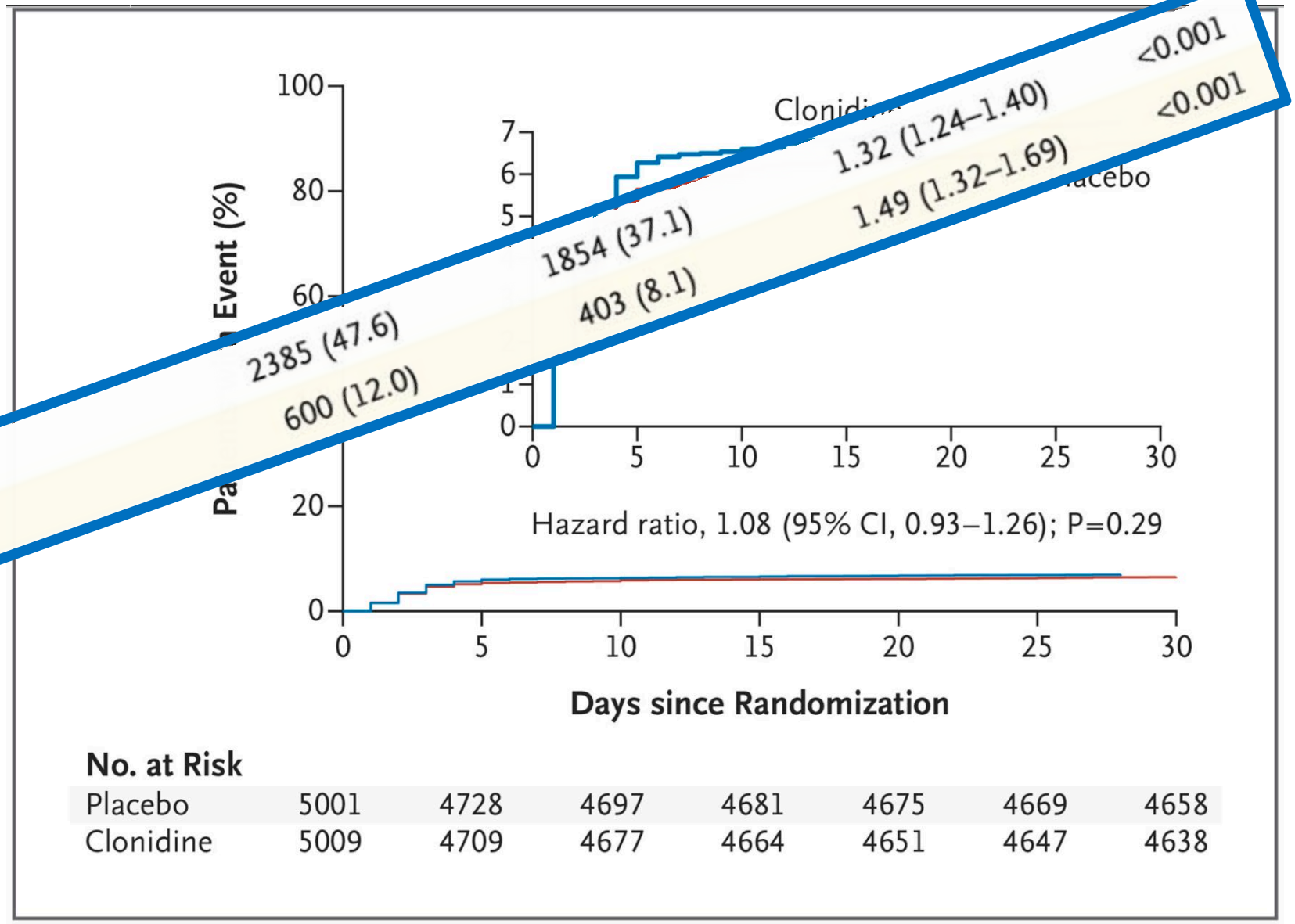


30 studies were included. Data on intra- and postoperative hemodynamic effects could be extracted from 13 studies. For dexmedetomidine, only three trials reported on hemodynamic outcomes.

Anesthesiology. 2012 Jun;116(6):1312-22. Effect of perioperative systemic α2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. Grégoire Blaudszun, Christopher Lysakowski, Nadia Elia, Martin R Tramèr

Clonidine

At 2 to 4 hours before surgery, patients who met the hemodynamic criteria (i.e., systolic blood pressure ≥105 mm Hg and heart rate ≥55 beats per minute) received 0.2 mg of oral clonidine or placebo and had a transdermal clonidine patch (whi releases 0.2 has placebo to their upper a chest; the patch remained there until 72 hours after surgery.



Clinically important hypotension	2385 (47.6)	1854 (37.1)	1.32 (1.24–1.40)	<0.001
Clinically important bradycardia	600 (12.0)	403 (8.1)	1.49 (1.32–1.69)	<0.001

N Engl J Med 2014;370:1504-1513. POISE-2 Trial. Clonidine in Patients Undergoing Noncardiac Surgery.

Regional Anesthesia and Acute Pain Medicine

Section Editor: **Richard Brull**

Clonidine Does Not Reduce Pain or Opioid Consumption After Noncardiac Surgery

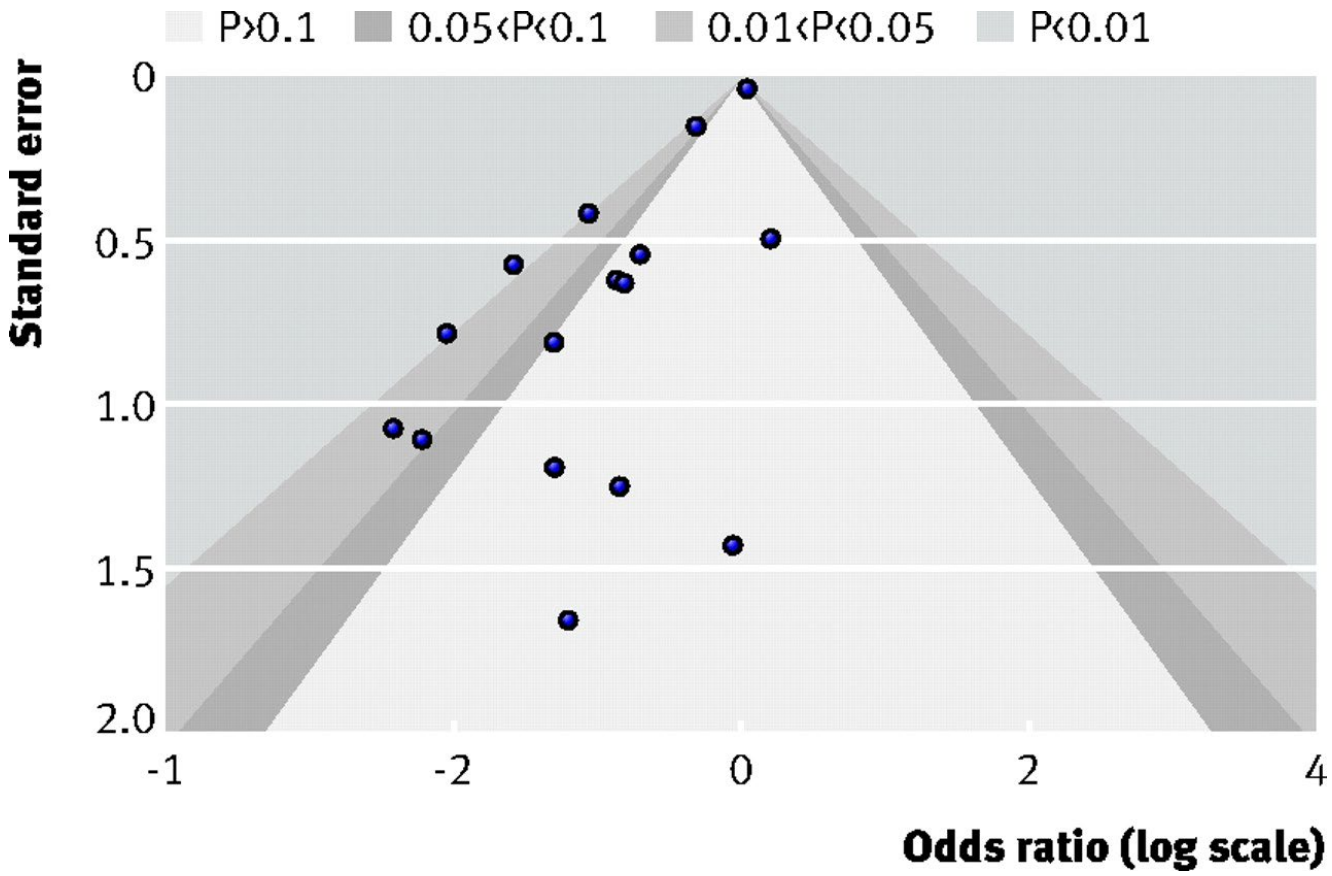
Opioid consumption was 63 (30, 154) mg morphine equivalents in the clonidine group, which was similar to 60 (30, 128) mg morphine equivalents in the placebo group.

Mean pain scores per patient were 3.6 ± 1.8 for clonidine patients and 3.6 ± 1.8 for placebo patients.

Clonidine does not reduce opioid consumption or pain scores in patients recovering from noncardiac surgery.

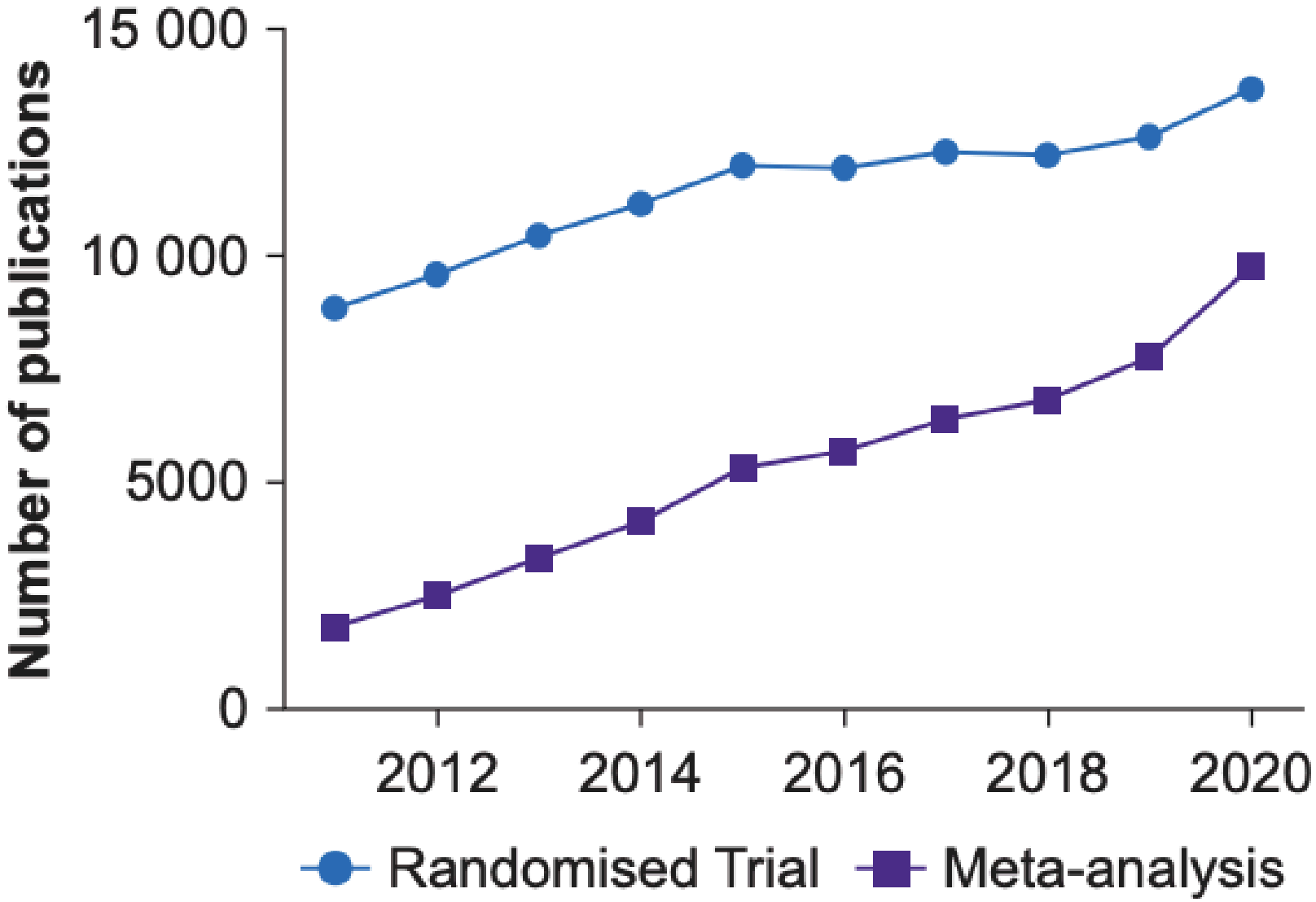
Anesth Analg. 2016 Sep;123(3):749-57.

On Meta-analyses



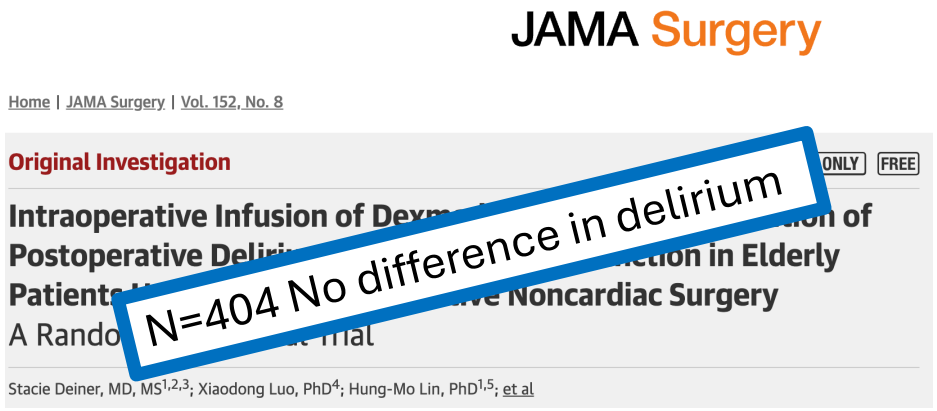
Contour enhanced funnel plot for trials of the effect of intravenous magnesium on mortality after myocardial infarction

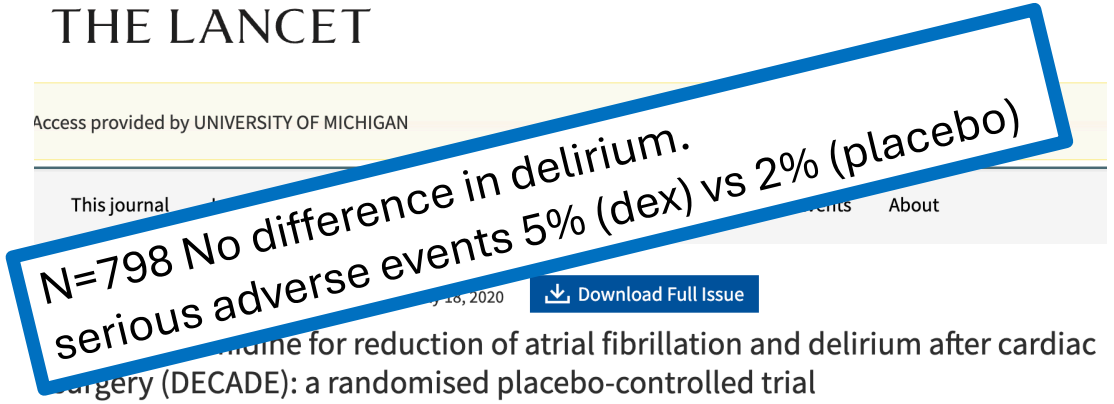
Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011;343:d4002

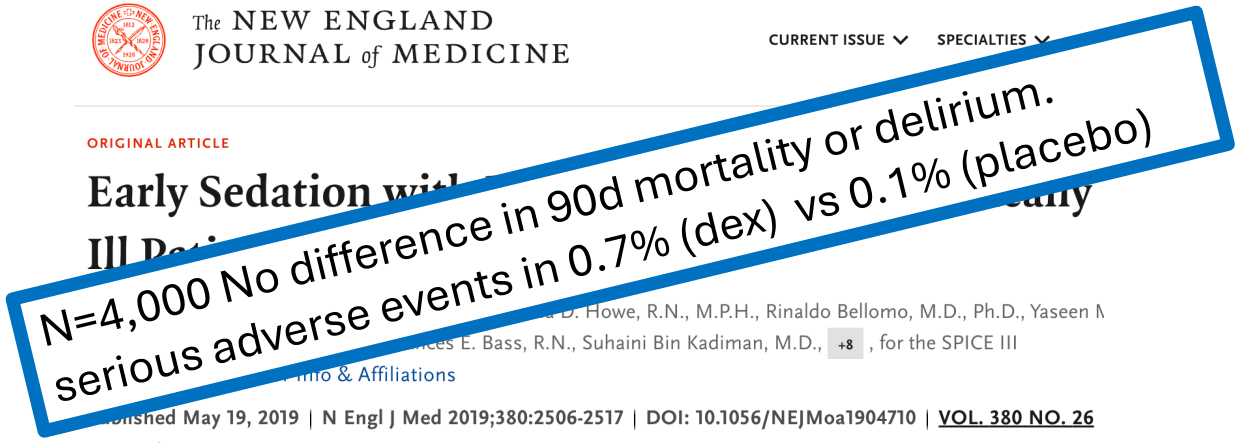


British Journal of Anaesthesia, 128 (2): 233e235 (2022). Meta-analyses of clinical trials: are we getting lemonade from lemons? Karsten Bartels and Daniel I. Sessler

Dexmedetomidine







Dexmedetomidine reduces opioid requirements.

Choosing dexmedetomidine as an analgesic adjunct should be informed by patient- and procedure-specific risks for its common side effects (bradycardia and hypotension).

Ketamine

Cochrane Database Syst Rev. 2018 Dec 20;2018(12):CD012033. doi: 10.1002/14651858.CD012033.pub4

Perioperative intravenous ketamine for acute postoperative pain in adults

130 studies with 8,341 participants. Ketamine was given to 4588 participants, and 3753 participants served as controls

Perioperative intravenous ketamine reduced postoperative opioid consumption over 24 hours by 8 mg morphine equivalents

Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial

*Michael S Avidan, Hannah R Maybrier, Arbi Ben Abdallah, Eric Jacobsohn, Phillip E Vlisides, Kane O Pryor, Robert A Veselis, Hilary P Grocott, Daniel A Emmert, Emma M Rogers, Robert J Downey, Heidi Yulico, Gyu-Jeong Noh, Yonghun H Lee, Christine M Waszynski, Virendra K Arya, Paul S Pagel, Judith A Hudetz, Maxwell R Muench, Bradley A Fritz, Witold Waberski, Sharon K Inouye, George A Mashour, on behalf of the PODCAST Research Group**

672 were randomly assigned, with 222 in the placebo group, 227 in the 0·5 mg/kg ketamine group, and 223 in the 1·0 mg/kg ketamine group.

There was no difference in delirium incidence between patients in the combined ketamine groups and the placebo group (19·45% vs 19·82%).

With increasing ketamine dose, more patients reported hallucinations 18% in the placebo group, 20% in the 0·5 mg/kg ketamine group, and 28% in the 1·0 mg/kg ketamine group and nightmares 8%, 12%, and 15%, respectively over 3 postoperative days

Lancet 2017; 390: 267–75

Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial

*Michael S Avidan, Hannah R Maybrier, Arbi Ben Abdallah, Eric Jacobsohn, Phillip E Vlisides, Kane O Pryor, Robert A Veselis, Hilary P Grocott, Daniel A Emmert, Emma M Rogers, Robert J Downey, Heidi Yulico, Gyu-Jeong Noh, Yonghun H Lee, Christine M Waszynski, Virendra K Arya, Paul S Pagel, Judith A Hudetz, Maxwell R Muench, Bradley A Fritz, Witold Waberski, Sharon K Inouye, George A Mashour, on behalf of the PODCAST Research Group**

	All groups (n=672)	Placebo (n=222)	0·5 mg/kg ketamine (n=227)	1·0 mg/kg ketamine (n=223)
Morphine equivalents POD0 (n=598)	18 (8–48)	17 (8–49)	17 (8–50)	18 (8–42)
Morphine equivalents POD1 (n=605)	32 (17–68)	33 (17–78)	32 (18–63)	30 (16–59)
Morphine equivalents POD2 (n=559)	24 (12–48)	25 (12–52)	24 (12–44)	22 (12–49)
Morphine equivalents POD3 (n=450)	19 (8–40)	22 (10–42)	17 (8–39)	16 (8–38)

Lancet 2017; 390: 267–75

Ketamine’s clinical efficacy as an intraoperative analgesic adjunct is modest.

Choosing ketamine as an analgesic adjunct should be informed by patient-specific risks for its common side effects (hallucinations, nightmares, tachycardia)

MPOG
MULTICENTER PERIOPERATIVE OUTCOMES GROUP

Acetaminophen
NSAIDs
Alpha-2 agonists
Ketaminez

MSQC
MICHIGAN SURGICAL QUALITY COLLABORATIVE

Acetaminophen
NSAIDs
Alpha-2 agonists
Ketamine
Dexamethasone
Lidocaine infusion
SNRI (duloxetine)
Methocarbamol
Gabapentinoid

Dexamethasone

Perioperative Single Dose Systemic Dexamethasone for Postoperative Pain

A Meta-analysis of Randomized Controlled Trials

Gildàsio S. De Oliveira, Jr., M.D.,* Marcela D. Almeida, M.D.,† Honorio T. Benzon, M.D.,‡ Robert J. McCarthy, Pharm.D.§

24 randomized clinical trials with 2,751 subjects were included.

Pain reduction:
Dexamethasone over placebo for pain at rest on 11-point VAS: ≤ 4 h, **-0.32** , 24 h, **-0.49**

Opioid consumption (IV MME):
-0.82 for dexamethasone intermediate dose 0.11–0.2 mg/kg
-0.85 for dexamethasone high-dose (more than 0.2 mg/kg)

Anesthesiology. 2011 Sep;115(3):575-88.

British Journal of Anaesthesia **110** (2): 191–200 (2013)
Advance Access publication 5 December 2012 · doi:10.1093/bja/aes431

BJA

Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis

N. H. Waldron, C. A. Jones, T. J. Gan, T. K. Allen and A. S. Habib*

45 studies involving 5,796 patients receiving dexamethasone 1.25–20 mg were included.

Patients receiving dexamethasone had lower pain scores at 2 h: **-0.49,** and 24 h **-0.83**

Dexamethasone-treated patients used less opioids at 2 h: **-0.87 mg morphine equivalents** and 24 h **-2.33 mg morphine equivalents**

Adverse Effects: No increase in infection or delayed wound healing with dexamethasone, but blood glucose levels were higher at 24 h: 0.39 mmol litre **7.02 mg/dL**

Dexamethasone has low
favorable side eff
art of
P
My suggestion: Since it is used primarily for PONV, may remove

IV Lidocaine compared to placebo or no treatment

The review included 68 trials (4525 randomized participants)

”We are **uncertain** whether IV lidocaine improves postoperative pain compared to placebo t at early time points (very low-quality evidence) after surgery.”

“We **ruled out** a clinically relevant reduction in pain with lidocaine at intermediate and at late time points.”

“We are **uncertain** whether lidocaine reduces
the risk of ileus
time to first bowel movement
risk of postoperative nausea
opioid consumption”

“The effect of IV lidocaine on adverse effects compared to placebo treatment is uncertain, as **only a small number of studies systematically analysed the occurrence of adverse effects (very low-quality evidence).**”

Cochrane Database Syst Rev. 2018 Jun 4;6(6):CD009642. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults

IV lidocaine has questionable or no efficacy fo
acute post-operative pain and lacks hi
RCT evidence.

Lidocai narrow therapeutic index.
P us adverse events include seizures,
dy hythmias, hypotension, and cardiac arrest.

My suggestion: Remove

BJA

British Journal of Anaesthesia, 128 (1): 118–134 (2022)

doi: 10.1016/j.bja.2021.08.032
Advance Access Publication Date: 29 October 2021
Review Article

SNRIs (duloxetine)

Selective serotonin reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors as adjuncts for postoperative pain management: systematic review and meta-analysis of randomised controlled trials

Li Wang[1,2,3,*], Joshua Tobe[1], Emily Au[4], Cody Tran[4], Jane Jomy[3,5], Yvgeniy Oparin[1], Rachel J. Couban[2] and James Paul[1]

- 24 RCTs with 2197 surgical patients (21 trials for SNRIs and three trials for SSRIs).
- Moderate-quality evidence
- Reduced postoperative pain (VAS) within 24 h: **-0.68**
- Opioid consumption within 24 h: **-12 mg**

SNRI concerns

- Duloxetine reaches steady-state plasma concentrations only within 3 days of dosing.

- SNRI discontinuation symptoms typically begin 2-4 days after the last dose and can last from a few weeks to several months:

"Discontinuation of antidepressants was associated with increased odds of dizziness (OR 5.52), nausea (OR 3.16), vertigo (OR 6.40), and nervousness (OR 3.15) compared to placebo discontinuation."

JAMA Psychiatry 2025;82;(9):896-904. doi:10.1001/jamapsychiatry.2025.1362

SNRIs have modest efficacy for acute post
operative pain and lack high-quali e.

The pha nd pharmacodynamic
p s do not lend themselves to
pe erative care.

My suggestion: Remove

Methocarbamol

From the FDA drug label:

“Methocarbamol is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute, painful musculoskeletal conditions.

The mode of action of methocarbamol has not been clearly identified, but may be related to its sedative properties. Methocarbamol does not directly relax tense skeletal muscles in man.”

And

“Since methocarbamol may possess a general CNS depressant effect, patients receiving methocarbamol tablets should be cautioned about combined effects with alcohol and other CNS depressants.”

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=de2e3af9-03ab-4dc8-b480-6866474ad1bd

Original research

Intravenous methocarbamol for acute pain after spine surgery: a target trial emulati

Paul Potnuru , Adriana Ba

p 8.rapm-2025-107010.

1,270 patients. Methocarbamol **not associated with significant reductions in postoperative pain scores.**

ORIGINAL ARTICLE

Associatio

Requirements

Cohort Study

matsu, MD, MS,* Michael D. Singleton, PhD,† Jiang Wu, MD,‡
Emily M. Dinges, MD,‡ and Laurent A. Bollag, MD‡

9,089 patients undergoing musculoskeletal surgery found that postoperative methocarbamol was associated with **significantly higher pain scores** and **higher opioid requirements**

Clin J Pain2023;39:452–457

Methocarbamol has no proven efficacy for post-operative pain.

Meth… …ects are likely from CNS de… …, a special concern for older patients.

My suggestion: Remove

Gabapentin - FDA package insert

----------DOSAGE AND ADMINISTRATION----------

- Postherpetic Neuralgia (2.1)
  - Dose can be titrated up as needed to a dose of 1800 mg/day
  - Day 1: Single 300 mg dose
  - Day 2: 600 mg/day (i.e., 300 mg two times a day)
  - Day 3: 900 mg/day (i.e., 300 mg three times a day)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence ≥8% and at least twice that for placebo) were:

- Postherpetic neuralgia: Dizziness, somnolence, and peripheral edema (6.1)

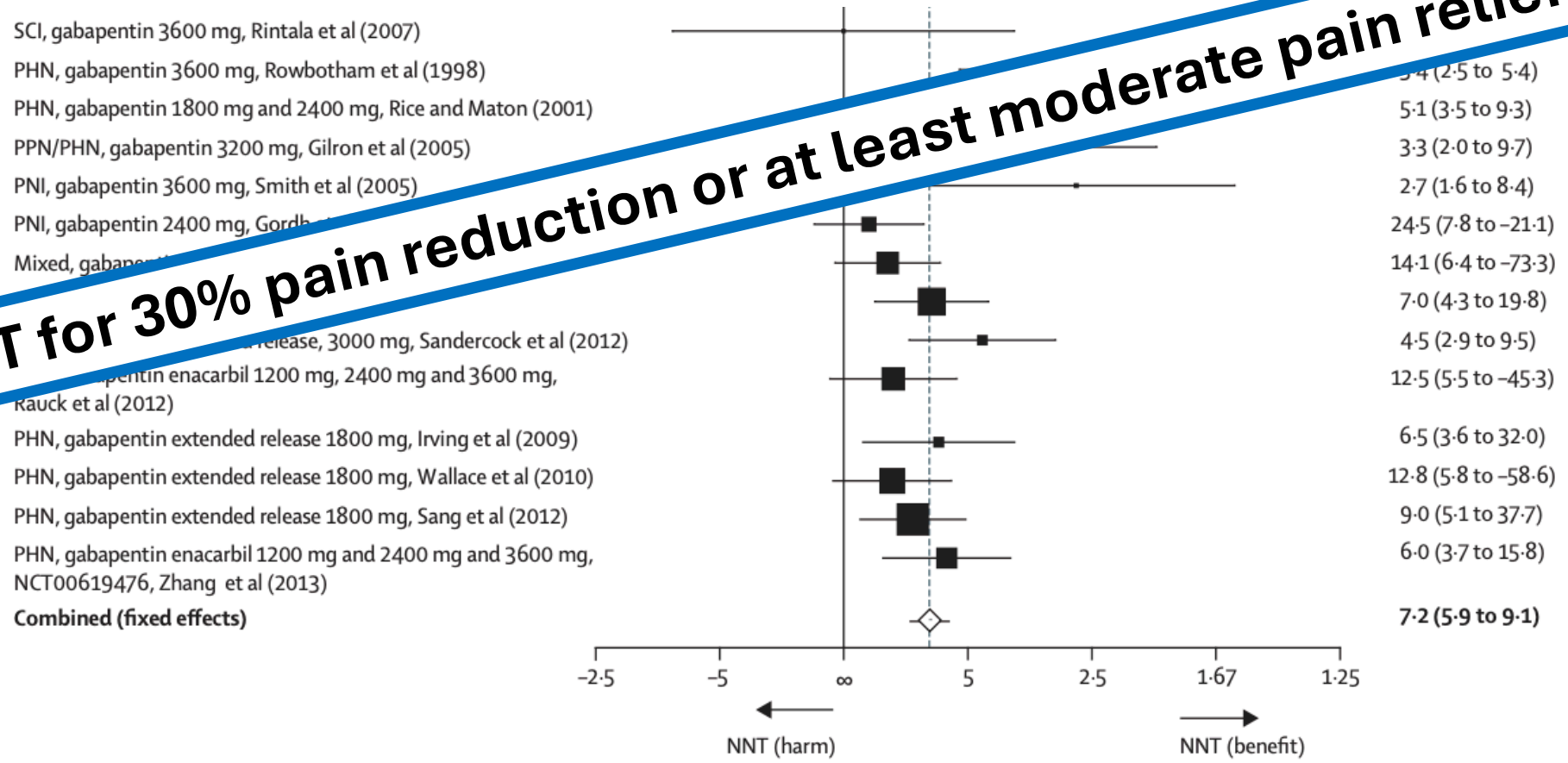
----------WARNINGS AND PRECAUTIONS----------

- Drug Reaction with Eosinophilia and Systemic Symptoms (Multiorgan hypersensitivity): Discontinue if alternative etiology is not established (5.1)
- Anaphylaxis and Angioedema: Discontinue and evaluate patient immediately (5.2)
- Driving Impairment; Somnolence/Sedation and Dizziness: Warn patients not to drive until they have gained sufficient experience to assess whether their ability to drive or operate heavy machinery will be impaired (5.3, 5.4)
- Increased seizure frequency may occur in patients with seizure disorders if NEURONTIN is abruptly discontinued (5.5)
- Suicidal Behavior and Ideation: Monitor for suicidal thoughts/behavior (5.6)
- Neuropsychiatric Adverse Reactions in Children 3 to 12 Years of Age: Monitor for such events (5.7)

Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis

Nanna B Finnerup, Nadine Attal*, Simon Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Maija Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Philip Siddall, Blair H Smith, Mark Wallace*

NNT for 30% pain reduction or at least moderate pain relief: 7.2



Lancet Neurol 2015; 162–73

Gabapentinoids for Acute Postoperative Pain

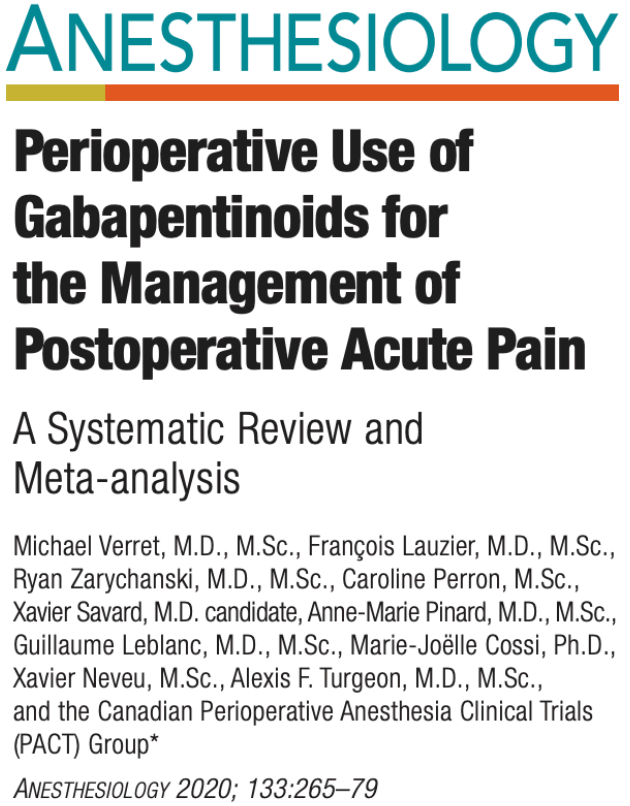
281 trials (N = 24,682 participants)

Conclusions:

No *clinically significant* analgesic effect for the perioperative use of gabapentinoids was observed.

There was also no effect on the prevention of postoperative chronic pain and **a greater risk of adverse events**.

These results do not support the routine use of pregabalin or gabapentin for the management of postoperative pain in adult patients.



Multicenter, double-blinded randomized controlled trial, adults undergoing major cardiac, thoracic, or abdominal surgery were randomized to receive either **gabapentin (600mg before surgery, 300mg twice daily for 2 days after surgery) or placebo**.

Primary outcome was length of hospital stay.

A total of **1,196 participants** were randomized

Among patients undergoing major cardiac, thoracic, and abdominal surgery, adding gabapentin to multimodal analgesic regimes **did not alter the length of hospital stay.**

Respiratory depression in 3 of the 1,196 or 0.25% of trial participants.

ANESTHESIOLOGY®

Gabapentin for Pain Management after Major Surgery: A Placebo-controlled, Double-blinded, Randomized Clinical Trial (the GAP Study)

Sarah Baos, Ph.D., Mandy Lui, M.Sc., Terrie Walker-Smith, B.Sc., Maria Pufulete, Ph.D., David Messenger, F.R.C.S., Reyad Abbadi, F.R.C.S., Tim Batchelor, F.R.C.S., Gianluca Casali, F.R.C.S., Mark Edwards, M.D., Nick Goddard, F.R.C.A., Mohammed Abu Hilal, F.R.C.S., Aiman Alzetani, F.R.C.S., Marius Vaida, F.R.C.A., Petr Martinovsky, F.R.C.A., Palinikumar Saravanan, F.R.C.A., Tim Cook, F.R.C.A., Rajiv Malhotra, F.R.C.A., Anna Simpson, Ph.D., Ross Little, F.R.C.A., Sarah Wordsworth, Ph.D., Elizabeth Stokes, D.Phil., Jingjing Jiang, Eu.H.E.M., Barnaby Reeves, Ph.D., Lucy Culliford, Ph.D., Laura Collett, M.Sc., Rachel Maishman, Ph.D., Nilesh Chauhan, F.R.C.A., Liz McCullagh, M.Pharm., Holly McKeon, M.Res., Samantha Abbs, M.Pharm., Jenny Lamb, B.A., Anna Gilbert, B.Sc., Chloe Hughes, David Wynick, Ph.D., Gianni Angelini, M.D., Mike Grocott, M.D., Ben Gibbison, M.D, Chris A. Rogers, Ph.D., for the GAP Investigators

ANESTHESIOLOGY 2025; 143:851–61

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Perioperative Gabapentin Use and In-Hospital Adverse Clinical Events Among Older Adults After Major Surgery

Chan Mi Park, MD, MPH; Sharon K. Inouye, MD, MPH; Edward R. Marcantonio, MD, ScM; Eran Metzger, MD; Brian T. Bateman, MD, ScM; Jessica J. Lie, MD, MPH; Su Been Lee, BA; Raisa Levin, MS; Dae Hyun Kim, MD, ScD

Retrospectove propensity score matching, n=237 872 (118 936 pairs), using data from the Premier Healthcare Database, included patients aged 65 years or older who underwent major surgery at US hospitals

EXPOSURES: De-novo Gabapentin use within 2 days after surgery.

The primary outcome was delirium

Compared with nonusers, gabapentin users had:

- **increased risk of delirium (4040 [3.4%] vs 3148 [2.6%]**
- new antipsychotic use
- pneumonia

WSJ Barron's MarketWatch IBD WSJ | Buy Side

THE WALL STREET JOURNAL.

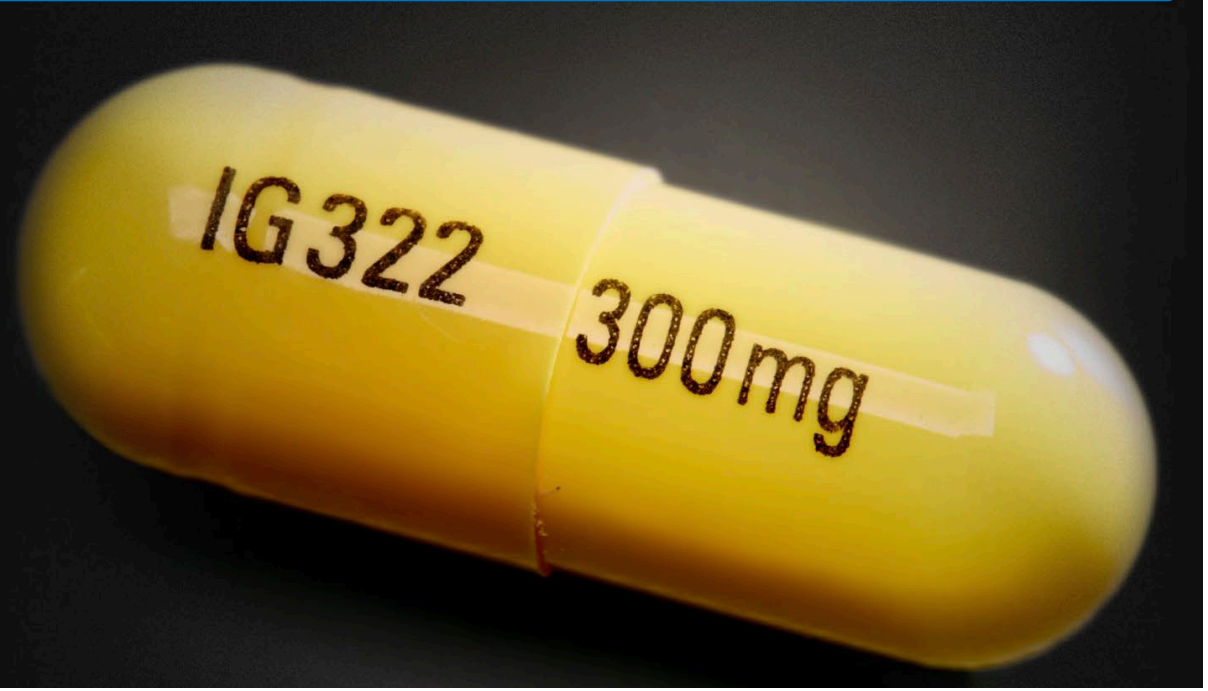
"One Pfizer medical director referred to the drug as the "'snake oil' of the twentieth century" in an email later made public. The drug's sales grew from almost $98 million in 1995 to more than $2 billion in 2003.

The Pfizer unit responsible for gabapentin ultimately pleaded guilty to criminal wrongdoing and was fined $430 million in 2004 for illegally promoting Neurontin's off-label use to doctors. It was one of the largest Medicaid-fraud settlements at the time, and the case led to calls for new marketing standards for pharmaceuticals."

The Hidden Risks of America's Most Popular Prescription Painkiller

Gabapentin has soared in popularity as an alternative to opioids, but patients are finding it can cause harm

733 Gift unlocked article Listen (15 min)

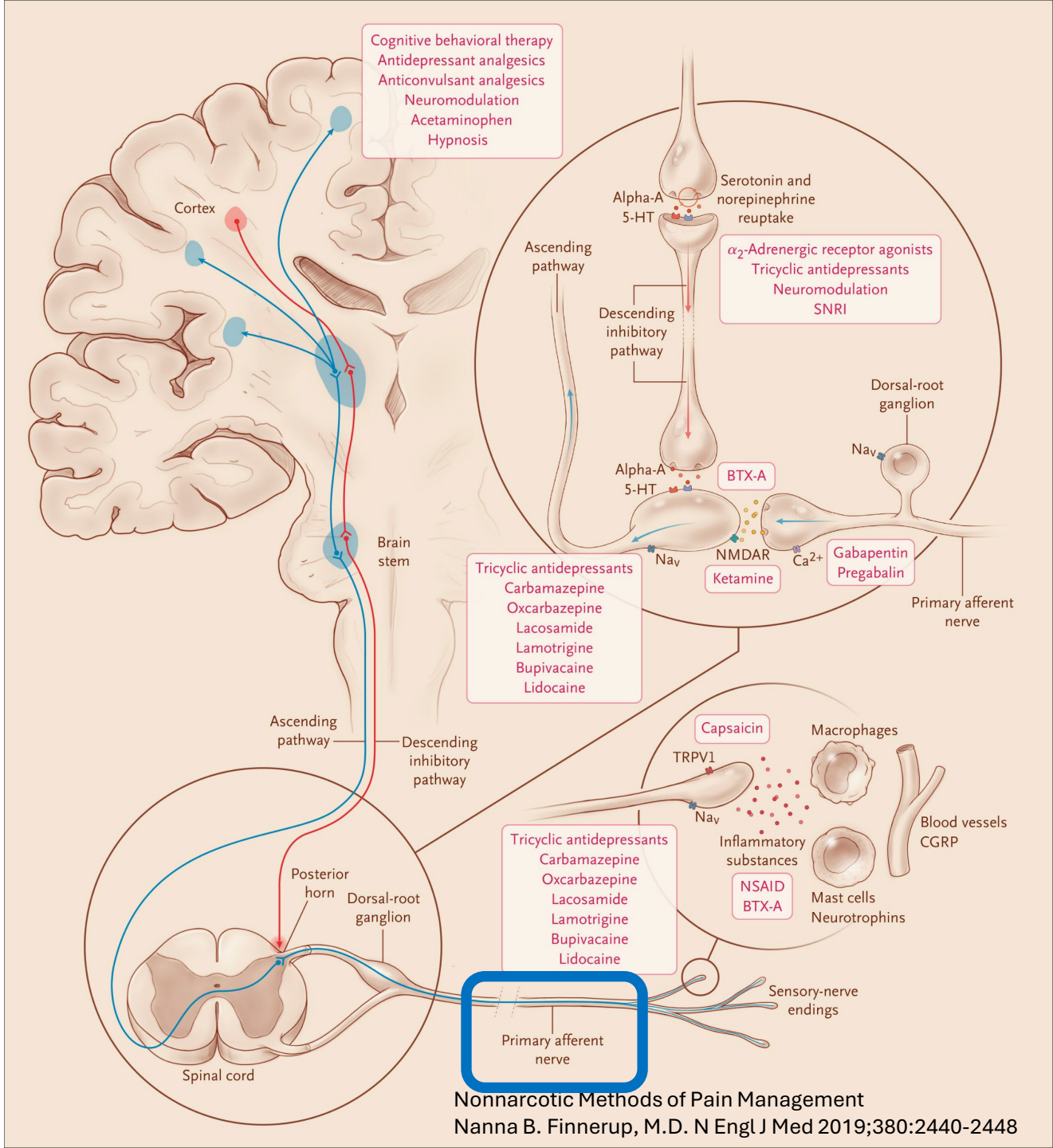


Betsy McKay, Shalini Ramachandran. WSJ. 12/24/2025.

Suzetrigine

(JOURNAVX®)

Voltage-gated sodium channel 1.8 ($Na_V1.8$) is a genetically and pharmacologically validated pain target that is selectively expressed in peripheral pain-sensing neurons and not in the central nervous system.

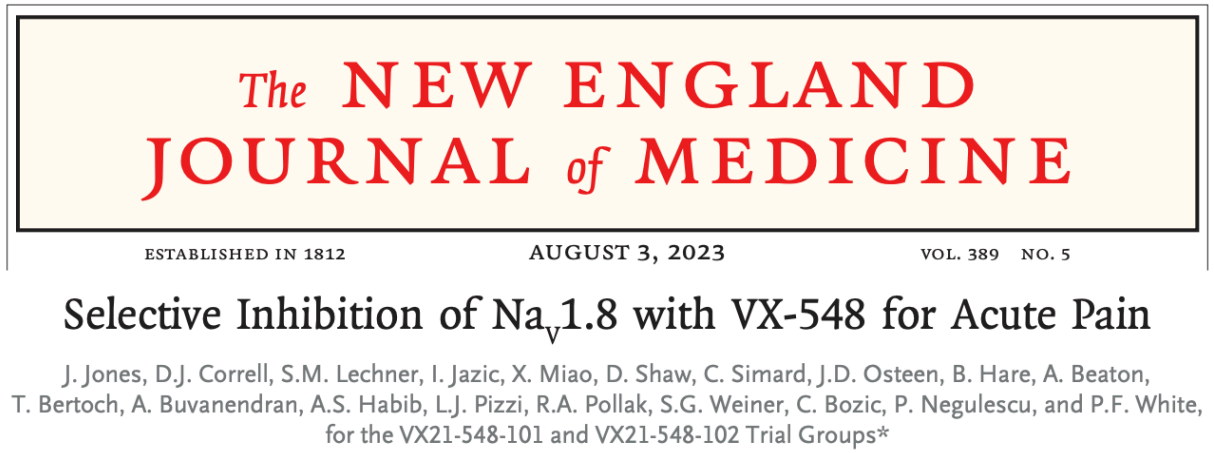


Nonnarcotic Methods of Pain Management
Nanna B. Finnerup, M.D. N Engl J Med 2019;380:2440-2448

Osteen JD et al., Pain Ther. 2025 Jan 8;14(2):655–674.

Suzetrigine

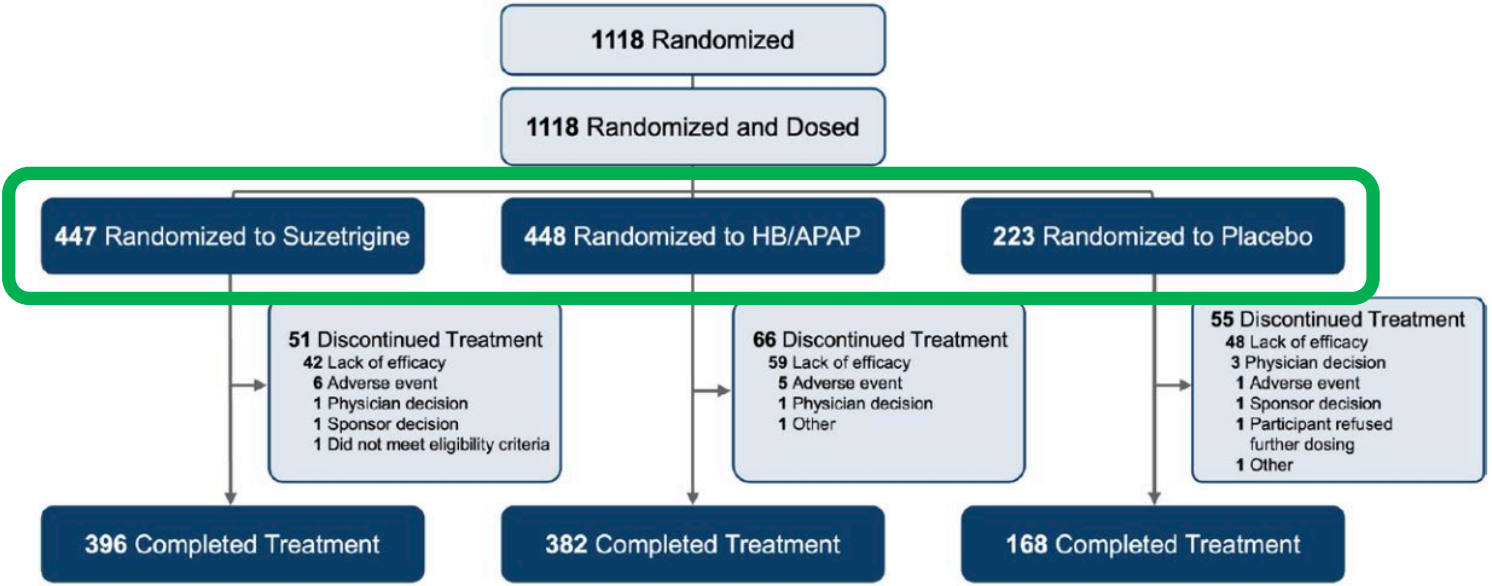
(JOURNAVX®)



A total of 303 participants were enrolled in the abdominoplasty trial and 274 in the bunionectomy trial.

“As compared with placebo, VX-548 at the highest dose, but not at lower doses, reduced acute pain over a period of 48 hours after abdominoplasty or bunionectomy.”

A Abdominoplasty



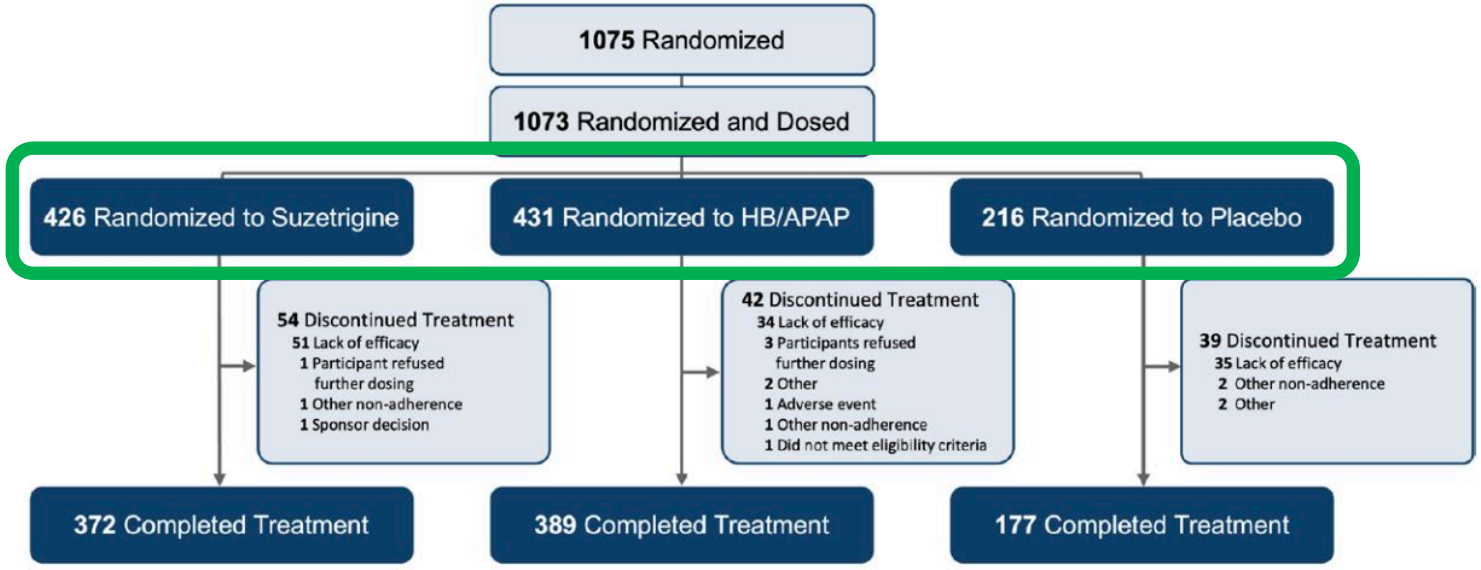
ANESTHESIOLOGY

Suzetrigine, a Nonopioid $Na_v1.8$ Inhibitor for Treatment of Moderate-to-severe Acute Pain: Two Phase 3 Randomized Clinical Trials

Todd Bertoch, M.D., Dominick D'Aunno, M.D., Jessica McCoun, M.D., Daneshvari Solanki, M.D., Louise Taber, M.D., Joshua Urban, M.D., Jessica Oswald, M.D., M.P.H., Matthew W. Swisher, M.D., Simon Tian, M.D., Xiaopeng Miao, Ph.D., Darin J. Correll, M.D., Paul Negulescu, Ph.D., Carmen Bozic, M.D., Scott G. Weiner, M.D., M.P.H.

ANESTHESIOLOGY 2025; 142:1085–99

B Bunionectomy



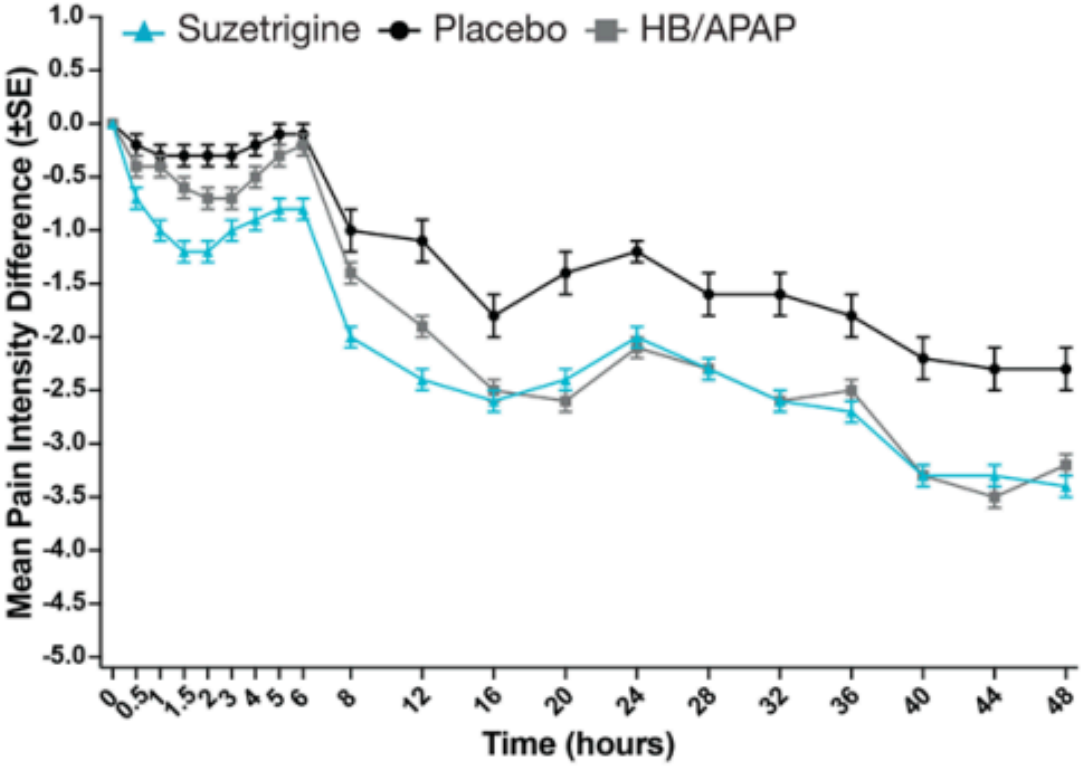
Suzetrigine (100 mg, then 50 mg every 12 h)

vs.

hydrocodone bitartrate/acetaminophen (5/325 mg every 6 h

Abdominoplasty

Prespecified analysis with rescue imputation: effect of study drug only



ANESTHESIOLOGY®

Suzetrigine, a Nonopioid $Na_v1.8$ Inhibitor for Treatment of Moderate-to-severe Acute Pain: Two Phase 3 Randomized Clinical Trials

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ANESTHESIOLOGY 2025; 142:1085–99

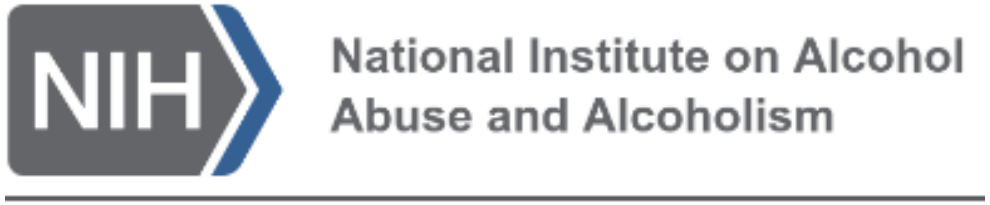
In Closing

Just because a medication may have analgesic properties and is a non-opioid, does not mean it should be prescribed to all surgical patients.

Measures for De-implementation could be included as CQI benchmarks.

Complex pain patients who may benefit from non-standard analgesic therapy require separate pain pathways from care-as-usual patients.

Funders



Departments of Anesthesiology and Psychiatry