

# A Gathering Storm: Evaluating Perioperative Opioids

Michael Bottros, MD

#### **Disclosure**

■ Nothing to disclose

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# **Objectives**

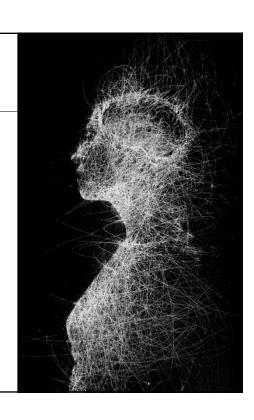
- Describe the history of opioid prescribing practices in the United States
- Describe the link between opioids and heroin
- Explain the components of an effective ERAS protocol

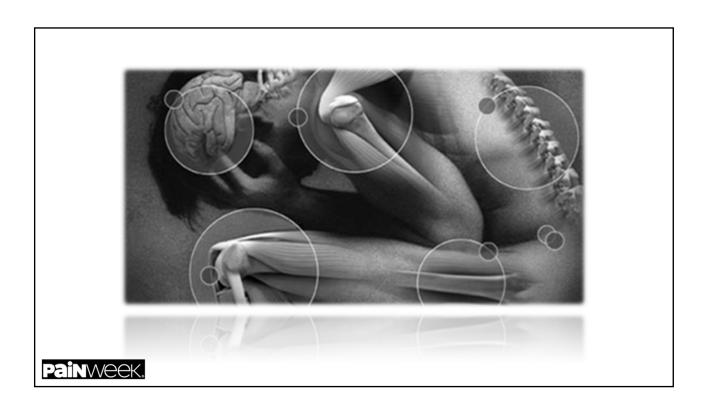


### **Outline**

- Introduction
- How did we get here?
- Persistent postoperative opioid use
- Increased unused opioids & illicit drug use
- The transition to heroin
- Rethinking the postoperative paradigm











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#### MODEL POLICY ON THE USE OF OPIOID ANALGESICS IN THE TREATMENT OF CHRONIC PAIN

#### INTRODUCTION

The Federation of State Medical Boards (FSMB) is committed to assisting state Medical Boards in protecting the public and improving the quality and integrity of health care in the United States. In 1997, the FSMB undertook an initiative to develop model guidelines and to encourage state medical boards and other health care regulatory agencies to adopt policies encouraging safe and effective treatment of patients with pain, including, if indicated, the use of opioid analgesics. [1]. The FSMB updated its guidelines in 2003 [2] so that its Model Policy would reflect the best available evidence on management of pain and give adequate attention to both the undertreatment and overtreatment of pain and the inappropriate use of opioid analgesics.

Through these initiatives, the FSMB has sought to provide a resource for use by state medical boards in educating their licensees about cautious and responsible prescribing of controlled substances while alleviating fears of regulatory scrutiny. The FSMB recognizes that inappropriate prescribing can contribute to adverse outcomes such as reduced function, opioid addiction, overdose, and death [3-5]. By promulgating its Model Policies, the FSMB has sought to provide a framework for the legitimate medical use of opioid analgesics for the treatment of pain while emphasizing the need to safeguard against their misuse and diversion.

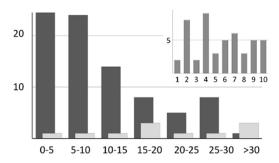




#### Focus Article

#### Pain Education in North American Medical Schools

Lina Mezei, Beth B. Murinson, and the Johns Hopkins Pain Curriculum Development Team Department of Neurology, Johns Hopkins School of Medicine, Baltimore, Maryland.



**Figure 1.** Frequency histogram, pain teaching hours by school. Main figure shows schools teaching 0 to 5 hours, 5 to 10 hours and so on. U.S. medical schools are shown as dark gray bars, Canadian schools as light gray. Inset shows expanded x-axis for 0 to 10 hours, U.S. schools only.



J Pain. 2011 Dec;12(12):1199-208

53.6%

### Top 20 Drugs for Service Year 2011 Rank Based on Total Paid

Rank	Drug Name	Brand Name/Generic	Paid Share		
1	OXYCONTIN	Brand Name	7.4%		
2	LIDODERM	Brand Name	4.9%		
3	LYRICA	Brand Name	4.6%		
4	GABAPENTIN	Generic	4.0%		
5	HYDROCODONE-ACETAMINOPHEN	Generic	3.8%		
6	CYMBALTA	Brand Name	3.4%		
7	CELEBREX	Brand Name	3.2%		
8	MELOXICAM	Generic	2.9%		
9	TRAMADOL HCL	Generic	2.5%		
10	OPANA FR	Brand Name	2.5%		
11	CYCLOBENZAPRINE HCL	Generic	2.0%		
12	FENTANYL	Generic	1.9%		
13	OXYCODONE HCI -ACETAMINOPHEN	Generic	1.6%		
14	FLECTOR	Brand Name	1.4%		
15	OXYCODONE HCL	Generic	1.4%		
16	METAXALONE	Generic	1.3%		
17	CARISOPRODOL	Generic	1.3%		
18	ZOLPIDEM TARTRATE	Generic	1.2%		
19	KADIAN	Brand Name	1.2%		
20	PERCOCET	Brand Name	1.1%		

Source: NCCI Medical Data Call, for Service Year 2011.

The 35 jurisdictions for which NCCI provides ratemaking services are AK, AL, AR, AZ, CO, CT, DC, FL, GA, HI, IA, ID, IL, KS, KY, LA, MD, ME, MO, MS, MT, NE, NH, NM, NV, OK, OR, RI, SC, SD, TN, UT, VA, VT, and WV. The seven independent bureau states for which NCCI collects the Medical Data Call are IN, MA, MN, NC, NJ, NY, and WI. Data used with permission.

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### Narcotics in Workers Compensation Are Highly Concentrated by Active Ingredient

by Active Ingredient
Top Narcotics' Active Ingredient for Service Year 2011
Rank Based on Total Paid

Rank	Active Ingredient	Paid Share
1	OXYCODONE HCL	30.6%
2	OXYCODONE HCL/ACETAMINOPHEN	15.0%
3	HYDROCODONE BIT/ACETAMINOPHEN	14.4%
4	OXYMORPHONE HCL	10.7%
5	MORPHINE SULFATE	9.6%
6	FENTANYL	8.9%
7	FENTANYL CITRATE	6.0%
8	HYDROMORPHONE HCL	2.2%
	ALL OTHER	2.6%

Source: NCCI Medical Data Call, for Service Year 2011.

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#### Brand Name OxyContin Is One-Fourth of All Narcotics Top Narcotics for Service Year 2011 Rank Based on Total Paid

Rank	Drug Name Brand (B) or Generic (G)	Active Ingredient(s)	Paid Share
1	OXYCONTIN (B)	OXYCODONE HCL	25.5%
2	HYDROCODONE-ACETAMINOPHEN (G)	HYDROCODONE BIT/ACETAMINOPHEN	13.0%
3	OPANA ER (B)	OXYMORPHONE HCL	8.7%
4	OXYCODONE HCL-ACETAMINOPHEN (G)	OXYCODONE HCL/ACETAMINOPHEN	8.6%
5	FENTANYL (G)	FENTANYL	6.6%
6	OXYCODONE HCL (G)	OXYCODONE HCL	4.8%
7	KADIAN (B)	MORPHINE SULFATE	4.2%
8	PERCOCET (B)	OXYCODONE HCL/ACETAMINOPHEN	3.9%
9	MORPHINE SULFATE ER (G)	MORPHINE SULFATE	2.4%
10	FENTORA (B)	FENTANYL CITRATE	2.4%

Source: NCCI Medical Data Call, for Service Year 2011.

The 35 jurisdictions for which NCCl provides ratemaking services are AK, AL, AR, AZ, CO, CT, DC, FL, GA, HI, IA, ID, IL, KS, KY, LA, MD, ME, MO, MS, MT, NE, NH, NM, NV, OK, OR, RI, SC, SD, TN, UT, VA, VT, and WV. The seven independent bureau states for which NCCl collects the Medical Data Call are IN, MA, MN, NC, NJ, NY, and WI.

Data used with permission.







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 $\label{thm:linear_problem} American\ Pain\ Society.\ Principles\ of\ Analgesic\ Use\ in\ the\ Treatment\ of\ Acute\ Pain\ and\ Cancer\ Pain.$ 

#### 106TH CONGRESS 2D SESSION

#### S. 3163

To designate the calendar decade beginning on January 1, 2001, as the "Decade of Pain Control and Research".

#### IN THE SENATE OF THE UNITED STATES

October 5 (legislative day, September 22), 2000 Mr. Hatch introduced the following bill; which was read twice and referred to the Committee on the Judiciary

#### A BILL

To designate the calendar decade beginning on January 1, 2001, as the "Decade of Pain Control and Research".

- 1 Be it enacted by the Senate and House of Representa-
- 2 tives of the United States of America in Congress assembled,
- 3 SECTION 1. DECADE OF PAIN CONTROL AND RESEARCH.
- 4 The calendar decade beginning January 1, 2001, is
- 5 designated as the "Decade of Pain Control and Research".

J Anesth Analg. 2005; 100:162–168.



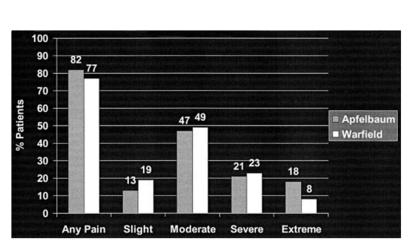


Figure 1. Overall pain after surgery.

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Anesth Analg. 2003;97:534-540.

### **Inadequately Managed Postsurgical Pain**

- Increased complications
- Increased resource utilization
- Increased healthcare costs related to longer hospital stays
- Higher rates of readmission
- Potential for progression from acute to chronic pain



Anesthesiology. 2004; 100: 1573–1581.

Anesthesiology. 2000; 93:1123–1133.



Long-term opioid management for chronic noncancer pain (Review)

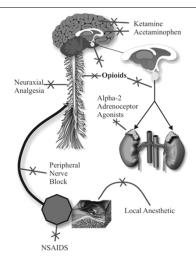
Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, Schoelles KM, Chou R

- ■62 randomized controlled trials in meta-analysis
- Opioids are more effective than placebo for nociceptive and neuropathic pain on a short-term basis
- There is weak evidence for long-term use



Cochrane Database Syst Rev. 2010;(1):CD006605.

# What works to decrease opioid use?







# Persistent opioid use

#### ORIGINAL INVESTIGATION

#### Long-term Analgesic Use After Low-Risk Surgery

A Retrospective Cohort Study

Asim Alam, MD; Tara Gomes, MHSc; Hong Zheng, MSc; Muhammad M. Mamdani, PharmD, MA, MPH; David N. Juurlink, MD, PhD; Chaim M. Bell, MD, PhD

- Retrospective cohort study, 1997-2008
- 391,139 opioid naïve patients, aged 66 years or older
- Short stay, "low-pain" procedures (cataract surgery, lap chole, TURP, or varicose vein stripping)
- 7.1% prescribed opioids within 7 days of surgery. ~10% of those at 1 year

Table 2. Risk of Long-term Analgesic Use After Low-Risk, Short-Stay Surgery

		Opioid Coh	ort	NSAID Cohort				
Primary Outcome	No. of Events in Non–Early Users  No. of Events in Early Users		Adjusted Odds Ratio (95% CI)	No. of Events in Non–Early Users	No. of Events in Early Users	Adjusted Odds Ratio (95% CI)		
All operations	27 288	2857	1.44 (1.39-1.50)	29 795	285	3.74 (3.27-4.28)		
Cataract surgery	26 584	2102	1.62 (1.54-1.67)	28 093	247	4.61 (3.98-5.35)		
Laparoscopic cholecystectomy	222	549	1.33 (1.13-1.56)	1089	15	1.14 (0.67-1.96)		
Transurethral resection of the prostate	425	123	1.33 (1.07-1.64)	440	17	4.10 (2.36-7.14)		
Varicose vein stripping	57	83	1.41 (0.99-2.02)	173	6	0.82 (0.35-1.95)		

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

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Arch Intern Med. 2012;172(5):425-430.

#### ORIGINAL INVESTIGATION

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Table 3. Distribution of Opioid Prescribing Among Patients Newly Dispensed an Opioid Within 7 Days After Surgery and at 1-Year Follow-up

	Frequency Prescribed, % <sup>a</sup>					
Opioid Name	First 7 Days After Surgery	1-Year Follow-up				
Codeine	93.4	87.5				
Fentanyl patch	0.01	1.6				
Hydromorphone	0.3	1.9				
Meperidine	0.7	1.0				
Morphine	0.1	2.6				
Oxycodone	5.4	15.9				
Long-acting oxycodone	0.04	1.9				

<sup>&</sup>lt;sup>a</sup>Calculated among people receiving at least 1 opioid prescription. If someone received multiple opioid types, they were counted multiple times.



Arch Intern Med. 2012;172(5):425-430.

# Rates and risk factors for prolonged opioid use after major surgery: population based cohort study

© OPEN ACCESS

Hance Clarke assistant professor<sup>123</sup>, Neilesh Soneji lecturer<sup>24</sup>, Dennis T Ko associate professor<sup>567</sup>, Lingsong Yun analyst<sup>4</sup>, Duminda N Wijeysundera assistant professor<sup>12578</sup>

- Population based retrospective cohort study, 2003-2010
- 39,140 opioid naïve patients, aged 66 years or older
- Main outcome measure: prolonged opioid use after discharge (>90 d)
- 49.2% were discharged with opioids; 3.1% continued for >90 days
- Adjusted risk factors:
  - Younger age
  - Lower household income
  - Specific comorbidities (DM, CHF, pulmonary disease)
  - Specific preop drugs (benzo, SSRI, ACEI)
  - Both open AND minimally invasive thoracic procedures



BMJ 2014;348:g1251

Table 1| Patterns of post-discharge opioid use across different surgical procedures. Values are proportions (%) with exact 95% binomial confidence intervals

		Duration of	f opioid use
Procedures	No of participants (n=39 140)	Early post-discharge* % (95% CI)	Prolonged post-discharge† % (95% CI)
Urological surgery‡:			
Radical prostatectomy (open and minimally invasive)	5193	65.2 (63.9 to 66.5)	2.8 (2.4 to 3.2)
Coronary artery bypass graft via sternotomy	9488	53.5 (52.4 to 54.5)	3.3 (2.9 to 3.6)
Intrathoracic surgery:			
Minimally invasive lung resection	720	65.7 (62.1 to 69.2)	6.3 (4.6 to 8.3)
Open lung resection	2423	72.4 (70.6 to 74.2)	8.5 (7.4 to 9.6)
Intra-abdominal surgery:			
Minimally invasive colorectal surgery	3202	44.1 (42.3 to 45.9)	3.2 (2.6 to 3.9)
Open colorectal surgery	8642	38.0 (37.0 to 39.1)	2.8 (2.4 to 3.1)
Gynaecological surgery:			
Minimally invasive hysterectomy	5287	35.7 (34.4 to 37.0)	1.5 (1.2 to 1.8)
Open hysterectomy	4185	47.3 (45.7 to 48.8)	2.5 (2.1 to 3.0)

<sup>\*≥1</sup> prescriptions for opioids within 1-90 days after surgery.

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BMJ 2014;348:g1251

- "Doctors and hospital administrators are asking, if an opioid addiction starts with a prescription after surgery or some other hospital-based care, should the hospital be penalized? As in: Is addiction a medical error along the lines of some hospitalacquired infections?"
- "Putting hospitals on the hook for the consequences of aggressive opioid prescribing makes sense to me."
- Martha Bebinger | Washington Post December 11, 2017







<sup>†≥1</sup> prescriptions for opioids within 1-90 days after surgery, along with ≥1 prescriptions for opioids within 91-180 days after surgery.

<sup>‡</sup>Subgroup specific results for open versus minimally invasive prostatectomy not reported owing to privacy regulations on reporting of small numbers of people within subgroups.

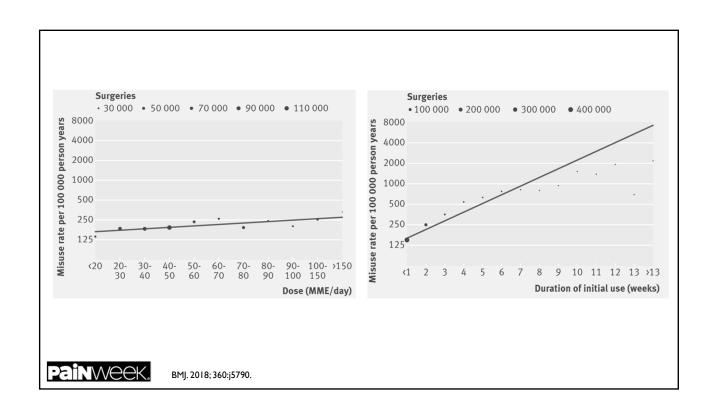
# Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study

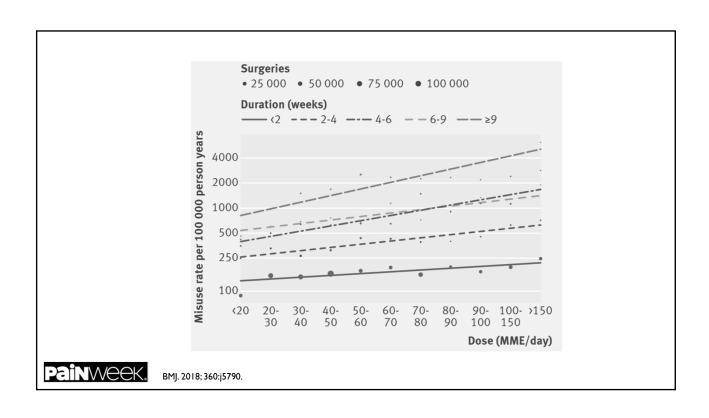
Gabriel A Brat, <sup>1,2</sup> Denis Agniel, <sup>1</sup> Andrew Beam, <sup>1</sup> Brian Yorkgitis, <sup>3</sup> Mark Bicket, <sup>4</sup> Mark Homer, <sup>1</sup> Kathe P Fox, <sup>5</sup> Daniel B Knecht, <sup>5</sup> Cheryl N McMahill-Walraven, <sup>5</sup> Nathan Palmer, <sup>1</sup> Isaac Kohane <sup>1</sup>

- Retrospective cohort study.
- 1,015,116 opioid naïve patients undergoing surgery.
- 56% patients received postop opioids.
- 0.6% (5,906 pts) were identified having a code for abuse.
- Total duration of opioid use was the strongest predictor of misuse.
- Each refill and additional week of opioid use was associated with an adjusted increase in misuse rate of 44%.



BMJ 2018; 360:j5790.

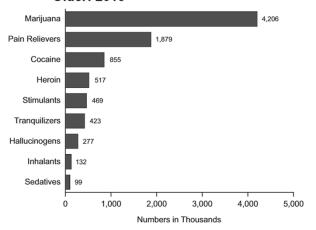






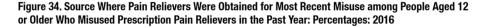
# Increased unused opioids & illicit drug use

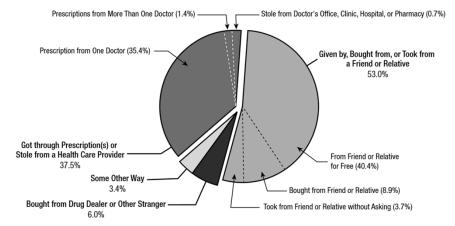
Figure 7.2 Specific Illicit Drug Dependence or Abuse in the Past Year among Persons Aged 12 or Older: 2013



Substance Abuse and Mental Health Services Administration. Results from the 2013 National Survey on Drug Use and Health. Volume 1: Summary of National Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014







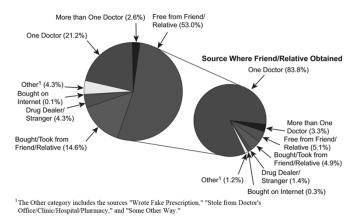
 ${\bf 11.5\ Million\ People\ Aged\ 12\ or\ Older\ Who\ Misused\ Prescription\ Pain\ Relievers\ in\ the\ Past\ Year}$ 

Note: Respondents with unknown data for Source for Most Recent Misuse or who reported Some Other Way but did not specify a valid way were excluded. Note: The percentages do not add to 100 percent due to rounding.

Substance Abuse and Mental Health Services Administration. Results from the 2016 National Survey on Drug Use and Health. Volume 1: Summary of National Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2017



Source Where User Obtained



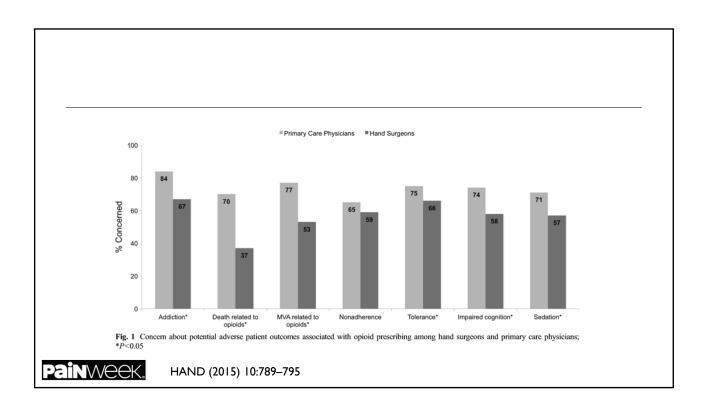
Substance Abuse and Mental Health Services Administration. Results from the 2013 National Survey on Drug Use and Health. Volume 1: Summary of National Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014

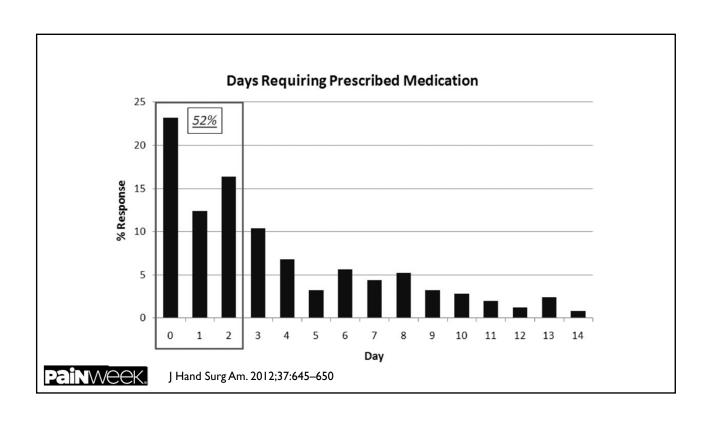
# Physicians' Knowledge & Attitudes about Opioid Abuse

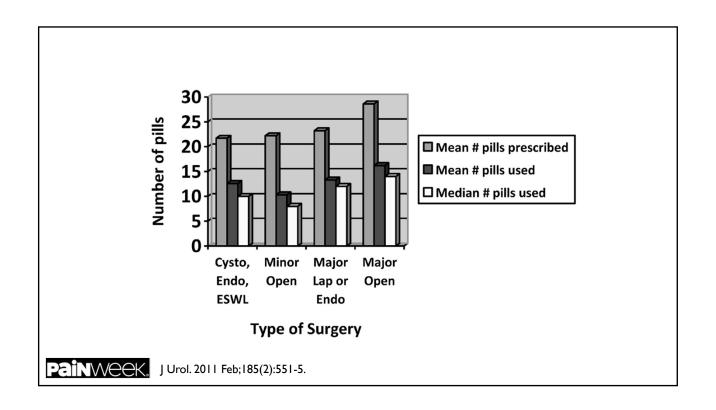
Clin J Pain 2016;32:279-284

Note: The percentages do not add to 100 percent due to rounding.

	%
To your knowledge, what is the most common route for abusing prescription opioids?	
Swallowing the pills whole	66
Crushing and swallowing the pills	13
Crushing and snorting the pills	10
Crushing, dissolving, and injecting the pills	9
Crushing and smoking the pills	2
What do you think is the most common source of prescription opioids	
for people who use them for nonmedical purposes?	
More than one doctor	69
A relative or friend	13
A single doctor	8
A drug dealer or stranger	7
The internet	3
	Strongly or Somewhat Agree (%
Abuse-deterrent formulations (ADFs)	
An ADF of a drug will have a lower addictive potential than a non-ADF of the same drug	46
ADFs of prescription opioids will result in large or moderate reductions of morbidity and mortality	27
I have a lot or some experience prescribing ADFs	12









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Original article

Painfully Obvious: A Longitudinal Examination of Medical Use and Misuse of Opioid Medication Among Adolescent Sports Participants

Philip Veliz, Ph.D. <sup>a.</sup> , Quyen M. Epstein-Ngo, Ph.D. <sup>a</sup>, Elizabeth Meier, Ph.D. <sup>a</sup>, Paula Lynn Ross-Durow, Ph.D. <sup>a</sup>, Sean Esteban McCabe, Ph.D. <sup>a</sup>, and Carol J. Boyd, Ph.D. <sup>b</sup> \*histince for Research on Women and Gender, University of Michigan, Ann Arbor, Michigan \*\*School of Nursing University of Michigan, Ann Arbor, Michigan

Article history: Received March 4, 2013; Accepted September 6, 2013 Keywords: Adolescents; Prescription medications; Opioid use; Opioid misuse; Sports participation

- 1540 adolescents
- 2009-2010 and 2011-2012 school years
- Those in organized sports vs those who were not
  - -2x prescribed an opioid
  - -10x greater risk for misuse by taking too much
  - -4x greater risk for misuse to get high

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J Adolesc Health. 2014;54:333-340.



#### The transition to heroin



#### **OPIOIDS, SUBSTANCE ABUSE & ADDICTIONS SECTION**

**Original Research Article** 

Prescription Opioid Abuse and Diversion in an Urban Community: The Results of an Ultrarapid Assessment

James A. Inciardi, PhD,\* Hilary L. Surratt, PhD,\* Theodore J. Cicero, PhD,† and Ronald A. Beard, MHS\*

\*Center for Drug and Alcohol Studies, University of Delaware, Coral Gables, Florida; †Department of Psychiatry, Washington University School of Medicine, St. Louis, Missouri, USA

- One male heroin user in his early 20s stated,
   "I started with Percocets and ended up shooting 10 bags of heroin a day."
- A 23-year-old male reported, "It led me into heroin. When I was in junior high my grandfather had cancer and he had Percocet and morphine pills, and after he died my Grandma still had a lot of his pill bottles around. I...started taking them, and...after that I was hooked."
- This theme was indicated by others as well: "They [prescription pills] are like just as strong as dope and weed. They are really gateway drugs. They get you there. They get you into that scene."

It was also explained by several focus group participants that the movement from prescription drugs to heroin was due to the high cost of prescription opioids on the street: "When I first started doing drugs I started taking the pills, like Xanax, Oxys, Percocets, anything that was prescription. After that I progressed into heroin and cocaine because...sometimes the prescription drugs are real expensive. Most pills like an Oxy can be \$40. So it was just getting too expensive for me."



Pain Med. 2009 Apr; 10(3):537-48

#### Joint Commission Online

In this issue

Revisions to pain management standard effective January 1, 2015 BrightStar Care® recognized as Enterprise Champion for Quality for second year New on the Web

Revisions to pain management standard effective January 1, 2015

Revisions to the Provision of Care, Treatment, and Services standard PC.01.02.07 - which addresses pain management – will be effective January 1, 2015. Following an extensive literature review, The Joint Commission revised the rationale and added a note to element of performance (EP) 4. Clinical experts in pain management provided feedback on these revisions and guidance on the future direction of pain management. The experts affirmed that treatment strategies may consider both pharmacologic and nonpharmacologic approaches. In addition, when considering the use of medications to treat pain, organizations should consider both the benefits to the patient, as well as the risks of dependency, addiction, and abuse of opioids. The revisions (below) will appear in the 2014 *Update* 2 to the accreditation manuals. Similar revisions are scheduled for the behavioral health care program (in the "Care, Treatment, and Services" chapter) with a July 1, 2015, effective date and will be published closer to that date. (Contact: Emi Datuin-Pal, BDatuin-Pal@jointcommission.org)

Effective January 1, 2015: For ambulatory care, critical access hospital, home care, hospital, nursing care center, and office-based surgery accreditation programs.

Standard PC.01.02.07: The [organization] assesses and manages the [patient's] pain.

[Revised] Rationale for PC.01.02.07 [New for ambulatory care and office-based surgery practice]

The identification and management of pain is an important component of [patient]-centered care. [Patients] can expect that their health care providers will involve them in their assessment and management of pain. Sub pharmacologic and nonpharmacologic strategies have a role in the management of pain. The following examples are not exhaustive, but strategies may include the following:

Nonpharmacologic strategies: physical modalities (for example, acupuncture therapy, chiropractic therapy, osteopathic manipulative treatment, massage therapy, and physical therapy), relaxation therapy, and cognitive behavioral therapy

Pharmacologic strategies: nonopioid, opioid, and adjuvant analgesics

EP 4: The [organization] either treats the [patient's] pain or refers the [patient] for treatment



[New] Note: Treatment strategies for pain may include pharmacologic and nonpharmacologic approaches. Strategies should reflect a [patient]-centered approach and consider the patient's current presentation, the health care providers' clinical judgment, and the risks and benefits associated with the strategies, including potential risk of dependency, addiction, and abuse.

#### Joint Commission Online

A complimentary publication of The Joint Commission

In this issue

Revisions to pain management standard effective January 1, 2015 BrightStar Care® recognized as Enterprise Champion for Quality for second year

#### Accreditation

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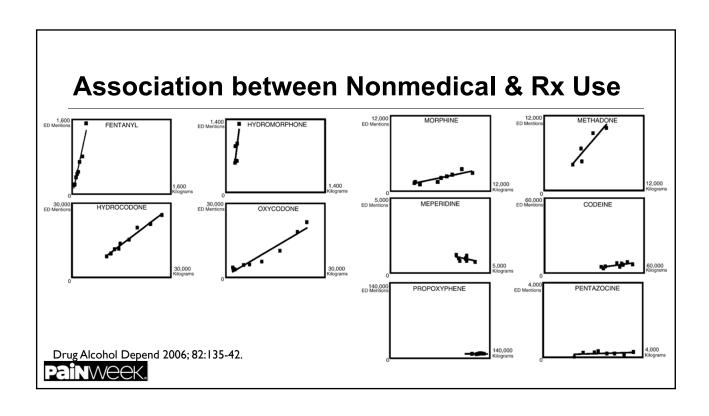
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[New] Note: Treatment strategies for pain may include pharmacologic and nonpharmacologic approaches. Strategies should reflect a [patient]-centered approach and consider the patient's current presentation, the health care providers' clinical judgment, and the risks and benefits associated with the strategies, including potential risk of dependency, addiction, and abuse.



	Opioid Prescrib	bing	Fatality	
Specialty	# of Prescriptions	% of All Opioid Prescriptions	Prescriptions Associated with Fatalities	% of All Fatalities Associated
Pain medicine	232,246	1.0	2,735	2.0
Physical medicine and rehabilitation	607,594	2.6	6,105	4.6
Psychiatry and neurology	221,394	1.0	2,015	1.5
Anesthesiology	245,629	1.0	1,961	1.5
Family medicine	5,626,869	24.1	40,107	30.2
Missing specialty	1,927,060	9.8	14,341	10.8
Emergency medicine	1,498,069	6.4	7,575	5.7
Podiatrist	278,571	1.2	1,384	1.0
Internal medicine	2,508,085	10.8	11,775	8.8
Orthopedic surgery	1,502,771	6.4	7,015	5.3
Dentist	2,038,377	8.7	6,534	4.9
Obstetrics and gynecology	644,763	2.8	1,532	1.2

# Medicaid Patients With CNCP in North Carolina

Proportion of all prescriptions and all opioid prescriptions filled for chronic noncancer pain patients 18 to 64 years of age, according to specialty for patients with provider specialty data

		n (%) of all opioid prescriptions filled	Opioid prescriptions as % of all prescriptions filled, according to specialty
Provider specialty	n (%) of all prescriptions filled (column %)	(column %)	(row %)
ENT	5186 (0.40)	560 (0.36)	10.80
Dentists	28,194 (2.17)	7492 (4.78)	26.57
GP/FM/DO	405,786 (31.16)	35,881 (22.89)	8.84
Internal medicine	262,846 (20.19)	22,188 (14.16)	8.44
Emergency medicine	87,903 (6.75)	19,924 (12.71)	22.67
Orthopedists	28,178 (2.16)	11,768 (7.51)	41.76
OB/GYN	49,686 (3.82)	5032 (3.21)	10.13
Other specialty	434,389 (33.36)	53,877 (34.38)	12.40
Total prescriptions	1,302,168 (100)	156,722 (100)	12.04

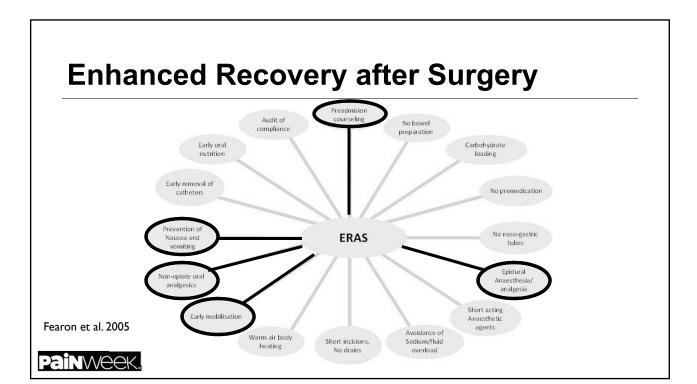
DO Doctor of osteopathic medicine; ENT Ear, nose and throat; GP General practitioner; FM Family medicine; OB/GYN Obstetrics and gynecology



Pain Res Manag. 2014 Jul-Aug; 19(4):179-85



# **The Opportunity**

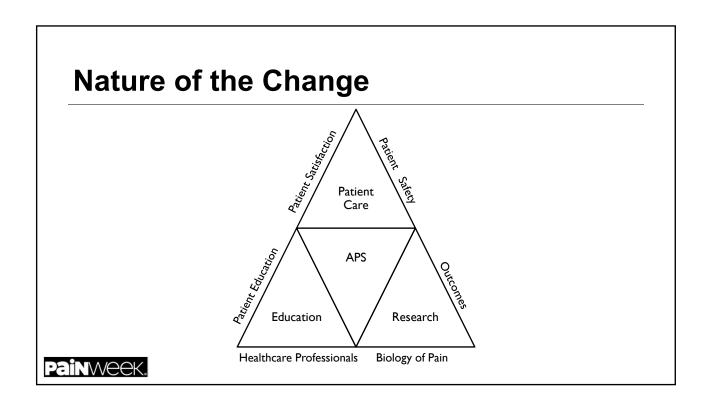


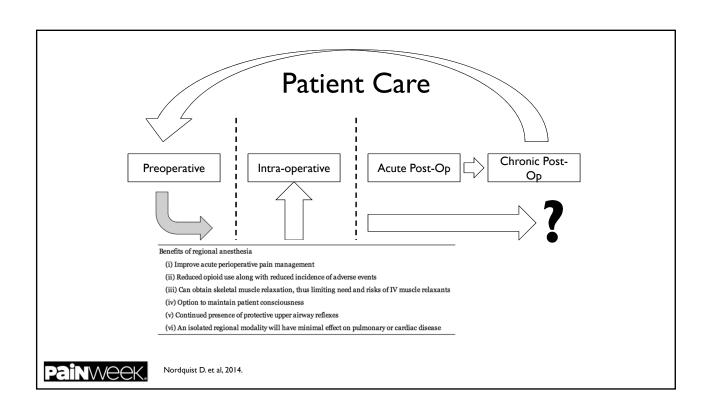
#### Identifying patients at risk for opioid abuse

- Key characteristics (odds ratio >2):
  - At least one prior prescription of buprenorphine (OR = 51.75) or methadone (OR = 2.97)
  - -At least one diagnosis of nonopioid drug abuse (OR = 9.89)
  - -Prior opioid prescriptions (OR = 2.23 for 1-5 prior Rxs; OR = 6.85 for 6+ prior Rxs)
  - -Having a family member diagnosed with opioid abuse (OR = 3.01)
  - -Mental illness (OR = 2.45)
  - -Hepatitis (OR = 2.36)



Pain Med. 2012 Sep;13(9):1162-73





Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery (Review)

Jørgensen H, Wetterslev J, Møiniche S, Dahl JB



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Golmane Labrary* 2008, Issue 4



#### Analysis I.I. Comparison I Epidural local anaesthetic (LA) vs opioid based regimens, Outcome I Effect on time (h) to first passage of stool.

Review. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery

Comparison: I Epidural local anaesthetic (LA) vs opioid based regimens

Outcome: I Effect on time (h) to first passage of stool

Study or subgroup	Epidural LA N	Mean(SD)	Opioid based analg N	Mean(SD)		Mean erence om,95% CI	Weight	Mean Difference IV,Random,95% CI
Wattwil 1989	20	70 (44)	20	103 (26)	-		12.2 %	-33.00 [ -55.40, -10.60 ]
Scheinin 1987	15	66 (28)	45	92 (32)	-		126%	-26.00 [ -42.98, -9.02 ]
Thom 1989	11	57 (44)	11	92 (22)	-		11.5 %	-35.00 [ -64.07, -5.93 ]
Wallin 1986	15	62 (18)	15	65 (27)	-	-	12.6%	-3.00 [ -19.42, 13.42 ]
Ahn 1988	16	57 (12)	14	192 (36)	•		12.4%	-135.00 [ -154.75, -115.25 ]
Riwar 1992	24	21 (19)	24	110 (35)			127%	-89.00 [ -104.93, -73.07 ]
Asantila 1991	20	46 (12)	40	59 (17)	+		13.1 %	-13.00 [ -20.44, -5.56 ]
Bredtmann 1990	57	71 (36)	59	96 (29)	-		129%	-25.00 [ -36.92, -13.08 ]
<b>Total (95% CI)</b> Heterogeneity: Tau <sup>2</sup> Test for overall effect	= 1521.37; Chi		228 = 7 (P<0.00001);  2 =	-96%	_		100.0 %	-44.64 [ -72.43, -16.85 ]
				-	100 -50 (	50	100	
				Favou	rs Epidural LA	Favours o	pioid based	

Painweek.

#### Analysis I.2. Comparison I Epidural local anaesthetic (LA) vs opioid based regimens, Outcome 2 Effect on time (h) to first passage of flatus.

Review. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery

Comparison: I Epidural local anaesthetic (LA) vs opioid based regimens

Outcome: 2 Effect on time (h) to first passage of flatus

Study or subgroup	Epidural LA		Opioid based analg		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Ahn 1988	16	48 (10)	14	128 (21)	-	14.4 %	-80.00 [ -92.04, -67.96 ]
Liu 1995	14	40 (7.5)	24	65 (13)	•	14.9 %	-25.00 [ -31.52, -18.48 ]
Riwar 1992	24	18 (12)	24	81 (18)	+	14.8 %	-63.00 [ -71.65, -54.35 ]
Scheinin 1987	15	66 (28)	45	92 (32)		13.6 %	-26.00 [ -42.98, -9.02 ]
Thom 1989	- 11	22 (16)	11	56 (22)		13.8 %	-34.00 [ -50.08, -17.92 ]
Wallin 1986	12	43 (20)	15	39 (18)	+	14.0 %	4.00 [ -10.53, 18.53 ]
Wattwil 1989	20	31 (22)	20	58 (14)	-	14.5 %	-27.00 [ -38.43, -15.57 ]
0 ,	= 661.34; Chi²		153 = 6 (P<0.00001);   <sup>2</sup> =9	95%	•	100.0 %	-36.11 [ -55.76, -16.47 ]
Test for overall effect	c Z = 3.60 (P =	0.00032)					
				-	00 -50 0 50	100	

Favours Treatment Favours Control



#### Analysis 1.3. Comparison | Epidural local anaesthetic (LA) vs opioid based regimens, Outcome 3 Effect on time (h) to return of gastrointestinal function (flatus or stool) - subgroups.

Review. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal panalysis, PONV and pain after abdominal surgery

Comparison: I Epidural local anaesthetic (LA) vs opioid based regimens

Outcome: 3 Effect on time (h) to return of gastrointestinal function (flatus or stool) - subgroups

Study or subgroup	Epidural LA		Opioid based analg		Mean Difference	Weight	M Differe
	N	Mean(SD)	N	Mean(SD)	IV,Random,959	G	IV,Random,955
I Epi LA vs systemic opi	oid						
Ahn 1988	16	48 (10)	14	128 (21)	-	14.5 %	-80.00 [ -92.04, -67.9
Bredtmann 1990	57	71 (36)	59	96 (29)	+	14.5 %	-25.00 [ -36.92, -13.0
Liu 1995	14	40 (7.5)	12	81 (10)	*	15.2 %	-41.00 [ -47.89, -34.1
Riwar 1992	25	18 (12)	25	81 (18)	*	15.0 %	-63.00 [ -71.48, -54.52
Scheinin 1987	15	66 (28)	15	91 (35)		12.3 %	-25.00 [ -47.68, -2.32
Wallin 1986	12	43 (20)	15	39 (18)	+	14.0 %	4.00 [ -10.53, 18.53
Wattwil 1989	20	31 (22)	20	58 (14)	-	14.6 %	-27.00 [ -38.43, -15.57
Subtotal (95% CI) Heterogeneity. Tau <sup>2</sup> = 5 Test for overall effect: Z 2 Epi LA vs epi opioid	73.76; Chi <sup>2</sup> =		160 6 (P<0.00001); I <sup>2</sup> =959	6	•	100.0 %	-37.24 [ -55.67, -18.82
Asantila 1991	20	46 (12)	20	55 (7)		266%	-9.00 [ -15.09, -2.91
Liu 1995	14	40 (7.5)	14	71 (15)	*	260 %	-31.00 [ -39.78, -22.22
Scheinin 1987	15	66 (28)	30	93 (28)	-	23.5 %	-27.00 [ -44.35, -9.65
Thom 1989	- 11	22 (16)	11	56 (22)		23.9 %	-34.00 [ -50.08, -17.92
Subtotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 1 Test for overall effect: Z 3 Epi LA vs epi LA/opioi	75.83; Chi <sup>2</sup> = 1 = 3.33 (P = 0.0		75 (P = 0.00008); I <sup>2</sup> =865	K	•	100.0 %	-24.42 [ -38.81, -10.03
Asantila 1991	20	46 (12)	20	62 (19)	=	49.8 %	-1600 [ -25.85, -6.15
Liu 1995	14	40 (7.5)	12	43 (14)	#	50.2 %	-3.00 [ -11.84, 5.84
Subtotal (95% CI) Heterogeneity. Tau <sup>2</sup> = 6 Test for overall effect: Z	1.70; $Chi^2 = 3$		<b>32</b> = 0.05); I <sup>2</sup> =73%		+	100.0 %	-9.31 [ -22.05, 3.42



#### Analysis 1.7. Comparison I Epidural local anaesthetic (LA) vs opioid based regimens, Outcome 7 Effect on the incidence of postoperative nausea.

Review: Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery

Comparison: I Epidural local anaesthetic (LA) vs opioid based regimens

Outcome: 7 Effect on the incidence of postoperative nausea

Study or subgroup	Epidural LA	Opioid based analg	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	Peto,Fixed,95% CI		Peto,Fixed,95% CI
Asantila 1991	5/20	8/40	-	13.5 %	1.34 [ 0.37, 4.86 ]
Beeby 1984	0/10	2/23		2.4 %	0.23 [ 0.01, 4.87 ]
Brodner 2000	5/22	13/81		14.8 %	1.58 [ 0.46, 5.44 ]
Cooper 1996	2/18	0/38		2.5 %	23.78 [ 1.19, 475.13 ]
Delilkan 1993	3/20	14/38		16.2 %	0.35 [ 0.11, 1.15 ]
George 1992	3/10	7/20	-	9.0 %	0.80 [ 0.17, 3.92 ]
Lee 1988	12/20	19/40	-	19.9 %	1.64 [ 0.56, 4.75 ]
Liu 1995	2/14	6/38	+	8.0 %	0.89 [ 0.17, 4.80 ]
Thom 1989	0/11	5/11		5.9 %	0.08 [ 0.01, 0.59 ]
Wattwil 1989	0/20	6/20		7.7 %	0.10 [ 0.02, 0.56 ]
Total (95% CI) Total events: 32 (Epidura Heterogeneity. Chi² = 2 Test for overall effect: Z Test for subgroup differe	1.61, df = 9 (P = 0.01) = 1.12 (P = 0.26)	-		100.0 %	0.76 [ 0.47, 1.23 ]
			0.01 0.1 I 10 100		
			0.01		



#### Analysis 1.8. Comparison I Epidural local anaesthetic (LA) vs opioid based regimens, Outcome 8 Effect on the incidense of postoperative vomiting.

 $Review. \quad \hbox{Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery} \\$ 

 ${\sf Comparison:} \quad {\sf I \ Epidural \ local \ anaesthetic \ (LA) \ vs \ opioid \ based \ regimens}$ 

Outcome: 8 Effect on the incidense of postoperative vomiting



#### Epidural versus Continuous Preperitoneal Analgesia during Fast-track Open Colorectal Surgery

A Randomized Controlled Trial

March 2013

Philippe Jouve, M.D., \* Jean-Etienne Bazin, M.D., Ph.D., † Antoine Petit, M.D., \* Vincent Minville, M.D., Ph.D., ‡ Adeline Gerard, M.D., \* Emmanuel Buc, M.D., Ph.D., § Aurelien Dupre, M.D., § Fabrice Kwiatkowski, Ph.D., I Jean-Michel Constantin, M.D., Ph.D., #, Emmanuel Futier, M.D.\*\*

Background: Effective postoperative analgesia is essential for early rehabilitation after surgery. Continuous wound infiltration (CWI) of local anesthetics has been proposed as an alternative to epidural analgesia (EA) during colorectal surgery. This prospective, double-blind trial compared CWI and EA in patients undergoing elective open colorectal

Methods: Fifty consecutive patients were randomized to receive EA or CWI for 48 h. In both groups, patients were managed according to Enhanced Recovery After Surgery recommendations. The primary outcome was the dynamic pain score measured during mobilization 24 h after surgery (H24) using a 100-mm verbal numerical scale. Secondary outcomes were time to functional recovery, analgesic technique-related

Results: Median postoperative dynamic pain score vas lower in the EA than in the CWI group (10 [interquartile range: 1.6–20] vs. 37 [interquartile range: 30–49], P < 0.001) and remained lower until hospital discharge. The median times to eturn of gut function and tolerance of a normal, complete diet were shorter in the EA than in the CWI group Probability (P < 0.01 each). Sleep quality was also better in the EA group, but there was no difference in urinary retention rate (P = 0.57). The median length of stay was lower in the EA than in the CWI group (4 [interquartile range: 3.4-5.3] days vs. 5.5 [interquartile range: 4.5-7] days; P = 0.006). Conclusion: Within an Enhanced Recovery After Surgery program, EA provided quicker functional recovery than CWI and reduced length of hospital stay after open colorectal surgery.





Thoracic surgery: T4-8

Upper abdominal (Whipple, gastrectomy, hepatic): T6-7

Mid-abdominal (GU): T7-10

Lower abdominal (TAH, AP, colectomy): T9-10



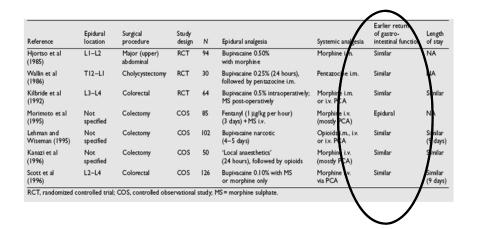
# **Catheter-Incision Congruence**

Reference	Epidural location	Surgical procedure	Study design	N	Epidural analgesia	Systemic analgesia	Earlier return of gastro- intestinal function	Length of stay
Scheinin et al (1987)	Middle of planned incision'	Colectomy	RCT	60	Bupivacaine 0.25% or morphine (48 hours)	Oxycodone i.m.	Epidural	NA.
Ahn et al (1988)	L2-L3	Rectal-sigmoid colectomy	RCT	30	Bupivacaine 0.25% (48 hours)	Pentazocine i.v	Epidural	*
Wattwil et al (1989)	TI2-LI	Abdominal hysterectomy	RCT	40	Bupivacaine 0.25% (~24 hours)	Ketobemidon: i.m.	Epidural	8 days versus 7 days
Seeling et al (1990)	T7-T11	Major abdominal	RCT	214	Bupivacaine 0.25% with fentanyl (~76 hours)	Piritramide i.ki.m.	Epidural	NA
Bredtmann et al (1990)	T8-T10	Colectomy	RCT	116	Bupivacaine 0.25% (72 hours)	Piritramide-ramadol i.m.	Epidural	20 days versus 19 days
Jayr et al (1993)	T7-TI I	Major abdominal	RCT	153	Bupivacaine 0.125% with morphine (4 days)	Morphine s.c	Epidural	Similar
Liu et al (1995a)	T8-T10	Colectomy	RCT	54	Bupivacaine (0.1-0.15%), MS, or both (60-100 hours)	Morphine Lv. PCA	Epidural	4 days versus 5 days
Scott et al (1996)	T6-T10	Colectomy	cos	128	Bupivacaine 0.10% with MS or morphine only	Morphine Lv. PCA	Epidural	9 days versus 9 days
de Leon- Casasola et al (1996)	T10-T12	Abdominal hysterectomy	cos	68	Bupivacaine 0.05% with morphine (~4 days)	Morphine Lv. PCA	Epidural	0 days versus 14 days



Balliere's Clin Anaesthesiol 1999;13:9-22

# **Catheter-Incision Incongruence**





Balliere's Clin Anaesthesiol 1999;13:9-22

# **Chronic Postsurgical Pain**

	Favours re	gional	Conventional pain	control		OR	OR
Study or subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Thoracotomy (e	pidural analge	esia)					
Ju 2008	26	48	31	43	43.4%	0.46 [0.19, 1.10]	
Lu 2008	9	62	12	28	31.4%	0.23 [0.08, 0.63]	
Senturk 2002	25	46	18	23	25.2%	0.33 [0.10, 1.04]	-
Subtotal (95% CI)		156		94	100.0%	0.34 [0.19, 0.60]	
Total events	60		61				
Heterogeneity: τ2=0.0	$00; \chi^2 = 1.04, dt$	f=2 (P=0	59); / <sup>2</sup> =0%				
Test for overall effect:	Z=3.69 (P=0.	0002)					
1.1.2 Breast cancer s	surgery (parav	ertebral l	olock)				
Ibarra 2011	5	15	7	14	39.3%	0.50 [0.11, 2.24]	-
Kairaluoma 2006	5	30	12	30	60.7%	0.30 [0.09, 1.00]	
Subtotal (95% CI)		45		44	100.0%	0.37 [0.14, 0.94]	
Total events	10		19				
Heterogeneity: τ2=0.0	00; $\chi^2$ =0.27, d	f=1 (P=0	60); f <sup>2</sup> =0%				
Test for overall effect:	Z=2.09 (P=0.	04)					
						-	<del></del>
						2000	0.1 0.2 0.5 1 2 5 1
						Favoi	urs experimental Favours contro



Andrae MH, 2013

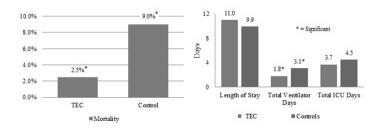
# **Epidurals in Trauma**

	TEC	Controls	P
N	158	301	N/A
Age (yrs)	53.4	52.2	0.44
Sex (Male/Female)	69%/31%	68%/32%	0.85
Mortality (%)	4 (2.5%)	27 (8.9%)	0.009
PE	4 (2.5%)	7 (2.3%)	0.89
DVT	5 (3.2%)	25 (8.3%)	0.034
ISS	18 (4-75)	18 (1-75)	0.016
Rib Fracture Count	6 (1-19)	6 (1-15)	0.054

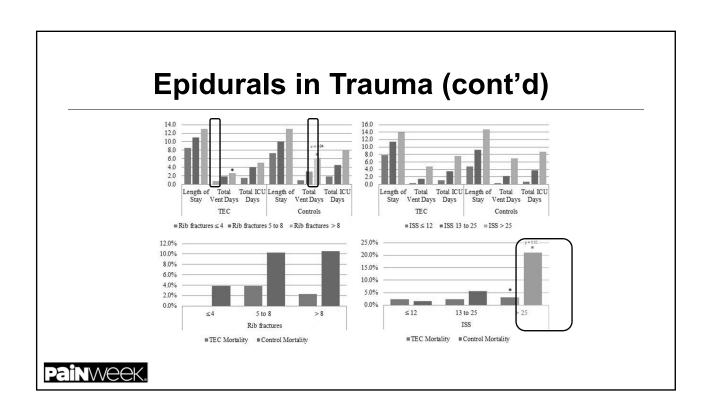


# **Epidurals in Trauma (cont'd)**

Thoracic Epidural Patients vs Matched Controls:







# PNAS

# Morphine paradoxically prolongs neuropathic pain in rats by amplifying spinal NLRP3 inflammasome activation



Peter M. Grace<sup>a,b,c,1</sup>, Keith A. Strand<sup>a,b</sup>, Erika L. Galer<sup>a,b</sup>, Daniel J. Urban<sup>d</sup>, Xiaohui Wang<sup>a,b,e,f,g,h</sup>, Michael V. Baratta<sup>a,b</sup>, Timothy J. Fabisiak<sup>a,b</sup>, Nathan D. Anderson<sup>a,b</sup>, Kejun Cheng<sup>l</sup>, Lisa I. Greene<sup>a,b</sup>, Debra Berkelhammer<sup>a,b</sup>, Yingning Zhang<sup>a,b</sup>, Amanda L. Ellis<sup>a,b</sup>, Hang Hubert Yin<sup>f,g,h,j</sup>, Serge Campeau<sup>a,b</sup>, Kenner C. Rice<sup>l</sup>, Bryan L. Roth<sup>d</sup>, Steven F. Maier<sup>a,b</sup>, and Linda R. Watkins<sup>a,b</sup>

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- Rodent model used to investigate whether administration of morphine following peripheral nerve injury would result in persistent neuropathic pain.
- Starting 10 days following sciatic chronic constriction injury (CCI) or sham surgery, animals were administered morphine (5mg/kg) or saline twice daily for 5 days.
- Results show that the brief course of morphine prolonged the duration of CCI-induced allodynia following treatment cessation (P <.001). First study to report such an effect.</li>
- The researchers also confirmed that this effect was mediated by dorsal spinal microglial reactivity, as well as NOD-like receptor protein 3 (NLRP3) inflammasome and related activation of IL-1β.



Proc Natl Acad Sci U S A. 2016 Jun 14;113(24):E3441-50.

### **Summary**

- Based on population-health statistics, a large number of people continue on opioids postoperatively
- Current postoperative prescribing practices are flooding the community with unused opioids
- Unused opioids are the main source of abused or diverted drugs
- Abused opioids appear to be a gateway to heroin and cocaine use
- Extending our reach beyond opioids can potentially impact both patients and society

