

The Pitfalls of Opioids in Workers Compensation

Brian D. Meek, M.D.

Board Certified Pain Management Physician

St. Peters, MO



Disclosures

➤ None

Outline

- ❖ Historic review
- ❖ Evaluating effects of opioids on the brain and nervous system
- ❖ Examining opioids in worker's compensation claims
- ❖ Recommendations for the paining patient
- ❖ Questions

How we arrived here...

- ◆ Initial opinion articles (1980 NEJM, 1986 *Pain*) stated minimal risk for opiate addiction
- ◆ American Pain Society publishes guidelines that advocated for doctors to expand their use of prescription narcotics to relieve pain
- ◆ Joint Commission issues pain management standards in 2001
- ◆ Patient expectation increases to have doctor “cure” their pain

Impact of opioid prescription

- ◆ Several medical societies recommend against the routine use of opiates for acute low back pain, yet use of potent analgesics continues to climb
- ◆ Opiates may be prescribed in response to patients' pain behaviors or demands rather than pain severity, objective physical findings, or pain duration
- ◆ Several studies have shown increased cost and healthcare utilization when opiates are prescribed
- ◆ Additional challenge in Worker's Compensation to address psychosocial factors contributing to pain

The Opiate Epidemic

NEW REPUBLIC

POLITICS | CULTURE | THE MAGAZINE

search...

SIGN IN

SUBSCRIBE NOW

International Orders | Give a Gift

HEALTH

MARCH 19, 2014

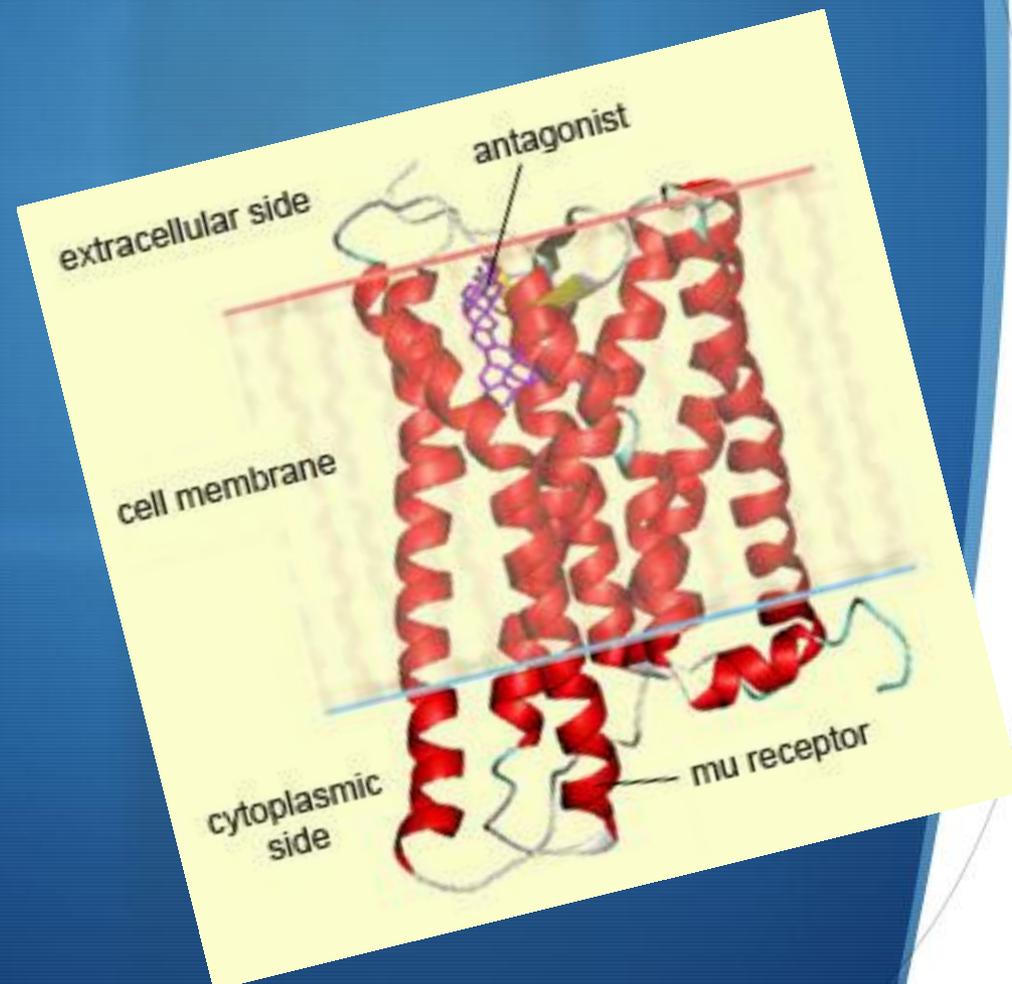
Drug Dealers Aren't to Blame for the Heroin Boom. Doctors Are.

BY **GRAEME WOOD**

 Share

 Tweet

Effects of Opioids



Systemic effects of opioid therapy

- ◆ Nervous system
 - ◆ Decreased pain
 - ◆ Sedation, slowed thinking, dizziness, myoclonus, itching
 - ◆ Worsening depression; dependence and addiction
- ◆ Respiratory system
 - ◆ Respiratory depression/apnea
- ◆ Gastrointestinal system
 - ◆ Constipation, nausea, vomiting
- ◆ Endocrine system
 - ◆ Decreased testosterone
- ◆ Immune system
 - ◆ Depressed immune function



Effects of chronic opioid exposure

Chronic opioid exposure

DESENSITIZATION
TOLERANCE

SENSITIZATION
(OIH)

PRONOCICEPTION

Dependence
Addiction

↔ Psychosocial factors

Increased opiate need

Clinically challenging overlay of tolerance, dependence, and sensitization.



Tolerance

- ◆ More medication is needed for the same clinical effect
- ◆ Occurs at the level of the cell
 - ◆ Less receptors for the drug to work
 - ◆ Production of fewer receptors
- ◆ Also more release of spinal levels of pain producing substances

Tolerance and dependence

TOLERANCE

Positive reinforcement

Euphoria, reward (mesocorticolimbic system)

Compensatory adaptations in regions that control somatic function, predominantly locus ceruleus. Symptomatic only on withdrawal.

Pain relief (pain systems)

DEPENDENCE

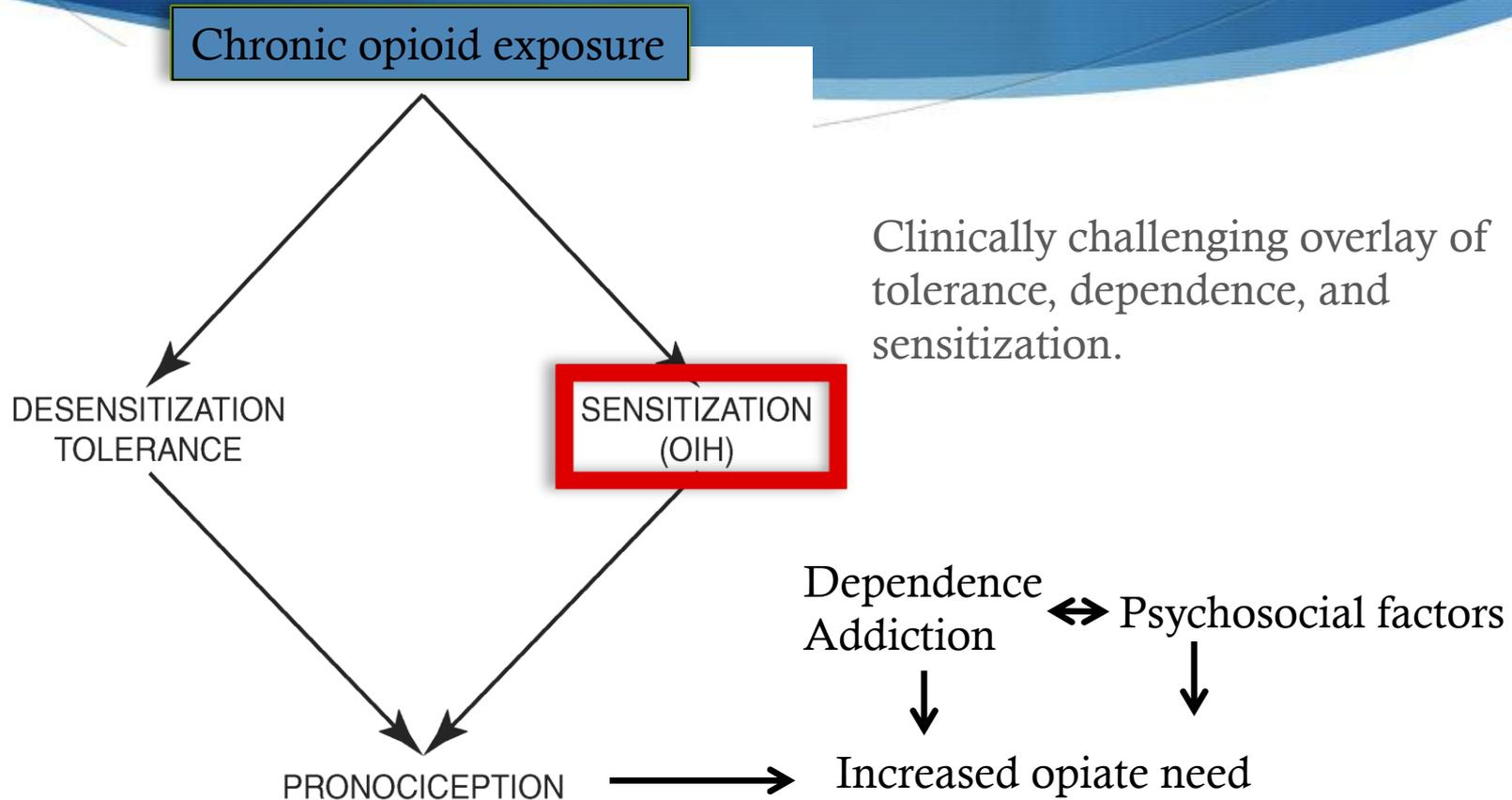
Negative reinforcement

Withdrawal anhedonia (let down)

Physical symptoms comprising central neurologic arousal and sleeplessness, irritability, tremor, agitation, diarrhea, vomiting, and phoresis

Withdrawal hyperalgesia

Effects of chronic opioid exposure



Sensitization/ Opioid-induced hyperalgesia (OIH)

Hyperalgesia is defined as an increased response to a stimulus which is normally painful.

OIH is the clinical syndrome where pain symptoms paradoxically worsen with increased exposure to opioids.

Q: Why would this
happen?

Opiate Induced Hyperalgesia



A: The Duality of the opioid receptor

Antinociceptive

- ◆ Opioid receptor closes Ca⁺ channels leading to less nerve activity
- ◆ Short term decrease in excitatory neurotransmitters
- ◆ Increases descending pain inhibition

Pronociceptive

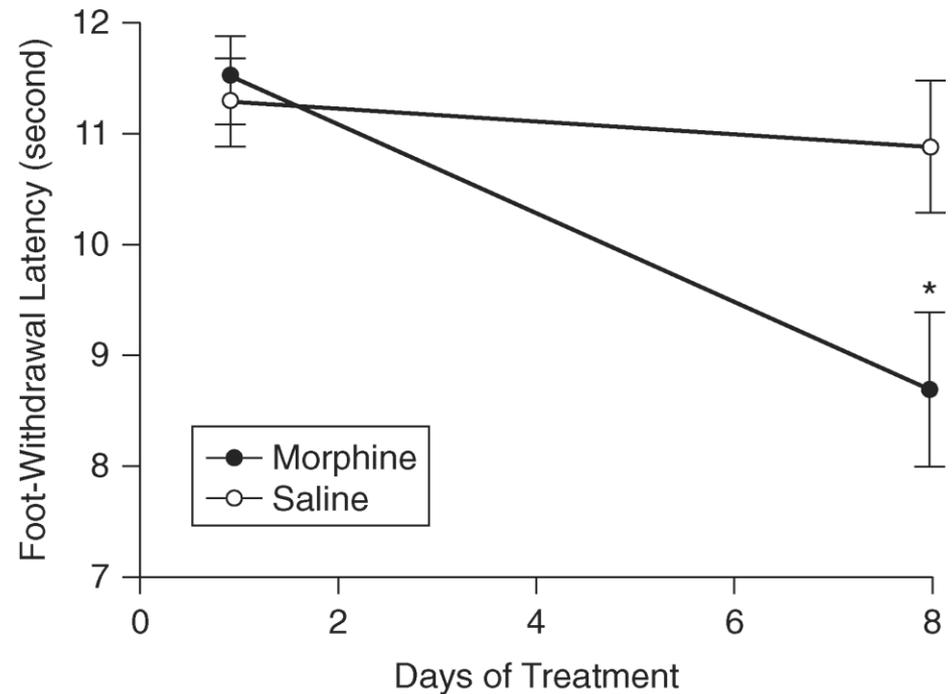
- ◆ Increased excitatory neurotransmitters with prolonged opioid receptor activation
- ◆ Prolonged exposure causes deactivation of cell membrane receptors
- ◆ Induction of painful spinal substances

Q: Does opioid-induced hyperalgesia exist?



OIH animal studies

Several *animal studies* have demonstrated that repeated administration of opiate medications creates a lasting reduction in baseline nociceptive threshold



OIH human clinical evidence

- ◆ Maintenance and withdrawal
 - ◆ Addicts maintained on methadone were 40-80% more sensitive to cold-pressor testing compared with addicts not maintained
- ◆ Chronic opiate use
 - ◆ Sensitivity to cold-pressor testing
 - ◆ Less relief diffuse noxious inhibitory control (DNIC) in opiate maintained patients
 - ◆ Increased pain with LA injection – direct correlation with opiate dose
- ◆ Volunteers
 - ◆ 30- to 90-minute infusion of remifentanyl dose-dependently aggravated preexisting skin hyperalgesia (up to 24 hours following infusion)

OIH Perioperative Evidence

Table 2 Studies in Patients Undergoing Surgery

Reference	Surgery	Intraoperative		Postoperative		Remarks
		Opioid	Dose	Opioid use	Pain	
Cooper (26)	Cesarean section	Fentanyl IT	0 vs. 25 µg	~60%↑	ND	N = 60; 23-hr observation
Chia (30)	Hysterectomy	Fentanyl IV	1 vs. 22 µg/kg	~120%↑	~30%↑	N = 60; 16-hr observation
Guignard (27)	Colectomy	Remifentanyl IV	0.1 vs. 0.3 µg/kg/min for 260 min	~85%↑	~50%↑	N = 50; 24-hr observation
Cortinez (31)	Gynecologic	Remifentanyl IV	0.1 vs. 0.23 µg/kg/min for 100 min	ND	ND	N = 60; 24-hr observation
Joly (28)	Colectomy	Remifentanyl IV	0.05 vs. 0.4 µg/kg/min for 260 min	~30%↑	ND ^{a,b}	N = 50; 48-hr observation
Lee (32)	Colorectal	Remifentanyl IV	N2O vs. 0.17 µg/kg/min for 140 min	ND	ND	N = 60; 24-hr observation
Crawford (29)	Scoliosis	Remifentanyl IV plus MS vs. MS alone	0.28 µg/kg/min for 460 min ^c	~30%↑	ND	N = 30; 24-hr observation

^aMeasures of secondary hyperalgesia were increased (~25%↓ in mechanical pain threshold and 120%↑ in area).

^bPrevented by intraoperative (0.5 mg/kg → 5 µg/kg/min) and postoperative (2 µg/kg/min for 48 hr) ketamine.

^cIntraoperative MS consumption was 198 versus 237 µg/kg/min for group R and MS, respectively.

Abbreviations: IT, intrathecal, IV, intravenous, ND, not different, N, number of patients.

OIH Perioperative Evidence



A photograph of a man in a white dress shirt and a red patterned tie sitting at a desk in an office. He is leaning back in his chair, holding his lower back with both hands, indicating pain. On the desk in front of him is a computer monitor, a keyboard, a mouse, and a telephone. To the right, there is a filing cabinet. The background consists of white vertical blinds. The entire image is tilted and framed by a blue border.

Opioids in Workers Compensation



Do opiates reduce pain and improve function in WC?

- ◆ Franklin et. al. prospectively evaluated injured workers with low back pain in Washington
- ◆ 42% (**781/1843**) received opiate in year following injury mostly soon after injury; 16% received opiates all 4 quarters
- ◆ Morphine equivalent dose (MED) increased significantly for those receiving opiates all 4 quarters

TABLE 1. Mean Morphine Equivalent Dose (mg) per Quarter Among Workers who Filled at Least 1 Opioid Prescription in the First Quarter

Quarters of Prescription Fills (n)	Q1 Mean (SD)	Q2 Mean (SD)	Q3 Mean (SD)	Q4 Mean (SD)
Q1 only (410)	465 (711)			
Q1 Q2 (103)	1209 (1452)	1053 (2436)		
Q1 Q2 Q3 (70)	1829 (2038)	2394 (3680)	1350 (2094)	
Q1 Q2 Q3 Q4 (111)	2364 (4019)	2518 (3446)	3077 (4998)	3824 (5998)

Q: What percentage of patients had 30% reduction of pain on opioids?

- A. 75%
- B. 50%
- C. 25%
- D. 15%

Q: What percentage of patients had 30% improvement of function with opioids?

- A. 75%
- B. 50%
- C. 25%
- D. 15%

Do opiates reduce pain and improve function in WC?

- ◆ Franklin et. al. prospectively evaluated injured workers with low back pain in Washington
- ◆ 42% (**781/1843**) received opiate in year following injury mostly soon after injury; 16% received opiates all 4 quarters
- ◆ Morphine equivalent dose (MED) increased significantly for those receiving opiates all 4 quarters
- ◆ Improvement by at least 30% of long term users (all 4 quarters):
 - ◆ Pain 26%
 - ◆ Function 16%
- ◆ After adjustment for baseline pain, function, and injury severity, the strongest predictor of longer term opioid prescription was total MED in the first quarter.

Impact of early opioid prescribing

- ◆ Webster et. al analyzed a cohort of 8443 claimants from a large WC database with new-onset LBP
- ◆ Goal of study was to evaluate the effect of morphine equivalent amount provided in the first 15 days on disability duration, medical cost, need for surgery, and late opioid use
- ◆ Covariates included age, gender, job tenure, and low back injury severity

Table 1. Demographic Characteristics of the Study Cohort

Cohort Characteristic	Total (n = 8443)	MEA Received in First 15 Days Postinjury				
		0 mg (n = 6651)	1–140 mg (n = 437)	141–225 mg (n = 494)	226–450 mg (n = 423)	450+ mg (n = 438)
Age (yr)	40.3 (10.4)	40.3 (10.4)	39.6 (10.3)	40.8 (10.7)	40.6 (9.5)	40.7 (9.7)
Female (%)	28.2	28.4	28.2	22.1	29.3	30.8
Tenure (yr)	7.5 (7.9)	7.6 (7.9)	7.0 (7.4)	7.5 (8.1)	7.5 (8.1)	6.2 (7.1)
MEA (mg)	81.9 (262.7)	0.0	85.9 (30.5)	181.3 (30.2)	339.6 (67.4)	960.4 (613.3)
Disability (days)	130.0 (209.9)	121.1 (204.3)	124.1 (202.3)	149.6 (217.4)	175.5 (232.7)	204.2 (245.0)
Medical costs (U.S.\$)	12,188 (34,569)	10,441 (30,555)	13,196 (29,474)	15,686 (34,656)	18,449 (37,774)	27,613 (70,343)
Surgery (%)	9.8	7.9	10.5	11.9	15.6	23.5
Late opioid (%)	10.4	7.2	13.5	18.8	23.4	34.3
High severity (%)	26.1	24.6	22.2	31.2	35.9	37.2

Table 2. Multivariate Linear Regression Model Examining Association Between Morphine Equivalent Amount (MEA) and Disability Duration (days) After Controlling for Severity, Age, Gender, and Job Tenure

Variable	Change in Mean Disability Duration	95% Confidence Intervals	<i>P</i>
MEA (mg)			
450+	69.1	49.3 to 89.0	<0.001
226–450	43.8	23.7 to 63.9	<0.001
141–225	21.9	3.2 to 40.6	0.022
1–140	5.2	–14.6 to 25.0	0.609
0	0.0	—	—
High severity	88.5	78.5 to 98.5	<0.001
Age (yr)	1.6	1.1 to 2.0	<0.001
Female gender	–0.1	–9.9 to 9.7	0.985
Tenure (yr)	–1.7	–2.3 to –1.1	<0.001

Table 3. Multivariate Linear Regression Model Examining Association Between Morphine Equivalent Amount (MEA) and Medical Costs (U.S.\$) After Controlling for Severity, Age, Gender, and Job Tenure

Variable	Change in Mean Medical Cost	95% Confidence Intervals	<i>P</i>
MEA (mg)			
450+	15,523	12,230 to 18,816	<0.001
226–450	6690	3348 to 10,033	<0.001
141–225	4399	1292 to 7506	0.006
1–140	3017	–270 to 6304	0.072
0	0	—	—
High severity	11,346	9686 to 13,006	<0.001
Age (yr)	111	34 to 187	0.005
Female gender	–723	–2353 to 907	0.385
Tenure (yr)	–146	–248 to –45	0.005

Table 5. Logistic Regression Model Examining Association Between Morphine Equivalent Amount (MEA) and Late Opioid Use After Controlling for Severity, Age, Gender, and Job Tenure

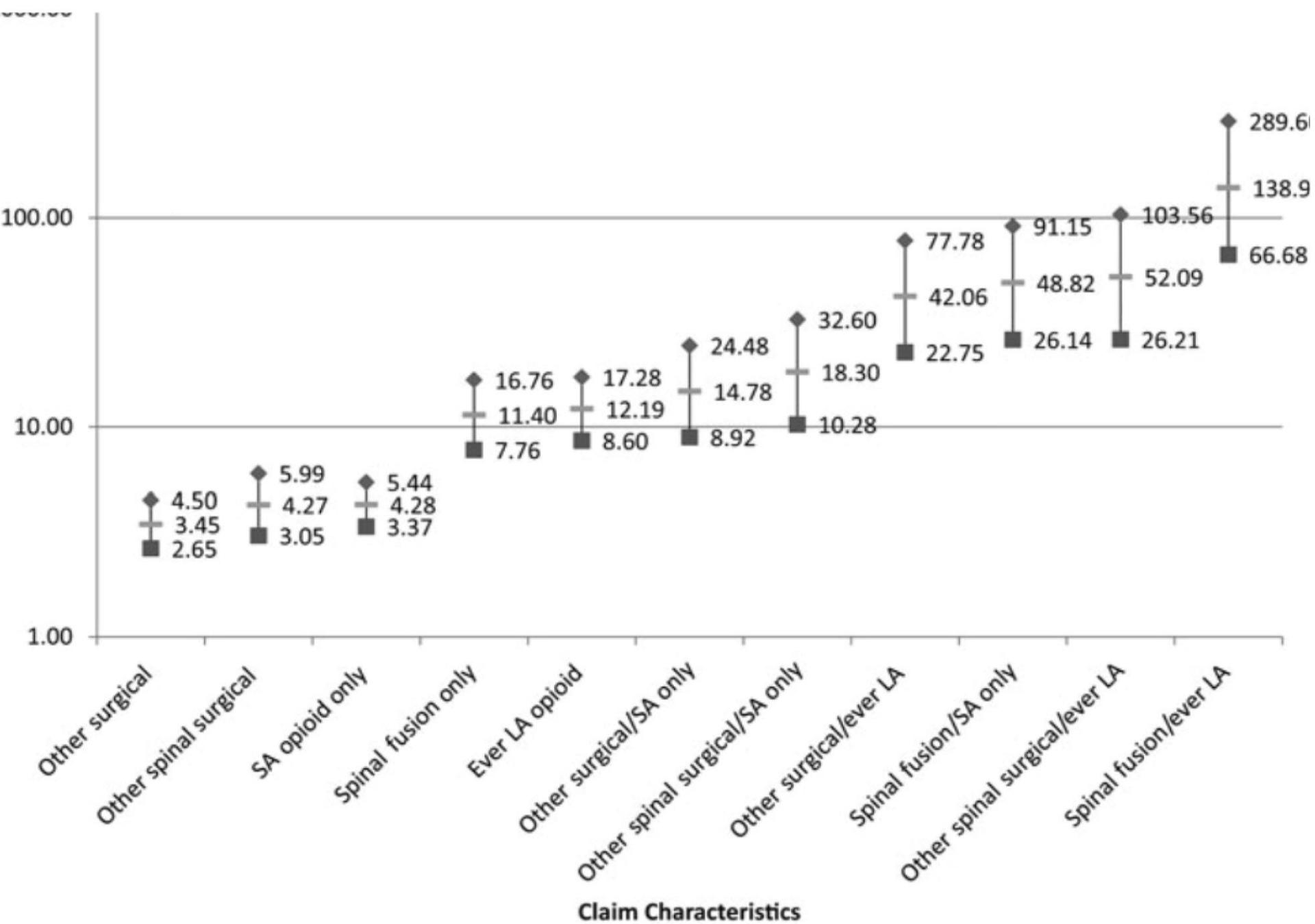
Variable	Odds Ratio	95% Confidence Intervals	<i>P</i>
MEA (mg)			
450+	6.14	4.92 to 7.66	<0.001
226–450	3.69	2.88 to 4.73	<0.001
141–225	2.89	2.25 to 3.69	<0.001
1–140	2.08	1.55 to 2.78	<0.001
0	—	—	—
High severity	2.02	1.74 to 2.34	<0.001
Age (yr)	1.02	1.01 to 1.02	<0.001
Female gender	1.02	0.87 to 1.20	0.783
Tenure (yr)	0.98	0.97 to 0.99	<0.001

Opioids and surgery

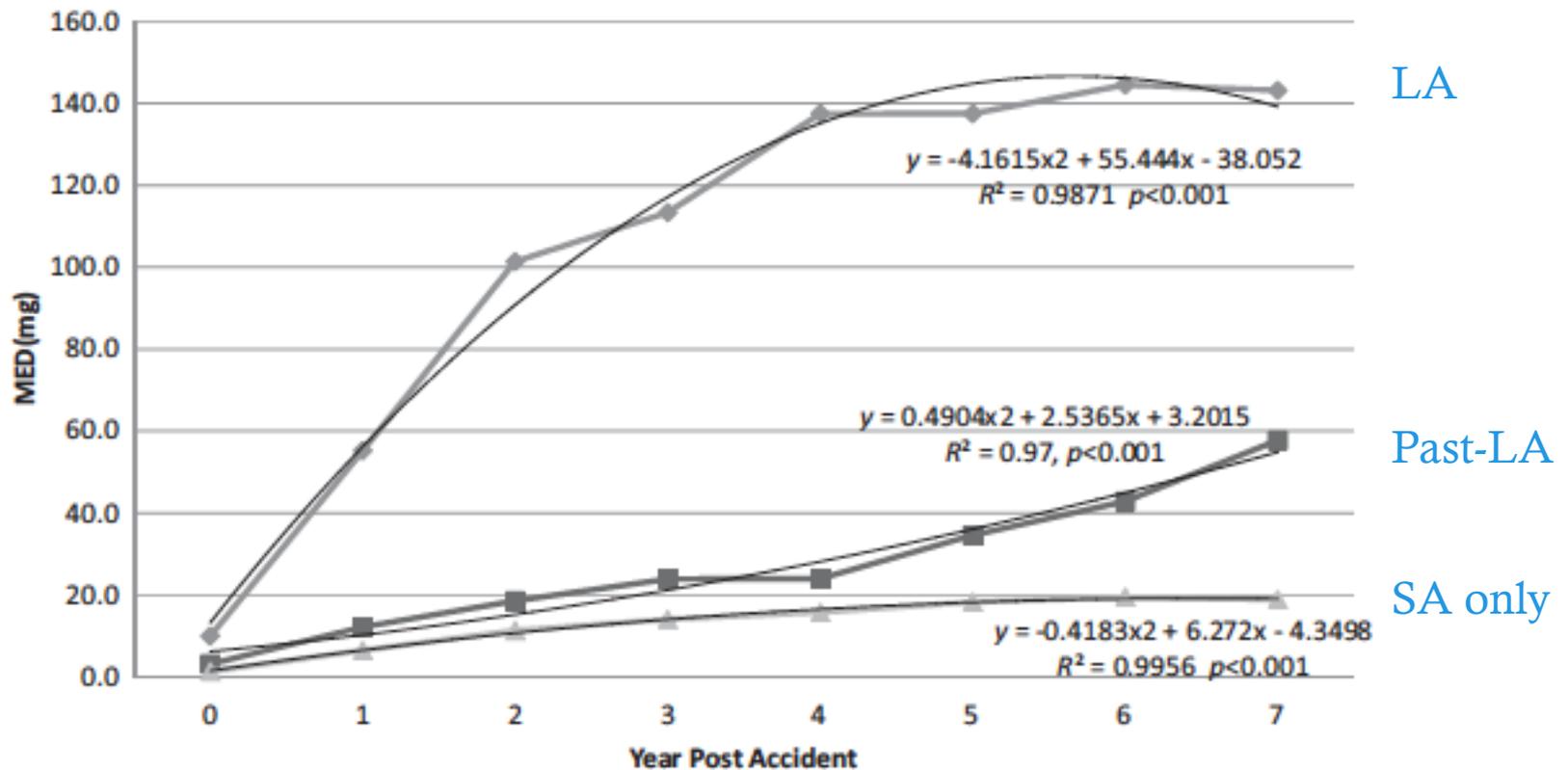
TABLE 3. The Association of Opioid Usage and Surgical Procedures With the Risk of Final Claim Cost

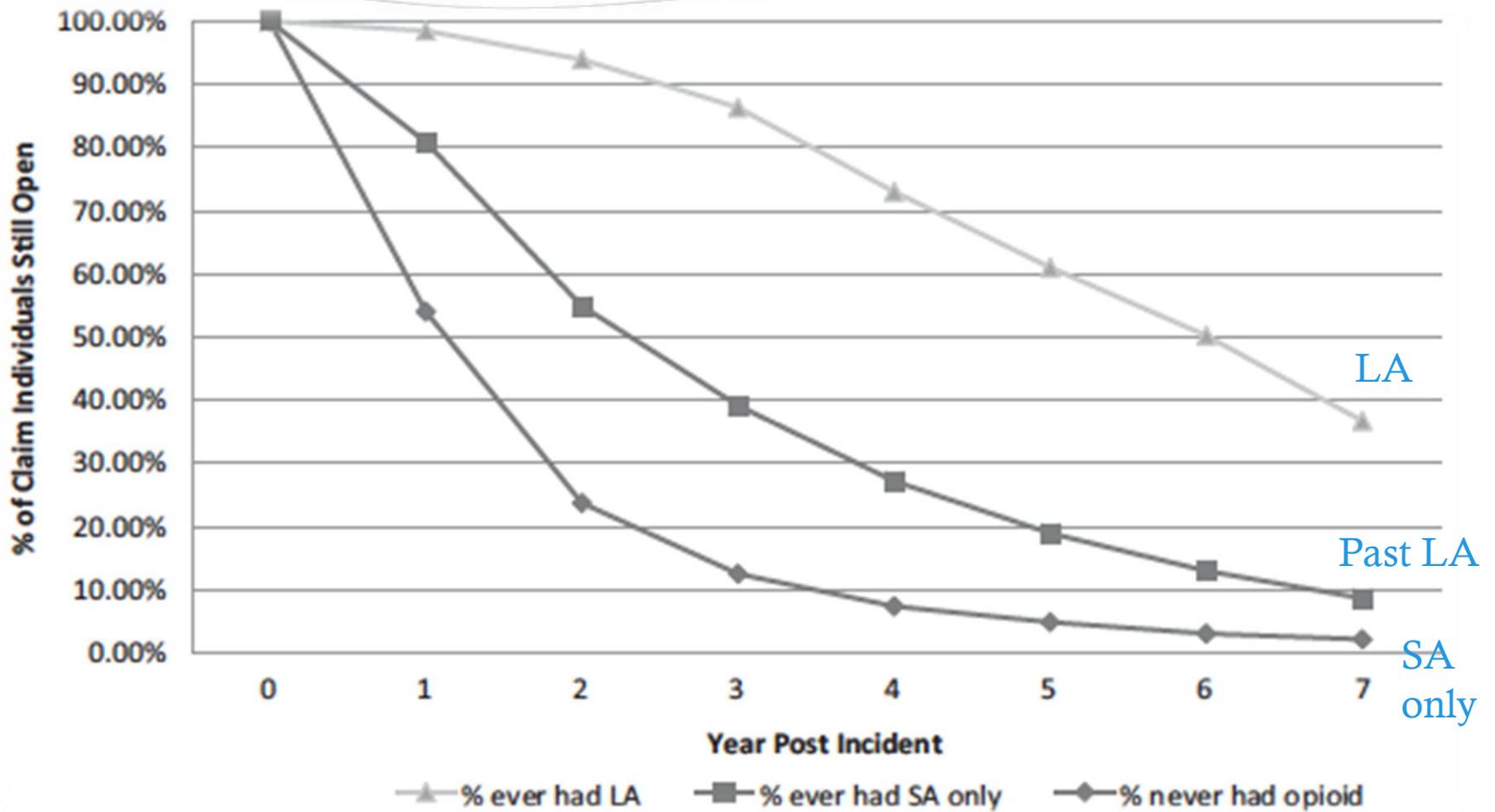
Variables	For Final Cost at \$50,000 to <\$100,000		For Final Cost at \geq \$100,000	
	OR	95% CI	OR	95% CI
Spinal injection vs nonspinal injection	1.16	0.87–1.55	1.87	1.43–2.44
SA opioid only vs nonopioid	4.78	3.83–5.96	4.28	3.37–5.44
Ever LA opioid vs nonopioid	6.84	4.67–10.02	12.19	8.60–17.28
Other surgical vs nonsurgical	3.66	2.87–4.66	3.45	2.65–4.50
Other spinal surgical vs nonsurgical	5.51	3.97–7.66	4.27	3.05–5.99
Spinal fusion vs nonsurgical	6.81	4.47–10.37	11.40	7.76–16.76

The ORs were from logistic regression model controlling for gender, attorney involvement, claim duration, and each other. The analysis used claims <\$50,000 as reference group. 95% CI, 95% confidence interval; LA, long-acting; OR, odds ratio; SA, short-acting.



What happens over time?





LA

Past LA

SA only

Recommendations for the paining patient



Recommendations for acute low back pain

- ◆ Focus on evidence-based care
- ◆ Identify and counsel and fears or misconceptions
- ◆ Address occupational safety issues
- ◆ Consider frequent visits for continued education and verification of treatment compliance
- ◆ Return to work
- ◆ Opioids not recommended; nonopioid analgesics can be considered

Recommendations for opioid management

- ◆ Prescribe opioids at minimum effective dose for the shortest duration possible
- ◆ Proper education of patient should be provided in regards to the risk of opioid medication
- ◆ Sustained-release/long-acting opioid formulations should not be prescribed for work-related injuries
- ◆ Obtain Pain Management consultation for
 - ◆ Opioid requirement greater than 40mg/d MED
 - ◆ Morphine equivalent dose greater than 450mg in first 15 days
 - ◆ Continued opioid prescriptions 3 months post injury

In conclusion...

- ◆ Opioid pain medication should be prescribed cautiously given potential risk and poorer outcomes in workers compensation
- ◆ Limited efficacy of chronic opioids may not be solely related to side effects or psychosocial factors, but a physiologic response to prolonged opioid exposure
- ◆ Understanding the evidence and effective alternatives will improve outcomes, ultimately reducing catastrophic claims

Questions?



References

- Cohen SP, Christo PJ, Wang S, et al. The effect of opioid dose and treatment duration on the perception of a painful standardized clinical stimulus. *Reg Anesth Pain Med* 2008; 33(3):199–206.
- Franklin et al. Opioid Use for Chronic Low Back Pain: A Prospective, Population-based Study Among Injured Workers in Washington State, 2002-2005. *Clin J Pain* 2009; 25:743–751.
- Gounder, Celine. “Who is responsible for the pain-pill epidemic” *The New Yorker*; November 8, 2013.
- Mao Jianren. Opioid-induced hyperalgesia. Informa Healthcare, New York: 2010.
- Tao et al. Impact of the Combined Use of Opioids and Surgical Procedures on Workers’ Compensation Cost Among a Cohort of Injured Workers in the State of Louisiana. *JOEM*; 54(12): 1513-1519
- Tao et. al Natural History of Opioid Dosage Escalation Post-Injury A Cohort Study of Injured Workers in the State of Louisiana. *JOEM*; 54(4): 439-444
- Ueda H, Inoue M. Peripheral morphine analgesia resistant to tolerance in chronic morphine-treated mice. *Neurosci Lett* 1999; 266(2):105–108.
- Webster BS et al. Relationship Between Early Opioid Prescribing for Acute Occupational Low Back Pain and Disability Duration, Medical Costs, Subsequent Surgery and Late Opioid Use. *Spine* 2007;32:2127–2132