Five Tips for Hospitalists Managing Opioids

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The past attitude about inpatient opioids: What happens in the hospital, stays in the hospital.
The past attitude about inpatient opioids:
What happens in the hospital stays in the hospital

Increasing awareness:
Inpatient opioids have many similar risks as in other contexts, and exist in a continuum with those contexts
Five common inpatient scenarios:

• 1. Opioids for pain in an opioid naïve person
• 2. The unseen medical complication of opioids
• 3. What is a “pain flare”? 
• 4. The nonfatal opioid overdose
• 5. Opioid addicts in pain
TIP 1.
For opioid naïve patients, keep post-operative and acute pain opioid prescriptions:

-Time limited
-Lowest reasonable dose
-Short acting only
Acute pain and post-operative opioid outcomes:

• Preventing chronic opioid use after surgery
• Predicting opioid addiction after surgery
• Opioid-related complications after surgery?
Probability of continued opioid use depending on initial total MME *(not opioid use disorder!)*

https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm?s_cid=mm6610a1_w
Predictors of ongoing opioid use after a hospital admission

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% confidence interval)</th>
<th>ρ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.19 (1.14–1.25)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Insurance, (ref = Medicaid)</td>
<td>1.04 (0.79–1.36)</td>
<td>0.78</td>
</tr>
<tr>
<td>Discount payment plan</td>
<td>0.73 (0.52–1.03)</td>
<td>0.07</td>
</tr>
<tr>
<td>Medicare</td>
<td>0.43 (0.25–0.73)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Commercial</td>
<td>0.54 (0.31–0.92)</td>
<td>0.02</td>
</tr>
<tr>
<td>Milligrams of morphine per hospital day, (ref = 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.01 &lt; 10</td>
<td>1.65 (1.09–2.52)</td>
<td>0.02</td>
</tr>
<tr>
<td>10 &lt; 51</td>
<td>2.08 (1.47–2.93)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>51 &lt; 100</td>
<td>2.23 (1.49–3.35)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>100+</td>
<td>3.37 (2.15–5.41)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Number of healthcare encounters in the 1 year preceding the index admission, (ref = 0)</td>
<td>0.05 (0.47–0.84)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Receipt of opioid at discharge, (ref = no)</td>
<td>2.33 (1.78–3.04)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Past year number of opioid prescriptions filled, (ref = 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.99 (1.46–2.71)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>2</td>
<td>3.31 (2.26–4.83)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>3</td>
<td>4.19 (2.47–7.12)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>4–9</td>
<td>9.87 (6.33–15.37)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Past year receipt of non-opioid analgesics, (ref = no)</td>
<td>1.92 (1.49–2.48)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Past year benzodiazepine receipt, (ref = no)</td>
<td>1.89 (1.26–2.82)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Three-year history of any substance use disorder, (ref = no)</td>
<td>1.24 (0.98–1.56)</td>
<td>0.07</td>
</tr>
<tr>
<td>Three-year history of a chronic pain diagnosis, (ref = no)</td>
<td>1.79 (1.41–2.26)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Surgery during index hospitalization, (ref = no)</td>
<td>0.57 (0.44–0.74)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>1.11 (1.05–1.17)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Number of subsequent hospitalizations within 12 months post hospital discharge, (ref = 0)</td>
<td>1.51 (1.39–1.64)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
1.4% continue opioids one year after surgery.
• Risk of post-op **opioid addiction 0.2%**

• Risk factors:
  • Tobacco use disorder RR=2
  • Preop Major Depressive D/o RR=1.6
  • Dose of opioids+10 MME/day=0.8% incr risk
  • Duration of opioids+7days=20% incr risk
(Risk of opioid use disorder)
• Inpatient post op risk cluster:
  • Higher inpatient dose of opioids
  • More hospital days on opioids
  • Longer hospital stay
  • Higher readmission rate (OR 1.3)
  • Higher in hospital mortality (OR 28.8)
  • Higher discharge to care facilities
  • $8225 extra cost to system

Unknown which of these are causative

Shafi Association of opioid related adverse drug events with clinical and cost outcomes among surgical patients JAMA surg may 23 2018
Tip 1 summary

- The exhaustive study of opioid effects is turning towards inpatient care.
- Post-op and inpatient opioids appear to be total dose dependent predictive of ongoing use.
- Duration of use may confer risk of addiction.
- Mental health, addictive history and poly-pharmacy are important risk factors.
- Inpatient opioid use may affect medical outcomes.
- Expect more detailed info in the coming years.
TIP 2.
Consider the medical complications of opioids:

- Falls/fractures/accidents
- Cardiovascular events
- Pneumonia
- Immunosuppression
- Respiratory compromise
- Sleep disordered breathing
- And the obvious ones:
  - Nausea, Pruritus, Constipations, QT prolongation
Opioids and fractures...

- All opioids are associated with falls and fractures
- Short acting opioids more likely
- First 14 days highest risk
- Tramadol: least fractures
- Codeine: most fractures


Opioid safety in older patients (vs ibuprofen)

- Opioids vs NSAIDs in the elderly
- Falls RR 4.5; all cause mortality 1.9
**Figure.** Kaplan-Meier curves for the cumulative incidence of the 6 composite safety measures. 

A, Composite cardiovascular events. B, Upper or lower gastrointestinal tract bleeding. C, Composite fracture. D, Any of the individual safety events resulting in hospitalization. E, Any of the individual safety events leading to immediate death or a hospitalization with death. F, All-cause mortality. P values were determined with the log-rank test. Coxibs indicates selective cyclooxygenase-2 inhibitors; nsNSAIDs, nonselective nonsteroidal anti-inflammatory drugs.
• Tennessee Medicaid patients initiating new long-acting opioid or analgesic anticonvulsant/tricyclic antidepressant in 1999-2012
• Excess out-of-hospital deaths: 67/10,000 person years
Opioid use predisposes to pneumonia:

Sedation and aspiration

Embargoed until Monday, April 24th at 1:30pm ET

Deaths Associated with Opioid Use and Possible Infectious Disease Etiologies Among Persons in the Unexplained Death (UNEX) Surveillance System — Minnesota, 2006–2015

Victoria Hall, R. Lynfield, N. Wright, L. Hiber, J. Palm, J. Christensen, K. Smith, S. Holzbauer
Opioid Analgesic Use and Risk for Invasive Pneumococcal Diseases: A Nested Case–Control Study

Andrew D. Wiese, PhD; Marie R. Griffin, MD, MPH; William Schaffner, MD; C. Michael Stein, MB, ChB; Robert A. Greevy, PhD; Edward F. Mitchell Jr., MS; Carlos G. Grijalva, MD, MPH

Article, Author, and Disclosure Information

Abstract

Background: Although certain opioid analgesics have immunosuppressive properties and increase the risk for infections in animals, the clinical effects of prescription opioid use on infection risk among humans are unknown.

Objective: To test the hypothesis that prescription opioid use is an independent risk factor for invasive pneumococcal disease (IPD).

Design: Nested case–control study.

Setting: Tennessee Medicaid database linked to Medicare and Active Bacterial Core surveillance system databases (1995 to 2014).

Patients: 1233 case patients with IPD aged 5 years and older matched to 24 399 control participants by diagnosis date, age, and county of residence.
Which opioids are most immuno-compromising?

• Different opioids may have different levels of immunosuppressive activity
• Long acting is worse
• Morphine, methadone and fentanyl may be worse

• Wiese clinical infectious disease 15 September 2018
New opioid rx doubles the mortality in older adults with copd

Opioids worsen sleep apnea...

- 45% patients on opioids have severe sleep apnea
- Often mixed OSA and CSA
- 17% pure central sleep apnea
- Increased obesity in opioid users

Published online 2014 Aug 15. doi: [10.5664/jcsm.3952](https://doi.org/10.5664/jcsm.3952)

Effect of Opioids on Sleep and Breathing in Chronic Pain Patients

M. Jeffery Mador, M.D. and Jennifer Henderson, D.O.

[Author information](https://doi.org/10.5664/jcsm.3952) ➤ [Article notes](https://doi.org/10.5664/jcsm.3952) ➤ [Copyright and License information](https://doi.org/10.5664/jcsm.3952) ➤ [Disclaimer](https://doi.org/10.5664/jcsm.3952)
Summary tip 2:

- Opioids have a variety of important medical complications
- Understanding of these issues is only now emerging
- These are rare events: they usually do not represent absolute contraindications to opioids
- We should begin to consider these complications in the risk benefit discussions of opioids
TIP 3.
Keep your DDX broad for a pain flare in a patient using opioids chronically:

- Inpatient admissions for pain flares often represent a complex mix of events
- The pragmatic solution for a given inpatient (give them opioids) may fuel a destructive cycle for the populations
- Consider all causes of the pain flare early in the admission
What is a pain flare?

• A pain flare is increased pain due to increased activity or progression of underlying disease
What else can a pain flare be?

• A pain flare is increased pain due to increased activity or progression of underlying disease

• Pain flares from *opioid withdrawal* and no change of disease activity
What else can a pain flare be?

• A pain flare is increased pain due to increased activity or progression of underlying disease

• Pain flares from *opioid withdrawal* and no change of disease activity
  • Or both increased disease activity and withdrawal
Differentiating disease activity from withdrawal

- Look at PMP for likely home supply of opioids
- Establish the time of the next opioid refill
- Determine the presence/absence of home opioids
- GI symptoms suggest withdrawal
- Look for biomarkers of the disease activity
- Immediate resolution of observed discomfort with opioids
What else can a pain flare be?

• A pain flare is increased pain due to increased activity or progression of underlying disease

• Pain flares from *opioid withdrawal* and no change of disease activity

• Pain flares from mental health crisis
What else can a pain flare be?

• A pain flare is increased pain due to increased activity or progression of underlying disease
• Pain flares from *opioid withdrawal* and no change of disease activity
• Pain flares from mental health crisis
  • Mental health crisis mixed with disease activity and withdrawal
Differentiating disease activity from mental health crisis

- Is the patient distractible?
- Do the pain symptoms not correspond with the disease physiology?
- Is there a known mental health diagnosis?
- Are there simultaneous obvious mental health symptoms?
What else can a pain flare be?

• A pain flare is increased pain due to increased activity or progression of underlying disease
• Pain flares from *opioid withdrawal* and no change of disease activity
• Pain flares from mental health crisis
• Drug seeking behavior
## DSM-5 addiction criteria

**FIGURE 1. DSM-IV and DSM-5 Criteria for Substance Use Disorders**

<table>
<thead>
<tr>
<th>DSM-IV Abuse&lt;sup&gt;a&lt;/sup&gt;</th>
<th>DSM-IV Dependence&lt;sup&gt;b&lt;/sup&gt;</th>
<th>DSM-5 Substance Use Disorders&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazardous use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Social/interpersonal problems related to use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Neglected major roles to use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Legal problems</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Withdrawal&lt;sup&gt;d&lt;/sup&gt;</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Tolerance</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Used larger amounts/longer</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Repeated attempts to quit/control use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Much time spent using</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Physical/psychological problems related to use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Activities given up to use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Craving</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

<sup>a</sup> DSM-IV Abuse

<sup>b</sup> DSM-IV Dependence

<sup>c</sup> DSM-5 Substance Use Disorders

- ≥1 criterion
- ≥3 criteria

AmJ Psych Aug 2013 170:8 Hasin et al
What else can a pain flare be?

- A pain flare is increased pain due to increased activity or progression of underlying disease
- Pain flares from *opioid withdrawal* and no change of disease activity
- Pain flares from mental health crisis
- Drug seeking behavior
  - All of the above!
Pain

- Disease progression
- Opioid withdrawal
- Opioid craving
- Mental health crisis
Often inpatients have multiple issues of these at once!
If a patient is ready for discharge but wont go unless they get opioids....

• .... You may have failed to identify a serious problem earlier in the admission (such as mental health crisis, withdrawal, opioid addiction)
When the most efficient solution to a patient’s request for opioids is to give them opioids when not indicated....

• ... you may be creating a worse problem in the future:
  For that patient
  For the practice of hospital medicine
TIP 3 summary

• Hospital admissions have been the “cheat code” for highly complex toxicological, psychiatric, addictive, and pain cases
• The easiest thing to do in the moment is to give opioids
• But long term this cycles back to worsen the problem
• Identify all contributors to the problem early in the hospital stay
TIP 4.
Nonfatal opioid overdoses require careful interventions:

- Diagnostic interview for opioid use disorder
- Counseling on and referral for medication assisted therapy
- Communication with outpatient providers
- Naloxone
Overdose Deaths Involving Opioids, United States, 2000-2016

- Any Opioid
- Other Synthetic Opioids (e.g., fentanyl, tramadol)
- Commonly Prescribed Opioids (Natural & Semi-Synthetic Opioids and Methadone)
- Heroin

FIGURE. Percentage of naloxone administrations by emergency medical services and percentage of opioid-related deaths, by age – 2012 and 2016


Source: Multiple Cause of Death Data, 2016, National Vital Statistics System, CDC.

The figure above consists of two line graphs showing the percentage of naloxone administrations by emergency medical services and the percentage of opioid-related deaths by age in 2012 and 2016.
Nonfatal overdose & hospitalization
la Rochelle Annals 2016
Risk for repeat overdose

- Nonfatal repeat overdose 29.5% first year
- Fatal repeat overdose 1.2% first year
  - Bzd HR 1.7
  - Heroin HR 1.6
  - Ventilation HR 1.9

Olfson et al Drug and alc dependence 1sept 2018 p112
One year after a nonfatal opioid overdose:

- 26% SUD related death
  - 130 fold increase mortality over general population
- 13% CV disease death
- 10% cancer death
- The rest, other: Suicide, COPD, HIV
Treatment post nonfatal overdose

• All cause mortality 4.7/100 person years
• Opioid overdose mortality 2.1/100 person years
• Few are offered life saving treatments:
  • 11% methadone 17% buprenorphine 6% naltrexone
  • Decreased all cause mortality 0.47; opioid OD mortality 0.41
  • Buprenorphine>methadone
  • Naltrexone no effect on mortality (low numbers)
• Meds only worked while patients were on them
• Larochelle ann int med 2018; 169: p137
Relationship between opioid MME and death
Other interventions for opioid overdose

• Dramatically lower the opioids prescribed
• Discontinue the benzodiazepines
• Check the PMP
• Communicate with the outpatient prescribers
• Very close follow up
• Careful counseling on risk of death- include loved ones
Tip 4 summary

• A nonfatal opioid overdose is a critical moment to intervene and coordinate life saving treatments with outpatient providers
5. Pain in a patient with opioid use disorder
Three FDA Approved Treatments for Opioids Addicts

• Methadone– full replacement drug
• Naltrexone– full blocker
• Buprenorphine– replacement AND blocker

• Any of these will change how opioids work for pain, but have minimal on any other medication
Buprenorphine

• Long half life
• Very high affinity
• Partial activity (40%) at Mu receptor
• Not for acute pain
• May interfere with full agonist opioids
• Often desirable to stop buprenorphine when treating pain with opioids
• Resuming buprenorphine may precipitate withdrawal
• Searchable on PMP
• Inpatient docs can continue it without a DEA waiver while inpatient
Methadone (for addiction)

- Long half life
- Very high affinity
- **Full activity** (40%) at Mu receptor
- Not for acute pain
- Coprescribing with full agonist opioids ok
- Not searchable on PMP
- Inpatient docs can continue/adjust methadone for current MMT patient as appropriate while inpatient
- In select circumstances, inpatient docs can initiate methadone for addiction while inpatient
Naltrexone

- Oral= 24-36 hours; IM=30 days
- Very high affinity
- **Antagonist** at Mu receptor
- Will block full agonist opioids
- Must stop naltrexone when treating pain with opioids
- Resuming naltrexone will precipitate withdrawal
- Not searchable on PMP
- Inpatient docs can continue it and prescribe at time of discharge
There are actually many ways to manage postop pain in a buprenorphine or methadone patient.

Some providers are now continuing buprenorphine.

If uncertain consult with an experienced doc.
Five common inpatient scenarios:

• 1. Opioids for pain in an opioid naïve person
• 2. The unseen medical complication of opioids
• 3. What is a “pain flare”? 
• 4. The nonfatal opioid overdose 
• 5. Opioid addicts in pain
Thanks!
Questions?