

## Perioperative Management of Patients on Buprenorphine

A concise review and recommendations for perioperative management

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## Disclosures

- None

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## Learning Objectives

1. Describe the mechanism of action and unique pharmacokinetic/pharmacodynamic properties of buprenorphine
2. Understand the clinical indications for buprenorphine use
3. Increase familiarity with perioperative management strategies for buprenorphine
4. Understand the importance of multimodal and multidisciplinary analgesic strategies

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Case

- 36 yo female with Crohn's Disease
- Small bowel obstruction with strangulation
- History of opioid addiction on Suboxone therapy



- What is optimal perioperative management?
- Would that change if this was elective surgery?

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Annals of Internal Medicine

IDEAS AND OPINIONS | 1 DECEMBER 1990

Improving Outcomes of Analgesic Treatment: Is Education Enough?

Mitchell B. Max, MD



The Joint Commission  
*The Source*

The Fifth "Vital Sign"  
Complying with Pain Management Standard PC.01.02.07

"Therapeutic use of opiate analgesics rarely results in addiction..."

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1980  
Vol. 302 No. 2

THE NEW ENGLAND  
JOURNAL OF MEDICINE

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

*To the Editor:* Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients<sup>1</sup> who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,<sup>1</sup> Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER  
HERSHEL JICK, M.D.  
Boston Collaborative Drug Surveillance Program  
Waltham, MA 02154 Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Sione D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

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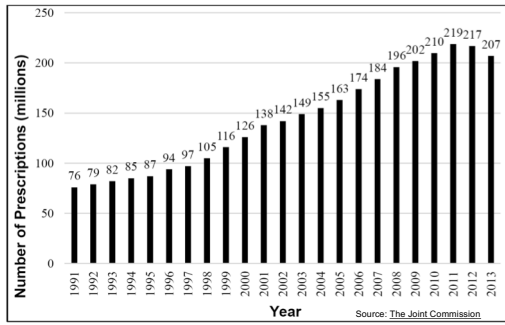
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Figure 1. Opioid Prescriptions Dispensed by U.S. Retail Pharmacies, 1991-2013.



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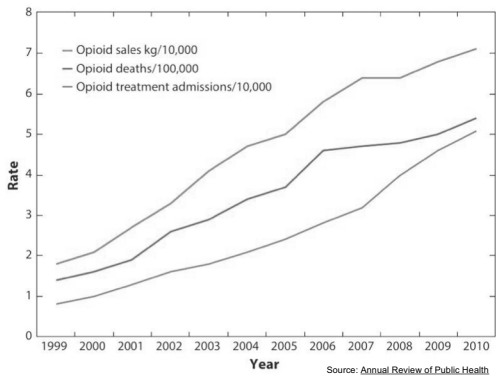
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Goals of Anesthesiologists?

1. Don't let your patient die
2. Try not to let your patient suffer

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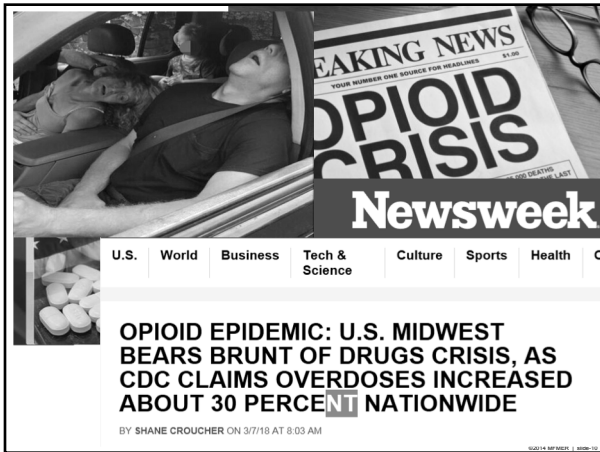
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**Opioid use disorder**

- Chronic neurobehavioral disease characterized by a pattern of *opioid use* that causes significant impairment or distress
  - Strong desire to *use opioids*
  - Increased tolerance to *opioids*
  - Withdrawal when *opioids* are discontinued
- More than 2 million Americans
- 2 common medication-assisted treatment strategies:
  - **Methadone**
    - Full  $\mu$ -receptor agonist, NMDA antagonist
    - Slow onset of action, long half life
  - **Buprenorphine**
    - Increasingly used for chronic pain

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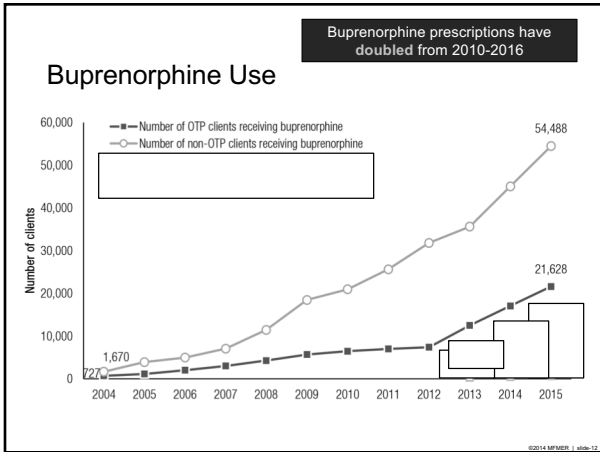
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### Buprenorphine Mechanism of Action



- Partial  $\mu$ -receptor agonist
  - High affinity, low activity, slow dissociation
  - 30x more potent than morphine
  - Reduces binding of other opioids by 80-95%
  - Competitively displaces traditional opioids
  - Reduces craving, withdrawal symptoms
  - Ceiling effect (less respiratory depression?)
- $\kappa$  and  $\delta$  receptor antagonist
  - Reduces subjective “high”, respiratory toxicity

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### Pharmacokinetics

- Rapid onset of action
  - 30-60 minutes sublingual
  - 5-15 minutes IV
- Broad inter-patient half-life variability (24-60 hrs)
- High volume of distribution, high protein binding
- Metabolized by liver CYP3A4
  - Norbuprenorphine – 25% potency
  - Avoid in severe hepatic dysfunction
- Primarily biliary excretion (15% urine)
  - Low risk in CKD (caution with GFR < 30 ml/min)

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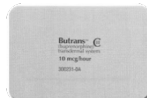
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### Formulations

- Sublingual
  - Subutex (tab) – buprenorphine
  - Zubsolv (tab) – buprenorphine + naloxone
  - Suboxone (film) – buprenorphine + naloxone
- Buccal
  - Bunavail – buprenorphine + naloxone
  - Belbuca – buprenorphine
- Transdermal
  - Butrans (patch) – buprenorphine, change every 7 days
- Subdermal
  - Probuphine (implant) – replaced every 6 months
- Injection
  - Sublocade – monthly subcutaneous injection
  - Buprenex – IV/IM injection



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### Why is buprenorphine used for chronic pain?

- Opioid-naïve patients with chronic pain, transdermal fentanyl  $\approx$  transdermal buprenorphine<sup>1</sup>
- In those with opioid use disorder, reductions in chronic pain noted after buprenorphine initiation<sup>2</sup>
- Slower development of opioid tolerance when compared to other full agonists (e.g. morphine)<sup>3</sup>
- Reduces opioid-induced hyperalgesia, in part related to Kappa receptor antagonism<sup>4</sup>
- Reduces treatment-resistant depression<sup>5</sup>

1. Mitra et al. Pain Med 2013. 4. Koppert et al. Pain 2005.  
2. Anderson et al. Anesthesiology 2017. 5. Karp et al. J Clin Psychiatry 2014.  
3. Gutwinski et al. Harm Reduct J 2016. ©2014 MPMER | 450-15

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### What is optimal perioperative management?

- Multiple approaches
- Little evidence (case reports, expert opinion)
- Same goals as for all patients:
  - Guide safely through perioperative period
  - Avoid iatrogenic harm (relapse, overdose)
  - Treat perioperative pain and suffering
  - Promote return to preoperative function

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### Risks with poor management?

- Pain under-treatment
- Pain over-treatment (e.g. respiratory events)
- Opioid use disorder relapse, return to addiction



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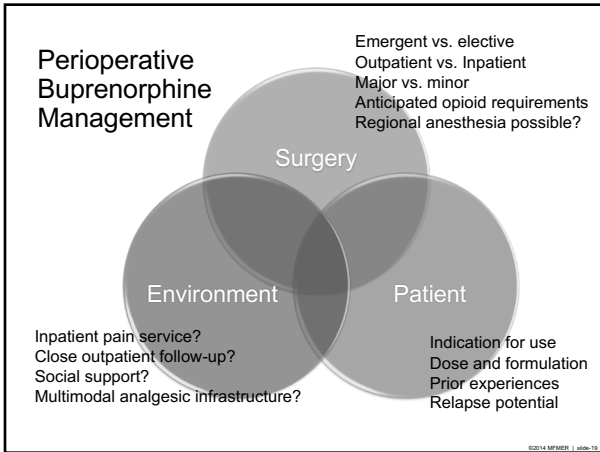
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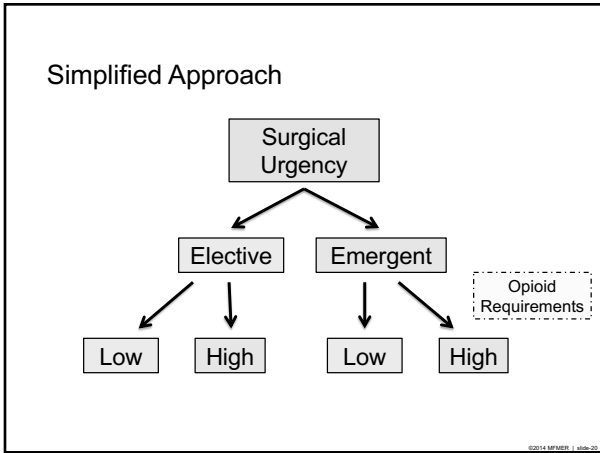
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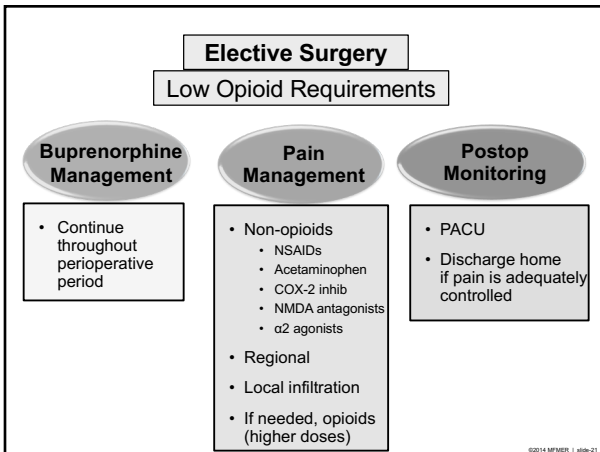
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**Elective Surgery**

Mod-High Opioid Requirements

Buprenorphine Management	Pain Management	Postop Monitoring
<ul style="list-style-type: none"> <li>• Discontinue 3-5 days before surgery</li> <li>• Discuss bridging with short course full agonist therapy to manage withdrawal symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• Non-opioids                             <ul style="list-style-type: none"> <li>• NSAIDs</li> <li>• Acetaminophen</li> <li>• COX-2 inhib</li> <li>• NMDA antag</li> <li>• α2 agonists</li> </ul> </li> <li>• Regional / Local</li> <li>• Full mu agonist therapy (higher doses, short acting, use PCA)</li> </ul>	<ul style="list-style-type: none"> <li>• PACU</li> <li>• Continuous respiratory monitoring (e.g. remote pulse oximetry)</li> <li>• Consider ICU admission for difficult to control pain</li> </ul>

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**Emergent Surgery**

Low Opioid Requirements

Buprenorphine Management	Pain Management	Postop Monitoring
<ul style="list-style-type: none"> <li>• Continue throughout perioperative period</li> <li>• No dose change or taper</li> </ul>	<ul style="list-style-type: none"> <li>• Non-opioids                             <ul style="list-style-type: none"> <li>• NSAIDs</li> <li>• Acetaminophen</li> <li>• COX-2 inhib</li> <li>• NMDA antag</li> <li>• α2 agonists</li> </ul> </li> <li>• Regional / Local</li> <li>• Opioids if needed</li> </ul>	<ul style="list-style-type: none"> <li>• PACU</li> <li>• Regular hospital floor</li> <li>• Discharge home if pain is adequately controlled</li> </ul>

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**Emergent Surgery**

Mod-High Opioid Requirements

Buprenorphine Management	Pain Management	Postop Monitoring
<ul style="list-style-type: none"> <li>• Ascertain timing of last dose</li> <li>• Discontinue (remove patch)</li> <li>• No additional doses to be given</li> </ul>	<ul style="list-style-type: none"> <li>• Non-opioids                             <ul style="list-style-type: none"> <li>• NSAIDs</li> <li>• Acetaminophen</li> <li>• COX-2 inhib</li> <li>• NMDA antagonists</li> <li>• α2 agonists</li> </ul> </li> <li>• Regional / Local</li> <li>• Full mu agonist therapy (higher doses, use PCA)</li> </ul>	<ul style="list-style-type: none"> <li>• PACU</li> <li>• ICU for respiratory monitoring and aggressive pain control</li> </ul>

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Why intensive care?

- To watch for the transition point
  - As buprenorphine dissociates from receptors, full  $\mu$ -agonists will have greater clinical effect and side effects
- Timing highly variable
  - Half life 24-60 hours

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Things to Consider with Discontinuation

- Preoperatively
  - Discussion with surgeon, original prescriber (pain, addiction specialist)
    - Create tapering plan and assess need for short-acting opioids after taper
  - Pre-emptive analgesia
  - Expectation setting

**Risks?** Increased care complexity, Increased burden for prescribers & patients

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Things to Consider with Discontinuation

- Intraoperatively
  - Multimodal analgesia
    - NSAIDS, acetaminophen
    - Gabapentinoids
    - Ketamine
    - $\alpha$ 2 agonists
    - NMDA antagonists
    - Local anesthetics
  - Anticipate higher doses of opioids
  - Clear communication with entire anesthesia and surgical team

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Things to Consider with Discontinuation

• Postoperative

- Pain service
- Care

**Multidisciplinary multimodal analgesia**

social support network

**Risks?** Increased complexity, increased burden for prescribers, introduces period of withdrawal, potential increase risk for relapse

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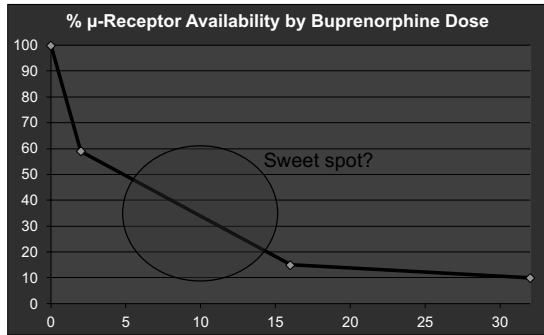
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Should we consider continuation at lower dose?



Data derived from Greenwald et al. Neuropsychopharmacology 2003 ©2014 MPMER | slide-29

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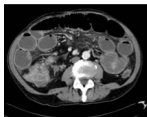
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Case

- 36 yo female with Crohn's Disease
- Small bowel obstruction with strangulation
- History of opioid addiction on Suboxone therapy



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### What about OB patients?

- Little evidence, most suggest continuation:
- Vaginal delivery or Cesarean
  - Continue buprenorphine therapy
  - Use neuraxial techniques when possible
    - Does not interfere with local anesthetics
  - Optimize non-opioid agents
    - Scheduled acetaminophen, NSAIDs
  - Short-acting full  $\mu$ -agonists available if necessary
    - Increased doses will likely be needed, particularly if regional anesthesia is not possible

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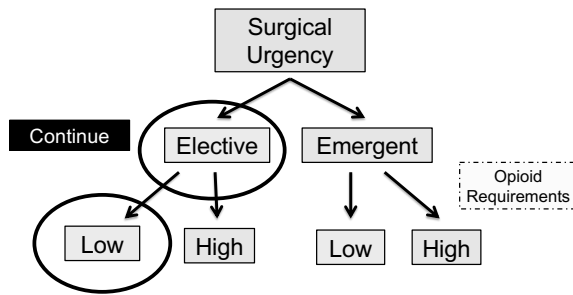
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### Review



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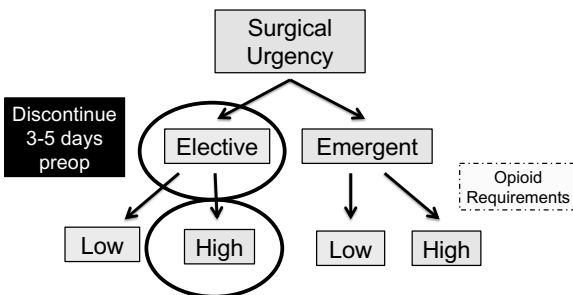
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### Review



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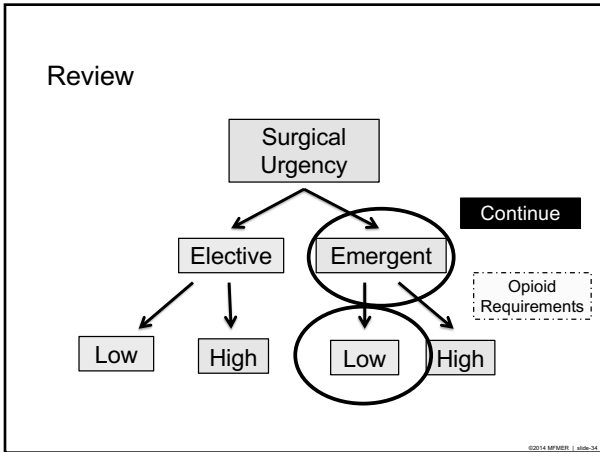
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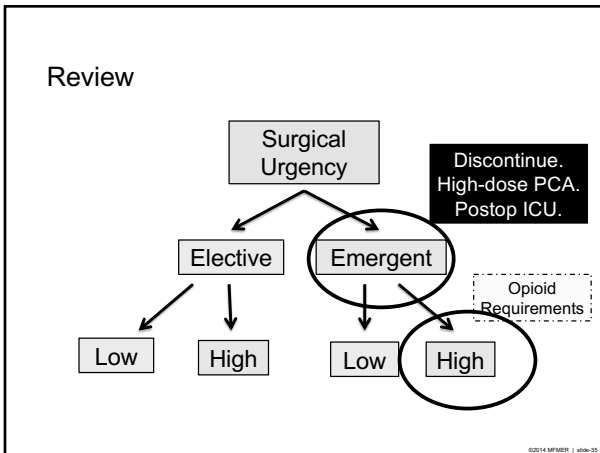
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Summary

- Buprenorphine use will continue to increase
- Surgical, patient, and environmental factors
- We must avoid under-treatment and over-treatment
- Multidisciplinary, multimodal analgesia

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Questions & Discussion

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