Hot topic: Management of patients with opioid addiction or dependence across the health care system

GMCCP Spring Educational Event/Business Meeting
Thursday June 2\textsuperscript{nd}, 2016

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Disclosures

• The speakers have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.
Objectives

• Explain current trends in overprescribing and abuse of opioids.
• Identify at least 3 efforts currently being implemented to help decrease overprescribing and abuse of opioids.
• Describe the role of opioid overdose education and naloxone distribution programs in reducing opioid overdose-related deaths.
• Identify key components of the VA Opioid Safety Initiative for patients on opioids with chronic, non-cancer pain.
• Summarize two pain management goals of therapy for patients with opioid addiction.
• Design a treatment plan for the management of pain in a patient with co-existing opioid addiction.
Opioid Overprescribing and Abuse: Ambulatory Considerations

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Ambulatory Pharmacy Clinical Coordinator
Residency Program Director – PGY1 Community Pharmacy
Aurora Health Care Metro, Inc.
Is there really a problem?
Medical examiner: Six probable overdose deaths in 24-hour period; 189 total for the year

White Americans Are Dying Younger as Drug and Alcohol Abuse Rises- New York Times

The Latest: Investigators consider overdose in Prince death

Opioids leading to new class of heroin abusers, study finds

888* Bodies and Counting
Opioids

• Natural opioids
  – Morphine and codeine

• Semi-synthetic opioids
  – Oxycodone, hydrocodone, hydromorphone, and oxymorphone

• Synthetic opioids
  – Methadone, tramadol, fentanyl
Opioid Prescribing

• 2000-2010:
  – Pain consistently discussed in 1 in 5 visits ambulatory visits related to non-malignant pain
  – Prescribing of non-opioid analgesics remained unchanged
  – Prescribing of opioids nearly doubled
    • 11.3% of visits \( \rightarrow \) 19.6% of visits

• 1999-2014:
  – Opioid prescription sales nearly quadrupled

Centers for Disease Control and Prevention. MMWR 2011; 60(43);1487-1492.
# US Opioid Prescribing: 2012

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Opioid Prescriptions [n, millions (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family practice</td>
<td>52.5 (18.2)</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>43.6 (15.1)</td>
</tr>
<tr>
<td>Non-physician prescriber&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32.2 (11.2)</td>
</tr>
<tr>
<td>General practice&lt;sup&gt;b&lt;/sup&gt;</td>
<td>32.2 (11.2)</td>
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<tr>
<td>Surgery&lt;sup&gt;c&lt;/sup&gt;</td>
<td>28.3 (9.8)</td>
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<tr>
<td>Dentistry</td>
<td>18.5 (6.4)</td>
</tr>
<tr>
<td>Pain medicine&lt;sup&gt;d&lt;/sup&gt;</td>
<td>14.5 (5)</td>
</tr>
<tr>
<td>Emergency medicine</td>
<td>12.5 (4.3)</td>
</tr>
<tr>
<td>Physical med and rehab</td>
<td>9.3 (3.2)</td>
</tr>
<tr>
<td>All others&lt;sup&gt;e&lt;/sup&gt;</td>
<td>45.3 (15.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>289 (100)</strong></td>
</tr>
</tbody>
</table>

<sup>a</sup>Non-physician prescriber: nurse practitioner, physician assistant; <sup>b</sup>General practice: osteopathic medicine, general practice, and preventive medicine; <sup>c</sup>Surgery: general, orthopedic, plastic, cardiothoracic, vascular, colorectal, spinal, neurologic; <sup>d</sup>Pain medicine: anesthesiology, pain medicine; <sup>e</sup>All others: cardiology, critical care, dermatology, endocrinology, gastroenterology, geriatrics, hematology, infectious disease, neurology, obstetrics and gynecology, oncology, otolaryngology, palliative care, pathology, pediatrics, podiatry, psychiatry, pulmonology, radiology, rheumatology, urology, veterinary, and “unspecified”

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Assessment Question

Which specialty accounts for nearly half of all dispensed opioid prescriptions in the United States?

A. Pain management
B. Orthopedics
C. Primary care
D. Emergency medicine
Assessment Question

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A. Pain management
B. Orthopedics
C. **Primary care**
D. Emergency medicine
Opioids

• Tolerance
  – Diminished response to a drug with repeated use

• Physical dependence
  – An adaptation to a drug that produces symptoms of withdrawal when the drug is stopped

• *Tolerance and physical dependence can both occur in the absence of opioid use disorder*
Opioids

• Opioid use disorder
  – Abuse, misuse or addiction
  – Problematic pattern of opioid use leading to clinically significant impairment or distress

• Overdose
  – Injury to the body when a drug is taken in excessive amounts
  – Can be fatal or nonfatal
Opioid Misuse in the US

- 2014: Nearly 2 million people abused or were dependent on opioids

- >1,000 people/day treated for misuse of opioids in the ED

- >70% of people abusing opioids get them through friends or relatives
  - Given, bought, or stolen
Source of Opioids for Non-Medical Users

- Prescribed by 1 or more physicians: 70.6%
- Other (e.g. fake prescriptions): 19.7%
- Bought from a drug dealer or other stranger: 5.5%
- Given by a friend or relative for free: 4.2%
- Bought from a friend or relative: 1.6%
- Stolen from a friend or relative: 0.8%

Wisconsin Department of Justice. A Dose of Reality: Medical. 2016.
US Opioid Overdose Deaths

• 1999-2014: Opioid overdose deaths quadrupled
  – 2014: >14,000 deaths from opioid-related overdoses
  – Highest risk:
    • 25-54 years old
    • Whites, American Indians & Alaskan Natives > Blacks and Hispanics
    • Men > Women

• Most common opioids in overdose deaths:
  – Methadone, oxycodone, hydrocodone
Opioid Overdose Deaths
United States, 2000-2014
WI Opioid Overdose Deaths

- WI Department of Health Services
  - 2014: 843 drug overdose deaths
    - 47% prescription opioids
    - 28% heroin

- WI Department of Justice
  - Opioid overdoses in people 12-25 years old have increased by 260%
Milwaukee County
Opioid Overdose Deaths

• 888* Bodies and Counting
  – Report released by the Office of Common Council President Michael J. Murphy

• 2012-2015 in Milwaukee County:
  – 888 overdose deaths due to opioids or heroin
    • Average age: 43 years old
    • 67% White, 24% Black, 6% Hispanic
    • Men > Women

Murphy M. 888* Bodies and Counting. 2016.
Assessment Question

According to the Centers for Disease Control and Prevention (CDC), since 1999, the rate of overdose deaths involving opioids has:

A. Not changed
B. Doubled
C. Tripled
D. Quadrupled
Assessment Question

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A. Not changed
B. Doubled
C. Tripled
D. Quadrupled
What efforts are being made to fight opioid abuse?
President Obama Is Taking More Steps to Address the Prescription Drug Abuse and Heroin Epidemic – the whitehouse

Senate approves bills to battle heroin, opiate abuse in Wis. – News 8000

Governor Walker signs series of bills aimed at curbing opiate abuse

Wisconsin Assembly passes HOPE bills targeting prescription drug abuse – The Cap Times

30 tons of prescription drugs collected smashes record, state AG says – WSJ

“888 bodies in three years:” Funding approved to find solution to heroin epidemic in Milwaukee

‘Dose of Reality’ campaign launched: Emphasizes dangers of misused prescription drugs

Wisconsin Department of Justice. A Dose of Reality: Medical. 2016.
Fox 6 Now. 2016.
Efforts to Curb Opioid Abuse

• National Efforts
  – CDC Guidelines for Prescribing Opioids for Chronic Pain
  – FDA Label Changes for Opioids
  – U.S. Department of Health and Human Services initiatives

• State & Local Efforts
  – State Prescription Drug Monitoring Program (PDMP)
  – Heroin, Opioid Prevention and Education (HOPE) Agenda
  – Pharmacy Society of Wisconsin Resources
  – Medication Collection
National Efforts to Curb Opioid Abuse
CDC Opioid Prescribing Guidelines

• Recommendations for primary care providers prescribing opioids for chronic pain in patients 18 years and older
  – Pain > 3 months or past time of normal tissue healing
  – Not related to active cancer, palliative, or end-of-life care

• Promote collaboration with behavioral health providers, pharmacists, and pain management specialists
CDC Opioid Prescribing Guidelines

• Twelve recommendations with goals to:
  – Improve communication about risks and benefits of opioid therapy
  – Improve safety and effectiveness of pain treatment
  – Reduce risks associated with long-term opioid therapy

• Areas for consideration:
  – Determining when to initiate or continue opioids for chronic pain
  – Opioid selection, dosage, duration, follow-up, and discontinuation
  – Assessing risk and addressing harms of opioid use
CDC Opioid Prescribing Guidelines

- Determining when to initiate or continue opioids for chronic pain
  - Prefer non-pharmaceutical therapy and non-opioid pharmaceutical therapy
    - Only consider opioid therapy if benefits for both pain and function > risks
  - Establish realistic goals for pain and function with patient before starting opioids
    - Consider how therapy will be discontinued if benefits < risks
  - Discuss risks and realistic benefits of opioids before starting and periodically during therapy
CDC Opioid Prescribing Guidelines

- Opioid selection, dosage, duration, follow-up, and discontinuation
  - When starting opioid therapy for chronic pain:
    - Immediate-release opioids preferred over extended-release or long-acting opioids
    - Start with lowest effective dose
      - Reassess benefits and risks if dose ≥ 50 morphine mg equivalents (MME) per day
      - Avoid doses ≥ 90 MME per day
    - Evaluate benefits and risks within 1-4 weeks of initiation or dose increase
      - Reevaluate every 3 months
      - Taper or discontinue if benefits < risk
CDC Opioid Prescribing Guidelines

• Opioid selection, dosage, duration, follow-up, and discontinuation
  – When starting opioid therapy for acute pain:
    • Prescribe lowest effective dose of immediate release opioids
    • Do not prescribe a greater quantity than needed
      – Generally 3 days or less
      – Rarely more than 7 days
CDC Opioid Prescribing Guidelines

• Assessing risk and addressing harms of opioid use
  – Evaluate risk factors for opioid-related harms before starting and periodically during therapy
    • Consider factors that increase risk for opioid overdose:
      – History of substance use disorder, opioid doses ≥ 50 MME per day, concurrent benzodiazepines
  • Create risk management strategies for patients
    – Offer naloxone via collaborative practice models with pharmacists
    – Use urine drug tests before starting therapy and then annually
    – Offer treatment for patients with opioid use disorder

CDC Opioid Prescribing Guidelines

• Assessing risk and addressing harms of opioid use
  – Review history of controlled substance prescriptions using state PDMP data when starting and periodically during therapy
    • Every prescription or at least every 3 months
  – Avoid prescribing opioids and benzodiazepines in combination if possible
    • Review the patient’s PDMP history
    • Consider involving pharmacists and pain specialists when opioids are used with other CNS depressants
FDA Label Changes for Opioids

• 2013: FDA required label changes for extended-release and long-acting opioids
  – Product indications, limitations of use, and warnings
  – Boxed warnings to more effectively communicate serious risks

FDA Label Changes for Opioids

• March 2016:
  – FDA requires label changes for immediate-release opioids
    • Boxed warning: risk of misuse, abuse, addiction, overdose & death
    • Immediate-release opioids reserved for pain severe enough to require opioids
    • Clarifies initial dosage, dosage changes and warns against abrupt discontinuation
    • Warns that chronic maternal use of opioids during pregnancy can result in neonatal opioid withdrawal syndrome

FDA Label Changes for Opioids

• March 2016:
  – FDA also requires updated labeling for all opioids
    • Safety information about:
      – Risk of serotonin syndrome
      – Effects on endocrine system
        ▪ Adrenal insufficiency & androgen deficiency
    • Clarifies risk of negative outcomes exists regardless of indication
      – Pain vs. medication-assisted treatment

U.S. Department of Health and Human Services initiatives

1. Provide training and educational resources to help reduce opioid overprescribing

2. Increase the use of naloxone

3. Expand the use of Medication-Assisted Treatment (MAT)
   – Use of buprenorphine or methadone plus counseling and behavioral therapies
State & Local Efforts to Curb Opioid Abuse
WI Prescription Drug Monitoring Program (PDMP)

• Collects information about monitored prescription drugs dispensed to patients in WI
  – Monitored prescription drugs
    • Controlled substances in schedules II-V
    • Tramadol – schedule IV drug effective August 18, 2014
  – Currently submit data within 7 days of monitored prescription drug dispensing
WI Prescription Drug Monitoring Program (PDMP)

• 2010:
  – Legislative direction for WI Pharmacy Examining Board (PEB) to create PDMP

• 2013:
  – January 1: Dispensers start collecting data
  – June 1: PDMP fully operational
  – October 1: Begin sharing data with other states
WI Prescription Drug Monitoring Program (PDMP)

• Current access to PDMP Data:
  – Direct access only available to dispensers, practitioners and their delegates
  – Must submit a formal request for PDMP data:
    • Patients and patient delegates
    • Healthcare review organizations
    • Federal and state agencies
    • DSPS investigatory staff
    • Medical examiners
    • Researchers
    • Law enforcement
Utilizing WI PDMP in Practice

• Creating an account - Search: WI PDMP
  – Database Access → Prescriber and Pharmacist
  – Training Guide for Wisconsin Practitioners and Pharmacists
    • Registration
      – Master & Delegate Accounts
        ▪ Need WI license number
    • Patient queries
      – WI recipient & multi-state queries
WI PDMP Statistics

• January-September 2015:
  – 8,242,636 monitored prescriptions dispensed
    • 6,581,973,371 tablets dispensed

• Top 5 monitored prescription drugs
  – Hydrocodone/acetaminophen
  – Dextroamphetamine/amphetamine
  – Tramadol
  – Oxycodone
  – Alprazolam
Assessment Question

Who can access data collected by the Wisconsin Prescription Drug Monitoring Program (PDMP) without having to submit a formal request for data or to provide sufficient proof to the Pharmacy Examining Board?

A. Patients and patient delegates
B. Pharmacists, practitioners, and their delegates
C. Law enforcement
D. Medical examiners
Assessment Question

Who can access data collected by the Wisconsin Prescription Drug Monitoring Program (PDMP) without having to submit a formal request for data or to provide sufficient proof to the Pharmacy Examining Board?

A. Patients and patient delegates

B. Pharmacists, practitioners, and their delegates

C. Law enforcement

D. Medical examiners
WI HOPE Agenda

• Heroin, Opioid Prevention and Education (HOPE) Agenda
  • Legislative agenda led by WI State Rep. John Nygren
  • 2013-2016:
    – 17 proposals introduced to combat Wisconsin’s heroin epidemic
    – All 17 proposals have been passed by WI state legislature and signed into law by Governor Walker
2013 WI Act 199

• Effective April 9, 2014:
  – Schedule II and III controlled substances may not be dispensed or delivered to a patient or patient’s representative without an identification card
  – Name on identification card and name of person picking up the medication must be recorded
  – Pharmacist may ask the patient to designate an authorized person to pick up the medication
2013 WI Act 199

• Exceptions:
  – Pharmacist has personal knowledge of the patient or authorized person picking up the medication
  – Medication is administered or dispensed directly to the patient by a practitioner
  – Medication is delivered to a health care facility to be administered in the health care facility
2015 WI Act 266

• Effective April 1, 2017:
  – PDMP data submission frequency will increase
    • No later than 11:59 PM of the next business day after dispensing
  – Will require prescribers to review PDMP data prior to issuing a prescription order unless:
    • Patient receiving hospice care
    • Prescription is for a number of doses intended to last 3 days or less
    • Monitored prescription drug is administered to the patient
    • Due to an emergency, not possible to review PDMP data before issuing a prescription
    • PDMP not operational or other technological failure, if the practitioner reports failure to the board
2015 WI Act 266

• Effective April 1, 2017:
  – Will allow law enforcement agencies to request PDMP data without court orders
  – Will add PDMP access for non-prescriber health care and substance abuse professionals
Assessment Question

Which of the following statements regarding 2013 Wisconsin Act 199 is FALSE?

A. For any schedule II or III controlled substance being dispensed or delivered, an identification card must be presented to the pharmacist, by the patient or the patient’s representative.

B. A record must be kept by the pharmacist that includes the name of the person on the identification card and the name of the person to whom a drug is being dispensed or delivered.

C. A pharmacist may request a patient to designate an authorized person to pick up a controlled substance.

D. There are no exceptions to the above controlled substance identification requirements enacted by Wisconsin Act 199.
Assessment Question

Which of the following statements regarding 2013 Wisconsin Act 199 is FALSE?

A. For any schedule II or III controlled substance being dispensed or delivered, an identification card must be presented to the pharmacist, by the patient or the patient’s representative.

B. A record must be kept by the pharmacist that includes the name of the person on the identification card and the name of the person to whom a drug is being dispensed or delivered.

C. A pharmacist may request a patient to designate an authorized person to pick up a controlled substance.

D. There are no exceptions to the above controlled substance identification requirements enacted by Wisconsin Act 199.
Additional State & Local Efforts

• Pharmacy Society of Wisconsin
  – Prescription Drug Abuse Prevention Education Toolkit
    • PSW Presentation
    • Information for providers, parents, teens, teachers, etc.

• Medication Collection
  – Department of Justice
    • National Prescription Drug Take-Back Day
    • Participating police departments
  – Dose of Reality
  – Milwaukee Metropolitan Sewerage District (MMSD)
Harm Reduction Initiatives: OEND & OSI

Anuja Vallabh, PharmD
PGY2 Psychiatric Pharmacy Resident
Clement J. Zablocki VA Medical Center
National Overdose Deaths
Number of Deaths from Prescription Opioid Pain Relievers

Source: National Center for Health Statistics, CDC Wonder
National Overdose Deaths
Number of Deaths from Heroin

Source: National Center for Health Statistics, CDC Wonder
National Overdose Deaths

Number of Deaths from Benzodiazepines

Source: National Center for Health Statistics, CDC Wonder
Combating the Opioid Overdose Epidemic

• Opioid Overdose Education and Naloxone Distribution (OEND) programs have been established since the 1990’s

• Harm reduction initiative

• Over 3-fold increase in programs from 2010 to 2014

• Key Components:
  – Prevention of overdose
  – Recognition of overdose
  – Reversal of overdose
  – Prescribing and dispensing naloxone

Centers for Disease Control and Prevention. MMWR. 2011;60(43):1487-1492.
# Outcomes of OEND Programs

<table>
<thead>
<tr>
<th>Article</th>
<th>Location</th>
<th>N</th>
<th>Population</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bennett et al, 2011</td>
<td>Pittsburgh</td>
<td>426</td>
<td>Needle exchange participants</td>
<td>89 individuals reported administering naloxone in response to 249 overdose episodes. 96% of overdoses were reversed when naloxone was used.</td>
</tr>
<tr>
<td>Walley et al, 2013</td>
<td>Massachusetts</td>
<td>2912</td>
<td>Opioid users, laypersons</td>
<td>Communities with greater OEND penetration were associated with fewer opioid overdose deaths.</td>
</tr>
<tr>
<td>McAuley et al, 2015</td>
<td>US, UK, Canada (Systematic Review)</td>
<td>1374</td>
<td>Needle exchanges, drug treatment centers</td>
<td>9% of naloxone kits distributed are likely to be used within the first 3 months of supply for every 100 people trained.</td>
</tr>
</tbody>
</table>

Naloxone

• Competitive, pure mu-opioid receptor antagonist
• Displaces opioid agonist from receptor
• No pharmacological effect in the absence of opioids
• Formulations: IV, SC, IM, IN

• Onset of Action:
  – IV: 2 minutes
  – IM/IN: 2-3 minutes

• Duration of Action: 20-90 minutes
  – Short-acting vs. long-acting opioids

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>IN Generic</th>
<th>IN Branded</th>
<th>IM Generic</th>
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<tbody>
<tr>
<td>Narcan® Nasal Spray</td>
<td>Evzio® Auto-injector</td>
<td></td>
<td></td>
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<table>
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<tr>
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<tr>
<td>Narcan® Nasal Spray</td>
<td>Evzio® Auto-injector</td>
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<table>
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<tr>
<th>FDA Approval for Public Use</th>
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<tbody>
<tr>
<td>11/18/2015</td>
<td></td>
<td></td>
<td></td>
<td>4/3/2014</td>
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<th>Sig</th>
<th>IN Generic</th>
<th>IN Branded</th>
<th>IM Generic</th>
<th>IM Branded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spray 1 ml (1/2 of syringe) into each nostril. Repeat after 2-3 minutes if no or minimal response.</td>
<td>Spray 0.1 ml into one nostril. Repeat with second device into other nostril after 2-3 minutes if no or minimal response.</td>
<td>Inject 1 ml in shoulder or thigh. Repeat after 2-3 minutes if no or minimal response.</td>
<td>Inject into outer thigh as directed by prompt.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assembly</th>
<th>IN Generic</th>
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<th>IM Generic</th>
<th>IM Branded</th>
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<th>Cost</th>
<th>IN Generic</th>
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<tbody>
<tr>
<td>$50</td>
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<th>IM Generic</th>
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<tbody>
<tr>
<td>IMS/Amphastar</td>
<td>Adapt Pharma</td>
<td>Hospira, Mylan</td>
<td>Kaléo</td>
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</table>
Supporting Laws - Wisconsin

Access Laws

• Civil and Criminal Protection for:
  – Prescribers
  – Dispensers
  – Lay Administrators
• Lay Distribution
• 3rd Party Prescribing
• Standing Order

Good Samaritan Laws

• Immunity from Prosecution for Possession of:
  – Controlled Substances
  – Drug Paraphernalia

*No immunity from arrest or charges for the above

VA OEND Program

- National directive in response to rising opioid overdose rates among Veterans
- National VA created non-prescriptive recommendations for issuing naloxone kits in May 2014 to support implementation of OEND programs on local levels
- OEND programs and naloxone prescribing may look different across VA facilities
- Naloxone kits are provided to local VA facilities at no cost
- Naloxone kits can be dispensed on-site or through the VA mail-order pharmacy
## National VA Recommendations

<table>
<thead>
<tr>
<th>Direct Association with Benefit</th>
<th>Indirect Association with Potential Benefit</th>
<th>Clinical Judgment of Potential Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Heroin or other injection drug use</td>
<td>• PTSD or other MH diagnosis</td>
<td>• Previous suicide attempt or on high-risk suicide list</td>
</tr>
<tr>
<td>• Substance use</td>
<td>• Any opioid prescription and known or suspected respiratory system disease; renal or hepatic disease</td>
<td>• Opioid induction, upward titration or rotation (for SUD or pain)</td>
</tr>
<tr>
<td>• Opioid or drug use disorder diagnosis</td>
<td>• High-dose opioid prescription (50 to 100 mg or more MEDD)</td>
<td>• Opioid induction, upward titration or rotation (for SUD or pain)</td>
</tr>
<tr>
<td>• High likelihood of opioid overdose or witnessing an opioid overdose.</td>
<td>• Concomitant benzodiazepine use or concurrent antidepressant prescription</td>
<td>• Aberrant opioid use / misuse (e.g., early fills; extra doses; overlapping, multi-site fills).</td>
</tr>
<tr>
<td></td>
<td>• Lost Tolerance</td>
<td></td>
</tr>
</tbody>
</table>

*Not an all-inclusive list*
Milwaukee OEND Program

- PGY1 Resident and Mental Health Pharmacist implemented the program from 9/2014 through 3/2015

Defined High Risk Veterans
Addressed Key Leaders
Created Note Template
Trained Staff
### OPIOD OVERDOSE RISK ASSESSMENT

Visit Location:*  
- [ ] Primary Care  
- [ ] Outpatient Mental Health  
- [ ] 3C Discharge  
- [ ] Dom 123  
- [ ] Home Based Primary Care  
- [ ] Spinal Cord Injury  
- [ ] Hematology/Oncology  
- [ ] Other: [ ]

Reason(s) for naloxone kit prescription:*  
- [ ] History of IV drug abuse or opioid use disorder  
- [ ] Prescribed opioids at doses > 100mg/day of morphine equivalence  
- [ ] Discharge from the domiciliary  
- [ ] Discharge from inpatient mental health (3C) for opioid/drug overdose  
- [ ] History of suicide attempt and/or has suicide flag  
- [ ] Other: [ ]

**RECOMMENDATION**

Dispense intranasal naloxone overdose rescue kit.  
- [ ] FIRST FILL  
- [ ] Subsequent Prescription  

[<< Click to REVIEW Patient Education Record/Learning Barriers/Preferences]
Prior to distributing the naloxone kit, the patient will be given an OEND pamphlet and educated on the following:

- Opioid overdose prevention handout

**PATIENT EDUCATION TOPIC:**
- Risk factors for opioid overdose
- Opioid overdose prevention
- Signs/symptoms of opioid overdose
- Proper administration of naloxone kit
- Proper storage of naloxone kit
- Proper disposal of naloxone kit
- Only reverses effects of opioid overdose
- Rescue Response
  - Importance of calling 911/EMS

**Level of Understanding:** *(None selected)*

**Instruction:** Instructed on risks and benefits

**Location:** MILWAUKEE
What are Opioids?

Opioids are a type of drug found in some pain or other prescription medications, and in some illegal drugs of abuse (e.g., heroin). In certain situations, opioids can slow or stop a person's normal breathing function.

Opioid harms
- Taking too much opioids can make a person pass out, stop breathing and die.
- Opioids can be addicking and abused.
- Tolerance to opioids can develop with daily use. This means that one will need larger doses to get the same effect.
- If a person stops taking opioids, he/she will lose tolerance. This means that a dose one takes when tolerant could cause overdose if it is taken again after being off of opioids.
- An opioid dose a person takes could cause overdose if shared with another person. Another person may not be tolerant.

Safe Use of Opioids

Safe use of opioids prevents opioid harms from happening to not only you, but also to family, friends and the public.

To use opioids safely
- Know what you're taking (e.g., color/shape/size/name of medication)
- Take your opioid medication exactly as directed
- Review the booklet Taking Opioids Responsibly for Your Safety and the Safety of Others with your provider
- DON'T mix your opioids with:
  - Alcohol
  - Benzodiazepines (Alprazolam/Xanax, Lorazepam/Ativan, Clonazepam/Klonopin, Diazepam/Vallium) unless directed by your provider
  - Medicines that make you sleepy

Ask a VA clinician if a naloxone kit is right for you

Important considerations:
- Naloxone works only for opioid overdose and may temporarily reverse opioid overdose to help a person start breathing again
- During an overdose the user cannot react, so someone else needs to give naloxone
- Encourage family and significant others to learn how to use naloxone (see "Overdose Resources" section)
- If you have a naloxone kit, tell family and significant others where you keep it
- Store naloxone kit at room temperature, out of the heat, cold and light (e.g., do not store in your car), otherwise naloxone will lose its effectiveness

Resources

- Local Emergency Services: 911
- National Poison Hotline: 1-800-222-1222
- Veteran Crisis Line: 1-800-273-TALK (8255), or text – 838255
- Taking Opioids Responsibly for Your Safety and the Safety of Others
- VA Substance Use Disorder Treatment Locator
  - www2.va.gov/directory/guide/SUD.asp
- VA Posttraumatic Stress Disorder (PTSD) Treatment Locator
  - www.va.gov/directory/guide/PTSD.asp
**Opioid Overdose**

- **Opioid overdose** occurs when a person takes more opioids than the body can handle, passes out, and has no or very slow breathing (i.e., respiratory depression).
  - Overdose can occur seconds to hours after taking opioids and can cause death.

**Signs of an Overdose***

**Check:** Appears sleepy, heavy nodding, deep sleep, hard to arouse, or vomiting

**Listen:** Slow or shallow breathing (less than 1 breath every 6–8 seconds); snoring, raspy, gurgling, or choking sounds

**Look:** Bluish or grayish lips, fingernails, or skin

**Touch:** clammy, sweaty skin

- If the person shows signs of an overdose, see next section “Responding to an Overdose”
  * Even if the person responds to an initial safety check, bystanders should continue to monitor any person with these signs constantly to make sure the person does not stop breathing and die.

**Overdose Resources**

- [SAMHSA Opioid Overdose Prevention Toolkit](http://store.samhsa.gov/product/Opioid-Prevention-Toolkit/SMA13-4742)

- [Community-Based Overdose Prevention and Naloxone Distribution Program Locator](http://hopeandrecovery.org/locations/)

- [Prescribe to Prevent](http://prescribetoprevent.org/video/)


---

**Responding to an Overdose**

1. **Check For A Response**
   - Lightly shake person, yell person’s name, firmly rub person’s sternum (bone in center of chest where ribs connect) with knuckles, hand in a fist
   - If person does not respond—Give Naloxone, Call 911

![Rub Sternum](image)

2. **Give Naloxone, Call 911**
   - If you have intranasal naloxone, spray one half of the naloxone cartridge into each nostril
   - If you have intramuscular naloxone, inject 1 mL into muscle of upper arm, upper thigh, or outer buttocks
   - If you have the naloxone auto-injector, pull device from case and follow voice instructions
   - When calling 911, give address and say the person is not breathing

![Inject Naloxone](image)

3. **Airway Open, Rescue Breathing (if overdose is witnessed)**
   - Place face shield (optional)
   - Tilt head back, lift chin, pinch nose
   - Give 1 breath every 5 seconds
   - Chest should rise

   ![Rescue Breathing](image)

4. **Chest Compressions (if collapse is unwitnessed)**
   - Place heel of one hand over center of person's chest (between nipples)
   - Place other hand on top of first hand, keep elbows straight, shoulders directly above hands
   - Use body weight to push straight down, at least 2 inches, at rate of 100 compressions per minute
   - Place face shield (optional)
   - Give 2 breaths for every 30 compressions

![Chest Compressions](image)

5. **Consider Naloxone Again**
   - If person doesn’t start breathing in 2–3 minutes, or responds to the first dose of naloxone and then stops breathing again, give second dose of naloxone
   - Because naloxone wears off in 30 to 90 minutes be sure to stay with the person until emergency medical staff take over or for at least 90 minutes in case the person stops breathing again

6. **Recovery Position**
   - If the person is breathing but unresponsive, put the person on his/her side to prevent choking if person vomits
VA Naloxone Kits

Intranasal Kit

Auto-injector Kit
Number of Kits Dispensed Within the VA

<table>
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<tr>
<th>Month</th>
<th>Kits Dispensed</th>
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<tbody>
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<td>Nov-14</td>
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<td>Feb-16</td>
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<tr>
<td>Mar-16</td>
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</tbody>
</table>

Total Kits Dispensed to Date: **27,588**
Number of Reversals through Feb 2015: **172**
**VA Opioid Safety Initiative (OSI)**

- System-wide effort to ensure the safe, effective, and judicious use of opioids

- Key clinical indicators measured:
  - Percent of Veterans dispensed opioids
  - Percent of Veterans dispensed an opioid and benzodiazepine
  - Percent of Veterans dispensed opioids long-term with a urine drug screen completed
  - Stratification by dispensed Morphine Equivalent Daily Dosing
VA OSI Progress Report

• Each VA facility is given a composite score to track OSI progress

• Every VA facility that is 1 SD above the median composite score must submit known system gaps and a corrective action plan

• Report generated identifying percentage and rank of opioid prescribers by VA facility

• Academic Detailers promote evidence based prescribing at the individual prescriber level
<table>
<thead>
<tr>
<th>VISN</th>
<th>Medical Center</th>
<th>Opioids</th>
<th>Opioid + BZD</th>
<th>UDS</th>
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</table>

Median + 1 Standard Deviation: 107
Resources

• SAMHSA

• http://prescribetoprevent.org

• How to broach topic of OEND with target patient populations
  – Introduction to Naloxone for People with Opioid Use Disorders
    • https://youtu.be/-qYXZDzo3cA
  – Introduction to Naloxone for People Taking Prescribed Opioids
    • https://youtu.be/NFzhz-PCzPc

• “How To” training videos
  – How to Use the VA Auto-Injector Naloxone Kit
    • https://youtu.be/-DQBCnrAPBY
  – How to Use the VA Intranasal Naloxone Kit
    • https://youtu.be/WoSfEf2B-Ds
  – How to Use the VA Intramuscular Naloxone Kit
    • https://youtu.be/Ig1LEw-PeTE
Managing Pain in the Patient with Coexisting Opioid Addiction

Brittany Jensen, PharmD
PGY1 Pharmacy Resident
Aurora Health Care Metro, Inc.
Goals of Therapy

• General patient population:
  – Minimize physiologic adverse effects of unrelieved pain
  – Avoid adverse effects of therapy
  – Maximize non-pharmacologic treatment approaches
  – Improve QOL
  – Educate about self-care of pain

Goals of Therapy

• Patients with opioid addictions:
  – Provide effective analgesia
  – Prevent withdrawal
  – Prevent relapse to addiction
  – Effective treatment of opioid addiction (maintenance opioid therapy)
  – Treatment of psychiatric disorders such as anxiety

Which of the following is not a treatment goal to consider in patients with suspected history of and/or active opioid addiction?

A. Prevent withdrawal
B. Minimize seriousness of pain
C. Treat symptoms
D. Prevent relapse
Treatment Modalities

• Non-pharmacologic
  – Physical Interventions
  – Psychological Interventions
  – Psychosocial Interventions

• Pharmacologic
  – Non-opioid Analgesics + Adjuvants
  – Opioid Analgesics
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

• Place in therapy
  – Nociceptive pain of mild to moderate intensity

• Use considerations in patients with addiction
  – Comorbid complications secondary to abuse
    • Cirrhosis
    • Cardiovascular
  – Concomitant bipolar disease and addiction
    • Lithium serum concentrations

Antidepressants

• Place in therapy
  – Management of most neuropathic pain

• Use considerations in patients with addiction
  – Several weeks before full effect
  – Avoid duloxetine in hepatic disease
  – Use Venlafaxine with caution in patients with hypertension

Anticonvulsants

• Place in therapy
  – Management of most neuropathic pain

• Use considerations in patients with addiction
  – Laboratory monitoring associated
  – Concomitant HIV
    • Impact of phenytoin and carbamazepine on blood counts
  – DDI between methadone and phenytoin

# Gabapentin

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Design, Setting, Population</strong></td>
</tr>
<tr>
<td>Randomized, 5-week, double blind, placebo-controlled trial</td>
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<tr>
<td>• Buprenorphine SL tablets +/- gabapentin (added week 2)</td>
</tr>
<tr>
<td>• 3x weekly opioid withdrawal scales, vitals, and urine drug screens</td>
</tr>
<tr>
<td><strong>Objective</strong></td>
</tr>
<tr>
<td>Whether the addition of gabapentin improves outcomes during buprenorphine-assisted detoxification</td>
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</table>
**Gabapentin**


| Results | • Self-reported and observer-rated opioid withdrawal ratings did not differ between groups during taper  
• Urine results showed a drug x time interaction  
• Probability of opioid-positive urines significant decreased over time in the gabapentin versus placebo groups during weeks 3-4 (OR=0.73, p=0.004) |

• Other considerations:  
  – Opioid sparing pre- and post-operatively  
  – Daytime somnolence
Topical Agents

• Place in therapy
  – Management of peripheral nociceptive and neuropathic pain

• Use considerations in patients with addiction
  – Opioid sparing potential
  – May experience delayed time to full effect
  – Few adverse effects

• Ex: amitriptyline, ketamine, lidocaine, capsaicin

Benzodiazepines (BZDs)

• NOT RECOMMENDED
• Addiction liability, relapse, functional impairment
• Alternatives to BZDs in treating anxiety related pain exist
  – Antidepressants or anticonvulsants

Treatment: Pharmacologic

- Non-opioid Analgesics/Adjuvants

- Opioid Analgesics
  - Opioid Maintenance Agents
  - Mixed Agonist/Antagonist Combinations
  - Pure Agonists
Opioid Maintenance

• Methadone
• Buprenorphine
  – Buprenorphine/naloxone
Opioid Maintenance - Methadone

• Synthetic, long-acting opioid agonist
• In addiction, promotes analgesia by a second mechanism:
  – NMDA receptor antagonist
• Produces tolerance less readily than other mu opioids
• Pharmacological properties make misuse particularly risky
Opioid Maintenance - Buprenorphine

• Partial opioid agonist
  – Partial agonist at the mu-opioid receptor
  – Antagonist at the kappa-opioid receptor

• May precipitate withdrawal if administered with a pure agonist
  – Blocks the effects of other opioids

• May exhibit ceiling effect

Mixed Agonist-Antagonist Agents

- Ex. Pentazocine, nalbuphine, butorphanol
- May reverse analgesia and precipitate withdrawal in opioid-dependent patients
- Ceiling effect precludes their use
Pure Agonist

• Place in therapy
  – Drug of choice in acute, severe pain
  – Conflicting evidence regarding long-term use in chronic pain

• Multiple formulations!
  – Immediate- versus Extended/Controlled-Release

Treat Guidel Med Lett. 2013 Apr;11(128):31-42
Pure Agonist

A. How long do they last?
   – Methadone half-life increases with repeated dosing

B. Time to full effect?
   – Ex. Fentanyl patch: Tmax 20-72 hours
     – Additional agents needed until full effect reached

C. Routes of administration
   – PO, SL, TD, IV, etc...

D. Renal dysfunction?
   – Delayed clearance of active drug
   – Consider fentanyl

E. Hepatic dysfunction?
   – Caution using agents combined with acetaminophen
Opioid Use Considerations
Norco, Oxy, Dilaudid... oh my!
Opioid Use Considerations

- Selection
- Scheduling
- Medication Supply
- Limitations
Less Addictive Option?

Abuse-deterrent formulations?..
Abuse-deterrent Formulation: Reformulated Oxycontin®

- More difficult to crush, break, or dissolve
- When dissolved, viscous gel difficult to inject

“Hard to crush and hard to snort”

Cone et al. Alcohol Drug Addiction. 2013
Lessons Learned From OxyContin


<table>
<thead>
<tr>
<th>Design, Setting, Population</th>
<th>Survey Study</th>
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<tbody>
<tr>
<td>Data from the ongoing Survey of Key Informants’ Patients program</td>
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<td>N = 10, 784</td>
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<td>January 1, 2009 – June 30, 2014</td>
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<tr>
<td>DSM-V diagnosis of opioid use disorder and primary drug of abuse (RX opioid or heroin)</td>
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<tr>
<th>Objective</th>
<th>Examine the factors that led to the initial steep decline in OxyContin abuse and levels of stable residual abuse since 2012</th>
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<table>
<thead>
<tr>
<th>Primary Measure</th>
<th>Past-month abuse of opioids</th>
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# Lessons Learned From OxyContin

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<th>Results</th>
<th>Past month abuse</th>
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<tr>
<td></td>
<td>January to June 2009</td>
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<tr>
<td></td>
<td>• 45.1% [95% CI, 41.2%-49.1%]</td>
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<tr>
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<td>July 2009 to December 2012</td>
</tr>
<tr>
<td></td>
<td>• 26% [95% CI, 23.6%-28.4%]</td>
</tr>
<tr>
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<td>• P-value &lt; 0.001</td>
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Reduction leveled off...
25-30% of the sample persisted in endorsing past-month abuse from 2012-2014 (at study end, 26.7% [95% CI, 23.7%-29.6%])
Figure 1. Respondents Who Endorsed Past-Month Use of OxyContin or Heroin Before and After the Introduction of an Abuse-Deterrent Formulation (ADF)
Figure 3. Drugs Used to Replace OxyContin After the Introduction of the Abuse-Deterrent Formulation (ADF)
Less Addictive Option?

Comparative abuse liability?..
## Abuse Risk Comparisons


| Design, Setting, Population | Data on prescription opioid abuse and routes of administration used from:  
|                            | • 2009 Addiction Severity Index-Multimedia Version Connect assessments  
|                            | Prescription volumes data from SID Health LLC  
|                            | N = 59,792  
|                            | 464 treatment facilities in 34 states  
| Objective                  | Examine how relative risks change when adjusted for prescription volume of the products, along with patterns of abuse via routes of administration for the products |
# Abuse Risk Comparisons


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<th>(+) Abuse Risk/100,000 RXs</th>
<th>Total No of RXs/100,000</th>
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<td>0.005</td>
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<td>ER fentanyl</td>
<td>0.044</td>
<td>0.0063</td>
<td>22.934</td>
</tr>
<tr>
<td>Methadone</td>
<td>0.278</td>
<td>0.0411</td>
<td>20.028</td>
</tr>
<tr>
<td>ER morphine</td>
<td>0.091</td>
<td>0.0111</td>
<td>26.059</td>
</tr>
<tr>
<td>ER oxymorphone</td>
<td>0.017</td>
<td>0.0177</td>
<td>2.896</td>
</tr>
</tbody>
</table>
ER oxycodone and methadone = statistically significant greatest abuse risk after adjusting for prescription volume

ER oxycodone: p-value < 0.0001
Methadone: p-value < 0.0001

Opioid Selection

- **Pharmacokinetics**
  - Select opioids with minimal rewarding properties, when effective
  - Avoid prescribing supra-therapeutic doses
    - Active metabolites in renal and hepatic dysfunction

- **Consider route of administration**
Opioid Scheduling

Long-acting agent + short-acting PRN?

• Problematic...

Two Alternative Approaches:

A. Schedule short-acting agent at specific times
B. Pre-medicate with short acting agent around activities

Opioid Medication Supply

• 71 Federal Register 52724:
  – Schedule II sequential fills

• For more information:
Opioid Therapy Limitations

• Diminished efficacy over time
• Intolerable adverse effects
• Risk of addiction/relapse
• Opioid-induced hyperalgesia (OIH)
• Drug interactions

Guideline Application

“Inconceivable!..”
### SAMHSA*:

**Pain Management in Substance Abuse Disorders**

<table>
<thead>
<tr>
<th>CNCP</th>
<th>Acute Pain Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In Recovery</td>
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</tr>
<tr>
<td>2. In Medication-assisted Recovery</td>
<td>2. On Agonist Therapy for Addiction or Pain</td>
</tr>
<tr>
<td>3. With Active Addiction</td>
<td>3. On Buprenorphine for Addiction</td>
</tr>
<tr>
<td></td>
<td>4. On Methadone for Addiction</td>
</tr>
</tbody>
</table>

*SAMHSA = Substance Abuse and Mental Health Services Administration*

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**Note:**

SAMHSA. Treatment Improvement Protocol (TIP) Series 54.  
HHS Publication No. (SMA) 12-4671.
CNCP Treatment

1. Treating patients in recovery
   - Non-pharmacologics
   - Non-opioid analgesics
   - Treat comorbidities
   - Initiate opioid therapy ONLY if:
     - Benefits outweigh risks
     - Limited duration

CNCP Treatment

2. Treating patients in medication-assisted recovery
   – Start with non-pharmacological and non-opioid therapy
   – Treat comorbidities
   – Closely monitor treatment outcomes for evidence of benefit and harm
CNCP Treatment

3. Treating patients with active addiction
   – Start with non-pharmacological and non-opioid therapy
   – Treat comorbidities
   – Consult pain management, behavioral health
   – If refusing consult, not recommended to prescribe scheduled medications except:
     • For acute pain or detoxification

Acute Pain Episodes

1. Treating patients in recovery
   – Non-pharmacologic
   – Non-opioid therapy
   – Treat comorbidities
   – Switching formulations
   – Reinforced recovery support

Acute Pain Episodes

2. Treating patients on agonist therapy for addiction or pain
   – Continue current opioid or an equivalent dose of an alternative
   – May require supplementation of additional opioids for short duration
   – Multimodal analgesia
   – Non-pharmacologic

Acute Pain Episodes

3. Patients on buprenorphine for opioid addiction

- Utilize non-opioid analgesics
- May have reduced benefit from full agonist opioids
- In some cases, discontinue buprenorphine while inpatient
  - ex. Surgical, consider d/c buprenorphine and supplement with fentanyl
  - Remember to transition back

- Non-pharmacologic
Acute Pain Episodes

4. Patients on methadone for opioid addiction

– Prescribe their usual daily dose of methadone +/- different opioid for management of acute pain
– Avoid conversion
– Non-opioid therapy
– Non-pharmacologic

KD is hospitalized secondary to injuries sustained in a MVA 6 hours ago. She has taken methadone 80 mg/day orally as opioid replacement therapy for 1 year after a 10-year history of heroin use. Which of the following is the most appropriate strategy for managing this patient’s acute pain?

A. Methadone 80 mg IV on the day of surgery plus morphine 10 mg orally every 4 hours postoperatively

B. Morphine sustained release in an equianalgesic dose to methadone 80 mg orally on the day of surgery plus immediate-release morphine orally postoperatively

C. Methadone 80 mg orally on the day of surgery plus morphine IV by PCA pump postoperatively
Summary

• Explore non-opioid analgesics/adjuvants first
  – Multimodal approach
  – Avoid benzodiazepines

• Be cognizant of opioid maintenance therapy and risk of withdrawal
  – Are they on buprenorphine or methadone prior to admission?

• Opioids may be considered for severe pain
  – Consider pain management consultation

• Every patient has the right to high-quality pain assessment and management
Questions?

GMCCP Spring Educational Event/Business Meeting
Thursday June 2nd, 2016

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