Opioid Therapy Risk Management: The VA Opioid Safety and Naloxone Distribution Initiatives

Mitchell Nazario, PharmD, CPE
VISN 8 PBM Program Manager, Pain Management
West Palm Beach VAMC
7305 N. Military Trail
West Palm Beach, FL 33411
Mitchell.nazario@va.gov
561-214-5231

CPE Information

- Target Audience: Pharmacists & Technicians
- ACPE#: 0202-0000-15-204-L01-P/T
- Activity Type: Knowledge-based

CPE Information and Disclosures

Mitchell Nazario, PharmD, CPE: "declare(s) no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

The American Pharmacist Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Learning Objectives

- At the completion of this activity, participants will be able to:
  - Discuss the Department of Veterans Affairs’ (VA) Opioid Safety Initiative.
  - List the 4 metrics of the Opioid Safety Initiative and strategies to address them.
  - Describe the role of the pain management Clinical Pharmacy Specialist (CPS).
  - State the Opioid Education and Naloxone Distribution initiative and strategies for implementation.
  - Recall how the Pharmacy Technician can assist the CPS in the implementation of these strategies.

Self-Assessment Question 1

Which of the following metrics are being monitored in the VA Opioid Safety Initiative?
[A. Percent of patients on ≥ 100mg MEDD]
[B. Percent of patients on dual opioid-benzodiazepine therapy]
[C. Percent of patients on opioids with a UDS]
[D. B & C]
[E. All of the above]

Self-Assessment Question 2

The combined use of opioids and benzodiazepines may increase the risk for
[A. Death from overdose]
[B. Hospital admission for substance abuse]
[C. Worsening of sleep apnea]
[D. B & C]
[E. All of the above]
Self-Assessment Question 3

Distribution of the Naloxone Kit should be discouraged since it will give the patient a false sense of security and encourage them to use extra amounts of their opioids

[A. True]  
[B. False]

Consequences of Chronic Pain

Physical Functioning\textsuperscript{1\textendash}3
- Decreased mobility
- Sleep disturbance
- Fatigue
- Loss of appetite

Mood\textsuperscript{1,2}
- Depression
- Anxiety
- Anger
- Irritability

Social Functioning\textsuperscript{1\textendash}3
- Diminished social relationships (family/friends)
- Decreased sexual function/intimacy
- Decreased recreational and social activities

Societal consequences\textsuperscript{4\textendash}7
- Increased healthcare utilization
- Disability
- Loss of workdays or employment
- Substance abuse

---

Death Rate by All Drug Poisoning Now Greater Than Vehicular Collisions

**Death Rates: United States (1999-2010)**\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths per 100,000 Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>10.2</td>
</tr>
<tr>
<td>2002</td>
<td>11.4</td>
</tr>
<tr>
<td>2004</td>
<td>12.6</td>
</tr>
<tr>
<td>2006</td>
<td>13.9</td>
</tr>
<tr>
<td>2008</td>
<td>14.2</td>
</tr>
<tr>
<td>2010</td>
<td>14.3</td>
</tr>
</tbody>
</table>

- Motor vehicle traffic
- All poisoning
- Drug poisoning
- Unintentional drug poisoning

---

Unintentional OD Deaths in the US

**Unintentional Overdose Deaths in the U.S.**\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths per 100,000 Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>20.4</td>
</tr>
<tr>
<td>2002</td>
<td>22.1</td>
</tr>
<tr>
<td>2004</td>
<td>23.8</td>
</tr>
<tr>
<td>2006</td>
<td>25.5</td>
</tr>
<tr>
<td>2008</td>
<td>27.2</td>
</tr>
<tr>
<td>2010</td>
<td>28.0</td>
</tr>
</tbody>
</table>

Unintentional overdose deaths per capita sales of opioids in morphine equivalents by year.

---

2013 Prescription Opioid Mortality

- 16,235 total\textsuperscript{1}
  - 13,486 (83%) unintentional\textsuperscript{2}
  - 17% intentional or undetermined\textsuperscript{2}
- 44 people die from prescription opioids everyday in the U.S.\textsuperscript{3}
- Almost 2 deaths every hour

---

Death from OD and Opioids Prescribing Patterns

**Risk of Death by Prescription Opioid Overdose for Chronic Non-Cancer Pain**

Data shows all unintentional prescription opioid overdose deaths (n = 705) in a random national sample of United Health Administration patients in 2004-2006. The risk of opioid overdose increased as opioid dose was escalated to 80 mg/day of morphine. Mortality risk related to opioid doses of or above 100 mg/day were compared with less than 20 mg/day, which increased 4.0-fold.
High-Dose Opioid Analgesics

- A 9-fold increase in opioid OD has been reported in patients receiving high dose opioids (> 100mg MEDD) compared to low dose (< 20mg MEDD).
- Patients on > 120mg MEDD were more likely to have alcohol or drug related encounters (intoxication, withdrawal, OD).
- A reduction in the proportion of patients receiving > 120mg MEDD resulted in a 50% reduction in opioid related deaths.

Opioid Use in the VA Population

- Veterans are twice as likely to die from accidental OD compared to non-Veteran population.
- Veterans with PTSD are more likely to:
  - Be prescribed opioids at higher doses
  - Receive opioids and sedative hypnotics (including benzodiazepines) concurrently
- Opioid use in Mental Health populations is associated with:
  - Opioid-related, alcohol, and non-opioid drug related accidents and overdoses
  - Self-inflicted injuries and violence related injuries
  - Higher incidence of wounds or injuries

BZD and Substance Abuse Admissions

- According to SAMHSA, the number of substance abuse treatment admissions involving the combination of benzodiazepines and opioids increased by 570% over the recent decade, from approximately 5,000 admissions in 2000 to more than 33,000 admissions in 2010.
- In contrast, treatment admissions for all other substances decreased by approximately 10% during the same period.

BZD and Mortality

- In 2010, there were more than 22,000 pharmaceutical overdose deaths in the United States.
- Opioids (75.2%) and benzodiazepines (29.4%) were the two drug classes most commonly involved in these deaths.
- Benzodiazepines were involved in 30.1% of opioid deaths—more than any other drug class.
- Similarly, opioids were involved in 77.2% of benzodiazepine deaths—again, more than any other drug class.

Benzodiazepine-Opioid Prescribing Patterns & Deaths among Veterans

- Random sample of Veterans, primarily male (n=420,386) who received VHA medical services and opioid analgesics between 2004-09.
- Evaluated Veterans who died from a drug overdose (n=2400) while receiving opioid analgesics.
- Main outcome measure: Death from drug overdose, defined as any intentional, unintentional, or indeterminate death from poisoning caused by any drug, determined by information on cause of death from the National Death Index.

- Results:
  - During the study period 27% (n=112,069) of veterans who received opioid analgesics also received benzodiazepines. About half of the deaths from drug overdose (n=1185) occurred when veterans were concurrently prescribed benzodiazepines and opioids in a dose-response fashion.
  - Risk of death from drug overdose increased with history of benzodiazepine prescription: adjusted HR were:
    - 2.33 (95% CI, 2.05 to 2.64) for former prescriptions versus no prescription.
    - 3.86 (3.49 to 4.26) for current prescriptions versus no prescription.

Benzodiazepine-Opioid Prescribing Patterns & Deaths among Veterans

- Random sample of Veterans, primarily male (n=420,386) who received VHA medical services and opioid analgesics between 2004-09.
- Evaluated Veterans who died from a drug overdose (n=2400) while receiving opioid analgesics.
- Main outcome measure: Death from drug overdose, defined as any intentional, unintentional, or indeterminate death from poisoning caused by any drug, determined by information on cause of death from the National Death Index.

- Results:
  - During the study period 27% (n=112,069) of veterans who received opioid analgesics also received benzodiazepines. About half of the deaths from drug overdose (n=1185) occurred when veterans were concurrently prescribed benzodiazepines and opioids in a dose-response fashion.
  - Risk of death from drug overdose increased with history of benzodiazepine prescription: adjusted HR were:
    - 2.33 (95% CI, 2.05 to 2.64) for former prescriptions versus no prescription.
    - 3.86 (3.49 to 4.26) for current prescriptions versus no prescription.
The Opioid Safety Initiative (OSI) is a system-wide effort to ensure opioid pain medications are used safely, effectively and judiciously.

The key clinical indicators measured by the OSI are:
- Percent of Veterans dispensed an opioid over time
- Percent of Veterans prescribed an opioid and a benzodiazepine over time
- Percent of Veterans dispensed opioids long-term with a urine drug screen completed over time
- Stratification of the percent of Veterans dispensed Morphine Equivalent Daily Dosing

What Can We Do?

To reduce/improve:
- Percent of Veterans Dispensed an Opioid Over Time
- Percent Patients on Dual Opioid-Benzo Prescribing
- Percent Patients on > 100mg MEDD

Non-Opioid Analgesics

<table>
<thead>
<tr>
<th>Systematic review of effectiveness in diabetic neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agent (# high quality trials)</td>
</tr>
<tr>
<td>Antidepressants (TCA)</td>
</tr>
<tr>
<td>Amitriptyline (3)</td>
</tr>
<tr>
<td>Desipramine (2)</td>
</tr>
<tr>
<td>Nortriptyline (1)</td>
</tr>
<tr>
<td>Antidepressants (SNRI)</td>
</tr>
<tr>
<td>Venlaflaxine (2)</td>
</tr>
<tr>
<td>Duloxetine (3)</td>
</tr>
<tr>
<td>Antiepileptics</td>
</tr>
<tr>
<td>Gabapentin (2)</td>
</tr>
<tr>
<td>Pregabalin (4)</td>
</tr>
<tr>
<td>Topicals</td>
</tr>
<tr>
<td>Capsaicin (2)</td>
</tr>
<tr>
<td>Lidocaine patch (2)</td>
</tr>
</tbody>
</table>

Non-Opioid and Non-Drug Therapeutic Interventions

- Pain Procedures
  - TPI
  - Nerve Blocks
  - Major Joint Injections
  - Facet Injections
  - Medial Branch Blocks
  - Radio Frequency Ablations
- Epidurals
- ITDDS
- DCS

- Other Pain Disciplines
  - Cognitive Behavioral Therapies
  - Physical Therapy
  - Occupational/Recreational Therapy
  - Acupuncture
  - Chiropractic
  - Holistic Therapies/Yoga

- Surgery
  - Fusions, Laminectomies, Kyphos
  - Knee arthroscopies, replacements
  - Hip replacements
  - Carpal Tunnel Release
When Opioids Are Indicated

Proper Patient Selection
Risk Analysis and Stratification

VA/DOD Recommendations for Opioid Use

A trial of opioid therapy is indicated for a patient with chronic pain who meets all of the following criteria:

- Moderate to severe pain that has failed to adequately respond to indicated non-opioid and nondrug therapeutic interventions
- The potential benefits of opioid therapy are likely to outweigh the risks (i.e., no absolute contraindications)
- The patient is fully informed and consents to the therapy
- Clear and measurable treatment goals are established
- The ethical imperative is to provide the pain treatment with the best benefit-to-harm profile for the individual patient.

VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.
http://www.va.gov/PAINMANAGEMENT/docs/CPG_opioidtherapy_fulltext.pdf

Risk-Benefit Analysis

Use With Caution

- Patient receiving treatment for Substance Use Disorder
- Medical condition in which OT may cause harm:
  - OSA not on CPAP, central sleep apnea
  - COPD, respiratory depression in unmonitored setting
  - QTc interval 450-500 ms that may increase methadone risk
- Risk for suicide or unstable psychiatric disorder
- Complicated pain (unresponsive headache)
- Conditions that may impact adherence to OT:
  - Cognitively impaired
  - Unwillingness or inability to comply with treatment plan
  - Social instability, Mental Health disorders

VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.
http://www.va.gov/PAINMANAGEMENT/docs/CPG_opioidtherapy_fulltext.pdf

Risk Stratification & Mitigation Tools

- Instruments that may be useful for predicting risk of future aberrant drug-related behaviors:
  - Opioid Risk Tool (ORT)
  - Screener and Opioid Assessment of Patients with Pain (SOAPP) Version 1
- Tools for Risk Mitigation:
  - Opioid Agreement
  - PDMP Monitoring
  - UDS Monitoring

VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.
http://www.va.gov/PAINMANAGEMENT/docs/CPG_opioidtherapy_fulltext.pdf

Opioid Risk Tool (ORT)

VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.
http://www.va.gov/PAINMANAGEMENT/docs/CPG_opioidtherapy_fulltext.pdf
Opioid Therapy Risk Report

FAQ: OT Patient Populations

Patient List Enables the Clinician to Quickly View Status of Key Risk Factors & Treatment Milestones

Initial Use Team Huddle

• Preplanning for upcoming patients
• Determine who needs I-meed consent, UDS, and face to face Visit
• Also quick glance to determine if patient should be considered for possible BHS or SUD tx

Patient List Page – More Features

Click patient name to go to the patient detail page
Sort results by data columns using the arrows

Click on Patient Name to Open a Details Report for that Patient
Opioid Therapy Risk Report
Patient Detail

- Make a Decision to Discontinue Opioids in patients with:
  - Side effects or medical complications
  - Stable patients with reduced pain levels
  - Opioid misuse and addiction
- Consider referring to a pain specialist
  - Inadequate Analgesia
- Stop the opioid and educate patient about potential withdrawal if there are clear signs of unsafe or illegal behaviors

Available at: http://www.healthquality.va.gov/guidelines/Paincare/CTT_DetailsFull.pdf

Opioid Reduction/Discontinuation Strategies

- Pace of taper related to risk, the greater the risk the faster the taper
- Slower taper for patients on high dose and longer duration with manageable risks
  - Reduce dose 10-25% every 1-4 weeks
  - Initial dose reduction may be > 25% in select patients (high dose)
- High risk requires faster discontinuation
- Stop opioids when there are clear signs of unsafe/illegal behaviors
- Do not treat withdrawal symptoms with opioids or benzodiazepines

Available at: http://www.healthquality.va.gov/guidelines/Paincare/CTT_DetailsFull.pdf

Benzodiazepine Reduction/Discontinuation Strategy

- Reduce dose 10-25% every 2 weeks ( Monitor patient closely)
- Initial dose reduction may be > 25% in select patients (high dose)
- High risk requires faster discontinuation
- Stop benzodiazepines when there are clear signs of unsafe/illegal behaviors
- Do not treat withdrawal symptoms with opioids or benzodiazepines


Additional Opioid-Benzo Reduction Strategies

- Clinical Reminders Order Check (CROC). Will alert the provider as he is entering a NEW order for an opioid/benzo
- Authorizations for Use/Consults
- eConsults
- Staff Education through Academic Detailing and use of Risk Reduction tools
  - Opioid Therapy Risk Reduction (Almanac)
  - URINE DRUG SCREENS & TOXICOLOGY TESTING
Beating the “Test”

Pass It Kit

Recommended Frequency of UDT

<table>
<thead>
<tr>
<th>Opioid Risk Classification</th>
<th>Recommended UDT/PDOP Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>Monthly (1/2 wk - 1X per month)</td>
</tr>
<tr>
<td>Moderate Risk</td>
<td>Regular (1/4 X 1X per week)</td>
</tr>
<tr>
<td>High Risk or opioid doses &gt; 120</td>
<td>Daily (1/8 X 2X per week)</td>
</tr>
</tbody>
</table>

Potential False Positives

VA OPIOID OVERDOSE EDUCATION AND NALOXONE DISTRIBUTION (OEND) PROGRAM

Approach to Ordering Toxicology Testing

- Ask patient and document when he took his last opioid dose prior to announcing the toxicology screen
- Perform observed collections
- Routine UDS will not pick-up synthetic and semi synthetic opioids, order specific tests separately.
- Understand opioid kinetics and metabolic pathways

Cut-Off Values and Detection Times

<table>
<thead>
<tr>
<th>Substance</th>
<th>Cut-Off Values</th>
<th>Detection Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>50</td>
<td>2-8 hours after use</td>
</tr>
<tr>
<td>Cocaine</td>
<td>150</td>
<td>2-4 hours after use</td>
</tr>
</tbody>
</table>

VA Academic Detailing Service, US Department of Veterans Affairs
VA OEND Initiative

VA Opioid Overdose Education and Naloxone Distribution (OEND)

Naloxone – Expanded Access is Recommended

VA Opioid Overdose Education and Naloxone Distribution (OEND)

We are Saving Lives!

VA Opioid Overdose Education and Naloxone Distribution (OEND)

VA National Formulary Naloxone Listings

<table>
<thead>
<tr>
<th>CN</th>
<th>Product</th>
<th>Form</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>102</td>
<td>NALOXONE INJ</td>
<td>SOLN</td>
<td>0.4mg</td>
</tr>
<tr>
<td>102</td>
<td>NALOXONE RESCUE</td>
<td>KIT</td>
<td></td>
</tr>
<tr>
<td>102</td>
<td>NALOXONE AUTO</td>
<td>AUTO</td>
<td></td>
</tr>
</tbody>
</table>

*Intranasal kits are currently not being assembled at CMOP but may still be stocked by some facilities.

Naloxone is on the VA Formulary, including solution for injection and kits containing naloxone for either intranasal or intramuscular administration (by syringe or auto-injector). Naloxone kits and auto-injectors (EVZIO) and overdose education complement, and do not replace, safe and responsible opioid use.

VA Opioid Overdose Education and Naloxone Distribution (OEND)

VA Opioid Overdose Education and Naloxone Distribution (OEND)

We are Saving Lives!

Reversal Reported

106
OSI Results

- From Quarter 4 Fiscal Year 2012 (beginning in July 2012) to Quarter 2 Fiscal Year 2015 (ending in March 2015)
  - There are:
    - 109,862 fewer patients receiving opioids (679,376 patients to 569,514 patients)
    - 33,871 fewer patients receiving opioids and benzodiazepines together (122,633 patients to 88,762 patients)
    - 74,995 more patients on opioids that have had a urine drug screen to help guide treatment decisions (160,601 patients to 235,596)
    - 91,760 fewer patients on long-term opioid therapy (438,329 to 346,569)

- From Quarter 4 Fiscal Year 2012 (beginning in July 2012) to Quarter 2 Fiscal Year 2015 (ending in March 2015)
  - The overall dosage of opioids is decreasing in the VA system as 12,278 fewer patients (59,499 patients to 47,221 patients) are receiving greater than or equal to 100 Morphine Equivalent Daily Dosing.
  - The desired results of the Opioid Safety Initiative have been achieved during a time that VA has seen an overall growth of 90,488 patients (3,959,852 patients to 4,050,340 patients) that have utilized VA outpatient pharmacy services.

Role of the Pharmacist and Pharmacy Technician

- Actively participate in local OSI/OEND Committees overseeing the implementation of the directives (P)
- Perform chart reviews for compliance with the OSI Metrics (P, PT)
- Provide staff education/academic detailing on the OSI metrics and strategies for implementation/compliance (P)
- Assist hospital staff in the administration and interpretation of urine and serum toxicology screening (P)
- Provide staff/patient/caregiver education on the administration of the naloxone kit (P/PT)
- Participate in the acquisition and distribution of the naloxone kits (PT)

Key Points

- We discussed:
  - The 4 key clinical indicators measured by the OSI
  - The key components of the OEND program which includes education and training regarding:
    - Opioid overdose prevention
    - Recognition of opioid overdose
    - Opioid overdose rescue response
    - Issuing naloxone
  - Other risk mitigation strategies include
    - Opioid Agreements, PDMP Monitoring, UDS

Answers to Self-Assessment Question 1

Which of the following metrics are being monitored in the VA Opioid Safety Initiative?  
[A. Percent of patients on > 100mg MEDD]  
[B. Percent of patients on dual opioid-benzodiazepine therapy]  
[C. Percent of patients on opioids with a UDS]  
[D. B & C]  
[E. All of the above]

Answers to Self-Assessment Question 2

The combined use of opioids and benzodiazepines may increase the risk for  
[A. Death from overdose]  
[B. Hospital admission for substance abuse]  
[C. Worsening of sleep apnea]  
[D. B & C]  
[E. All of the above]
Answers to Self-Assessment Question 3

Distribution of the Naloxone Kit should be discouraged since it will give the patient a false sense of security and encourage them to use extra amounts of their opioids

[A. True]
[B. False]

Closing Remarks

Mitchell Nazario, PharmD, CPE
VISN 8 PBM Program Manager, Pain Management
West Palm Beach VAMC
7305 N. Military Trail
West Palm Beach, FL 33411
Mitchell.nazario@va.gov
561-214-5231