Opioid and Benzodiazepine Use in the Veteran Population

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Dr. Nari Hsiu, DO (she/her)
Psychiatrist & Addiction Medicine

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Learning Objectives

• Review the development of complex, persistent opioid dependence.
• Briefly compare complex persistent opioid dependence with opioid use disorder.
• Review benzodiazepine use in the veteran population with a brief overview of risks of benzodiazepine use
Complex Persistent Opioid Dependence Background

• In the United States, appx 40 million US adults struggle with moderate to severe chronic pain.

• In the 1980s, opioid treatment emerged and evolved into “long-term opioid treatment” aka LTOT.
  • Defined as more than 90 days of opioid use per year.
  • Typically lasting on the order of years.

• Long-term opioid treatment has increased from:
  • 1.8% of US Adults (or 4 million) in 2000
  • to 5.4% of US Adults (or 13 million) in 2014
Complex Persistent Opioid Dependence in the Veteran Population

• Between 2009-2011, of 1.8M individuals with an opioid prescription, 44% met criteria for LTOT. (Vanderlip et al, 2014.)

• Factors that increase opioid prescribing:
  • Exposure to combat trauma
  • Injuries that are explosive/non-explosive or penetrating/blunt/burns
  • Surgeries to manage injuries

• Retrospective study in 2021 by Beyer et al. *Annals of Surgery*:
  • Of 9,284 subjects, 23.3% developed persistent opioid use
  • 8 years later, 6.8% developed OUD with median time to dx at 3 years
Risks of long-term opioid treatment

- Misuse
  - Taking medications inappropriately (e.g., requesting early refills) or diversion
- Addiction
  - Euphoric properties from opioids may render them addictive
- Overdose
  - Accidental vs. intentional
- Mortality
  - Higher doses are associated with increased mortality due to risks for overdose

- Despite increased utilization of opioids, most US Adults report that they are inadequate for pain control.
  - Pain control management is multi-modal
Figure 2. National Drug Overdose Deaths*, Number Among All Ages, 1999-2022

*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.
Shift in Opioid Prescribing

• Due to the risks outweighing the benefits, public health officials addressed these concerns.
• In 2016, the CDC released their Guideline for Prescribing Opioid for Chronic Pain
  • Recommended tapering dose of long-term opioids to 90 MEDD or less leading to forced tapers.
• Opioid tapering led to the emergency of clinical destabilization, increased pain, impaired function, and anhedonia.
  • This unmasked the physiological and psychological dependence associated with long-term opioid treatment.
  • CPOD emerged
Complex Persistent Opioid Dependence vs. Opioid Use Disorder

• **CPOD:**
  • not a DSM-5 diagnosis
  • Characterized by physiological dependence (tolerance, withdrawal symptoms) increased pain and decreased function that is unmasked with tapering of long-term opioid treatment
  • No evidence of intoxication, euphoria with use.
  • Arises from prescription opioids (iatrogenic)

• **Opioid Use Disorder**
  • DSM-5 diagnosis
  • Characterized by lack of control, cravings, and consequences with impaired function in various domains (social, occupational, behavioral) and physiological dependence
  • Arises from prescription opioids (iatrogenic) and/or recreational drug use
Complicating Factors

• Inadequate pain control can manifest with anxiety, depression, insomnia, refill aberrancies, and medication-seeking behaviors.
  • Distinction is whether it is pain-driven

• Inadequate pain control is therefore not considered a “use disorder” despite the above symptoms.

• Risk for alienating patients with CPOD by giving them a substance use disorder diagnosis.
Treatment

• Opioid agonist therapy is gold standard treatment for opioid use disorder and can be beneficial in complex persistent opioid dependence.

• The level of clinical instability can be comparable between OUD and CPOD.

• Treatment of pain is multi-modal and can be addressed through working with a pain specialist, pain psychologist, using non-opioid medications to manage pain, acupuncture, physical therapy, and managing expectations for pain.
Key Points

• CPOD and OUD are two clinically distinct disorders with different origins.
• CPOD was born out of long-term opioid treatment with the changes in the CDC Guidelines unmasking physiological and psychological dependence on opioids. Typically, without functional impairment seen in Opioid Use Disorder.
Benzodiazepines

• Background:
  • In 1960, Chlordiazepoxide entered the market
  • Initially considered safe as a “minor tranquilizer” with low risk for side effects, misuse, or dependence
  • In the 1970s, benzodiazepines became the most prescribed medications in the world.
    • 1975: FDA restricted them due to increasing concerns of misuse, dependence
  • In 2016, FDA placed a black box warning that benzodiazepines should not be prescribed to patients concurrently taking opioids due to risk for overdose death.
Benzodiazepine Use Disorder: Reasons for Use

- Relax or relieve tension: 46.3%
- Experiment: 10.5%
- Get high/hooked: 11.8%
- Help with sleep: 5.7%
- Help with emotions: 2.2%
- Increase or decrease effects of other drugs: 1.8%
- Other reason: 1.5%

National Institute on Drug Abuse
Benzodiazepine Use in the Veteran Population

• American Psychiatric Association & VA/DoD Clinical Guidelines caution against use of benzodiazepines in patients with PTSD.
  • Risks associated with use
  • Lack of evidence supporting improvement in PTSD symptoms.
  • Risk for weakening the treatment effects of exposure-based therapies for PTSD.

• Commonly prescribed:
  • Estimated that 30% of Veterans with PTSD are prescribed a benzodiazepine

• In 2010, 61% of benzodiazepine users received > 90 days supply. (Hawkins et al, 2012)
  • 11% had alcohol use disorder
  • 47% were prescribed opioids long-term
Risks of Benzodiazepine Use

There are more effective and less harmful treatments available for sleep problems, nightmares, PTSD, pain, and anxiety.

- Feeling tired or drowsy
- Memory and thinking problems
- Depression, mood changes, irritability, anger
- PTSD symptoms may get worse
- Becoming physically dependent
- Withdrawal symptoms
- COPD and sleep apnea may get worse
- Pneumonia
- Car accidents
- Arrest for driving while impaired
- Unsteady walking
- Increased risk of falls, broken bones, or concussion

Overdose—especially when combined with alcohol, strong pain medications (opioids), and street drugs

- Birth defects
- Baby may need emergency care because of withdrawal symptoms

The overdose deaths of Heath Ledger, Amy Winehouse, Michael Jackson, and Elvis Presley involved benzodiazepines.

How ready are you to make a change?

Readiness scale

VA Academic Detailing
Overdose deaths show high prevalence of combined opioids and benzodiazepines:
- 30.1% of all opioid overdose deaths in 2010 involved benzodiazepines
- 77.2% of benzodiazepine overdose deaths involved opioids (Jones, et al. 2013)
Figure 2. National Drug Overdose Deaths*, Number Among All Ages, 1999-2022

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Benzodiazepines and Addiction

- Patients prescribed chronic benzodiazepines become physically dependent 58–100%.
- Patients newly started on benzodiazepines develop a substance use disorder 5–10%.
- Patients with substance use disorder history will develop benzodiazepine use disorder 50%.

Guina, J., et al.,

- Benzodiazepines are often not the primary substance used (alcohol, opioids, stimulants) → screen for other use disorders.
- Physical dependence can develop within weeks of starting.

U.S overdose deaths involving a benzodiazepine

- Number of Deaths
- Year
- NIDA, CDC wonder
- 0, 2,000, 4,000, 6,000, 8,000, 10,000
Treatment

• Address the underlying cause for using benzodiazepines (untreated PTSD, anxiety, alcohol use, other substance use)

• Consider tapering the medication if there is evidence of misuse, diversion, or comorbid psychiatric or medical conditions that would put patients at increased risk for complications.

• Benzodiazepines should not be abruptly stopped due to risk for seizures.
Key Points

• Benzodiazepines are effective medications to manage anxiety however carry risk for misuse, dependence, and addiction.

• Benzodiazepines with concurrent opioid use increases the risk for overdose.

• Benzodiazepines should not be abruptly stopped due to risk for seizures.
References


