*VA Data about Prescription Opioids and Overdose and Suicide: Clinical Implications*

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*Original Title: Surprising VA Data About Opioid Discontinuation*, Overdose and Suicide: Clinical Implications  
*Methodological concerns in defining this group were brought to our attention and we are working on re-classifying patients and using more appropriate analyses. These concerns will be discussed during the presentation and we hope will be informative for people doing work in this area.

Moderator: John Eadie, Coordinator, Public Health and Prescription Drug Monitoring Program Project, National Emerging Threat Initiative, A National HIDTA Initiative
Disclosures

- Ajay Manhapra, MD; Elizabeth Oliva, PhD; Friedhelm Sandbrink, MD; and John Eadie have disclosed no relevant, real, or apparent personal or professional financial relationships with proprietary entities that produce healthcare goods and services.

- Stefan Kertesz, MD, MSc – Stock ownership: Abbott, Merc; Spouse stock: Abbott, Merck and Johnson & Johnson
Disclosures

- All planners/managers hereby state that they or their spouse/life partner do not have any financial relationships or relationships to products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

- The following planners/managers have the following to disclose:
  - Kelly J. Clark, MD, MBA, FASAM, DFAPA – Consulting fees: Braeburn, Indivior
Learning Objectives

- Recognize that most patients who are prescribed opioids who end up dying from overdose or suicide are below 90 mg morphine equivalent daily dose and have a mental health or substance use disorder.
- Describe the important role of comorbidities in addressing risk for overdose and suicide among patients prescribed opioids.
- Identify strategies for addressing opioid prescribing among complex patients on long-term opioids for chronic pain.
Drs. Ajay Manhapra, Elizabeth Oliva, and Friedhelm Sandbrink have no personal or professional financial relationships with proprietary entities that produce health care goods and services.

Dr. Stefan Kertesz reports that prior to 2018, he owned stock in Merck & Co. and Abbot Laboratories amounting to less than 3% of assets.

The presentation is the personal opinion of the presenters and does not reflect the official views of the Department of Veterans Affairs or any other Federal Agency.
Clinical Considerations in Addressing Overdose and Suicide Among Patients Prescribed Opioids

- Moving beyond Morphine Equivalent Daily Dose (MEDD) and opioids
  - Based on previous observational research, many assume that overdose is mostly an opioid dose-related event
  - Re-examining data from these studies suggests that:
    - Most patients who die are below commonly recommended MEDD thresholds
    - MH/SUD diagnoses and other comorbidities play just as critical a role, and in some cases an even more critical role than opioids, in overdose and/or suicide outcomes
Clinical Considerations in Addressing Overdose and Suicide Among Patients Prescribed Opioids

- Those at greatest risk of overdose/suicide tend to be complex patients with multiple comorbidities in addition to pain
  - These complex patients may be more likely to drop out of care and/or have trouble adhering to treatment regimens
- Patient-centered risk mitigation addressing comorbidities is important *for all patients*, regardless of MEDD threshold or if opioids are no longer part of the patient’s treatment plan
Three Research Questions Examined in VHA Data Among ALL Patients Prescribed Opioids

STUDY 1

1. What is the relationship between MEDD and overdose and suicide mortality, including when taking into consideration MH/SUD diagnoses?

STUDY 2

2. Have there been any changes in overdose and/or suicide mortality rates following implementation of VHA safety initiatives?

3. (original question) Among patients prescribed opioids in Year 1, is being prescribed an opioid in Year 2 associated with differences in overdose or suicide mortality?
   • What is the role of MH/SUD diagnoses (e.g., main and interaction effects)?
Background
### Pain Management and Opioid Safety as Foundational Services in VHA

- Chronic pain is more common in Veterans than in the non-veteran US population, more often severe and in the context of comorbidities.
- Pain severity and co-concurrence with mental health comorbidities result in high impact pain (e.g., substantial restrictions in work, social, and self-care).
- Behavioral Health Autopsy report (2015): “The most frequently identified risk factor among Veterans who died by suicide was pain”.
- Pain, medical and/or mental comorbidities are often related to military service and/or require Veteran-specific expertise.
- Veterans in VHA had nearly twice the rate of fatal accidental poisoning than adults in general US population (data from 2005).*

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**VHA: Pain Management and Opioid Safety is included in the list of “Foundational Services”**

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* Bohnert et al., Med Care 2011

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#Rx Summit  www.NationalRxDrugAbuseSummit.org
TIMELINE OF VA INITIATIVES TO IMPROVE OPIOID SAFETY

2007
- Launched the Buprenorphine in VA (BIV) Initiative
- Opioid High Risk Medication Initiative

2008
- Policy required access to medication for opioid use disorder

2009
- VA Pain Directive - established Stepped Care Model for Pain

2010
- VA-DoD Clinical Practice Guideline (CPG) Opioid Therapy in Chronic Pain (FIRST)

2011
- Created standardized metrics for pain management therapies to pilot opioid safety initiative in 2012

2013
- Launched the Opioid and Psychotropic Drug Safety Initiatives (OSI & PDSI)

2014
- Targeted interventions for opioid reduction and opioid overdose education and naloxone distribution (OEND)

2016
- VA-DoD CPG on Management of Substance Use Disorders
- Comprehensive Addiction and Recovery Act (CARA)

2017
- VA-DoD CPG Opioid Therapy for Chronic Pain
- Launched Academic Detailing OUD Campaign
- Launched PDSI Phase 3
S.T.O.P. P.A.I.N. HIGHLIGHTS 8 VA BEST PRACTICES
(PRE-SUMMIT WORKSHOP)

- S – Stepped Care Model for Opioid Use Disorder & Pain
- T – Treatment alternatives/Complementary care
- O – Ongoing monitoring of usage
- P – Practice Guidelines
- P – Prescription monitoring
- A – Academic Detailing
- I – Informed Consent
- N – Naloxone distribution
Addressing the Opioid Epidemic in the United States
Lessons From the Department of Veterans Affairs

Over the past 15 years, more than 165,000 people in the United States have died from overdoses related to prescription opioids, and millions more have suffered adverse consequences. The misuse and abuse of prescription opioids have contributed to a precipitous increase in heroin and fentanyl overdoses.

Patients treated in the health care system of the Department of Veterans Affairs (VA) are part of this epidemic. Over half of veterans using the VA, compared with a third of the general population, receive opioid prescriptions. VA expanded its opioid treatment capacity and developed comprehensive guidelines to address opioid misuse. However, the VA faces challenges in addressing the epidemic’s data capabilities and continues to explore strategies to improve the safety of opioid prescribing, while expanding alternative pain therapies (Figure). By mid-2016 compared with mid-2012, the number of veterans dispensed an opioid each quarter had decreased by 172,000, or about 25%. Moreover, there were 57,000 (47%) fewer patients receiving concomitant opioids and benzodiazepines and 22,000 (36%) fewer patients receiving daily opioid dosages of more than 100 morphine-milligram equivalents, both measures of potentially unsafe opioid use. Between 2010 and 2015, the rate of

Strategies to Address the Opioid Epidemic

The VA has employed 4 broad strategies to address the opioid epidemic: education, pain management, risk mitigation, and addiction treatment (eTable in the Supplement). The VA details use sophisticated dashboards with real-time prescriber-level data to engage clinicians in adopting best practices around opioid prescribing. This focus is not simply on reducing opioid medications, but rather on improving the safe use of opioids. Beyond detailing, the VA developed an overdose education and naloxone distribution system that has distributed tens of thousands of naloxone doses and developed standardized patient and provider education to complement local efforts outside of the VA that

Gellad, Good CB, and Shulkin. JAMA Intern Med. 2017 May 1;177(5):611-612
Clinical Considerations in Addressing Overdose and Suicide Among Patients Prescribed Opioids

- Moving beyond Morphine Equivalent Daily Dose (MEDD) and opioids
  - Based on observational research, we tend to assume that overdose in Rx-receiving patients is dose-driven
  - Re-examining data from these studies suggests that:
    • Most patients who die are below recommended MEDD thresholds
    • MH/SUD diagnoses and other comorbidities play just as critical a role, and in some cases an even more critical role than dose in overdose and/or suicide outcomes
Review of Risk Factors for Overdose and OUD

Risk factors are related to:
- Opioid prescribing
- Interaction with other medication/drugs
- Medical comorbidities
- Mental health comorbidities

“Opioid dosage was the factor most consistently analyzed and also associated with increased risk of overdose. Other risk factors include concurrent use of sedative hypnotics, use of extended-release/long-acting opioids, and the presence of substance use and other mental health disorder comorbidities.”

Park et al., J Addict Med 2016
Review of 15 articles published between 2007 and 2015 that examined risk factors for fatal and nonfatal overdose in patients receiving opioid analgesics
Higher Dosage Associated with Increased Risks from Opioids

Hazard Ratios (HR):

**Mortality (all causes):**
- HR 1.64 for LA opioids

**Overdose deaths (unintentional):**
- HR 7.18-8.9 for MME > 100 mg/d

**Opioid use disorder on long-term opioids (> 90 d):**
- HR 15 for 1-36 mg/d MME
- HR 29 for 36-120 mg/d MME
- HR 122 for > 120 mg/d MME

Edlund et al., 2014
Most Opioid Overdoses In Patients with No or Lower Dose Opioids (Bohnert et al, JAMA 2011)

<table>
<thead>
<tr>
<th>Table 2. Unadjusted Rate of Prescription Opioid Overdose Death by Opioid Dose and Fill Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>Patients With Chronic Noncancer Pain Diagnoses</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Maximum prescribed daily opioid dose, mg/d</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-&lt;20</td>
</tr>
<tr>
<td>20-&lt;50</td>
</tr>
<tr>
<td>50-&lt;100</td>
</tr>
<tr>
<td>≥100</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Patients With Acute Pain Diagnoses</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Maximum prescribed daily opioid dose, mg/d</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-&lt;20</td>
</tr>
<tr>
<td>20-&lt;50</td>
</tr>
<tr>
<td>50-&lt;100</td>
</tr>
<tr>
<td>≥100</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Patients With Substance Use Disorder Diagnoses</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Maximum prescribed daily opioid dose, mg/d</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-&lt;20</td>
</tr>
<tr>
<td>20-&lt;50</td>
</tr>
<tr>
<td>50-&lt;100</td>
</tr>
<tr>
<td>≥100</td>
</tr>
</tbody>
</table>
### Most Overdose/Serious Opioid-Induced Respiratory Depression In Patients with No or Lower Dose Opioids
(Zedler et al., Pain Med 2015)

#### Table 1 Continued

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases (n = 817)</th>
<th>Controls (n = 8,170)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAXIMUM PRESCRIBED DAILY MED (mg), Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>98.7 (122.1)</td>
<td>24.2 (48.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum Prescribed Daily MED Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1—&lt;20</td>
<td>35 (4.3)</td>
<td>1,331 (16.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20—&lt;50</td>
<td>227 (27.8)</td>
<td>2,614 (32)</td>
<td></td>
</tr>
<tr>
<td>50—&lt;100</td>
<td>163 (20)</td>
<td>718 (8.8)</td>
<td></td>
</tr>
<tr>
<td>≥100</td>
<td>268 (32.8)</td>
<td>273 (3.3)</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>693 (84.9%)</strong></td>
<td><strong>4,936 (60.4%)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Missing</strong></td>
<td><strong>124 (15.1%)</strong></td>
<td><strong>3,234 (39.6%)</strong></td>
<td></td>
</tr>
</tbody>
</table>
No Clear Cut-Point to Distinguish Opioid Overdose Cases; Majority of Opioid Overdose Deaths Among Patients Below 100 MEDD (Bohnert et al., Med Care 2016)

- Median dosage for patients with opioid overdose was 60 MEDD; i.e., vast majority below 100 MEDD

Average opioid dosages
Cases (overdose deaths):
98.1 MEDD (SD 112.7)

Controls:
47.7 MEDD (SD 65.2)
MH/SUD-related Factors Account for Similar OSORD Risk as Opioid-related Factors in VHA sample
(Zedler et al., Pain Med 2015)

Table 3

<table>
<thead>
<tr>
<th>Question</th>
<th>Points for Yes Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past 6 months, has the patient had a healthcare visit (outpatient, inpatient or ED)</td>
<td></td>
</tr>
<tr>
<td>involving any of the following health conditions?</td>
<td></td>
</tr>
<tr>
<td>1. Opioid dependence?</td>
<td>15</td>
</tr>
<tr>
<td>2. Chronic hepatitis or cirrhosis?</td>
<td>9</td>
</tr>
<tr>
<td>3. Bipolar disorder or schizophrenia?</td>
<td>7</td>
</tr>
<tr>
<td>4. Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)?</td>
<td>5</td>
</tr>
<tr>
<td>5. Chronic kidney disease with clinically significant renal impairment?</td>
<td>5</td>
</tr>
<tr>
<td>6. An active traumatic injury, excluding burns (e.g., fracture, dislocation, contusion, laceration, wound)?</td>
<td>4</td>
</tr>
<tr>
<td>7. Sleep apnea?</td>
<td>3</td>
</tr>
<tr>
<td>Does the patient consume:</td>
<td></td>
</tr>
<tr>
<td>1. An extended-release or long-acting (ER/LA) formulation of any prescription opioid?</td>
<td></td>
</tr>
<tr>
<td>(e.g., OxyContin, Oramorph-SR, methadone, fentanyl patch)</td>
<td></td>
</tr>
<tr>
<td>1. Methadone? (Methadone is a long-acting opioid so also check “ER/LA formulation” [9 points])</td>
<td></td>
</tr>
<tr>
<td>2. Oxycodone? (If it has an ER/LA formulation [e.g., OxyContin] also check “ER/LA formulation” [9 points])</td>
<td></td>
</tr>
<tr>
<td>3. A prescription antidepressant? (e.g., fluoxetine, citalopram, venlafaxine, amitriptyline)</td>
<td></td>
</tr>
<tr>
<td>4. A prescription benzodiazepine? (e.g., diazepam, alprazolam)</td>
<td></td>
</tr>
<tr>
<td>Is the patient’s current maximum prescribed opioid dose?</td>
<td></td>
</tr>
<tr>
<td>1. ≥100 mg morphine equivalents per day?</td>
<td>16</td>
</tr>
<tr>
<td>2. 50–&lt;100 mg morphine equivalents per day?</td>
<td>9</td>
</tr>
<tr>
<td>3. 20–&lt;50 mg morphine equivalents per day?</td>
<td>5</td>
</tr>
</tbody>
</table>

Total point score (maximum 115)

- MH/SUD-related factors 29% of index
- Model ORs:
  - Opioid dep=4.5
  - Bipolar/SZ=1.9
  - Benzo=1.5
  - Antidep=2.0

- Opioid-related factors 32% of index
- Model ORs:
  - ER/LA=2.5
  - Methadone=2.4
  - ≥100 MEDD=5.0

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Table 3  CIP-based risk index for serious opioid-induced respiratory depression (RIOSORD)

<table>
<thead>
<tr>
<th>Question</th>
<th>Points for “yes” response</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past 6 months, has the patient had a health care visit (outpatient, inpatient, or ED) involving any of the following health conditions?†</td>
<td>25</td>
</tr>
<tr>
<td>• Substance use disorder (abuse or dependence)?</td>
<td></td>
</tr>
<tr>
<td>(This includes alcohol, amphetamines, antidepressants, cannabis, cocaine, hallucinogens, opioids, and sedatives/antianxiolytics)</td>
<td></td>
</tr>
<tr>
<td>• Bipolar disorder or schizophrenia?</td>
<td>10</td>
</tr>
<tr>
<td>• Stroke or other cerebrovascular disease?</td>
<td>9</td>
</tr>
<tr>
<td>• Kidney disease with clinically significant renal impairment?</td>
<td>8</td>
</tr>
<tr>
<td>• Heart failure?</td>
<td>7</td>
</tr>
<tr>
<td>• Nonmalignant pancreatic disease (e.g., acute or chronic pancreatitis)?</td>
<td>7</td>
</tr>
<tr>
<td>• Chronic pulmonary disease (e.g., emphysema, chronic bronchitis, asthma, pneumoconiosis, asbestosis)?</td>
<td>5</td>
</tr>
<tr>
<td>• Recurrent headache (e.g., migraine)?</td>
<td>5</td>
</tr>
<tr>
<td>Does the patient consume:</td>
<td></td>
</tr>
<tr>
<td>• Fentanyl?</td>
<td>13</td>
</tr>
<tr>
<td>• Morphine?</td>
<td>11</td>
</tr>
<tr>
<td>• Methadone?</td>
<td>10</td>
</tr>
<tr>
<td>• Hydromorphone?</td>
<td>7</td>
</tr>
<tr>
<td>• An extended-release or long-acting formulation of any prescription opioid?‡</td>
<td>5</td>
</tr>
<tr>
<td>• A prescription benzodiazepine?</td>
<td>9</td>
</tr>
<tr>
<td>• A prescription antidepressant?</td>
<td>8</td>
</tr>
<tr>
<td>Is the patient’s current maximum prescribed opioid dose ≥100mg morphine equivalents per day? (Include all prescription opioids consumed on a regular basis)</td>
<td>7</td>
</tr>
<tr>
<td>Total point score (maximum = 146)</td>
<td></td>
</tr>
</tbody>
</table>

- MH/SUD-related factors 36% of index
- Model ORs: SUD=12.7, Bipolar/SZ=2.8, Benzo=2.3, Antidep=2.2
- Opioid-related factors 36% of index
- Model ORs: Fentanyl=3.7, Methadone=2.8, ER/LA=1.7, ≥100 MED=2.0
MH and SUD Diagnoses Were Largest Predictors of Opioid Overdose in Kaiser Predictive Model
(Glanz et al., JGIM 2018)

Table 3 Unadjusted and Adjusted (final) Cox Regression Models for Predicting 2-Year Overdose Risk for Patients Prescribed Chronic Opioid Therapy at the Derivation Site

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unadjusted model</th>
<th>Adjusted model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>β coefficient</td>
</tr>
<tr>
<td></td>
<td>(95 CI†)</td>
<td>(95 CI†)</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.93 (0.88–0.98)</td>
<td>-0.06915</td>
</tr>
<tr>
<td>Age-squared</td>
<td>1.00 (1.00–1.00)</td>
<td>0.0005626</td>
</tr>
<tr>
<td>Mental health diagnosis</td>
<td>4.18 (2.88–6.07)</td>
<td>1.22076</td>
</tr>
<tr>
<td>Psychotropic prescription</td>
<td>2.82 (1.88–4.25)</td>
<td>1.24387</td>
</tr>
<tr>
<td>Substance abuse/dependence diagnosis</td>
<td>6.01 (4.03–8.96)</td>
<td>0.42788</td>
</tr>
<tr>
<td>Tobacco use or tobacco abuse/dependence diagnosis</td>
<td>2.31 (1.60–3.32)</td>
<td></td>
</tr>
<tr>
<td>History of opioid prescriptions in the year prior to initiating chronic opioid therapy</td>
<td>1.43 (1.00–2.05)</td>
<td></td>
</tr>
<tr>
<td>Long-acting or extended-release opioid formulation</td>
<td>2.47 (1.25–4.87)</td>
<td>0.68552</td>
</tr>
<tr>
<td>Daily opioid dose (per 10 mg morphine equivalents)**</td>
<td>1.01 (0.99–1.03)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C diagnosis†</td>
<td>2.82 (1.04–7.63)</td>
<td></td>
</tr>
</tbody>
</table>
MH and SUD Diagnoses Account for More Opioid Overdose Risk than Opioids (Glanz et al., JGIM 2018)

Table 5: Point-Based System* to Calculate 2-Year Risk of Opioid Overdose Based on Model Coefficients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>18–25</td>
<td>98</td>
</tr>
<tr>
<td>26–30</td>
<td>94</td>
</tr>
<tr>
<td>31–35</td>
<td>91</td>
</tr>
<tr>
<td>36–40</td>
<td>88</td>
</tr>
<tr>
<td>41–45</td>
<td>85</td>
</tr>
<tr>
<td>46–50</td>
<td>84</td>
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<tr>
<td>51–55</td>
<td>83</td>
</tr>
<tr>
<td>56–60</td>
<td>82</td>
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<tr>
<td>61–65</td>
<td>83</td>
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<tr>
<td>66–70</td>
<td>84</td>
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<td>71–75</td>
<td>84</td>
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<td>76–80</td>
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<td>81–85</td>
<td>87</td>
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<td>86–90</td>
<td>89</td>
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<tr>
<td>91–95</td>
<td>92</td>
</tr>
<tr>
<td>96–100</td>
<td>96</td>
</tr>
<tr>
<td>Mental health diagnosis</td>
<td>22</td>
</tr>
<tr>
<td>Substance abuse/dependence diagnosis</td>
<td>22</td>
</tr>
<tr>
<td>Tobacco use or tobacco abuse/dependence diagnosis</td>
<td>8</td>
</tr>
<tr>
<td>Long-acting or extended-release opioid formulation</td>
<td>12</td>
</tr>
</tbody>
</table>

*Scores of summed points, based on patient characteristics, indicate low (≤ 85), medium (86–103) or high risk (≥104)

- **MH/SUD diagnoses**
  - 27% of max points; 69% of non-age related points
- **Opioid-related factor**
  - 7% of max points; 19% of non-age related points
MH/SUD and Non-Opioid Related Factors Have Higher Odds Ratios than Opioid-Related Factors in VHA Predictive Model

Risk increased slightly with increasing MEDD
• e.g., 120 MEDD would increase modeled risk by about as much as a PTSD or AUD diagnosis

STORM Analysis: Oliva et. al. Psych. Services 2017
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High Odds Ratios for Other Evidence-Based Sedating Pain Medications

Odds Ratios for Overdose/Suicide-Related Events

- Having TCAs, SNRIs and Anti-convulsants is associated with increased risk
  - Association could be related to unmanaged pain, cumulative sedation, depressive symptoms, etc.

<table>
<thead>
<tr>
<th>Medication Combination</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid + Sedatives and hypnotics (e.g., benzo, barbiturates)</td>
<td>1.4</td>
</tr>
<tr>
<td>Opioid + 1 other evidence-based sedating pain med (TCA, SNRI, Anti-convulsants)</td>
<td>2.1</td>
</tr>
<tr>
<td>Opioid + 2 other evidence-based sedating pain med</td>
<td>3.6</td>
</tr>
<tr>
<td>Opioid + 3 other evidence-based sedating pain med</td>
<td>6.1</td>
</tr>
</tbody>
</table>

STORM Analysis: Oliva et. al. Psych. Services 2017

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Sum-up so far...

- Opioid dose a risk factor in most studies of overdose in the prescription-receiving population
- Concurrent sedatives and use of extended-release/long-acting opioids also associated with risk
- Most prescription-receiving patients with overdose deaths are at low dose or no prescribed opioids when death happens
- MH/SUD comorbidities highly associated with overdose/suicide
- Receiving opioid Rx, high dose in particular, may be a marker of risk versus a cause of risk
Current Studies
Three Research Questions Examined in VHA Data Among ALL Patients Prescribed Opioids

**STUDY 1**

1. What is the relationship between MEDD and overdose and suicide mortality, including when taking into consideration MH/SUD diagnoses?

**STUDY 2**

2. Have there been any changes in overdose and/or suicide mortality rates following implementation of VHA safety initiatives?

3. (original question) Among patients prescribed opioids in Year 1, is being prescribed an opioid in Year 2 associated with differences in overdose or suicide mortality?
   - What is the role of MH/SUD diagnoses (e.g., main and interaction effects)?
Limitations of Our Studies

- Examined whether patients were prescribed opioids, not whether they filled the prescriptions.

- Not measured: patient or provider behaviors, patient response and adherence to medicines.

- These data examine ALL patients prescribed opioids:
  - Future research should examine those on chronic opioids.

- These analyses were not designed to measure tapering:
  - Working with colleagues to examine tapering in administrative data.

- Administrative data-based analyses:
  - Working with colleagues to use chart review approach to better understand context surrounding overdose and suicide deaths and opioid prescribing patterns:
    - Helped us identify issues with previous “discontinuation” definition—revamping analytical approach for Research Question 3 to address these issues.
Observational data

- “Observational data” means “observed, outside of an interventional trial” and cannot prove causation
- It may reveal signals of interest
- All studies of overdose in populations receiving prescription opioids have used observational data
- Important questions to ask of observational studies
  - What associations were found and how strong?
  - What aspects of the problem might not be captured in the data?
  - Are there characteristics of the people, treatments and contexts that could account for reported associations?
- Question to ask: *Do I wish to infer causality?*
  
  *Correlation ≠ Causation*
Three Research Questions Examined in VHA Data Among ALL Patients Prescribed Opioids

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   • What is the role of MH/SUD diagnoses (e.g., main and interaction effects)?
General Method

- **Patient Population:** VHA patients who received an outpatient opioid analgesic prescription from VHA

- **Data Sources:**
  - VHA Electronic Medical Record (EMR) data-extracts from VHA’s Corporate Data Warehouse
    - Prescription information, demographics, mental health and substance use disorder diagnoses (MH/SUD), medical conditions
  - National Death Index (NDI) data from VA/Department of Defense (VA/DoD) Suicide Data Repository
    - Overdose mortality and suicide mortality
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   • What is the role of MH/SUD diagnoses (e.g., main and interaction effects)?
### Study 1: Descriptive Information

Table 1. Number and percentage of patients across morphine equivalent daily dose (MEDD) ranges by mental health (MH) and/or substance use disorder (SUD) diagnosis and deaths due to overdose and/or suicide in Fiscal Year 2013

#### Overall sample

<table>
<thead>
<tr>
<th></th>
<th>All dose groups</th>
<th>0-10 MEDD</th>
<th>&gt;10-20 MEDD</th>
<th>&gt;20-50 MEDD</th>
<th>&gt;50-90 MEDD</th>
<th>&gt;90-200 MEDD</th>
<th>&gt;200 MEDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1,394,907</td>
<td>223,906</td>
<td>443,937</td>
<td>465,558</td>
<td>158,692</td>
<td>68,354</td>
<td>34,460</td>
</tr>
<tr>
<td>% of the overall sample</td>
<td>100.0%</td>
<td>16.0%</td>
<td>31.8%</td>
<td>33.4%</td>
<td>11.4%</td>
<td>4.9%</td>
<td>2.5%</td>
</tr>
<tr>
<td>MH and/or SUD diagnosis (N)</td>
<td>681,861</td>
<td>94,878</td>
<td>197,756</td>
<td>234,293</td>
<td>90,252</td>
<td>42,321</td>
<td>22,361</td>
</tr>
<tr>
<td>MH and/or SUD diagnosis—% in each dose category (column %)</td>
<td>48.9%</td>
<td>42.4%</td>
<td>44.5%</td>
<td>50.3%</td>
<td>56.9%</td>
<td>61.9%</td>
<td>64.9%</td>
</tr>
</tbody>
</table>

#### Those who died due to overdose and/or suicide

<table>
<thead>
<tr>
<th></th>
<th>All dose groups</th>
<th>0-10 MEDD</th>
<th>&gt;10-20 MEDD</th>
<th>&gt;20-50 MEDD</th>
<th>&gt;50-90 MEDD</th>
<th>&gt;90-200 MEDD</th>
<th>&gt;200 MEDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1,305</td>
<td>101</td>
<td>274</td>
<td>428</td>
<td>224</td>
<td>152</td>
<td>126</td>
</tr>
<tr>
<td>Percentage of all who died (row %)</td>
<td>100.0%</td>
<td>7.7%</td>
<td>21.0%</td>
<td>32.8%</td>
<td>17.2%</td>
<td>11.6%</td>
<td>9.7%</td>
</tr>
<tr>
<td>MH and/or SUD diagnosis (N)</td>
<td>935</td>
<td>66</td>
<td>185</td>
<td>306</td>
<td>176</td>
<td>114</td>
<td>88</td>
</tr>
<tr>
<td>MH and/or SUD diagnosis—% in each dose category (column %)</td>
<td>71.6%</td>
<td>65.3%</td>
<td>67.5%</td>
<td>71.5%</td>
<td>78.6%</td>
<td>75.0%</td>
<td>69.8%</td>
</tr>
</tbody>
</table>
Study 1: FY2013 Overdose/Suicide Mortality

Percentage of Overall FY13 Overdose/Suicide Deaths

Morphine Equivalent Daily Dose (MEDD) Range

- 0-10 MEEDD: 7.8%, SUD diagnosis: 2.5%, MH-only diagnosis: 2.6%, No MH/SUD diagnosis: 2.7%
- >10-20 MEEDD: 6.2%, SUD diagnosis: 6.8%, MH-only diagnosis: 6.8%, No MH/SUD diagnosis: 6.8%
- >20-50 MEEDD: 32.7%, SUD diagnosis: 8.0%, MH-only diagnosis: 11.1%, No MH/SUD diagnosis: 9.3%
- >50-90 MEEDD: 17.2%, SUD diagnosis: 6.9%, MH-only diagnosis: 6.6%, No MH/SUD diagnosis: 3.7%
- >90-200 MEEDD: 11.6%, SUD diagnosis: 4.4%, MH-only diagnosis: 4.3%, No MH/SUD diagnosis: 2.9%
- >200 MEEDD: 9.7%, SUD diagnosis: 3.4%, MH-only diagnosis: 3.4%, No MH/SUD diagnosis: 2.9%
Study 1: Key Findings

- Almost 4 out of every 5 patients who died from overdose/suicide were prescribed doses below 90 MEDD

- Almost 3 out of every 4 overdose/suicide deaths were among patients with MH/SUD diagnoses
Study 1: Conclusions and Discussion

- Overdose and suicide deaths were most frequent among patients prescribed low to moderate opioid doses and patients with comorbid MH/SUD diagnoses.

- Findings highlight limitation of using MEDD thresholds as a solitary marker of risk in population-based risk mitigation strategies.
  - While our findings are consistent with research showing that relative risk increases with higher MEDD, adherence to a common standard of flagging persons above 90 MEDD as high-risk would have missed the vast majority of patients who died from overdose/suicide in our study.

- VHA has taken a multifaceted approach to risk mitigation and these findings will help inform those efforts.
  - see Gellad et al., 2017; VHA’s S.T.O.P. P.A.I.N. initiative.
Three Research Questions Examined in VHA Data Among ALL Patients Prescribed Opioids

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   • What is the role of MH/SUD diagnoses (e.g., main and interaction effects)?
Study 2: Background Information

- **Inclusion criteria:** VHA patients with an outpatient opioid analgesic prescription from VHA in index years FY2010 or FY2013
  - Originally examined follow-up year opioid prescribing: “Opioids Year 2” vs. “No Opioids Year 2” (latter previously labeled “opioid discontinuation”, found this was frequently misinterpreted)
    - Issues with this approach in classifying “No Opioids Year 2” group
      - Did not take into consideration opioid release or days supply data

- **Exclusion criterion:** Patients who died during index year

- **FY2010-2011 Cohort**
  - N=1,263,660; 46.9% MH/SUD diagnosis
    - Overdose deaths=1,035
    - Suicide deaths=661

- **FY2013-2014 Cohort**
  - N=1,352,579; 49.2% MH/SUD diagnosis
    - Overdose deaths=1,014
    - Suicide deaths=668
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>N=1,263,660</td>
<td>Overdose (n=1,035)</td>
<td>Suicide (n=661)</td>
<td>Overall (n=1,352,579)</td>
</tr>
<tr>
<td>Age (M, SD)</td>
<td>59.2 (14.2)</td>
<td>51.5 (11.6)</td>
<td>58.2 (14.5)</td>
<td>59.6 (14.2)</td>
</tr>
<tr>
<td>Currently married</td>
<td>48.4%</td>
<td>24.6%</td>
<td>37.1%</td>
<td>49.2%</td>
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<tr>
<td>Female</td>
<td>7.7%</td>
<td>7.9%</td>
<td>3.8%</td>
<td>8.3%</td>
</tr>
<tr>
<td>OEF/OIF</td>
<td>5.5%</td>
<td>7.0%</td>
<td>6.0%</td>
<td>7.7%</td>
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<tr>
<td>Race/Ethnicity</td>
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<td></td>
</tr>
<tr>
<td>White</td>
<td>72.1%</td>
<td>78.6%</td>
<td>80.0%</td>
<td>70.6%</td>
</tr>
<tr>
<td>Black</td>
<td>18.0%</td>
<td>9.8%</td>
<td>4.1%</td>
<td>18.4%</td>
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<tr>
<td>Hispanic</td>
<td>5.4%</td>
<td>4.2%</td>
<td>3.0%</td>
<td>5.9%</td>
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<tr>
<td>Asian</td>
<td>1.3%</td>
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<td>.6%</td>
<td>1.3%</td>
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<tr>
<td>Native Am</td>
<td>.7%</td>
<td>1.0%</td>
<td>.8%</td>
<td>.5</td>
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<tr>
<td>Urban</td>
<td>61.0%</td>
<td>70.2%</td>
<td>57.9%</td>
<td>62.1%</td>
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<tr>
<td>Rural</td>
<td>37.4%</td>
<td>28.3%</td>
<td>40.7%</td>
<td>36.4%</td>
</tr>
<tr>
<td>Highly Rural</td>
<td>1.6%</td>
<td>1.5%</td>
<td>1.4%</td>
<td>1.5%</td>
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</table>
### Study 2: Descriptive Information cont.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall N=1,263,660</td>
<td>Overdose (n=1,035)</td>
<td>Suicide (n=661)</td>
<td>Overall N=1,352,579</td>
</tr>
<tr>
<td>MH/SUD</td>
<td>46.9%</td>
<td>81.2%</td>
<td>64.1%</td>
<td>49.2%</td>
</tr>
<tr>
<td>Depr d/o</td>
<td>30.2%</td>
<td>56.5%</td>
<td>46.9%</td>
<td>30.5%</td>
</tr>
<tr>
<td>PTSD</td>
<td>17.0%</td>
<td>28.7%</td>
<td>20.9%</td>
<td>19.4%</td>
</tr>
<tr>
<td>AUD</td>
<td>10.3%</td>
<td>34.4%</td>
<td>17.7%</td>
<td>10.2%</td>
</tr>
<tr>
<td>OUD</td>
<td>1.9%</td>
<td>18.4%</td>
<td>6.7%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Medical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>60.1%</td>
<td>54.7%</td>
<td>56.9%</td>
<td>59.6%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28.2%</td>
<td>17.3%</td>
<td>22.2%</td>
<td>29.6%</td>
</tr>
<tr>
<td>COPD</td>
<td>19.1%</td>
<td>24.8%</td>
<td>22.7%</td>
<td>19.3%</td>
</tr>
<tr>
<td>MEDD (M, SD)</td>
<td>34.5 (81.7)</td>
<td>61.2 (76.9)</td>
<td>47.7 (69.4)</td>
<td>33.1 (49.3)</td>
</tr>
<tr>
<td>Sedative co-prescription</td>
<td>23.1%</td>
<td>50.4%</td>
<td>45.1%</td>
<td>23.0%</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------</td>
<td>------------------</td>
<td>--------------------</td>
<td>------------------</td>
</tr>
<tr>
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<td>Overall N=1,263,660</td>
<td>Overdose (n=1,035)</td>
<td>Suicide (n=661)</td>
<td>Overall N=1,352,579</td>
</tr>
<tr>
<td>Sedating medications</td>
<td>SNRI</td>
<td>5.1%</td>
<td>10.9%</td>
<td>6.1%</td>
</tr>
<tr>
<td></td>
<td>TCAs</td>
<td>11.3%</td>
<td>22.6%</td>
<td>11.3%</td>
</tr>
<tr>
<td></td>
<td>Anticonv</td>
<td>22.5%</td>
<td>35.5%</td>
<td>22.6%</td>
</tr>
<tr>
<td>Tier</td>
<td>LA</td>
<td>10.1%</td>
<td>28.0%</td>
<td>9.2%</td>
</tr>
<tr>
<td></td>
<td>Chronic SA</td>
<td>24.5%</td>
<td>31.5%</td>
<td>33.5%</td>
</tr>
<tr>
<td></td>
<td>Acute SA</td>
<td>42.2%</td>
<td>28.5%</td>
<td>32.7%</td>
</tr>
<tr>
<td></td>
<td>Tramadol</td>
<td>20.2%</td>
<td>12.0%</td>
<td>15.5%</td>
</tr>
</tbody>
</table>
Three Research Questions Examined in VHA Data Among ALL Patients Prescribed Opioids

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Overdose and Suicide Mortality Rates
FY2010-11 vs. FY2013-14
Overdose Rate Significantly Decreases Among VHA Patients Prescribed Opioids
Overall Overdose and Suicide Mortality Rates

Deaths per 100,000 VHA Patients Prescribed Opioids In the Prior Year

- Overdose Mortality
  - FY2011: 80
  - FY2014: 72
  - 8% difference

- Suicide Mortality
  - FY2011: 50
  - FY2014: 48
Key Points

- Despite population based increases in overdose and suicide, among patients prescribed outpatient opioids by VHA, overdose rates significantly decreased and there was no significant change in suicide.
- Implementation of VHA safety initiatives occurred over this timeframe.
- MAY suggest that VHA efforts have been helpful.
- Alternative interpretation:
  - VHA could be selecting patients with lower risk for opioid prescribing.
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Classifying “No Opioids in Year 2”

- Originally examined follow-up year opioid prescribing
  - No Opioids Year 2
    - FY2011—31%, FY2014—32%

- Approach did not take into consideration opioid release or days supply data
  - Patients, particularly at the beginning of the follow-up fiscal year (Year 2) may have still been receiving opioids (confounding interpretation of results)

FY2011 Suicide Deaths Per 100,000 Patients: Original Classification

FY2014 Suicide Deaths Per 100,000 Patients: Original Classification
FY2011 Overdose Deaths Per 100,000 Patients: Original Classification

FY2014 Overdose Deaths Per 100,000 Patients: Original Classification
What Can We Say About Year 2 Opioid Prescribing?

- Original abstract suggested “No Opioids in Year 2” compared to “Opioids in Year 2” was not significantly associated with overdose mortality but was significantly associated with increased suicide mortality. Revised abstract does NOT include these analyses given methodological issues that confound analyses and interpretation.
  - Revised analytic approaches will include interrupted time series and survival analyses.
    - Will consider opioid type, dose, release, and days supply; MH/SUD diagnoses, and medical comorbidities.
  - Will continue chart review and tapering analyses.

- Year 1 descriptive data of those who die of overdose or suicide in Year 2 highlight a few important clinical considerations:
  - MH/SUD diagnoses (e.g., AUD and OUD diagnoses)
  - Current marital status (lower rate among patients who overdose; education should emphasize overdose prevention and identify potential responders)
  - Sedating medications (benzos, TCAs, SNRIs, anti-convulsants)
  - Opioid type (large % of overdose [~40%] and suicide [~47%] deaths among those prescribed acute short-acting opioids or tramadol)
Cautionary Tale

- Original abstract had findings that were not interpretable because of issues classifying “No Opioids Year 2” group

- Lessons Learned
  - Opioid vs. no opioid
    - Prescription?
    - Release?
    - Days Supply?
  - Looking at healthcare data when want to know about pharmacological relationships is challenging
  - Including consistent information on length of time with no opioid may be helpful when analyzing and interpreting these types of data
Key Points

- Most VHA patients prescribed opioids who die from overdose/suicide are prescribed BELOW 90 MEDD and have MH/SUD diagnoses
- Overdose mortality rates have significantly decreased among VHA patients prescribed opioids
  - May suggest that VHA initiatives (e.g., discussed during VHA S.T.O.P. P.A.I.N. workshop) are having an impact
- Important to ensure approach to classifying patients as having no opioids includes release dates and days supply
What Can Clinicians Do With This Information?

Strategies for Addressing Opioid Prescribing Among Complex Patients on Long-Term Opioids or Chronic Pain
Three Clinical Reflections

- Drs. Ajay Manhapra and Stefan Kertesz
  - PC-based
- Dr. Friedhelm Sandbrink
  - Pain clinic
- Important considerations across settings
  - Patient-centered approaches that address broad array of patient risk factors, not just opioid-related risk
  - What to do about patients currently prescribed opioids?
  - How to identify and treat prescription opioid-related Opioid Use Disorder (OUD)
Ajay Manhapra, MD, ABAM

- VA Hampton Health Care System
- Yale University
- Director, High Risk Pain PACT
- Internal Medicine & Addiction Medicine

- Views are his own and do not represent positions of the US Department of Veterans Affairs
Overdose and Suicide Deaths: Complicated!!

- Our data suggest
  - Opioid dose strength explains little
  - Mental illness and SUD more significant
- Time to rethink dose reduction as a simple and effective overdose and suicide risk reduction strategy
- Clinically
  - How do we make sense of this?
  - What do we do?
Overdose and Suicide: Complex Problem Requiring a Comprehensive Approach

- Pain
- Opioid need and dependence
- SUD, Medication dependence
- Other Psychological factors
- Physical illness
- Mental illness
Random Sample of Discontinuations from 2012 (N=600)
Psychiatric, SUD and medical comorbidity (multi-morbidity)

- Higher rates of disabling chronic pain
- Requires larger opioid dose for acute pain
- Gets started on high dose LTOT more often
- Receive benzo co-prescription more often
- Higher burden of psycho-polypharmacy
- Higher risk of aberrancy and OUD on LTOT
- Higher risk of developing opioid related complications
- Higher risk of dying due to opioids
- Higher risk of suicide
- Higher risk of problems with tapering
- Higher utilization of healthcare
“Overdose” deaths as a multidrug and multisystem event:

Much more common than you think!!!!!!
Pain: Not a singular experience!

- Depression
- Dysphoria
- Anhedonia
- Decreased libido, disinterest, isolation, social withdrawal
- Sleep disorders
- Changes in cognition
- Lethargy
- Anorexia
- Immobilization
- Irritability
- Anger
- Anxiety
- Changes in cognition
Opioid Pain relief: More than analgesia

Pain intensity reduced

Nociceptive phenomenon mediated through pain pathways

Negative affect reduction

Mediated through Emotional (limbic) pathways

Relief

Mediated through Reward pathways

Shared pathway for relief from other unpleasant affective states: PTSD, depression, anxiety, fear, anger, insomnia etc.
Diagnostic dichotomy vs. Clinical reality

Distinct treatment options

Not OUD/Addiction
Particular set of behaviors absent

OUD/Addiction
Particular set of behaviors present

CDC:
0.7% in low dose
6% in very high dose

Predictable use
Compulsive use

Proportion of patients on long term opioids

Early Dependence → Complex dependence → OUD/Frank addiction

Most patients with chronic pain and problems on opioids

We don’t talk much about the grey areas

#Rx Summit www.NationalRxDrugAbuseSummit.org
Opioids: The boon and the curse

- Provides more than a simple pain relief
- Also provides emotional relief and “relief”
- “Relief” is a powerful “reward”
- Promotes automatic reward based learning with repeated use
- Reward based learning leads to
  - Simple dependence in most
  - Complex dependence in a substantial portion
  - Addiction in a minority
Complex Opioid Dependence: More Than Short Term Physical Withdrawal

- Effect of complex dependence with repeated opioid use
  1. Escalating pain and other psychological symptoms independent of primary pathology
  2. Volatility of pain and other symptoms
  3. Relief with each opioid dose becomes lower and shorter and opioid dose need increases
  4. These changes become difficult to reverse
  5. Opioid cessation or dose reduction results in withdrawals, both acute and protracted
     - Acute: Dominated by physical symptoms
     - Protracted abstinence: Cognitive and affective symptoms, worsening pain and disability persist for months to years
Cessation of Long Term Opioid Use: More Than Acute Withdrawal

- Acute withdrawals: Physical symptoms dominate
- Protracted abstinence: Cognitive and affective symptoms, worsening pain and disability persist for months to years
  - Worsening pain and function
  - Emotional dysregulation and volatility
  - Mood problems
  - Sleep disturbance
  - Medical destabilization
  - Psychiatric instability
Frequent, but not among all

Accumulating anecdotal experience: Significant problems with opioid tapering in a proportion of patients
Re-Explain the Pain
A new diagnosis

• A neurobiology based understanding of pain
• Chronic Pain: Mindless responses to persistent fear/danger
• Multimorbidity drives persistent fear

Relieve multi-morbid distress/fear

• Manage dependencies & distressing illnesses (psych and medical)
• Reduce polypharmacy
• Treat overwhelming distress from pain: multi-modal treatments

Retrain one’s brain to improve function

• Graded exposure and extinction of mal-adaptive behaviors
• Graded mobilization
• Shift locus of control to patient
• CBT, ACT & mindfulness if treatment resistant

Calm the crisis
Stabilize and improve
Self-manage

Only a small part of the treatment plan
Friedhelm Sandbrink, MD

- Director, VA National Pain Management Program

- Views are his own and do not represent positions of the US Department of Veterans Affairs
Approaching Opioid Tapering

- Integrated approach with patient buy-in and active participation leads to improved pain control and enhanced quality of life
- Goal is to improve function and long-term outcome while reducing risk
- Provider approach: empathetic, personalized, building trust
- Patients are often scared about opioid dosage reduction, even desperate or terrified
- Features of opioid use disorder may not be apparent, but manifest with opioid dosage reduction
Approaching Opioid Tapering

- Expectations should be clear and reasonable/achievable. The patient needs a clear plan that appears manageable and helps avoid or minimize fear or anxiety.

- Close collaboration with mental health providers including addiction medicine is recommended for many patients - evaluation for OUD and, if present, referral to Medication-Assisted Treatment is usually indicated.

- Caution: Involuntary tapers may carry significantly greater risk than voluntary tapers, and interfere with collaborative provider/patient relationship and shared decision making.
Opioid Tapering Considerations

- Slow tapering allows physiological and psychological adaptations to occur and provides opportunity for ongoing monitoring and support.

- Several factors go into the speed of taper selected:
  - Slower, more gradual tapers are often the most tolerable and can be completed over a several months to years based on the opioid dose.
  - The longer the duration of the opioid therapy, the longer the taper (but: individualize!)
  - CDC: “… patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages.”

- Common approach: tapering with dose reduction of 5-20% every 4 weeks.
Opioid Tapering Considerations

- Expectations regarding opioid tapering should be clear and reasonable/achievable. A clear plan that appears manageable to the patient helps avoid or minimize fear or anxiety.

- Rapid opioid dosage reductions may be required in situations where the urgent safety concerns and risks of continuing the opioid outweigh the risks of a rapid taper.

- Sudden interruption of opioid prescribing must be avoided for opioid dependent patients with few exceptions (urgent safety issues, diversion, etc.).

- Involuntary opioid tapering is generally not recommended.

- F/u is recommended within 1 to 4 weeks after dosage adjustment, and more frequent if clinically indicated.

- Contact information to allow for feedback and, if needed, urgent follow-up to address concerns.
Patient-Centered Opioid Tapering

- Community-based outpatient pain specialty clinic
- High dose opioid patients were sent a letter to volunteer for opioid dose reduction with education/support
- 110 eligible, 82 (75%) enrolled; 68 provided baseline data; 51 provided 4-month follow-up
- Baseline MEDD 288 (153-587) mg, median 6 year duration (3-9) of opioid use
- After 4 months: median MEDD 150 (54-248) mg
- Starting dose, baseline pain intensity, years on opioids, or any psychosocial variable did not predict likelihood of >50% dosage reduction
- Pain intensity and pain interference did NOT increase with opioid reduction

Darnall et al., JAMA Int Med 2018
Stefan G. Kertesz, MD, MSc

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- Views are his own and do not represent positions of the US Department of Veterans Affairs
Findings

- Voluntary + well-run programs
- Dose reduction can be achieved for some patients
- Some do feel better
- Rated as “low quality evidence”

Limitations

- No studies of mandatory, involuntary opioid discontinuation
- Insufficient evidence on adverse events such as “overdose, switch to illicit opioids, onset of suicidality”
Two Windows Into Taper and Cessation

- N=600 discontinued patients’ records (2011-12)
- Half with SUD & half without
- Most discontinuations initiated by clinician (85%)
- Most discontinuations related to aberrant behaviors
- This was not an outcomes study

- 110 high-dose patients invited to attempt reduction voluntarily and with support
- 75% enrolled, 51 (62%) provided follow-up
- Median dose fell 288 → 150 MME

Lovejoy et al., Pain 2017
Darnall et al., JAMA Int Med 2018
Figure. Change in Opioid Morphine Equivalent Daily Dose and Absolute Change in Pain Intensity Score From Baseline to Month 4 for Study Completers

NRS indicates numeric rating scale.
Regardless of Setting, Clinicians Are Navigating Complex Terrain

- Quality metrics on dose
- PDMP
- Law enforcement risk
- Medical Board rules
- Employer Rules

What do clinicians need?
- Guidance
- Safe harbor
- Resources

What do patients need?
- Respect
- Care for complex comorbid conditions
- A say in their care
Opiate Advice Team
Birmingham VA Medical Center

- Clinicians historically “flagged” and ended opioid therapy after aberrant behaviors
- Our new system: Opiate Advice Team consult
  - Clinician requests review for flag
  - We review chart, PDMP and risk profile
  - Flag decision based safety risk
  - Flag does not stop/start or foreclose an opioid
  - Flag is accompanied by an advisory review
  - It can include recommended referral to “Pain Risk Mitigation Clinic” and resource suggestions
Conclusions

- Opioid overdose and suicide risks are complex; opioid dosage and opioid/sedative co-prescribing are only one of many factors contributing to risk
- MH/SUD co-morbidities are common in patients prescribed opioid medication and contribute greatly to risk
- A focus on opioid tapering alone is not going to be sufficient
- Clinical guidance should emphasize biopsychosocial pain care that is individualized and patient-centered, i.e., Whole Person care
In Summary

- Opioid related overdose and suicide risk is determined by a complex set of factors
  - Opioid dose needs
  - Mental illness
  - SUD (current or prior)
  - Medical illnesses
  - Psycho-polypharmacy
  - Polysubstance use
  - Acute healthcare service utilization for the above
- And, not just the dose and benzo co-prescription
Overdose and Suicide: Complex Problem Requiring a Comprehensive Approach

Pain

Mental illness

Physical illness

Opioid need and dependence

SUD, Medication dependence

Other Psychological factors
VA Data about Prescription Opioids and Overdose and Suicide: Clinical Implications

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Original Title: Surprising VA Data About Opioid Discontinuation*, Overdose and Suicide: Clinical Implications

*Methodological concerns in defining this group were brought to our attention and we are working on re-classifying patients and using more appropriate analyses. These concerns will be discussed during the presentation and we hope will be informative for people doing work in this area.

Moderator: John Eadie, Coordinator, Public Health and Prescription Drug Monitoring Program Project, National Emerging Threat Initiative, A National HIDTA Initiative

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