Opiate-Use Disorder in American Indians

HOW SEVERE? RONALD SHAW, M.D.
HOW TO PREVENT?
HOW TO TREAT? OSAGE NATION HEALTH SERVICES
Why the concern now?

- Markedly increased fatal opioid death rate, i.e. people are dying at increasing rates
- When people merely suffered, the approach was more of that of therapeutic nihilism
- Stigma was and is a formidable obstacle in designing and accepting effective prevention and treatment strategies, e.g. MAT->"substituting one drug for another"
- Total overdose death rates remain high and includes overdoses from methamphetamine and alcohol-related accidents
- Many opioids are legal and methamphetamine is not (with rare exception)
### TABLE 2. Number and age-adjusted rates (per 100,000 population) of total drug overdose deaths for American Indians/Alaska Natives and non-Hispanic whites, by sex, age, and rural/urban residence — Washington, 2013–2015

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>American Indian/Alaska Native</th>
<th>Non-Hispanic white</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>116</td>
<td>51.8 (42.7–64.7)</td>
</tr>
<tr>
<td>Female</td>
<td>68</td>
<td>30.1 (23.3–39.2)</td>
</tr>
<tr>
<td><strong>Age group (yrs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>18</td>
<td>8.4 (5.0–13.2)</td>
</tr>
<tr>
<td>25–39</td>
<td>59</td>
<td>57.0 (43.4–73.5)</td>
</tr>
<tr>
<td>40–54</td>
<td>76</td>
<td>29.7 (20.7–112.3)</td>
</tr>
<tr>
<td>≥55</td>
<td>31</td>
<td>39.4 (26.8–55.9)</td>
</tr>
<tr>
<td><strong>County type of residence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metropolitan (urban)</td>
<td>160</td>
<td>43.3 (36.7–51.5)</td>
</tr>
<tr>
<td>Nonmetropolitan (rural)</td>
<td>24</td>
<td>30.5 (19.3–48.1)</td>
</tr>
</tbody>
</table>

TABLE 1. Corrected* and uncorrected age-adjusted total drug, opioid-involved, and heroin-involved overdose mortality rates (per 100,000 population) and rate ratios for American Indians/Alaska Natives and non-Hispanic whites — Washington and United States, 2013–2015

<table>
<thead>
<tr>
<th>Race</th>
<th>Population</th>
<th>Type of drug overdose rate (95% CI)</th>
<th>Total drug</th>
<th>Opioid-Involved</th>
<th>Heroin-Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian/Alaska Native</td>
<td>WA (corrected)</td>
<td>40.9 (35.1–48.0)</td>
<td>27.5 (22.8–33.5)</td>
<td>16.7 (13.1–21.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>WA (uncorrected)</td>
<td>28.7 (23.7–33.7)</td>
<td>19.6 (15.7–24.2)</td>
<td>11.9 (8.9–15.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>US (uncorrected)</td>
<td>13.2 (12.5–13.8)</td>
<td>7.6 (7.1–8.0)</td>
<td>2.4 (2.1–2.6)</td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>WA (corrected)</td>
<td>15.1 (14.5–15.7)</td>
<td>10.2 (9.7–10.7)</td>
<td>4.1 (3.7–4.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>WA (uncorrected)</td>
<td>15.7 (15.0–16.3)</td>
<td>10.6 (10.1–11.2)</td>
<td>4.3 (4.0–4.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>US (uncorrected)</td>
<td>19.2 (19.1–19.3)</td>
<td>12.1 (12.0–12.2)</td>
<td>4.4 (4.4–4.5)</td>
<td></td>
</tr>
</tbody>
</table>

**AI/AN:NHW rate ratios**

| WA AI/AN:NHW (corrected) | — | 2.7 (2.3–3.1) | 2.7 (2.3–3.2) | 4.1 (3.2–5.2) |
| WA AI/AN:NHW (uncorrected) | — | 1.8 (1.3–2.6) | 1.8 (1.5–2.3) | 2.8 (2.1–3.6) |
| U.S. AI/AN:NHW (uncorrected) | — | 0.69 (0.65–0.72) | 0.63 (0.59–0.67) | 0.55 (0.49–0.61) |
| WA AI/AN (corrected:uncorrected) | — | 1.4 (1.0–2.1) | 1.4 (1.1–1.8) | 1.4 (1.0–2.0) |

Sources: Washington Center for Health Statistics Death Files 2013–2015 linked with the Northwest Tribal Registry (corrected data); CDC WONDER online database, Multiple Cause of Death data 2013–2015 (uncorrected data).
How many have died?


Source: Washington Center for Health Statistics Death Files 1999–2015, corrected for AI/AN misclassification through linkage with the Northwest Tribal Registry.

Abbreviations: AI/AN = American Indian/Alaska Native; NHW = non-Hispanic white.

* Per 100,000 persons.
† Three-year rolling averages.
§ Total drug overdose deaths include opioid-involved and nonopioid-involved deaths; opioid-involved deaths include heroin-involved deaths.
How many are dying?
Who is dying from Opiate overdose?

OVERDOSE Deaths Involving Opioids among Native Americans U.S. 2000-2016

- Deaths per 100,000 population
- Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2016 on CDC WONDER Online Database
Who is dying in the Indian population?

The opioid overdose death rate among Native American males significantly exceeds the rate among Native American females (10.0 per 100,000 vs. 7.0 per 100,000). Opioid overdose deaths are significantly more common among Native Americans between the ages of 25-64.

SOURCE: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2016 on CDC WONDER Online Database
Which Opiate is Killing Us?

HEROIN Overdose Deaths among Native Americans by Sex & Age, U.S. 2014-2016

More than twice as many Native American men (4.0 per 100,000) die from a heroin overdose than Native American women (1.8 per 100,000).

The most common age groups when heroin overdose deaths occur are during ages 25-34 (6.9 per 100,000) and ages 35-44 (5.4 per 100,000).

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2016 on CDC WONDER Online Database.
<table>
<thead>
<tr>
<th>Type of Substance Use</th>
<th>Grade 8 American Indian, % (95% CI)</th>
<th>MTTF, %&lt;sup&gt;a&lt;/sup&gt;</th>
<th>RR (95% CI)</th>
<th>Grade 10 American Indian, % (95% CI)</th>
<th>MTTF, %&lt;sup&gt;a&lt;/sup&gt;</th>
<th>RR (95% CI)</th>
<th>Grade 12 American Indian, % (95% CI)</th>
<th>MTTF, %&lt;sup&gt;a&lt;/sup&gt;</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>15.8 (10.7-22.7)</td>
<td>7.3</td>
<td>2.1 (1.4-3.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24.1 (20.0-28.7)</td>
<td>19.9</td>
<td>1.2 (1.0-1.5)</td>
<td>30.7 (25.1-36.9)</td>
<td>33.2</td>
<td>0.9 (0.8-1.1)</td>
</tr>
<tr>
<td>Been drunk</td>
<td>9.6 (5.8-15.4)</td>
<td>1.8</td>
<td>5.3 (3.3-8.9)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16.5 (12.9-20.8)</td>
<td>9.0</td>
<td>1.8 (1.4-2.4)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23.2 (17.7-29.8)</td>
<td>20.4</td>
<td>1.1 (0.8-1.5)</td>
</tr>
<tr>
<td>Binge drinking</td>
<td>11.8 (6.4-20.6)</td>
<td>3.4</td>
<td>3.5 (2.0-6.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16.6 (13.6-20.0)</td>
<td>9.7</td>
<td>1.7 (1.4-2.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>22.8 (18.3-28.1)</td>
<td>15.5</td>
<td>1.5 (1.2-1.9)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Marijuana</td>
<td>22.5 (16.1-30.5)</td>
<td>5.4</td>
<td>4.2 (3.1-5.8)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>35.1 (28.2-42.8)</td>
<td>14.0</td>
<td>2.5 (2.0-3.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>39.3 (32.1-46.9)</td>
<td>22.5</td>
<td>1.7 (1.4-2.2)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Any illicit drug, not marijuana&lt;sup&gt;c&lt;/sup&gt;</td>
<td>6.4 (4.6-8.9)</td>
<td>2.7</td>
<td>2.7 (1.7-3.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6.7 (3.8-11.7)</td>
<td>4.4</td>
<td>1.5 (0.9-2.7)</td>
<td>9.7 (7.0-13.3)</td>
<td>6.9</td>
<td>1.4 (0.9-2.0)</td>
</tr>
<tr>
<td>Inhalants</td>
<td>4.9 (3.4-7.2)</td>
<td>1.8</td>
<td>2.7 (1.8-4.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.2 (1.2-3.9)</td>
<td>1.0</td>
<td>2.2 (1.2-4.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.1 (1.2-3.6)</td>
<td>0.8</td>
<td>2.6 (1.2-6.1)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>1.4 (0.7-2.9)</td>
<td>0.8</td>
<td>1.8 (0.9-3.5)</td>
<td>1.6 (0.9-3.0)</td>
<td>1.5</td>
<td>1.1 (0.5-1.9)</td>
<td>2.7 (1.8-4.2)</td>
<td>1.9</td>
<td>1.4 (0.9-2.3)</td>
</tr>
<tr>
<td>Narcotics other than heroin</td>
<td>1.3 (0.7-2.3)</td>
<td>NA</td>
<td>NA</td>
<td>2.8 (1.6-4.9)</td>
<td>NA</td>
<td>NA</td>
<td>4.9 (2.8-8.2)</td>
<td>1.7</td>
<td>2.9 (1.6-5.2)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>1.6 (0.8-3.4)</td>
<td>1.7</td>
<td>0.9 (0.5-1.8)</td>
<td>2.5 (1.5-4.1)</td>
<td>2.7</td>
<td>0.9 (0.5-1.6)</td>
<td>4.3 (2.8-7.3)</td>
<td>3.0</td>
<td>1.5 (0.8-2.6)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>1.2 (0.6-2.5)</td>
<td>0.3</td>
<td>4.0 (1.9-9.4)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.4 (1.3-4.4)</td>
<td>0.3</td>
<td>8.0 (3.7-17.6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.1 (2.8-6.1)</td>
<td>0.5</td>
<td>6.8 (3.5-13.1)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Crack</td>
<td>0.8 (0.3-2.1)</td>
<td>0.2</td>
<td>4.0 (1.5-10.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.3 (5.9-2.9)</td>
<td>0.2</td>
<td>6.5 (2.5-15.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.7 (0.6-4.8)</td>
<td>0.5</td>
<td>3.4 (1.6-12.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>LSD</td>
<td>1.5 (0.8-2.8)</td>
<td>0.4</td>
<td>3.8 (2.3-9.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.5 (0.6-4.2)</td>
<td>0.7</td>
<td>2.1 (0.8-6.4)</td>
<td>2.5 (1.4-4.6)</td>
<td>1.0</td>
<td>2.5 (1.2-5.1)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hallucinogens other than LSD</td>
<td>2.2 (1.3-3.8)</td>
<td>0.3</td>
<td>7.3 (4.1-13.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.7 (1.8-7.4)</td>
<td>0.5</td>
<td>7.4 (3.4-15.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.8 (1.7-4.5)</td>
<td>0.7</td>
<td>4.0 (2.2-7.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Heroin</td>
<td>0.8 (0.3-2.1)</td>
<td>0.2</td>
<td>4.0 (1.4-10.9)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.6 (0.2-1.3)</td>
<td>0.2</td>
<td>3.0 (1.2-8.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.5 (0.1-3.2)</td>
<td>0.2</td>
<td>2.5 (0.3-18.3)</td>
</tr>
<tr>
<td>Crystal meth&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.0 (0.4-2.4)</td>
<td>0.3</td>
<td>3.3 (2.6-4.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.4 (0.8-2.7)</td>
<td>0.2</td>
<td>7.0 (3.1-14.9)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.3 (1.6-6.8)</td>
<td>0.4</td>
<td>8.3 (3.0-19.1)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>10.6 (7.8-14.2)</td>
<td>2.6</td>
<td>4.1 (2.9-5.8)</td>
<td>15.1 (10.4-21.3)</td>
<td>4.9</td>
<td>3.1 (2.1-4.7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23.1 (17.9-29.4)</td>
<td>10.5</td>
<td>2.2 (1.6-2.9)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Racial disparities in overdose deaths

In 2016, African Americans were two times more likely to die of a drug overdose than whites.

In 2016, American Indians were almost six times more likely to die of drug overdose than whites.
Groups at Greatest Risk for Prescription Drug Abuse/Overdose

- Men aged 25-54 have the highest prescription drug overdose rates, although rates for women 25-54 are increasing faster.
- People in rural counties are about two times as likely to overdose on prescription painkillers as people in big cities.
- Teens/young adults
- Soldiers and veterans
Groups at Greatest Risk for Prescription Drug Abuse/Overdose

- Individuals with occupational injuries
- Individuals with mental illness or past substance abuse
- Whites and American Indians or Alaska Natives are more likely to overdose on prescription painkillers.
Prescription Drug Abuse – American Indians

- Data indicate high usage of illicit drugs by American Indians and outline the need for targeted resources and outreach.
- American Indian and Alaskan Native populations show high percentages of:
  - Lifetime abuse (64.8 percent)
  - Past year illicit drug use (27.1 percent)
  - Current non-medical use of prescription drugs (6.2 percent)
Source of Nonmedical Pain Relievers Among Persons Aged 12 or Older Who Used in the Past 12 Months

- From a friend or relative for free: 54.0%
- Bought drug from a friend or relative: 10.9%
- Prescription from one doctor: 19.7%
- Drug from dealer/other stranger: 4.3%
- Internet: 0.2%
In 2008, there were 14,800 prescription painkiller deaths. For every 1 death there are:

- 10 treatment admissions for abuse
- 32 emergency dept visits for misuse or abuse
- 130 people who abuse or are dependent
- 825 nonmedical users
Risk factors for American Indian Opiate Use Disorder

- higher incidence of historical trauma
- higher incidence of adverse childhood experiences
- lack of access to medical care and/or non-opioid treatment options
- stigma in pursuing chemical health treatment and recovery supports
- lack of access to culturally responsive treatment programs
- lack of trust with Western medicine interventions
- failure to appropriately diagnose physical or mental health symptoms
- lack of research about the effectiveness of interventions within people of color and American Indian communities
- access to illicit drugs within the community
- racial bias on the part of providers who prematurely and/or abruptly discontinue opioids
- illicit drugs are currently addressing symptoms
- cultural acceptance of sharing prescription medications with loved ones
Historical Trauma

- Historical loss
  - Loss of population/land/culture
- Historical loss symptoms
  - Depression
  - SUD
  - Dysfunctional parenting
- Physiological stress involving the Hypothalamic pituitary axis and the amygdala of the brain
  - “a legacy of chronic trauma and unresolved grief”
  - A part of “culturally competent care”
Text Box 1
DSM-5 Criteria for Opioid Use Disorder OUD Presented in the Author’s Mnemonic

Long Time Craving Control $\rightarrow$ TRASHed $\rightarrow$ Withdrawn
Longer use or larger amounts used than intended
Time spent obtaining opioids, using, or recovering from use
Craving opioids
Failed attempts to control or cut back opioid use
Opioid tolerance
Role failure due to opioid use
Activities reduced because of recurrent opioid use
Social problems resulting from recurrent opioid use
Health problems resulting from recurrent opioid use
Dangerous opioid use: use despite risk of physical hazard
Opioid withdrawal syndrome

In the above mnemonic, the satisfaction of two or more criteria in a 12-month period defines opioid use disorder. Criteria are listed in order of severity, progressing from milder criteria to those criteria that most impair function or cause distress. Severity scaling is determined by the number of criteria that are met and may be remembered by “5 or 4 is a moderate score” (2–3 = mild; $\geq 6$ = severe).
Opiate binding receptors
### Comparison of FDA-Approved Medications to Treat Opioid Use Disorder with Physiological Opioid Dependence

<table>
<thead>
<tr>
<th>Medication</th>
<th>MOR intrinsic activity</th>
<th>MOR binding</th>
<th>Differential pharmacology affecting MOR activation at therapeutic dose</th>
<th>Mechanism of relapse prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Partial agonist</td>
<td>High affinity</td>
<td>$K_i = 0.2$ nM</td>
<td>Slow MOR dissociation allows thrice-weekly sublingual dosing and possibility of high-dose weekly formulations(^\text{13-15}); Highest known MOR affinity makes rescue from overdose by naloxone less effective(^\text{16}); rapid precipitation of withdrawal if full agonists present</td>
</tr>
<tr>
<td>Methadone</td>
<td>Full agonist</td>
<td>High affinity</td>
<td>$K_i = 3.4$ nM</td>
<td>Long terminal half-life (up to 120 hours) with delayed steady-state efficacy poses increased MOR toxicity risk during induction phase(^\text{17}); Multiple drug-drug interactions pose both opioid-toxicity and withdrawal risks during treatment(^\text{18})</td>
</tr>
<tr>
<td>Naltrexone ER</td>
<td>Antagonist</td>
<td>High affinity</td>
<td>$K_i = 0.26-0.34$ nM</td>
<td>Lack of MOR agonism associated with delayed stabilization of opioid craving(^\text{19}); Safety concern based on rodent data demonstrating chronic naltrexone exposure increases respiratory-depression risk upon opioid agonist reexposure(^\text{20})</td>
</tr>
</tbody>
</table>

\(^*\) Equilibrium dissociation constant for the test compound and relative values are from Voipe et al. (2011)\(^\text{21}\)

\(^1\) Equilibrium dissociation constant is from Yuen et al. (2013)\(^\text{22}\)

MOR, mu-opioid receptor; ER, extended release; nM, nanomoles.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Percentage opioid free on medication</th>
<th>Percentage opioid free on placebo/detoxification</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naltrexone ER</td>
<td>36</td>
<td>23</td>
<td>Krupitsky et al. (2011)</td>
</tr>
<tr>
<td>Buprenorphine/naloxone</td>
<td>20-50</td>
<td>6</td>
<td>Fudala et al. (2003)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weiss et al. (2011)</td>
</tr>
<tr>
<td>Buprenorphine/naloxone</td>
<td>60</td>
<td>20</td>
<td>Woody et al. (2008)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mattick et al. (2009)</td>
</tr>
<tr>
<td>Methadone</td>
<td>60</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

ER, extended release.

a The randomized, controlled clinical trials summarized here paired medication maintenance with evidence-based psychosocial treatments and opioid use self-report data that were confirmed with urine toxicology. Clinical settings for treatment delivery may affect the rates of opioid use in the nonmedication control groups. The trials predominantly used adult opioid use disorder populations, with the majority being heroin dependent or having mixed dependence on heroin and prescription opioids.

b All medications are FDA approved.

c Population was prescription opioid-dependent patients.

d Population was youth aged 14-21 years.
Components of Successful Treatment

Evaluation
Appropriate detoxification
Identification of co-occurring disorders
Appropriate pharmacotherapy of co-occurring disorders
Appropriate pharmacotherapy of substance use disorder
Comprehensive curriculum to include 12 step facilitation
Family therapy
Discharge planning
Who needs to be admitted to a facility?

- Acute intoxication or medical instability
- Acute withdrawal other than opiate
- Homeless
- Inadequate support system
- No transportation to outpatient therapy
- Complicating medical/psychiatric co-morbidity
Who may be treated as an outpatient:

Stable and sober environment
Non-suicidal
No significant psychotic symptoms
Outpatient program sufficiently intense enough to address patients severity of illness
Opiate dependent patients do not all or even most do not require medical detoxification
Patients are not done with treatment when program completed-up to a years outpatient treatment/counseling is recommended
Medial Complications of Opiate Use Disorder

Accidental Overdose Death
High risk sexual behaviors-STD
Hepatitis B and C/HIV
Family and parental dysfunction
Incarceration
Unemployment
Depression/anxiety
Opiate withdrawal
Socioeconomic Effects of Opioid Use Disorder

Adverse childhood experiences
Joblessness
Medical costs
Incarceration
Loss of or disregard for cultural influence
Unintended modeling for children
Loss of normal emotional development in adolescence
Going Forward

Defeat the stigma against addictive disease and MAT
Youth prevention using cultural strengths and identification as tools
Early detection and treatment
Availability of MAT providers in I/T/U treatment programs
Increase intensity of treatment of outpatient programs
Wellness courts to emphasize recovery instead of punishment
Address the psychosocial context
Support and encourage physician conservatism in prescribing opioids