Ensuring balance in the Medical Use of Opioids

Wisconsin State Capital
February 18th, 2015

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WHO Collaborating Center for Pain Policy and Palliative Care
UW Carbone Cancer Center
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Website: http://www.painpolicy.wisc.edu
POLICY IMPACT

PRESCRIPTION PAINKILLER OVERDOSES

National Center for Injury Prevention and Control
Division of Unintentional Injury Prevention
Policy Impact: Prescription Painkiller Overdoses

What's the Issue?

In a period of nine months, a tiny Kentucky county of fewer than 12,000 people sees a 53-year-old mother, her 35-year-old son, and seven others die by overdosing on pain medications obtained from pain clinics in Florida. In Utah, a 13-year-old fatally overdoses on oxycodone pills taken from a friend’s grandmother. A 20-year-old Boston man dies from an overdose of methadone, only a year after his friend also died from a prescription drug overdose.

These are not isolated events. Drug overdose death rates in the United States have more than tripled since 1990 and have never been higher. In 2008, more than 36,000 people died from drug overdoses, and most of these deaths were caused by prescription drugs.

100 people die from drug overdoses every day in the United States.

Drug overdose death rates in the US have more than tripled since 1990.
Real Life Situation

• 55 yo woman with Pancreatic cancer:
  – methadone for pain
• After death, tablets placed in bathroom cabinet
• ???? Diversion
• 17 year old boy takes single 5 mg tablet
• Mother notices toxicity: Taken to ER
• ER administers Naloxone:
  – Clinical improvement: Discharged
• Found dead the next morning.
Real Life Situation

- 55 yo woman with Pancreatic cancer:
  - methadone for pain; Dies from cancer
- After death, tablets placed in bathroom cabinet
- ???? “Diversion”
- 17 year old boy takes single 5 mg tablet
- Mother notices toxicity: Taken to ER
- ER administers Naloxone:
  - Clinical improvement: Discharged
- Found dead the next morning.
1842: Jeanne Garnier, a widow
Founder of the Women of Calvary

“I started my hospice with 50 Francs;
...............providence did the rest.”

A house for patients at the end of the lifetime
An image, too often unhoped-for, which bring comfort,
a start of happiness in the medium of the suffering.
A house where one speaks again of the life,
even if is also there to die.

1875: Paris
1899: Calvary Hospice, New York
New Opioid Medicines

• Laudanum (opium in alcohol base)
• 1811: Morphine
  – Sertturner, Morpheus: Civil War veterans.
• 1874: Heroin
  – Wright (Bayer. 1898)
• 1916: Oxycodone
“Addiction” History

• Opioid addiction
  – 1900: Opium less problems than alcohol
    • Elderly white woman and civil war veterans
  – 1915: Harrison Act
  – 1920: Dangerous Drug Act
  – 1938: 25,000 MDs arraigned on narcotics charges
    • 3,000 served penitentiary sentences.
  – World War II
    • No addiction
    • Heroin usage increase post war
    • Addiction: immigrant young adults in poor areas.
New Opioids

- Laudanum (opium in alcohol base)
- 1811: Morphine
  - Serturner, Morpheus: Civil War veterans.
- 1874: Heroin
  - Wright (Bayer. 1898)
- 1916: Oxycodone
- 1920: Hydrocodone
- 1932: Pethidine (Demerol)
  - Germany: Anti-spasmodic and analgesic
- 1938: Methadone
  - Dolorphine
  - End Pain
Cecily Saunders

1850
Nottingham
1950
Sydney
2000
London

Nurse
Social Worker
Physician

1957: St Joseph’s Hospice

Documented use of regular morphine at St Luke’s
St Christopher’s Hospice
New Opioids

- Laudanum (opium in alcohol base)
- 1811: Morphine
  - Sertturner, Morpheus: Civil War veterans.
- 1874: Heroin
  - Wright (Bayer, 1898)
- 1916: Oxycodone (Germany)
- 1920: Hydrocodone
- 1932: Pethidine (Demerol)
  - Germany: Anti-spasmodic and analgesic
- 1938: Methadone (Germany)
  - Dolorphine: End Pain
- 1960: Fentanyl
Establishes a Framework to:

1. Prevent abuse and diversion, and

2. Ensure the availability of drugs for medical purposes
“the medical use of narcotic drugs continues to be indispensable for the relief of pain and suffering... adequate provision must be made to ensure the availability of narcotic drugs for such purposes....

(Preamble, p. 13)
"Do what good we can to those around us... There are still so many we cannot reach except by prayer; Let us then pray for the dying today, those for whom tomorrow will be too late."

-Venerable Mary Potter
Founder, Little Company of Mary Sisters
The WHO three-step analgesic ladder

Wisconsin Cancer Pain Initiative

- **1970s: Heroin for pain relief**
  - June Dahl, PhD
  - Professor of Pharmacology
  - David Joranson, MSW
  - WI Controlled Substances Board

- **1985: CSB initiated WCPI**
  - US Assistant Surgeon General
  - U.S. PHS' Interagency Committee on Pain & Analgesia
  - Supportive message from NIDA Director, Charles Shuster.

- **1988: Natl Inst for Drug Abuse --> funded WCPI**
  - To analyze drug use and diversion following a campaign to improve treatment of severe pain due to cancer.
  - No increase in Morphine related crime:
    with increased morphine consumption
PAIN AND ITS TREATMENT IN OUTPATIENTS WITH METASTATIC CANCER

Charles S. Cleeland, Ph.D., René Gonin, Ph.D., Alan K. Hatfield, M.D., John H. Edmonson, M.D., Ronald H. Blum, M.D., James A. Stewart, M.D., and Kishan J. Pandya, M.D.

Abstract  Background and Methods. Pain is often inadequately treated in patients with cancer. A total of 1308 outpatients with metastatic cancer from 54 treatment locations affiliated with the Eastern Cooperative Oncology Group rated the severity of their pain during the preceding week, as well as the degree of pain-related functional impairment and the degree of relief provided by analgesic drugs. Their physicians attributed the pain to various factors, described its treatment, and estimated the impact of pain on the patients' ability to function. We assessed the adequacy of prescribed analgesic drugs using guidelines developed by the World Health Organization, studied the factors that influenced whether analgesia was adequate, and determined the effects of inadequate analgesia on the patients' perception of pain relief and functional status.

Results. Sixty-seven percent of the patients (871 of 1308) reported that they had had pain or had taken analgesic drugs daily during the week preceding the study, and 36 percent (475 of 1308) had pain severe enough to impair their ability to function. Forty-two percent of those with pain (250 of the 597 patients for whom we had complete information) were not given adequate analgesic therapy. Patients seen at centers that treated predominantly minorities were three times more likely than those treated elsewhere to have inadequate pain management. A discrepancy between patient and physician in judging the severity of the patient's pain was predictive of inadequate pain management (odds ratio, 2.3). Other factors that predicted inadequate pain management included that physicians did not attribute to cancer (odds ratio, 1.9), better performance status (odds ratio, 1.8), age of 70 years or older (odds ratio, 2.4), and female sex (odds ratio, 1.5). Patients with less adequate analgesia reported less pain relief and greater pain-related impairment of function.

1996: Pain and Policy Study Group
WHO CC for Pain Policy & Palliative Care
- Cancer Control
- Access to Controlled Medications Program

Close Ties with INCB
- Opioid Consumption Data
“Balance” is the Fundamental Principle

National policy should establish a drug control system that prevents diversion and ensures adequate availability for medical use.

Drug control measures should not interfere with medical access to opioid.
PPSG Global Activities

Italy reforms national policy for cancer pain relief and opioids

C. BLENGINI, MEDICO DI MEDICINA GENERALE/MEMBER OF MINISTRY OF HEALTH WORKGROUP OF THE COMMISSIONE UNICA DEL FARMACO TO ADDRESS INADEQUATE PAIN MANAGEMENT/MEMBER OF ITALIAN WHO COLLABORATING CENTER FOR CANCER PAIN RELIEF AND PALLIATIVE CARE (CHIEF, PROF. VITTORIO VENTfone), Dogliani Cuneo, Italy,
D. E. JORNSON, SENIOR SCIENTIST AND DIRECTOR, University of Wisconsin Comprehensive Cancer Center, Pain Policy Studies Group/WHO Collaborating Center for Policy and Communications in Cancer Care, Madison, Wisconsin, USA & K. M. RYAN, SENIOR POLICY ANALYST, University of Wisconsin Comprehensive Cancer Center, Pain Policy Studies Group/WHO Collaborating Center for Policy and Communications in Cancer Care, Madison, WI, USA
## Progress in the world
(Salzburg 2006)

<table>
<thead>
<tr>
<th>Country</th>
<th>Days/Supply</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>7 days</td>
<td>28 days</td>
</tr>
<tr>
<td>Mexico</td>
<td>5 days</td>
<td>30 days</td>
</tr>
<tr>
<td>Italy</td>
<td>8 days</td>
<td>1 month</td>
</tr>
<tr>
<td>Germany</td>
<td>1 day</td>
<td>no limit</td>
</tr>
<tr>
<td>Poland</td>
<td>100 mg</td>
<td>4.0 grams</td>
</tr>
<tr>
<td>Peru</td>
<td>1 day</td>
<td>14 days</td>
</tr>
<tr>
<td>India</td>
<td>5 lic</td>
<td>2 lic Mor</td>
</tr>
<tr>
<td>Uganda</td>
<td>No morphine</td>
<td>Morphine + RN</td>
</tr>
<tr>
<td>Romania</td>
<td>3 d supply</td>
<td>30 d supply</td>
</tr>
</tbody>
</table>
### Table 1. Top 100 Drugs by Total Sales

<table>
<thead>
<tr>
<th>Rank</th>
<th>Drug (brand name)</th>
<th>Sales from October 1, 2012, through September 30, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abilify</td>
<td>$6,391,050,009</td>
</tr>
<tr>
<td>2</td>
<td>Nexium</td>
<td>$6,086,840,503</td>
</tr>
<tr>
<td>3</td>
<td>Cymbalta</td>
<td>$5,432,152,672</td>
</tr>
<tr>
<td>4</td>
<td>Humira</td>
<td>$5,352,226,238</td>
</tr>
<tr>
<td>5</td>
<td>Crestor</td>
<td>$5,318,542,115</td>
</tr>
<tr>
<td>6</td>
<td>Advair Diskus</td>
<td>$5,114,309,392</td>
</tr>
<tr>
<td>7</td>
<td>Enbrel</td>
<td>$4,673,141,322</td>
</tr>
<tr>
<td>8</td>
<td>Remicade</td>
<td>$4,058,128,532</td>
</tr>
<tr>
<td>9</td>
<td>Copaxone</td>
<td>$3,788,545,102</td>
</tr>
<tr>
<td>10</td>
<td>Neulasta</td>
<td>$3,537,574,204</td>
</tr>
<tr>
<td>11</td>
<td>Rituxan</td>
<td>$3,298,174,917</td>
</tr>
<tr>
<td>12</td>
<td>Spiriva Handihaler</td>
<td>$3,002,430,799</td>
</tr>
<tr>
<td>13</td>
<td>Atripla</td>
<td>$2,912,549,658</td>
</tr>
<tr>
<td>14</td>
<td>Januvia</td>
<td>$2,825,267,039</td>
</tr>
<tr>
<td>15</td>
<td>Lantus Solostar</td>
<td>$2,778,551,072</td>
</tr>
<tr>
<td>16</td>
<td>Avastin</td>
<td>$2,690,641,154</td>
</tr>
<tr>
<td>17</td>
<td>Oxycontin</td>
<td>$2,637,737,756</td>
</tr>
<tr>
<td>18</td>
<td>Lantus</td>
<td>$2,515,137,058</td>
</tr>
<tr>
<td>19</td>
<td>Lyrica</td>
<td>$2,324,979,374</td>
</tr>
<tr>
<td>20</td>
<td>Truvada</td>
<td>$2,278,264,056</td>
</tr>
<tr>
<td>21</td>
<td>Epogen</td>
<td>$2,214,743,254</td>
</tr>
<tr>
<td>22</td>
<td>Celebrex</td>
<td>$2,183,115,416</td>
</tr>
<tr>
<td>23</td>
<td>Diovan</td>
<td>$2,137,198,878</td>
</tr>
<tr>
<td>24</td>
<td>Herceptin</td>
<td>$1,933,127,070</td>
</tr>
<tr>
<td>25</td>
<td>Namenda</td>
<td>$1,900,527,136</td>
</tr>
<tr>
<td>26</td>
<td>Gleevec</td>
<td>$1,874,835,782</td>
</tr>
<tr>
<td>27</td>
<td>Lucentis</td>
<td>$1,794,896,441</td>
</tr>
<tr>
<td>28</td>
<td>Vyvanse</td>
<td>$1,709,395,031</td>
</tr>
<tr>
<td>29</td>
<td>Zetia</td>
<td>$1,652,217,183</td>
</tr>
<tr>
<td>30</td>
<td>Suboxone</td>
<td>$1,554,971,998</td>
</tr>
</tbody>
</table>

### Table 2. Top 100 Drugs by Prescription Volume

<table>
<thead>
<tr>
<th>Rank</th>
<th>Drug (brand name)</th>
<th>Total prescriptions* from October 1, 2012, through September 30, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Crestor</td>
<td>23,736,668</td>
</tr>
<tr>
<td>2</td>
<td>Synthroid</td>
<td>23,407,581</td>
</tr>
<tr>
<td>3</td>
<td>Nexium</td>
<td>20,686,735</td>
</tr>
<tr>
<td>4</td>
<td>Cymbalta</td>
<td>19,436,224</td>
</tr>
<tr>
<td>5</td>
<td>Ventolin HFA</td>
<td>17,531,384</td>
</tr>
<tr>
<td>6</td>
<td>Advair Diskus</td>
<td>16,604,511</td>
</tr>
<tr>
<td>7</td>
<td>Diovan</td>
<td>13,101,107</td>
</tr>
<tr>
<td>8</td>
<td>Vyvanse</td>
<td>10,409,180</td>
</tr>
<tr>
<td>9</td>
<td>Spiriva Handihaler</td>
<td>9,594,938</td>
</tr>
<tr>
<td>10</td>
<td>Lantus</td>
<td>9,496,964</td>
</tr>
<tr>
<td>11</td>
<td>Lyrica</td>
<td>9,406,166</td>
</tr>
<tr>
<td>12</td>
<td>Celebrex</td>
<td>9,288,870</td>
</tr>
<tr>
<td>13</td>
<td>Lantus Solostar</td>
<td>9,052,819</td>
</tr>
<tr>
<td>14</td>
<td>Abilify</td>
<td>8,922,954</td>
</tr>
<tr>
<td>15</td>
<td>Januvia</td>
<td>8,745,980</td>
</tr>
<tr>
<td>16</td>
<td>Namenda</td>
<td>8,464,036</td>
</tr>
<tr>
<td>17</td>
<td>Nasonex</td>
<td>8,388,973</td>
</tr>
<tr>
<td>18</td>
<td>Viagra</td>
<td>7,751,484</td>
</tr>
<tr>
<td>19</td>
<td>Zetia</td>
<td>7,714,153</td>
</tr>
<tr>
<td>20</td>
<td>Suboxone</td>
<td>7,658,467</td>
</tr>
<tr>
<td>21</td>
<td>Cialis</td>
<td>7,469,372</td>
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<tr>
<td>22</td>
<td>Bystolic</td>
<td>6,795,951</td>
</tr>
<tr>
<td>23</td>
<td>Tamiflu</td>
<td>6,415,670</td>
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<tr>
<td>24</td>
<td>Flovent HFA</td>
<td>6,154,584</td>
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<tr>
<td>25</td>
<td>Oxycontin</td>
<td>6,005,158</td>
</tr>
<tr>
<td>26</td>
<td>Symbicort</td>
<td>5,908,888</td>
</tr>
<tr>
<td>27</td>
<td>Dextlan</td>
<td>5,196,674</td>
</tr>
<tr>
<td>28</td>
<td>Nuvaring</td>
<td>5,188,089</td>
</tr>
<tr>
<td>29</td>
<td>Benicar</td>
<td>5,018,438</td>
</tr>
<tr>
<td>30</td>
<td>Levemir</td>
<td>4,749,858</td>
</tr>
</tbody>
</table>
“Sir,—It has been wittily remarked that there are three kinds of falsehood:

  the first is a ‘fib,’

  the second is a downright lie, and

  the third and most aggravated is statistics...”

The National Observer, London. 8 June, 1891.
Amount of prescription painkillers sold by state per 10,000 people (2010)

SOURCE: Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 2010

Drug overdose death rates by state per 100,000 people (2008)

Policy Impact: Prescription Painkiller Overdoses

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In a period of nine months, a tiny Kentucky county of fewer than 12,000 people sees a 53-year-old mother, her 35-year-old son, and seven others die by overdosing on pain medications obtained from pain clinics in Florida.1 In Utah, a 13-year-old fatally overdoses on oxycodone pills taken from a friend's grandmother.2 A 20-year-old Boston man dies from an overdose of methadone, only a year after his friend also died from a prescription drug overdose.3

These are not isolated events. Drug overdose death rates in the United States have more than tripled since 1990 and have never been higher. In 2008, more than 36,000 people died from drug overdoses, and most of these deaths were caused by prescription drugs.4

100 people die from drug overdoses every day in the United States.4

Drug overdose death rates in the US have more than tripled since 1990.5
Methadone's share of prescription painkillers dispensed in each state

Source: Drug Enforcement Administration Automation of Reports and Consolidated Orders System (ARCOS), 2010

Numbers account for differences in drug strength.
Painkillers (Click on the legend to highlight the drug. Shift-click to highlight multiple drugs.)

Washington drug use by type since 1997, in grams

Washington drug deaths by type since 1997

Note: Morphine use in 2000 is an estimate. These death statistics were derived from state research and vary from The Times' analysis.
Source: U.S. Drug Enforcement Administration and state Department of Health TIMES
Source: Seattle Times analysis of state death records.
Death rate from overdoses caused by a single prescription painkiller

Source: Substance Abuse and Mental Health Services Administration, Center for Behavioral Statistics and Quality, Drug Abuse Warning Network Medical Examiner Component, 2009.
Average number of days of therapy dispensed per prescription for selected opioids through U.S. outpatient retail pharmacies, Year 2011

MS Health, Vector One®: National (VONA). Extracted September 2012

- Hydrocodone Combination: 14.2 days
- Oxycodone Combination: 14.0 days
- Oxycodone ER: 27.3 days
- Oxycodone IR: 21.5 days
- Morphine ER: 28.2 days
- Morphine IR: 18.4 days
- Hydromorphone: 17.4 days
## Diagnoses Associated with Use (by grouped ICD-9 codes) for Selected Opioids as Reported by Office-Based Physicians in the U.S., Jan 2007-Nov 2011 cumulative

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hydrocodone Combo</th>
<th>Oxycodone Combo</th>
<th>Oxycodone IR</th>
<th>Morphine ER</th>
<th>Morphine IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Market</td>
<td>2,850 N(000)</td>
<td>1,406 N(000)</td>
<td>566 N(000)</td>
<td>2,618 N(000)</td>
<td>407 N(000)</td>
</tr>
<tr>
<td>Diseases of the Musculoskeletal System and Connective Tissue (710-739)</td>
<td>699 N(000)</td>
<td>287 N(000)</td>
<td>230 N(000)</td>
<td>1,781 N(000)</td>
<td>226 N(000)</td>
</tr>
<tr>
<td>Disease of Respiratory System (462-493)</td>
<td>594 N(000)</td>
<td>31 N(000)</td>
<td>2 N(000)</td>
<td>464 N(000)</td>
<td>226 N(000)</td>
</tr>
<tr>
<td>Fractures, Sprains, Contusions, Injuries (800-999)</td>
<td>547 N(000)</td>
<td>368 N(000)</td>
<td>43 N(000)</td>
<td>89 N(000)</td>
<td>15 N(000)</td>
</tr>
<tr>
<td>All others</td>
<td>360 N(000)</td>
<td>102 N(000)</td>
<td>13 N(000)</td>
<td>64 N(000)</td>
<td>27 N(000)</td>
</tr>
<tr>
<td>Follow up examinations</td>
<td>286 N(000)</td>
<td>198 N(000)</td>
<td>11 N(000)</td>
<td>113 N(000)</td>
<td>21 N(000)</td>
</tr>
<tr>
<td>Headaches and Nerve Pain (337-359)</td>
<td>98 N(000)</td>
<td>51 N(000)</td>
<td>213 N(000)</td>
<td>392 N(000)</td>
<td>81 N(000)</td>
</tr>
<tr>
<td>Fever and General Symptoms (780-789)</td>
<td>96 N(000)</td>
<td>53 N(000)</td>
<td>28 N(000)</td>
<td>64 N(000)</td>
<td>25 N(000)</td>
</tr>
<tr>
<td>Neoplasms (140-239)</td>
<td>70 N(000)</td>
<td>5 N(000)</td>
<td>31 N(000)</td>
<td>102 N(000)</td>
<td>2 N(000)</td>
</tr>
<tr>
<td>Disease of Genitourinary System (392-628)</td>
<td>62 N(000)</td>
<td>3 N(000)</td>
<td>1 N(000)</td>
<td>11 N(000)</td>
<td>9 N(000)</td>
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<tr>
<td>Bacterial, Viral and Parasitic Infections (001-138)</td>
<td>39 N(000)</td>
<td>4 N(000)</td>
<td>1 N(000)</td>
<td>8 N(000)</td>
<td>2 N(000)</td>
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<table>
<thead>
<tr>
<th>Year</th>
<th>Hydrocodone</th>
<th>Oxycodone</th>
</tr>
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<tr>
<td></td>
<td>Toxic</td>
<td>Patients-days</td>
</tr>
<tr>
<td></td>
<td>Exposures</td>
<td>of Therapy</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>2002</td>
<td>17,429</td>
<td>851,393,000</td>
</tr>
<tr>
<td>2003</td>
<td>19,578</td>
<td>900,187,000</td>
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<tr>
<td>2004</td>
<td>22,654</td>
<td>981,437,000</td>
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<tr>
<td>2005</td>
<td>22,229</td>
<td>1,128,031,000</td>
</tr>
<tr>
<td>2006</td>
<td>22,244</td>
<td>1,275,681,000</td>
</tr>
</tbody>
</table>

*DEPI analysis using numbers from tables 4 and 6 in DEA report. Sources: NPDS and NPA Plus; * Total Number Patient-days of Therapy provided by DEA
Figure 1 Hydrocodone and Oxycodone Toxic Exposures per Million Patient-days of Therapy, NPDS 2002-2006*

* DEPI analysis using data from Table 5 above. Source: Total Number Patient-days of Therapy provided by DEA.
In 2010, 2 million people reported using prescription painkillers nonmedically for the first time within the last year—nearly 5,500 a day.7

Where the drugs come from
Almost all prescription drugs involved in overdoses come from prescriptions originally; very few come from pharmacy theft. However, once they are prescribed and dispensed, prescription drugs are frequently diverted to people using them without prescriptions. More than three out of four people who misuse prescription painkillers use drugs prescribed to someone else.7

Most prescription painkillers are prescribed by primary care and internal medicine doctors and dentists, not specialists.10 Roughly 20% of prescribers prescribe 80% of all prescription painkillers.11,12,13

Who is most at risk
Understanding the groups at highest risk for overdose can help states target interventions. Research shows that some groups are particularly vulnerable to prescription drug overdose:
Misuse of opioids

“using the medication differently than prescribed, taking the medication at higher doses, administering it alternatively, or taking the medication in conjunction with other substances (e.g. other medications, alcohol, etc.).”
Figure 1. Percentages of Year-Before-Last Initiates Not Using the Initiated Substance in the Past Year, by Substance: 2004-2006

- Crack: 75.6%
- Inhalants: 72.6%
- Heroin: 69.4%
- Sedatives*: 63.7%
- Hallucinogens: 61.5%
- Stimulants*: 59.1%
- Tranquilizers*: 58.8%
- Cocaine (Not Including Crack): 57.5%
- Pain Relievers*: 56.6%
- Marijuana: 42.4%
- Alcohol: 25.7%

Source: SAMHSA, 2004-2006 NSDUHs.

Figure 2. Percentages of Year-Before-Last Initiates Who Were Dependent on the Initiated Substance in the Past Year, by Substance: 2004-2006

- Heroin: 13.4%
- Crack**: 9.2%
- Marijuana: 5.8%
- Stimulants*: 4.7%
- Cocaine (Not Including Crack)**: 3.7%
- Alcohol: 3.2%
- Pain Relievers*: 3.1%
- Sedatives*: 2.4%
- Hallucinogens: 1.9%
- Tranquilizers*: 1.2%
- Inhalants: 0.9%

Source: SAMHSA, 2004-2006 NSDUHs.
Policy Impact: Prescription Painkiller Overdoses

What’s the Issue?

In a period of nine months, a tiny Kentucky county of fewer than 12,000 people sees a 53-year-old mother, her 35-year-old son, and seven others die by overdosing on pain medications obtained from pain clinics in Florida.1 In Utah, a 13-year-old fatally overdoses on oxycodone pills taken from a friend’s grandmother.2 A 20-year-old Boston man dies from an overdose of methadone, only a year after his friend also died from a prescription drug overdose.3

These are not isolated events. Drug overdose death rates in the United States have more than tripled since 1990 and have never been higher. In 2008, more than 36,000 people died from drug overdoses, and most of these deaths were caused by prescription drugs.4

100 people die from drug overdoses every day in the United States.4

Drug overdose death rates in the US have more than tripled since 1990.5

*Deaths are those for which poisoning by drugs (licit, prescription, and over-the-counter) was the underlying cause.
“Balance” is the Fundamental Principle

National policy should establish a drug control system that prevents diversion and ensures adequate availability for medical use.

Drug control measures should not interfere with medical access to opioid.
Symptom Trends in the Last Year of Life From 1998 to 2010: A Cohort Study

Adam E. Singer, MPhil; Daniella Meeker, PhD, MS; Joan M. Teno, MD, MS; Joanne Lynn, MD, MA, MS; June R. Lunney, PhD, RN; and Karl A. Lorenz, MD, MSHS

Background: Calls for improvement in end-of-life care have focused attention on the management of pain and other troubling symptoms at the end of life.

Objective: To describe changes in pain intensity and symptom prevalence during the last year of life from 1998 to 2010.

Design: Observational study.

Setting: The HRS (Health and Retirement Study), a nationally representative longitudinal survey of community-dwelling U.S. residents aged 51 years or older.

Participants: 7204 HRS participants who died while enrolled in the study and their family respondents.

Results: Between 1998 and 2010, proxy reports of the prevalence of any pain increased for all decedents from 54.3% (95% CI, 51.6% to 57.1%) to 60.8% (CI, 58.2% to 63.4%), an increase of 11.9% (CI, 3.1% to 21.4%). Reported prevalences of depression and periodic confusion also increased for all decedents by 26.6% (CI, 14.5% to 40.1%) and 31.3% (CI, 18.6% to 45.1%), respectively. Individual symptoms increased in prevalence among specific decedent categories, except in cancer, which showed no significant changes. The prevalence of moderate or severe pain did not change among all decedents or in any specific decedent category.
Case 1:

- Your colleague is treating a patient for painful malignant brachial plexopathy by using gabapentin and long-acting morphine at 300 mg twice daily plus short-acting morphine 30 mg up to every 2 hours, as needed. He tells you that the patient’s pain is severe despite five to six rescues per day and that the patient appears to have no adverse effects. He proposes to increase the long-acting morphine to 600 mg twice daily plus short acting morphine 90 mg up to every 2 hours, as needed. What do you say? (check all that apply)

- Good idea
- Not a good idea because of the risk of serious toxicity, particularly respiratory depression
- Not a good idea because of the likelihood of adverse effects of somnolence and mental clouding
- Not a good idea because of the risk of drug abuse or addiction at the higher dose
- Not a good idea because of more rapid tolerance leading to ineffective opioid therapy later
- Not a good idea because of the phenomenon of opioid-induced hyperalgesia
- Not a good idea because of the regulatory climate that puts doctors under scrutiny if relatively high doses are prescribed
- No comment

89%: an incorrect answer
Case 2

• A 40-year-old man with metastatic lung cancer reports that bone pain is steadily worsening despite treatment with long-acting oxycodone 160 mg twice daily. There are no adverse effects, and the patient continues to receive chemotherapy and is working part-time. What would you recommend? (check all that apply)

• Increase the oxycodone to 160 mg three times daily
• Add a rescue medication, specifically oxycodone 5 mg plus acetaminophen 325 mg, two tablets four or five times daily, as needed
• Add a short-acting opioid such as morphine
• Add a rapid onset opioid such as oral transmucosal fentanyl citrate
• Switch to the transdermal fentanyl patch, 50 g/h, patch changed every 3 days
• Add pregabalin

60% did not have a correct answer
Disparity in Consumption: High vs. Low- and Middle-income countries (LMIC)

2010 Population
- HIC (16%)
- LMIC (84%)

2010 Morphine Consumption (kg)
- High Income (90%)
- LMIC (10%)
The central principle of balance:

- a dual obligation of govts to establish a system of control
  - that ensures the *adequate availability* of controlled substances for medical and scientific purposes, while simultaneously *preventing abuse, diversion and trafficking*.  

- Many controlled medicines are essential medicines and are *absolutely necessary for the relief of pain*, treatment of illness and the prevention of premature death.

- To ensure the rational use of these medicines, govts should
  - both enable & empower healthcare professionals to prescribe, dispense & administer them according to individual medical needs of patients, ensuring a sufficient supply is available to meet those needs.
  - While misuse of controlled substances poses a risk to society, *the system of control is not intended to be a barrier to their availability for medical and scientific purposes*, nor interfere in their legitimate medical use for patient care.

*CND. Resolution 53/4: Promoting adequate availability of internationally controlled licit drugs for medical and scientific purposes while preventing their diversion and abuse.*

Prescription Drug Abuse Prevention Plan (April, 2011)

Office of National Drug Control Policy (ONDCP)
ONDCP

Prescription Drug Abuse Prevention Plan

- Domain #2: Tracking and Monitoring
  - PMPs
  - Electronic prescribing
  - Epidemiology
- Domain #3: Proper Medication Disposal
- Domain #4: Enforcement
  - Reduce “doctor shopping” and “pill mills”
ONDCP

Prescription Drug Abuse Prevention Plan

- Domain #1: Education
  - Healthcare practitioners
    - REMS
    - Continuing Education
    - Curricula in health professional schools
    - Methods to facilitate and assess adequateness and effectiveness of pain treatment
  - Parent, youth, and patient
  - Research and development
What is the right number of pain medicines to give to a 50 year old man after wisdom teeth removal?

“Enough tablets so that I or my colleagues don’t get called after hours for a refill?”

Partial Refills of Post operative opioids ??
Hydrocodone #20 12 tablets initially
further 8 tablets prn between days 3-5
Real Life Situation

- 55 yo woman with Pancreatic cancer:
  - methadone for pain
- After death, tablets placed in bathroom cabinet
- Diversion  Disposed
- 17 year old boy takes single 5 mg tablet
- Mother notices toxicity: Taken to ER
- ER administers Naloxone:
  - Clinical improvement: Discharged
- Found dead the next morning.