Tackling the opioid issue: the US perspective

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Opioids have been oversold: CDC has termed prescription opioid abuse an “epidemic”
Prescription Painkiller Overdoses

A growing epidemic, especially among women
July 2013
Vitalsigns™

48,000
Nearly 48,000 women died of prescription painkiller overdose between 1999 and 2010.

400%
Deaths from prescription painkiller overdoses among women have increased more than 400% since 1999, compared to 265% among men.

30
For every woman who dies of a prescription painkiller overdose, 3 go to the emergency department for painkiller misuse or abuse.

About 18 women die every day of a prescription painkiller overdose in the US, more than 6,600 deaths in 2010. Prescription painkiller overdoses are an under-recognized and growing problem for women.
Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010

CDC. MMWR 2011. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm60e1101a1.htm?s_cid=mm60e1101a1_w. Updated with 2009 mortality and 2010 treatment admission data.
Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)

1999 (range 1 - 50)

15 - 18

45 or more

Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.
Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)

2009
(range 1 – 379)

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.
Drugs Control and Access to Medicines Consortium Copyright © 2009-2011 The Board of Regents of the University of Wisconsin System.
Sources: International Narcotics Control Board; United Nations population data
Figure 4: Pharmaceutical opioid base supply (grams) Australia from 1991-2007

**Huxtable CA et al** *Anaesth Intensive Care* 2011; 39 : 804-823

**Figure 1:** Coronial deaths involving oxycodone and oxycodone supply, Victoria, 2000-2009. Reproduced with permission from Rintoul et al.
Why the interest in selling opioids?
US Characteristics

- Large market
- Post-graduate medical education largely industry funded
- Fragmented healthcare
- Open to multiple prescribers, doctor shopping and pill mills
Opioids Market to 2017 - Steady Uptake of Oxycontin and High Incidence Of Diseases Such As Cancer And Arthritis to Drive the Market
GBI Research, June 2011, Pages: 177

“Opioids Market to 2017 - Steady Uptake of Oxycontin and High Incidence Of Diseases Such As Cancer And Arthritis to Drive the Market” provides insights into global Opioids market and market forecast until 2017. Report is built using data and information sourced from proprietary databases, primary and secondary research and in-house analysis by GBI Research’s team of industry experts.

The report provides an in-depth analysis of the top five therapeutic indications for which often opioids are prescribed which includes fibromyalgia, neuropathic pain, cancer pain, osteoarthritis pain, rheumatoid arthritis pain, low back pain and post operative pain. The report also examines the global opioids treatment usage patterns for the covered indication. In addition, the report also includes insights into the opioids R&D pipeline.

Opioids Remain The Mainstay of Chronic Pain Treatment

Pain is a disabling symptom that can occur at any point in the course of an illness.
Market Overview

U.S. Opioid Pain Management Market Offers Financial and Therapeutic Potential

The U.S. opioid pain management market generated revenues of $11,063.3 million in 2009 and is expected to reach $15,330.0 million in 2016. Many pain management experts consider opioids the best medication available for managing moderate to severe pain as well as cancer pain. The ineffectiveness of non-opioids in the treatment of pain has boosted market growth. Evidence points to the fact that opioids have been highly effective in the treatment of certain types of pain. With the rapid growth of the ageing population, the prevalence of painful conditions has escalated. According to the U.S. Census Bureau, the fastest growing segments of the U.S. population are the older age brackets. 'This population segment presents the greatest risk for painful conditions such as osteoarthritis, rheumatoid arthritis, and hip/back problems,' notes the analyst of this research service. 'Trends indicate that this population segment will increase by 22.1 percent from 39.5 million in 2009 to 48.2 million in 2016, widening the scope for the market.' The high incidence of certain diseases, particularly cancer and arthritis, is also likely to help spearhead the growth in this domain.
How oversold?

Benefits overplayed: Risks underplayed
Why not prescribe opioids?

1980s, persuaded to use opioids for chronic non-cancer pain based on:

1) the moral argument that this type of pain causes as much suffering and deserves treatment as much as cancer pain

2) the “scientific” argument that enduring analgesia can be achieved at stable doses with minimal risk of addiction

Sullivan and Ballantyne Arch Int Med 2012;172:1342-3
Arguments for liberal prescribing of opioids for chronic pain

Indispensable for the treatment of pain and suffering

Uncontrolled pain may have deleterious physical effects

Persistent pain destroys autonomy and dignity and compromises decision-making capacity

Low addiction rates (up to 5%) reported
Patients Bill of Rights

“You have the right to know your treatment options and to participate in decisions about your care. Parents, guardians, family members, or other individuals that you designate can represent you if you cannot make your own decisions.”


“Intractable pain” statutes

“Controlled substances and, in particular, narcotic analgesics may be used in the treatment of pain experienced by a patient with a terminal illness or chronic disorder. These drugs have legitimate clinical use and the physician should not hesitate to prescribe, dispense or administer them when they are indicated for a legitimate medical purpose.”

Joranson & Gilson 1997. DEA 1990
Initially based only on observational data

- Generally achieve improvement in pain
- Although there are a few outliers, generally these patients are followed for no more than 2 yrs
- Doses are moderate (up to 200 MED), with a few outliers (> 2000 MED)
- Findings on function and quality of life are equivocal
- No conclusions on addiction risk

The evidence – epidemiological

- Later, industrially funded RCTs confirmed the short-term analgesic efficacy of opioids and the analgesic equivalence of new opioids, but did nothing to support long term efficacy or safety

- New evidence for concern comes mostly from epidemiological data because long term trials have never been conducted, and may not be practical
Long acting opioids were promoted with the message that they would provide better analgesia with less risk of addiction

- Improvement in efficacy was suggested on the basis of less pain re-emergence
- Supposed low risk of addiction was inappropriately supported with inpatient data, and weak observational data
- It was proposed that the steady state produced would produce less euphoria and therefore less likelihood of addiction
- Additionally, it was proposed that less focus on taking medication would be protective and allow distraction

Aberrant drug abuse behaviors are common in pain patients

63% admitted to using opioids for purposes other than pain\(^1\)

35% met DSM V criteria for addiction\(^2\)

The Purdue Frederick Company, Inc. and Top Executives Plead Guilty to Misbranding OxyContin; Will Pay Over $600 Million

ABINGDON, Va., May 10 /PRNewswire-USNewswire/ -- The Purdue Frederick Company, Inc., along with its President, Chief Legal Officer, and former Chief Medical Officer have pleaded guilty to charges of misbranding Purdue's addictive and highly abusable drug OxyContin. John L. Brownlee, United States Attorney for the Western District of Virginia, and Virginia Attorney General Bob McDonnell announced today. Purdue and the three executives will pay a total of $634,515,475. OxyContin is a Schedule II prescription pain relief medication, classified as having the highest potential for abuse of legally available drugs. The Purdue Frederick Company, Inc., and the three executives have admitted that Purdue fraudulently marketed OxyContin by falsely claiming that OxyContin was less addictive, less subject to abuse, and less likely to cause withdrawal symptoms than other pain medications when there was no medical research to support these claims and without Food and Drug Administration approval of these claims.
Chronic opioid use (>90 d/yr) in patients with MH and SUD diagnoses

Schwartz et al 2006;45:136-142
Sullivan et al Arch Intern Med 2006;166:2087-93
Edlund et al Pain 2007;129:355-362
Weisner et al Pain 2008;145:287-93
Martin et al J Gen Intern Med 2011;26:1450-7
Phifer et al Pain 2011;152:2233-40
Seal et al JAMA 2012;307:940-7

Edlund et al Drug Alcohol Depend 2010; 112:90-98
Crude association of daily dosage of opioid analgesics with risk of unintentional drug overdose death, New Mexico, October, 2006—March, 2008


Gomes et al., Arch Int Med, 2011

Dunn et al., Annals Int Med, 2010

Bohnert et al., JAMA, 2011
<table>
<thead>
<tr>
<th>Type of pharmaceutical</th>
<th>Related causes of death (defining ICD10 codes)</th>
<th>No. of deaths</th>
</tr>
</thead>
</table>
| Opioid analgesics       | • Overdose (OD codes* with T40.2-T40.4)  
• Overdose without benzodiazepine or antidepressant                                                            | 14,800  
9,926        |
| All non-opioid analgesics | • Overdose (X40, X60, Y10)                                                                                         | 611           |
| --- Acetaminophen       | • Overdose (OD codes with T39.1)                                                                                | 913  
4,059        |
|                         | • Toxic liver disease/liver failure from any cause except alcohol or viruses (K71-K72)                              |               |
| --- NSAIDS              | • Overdose (OD codes with T39.0,T39.2,T39.3)  
• GI ulcers/gastritis from any cause (K25-K29)                                                                     | 683  
3,364        |
| Antidepressants         | • Overdose (OD codes with T43.0-43.2)  
• Overdose without opioid analgesic                                                                                   | 3,610  
1,662        |
| Benzodiazepines         | • Overdose (OD codes with T42.4)  
• Overdose without opioid analgesic                                                                                   | 5,010  
1,377        |

*OD (overdose) codes for underlying causes of death are X40-X44, X60-X64, X85, and Y10-Y14.
Metrics that encourage opioid prescribing
Guidelines were not effective, so a group of concerned individuals approached credentialing body JCAHO.

In 2001 JCAHO introduced pain management standards into its requirement for accreditation.

The mandate required pain’s recognition, assessment, documentation and treatment and required that systems be in place to achieve these goals.

The “fifth vital sign” rapidly became instantly popular.

Some institutions went as far as writing dosing protocols related to pain scores.

Photo taken at the The 7th International Conference on Pain and Chemical Dependency, June 2007
Prescribing against a better judgment in order to maintain patient satisfaction
Health care organizations frequently utilize patient satisfaction ratings as an integral part of marketing and benchmarking of services.

Clinicians may feel threatened into prescribing in order to meet the satisfaction metrics by which they and their practices are judged.
## CARE PROVIDER

During your visit, your care was provided primarily by a doctor, physician assistant (pa), nurse practitioner (np), or midwife. Please answer the following questions with that health care provider in mind.

<table>
<thead>
<tr>
<th>Question</th>
<th>Very Poor</th>
<th>Poor</th>
<th>Fair</th>
<th>Good</th>
<th>Very Good</th>
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</thead>
<tbody>
<tr>
<td>1) Friendliness/courtesy of the care provider</td>
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<td>2) Explanations the care provider gave you about your problem or condition</td>
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<td>3) Concern the care provider showed for your questions or worries</td>
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<td>4) Care provider's efforts to include you in decisions about your treatment</td>
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<td>5) Information the care provider gave you about medications (if any)</td>
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<td>6) Instructions the care provider gave you about follow-up care (if any)</td>
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<td>7) Degree to which care provider talked with you using words you could understand</td>
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<td>8) Amount of time the care provider spent with you</td>
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<td>9) Your confidence in this care provider</td>
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<td>10) Likelihood of your recommending this care provider to others</td>
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11) Comments (describe good or bad experience):

...
Patient Satisfaction, Prescription Drug Abuse, and Potential Unintended Consequences

Aleksandra Zgierska, MD, PhD
Michael Miller, MD
David Rabago, MD

Patient-centered care can improve treatment outcomes, and its implementation has become the focus of national and local efforts to optimize health and health care delivery. Patients' satisfaction with care is one of the pillars of patient-centered care.1 As such, behaviors. Medical quality committees and even licensure boards can determine that care is substandard if clinicians exclude these components. Before prescribing opioids, clinicians may be expected to recommend nonopioid interventions and refer patients to consultants even if what the patient wants is an opioid prescription. Combined with overall poor treatment outcomes in chronic pain and difficulties reported by most clinicians regarding issues surrounding prescription drug abuse, it is not surprising that clinicians' satisfaction and comfort level with management of care for

Zgierska et al JAMA 2012;307:1377-8
The problem the US is left with: a large population of opioid dependent patients
NOT ABLE TO COME OFF

- Once started on a course of COT, how long do patients remain on opioids?

- TROUP study of COT recipients (used at least 90 days without a 32 day gap)

- Outcome: 6 months without any opioid Rx

COT discontinuation

Longer duration and higher doses associated with:

- Higher rates of overdose and death
- Less likelihood of being able to wean if necessary
  - Difficulty controlling acute pain, surgical recovery, terminal pain
  - Continued use during pregnancy – neonatal abstinence
- Higher rates of mental health & substance use disorder, less able to control usage
- Higher rates of falls and fractures in the elderly
- Less likelihood of returning to function or work
- Higher rates of endocrinopathy affecting fertility, libido & drive
- Higher rates of immune dysfunction

CONCLUSIONS

• Opioid use has increased throughout much of the developed world, but more in the US

• Aggressive marketing practices and market driven healthcare have contributed

• The US now has a large population of opioid dependent individuals
REFERENCES