Setting the Stage: The Impact of Opioid Use and Abuse

Kim Templeton, MD
Professor of Orthopaedic Surgery
University of Kansas Medical Center
Steering Committee, Kansas Partnership for Pain Management
Why is Pain Important?

- Represents over 80% of complaints for those seeking acute care
- Chronic (non-malignant) pain estimated to affect 34-100 million people
- Can lead to depression, lost time from work, decrease quality of life
IOM Report

Examined pain as a public health problem

HHS asked the IOM to assess the state of the science regarding pain research, care, and education and to make recommendations to advance the field

Raised awareness of the deficits in pain treatment
Underlying Principles

- Pain management is a moral imperative
- Chronic pain can be a disease in itself
- The value of comprehensive treatment
- The need for interdisciplinary approaches
- The importance of prevention
- Wider use of existing knowledge
- Recognition of the conundrum of opioids
- Collaborative roles for patients and clinicians
- The value of a public health and community-based approach
Need to Foster a Cultural Transformation

• Pain is a national challenge
  All people are at risk for pain
  Pain is a uniquely individual, subjective experience

• Comprehensive and interdisciplinary (e.g., biopsychosocial) approaches are the most important and effective ways to treat pain

• Such care is difficult to obtain because of structural barriers – including financial and payment disparities

• A cultural transformation is needed to better prevent, assess, treat, and understand pain

• Focus on patient and provider education and research

• It does NOT say that everyone with pain should be treated with opioids
Pain as the “5th Vital Sign”?

Blood Pressure
Pulse
Respiratory rate
Temperature
Pain? Symptom or sign?
5\textsuperscript{th} Vital Sign?

An attempt to improve the management of pain, especially chronic pain
American Pain Society adopted guidelines for treating pain-1995
5\textsuperscript{th} Vital Sign adopted by the VA in 1999
Joint Commission used as an example in 2001
Pain vs function?
Use of Opioids

Effective for acute pain

Role in chronic pain (especially MSK, HA) not established

65% of opioid prescriptions in 2014 were for short term (<3 weeks) therapy (Volkow et al)

Other modalities for chronic pain?
How do Opioids Work?

Bind to mu-opioid receptors

Primarily in areas of the brain that regulate pain perception, emotional responses, pleasure

Also bind to areas in the brain stem responsible for controlling respiration

Receptors in spinal cord alter perception of pain
Other Sites of Action

Gastrointestinal tract-slow motility

Skin- can lead to increased sensitivity or pain with touch, with paradoxical increase in opioid dose to deal with pain
Opioids interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects (euphoria) and pain relief.

Inhibits production of endogenous opioids—cessation leads to dysphoria.

Overdose treatment blocks this interaction.
Types of opioids

Natural opioid analgesics
  morphine, codeine
Semi-synthetic opioid analgesics,
  oxycodone (Percocet, Oxycontin), hydrocodone (Vicodin, Lortab), hydromorphone (Dilaudid)
Synthetic opioids
  methadone, tramadol, fentanyl (legal and illicit)
Heroin, illegally-made opioid synthesized from morphine
The problem with opioids: different than other medications

Pain is subjective – no data to measure outcomes

Changes in regimen cannot be done quickly due to physiologic responses and complexity of involved systems

Used across various practice specialties

Opioids do not have a maximum daily dose as most other medications do

One of many ways to address pain but frequently used as the first, and maybe only, option
Misuse/Abuse of Opioids

Use of opioids in doses or length of treatment not indicated by clinical condition or for reasons other than pain relief (e.g., euphoria)

When/how/in whom does pain relief from opioids transition to misuse/abuse?

Can involve prescriptions for a given patient or those obtained from family/friends, or black market
Physiology and potential problems

**Physical dependence** - normal adaptations to exposure of drug creating a physiological reliance on the drug

**Addiction** - a primary, chronic and relapsing brain disease characterized by an individual pathologically pursuing reward (rare, ~3-4%)

**Tolerance** - need for higher doses to achieve pain relief or euphoric response; common

**Withdrawal** – wide range of symptoms that occur after stopping or reducing opioids

**Long term changes to the brain** in decision making and behavior regulation
Defining opioid use disorder

Problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least 2 of the following, occurring within a 12-month period:

1. Opioids taken in larger amounts or longer period than intended.
2. Persistent desire or unsuccessful efforts to cut down.
3. Time spent in activities necessary to obtain the opioid or use the opioid.
4. Craving or urge to use opioids.
5. Opioid use resulting in a failure to fulfill obligations at work, school, or home.
6. Continued opioid use despite having recurrent social or interpersonal problems caused by effects of opioids.
7. Social, occupational, or recreational activities are given up because of use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is due to opioids.
10. Tolerance, as defined by either (a) need for markedly increased amounts of opioids to achieve desired effect or (b) diminished effect with continued use of the same amount of opioid.
11. Withdrawal, as manifested by either (a) opioid withdrawal syndrome or (b) opioids taken to relieve withdrawal symptoms.

DSM - 5
Risk Factors for Addiction

Daily dose >100 MME (morphine milligram equivalents)
Long term use (>3 months)
Depression
History of abusing other substances (e.g., alcohol)
Adolescents
Input from Industry

Opioid addiction is rare
Opioids are safe and effective for chronic pain
Opioids can be easily discontinued
Which of these is true??
The “Perfect Storm” for the Opioid Crisis

Increased focus on pain and pain management
Public view that pain should be avoided and can be prevented
Pain scores used to assess HCP/hospital “quality”
Heavy marketing by Pharma
More types of opioids available and marketed
More opioids in the system
Increased acceptance of using medications for other than intended purposes
Opioid Prescriptions Dispensed by US Pharmacies

Trend toward more prescriptions started prior to the 5th vital sign program

More closely paralleled new formulations of opioids that became available

The US makes up about 4.6% of the world’s population but consumes 80% of its opioids and 99% of the world’s hydrocodone

Data from NIDA
We’ve Been Here Before…

Latter half of 19\textsuperscript{th} century

Limited ability to assess or treat sources of pain

Opioids used to treat adults and children (e.g., pain, diarrhea)

“Likely to soothe any human or animal”

Decreased use with development of alternatives (e.g., aspirin) and education of physicians
Some states have more opioid prescriptions per person than others.

Number of opioid prescriptions per 100 people:
- 52-71
- 72-82.1
- 82.2-95
- 96-143

SOURCE: IMS, National Prescription Audit (NPA™), 2012.
Sources of Prescription Opioids Among Past-Year Non-Medical Users

![Diagram showing sources of prescription opioids among past-year non-medical users.](chart)

- Given by a friend or relative for free
- Prescribed by ≥1 physicians
- Stolen from a friend or relative
- Bought from a friend or relative
- Bought from a drug dealer or other stranger
- Other

Number of Days of Past-Year Non-Medical Use:
- Any
- 1-29
- 30-99
- 100-199
- 200-365

Percent of Users

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*Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.*

*Estimate is statistically significantly different from that for highest-frequency users (200-365 days) (P<.05).*

*Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchases on the internet; and obtained some other way.*

Opioids for Chronic Pain

Issues with misuse, abuse, diversion

938, 586 UDS from pts treated with opioids and/or benzo for chronic pain

Males more likely than females to have illicit drug noted

Couto et al 2009
FIG. 1. Aggregate test results of patients administered urine drug screening using RxGuardian testing (January 2006–January 2009). Note that all categories add to a total greater than 100% as a single patient can fall into more than 1 category. $N = 938,420$. 
Heroin

Seen by the brain as morphine
Similar effects in brain to other opioids
May be cheaper and easier to get
Nearly 80 percent of Americans using heroin have reported misusing prescription opioids prior to using heroin

Less than 4 percent of people who had misused prescription pain medicines started using heroin within 5 years—prescription opioid misuse is just one factor leading to heroin use
Heroin

Highly addictive

Similar issues with overdosing and death

Unsure purity

May be mixed with black market fentanyl
Opioids and Heroin

People with abuse of dependence on
Alcohol 2x
Marijuana 3x
Cocaine 15x
Prescription opioids 40x
More likely to have abused or have dependence on heroin

Abuse Disorders/Addiction

2.1 million Americans with abuse disorders related to prescription opioids
467,000 Americans addicted to heroin

NIDA 2012
Opioid Overdoses

Overdose by respiratory depression (slowed breathing) which may cause death
Tolerance to pain relief or euphoria develops quickly
Receptors in brain stem develop tolerance more slowly
Respiratory depression most likely when dose is increased to achieve pain relief or to maintain euphoria
Overdoses

States with highest sales per capita of prescription opioids show the highest rates of opioid overdose fatalities

High daily dose of opioid pain relievers exceeding 100 MME greatly increases risk of fatal overdose

Benzodiazepines were involved in nearly a third of opioid overdose fatalities

Patients receiving opioid prescriptions from four or more prescribers and/or pharmacies had an increased risk of overdose
Opioid Overdose Deaths

47,055 in the US in 2014 (more than any previous year)

In 2014 drug overdose deaths were the leading cause of injury death in the US outpacing motor vehicle deaths by 150%

More than 3 out of 5 drug overdose deaths in 2014 involved opioids

CDC
Opioid Overdose Deaths

More likely to occur among those taking prescription opioids vs illicit or heroin

More common among men but greater increase in number among women (265% vs 415%)

Greatest incidence among adults age 45-54

Greatest rate of increase in overdose- adults age 55-64

Highest rate of increase of opioid-related deaths- Caucasian women age 55-64
How to Address the Opioid Epidemic?

Primary prevention - prevent new cases of addiction
Secondary prevention - early identification and treatment of those at risk of addiction
Tertiary prevention - increased access to treatment for addiction
How do we solve the problem?

Public and health care provider education about the role of opioids and other interventions in pain management

Pain as 5th Vital Sign? (no indication of impact, AMA stance)

Pain vs function

Change in satisfaction/quality measures

Control of internet or black market sources (e.g., illicit fentanyl)

Research to better understand pain and how to manage it

Research into identifying those at risk of abuse

Limitations on prescriptions?
Sex Differences in Pain

Chronic pain is more prevalent in females

Certain pain conditions are more prevalent in women

Women may have greater pain severity

Women may be more sensitive to painful stimuli
Mechanisms Underlying Sex Differences in Pain

Biological
- Sex hormones: Estradiol and progesterone (pro and anti-nociceptive); testosterone (anti-nociceptive)
- Research still limited – modulatory mechanisms need to be assessed

Pain processing

Endogenous opioid system
- High estradiol/low progesterone $\rightarrow$ ↓ pain sensitivity & ↑ brain mu-opioid receptor binding
- Low estradiol $\rightarrow$ ↓ brain mu-opioid receptor binding
Summary of Gender Bias in Pain Treatment

In general, studies seem to point to:

Women being offered psychological or pharmacotherapy (opioids, sedatives, or both) at higher doses for longer periods of time

Men being offered physiotherapy, radiologic studies, surgery, analgesics
Sex-Based Differences

Women are more likely to misuse/abuse opioids
Longer time to onset - more likely to misuse?
Due to increased number of opioid prescriptions (vs other inventions for men)
Other factors that increase risk of abuse? (e.g., depression)
Social acceptance of expressing pain?
Seen at all ages (can contribute to cognitive issues in older adults)
Data from Kansas PDMP

Females account for almost two-thirds of MPE rates

![Line graph showing age-adjusted MPE rates per 100,000 population for female and male patients from Jan-Jun 2011 to Jan-Jun 2015.](image)

- Female MPE Patients:
  - Jan-Jun 2011: 51.2
  - Jan-Jun 2012: 63.4
  - Jan-Jun 2013: 63.4
  - Jan-Jun 2014: 63.4
  - Jan-Jun 2015: 63.4

- Male MPE Patients:
  - Jan-Jun 2011: 23.7
  - Jan-Jun 2012: 28.4
  - Jan-Jun 2013: 28.4
  - Jan-Jun 2014: 28.4
  - Jan-Jun 2015: 28.4

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Data Source: Kansas Board of Pharmacy, Kansas Tracking and Reporting of Controlled Substance (2010-2012, 2015). Kansas population was based on the U.S. Census County Vintage 2015 post-censal estimate of the resident population of the United States by single year of age, bridge-race category and age-adjusted to the U.S. 2000 standard population. Credit: Images created by Iconarray.com. Risk Science Center and Center for Bioethics and Social Sciences in Medicine, University of Michigan. Accessed 2016-08-19. Comparison of indicators do not imply statistical significance. Each point estimate may include the same patients.
Thank you!