Opioid Crisis
More Limitations and Monitoring are Needed

United States, 2017
• Total deaths: 46,394
• Prescription opioid death rate: 4.4
• Non-prescription opioid death rate: 12.0
(Rates per 100,000 populations)

New Mexico, 2017
• All opioid deaths: 329
• Prescription opioid death rate: 7.1
• Non-prescription opioid death rate: 11.6
(Rates per 100,000 populations)

Richard Larson MD, PhD
Executive Vice Chancellor
Vice Chancellor for Research

Source: CDC Wonder Database
Adapted From https://www.cdc.gov/drugoverdose/data/statedeaths.html

What is the Problem?

• Increased opioid prescriptions
• Increased opioid prescription doses
  • More prescriptions ➔ more opioid use disorders ➔ more prescription opioid overdoses
• Prescription use disorders ➔ illicit opioid use

Prescription Opioids

<table>
<thead>
<tr>
<th></th>
<th>2002</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total MME Sold</td>
<td>123.7 billion</td>
<td>167 billion</td>
</tr>
<tr>
<td>Use Disorder Cases</td>
<td>1.5 million</td>
<td>1.7 million</td>
</tr>
<tr>
<td>Overdose Deaths</td>
<td>4,416</td>
<td>14,495</td>
</tr>
<tr>
<td>MME=Milligrams of Morphine Equivalents</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2 SAMHSA Key Substance Use and Mental Health Indicators in the US, Retrieved from http://samhsa.gov/data/
3 Centers for Disease Control and Prevention, CDC WONDER database. Retrieved from http://wonder.cdc.gov/
Prescription Opioid Use is more Common than Heroin Use

- Prescription opioid misuse represents 97.2% of all opioid misuse
- Prescription opioid misuse leads to heroin use in 3.6% of people


11.1 million prescription opioid misusers (97.2% of total opioid misusers) 1
562,000 prescription opioid misusers AND heroin users (1.8%) 2
886,000 people heroin users (7.8%) 1
324,000 people: heroin users only (2.8%) 1

Prescription Opioids

- 191 million prescriptions dispensed by US pharmacies (2017) 1
- Of those prescriptions, 80 million (42%) exceed a 30 day supply 2
- 80% of patients receive opioids after low risk surgery or outpatient procedures 3
- 6% of surgical outpatients became chronic users 2
- 6% of patients issued new prescriptions became chronic users 3
- No evidence that opioid therapy is more effective than non-opioid therapies in treating long-term pain 4

Sources: 1Hah et al, Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic, Anesth. 125(5) p 1733-1740, 2017
4Dowell et al, CDC Guideline for prescribing opioids for chronic pain -US, March 2016, 65(1);1-49

Clinical Scenarios in which Opioids are Prescribed

Low Risk
- Low back pain 1
- Headache 2
- Tooth extractions 3
- Low-risk surgery (varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, carpal tunnel) 4
- Osteoarthritis 5
- Depression 6,7
- Anxiety Disorder 7
- Fibromyalgia 8
- Minor Injuries (musculoskeletal pain, joint fracture or dislocation, chronic abdominal pain) 9

High Risk 1
- Cancer 4
- Some neuropathic pain conditions 5
- Palliative and hospice care 8

2Tepper, Opioids should not be used in migraine, Headache, 52 Supple 1, p 30-50, 2012
3Gupta et al, Multiple opioid prescriptions among privately insured dental patients in the United States, J Am Dent Assoc., 149(7), p 619-627, 2018
5Krebs et al, Effect of opioid vs non-opioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain, JAMA, 319(9) p 827-882, 2018
6Mazereeuw et al, Depression in chronic pain: might opioids be responsible?, Pain, 159(11), p 2142-2145, 2018
9Waddell et al, Opioid-light initiative: a multi-modal approach to reduce opioid prescribing in the emergency department; retrieved from https://www.ashp.org/Membership-Center/Member-Spotlight-Gallery/Opioid-Case-Study-Baptist-Memorial-Healthcare
“Estimated” Opioid Prescriptions

- Aggressive Marketing
- Lax Distribution Controls
- Physician Perception & Training
- Physician Prescribing Practice

- Oncologic, Nausophaetic Pain (120M Prescriptions, 310M Americans)
- Low-Risk Clinical Scenario (surgery, back pain, minor injury, dental) (75M Prescriptions, 47M Americans)

4. Hooten et al, Incidence and Risk Factors for Progression From Short-term to Episodic or Long-term Opioid Prescribing: A Population-Based Study; Mayo Clinic Proc.; 90(7) p 850-6
5. Dowell et al, CDC Guideline for prescribing opioids for chronic pain - US, March 2016, 65(1);1-49

Overprescribing Leads to Diversion and Misuse

- More than two-thirds of patients reported unused prescription opioids after surgery.
- The quantity of unused opioid tablets ranged from 42% to 71% of pills dispensed.
- More than half (53%) of people who misused prescription opioids in 2017 received them from a friend or relative, often for free.

Percent of Patients Who Reported Unused Opioids Prescribed After Surgery

- General
- Dental
- Gastroenterology
- Ophthalmology
- Orthopedics

When Digging a hole; First Stop Digging...

- Less prescriptions will lead to less misuse and overdoses.
What Drives Increased Misuse?

- Marketing
- Distribution
- Days prescribed
- Dose prescribed
- Immediate-release vs. long acting

Days’ Prescription Increases Risk of Long-term Opioid Use

Key Issues:
- The probability of long-term opioid use increases most sharply in the first days of therapy
  - 3 days use = 8% risk at 1 yr.
  - 7 days use = 16% risk at 1 yr.
  - 3 days use = 4% risk at 3 yrs.
  - 7 days use = 8% risk at 3 yrs.


Higher Dosages Increase Overdose Risk

<table>
<thead>
<tr>
<th>Dosage in MME/day</th>
<th>Overdose odds ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>1</td>
</tr>
<tr>
<td>20 to &lt;50</td>
<td>1.3-1.9</td>
</tr>
<tr>
<td>50 to &lt;100</td>
<td>1.9-4.6</td>
</tr>
<tr>
<td>100 or greater</td>
<td>2-8.9</td>
</tr>
</tbody>
</table>

*Odds based on single studies

Long-Acting Opioids Increase Risk of Chronic Use

37% of working-age adults prescribed long-acting opioids transitioned to chronic opioid therapy, compared to 1.3% of those prescribed immediate-release opioids.

Source: Thornton et al, Predictors of Transitioning to Incident Chronic Opioid Therapy Among Working-Age Adults in the United States, Am Health Drug Benefits, 11(1), p 12-21, 2018

Do Limitations Reduce Misuse or Overdose?

Opioid Prescriptions Peak in 2012

New Restrictions
- Insurance Coverage
- Formulary Restrictions
- Pill Mill Laws
- Hydrocodone Rescheduling

Lower Rates of Opioid Prescribing Led to Reduced Misuse and Deaths 2007-2014

- Opioid prescribing peaked in 2012.
- Lower prescription rates led to lower misuse and deaths.
- Opioid misuse declined from 49 per 1,000 to 39 per 1,000.

Other examples: Did Prescription Restrictions Work?

- After Florida lawmakers implemented a series of restrictions on pain clinics, Florida’s overdose death rates from opioid analgesics declined 27%, and oxycodone deaths declined 52% from 2010 to 2012.

Florida Drug Overdose Death Rates for Selected Drugs; Dates of Policy and Enforcement Actions

- Opioid overdose deaths in Florida declined significantly after state lawmakers enacted:
  - Pain clinic regulations
  - Mandatory prescription drug-monitoring program requiring
  - Wholesale distributor regulations
  - Law enforcement actions
Attempts to Decrease Over-Prescribing

- As of April 2018, 21 states had set legal limits on supply, dosage, or both.
- 7 other states have authorized regulatory restrictions.
- Most of the laws limit first-time prescriptions to a certain number of days supply. Those limits range from 3-14 days, with 7 being the most common.
- 7 states that enacted laws limiting opioid prescribing before 2017 showed a significant decline in prescription opioid death rates compared with 30 states that did not enact such laws through 2017. (Wilcoxon p=0.012)

Laws Setting Limits on Certain Opioid Prescriptions

<table>
<thead>
<tr>
<th>Statutory Limit: 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statutory Limit: 7 days</td>
</tr>
<tr>
<td>Statutory Limit: 5 days</td>
</tr>
<tr>
<td>Statutory Limit: 3-4 days</td>
</tr>
</tbody>
</table>

Through Regulation

- Direction or Authorization to Other Entity to Set Limits or Guidelines
- No Limits
- No Information

Source/Map: National Conference of State Legislatures

What Else Can Be Considered?

Has it worked?

<table>
<thead>
<tr>
<th>Approach</th>
<th>Sensitivity (Range)</th>
<th>Specificity (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-Assessment Instruments¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Screener and Opioid Assessment for Patients with Pain²</td>
<td>90.83%*</td>
<td>33-69.3%*</td>
</tr>
<tr>
<td>• Opioid Risk Tool (ORT)¹</td>
<td>58.8-82%*</td>
<td>22-38.4%*</td>
</tr>
<tr>
<td>• Drug Abuse Screening Test (DAST)¹</td>
<td>70%</td>
<td>10%</td>
</tr>
<tr>
<td>• Current Opioid Misuse Measure²</td>
<td>52%</td>
<td>50.6%</td>
</tr>
<tr>
<td>• Current Opioid Misuse Measure (COMM)¹</td>
<td>52.1%</td>
<td>50.6%</td>
</tr>
<tr>
<td>• EM Providers Clinician Assessment Questionnaire²</td>
<td>81%</td>
<td>33%</td>
</tr>
<tr>
<td>• Emergency Provider Impression Data Collection Form²</td>
<td>72.7%</td>
<td>63.2%</td>
</tr>
</tbody>
</table>

Source: *Ranges based on multiple studies

¹ Sahota et al, Screening ED patients for opioid drug use: a qualitative systematic review, Oct 2018, Vol. 85:139-146
² Dowell et al, CDC Guideline for prescribing opioids for chronic pain - US, March 2016, 65(1);1-49
³ Davis et al, Physician continuing education to reduce opioid misuse, abuse and overdose: Many opportunities, few requirements, June 2016, Vol. 163, 100-107

Urine Testing

- 92% Sensitivity, 93% Specificity
- Easily defeated. Urine adulteration to defeat positive drug screening is a major challenge for clinical and forensic laboratories

Opioid Management

- Plans intended to mitigate risk of misuse or addiction in patients prescribed opioids for chronic pain
- The CDC found no studies that evaluated the effectiveness of opioid management plans

Training

- Only five states (Conn., Iowa, Maryland, South Carolina and Tenn.) require all physicians to obtain continuing medical education on pain management and controlled substance prescribing
- Fewer than half of states require any physicians to obtain such training
What Else Can Be Considered?

- Stewardship Boards or other activities to educate
- Further Limitations on prescriptions:
  a) Limit days of prescription
  b) Limit reimbursement or conditions
  c) Limit prescribing to minors
- Research into non-opioid analgesics
- Replacement of opioid prescriptions with non-opioid drugs

Questions?

Richard Larson, MD, PhD
Executive Vice Chancellor
Vice Chancellor for Research
UNM Health Sciences Center
RLarson@salud.unm.edu
505-272-5102

Medicare Tightened Daily Dose Restrictions On Hydrocodone Products

- Formularies used quantity limits and prior authorization to restrict opioid dosages, 2006 to 2015.

Private Insurance Limits Opioid Prescribing

- Opioid prescribing rates declined after Blue Cross of Massachusetts implemented prior approval and quantity limits in July 2012.

Limits on Opioid Prescribing Held Deaths in Check for Two Years

- Prescription opioid deaths remain flat from 2012 to 2014.