Measuring an epidemic: using EHR data to track trends in opioid prescribing

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You Draw It: Just How Bad Is the Drug Overdose Epidemic?

By JOSH KATZ   APRIL 14, 2017

The number who die each year from...

- Drug overdoses: 52,404
- Car accidents: 37,757
- Guns: 35,763
- H.I.V.: 6,465
An influential report of a small case series of atypical chronic pain patients using opioids long-term

*Pain, 25 (1986) 171–186*
Elsevier

**Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases**

Russell K. Portenoy and Kathleen M. Foley

*Pain Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, and Department of Neurology, Cornell University Medical College, New York, NY 10021 (U.S.A.)*

(Received 10 June 1985, accepted 28 October 1985)

Addiction: “Misunderstanding of addiction and mislabeling of patients as addicts result in unnecessary withholding of opioid medications.”

Tolerance: “For most opioids, there does not appear to be an arbitrary upper dosage limit.”

Diversion: “Efforts to stop diversion should not interfere with prescribing opioids for pain management.”

Overdose: “Respiratory depression induced by opioids tends to be a short-lived phenomenon, generally occurs only in the opioid-naive patient, and is antagonized by pain.”
"There’s no question that our best, strongest pain medicines are the opioids, but these are the same drugs that have a reputation for causing addiction and other terrible things."

“They don’t wear out. They go on working.”

“They do not have serious medical side effects…these drugs should be used much more than they are for patients in pain…”

Promotional video, Purdue Pharma, 1999
National, state, local policies

- The Oregon Intractable Pain Act, passed in 1995, allowed physicians to prescribe controlled substances for treatment of chronic pain without sanction from the Oregon Medical Board. The Oregon Pain Commission advocated for appropriate patient access to pain management...

- Joint Commission on Accreditation of Healthcare Organizations (JCAHO) – 2001. All patients assessed for pain (5th vital sign)
Opioid Prescriptions Dispensed by US Retail Pharmacies IMS Health, Vector One

Nora Volkow report to congress May 14, 2014 (NIDA website)
Paula is taking me on a driving tour of Man, the tiny West Virginia town where she has spent her entire life. Because I don't know my way around the hollows and gullies and creeks that carve through these hills, Paula is at the wheel. And because Paula isn't a morning person, we've set out on our tour at midnight. It's dark; the only illumination comes from our headlights cutting through the mist that rolls down from the hills.

The tour Paula is leading isn't sanctioned by the local chamber of
Deadly abuse of methadone tops other prescription drugs

By Donna Leinwand, USA TODAY

Methadone, a painkiller that has been used to treat heroin addicts for decades, has emerged as an increasingly popular and deadly street drug, joining narcotics such as Vicodin and OxyContin as frequently abused prescription drugs.

Fatal overdoses of methadone rose at a higher rate than those involving any other narcotic from 1999 through 2004, according to a recent study by the National Center for Health Statistics (NCHS). The number of deaths from methadone in 2004 (3,849) represented a 390% rise from 1999, the study said.

ON THE STREET: Painkiller becomes more available

Methadone was cited in nearly 13% of all the overdose deaths reported in the USA in 2004, up from about 4% five years earlier. Among drugs cited in fatal overdoses, only cocaine kills more people than methadone.
Heroin isn't the drug that's killing most Oregonians

- More people in the 35- to 54-year-old age group die of unintentional overdoses than from motor vehicle accidents. Methadone is a particularly bad actor…

- More individuals die from overdoses of prescription medications than heroin, cocaine and methamphetamine combined…
Overdose Deaths Involving Opioids, United States, 2000-2015

Sales per 100,000 population

Any Opioid

Commonly Prescribed Opioids
(Natural & Semi-Synthetic Opioids and Methadone)

Heroin

Other Synthetic Opioids
(e.g., fentanyl, tramadol)

What happened?

Opioid Overdose Deaths

- Economic & Political Pressures
- Sociocultural Zeitgeist
- Professional guidelines
For every action...?

- Beginning 2000 - Anecdotes in the popular press.
- 2007 – Purdue pharmaceutical settlement
- 2010 – Oxycontin reformulated to prevent injection use
- Prescription drug monitoring programs (PDMPs) – 25 in 2005. 46 in 2011
- 2011 – ONDCP report – **Epidemic**: Responding to America’s Prescription Drug Abuse Crisis
- 2011 – Portland, OR local FQHC policies
- 2014 opioid/acetaminophen combinations rescheduled from category 3 to 2
- 2016 CDC safe prescribing guideline published
- 2016 Surgeon general communication to all prescribers
Oregon House passes bill seeking to stem opioid epidemic

BY ANDREW SELSKY
The Associated Press
6:50 P.M., APRIL 10, 2017

SALEM — Seeking to stem the opioid epidemic in Oregon and prevent overdose deaths, the state House of Representatives unanimously approved a proposed law on Monday that would provide safe-use recommendations to those who prescribe such pain-killing drugs.

However, provisions in the bill that would have limited health-care practitioners to prescribing a maximum seven-day supply of opioids to patients, as directed by the Oregon Health Care Commission, were removed and the bill was scaled back to encouraging safe-use practices but not restricting prescribing.

The bill was approved without amendments, and would now move to the Senate for consideration. It is one of several bills aimed at addressing the opioid epidemic that have been introduced this legislative session.
Timeline 2

- Portenoy paper 1986
- Oxycontin promotion 1996
- Pain Society guidelines
- Stopping
- NDMP
- PDMPs
- Medical residency
- Practicing in urban Portland
- Teaching behavioral medicine
- CDC guidelines
- Surgeon general letter 2016
It’s complicated

Pain

Substance Use Disorders

Overdose Deaths

Pain Medicine
**Lack of evidence**

- “In the United States guideline [2009], 21 of 25 recommendations were viewed as supported by only low-quality evidence.”

- “In other words, the developers of the guidelines found that what we know about opioids is dwarfed by what we don’t know.”
  
What do we want to know?

- What policies led to over-prescribing of opioids?
- What policies will lead to more appropriate prescribing?
- What pain conditions most commonly lead to opioid use?
- What other patient characteristics are associated with opioid use for pain? With overdose?
- Are some opioids better than others? Are some delivery methods better? LA vs SA? Benefits/Harms?
- What are the best ways to monitor patient opioid use risk?
- How can we identify overdoses in ambulatory records? In ED records?
- How can we better treat pain if not with opioids?
- How can we better treat substance use disorders and overdose to which overprescribing has contributed?
The principles of research into comparative effectiveness are well suited for addressing these and other research gaps. Rather than evaluating whether yet another opioid is more effective than nothing in low-risk patients, such research focuses on the benefits and harms of interventions in populations similar to those encountered in clinical practice, emphasizing the need to understand the trade-offs between different interventions (e.g., different opioids).

These principles can be applied to the evaluation of different strategies for risk assessment, patient selection, dosing, management and monitoring, using a broad range of study designs, including observational studies of large databases or registries.
How have we studied opioids in populations up to now?

- **NSDUH - National Survey on Drug Use and Health**

- **NHANES – National Health and Nutrition Examination Survey**

- **NAMCS – National Ambulatory Medical Care Survey**
Pharmacy Claims Databases


In 2010 Florida was home to 98 of the 100 U.S. physicians who dispensed the highest quantities of oxycodone.


Opioid prescription rates for selected drugs calculated from IMS Health National Prescription Audit (NPA) decreased significantly 2010 to 2012, and especially oxycodone (24%).

Florida Medical Examiners Commission (FMEC) data from 200102012 showed opioid overdose deaths declined 27%, again, especially those attributable to oxycodone (52%).

Prescription Drug Monitoring Programs (PDMPs)


How can we better leverage clinical data warehouses to track opioid prescribing?

- Most major institutions began implementing EHRs after 2005 – if this tool had been available in 1990, could we have understood the problem better and addressed it earlier?

- Clinical data is a more granular look at details of encounters in which opioids have been prescribed.
Clinical data entry

Data warehouse structure and organization

Extraction into population reports with meaning
Studies using EHR data

- The CONSORT study


Introducing the ADVANCE Clinical Data Research Network

Jon Puro, MPA:HA
Principle Investigator, ADVANCE
The ADVANCE CDRN Partners

OCHIN, Inc.
97 health systems; 597 clinics; 17 states

Health Choice Network (HCN)
24 health systems; 466 clinics; 8 states

Legacy Health System

Care Oregon Medicaid Managed Care Plan

American Academy of Family Physicians, Robert Graham Center

Fenway Health
3 clinics; 1 state

Kaiser Permanente NW Center for Health Research

Oregon Health and Sciences University (OHSU)
The ADVANCE CDRN
**ADVANCE Research Data Warehouse (RDW) includes:**

<table>
<thead>
<tr>
<th>PCORnet CDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics (DOB, sex, race, etc.)</td>
</tr>
<tr>
<td>Enrollment</td>
</tr>
<tr>
<td>Encounter</td>
</tr>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>Labs</td>
</tr>
<tr>
<td>Prescribing and Dispensing</td>
</tr>
<tr>
<td>Death date and cause</td>
</tr>
<tr>
<td>Vital Signs (height, weight, tob.)</td>
</tr>
<tr>
<td>Condition (incl. Problem List)</td>
</tr>
<tr>
<td>Patient Reported Outcomes</td>
</tr>
</tbody>
</table>

Plus additional data needed for research on the safety net:

- **Federal Poverty Level (FPL)**
- **Household income and size**
- **Insurance status (incl. uninsured)**
- **Homeless status**
- **Migrant/seasonal worker status**
- **Veteran status**
- **Community Vital Signs**
OVERVIEW:

- ADVANCE prescribing data

- Methods used in identifying opioid medications
  - Step I: Identify opioid classes using RxClass and RxNav
  - Step II: Identify additional opioid medications with missing RxNorms using text searches; obtain RxNorms using RxMix.

- Preliminary results
**Terminology**

- **RxNorm**: Standardized terminology for identifying both generic and brand-name drugs.
- **RxCUI**: RxNorm concept unique identifier for a clinical drug.
- **Raw_Rx_Med_Name**: An optional field in the prescribing CDM table.
- **RxClass**: Web based application to look at drug class hierarchies to find RxNorm.
- **RxNav**: Web based application to search for different drug characteristics across different classification systems.
- **RxMix**: Web based application that can be used to create programs to search for RxNorm functions. Allow users to run programs instantly or in batch mode.
- **NDC**: National Drug Code. It is a unique 10-digit, 3-segment number. It is a universal product identifier for human drugs in the US.
Advance prescribing data

- All prescribed medications are included, even if some cannot be mapped to RxNorm.
  - >95% mapped to RxNormCUI.

- Medication reconciliation/active med list records are not included in the Prescribing table.

- Contain optional fields such as Raw_Rx_Med_Name and Raw_RxNorm_CUI.
  - Raw_Rx_Med_Name may contain both generic and brand named medications.
Step I: using RxClass and RxNav

- **RxClass**
  - Web based application created by NIH to look at drug class hierarchies to find RxNorm.
    - NDC code cannot be used in the search.
    - Shows links to clinical drugs (brand and generic), to their active ingredients, drug components, and related brand names.
  - Contain 9 drug class trees:
    - Anatomical Therapeutic Chemical (ATC1-4)
    - Established Pharmacologic Classes (EPC)
    - MeSH Pharmacologic Actions (MESHPA)
    - Disease
    - Chemical Structure (Chem)
    - Mechanism of Action (MoA)
    - Physiologic Effect (PE)
    - Pharmacokinetics (PK)
    - VA Classes (VA)
Step I: using RxClass and RxNav

RxClass: https://mor.nlm.nih.gov/RxClass/
Step I: using RxClass and RxNav

RxNav: https://mor.nlm.nih.gov/RxNav/
Step I: using RxClass and RxNav
Step II: Pattern SEARCH on GENERIC Names of opioid drugs

- Missing RxNormCUI information

- Pattern search on generic opioid medications
  - Hydrocodone
  - Oxycodone
  - Tramadol
  - Codeine
  - Morphine
  - Methadone
  - Fentanyl
  - Hydromorphone
  - Oxymorphone
  - Meperidine
  - Tapentadol

- Use RxMix to identify the RxCUIs
Step II: Pattern SEARCH on GENERIC Names of opioid drugs

https://mor.nlm.nih.gov/RxMix/
Methods

**STEP 1**

- RxNorm is Populated
  - Use RxClass to identify opioid medications
  - Use RxNav to download a list of RxCUIs
  - Compile/Combine list of RxCUIs
  - Import RxNorm file to SQL

**STEP 2**

- RxNorm is missing
  - Run a pattern search on generic names of opioid medications
  - Save file as a .txt file
  - Use RxMix to upload input file for batch job (FindRxCuibyString)
  - Import RxNorm file to SQL

Link to CDM (by Rxnorm) or by Raw_Rx_Med_Name to create final opioid flags

Result with missing RxCUIs, clean med name and resubmit batch job
Percentage of adults with $\geq 1$ opioid prescription by year
Percentage of adults with $\geq 1$ opioid prescription by age group
4. Percentage of adults with $\geq 1$ opioid prescription in 2016 by sex and age group

5. Percentage of adults with $\geq 1$ opioid prescription in 2016 by payor type
6. Percentage of adults with >=1 opioid prescription in 2016 by Race

7. Percentage of adults with >=1 opioid prescription by sex and ethnicity
8. Percentage of all adults with >=10 opioid prescription by year.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Orders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>160,766</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>106,238</td>
</tr>
<tr>
<td>Tramadol</td>
<td>61,523</td>
</tr>
<tr>
<td>Codeine</td>
<td>35,743</td>
</tr>
<tr>
<td>Morphine</td>
<td>23,770</td>
</tr>
<tr>
<td>Methadone</td>
<td>12,287</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>8,797</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>3,471</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>380</td>
</tr>
<tr>
<td>Meperidine</td>
<td>254</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>222</td>
</tr>
</tbody>
</table>
Defining chronic opioid use using population data - Annual number of prescriptions vs. a predefined MME

- EHR Order Data
  - Unique Med Order ID
  - Unique Patient ID
  - Date of prescription order
  - Name of medication
  - Unit of medication (MG, MG/ML, MCG/HR)
  - Strength of ordered medication per unit
  - Number of units ordered
  - Frequency at which it should be taken
  - Example: Order20010111, MRN1002010, 1/25/2015, Oxycontin, Mg, 10, 90, Take one three times daily.

- And extrapolate:
  - Number of morphine milliequivalents per prescription (from name, strength, unit, number of units)
  - Long acting vs. short acting medicine (from name)
  - Initiation date
One Urban FQHC in Portland

- 8080 adults with at least one ambulatory visit in 2015
- Followed forward for one year after index visit and opioid prescriptions assessed.
- 1757 with at least one prescription for an opioid (22%)
- 15160 distinct opioid prescription orders (avg 8.6)
  - 81% did not have a discrete “sig”, so expected frequency wasn’t clear.
- The clinic keeps a list of “chronic opioid users” = 540 patients (in 2015)
Count of opioid prescriptions for each patient

Number of opioid prescriptions per patient

Number of opioid prescriptions: 0, 100, 200, 300, 400, 500, 600

Count of patients: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47

Number of patients: 0, 10, 20, 30, 40, 50, 60
FQHC 2015
8080 adults, 1757 with at least 1 opioid prescription

<table>
<thead>
<tr>
<th>Opioid type</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long acting</td>
<td>46</td>
<td>3%</td>
</tr>
<tr>
<td>Short acting</td>
<td>227</td>
<td>13%</td>
</tr>
<tr>
<td>Both LA and SA</td>
<td>1479</td>
<td>84%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid number</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>477</td>
<td>27%</td>
</tr>
<tr>
<td>&gt;8</td>
<td>683</td>
<td>39%</td>
</tr>
<tr>
<td>&gt;10</td>
<td>613</td>
<td>35% (7.6% of clinic adults)</td>
</tr>
</tbody>
</table>
# Milligram Morphine Equivalents (MMEs)

<table>
<thead>
<tr>
<th>Major Group</th>
<th>Type of Opioid</th>
<th>Morphine equivalent conversion factor per mg of opioid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting Non-Schedule II</td>
<td>Propoxyphene (with or without aspirin/acetaminophen/ibuprofen)</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>Codeine + (acetaminophen, ibuprofen or aspirin)</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Hydrocodone + (acetaminophen, ibuprofen, or aspirin) Hydrocodone and homatropine</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Tramadol with or without aspirin</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>Butalbital and codeine (with or without aspirin, ibuprofen, acetaminophen)</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Dihydrocodeine (with or without aspirin, ibuprofen, acetaminophen)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>Pentazocine (with or without aspirin, ibuprofen, acetaminophen)</td>
<td>0.37</td>
</tr>
<tr>
<td>Short-acting, Schedule II</td>
<td>Morphine sulfate</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Codeine sulfate</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Oxycodone (with or without aspirin, acetaminophen, ibuprofen)</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Hydromorphone</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>Meperidine hydrochloride</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Fentanyl citrate transmucosal^2</td>
<td>0.125</td>
</tr>
<tr>
<td></td>
<td>Oxymorphone</td>
<td>3.0</td>
</tr>
<tr>
<td>Long-acting (Schedule II)</td>
<td>Morphine sulfate sustained release</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Fentanyl transdermal^3</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Levorphanol tartrate</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>Oxycodone HCL controlled release</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Methadone</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Milligram morphine equivalents prescribed for the year

<table>
<thead>
<tr>
<th>Total MME</th>
<th>Total/365</th>
<th>No. Patients (% of 1757)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1825</td>
<td>&lt;5</td>
<td>949 (54)</td>
</tr>
<tr>
<td>1826-5474</td>
<td>5-14.9</td>
<td>262 (14.9)</td>
</tr>
<tr>
<td>5475-18249</td>
<td>15-49.9</td>
<td>296 (16.8)</td>
</tr>
<tr>
<td>18250-32849</td>
<td>50-89.9</td>
<td>97 (5.5)</td>
</tr>
<tr>
<td>&gt;32850</td>
<td>&gt;=90</td>
<td>153 (8.7)</td>
</tr>
</tbody>
</table>
Opportunities

- Medication orders are mostly defined vocabulary from that clinicians select from lists, and therefore reliably accurate.

- There is a great deal of unexplored data in the clinical records concerning visits and patient characteristics that have yet to be explored and tracked.

- Thus far, studies have been retrospective analyses. Do they need to be?
  - Once opioid prescriptions are appropriately identified, there is opportunity for regular surveillance on a nearly real time basis.
**Challenges**

- The larger the study population, the more generalizable. Combining data from different EHRs is complicated.

- The data is only as good as the entry. Example: clinicians free-text the patient instructions, or “sig”, it becomes difficult to calculate a daily MME.

- Electronic health records count prescription orders, not fills. But perhaps we can assume excellent medication adherence when it comes to opioids.
Next steps:

- Continue organizing and exploring ADVANCE data as infrastructure for further studies
- New CDC Prescribing Guidelines – can we tease out the effect?
- Benzodiazepines
- Funding
Future directions

- Linking to other data sets
  - Social determinants of health data
  - Prescription drug monitoring program data
  - State vital statistic registries

- Patient reported data (adverse childhood experiences)

- Identifying overdoses in EHRs?

- Pain!
Questions, Answers, and Discussion

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