Opioid Therapy at a Time of Crisis

Steven D. Passik, PhD

Dedication

• This talk is dedicated to Ken Kirsh, Simon Budman, and Howard Smith in honor of their multiple insights and contributions to opioid safety

Disclaimer and Disclosure

• The views expressed in this talk are my own and not those of my employer.
• Full time employee Collegium Pharmaceuticals
  • VP, Scientific Affairs, Education and Policy
Conflict of Interest Disclosure

Information
• Conflicts of interest listed for ALL contributors
  • Steven D. Passik, PhD Full time employee Collegium Pharmaceuticals

A conflict of interest is a particular financial or non-financial circumstance that might compromise or appear to compromise, professional judgment. Anything that fits this should be included. Examples are owning stock in a company whose product is being evaluated, being a consultant or employee of a company whose product is being evaluated, etc.
• Taken in part from “On Being a Scientist: Responsible Conduct in Research”. National Academies Press. 1995.

Learning Objectives
• Evaluate the notion of the opioid epidemic and the data used to support it
• Understand the limitations of present opioid policy
• Identify 5 potential ways to improve opioid safety

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The Opioid Pendulum: Where Are We Now?

Opioid Prescribing and the Healthcare System

- What has increased opioid prescribing exposed in our healthcare system?
  - Where does our healthcare system fall?
    - Chronicity
    - Conditions with major motivational/psychiatric component
    - CARE COORDINATION: Communication among professionals
    - Ongoing risk assessment
    - Conditions that intersect badly with SES
    - Stigmatization

Sensitivities in Questioning the Opioid Status Quo

- Can you question some of the key assumptions?
- Can you question the interpretation of data?
- Can you ask for a sense of scale?
  - Without being callous to the multiple parties who are hurting and have suffered pain and loss?
  - I say, we can (must) but we must search for solutions that don't address one side's losses at the cost of the other's

Prevalence of Overdose Deaths Among Opioid Analgesic Patients in NC

0.02%

Even with the cost-offsets within the health system from having fewer patients abusing opioids, use of ADF opioids resulted in an additional $533 million net spending over five years from the health care system perspective (Table ES7). The lower abuse-related costs of ADF opioids compared to non-ADF opioids were outweighed by the higher prescription costs of ADF opioids.

Using ADF opioids resulted in additional costs of $231,500 for preventing one new case of abuse and approximately $80,500 for preventing one abuse-year. Given the small benefit observed in overdose deaths, the cost to prevent an overdose death was estimated to be approximately $1.4 billion (Table ES8).

Over a five-year time-horizon, our base case analysis indicated that there were approximately 2,300 fewer new cases of abuse in the ADF opioid cohort and approximately 6,600 fewer abuse-years incurred compared to the non-ADF opioid cohort, with a small reduction in opioid overdose-related deaths of less than one.

Assume ICER report is accurate (or even worst case)

They predict converting the entire opioid market to branded ADFs (ER and IR) will cost an additional $511 million over five years (or $102.2 million per year).

In 2016 the Congressional Budget Office estimated US health coverage as follows:

- US population in 2016 = approximately 325 million
- 53 million Americans aged 65 or over were covered by Medicare
- 245 million Americans received either employer-based (155 million) or non-employer based (90 million) health insurance
- Cost of converting the entire opioid market to branded ADFs (ER and IR) would be:

\[
\text{Cost per person per year} = \frac{\$102.2 \text{ million}}{298 \text{ million people}} = \$0.34/\text{person per year}
\]
What is an Epidemic?

- ...affects a greater number of people than is usual for the locality or one that spreads to areas not usually associated with the disease...
- Epidemics are about expectations and geography
  - Is chronic pain (still) an epidemic?
  - Is opioid abuse?

Expectations:
Was the Healthcare System Ready for More Opioids?

- Shortly after the increase in Rxing in the early 90s
- Early reports that despite unprecedented increases in opioid manufacturing quotas approved by DEA in ARCOS, no increases in DAWN mentions were noted – and people believed it!*
- Prescription Drug Monitoring Programs (PDMP) were primitive, abuse deterrents and better opioids were science fiction, LCMS drug testing didn't come back from the lab for 2 weeks, addiction training wasn't common.....


All Tools Clinicians Have Needed Are Now In Place

- PDMPs: are the other prescribers of controlled substances
- LC-MS/MS drug testing in 24 hours: is the patient taking their prescribed medication? And only their prescribed medications – no other licit or illicit opioids?
- Genetic Testing: is the patient on the best opioid for them – most likely to get best response at most reasonable dose
- Screening Tools: ascertain risk level and accommodate opioid delivery to it
- Giveback Programs: ensure safe disposal and decrease opioids available for diversion
3rd Party Payors

- Frequent visits
- Urine screens
- Psychological care
- Abuse deterrent opioids
- Less drug per prescription

Opioid Crisis: Trump Gets It

...Pledges more arrests and prosecutions, but no national emergency declaration

by Shannon Firth, Washington Correspondent, MediPage Today
August 29, 2017

- “Strong law enforcement is absolutely vital to having a drug-free society.”
- The president also channeled former first lady Nancy Reagan’s “just say no” approach to combating drug use.
- “The best way to prevent drug addiction and overdose is to prevent people from abusing drugs in the first place. If they don’t start, they won’t have a problem. If they do start, it’s awful tough to get off. So we can keep them from going on, and maybe by talking to youth and telling them ‘No good; really bad for you’ in every way. But if they don’t start, it will never be a problem.”

Trying to Get to a Rational Opioid Policy

- Most policy on the state and federal level attempts to limit the number, length and extent of opioid exposures.
- Opioid exposures will never drop to zero; nor should this be the goal.
- And while a correction was necessary, equal attention should be paid to the need to make the exposures that do occur as safe as they can possibly be.
Prescribing rates are Dropping

But the Death Rate Keeps Climbing

What Really is the Risk of Addiction in an Opioid Exposure?

- Was there any truth to Porter and Jick?
- Extremely low risk of addiction in non-addicts exposed to opioids for a short time in a structured setting (4/11882 <1%)
- Dunbar and Katz
  - 20 patients treated with opioids in outpatient setting for non-cancer pain. 9 with a prior history of opioid abuse (high risk).
  - Among high risk people aberrant behaviors were noted in 44% to 100%. In the no prior opioid abuse (low risk) group aberrant behaviors were noted in 0%-20%. Of those who would manifest signs of loss of control 55% manifest problems almost immediately.

Dunbar SA, Katz NP, Chronic Opioid Therapy for Nonmalignant Pain in Patients with a History of Substance Abuse: Report of 20 cases, JPSM 1996
Addiction Is Not Simply a Disease of Exposure

Burroughs: Exposure

Current

▪ Exposure is necessary not sufficient
▪ Exposure to drug
▪ Vulnerable person
▪ Vulnerable time


Understanding the demand side of the prescription opioid epidemic: Does the initial source of opioids matter?

Theorens J, Clever, Matthew S. 2016

▪ Conclusions: “Our results suggest that self-treatment of co-morbid psychiatric disturbances is a powerful motivating force to initiate and sustain abuse of opioids and that the initial source of drugs – a prescription of experimentation – is largely irrelevant in the progression to a substance use disorder.”

Passik’s 5 Suggestions for Improving Opioid Safety

1. Establish the Well Opioid Visit
   ▪ Develop next generation PDMP software
2. Develop new treatments for acute pain in young people
3. Limit short acting opioids for chronic pain
4. Eliminate MISE limits for opioids to which they don’t apply
   ▪ Develop a more specific opioid-benzodiazepine MISE or have 2 cutoffs one for patients on benzos and one for those not on benzos
5. Eliminate fail-first policies for ADFs LAOs
The Well Opioid Visit

- A 45 minute visit 4/year minimum
- Qualified clinician is reimbursed fully for the amount of time and cognitive effort that is required to truly
  - Evaluate the patient
  - Review results of all surveillance (not simply most recent results, but trends)
  - Next generation PDMP software that detects potential problems and notifies the prescriber
  - Address aberrant drug related behavior
  - Evaluate mental state, goal attainment, functional restoration
  - Address barriers
  - Amend strategy and treatment plan especially if risk level has changed

Risk Management Is a Package Deal

- Screening and risk stratification
- Use of PMP data
- Compliance Monitoring
  - Urine screening
  - Pill/Patch counts
- Education regarding drug storage and sharing
- Psychotherapy and highly "structured" approaches
- Better/safer opioid products

New treatments for acute pain in young people
New treatments for acute pain in young people

Limit Short Acting Opioids for Chronic Pain
Fig 2. Rates of IR and ER opioid analgesic Intentional Abuse, RADARS System Poison Center Program.

- Data are displayed according to calendar quarter. (A) Rates of Intentional Abuse adjusted for population; a cubic model was fit for both IR and ER formulations over time. (B) Rates adjusted for prescriptions dispensed; a quadratic model was fit for both IR and ER formulations over time. (C) Rates adjusted for grams dispensed; a quadratic model was fit for both IR and ER formulations over time. The red boxes represent the point with the highest expected rate during the study period.


Fig 3. Rates of IR and ER opioid analgesic diversion, RADARS Drug Diversion Program.

- Data are displayed according to calendar quarter. (A) Rates of endorsement adjusted for population. (B) Rates adjusted for prescriptions dispensed. (C) Rates adjusted for grams dispensed. For each, a cubic model was fit for both IR and ER formulations over time. The red boxes represent the point with the highest expected rate during the study period.


Eliminate MSE Limits for Certain Opioids

- MSE limits have been recommended in CDC guidelines for primary care prescribing opioids primarily as a way to limit abuse, addiction and overdose when patients are managed by non-specialists.
- If primary care physicians cannot alter their workflow and are locked in to 8-15 minute visits, once-a-month with the ability to incorporate only minimal monitoring, then some limitations are appropriate.
- However, these limits were not meant to apply to qualified specialists. Yet, due to their enforcement via state laws and payer policies, they are fast becoming the “law of the land.”
- Some have questioned the scientific merit of MSE limits in general.
- Their application to certain opioid medications is often particularly irrational.
- And these are medications that we might societally want to encourage use of in a crisis due to low rates of abuse and overdose.
Eliminate MSE Limits for Certain Opioids

Assessment of the abuse of tapentadol immediate release: The first 24 months
Dart RC, Cicero TJ, Suralti HL, Rosenblum A, Bartelson BB, Adams EH

Eliminate Fail First Policies for ADF LAOs

- Most payors require a patient to fail one or even two non-ADFs before they can have access to an ADF
- Many do so because the patient isn’t considered high enough risk nor have they exhibited sufficient evidence of drug abuse
- This ignores the importance of the risk around the patient – eg, teenagers, substance abusers – that might necessitate an ADF to avoid diversion
- They site the lack of evidence supporting ADF prevention of abuse and diversion but have created a Catch-22 insofar as their policies prevent market uptake and thus data cannot accrue to determine the impact of ADF on prevention
- Even in the absence of definitive evidence – is this a socially responsible way to respond to a public health crisis?

Eliminate Fail First Policies for ADF LAOs

There’s little evidence abuse-deterrent opioids work. Why should we use them?

By C. Bernice Good, Chrsitina Woodhouse, and William Sharrer / August 8, 2017
The Right Question About Opioids for Chronic Pain

• The wrong question is, “Should we use opioids to treat chronic pain?”

• The right question is, “In which patients should we use opioids, at what doses, for how long, with which adjunctive treatments, and with what precautions?”