Opioid Correction vs Opioid Trauma: Where Policy Meets Chronic Pain

STEFAN G. KERTESZ, MD, MSC

PROFESSOR, UNIVERSITY OF ALABAMA AT BIRMINGHAM

BIRMINGHAM VAMC OPIOID SAFETY INITIATIVE, RISK MITIGATION TEAM, OPIOID ADVICE TEAM

DIRECTOR, HOMELESS PATIENT-ALIGNED CARE TEAM

@STEFANKERTESZ

Disclosures and a comment

- No pharmaceutical grants, honoraria, contracts, history of such
- I had stock in Abbot & Merck (<3%), sold it. My wife has same + J&J
- Opinions: not formal positions of any federal agency
- This talk includes learning from several

Adam J. Gordon, MD
VA Salt Lake City
U. Utah

Ajay Manhapra, MD
VA Hampton HCS
Yale U.

Sally Satel, MD
American Enterprise Institute
Yale U.

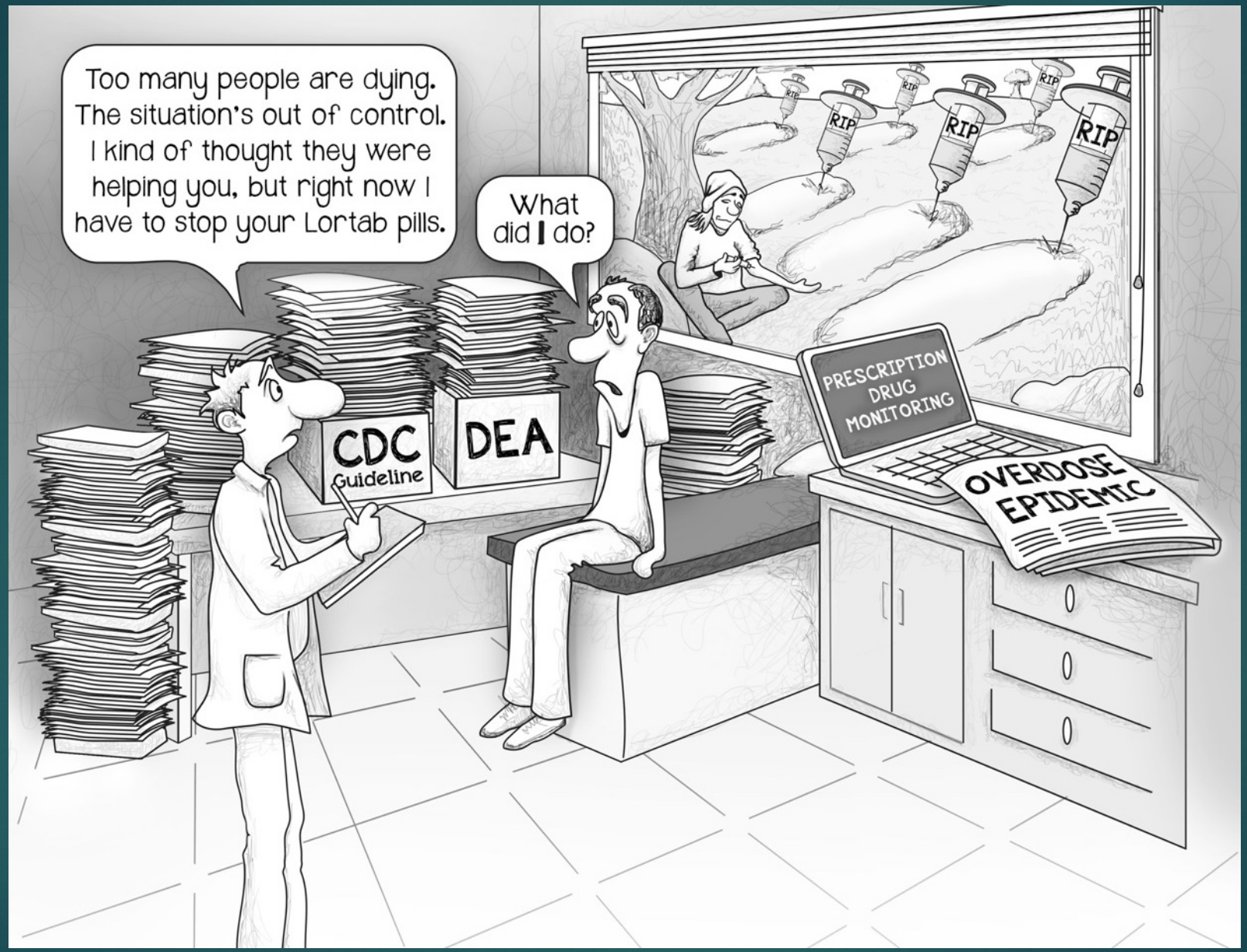
Time of tragedy call for questions

- >49,000 opioid OD deaths (USA, 2017)
- Among many parties implicated, **doctors**
- A need to "do something" risks upending key questions:

How do we know that what we think is right, is right?

Could what seems right be wrong?

For whom might it not be right?



Published in Kertesz, SG. *Turning the Tide or Riptide: the Changing Opioid Epidemic.* Substance Abuse, 2017

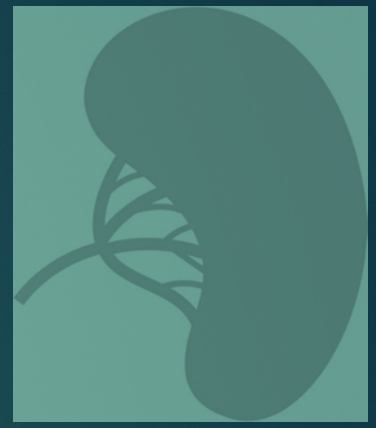
A thesis of sorts

- I hope we can agree:
  - Opioids were overprescribed
  - This caused harm
  - A systems-level decline in opioid reliance is desirable
- My thesis:
  - Forced reductions are highly incentivized, and/or mandated
  - This violates ethical and evidentiary norms of medical practice
  - Adverse consequences are evident
  - Better approaches are available

Here’s what’s next

- Case example
- Review of policies
  - Relationship to the CDC Guideline
  - Comment on shortages
- Data regarding the opioid tapers and discontinuations
- My policy suggestion

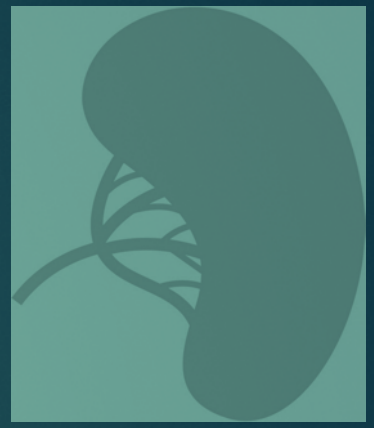
73 yo man with kidney transplant



- Chronic pain/polyarthritis late 1990's, renal transplant 2003
- Opioids since 2001, doses ~105-140 MME through 2014
  - Reduced dose with 30-60% cuts from 2014 to 2016
  - Down to 22.5 MME by July of 2017
- Progressive loss of energy → inability to keep up with meds
- 3/2017: admitted with renal failure
  - 1970s: 2 psych hospitalizations, prior alcohol use until 1989
- Evaluation
  - Renal biopsy: acute **and** chronic rejection
  - Acute rejection is prevented by meds he no longer could manage

- *Approved for presentation at the 2017 AMERSA meeting*

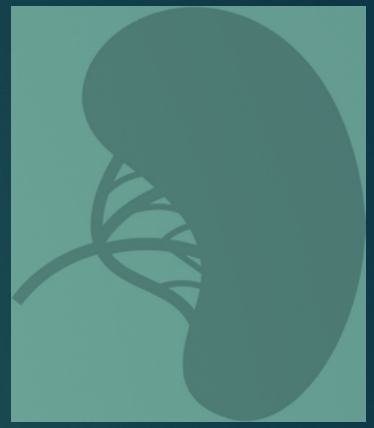
73 year old man



- Dialysis--→ restabilized
  - Bumped to oxycodone 10 mg four times a day
- PCP reduced immediately
- Readmitted twice in next 6 months
- Died in September, 2017

- Hydromorphone 0.4 mg/hour for final 24 hours

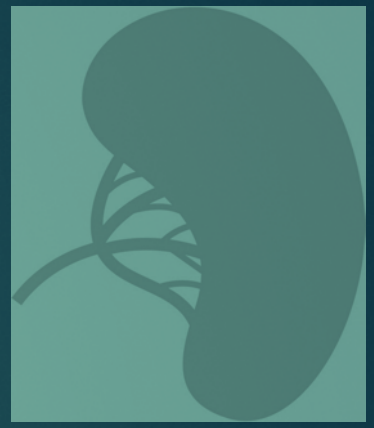
Policy Questions I have



- Did this human being's opioid reduction count as **entirely favorable in metrics** upheld by National Committee for Quality Assurance, by CMS, by the OIG (HHS), by state health authorities, by Congress, by VA, by DoJ and by all potential payers?

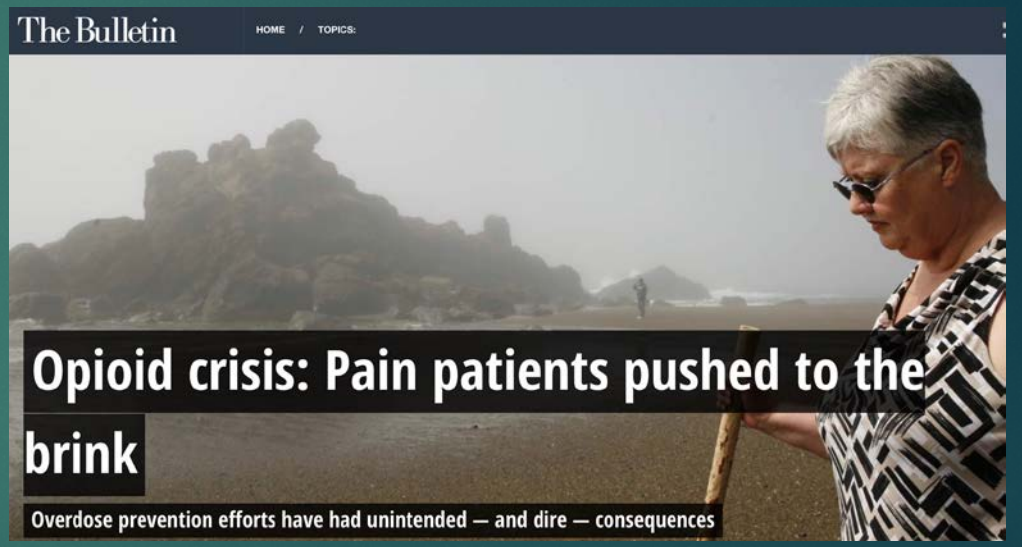
- Was this man **protected** by this reduction?

Clinical Interpretation



- **Not** acute withdrawal
- This **is** prolonged abstinence syndrome
  - Resurgent pain & dependence, “Things Fall Apart”
- Never qualified for Opioid Use Disorder
- Some patients really feel better after slow taper
- Other outcomes we see often: churning of medications, ineffective procedures, medical deterioration, loss of care relationships, illicit substances/alcohol & suicidality,

Our count: 50 **suicides** with explicit mention of pain + opioid reduction (from public reports or social media)

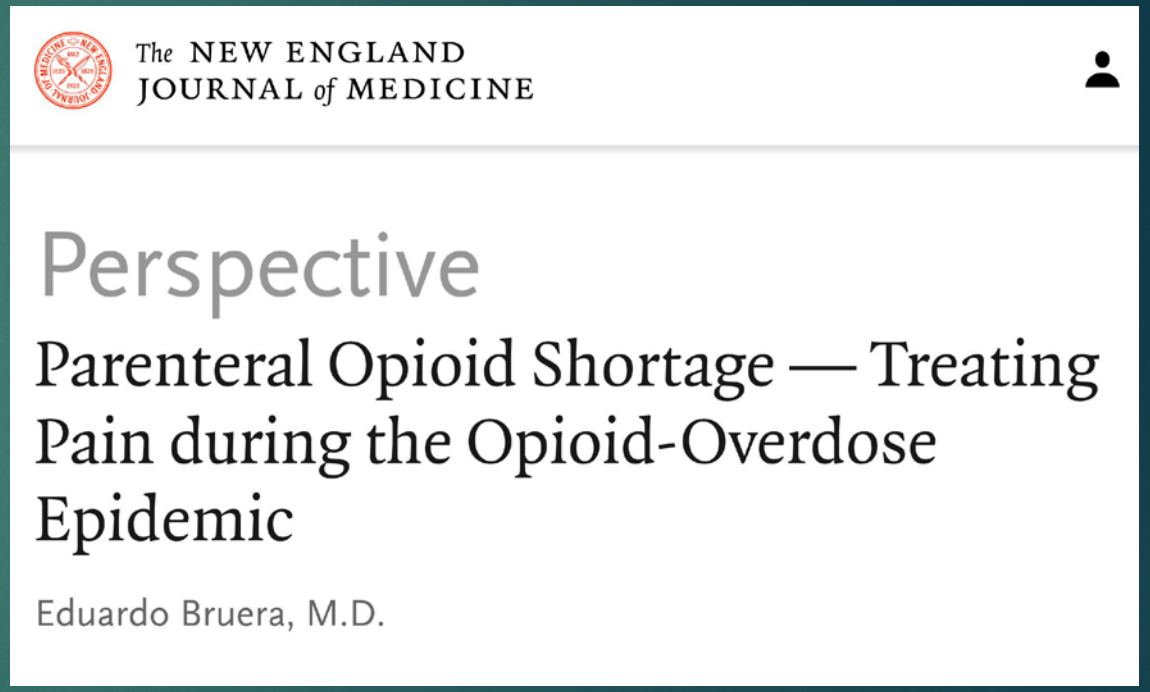


Prescription Opioid Control Policies

WHY IS THIS HAPPENING?

Sidebar: Parenteral Opioid Supply

- Parenteral opioid shortages : affected 86% of facilities in 4/18[1]
- Manufacturing shortfalls (Pfizer) + a tightly regulated supply chain[2,3]
- Consequences include:
  - Swapping products, formulations
  - Medical error
  - Turfing opioid care to a small group of providers[3]
- A political mandate to tightly control supply chain is part of this



1. ASHP report 4/2018; 2. Ross C. STATNews 3/15/2018; 3. Bruera, E. NEJM. 8/16/18.

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

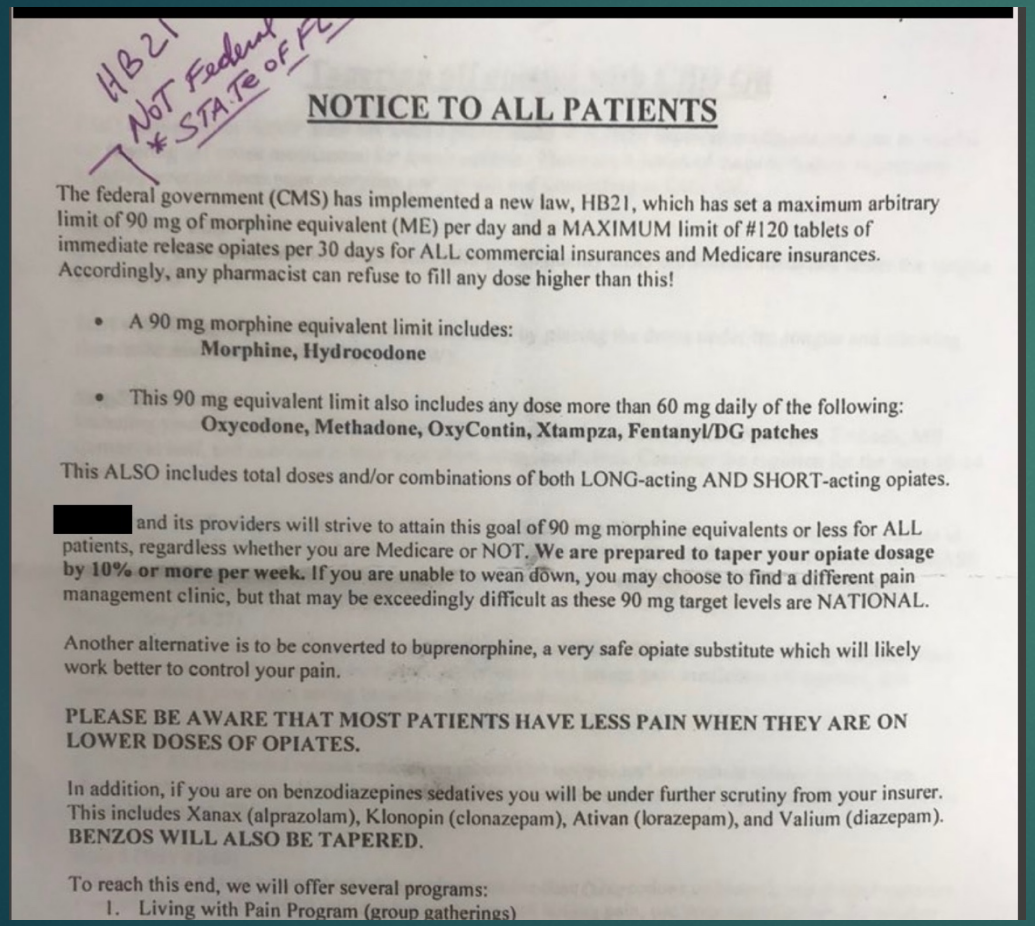
- Try to reduce tendency to start opioids
- Evaluate risks and benefits
- Go for lowest effective dose
- **For patients already on opioids, evaluate harm vs benefit** (#7)
  - **No dose target**
  - **No mandated reductions**

- Evidence quality: Low, for most recommendations

Rx Control Ascendant

- Tightened production (DEA)
- State restrictions (28 states with laws)
- Quality indicators based on pill dose/count used by everyone
- Payers *effectively* impose nonconsensual taper
- Pharmacies invoke liability, corresponding responsibility to reject:
  - the prescription, the prescriber or the patient
- Fear of investigation
- **A single Rx is now subject to multiple high-stakes conflicting mandates**

Example A: medical practice to patients



HB21 Not Federal * STATE OF FL

NOTICE TO ALL PATIENTS

The federal government (CMS) has implemented a new law, HB21, which has set a maximum arbitrary limit of 90 mg of morphine equivalent (ME) per day and a MAXIMUM limit of #120 tablets of immediate release opiates per 30 days for ALL commercial insurances and Medicare insurances. Accordingly, any pharmacist can refuse to fill any dose higher than this!

- A 90 mg morphine equivalent limit includes:
  Morphine, Hydrocodone
- This 90 mg equivalent limit also includes any dose more than 60 mg daily of the following:
  Oxycodone, Methadone, OxyContin, Xtampza, Fentanyl/DG patches

This ALSO includes total doses and/or combinations of both LONG-acting AND SHORT-acting opiates.

[redacted] and its providers will strive to attain this goal of 90 mg morphine equivalents or less for ALL patients, regardless whether you are Medicare or NOT. **We are prepared to taper your opiate dosage by 10% or more per week.** If you are unable to wean down, you may choose to find a different pain management clinic, but that may be exceedingly difficult as these 90 mg target levels are NATIONAL.

Another alternative is to be converted to buprenorphine, a very safe opiate substitute which will likely work better to control your pain.

PLEASE BE AWARE THAT MOST PATIENTS HAVE LESS PAIN WHEN THEY ARE ON LOWER DOSES OF OPIATES.

In addition, if you are on benzodiazepines sedatives you will be under further scrutiny from your insurer. This includes Xanax (alprazolam), Klonopin (clonazepam), Ativan (lorazepam), and Valium (diazepam). **BENZOS WILL ALSO BE TAPERED.**

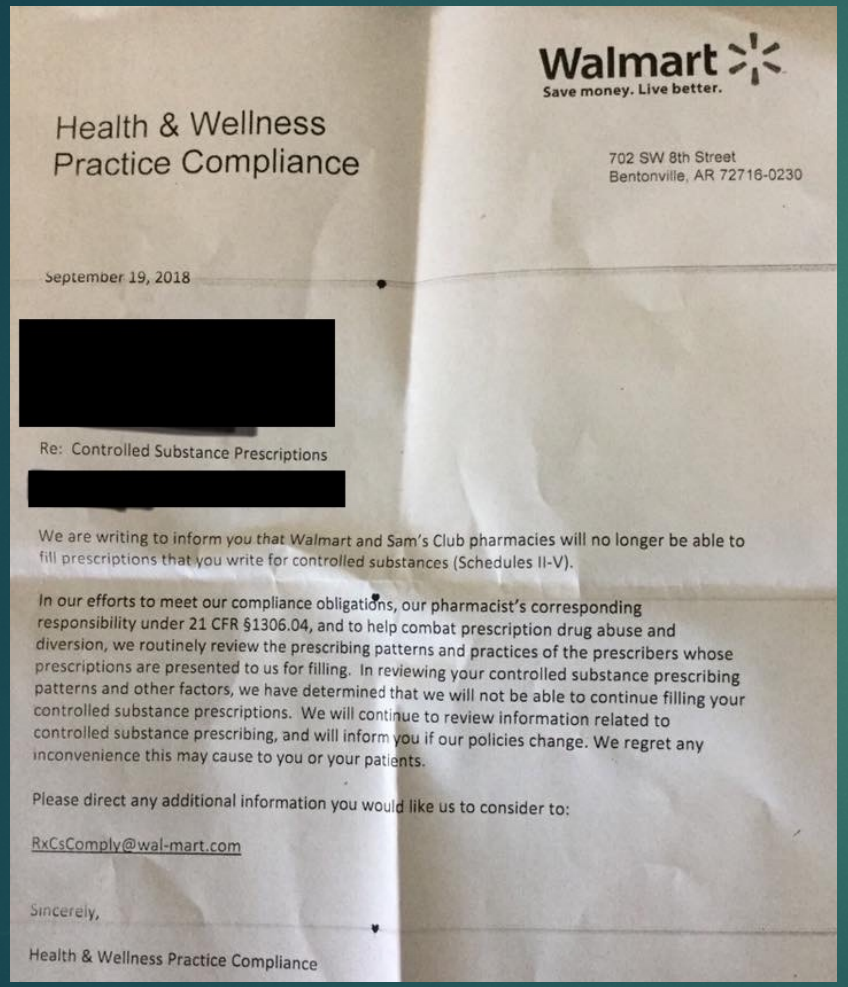
To reach this end, we will offer several programs:

1. Living with Pain Program (group gatherings)

- 2018: “CMS has implemented a new law” “HB21” with max of 90 MME

  (Mis-citations of authority are routine)
- Will taper by >10% a week
- Most patients “have less pain when they are on lower doses”
- Care offers:
  - Group support or psychologist
  - CBD or Buprenorphine

Example B: Walmart to prescriber



Walmart
Save money. Live better.

Health & Wellness
Practice Compliance

702 SW 8th Street
Bentonville, AR 72716-0230

September 19, 2018

[redacted]

Re: Controlled Substance Prescriptions

[redacted]

We are writing to inform you that Walmart and Sam's Club pharmacies will no longer be able to fill prescriptions that you write for controlled substances (Schedules II-V).

In our efforts to meet our compliance obligations, our pharmacist's corresponding responsibility under 21 CFR §1306.04, and to help combat prescription drug abuse and diversion, we routinely review the prescribing patterns and practices of the prescribers whose prescriptions are presented to us for filling. In reviewing your controlled substance prescribing patterns and other factors, we have determined that we will not be able to continue filling your controlled substance prescriptions. We will continue to review information related to controlled substance prescribing, and will inform you if our policies change. We regret any inconvenience this may cause to you or your patients.

Please direct any additional information you would like us to consider to:

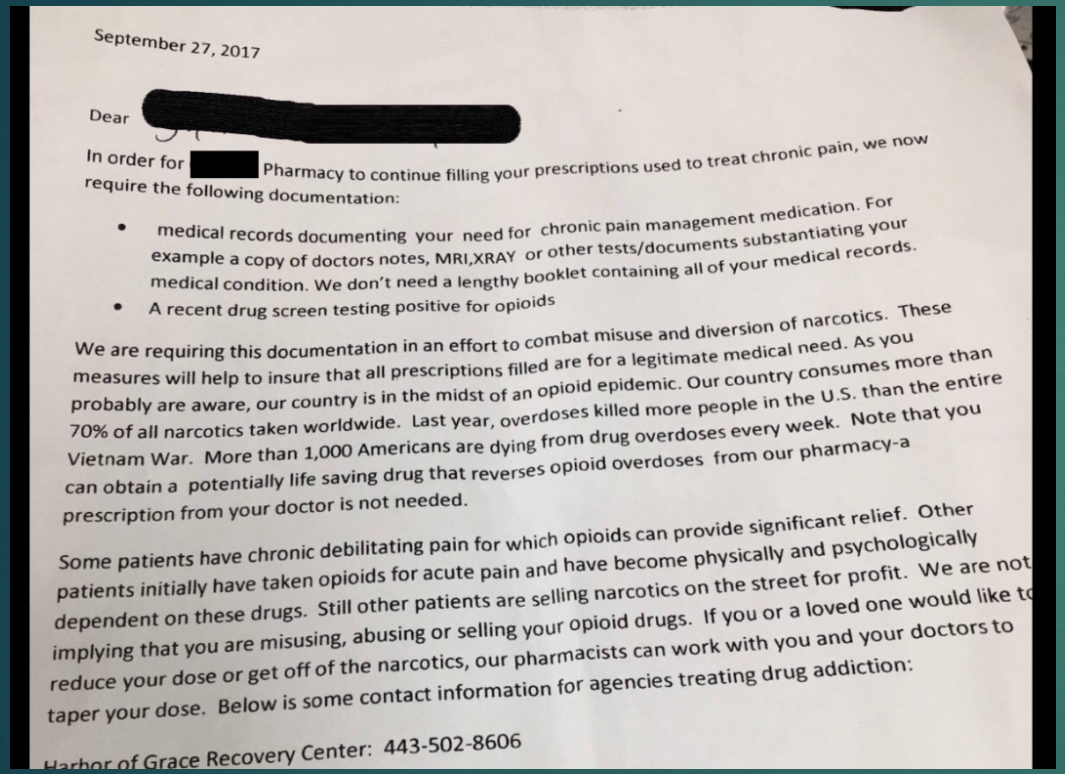
RxCsComply@wal-mart.com

Sincerely,

Health & Wellness Practice Compliance

- Cites "corresponding responsibility" 21CFR §1306.04
- "In reviewing your controlled substance prescribing patterns and other factors…
- …we have determined that **we will not be able to continue filling your controlled substance prescriptions**"

Example C: private pharmacy to patient



September 27, 2017

Dear [redacted]

In order for [redacted] Pharmacy to continue filling your prescriptions used to treat chronic pain, we now require the following documentation:

- medical records documenting your need for chronic pain management medication. For example a copy of doctors notes, MRI,XRAY or other tests/documents substantiating your medical condition. We don't need a lengthy booklet containing all of your medical records.
- A recent drug screen testing positive for opioids

We are requiring this documentation in an effort to combat misuse and diversion of narcotics. These measures will help to insure that all prescriptions filled are for a legitimate medical need. As you probably are aware, our country is in the midst of an opioid epidemic. Our country consumes more than 70% of all narcotics taken worldwide. Last year, overdoses killed more people in the U.S. than the entire Vietnam War. More than 1,000 Americans are dying from drug overdoses every week. Note that you can obtain a potentially life saving drug that reverses opioid overdoses from our pharmacy-a prescription from your doctor is not needed.

Some patients have chronic debilitating pain for which opioids can provide significant relief. Other patients initially have taken opioids for acute pain and have become physically and psychologically dependent on these drugs. Still other patients are selling narcotics on the street for profit. We are not implying that you are misusing, abusing or selling your opioid drugs. If you or a loved one would like to reduce your dose or get off of the narcotics, our pharmacists can work with you and your doctors to taper your dose. Below is some contact information for agencies treating drug addiction:

Harbor of Grace Recovery Center: 443-502-8606

- "We now require the following documentation…"
  - **Medical records, for example: MRI, X-ray, doctors' notes,**
  - **A recent urine drug test positive for the opioid**
- This liability reduction exercise positions the pharmacist as ultimate assessor of pain care quality

Example D: Insurer to Patient

Our decision to deny coverage for this medication(s) is therefore unchanged. Our decision does not reflect any view about the appropriateness of this medication(s). Only you and your provider can make decisions about your care.

that you take in a day is called the morphine equivalent dosage (MED). We reviewed your health plan language, benefits, and plan guidelines. We reviewed information sent on appeal Your health plan covers up to 90 MED per type of opioid medicine per day. For Xtampza E that would be up to 54 mg per day. Your health plan only covers a higher dose if you have

- Coverage policy effectively mandates the dose reduction that the CDC Guideline did not endorse

Example E: Medicaid in Oregon

- Oregon Medicaid
  - 2018: no opioids for back disorders of any kind, no matter the history and no matter the diagnosis
  - 2019 proposal: mandatory taper to 0 mg for all Medicaid patients on opioids long term

OPINION | COMMENTARY

Oregon Overshoots on Opioids

A ban on Medicaid coverage would be cruel to patients.

By Sally Satel and Stefan Kertesz

Aug. 16, 2018 7:21 p.m. ET

WSJ | OPINION

Example F: Prosecutorial warning

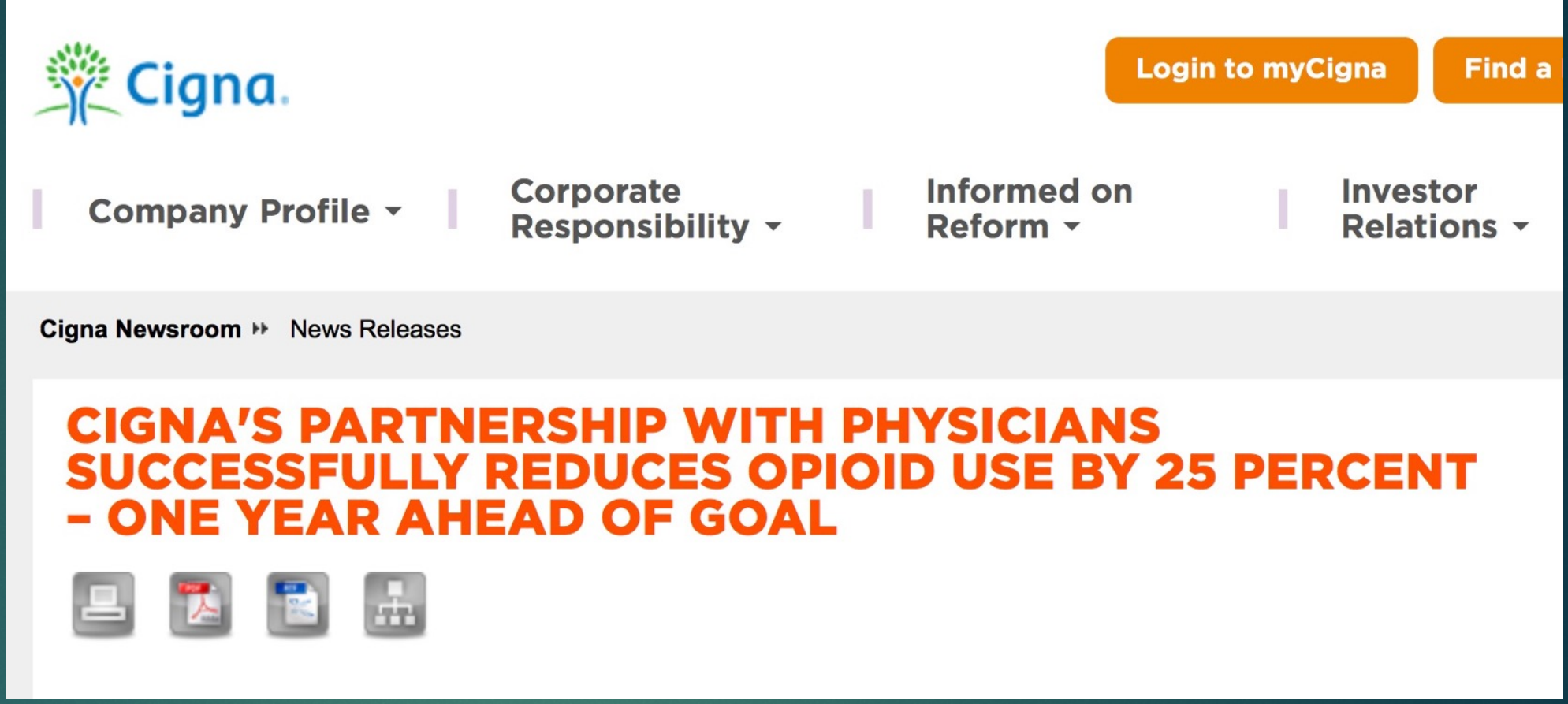
Prosecutors notify 30 doctors about excessive opioid prescriptions

U.S. Attorney BJay Pak at news conference announcing indictment of former medical examiner Joe Burton. (Curtis

- 30 MDS "identified for prescribing opioids in ..greater quantities or doses than their peers"
- "DoJ has not determined if the 30 doctors ...put on notice have broken the law"
- "Part of an initiative by the U.S. Department of Justice to reduce opioid prescriptions by one-third over the next 3 years"
- Will threat of prison reduce prescribing? Probably

Atlanta Journal Constitution, 10/5/2018

The payoff

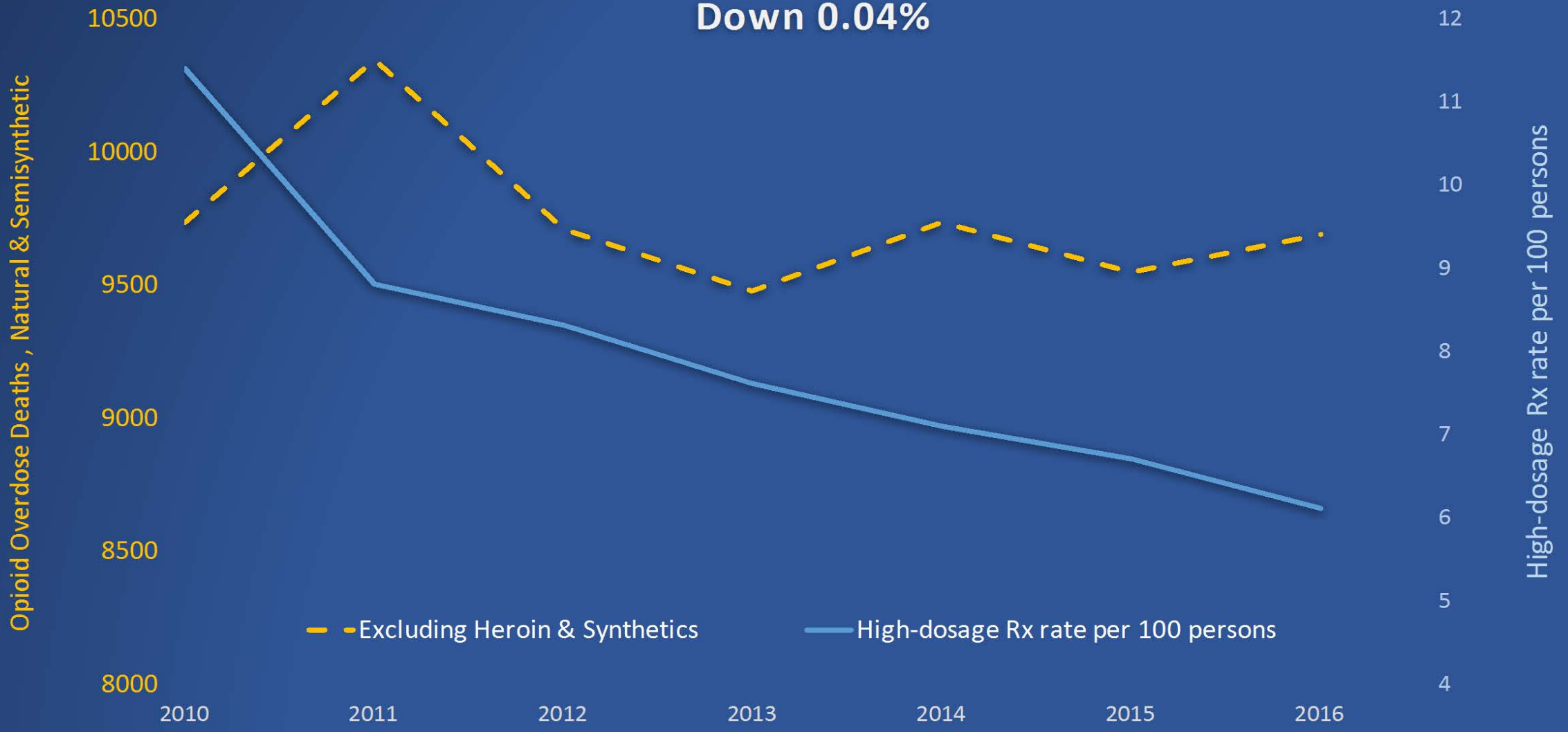


I hope you notice we have not talked about ***PATIENT OUTCOMES,***

Opioid prescriptions falling in US since 2012

1. USA: Prescriptions per 100,000 (Bohnert, 2018)

Since 2010: hi-dose Opioid Rx Down 46%
OD with natural/semisynthetic opioids (excluding heroin/fentanyl): Down 0.04%



Overall Natural & Semisynthetic figures from CDC: https://www.cdc.gov/nchs/data/databriefs/db294_table.pdf#page=4
Excluding Heroin & Synthetics from National Center for Health Statistics NVSS, by Clayton Hale, American Enterprise Institute
High-dose prescribing from CDC Surveillance Report: https://www.cdc.gov/drugoverdose/pdf/pubs/2017-cdc-drug-surveillance-report.pdf

The Policy Conundrum

- Agencies have prioritized opioid counts (dose, # of persons receiving) as ***the*** indicators of quality, safety & good faith
- Most invoke the CDC***, inaccurately***
- Opioid counts are de facto standards for legal risk & professional responsibility

- There is a case to be made that taper, consensual or not, is helpful to some individuals
- Science on ***institutionally mandated*** taper requires discussion
- Policy has moved ahead of science here

- The patient who receives any longstanding Rx, but especially high dose, is <u>a liability</u> to all concerned
- *And what do professionals normally do with liabilities?*

Crucially, the mandating agencies ***do not measure*** *and* ***are not accountable*** *for <u>any</u> patient outcomes, including mortality, tied to their policies*

Where’s the data supporting these mandates?

REVIEWS | 1 AUGUST 2017

Patient Outcomes in Dose Reduction or Discontinuation of Long-Term Opioid Therapy: A Systematic Review FREE

Findings

- Voluntary, well-run programs
- Dose reduction were achieved for *some* patients
- Some really feel better

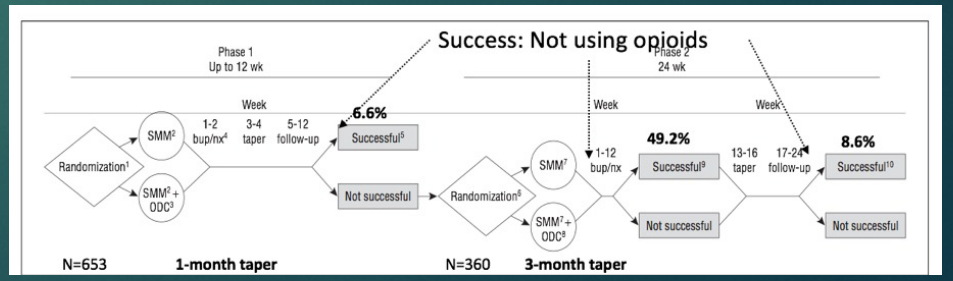
Limitations

- No studies of mandated policies
- Insufficient data on adverse events “overdose, switch to illicit opioids…suicidality”

Frank et al. ***Annals of Internal Medicine***. August 1, 2017

Does tapering work? For Prescription Opioid Use Disorder, not that well

- RCT, funded by NIDA
- Prescription opioid use disorder (n=653)
  - Most started with pain
- Tapered, +/- buprenorphine
- **One year failure rate: <u>91.4%</u>**



Weiss et al Arch Gen Psych 2011

General Hospital Psychiatry 47 (2017) 29–35

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych

Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users

Michael I. Demidenko[a], Steven K. Dobscha[a,b], Benjamin J. Morasco[a,b], Thomas H.A. Meath[a,c], Mark A. Ilgen[d,e], Travis I. Lovejoy[a,b,f,*]

[a] VA Center to Improve Veteran Involvement in Care, VA Portland Health Care System, 3710 SW U.S. Veterans Hospital Road, Mail Code: R & D 66, Portland, OR 97239, United States

[b] Department of Psychiatry, Oregon Health & Science University, 3181 SW U.S. Sam Jackson Park Road, Portland, OR 97239, United States

[c] Center for Health Systems Effectiveness, Oregon Health & Science University, 3181 SW Sam Jackson Park Road, Mail Code: MDYCHSE, Portland, Oregon 97239, United States

[d] VA Center for Clinical Management Research, 2215 Fuller Road, VA Ann Arbor Health Care System, Ann Arbor, MI 48109, United States

[e] Department of Psychiatry, University of Michigan, SPC 5763 2700, 4250 Plymouth Road, Ann Arbor, MI 48109, United States

[f] School of Public Health, Oregon Health & Science University, 3181 SW U.S. Sam Jackson Park Road, Mail Code: CB 669, Portland, OR 97239, United States

Where's the data?

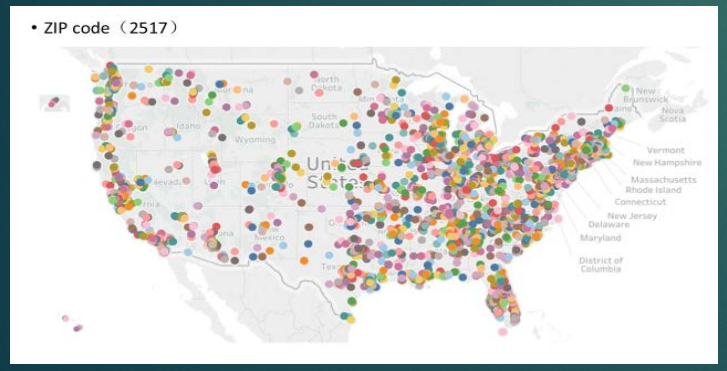
- **No study has shown dose reduction to be protective, safetywise**
- **The mandated policies all seem to violate the CDC Guideline**

- Four preliminary studies (at scientific meetings or briefed to FDA) in 2018, signaled concern that outcomes are not consistently good
  - All retrospective and observational
  - None prove cause and effect

- Example: Among Veterans tapered to 0 mg from high dose (>90 MME), 30% were dead within 6 months of last prescription. Causes of death not yet analyzed (Minegishi, AcademyHealth, 2018)

What pain patients say: Online survey N=3155

- 3155 pain patients via pain-related websites
- Not representative, exploratory
- All 50 states
- by Terri Lewis, PhD



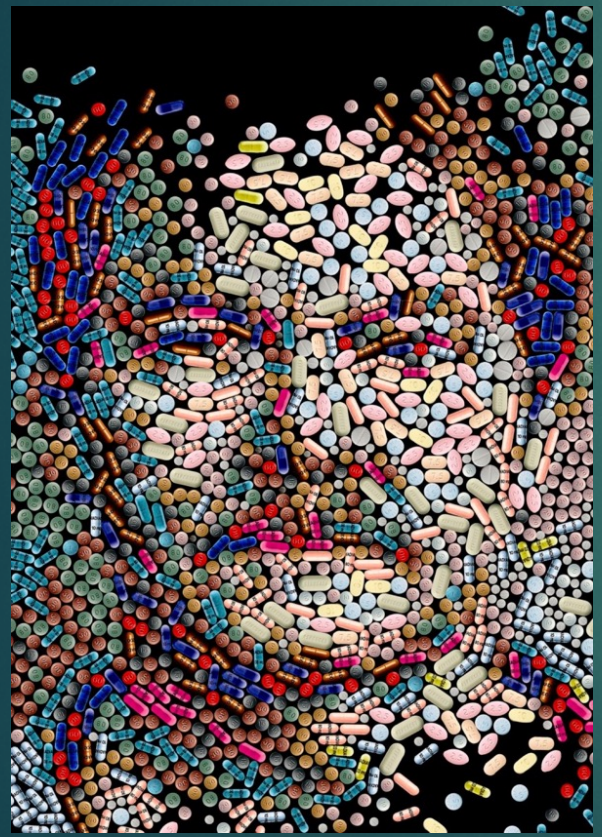
- Demographics: 62% over 50, 78% female, 95% white, 95% are the patient with pain responding

- Discharged from PC due to needing pain care: 20%
- Discharged from pain management care: 25%
- Losing pain care increased hopelessness/suicidal feelings: 53%
- Told I need to accept services I do not want in order to get services I need: 28%

A Better Approach

"STEWARDSHIP" IS FOR PEOPLE, NOT PILLS

Let's focus on the people who more often receive high doses



- Multiple diagnoses
- Psychiatric diagnoses
- Substance Use Disorder, present or remitted
- Higher rates of Polypharmacy:
  - Antidepressant, benzo
- Caveat: some people at high dose have none of these
- In large databases (like VA) these factors in combination account for a greater component of opioid-related morbidity than dose

Morasco, Pain. 2015. Kobus, J Pain. 2012. Oliva, 2017.

Systems-level correctives

- No patient is safe if no doctor can assume their care
- We have to **reverse** metrics, policies, and legal threats that jeopardize protection of legacy patients, nearly all of which violate the CDC Guideline while invoking its authority
- Any entity using metrics based on Rx #'s must **collect patient outcomes**
  - Dead or alive?
  - Continuous care or loss of care?
  - Hospitalized or not?
- They must publicly report outcomes and be held accountable

Enacting health policy with (a) no patient outcomes and (b) no accountability?

That's how we got into this mess in the first place

A time of tragedy, a time for choosing

- We professionals, regulators and payers are implicated in a massive social crisis
- Appropriately we are under pressure
- Our patients are in the same boat, but more vulnerable
- None of us has complete knowledge of what is right, but these are the questions we must ask:

How do we know that what we think is right, is right?

Could what seems right be wrong?

For whom might it not be right?

Thank you for your attention

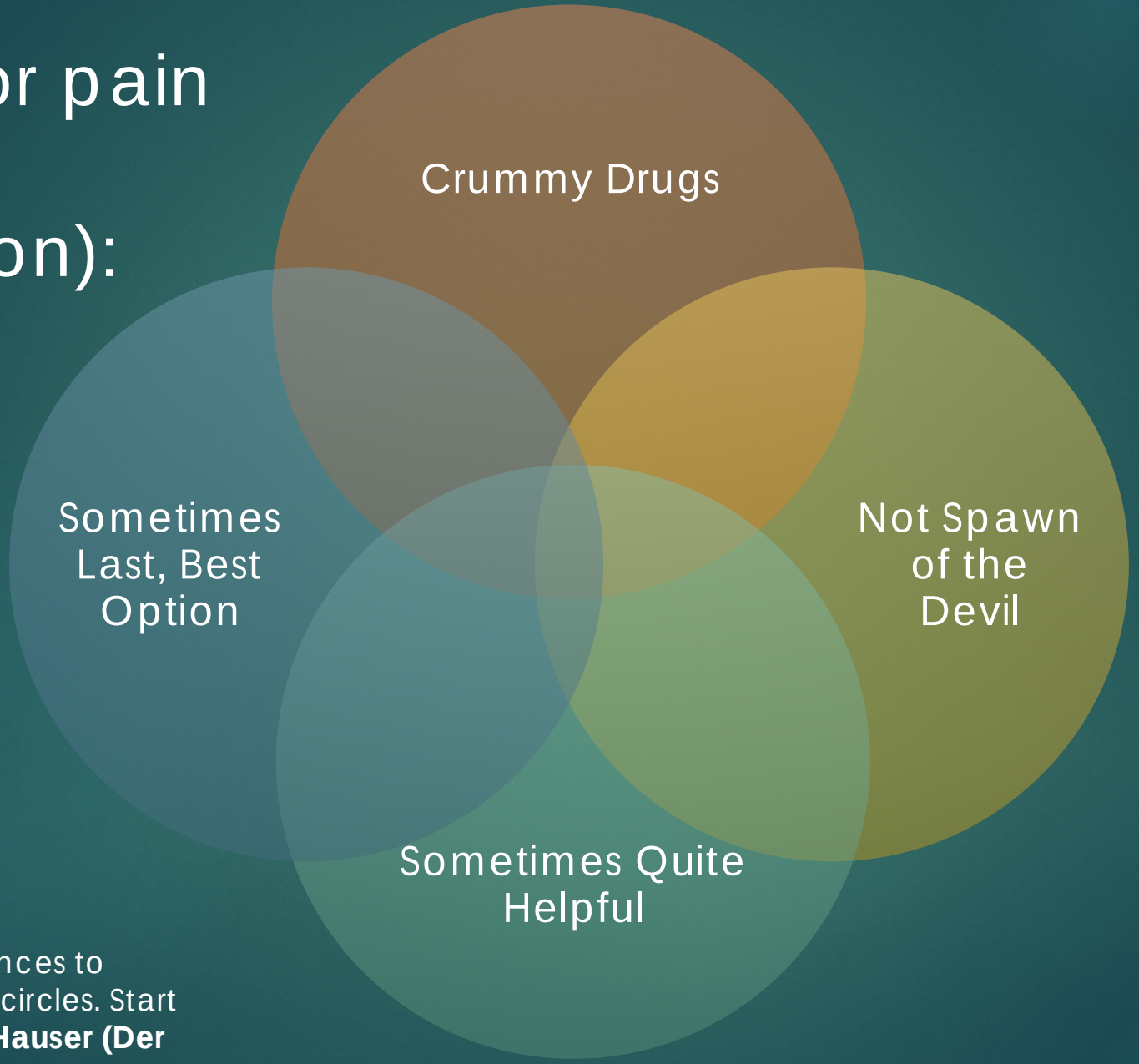
- @StefanKertesz
- skertesz@uabmc.edu
- I reserve the right to conclude that some ideas in this talk need improvement, at some future time

Extra slides follow

Pain care? Opioids?

A BRIEF COMMENT

Opioids for pain are (my opinion):



I am glad to provide references to substantiate each of these circles. Start with **Krebs (JAMA, 2018) & Hauser (Der Schmerz, 2015)**

Opioids and Chronic Pain?

- A 1-year trial (Krebs, 2018) of voluntary patients with chronic musculoskeletal pain : no superior outcome for A vs B
  - A. An aggressive opioid approach (3 tiers of potency/escalation), versus
  - B. A tiered set of non opioid offers with low-potency opioid for 3rd tier

- My take: the (usually) riskier therapy of opioids is not, on average, a better choice, to holding low-potency opioid in reserve
  - But no treatment has consistent benefit for most patients

- In long-term open-label follow-up, 25-33% stay on at stable dose

Krebs, 2018
Hauser, 2015

A correlation of dose and mortality

- Prescription Opioid OD deaths, unintentional, 2004-2008
- Restricted to deaths where Rx contributed, in whole or in part
- Dose **was** a risk factor

Table 3. Cox Proportional Hazards Models of Risk of Death by Prescription O

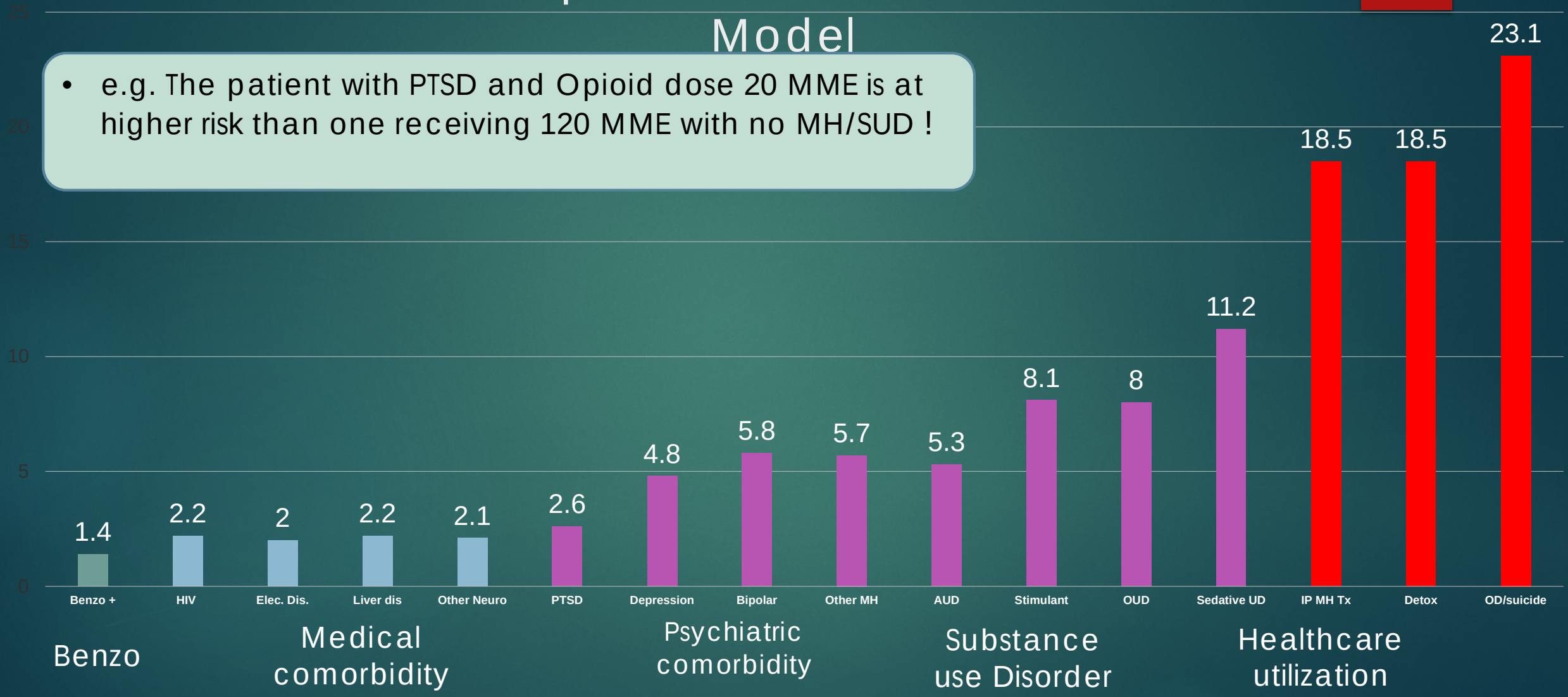
Predictors of OD in Veterans Rx'd opioids long or short term Bohnert, JAMA. 2011:1315-1321	Chronic Pain (n = 111 759)
Opioid fill type	
Regularly scheduled only	1 [Reference]
As needed only	1.10 (0.85-1.43)
Simultaneous as needed and regularly scheduled	1.34 (0.99-1.79)
Maximum prescribed daily opioid dose, mg/d	
1-<20	1 [Reference]
20-<50	1.88 (1.33-2.67)
50-<100	4.63 (3.18-6.74)
≥100	7.18 (4.85-10.65)
Pain-related diagnoses	
Cancer	0.99 (0.72-1.36)
Chronic bodily pains	0.69 (0.35-1.33)

Dose is a risk factor in this study

Bohnert JAMA 2011. Apr 6;305(13):1315-21. doi: 10.1001/jama.2011.370.

Mental health and Non-Opioid Related Factors Have Higher Odds Ratios than Opioid-Related Factors in VHA Predictive Model

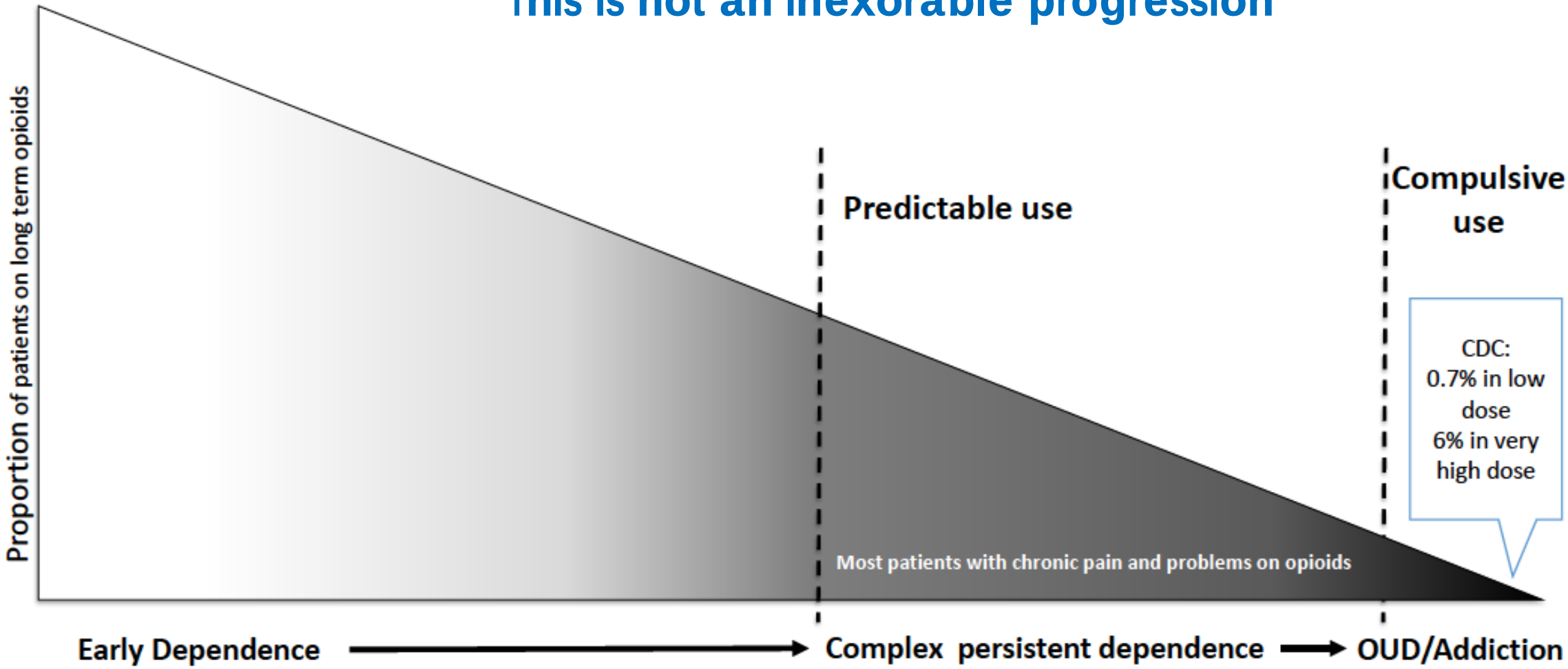
- e.g. The patient with PTSD and Opioid dose 20 MME is at higher risk than one receiving 120 MME with no MH/SUD !



STORM Analysis: Oliva et. al. Psych. Services 2017

Clinical reality: Not Black & White, But many shades of grey!!

This is not an inexorable progression



Manhapra, Arias, Ballantyne, Substance Abuse 2017

Manhapra & Becker; Medical Clinics of North America 2018

"All the News That's Fit to Print"

The New York Times

National Edition

Clouds and sunshine north. Mostly cloudy south. Highs in upper 40s to lower 60s. Cloudy south tonight. A few showers late. Partly cloudy north. Weather map is on Page B7.

VOL. CLXVII ... No. 57,915 © 2018 The New York Times Company WEDNESDAY, MARCH 28, 2018 Printed in Chicago $3.00

Thousands of mourners gathered on Tuesday

Putin Is Facing Fury of Public Over Mall Fire

By ANDREW HIGGINS

MOSCOW — At the end of a month that has seen him unveil new "invincible" missiles, announce a space mission to Mars and secure a sky-high vote in Russia's election, President Vladimir V. Putin faced a grim reality on the ground Tuesday: a nation enraged by the deaths of children trapped in a burning mall in Siberia.

Mr. Putin traveled to the town of Kemerovo to lay flowers next to a memorial for the at least 64 people, many of them children, who died in the fire on Sunday. Some of them died as they banged on locked exit doors and screamed into cellphones for help from their

Trump Backers See Trade Deal As a Validation

AT LEAST 12 STATES READY TO SUE U.S. OVER THE CENSUS

Could Send Patients Into Withdrawal

weigh the harm for that patient," said Dr. Joanna L. Starrels, an opioid researcher and associate professor at Albert Einstein College of Medicine. "That takes a lot of clinical judgment. It's individualized and nuanced. We can't codify it with an arbitrary threshold."

Underlying the debate is a fundamental dilemma: how to curb access to the addictive drugs while ensuring that patients who need them can continue treatment.

The rule means Medicare would deny coverage for more than seven days of prescriptions

Medicare officials thought they had finally figured out how to do their part to fix the troubling problem of opioids being overprescribed to the old and disabled: In 2016, a staggering one in three of 43.6 million beneficiaries of the federal health insurance program had been prescribed the painkillers.

Medicare, they decided, would now refuse to pay for long-term, high-dose prescriptions; a rule to that effect is expected to be approved on April 2. Some medical experts have praised the regulation as a check on addiction.

But the proposal has also drawn a broad and clamorous blowback from many people who would be directly affected by it, including patients with chronic pain, primary care doctors and experts in pain management and addiction

patients with cancer or in hospice. (Morphine equivalent is a standard way of measuring opioid potency.)

According to Demetrios Kouzoukas, the principal deputy administrator for Medicare, it aims to further reduce the risk of participants "becoming addicted to or overdosing on opioids while still maintaining their access to important treatment options."

The Centers for Medicare and Medicaid Services estimates that about 1.6 million patients currently have prescriptions at or above those levels. The rule, if approved as expected at the end of a

riod, would take effect on Jan. 1, 2019.

Dr. Stefan G. Kertesz, who teaches addiction medicine at the

Continued on Page A12

protracted trade standoff at a moment when it needs the South as an ally.

The trade deal came as the Chinese state news media reported that North Korea's leader, Kim Jong-un, made an unannounced visit to Beijing to meet with President Xi Jinping weeks before planned summit meetings with American and South Korean leaders.

The political success of the trade agreement — and its ability to be replicated in other negotia-

Continued on Page A8

Kim Meets With Xi

he North Korean leader made a secret trip to Beijing to engage in surprise talks with the president of China. Page A8.

ministration to undermine that goal, which will result in an undercount of the population and threaten federal funding for our state and cities."

The Constitution requires that every resident of the United States be counted in a decennial census, whether or not they are citizens. The results are used not just to redraw political boundaries from school boards to House seats, but to allocate hundreds of billions of dollars in federal grants and subsidies to where they are needed most. Census data provide the baseline for planning decisions made by corporations and governments alike.

Opponents of the added citizenship question said it was certain to depress response to the census from noncitizens and even legal immigrants. Critics accused the administration of adding the ques-

"The decision to taper opioids should be based on whether the benefits for pain and function outweigh the harm for that patient," said Dr. Joanna L. Starrels, an opioid researcher and associate professor at Albert Einstein College of Medicine. "That takes a lot of clinical judgment. It's individualized and nuanced. We can't codify it with an arbitrary threshold."

Two Epidemiologic Hopes

Overdose

- Overdoses protection by reducing Rx doses (shielding)

Addiction

- Addiction will be prevented by prescribing less (preventing)