THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Knowledge that will change your world

Care for Patients On Long Term Opioids

STEFAN G. KERTESZ, MD, MSC

PROFESSOR, UNIVERSITY OF ALABAMA AT BIRMINGHAM

OPIOID SAFETY, RISK MITIGATION, OPIOID ADVICE TEAM: BIRMINGHAM VA MEDICAL CENTER

Please use this slide in your presentation (slide 2)

Disclosure Information for re for Patients on Long-Term Opioids Stefan G. Kertesz

2. Under ACCME guidelines:
   a) I have no financial affiliations, grants or honoraria but
   b) My wife owns stock in her own portfolio in Merck, Abbot, Johnson & Johnson (<7.5% of her assets)

AND

3. I intend to reference the following off-label or investigational use of drugs or products in my presentation: _buprenorphine/naloxone in pain with opioid dependence (not FDA approved, but cited by US Dept of Health and Human Services, 2019)

Acknowledgments

- These are my views, and I'm not representing the US Government or Department of Veterans Affairs
- I have modified certain slides and concepts from
  - Ajay Manhapra, MD: Yale University School of Medicine
  - Dan Alford, MD: Director, Clinical Addiction Research and Education (CARE), Boston Univ.

Objectives
(as a result of this talk, attendees will be able to)

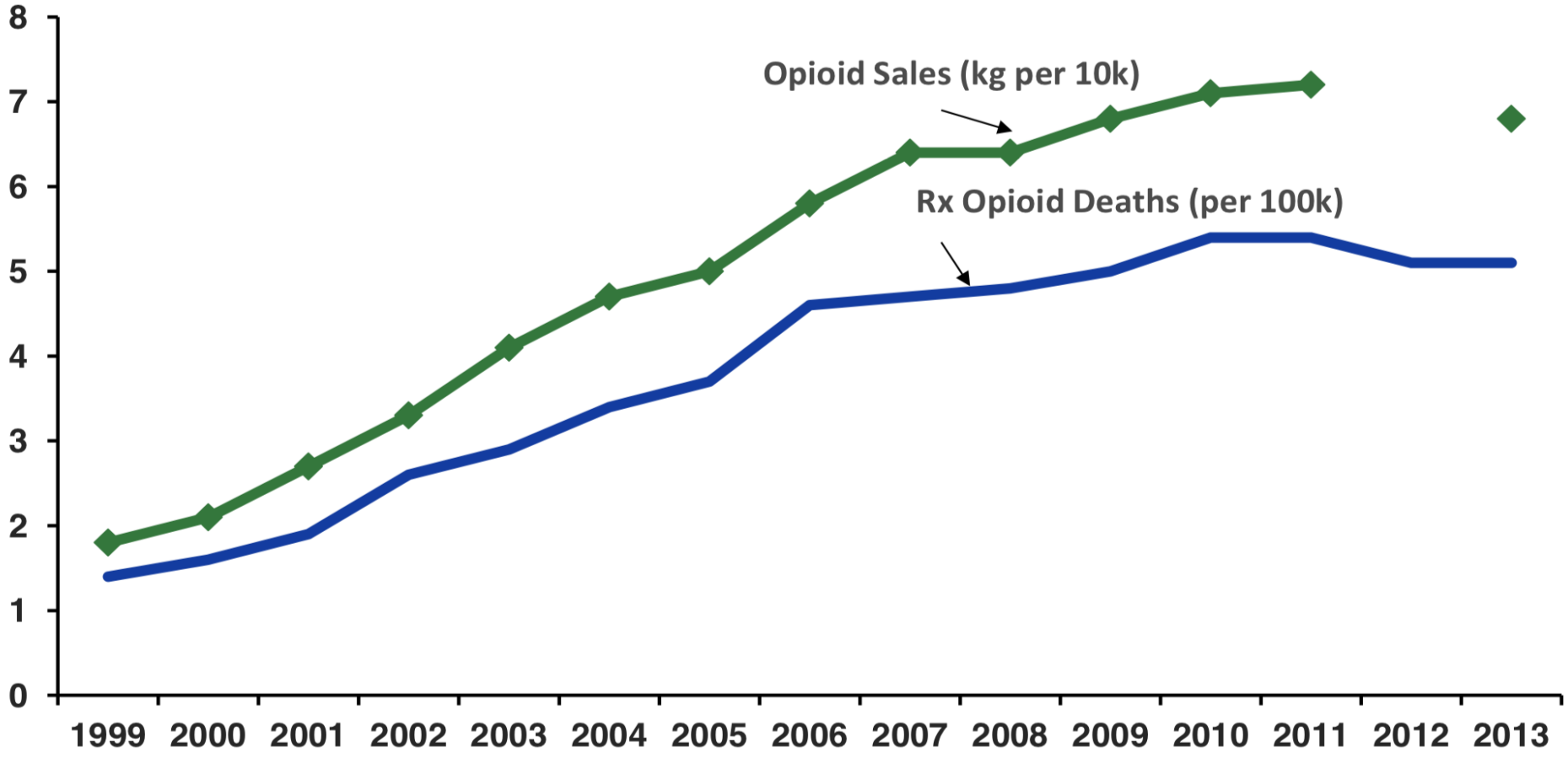
- Summarize the policy **context** relating opioid prescribing in the US
- Describe a psycho-physiologic **model** for chronic pain and its relevance for care planning
- Articulate **evidence** re: opioids in chronic pain, pro & con
- Differentiate forms of **dependence** that can emerge on opioids
- Adhere to reasonable **standards** for prescribing practice
- Detail evidence on favorable use of **taper**, and common policy missteps

The Policy Context

The context is ~70,000 drug overdose deaths in 2017, with 45,000 involving opioids

TRAGEDY CREATES PRESSING QUESTIONS

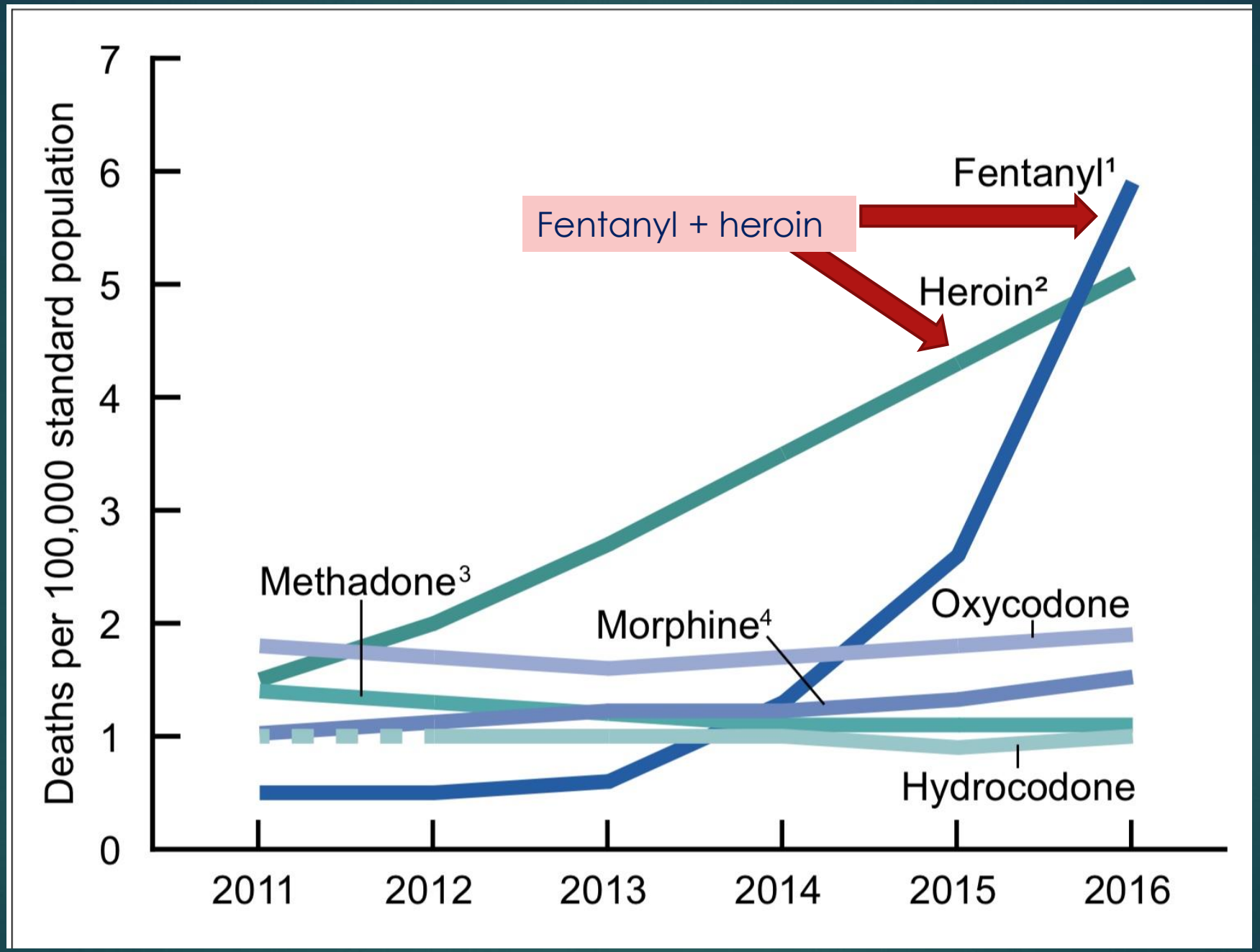
Sharp increases in opioid prescribing coincides with sharp increases in Rx opioid deaths



National Vital Statistics System, DEA's Automation of Reports and Consolidated Orders System.

From CDC (Grant Baldwin, 2015)

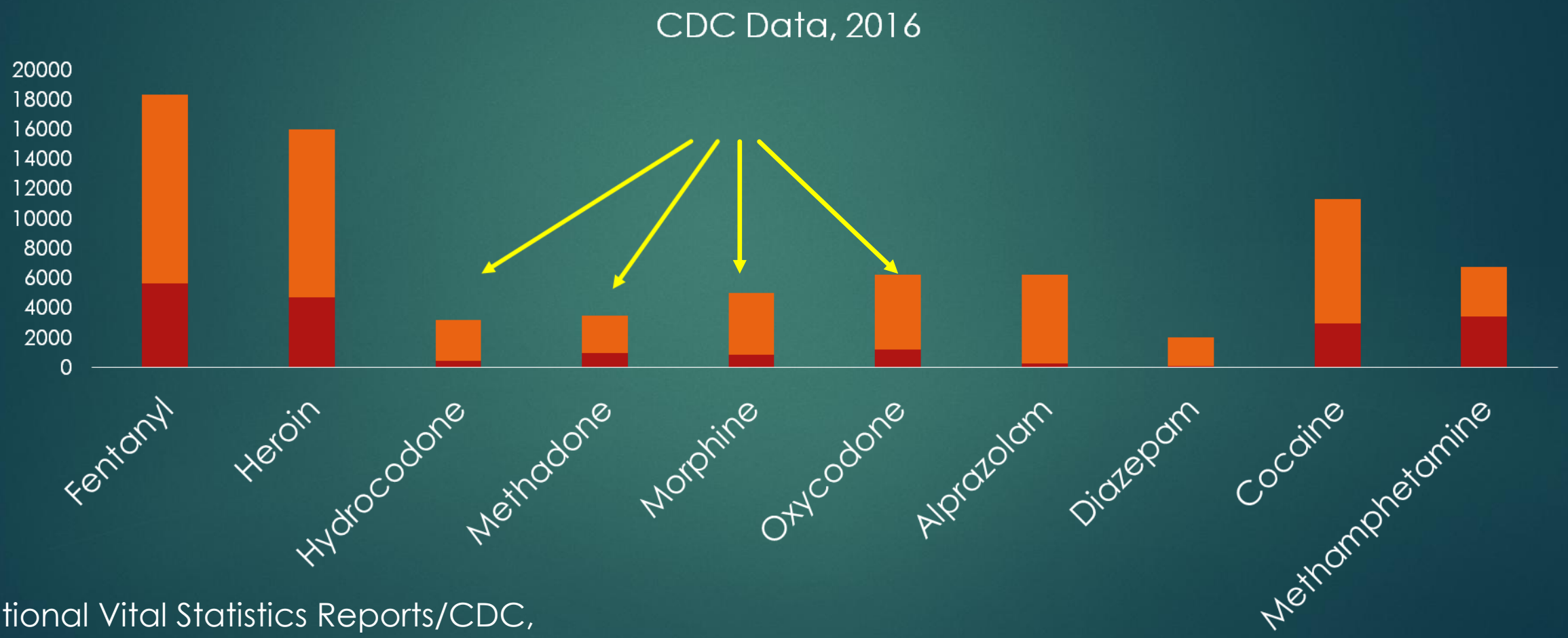
sz, MD, MSc



Hedegaard, 12/12/18

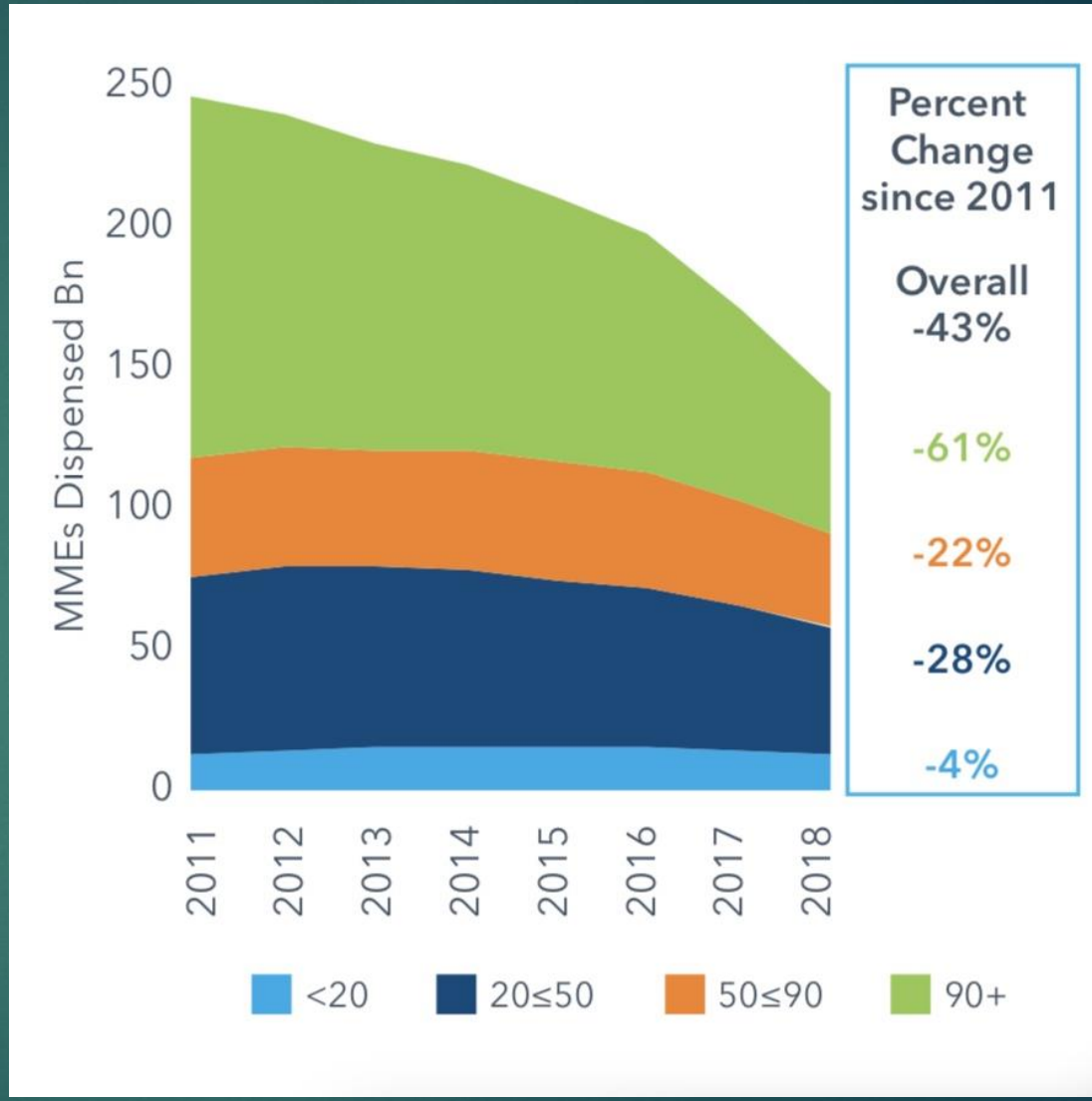
Most "drug overdose" is a "polysubstance poisoning"

"prescription opioid overdose" is a problematic term



National Vital Statistics Reports/CDC, 12/12/18

Prescriptions are in decline



The Washington Post
Democracy Dies in Darkness

Health

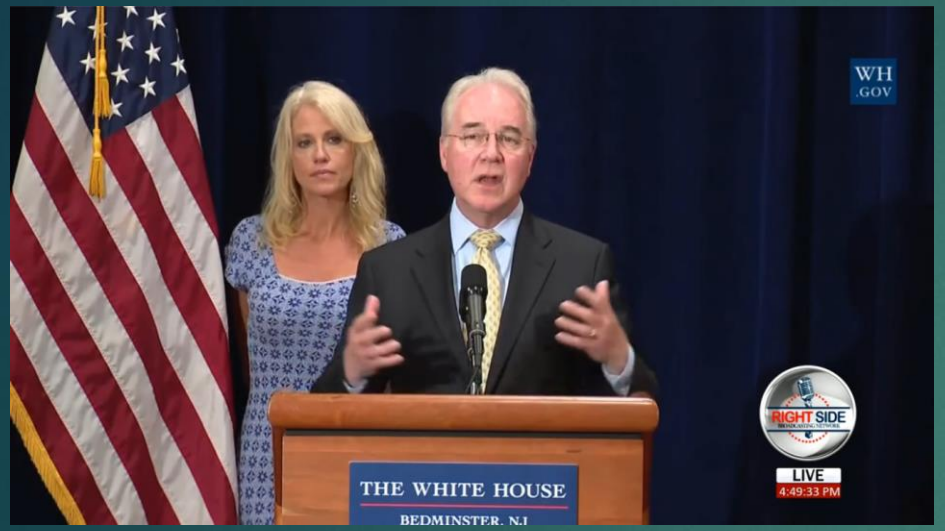
Opioid crackdown forces pain patients to taper off drugs they say they need

Hank Skinner and his wife, Carol, are no strangers to pain, having collectively experienced multiple illnesses and surgeries. Hank relies on a fentanyl patch but is now being forced to lower his dosage. (Salwan Georges/The Washington Post)

By **Joel Achenbach** and **Lenny Bernstein**

September 10, 2019 at 9:54 a.m. CDT

Our crisis can be framed 2 ways



"What is the NIH doing?
..hopefully, pain medication that is not addictive or narcotic"

Tom Price, Secretary HHS
8/8/2017

"We recognize that this is a polydrug problem in our nation, that we are a nation that consumes legal and illegal drugs at an alarming rate"
"…this involves public health, the medical community, healthcare delivery system, law enforcement, devastated families and those in treatment and recovery"

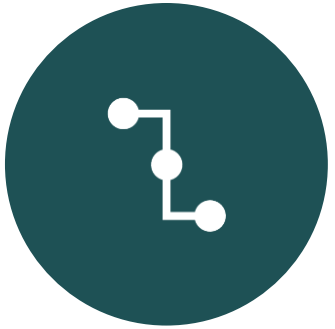
KellyAnne Conway, 8/8/2017

How you conceptualize "the problem" tends to guide the solution you favor

- Overdose deaths and addiction (this is the top-line question)
  - How much weight do you assign to pain care and prescriptions?
- Pain
  - What is it, and how do we care for it
  - This gets overshadowed

Policy context summarized

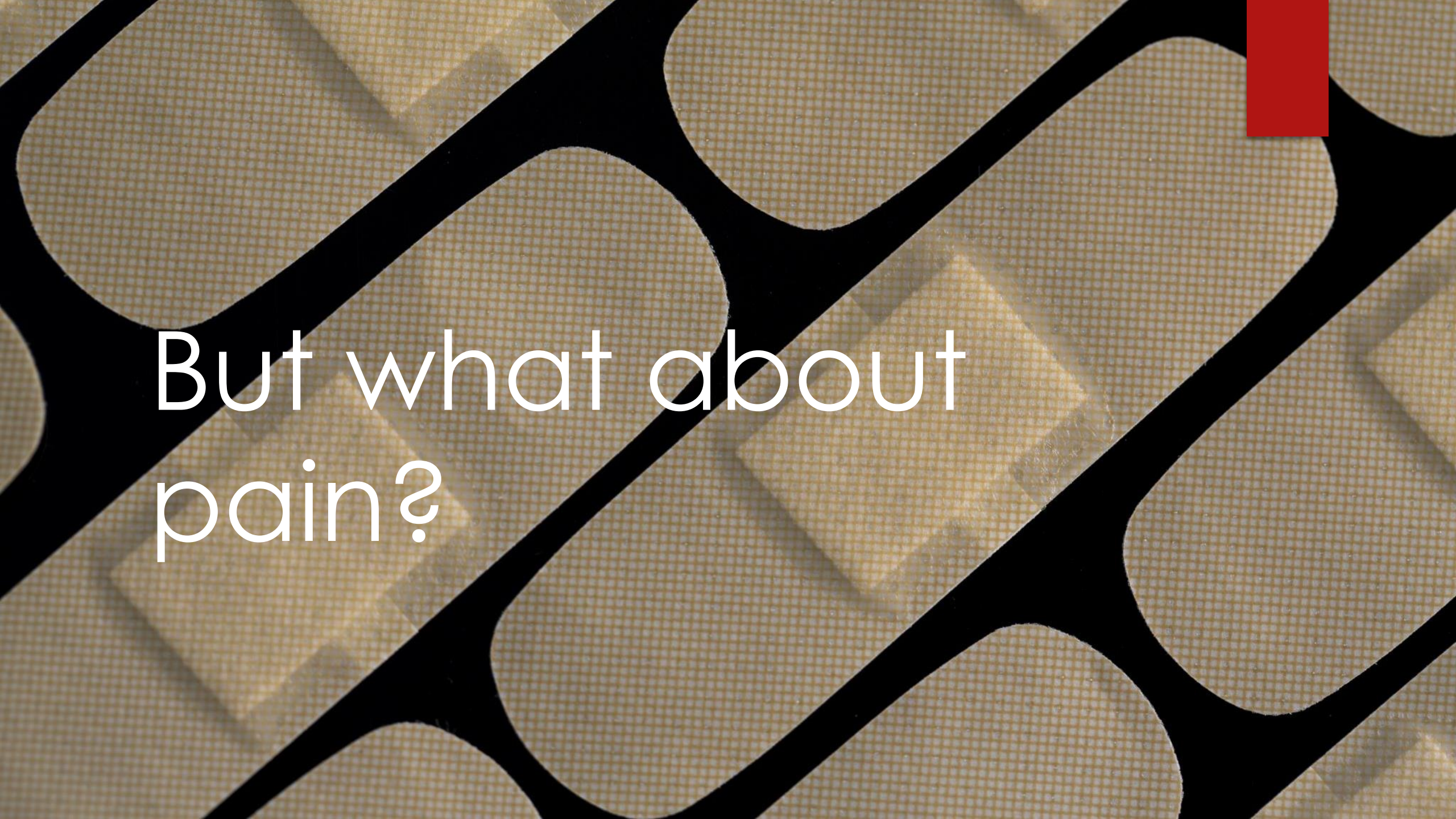
There is a relationship between opioid prescribing and our crisis



There are other causal factors

Prescriptions are the attractive point of leverage for policy & litigation

Benefits and downsides of our course correction remain to be determined


But what about pain?

What about chronic pain?

- 23.4 million: severe and debilitating chronic pain (1)
- ~10 million: on chronic opioids (2)
- Chronic pain can be a ***terrible*** experience
- Any single treatment for severe chronic pain
  - Predominantly short-term trial data
  - Works well for a minority, usually
  - Offers modest benefit, on average

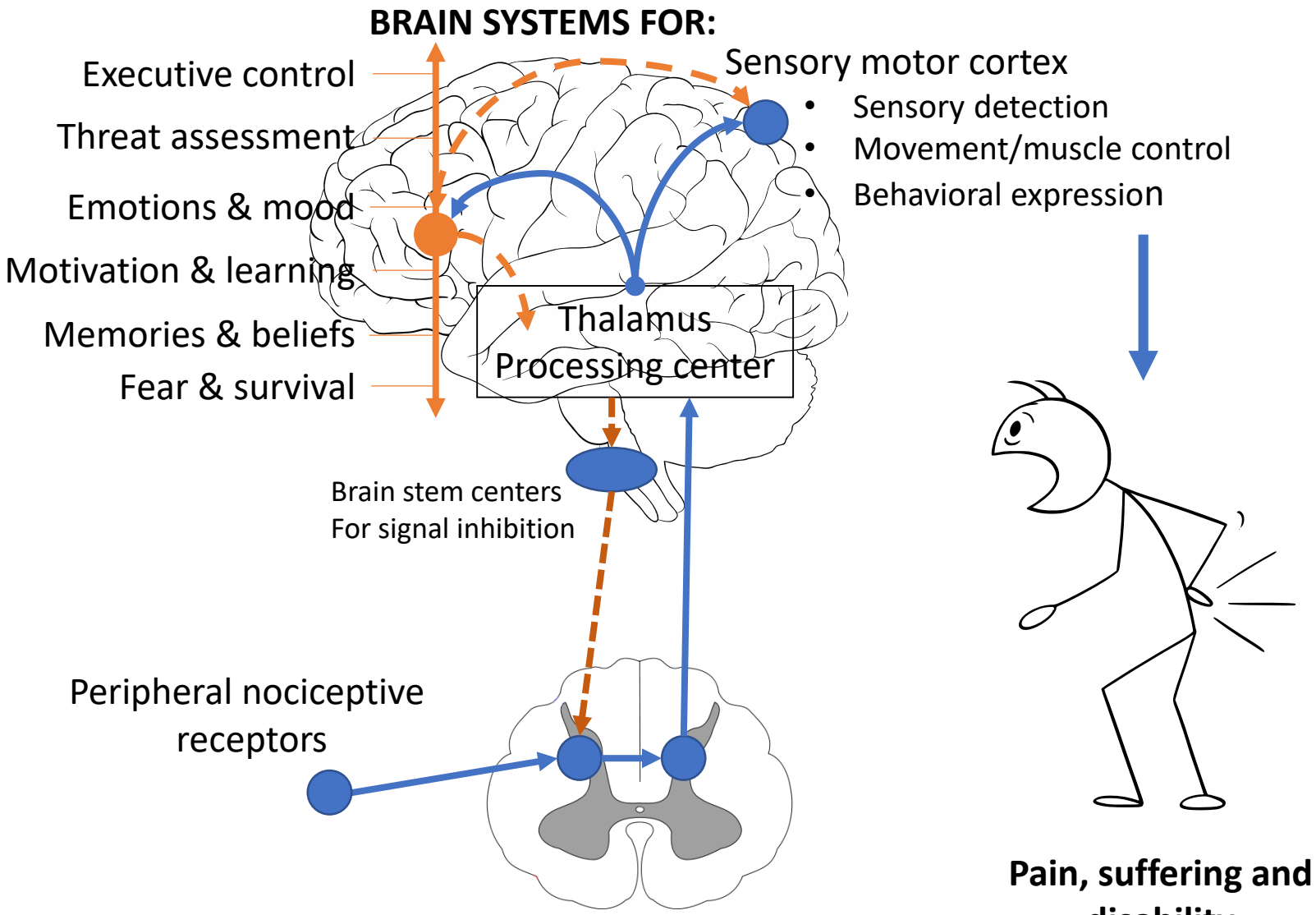
1. Nahin RL. J Pain. 2015 (NHIS data). 2. Mojtabai, 2018 (NHIS data).

The Model for Pain

Ineffective models impede clear thinking

Let's discuss acute and chronic pain

Summary of pain processing: Acute Pain



Summary of pain processing: Acute Pain

Central pain generators:

Factors that affect the brain pathways

Grief, infections, panic. Etc.

Social stressors

Psychological factors

BRAIN SYSTEMS FOR:

Executive control

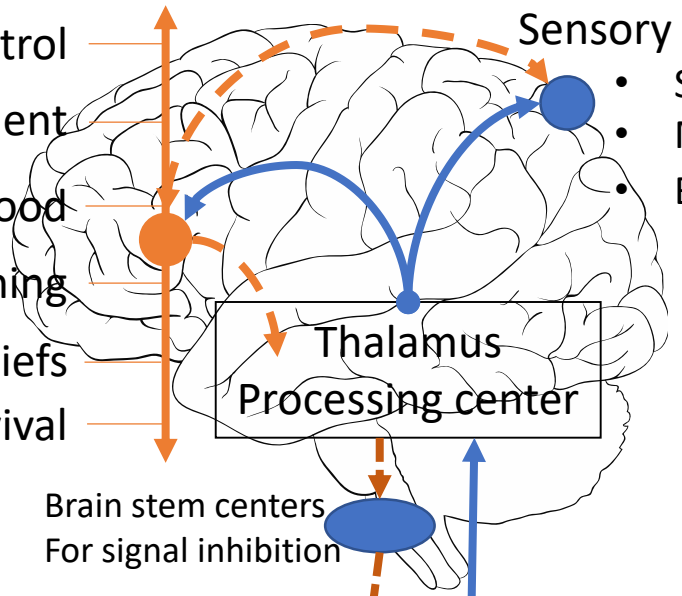
Threat assessment

Emotions & mood

Motivation & learning

Memories & beliefs

Fear & survival

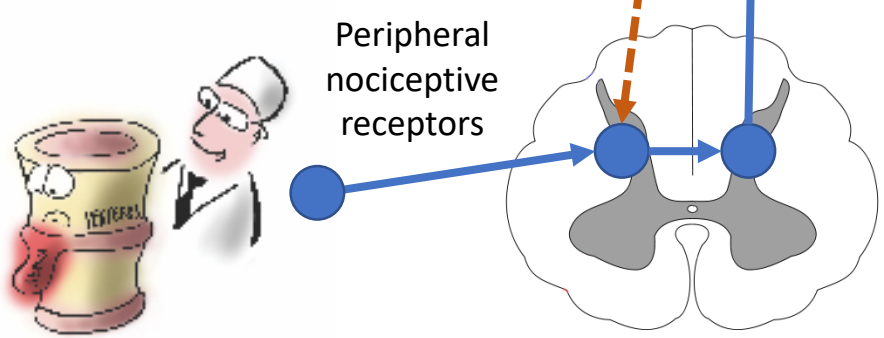


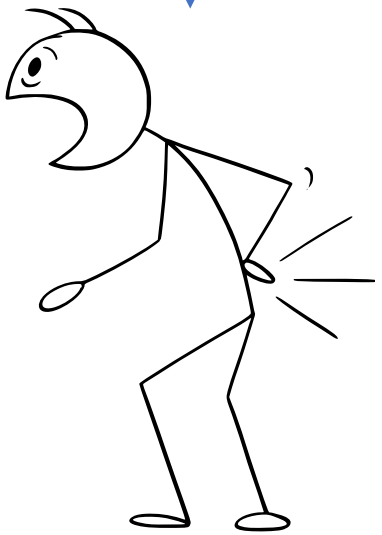
- Sensory detection
- Movement/muscle control
- Behavioral expression

Peripheral Pain generators:

Factors that affect pain site

Acute disease, Injury, Degeneration





Pain, suffering and disability

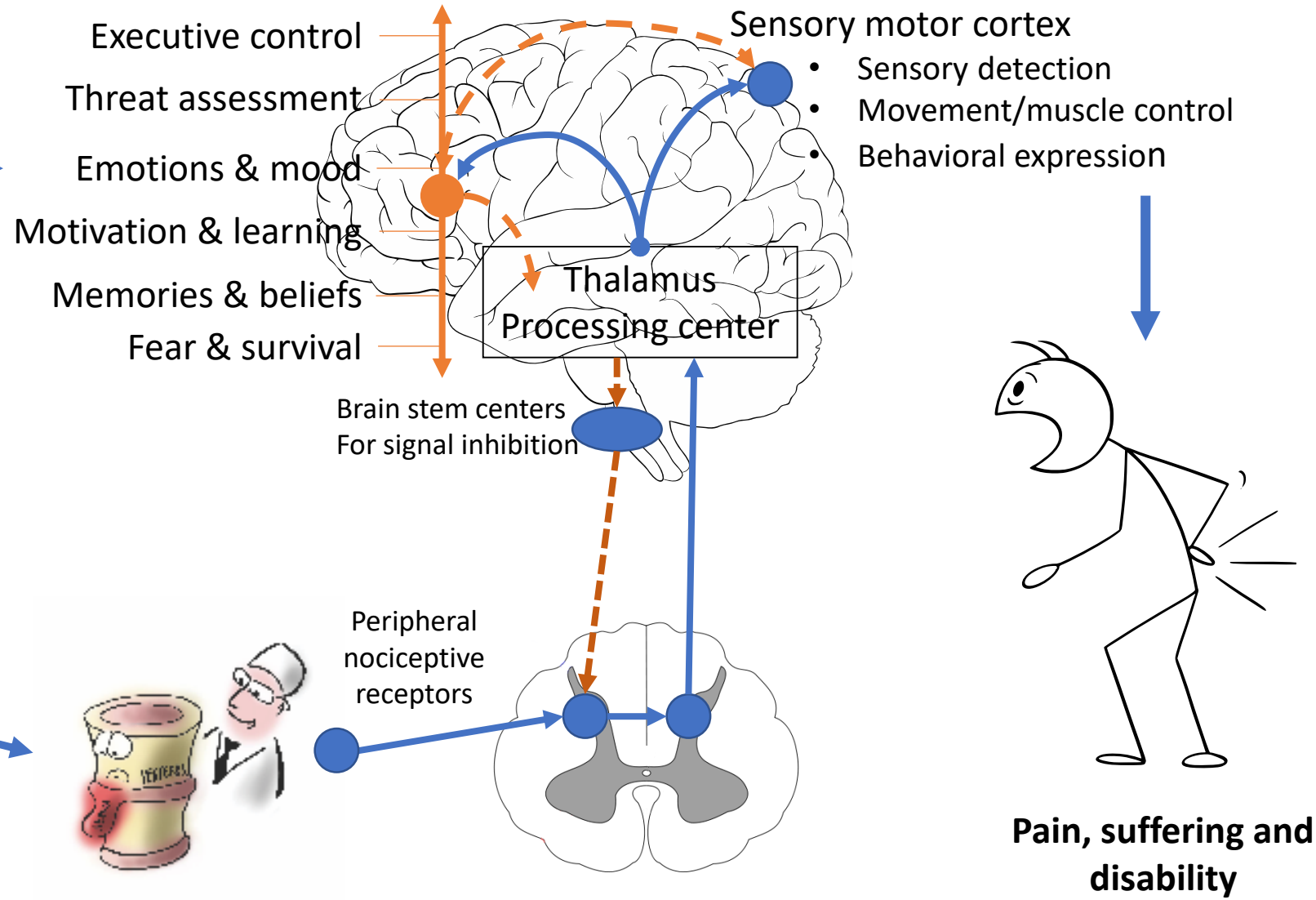
Ajay Manhapra MD

Summary of pain processing: Chronic pain

Central pain generators: Factors that affect the brain pathways

1. **Social stressors**
2. **Psychological factors**
3. **Distressing Illnesses**
   - **Psychiatric**
   - **Medical**
   - **Substance use**
   - **Medication dependence**
   - **Multiple medications**

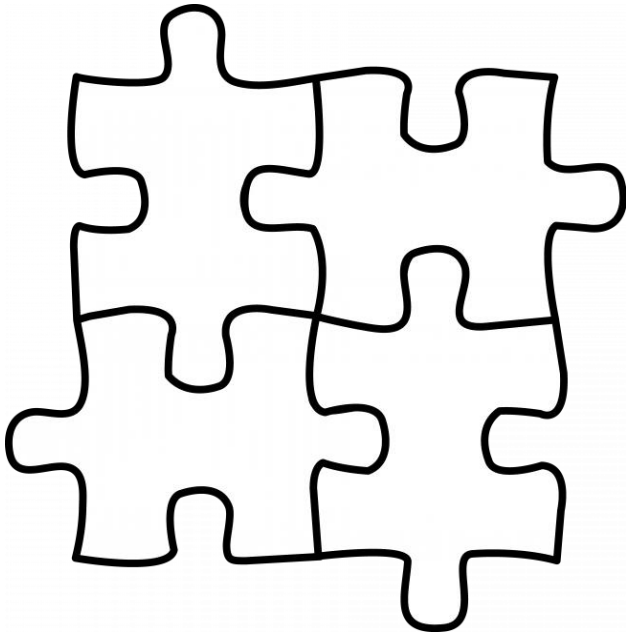
Peripheral Pain generators:
Factors that affect pain site
Chronic Disease, Injury, Degeneration



Ajay Manhapra MD

Implications for assessment and care

offer a narrative "how did we get here"



Look back in time: what past care and expectations got us here?

Assess:

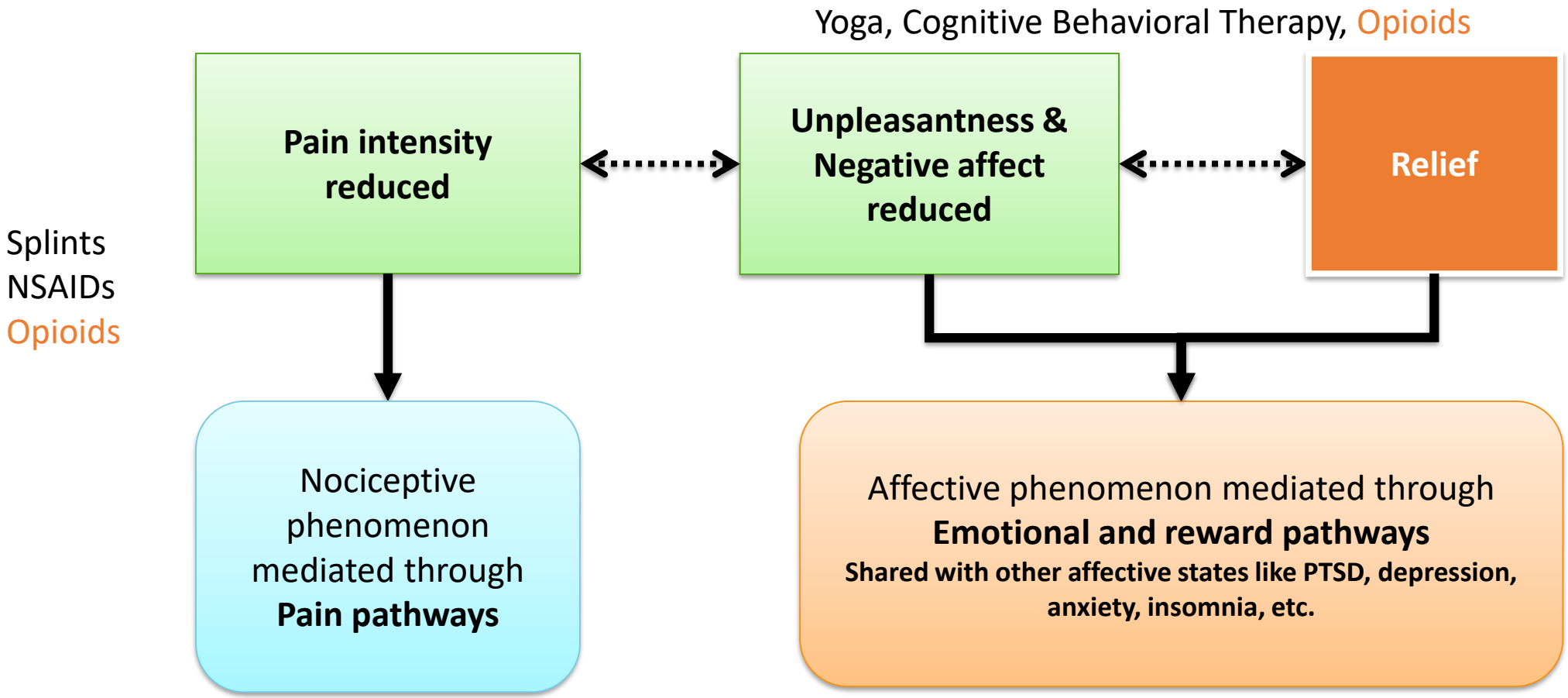
- Social stressors
- Psychological factors
- Distressing Illnesses, meds
- Peripheral pain generators

- Harm or benefit of current treatments

Plan:

- Emphasize activity goals
- Where "drivers" can be addressed, address them
- Address distress that impedes recovery-oriented activity

Pain relief: not just **anti-nociception**

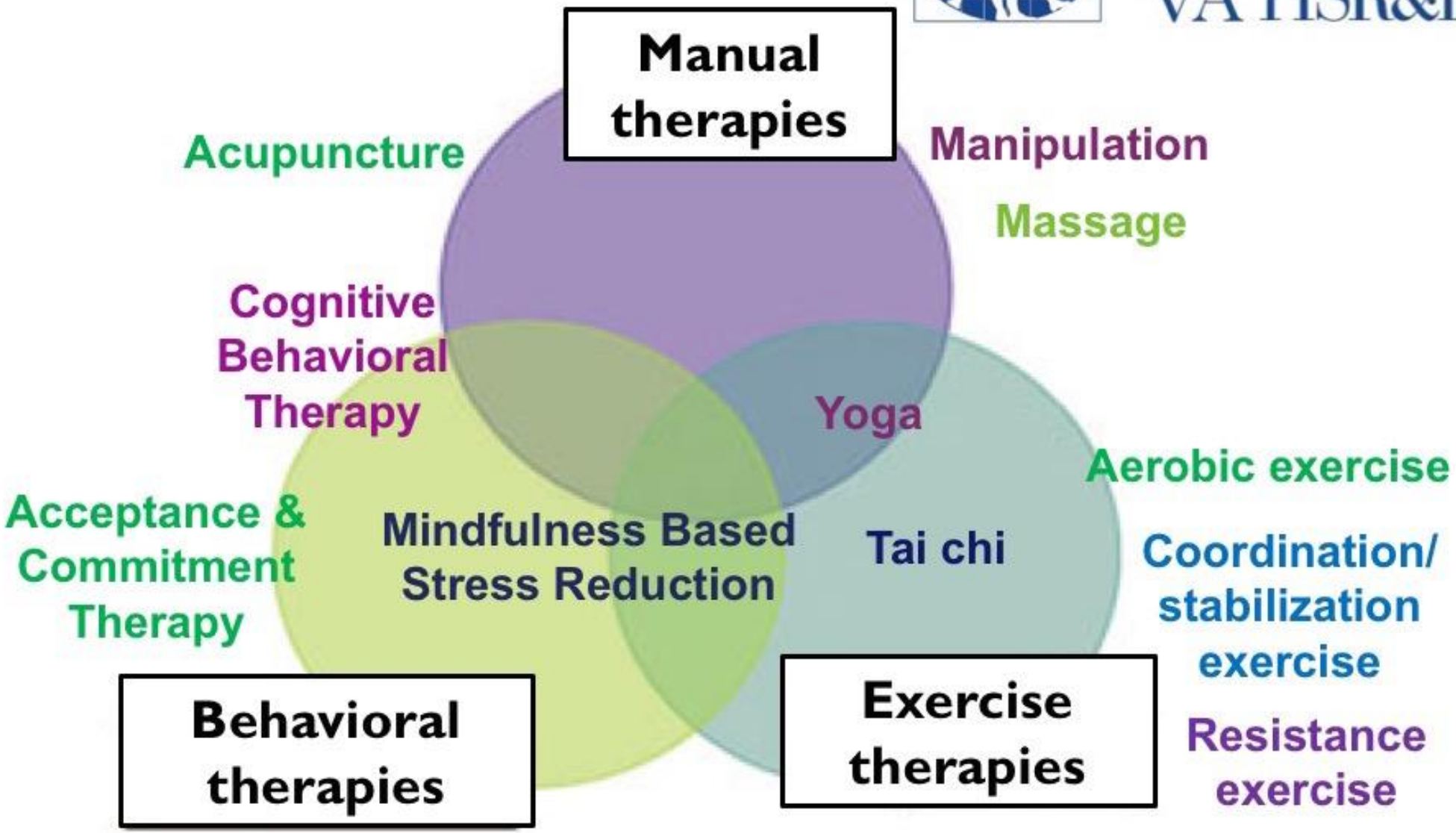


Manhapra, Arias, Ballantyne, Substance Abuse 2017

The Evidence

Therapies with sufficient evidence

STATE OF THE ART CONFERENCE
Non-pharmacological Approaches to Chronic Musculoskeletal Pain Management
VA HSR&D



So opioids for chronic pain?

EVIDENCE DISCUSSION, THEN PRACTICALITIES

"The pain medication conundrum"

Opinion The New York Times

- Undertreating pain, we are admonished…it violates the basic ethical principles of medicine. On the other hand, we are lambasted for overprescribing pain medications… creating an epidemic of overdose deaths.
- For patients with chronic pain, especially those with syndromes that don't fit into neat clinical boxes, being judged by doctors to see if they "merit" medication is humiliating and dispiriting. This type of judgment, with its moral overtones and suspicions, is at odds with the doctor-patient relationship we work to develop.

"As Mr. W. and I sat there sizing each other up, I could feel our reserves of trust beginning to ebb. I was debating whether his pain was real or if he was trying to snooker me. He was most likely wondering whether I would believe him…"

Danielle Ofri, MD, Associate Professor at NYU and a physician at Bellevue Hospital, *August 2015*

Slide c/o Dan Alford, MD (Boston Univ.)

Opioid Efficacy for Chronic Pain

Meta-analyses (3-6 m f/u)

- **Opioids vs placebo**
  (high quality studies)
  Opioids with statistically significant, but small, improvements in pain[1,2] and physical functioning.[2]

- **Opioids vs nonopioids**
  (low-mod quality studies)
  Similar benefits[2]

RCT[3] found opioids **not superior** to nonopioids for improving musculoskeletal pain-related function over 12 months

Study limitations: [4]

- *Excluded patients already on long-term opioids*
- *89% of eligible patients declined to be enrolled*

Two longer term follow-up studies found **44.3%** on chronic opioids for chronic pain had **at least 50% pain relief** [5]

1. Meske DS, et al. *J Pain Res.* 2018
2. Busse JW, et al. *JAMA*. 2018
3. Krebs EE, et al. *JAMA*. 2018
4. Webster L. *Pain Med.* 2019
5. Noble M, et al. *Cochrane Syst Rev.* 2010

Slide c/o Dan Alford, MD (Boston Univ.)

Aren't opioids no better than Tylenol?

JAMA | Original Investigation

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain

The SPACE Randomized Clinical Trial

Erin E. Krebs, MD, MPH; Amy Gravely, MA; Sean Nugent, BA; Agnes C. Jensen, MPH; Beth DeRonne, PharmD; Elizabeth S. Goldsmith, MD, MS; Kurt Kroenke, MD; Matthew J. Bair; Siamak Noorbaloochi, PhD

- For adults with hip, knee or low back pain (n=248)
- Who volunteered to be in a trial
- 4485 identified, 2377 not eligible and 1843 declined
- This is a one-year trial

Interventions

- All medications in both arms on VA formulary
- Each arm included 3 medication steps

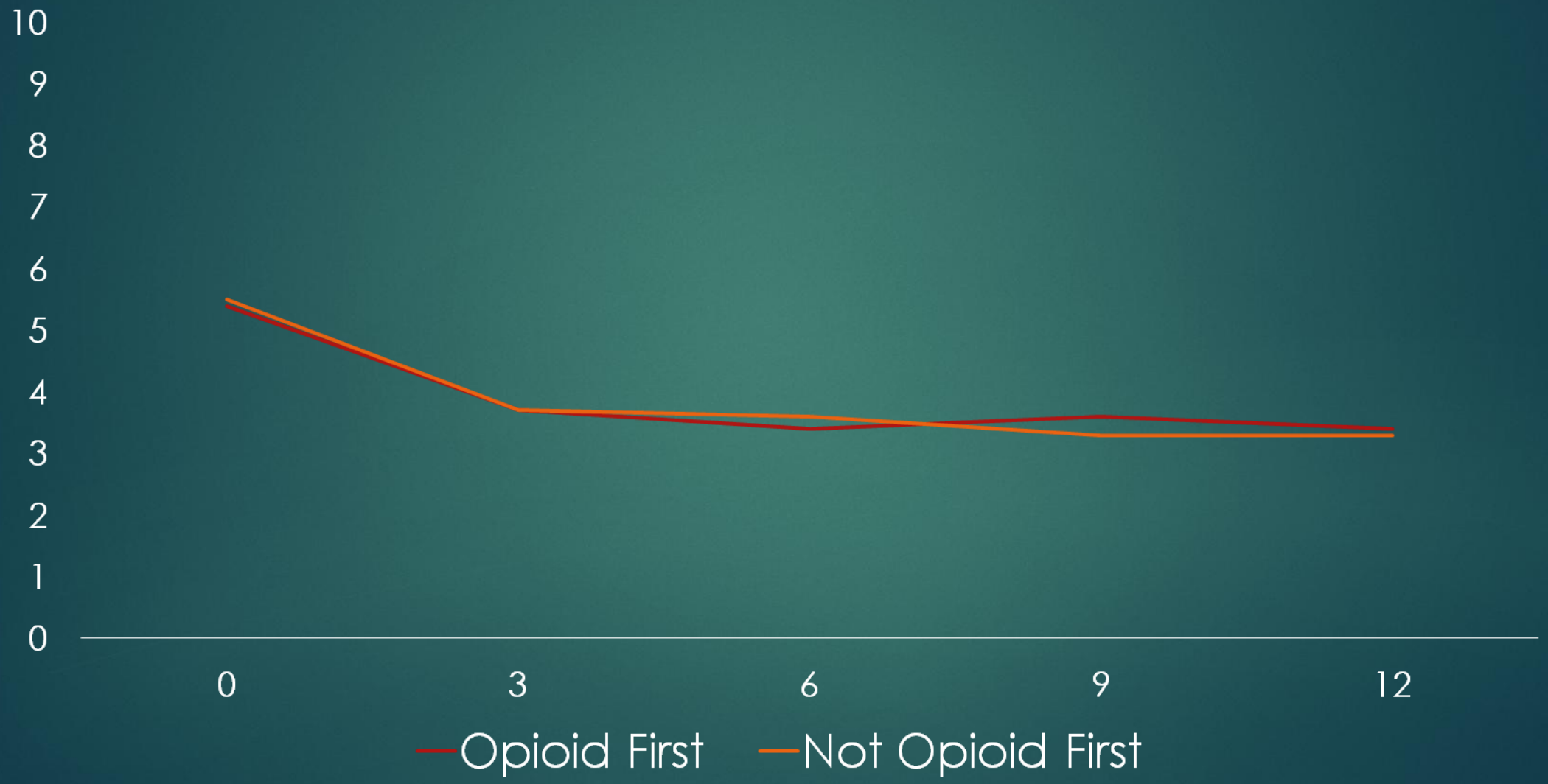
Not opioid first

Table: Example medications within arms

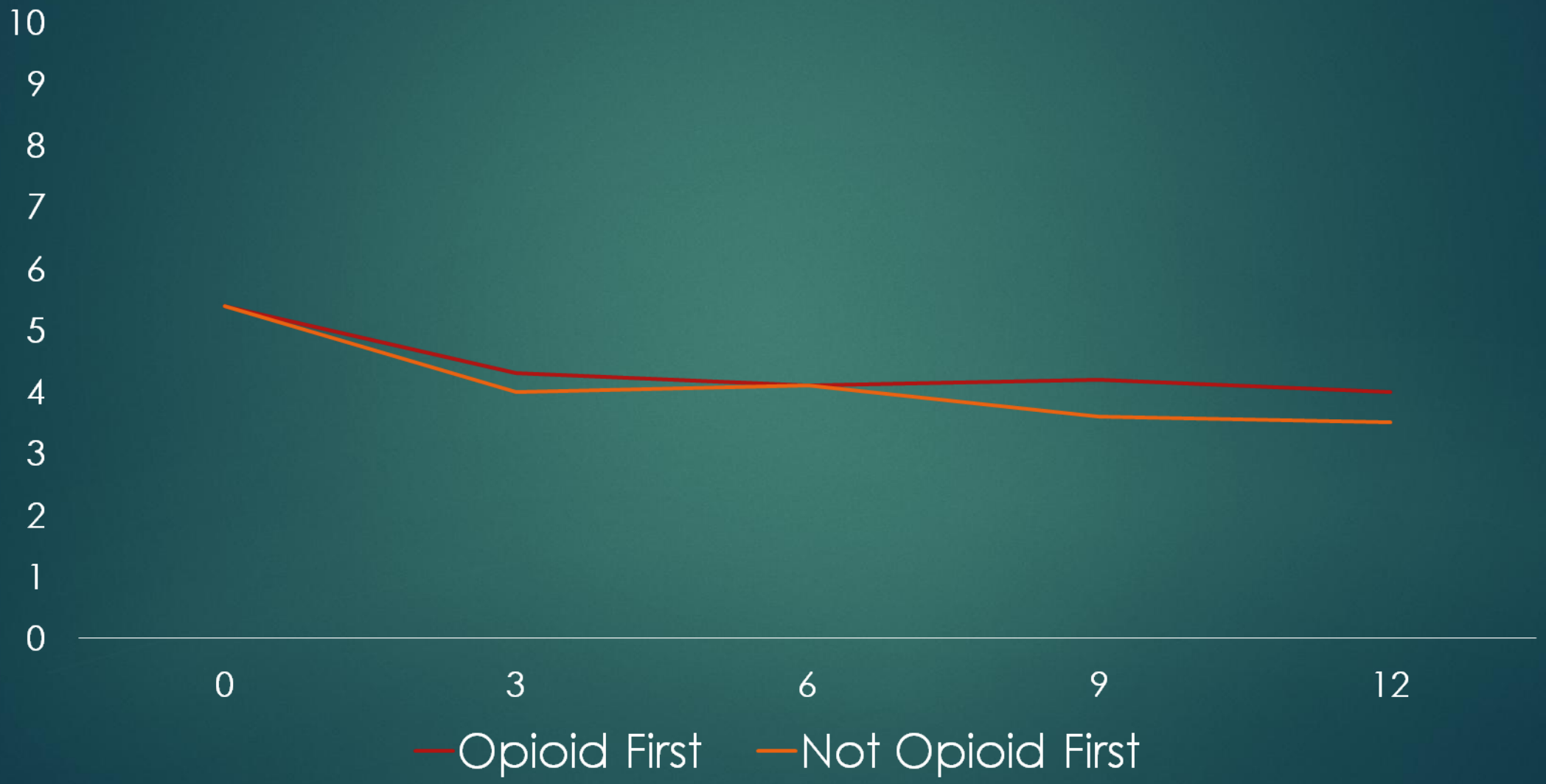
Opioid first

	Opioid arm	Non-opioid arm
Step 1	Morphine IR* Hydrocodone/APAP	Acetaminophen* Naproxen
Step 2	Morphine SR Oxycodone SA	Nortriptyline Capsaicin topical Gabapentin
Step 3	Fentanyl transdermal	Tramadol

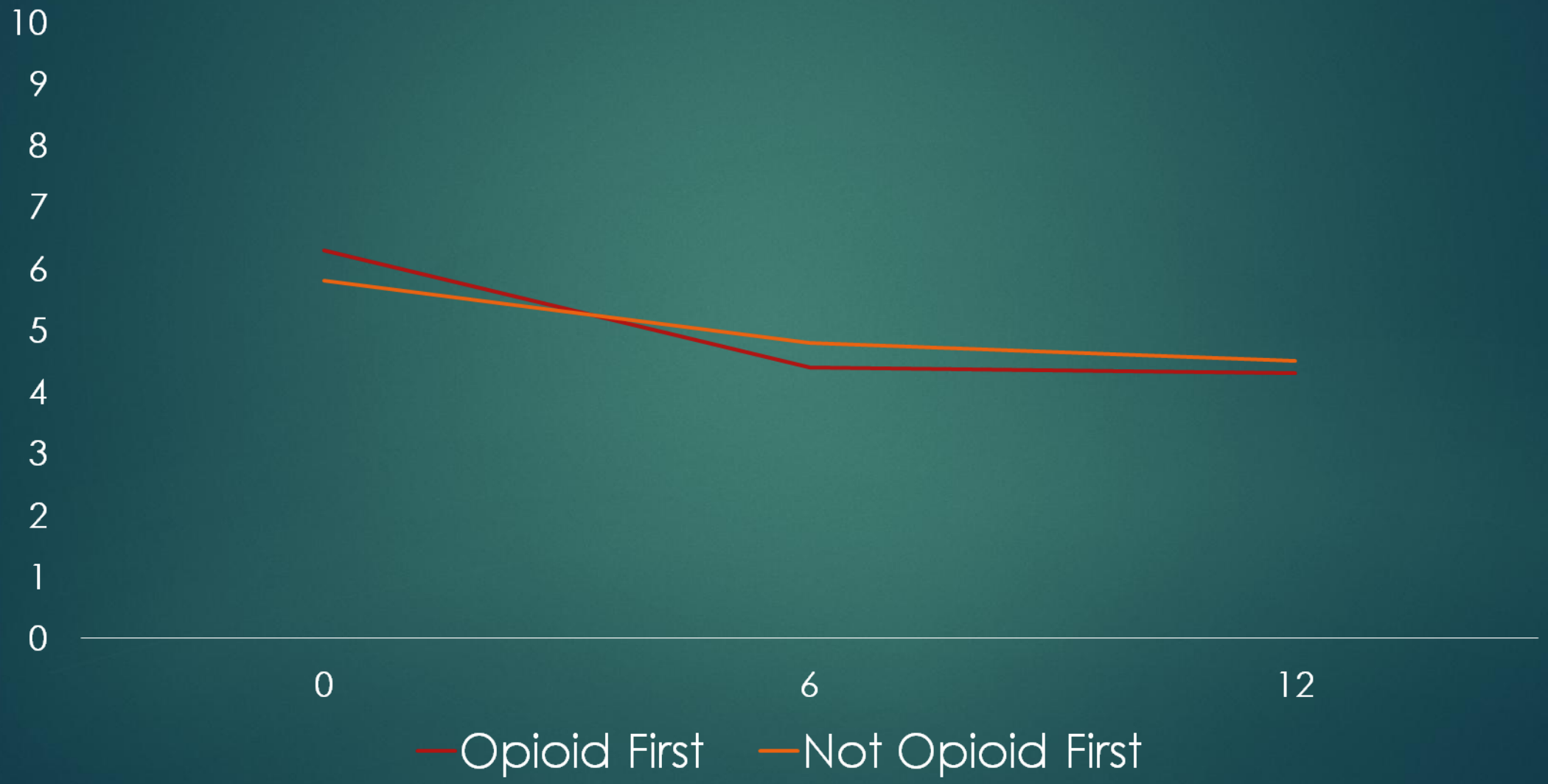
Brief Pain Inventory Scores (p=0.58)



Pain Scores (p=0.03)



Depression scores (p=0.13)



SPACE trial: my take

- Opioids were not "ineffective"
- Intensive opioids weren't better than a systematic step-up of therapies, with low dose opioids, reserved for a few
- Opioids did not cause depression
- Both groups improved, a lot
- SPACE trial doesn't reflect all people I care for
  - Pain = 5/10
  - Improvements for 60%
  - vs 30-40% for most therapies in most trials

- If aggressive opioids for patients **like these** was your approach….let it go

Who might need opioid therapy?

- Opioids are not 1st-line or routine for chronic pain
  - Exceptions might be invoked on ethical grounds
- Some pain-related distress can be mitigated with medications, including opioids, but you have to anticipate risks
- Generally combine with other therapies

https://www.cdc.gov/drugoverdose/pdf/prescribing/Guidelines_Factsheet-a.pdf

How often do adults starting opioids develop new addiction-ish behaviors?

- Chronic non-cancer pain, 18-75 years (mean age 47, n=180)
- Excluded: drug/alcohol/psych problems in last 3 months
- Mean dose: 19 MME (SD 27)
- 28% stopped the opioids
- Very few aberrant behaviors
- Urine drug tests: cannabis (8.4% baseline, 9.7% 12 months)
- Prescribed opioids not detected in the urine: 16%
- Group mean pain score didn't fall significantly

Cheatle, Pain Medicine 2018; 19: 764–773

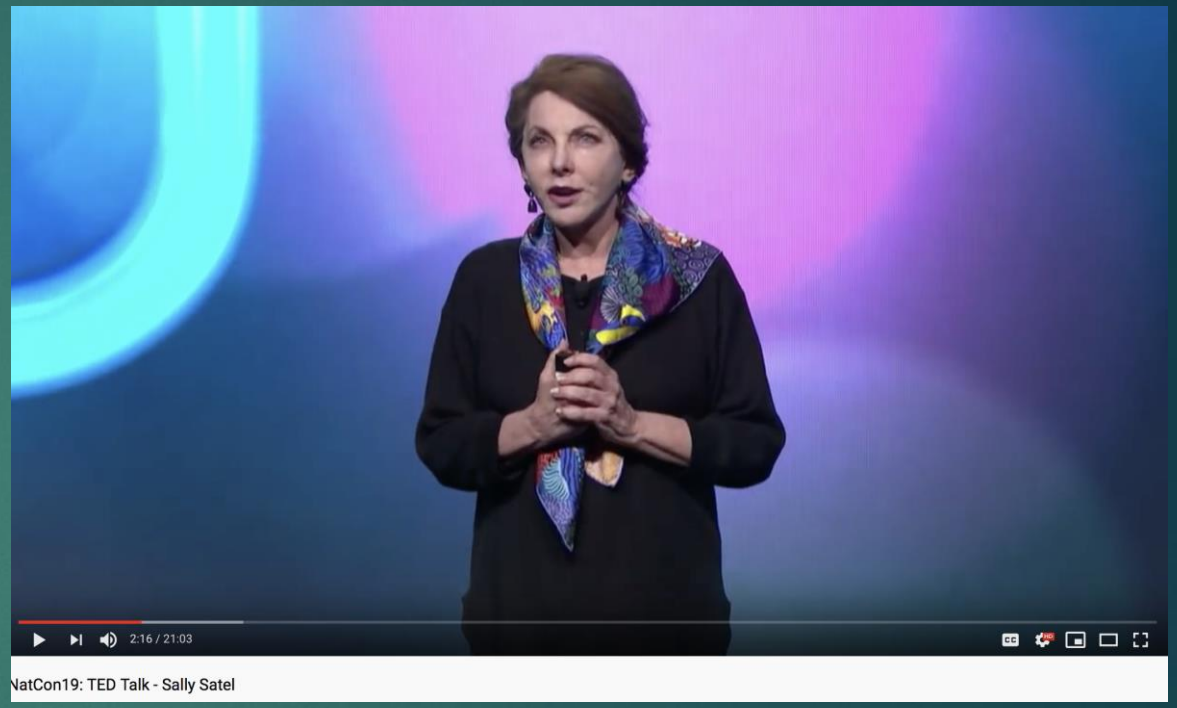
Dx: "Opioid Use Disorder" (OUD)

2 or more		
Taken more than intended	Taking too much	
Unsuccessful cutting down or controlling use		
Craving	Craving	
Recurrent failure in role obligations	Life problems	
Use despite social problems		
Important activities given up due to use		
Recurrent use in hazardous context		
Continued use despite knowing it's causing harm		
Withdrawal	Physiologic dependence	Not if under appropriate medical supervision
Tolerance		

2 -3 criteria over 12 months :"mild" 4-5: "moderate" 6 or more: "severe"

How many develop addiction?

- Average "de novo" addiction: <1% to 6.5%
- We are **not equally liable** to addiction
- Study of misuse/poisoning post-op Rx
  - 500% increased odds for persons aged 15 to 25



"Comforting Fictions" About Addiction
NatCon19 TED Talk – April 8, 2019
Sally Satel, MD

Edlund, Clin J Pain. 2014; Brat et al. BMJ 2018;360:j5790

Can I treat opioid use disorder?

Meds

- For OUD 3 meds have evidence
  - Methadone (clinics)
  - Long-acting naltrexone (off other opioids 7 days, less evidence)
  - **Buprenorphine/naloxone**(off other opioids 12-36 hours)

- Please note: much recovery unfolds in ways separate from what doctors do

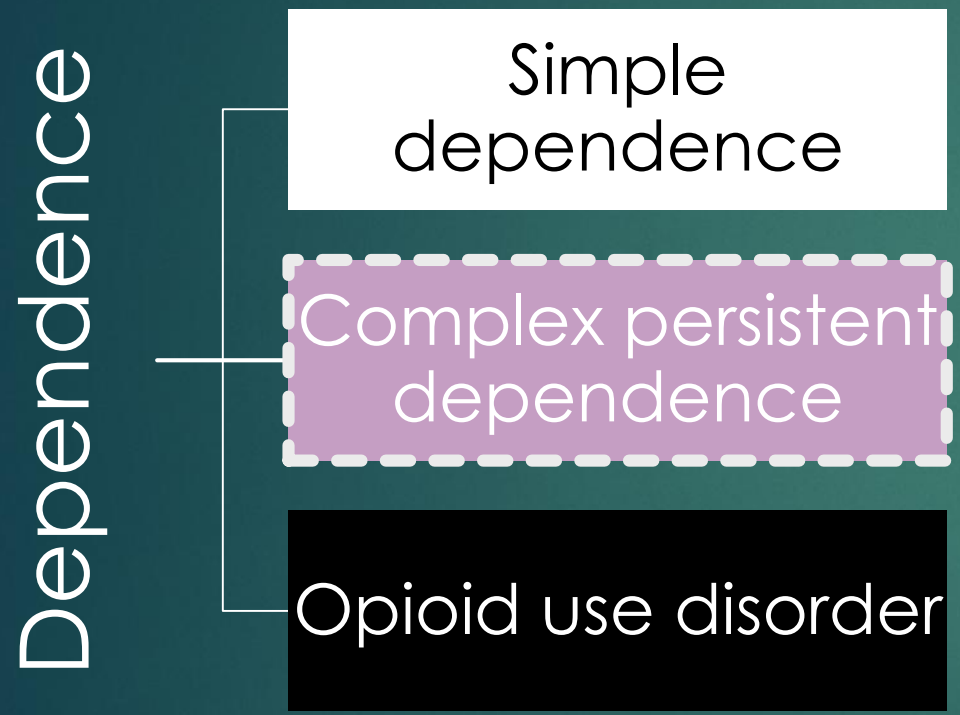
Legal

- In hospital, no restriction
- To prescribe BUP/NLX for OUD, do a training + upload certificate to SAMHSA… they forward to DEA… wait 45 days

- Free training: **https://pcssnow.org/about/**

- FYI: you can prescribe various forms of buprenorphine for pain, and the "waiver" is not needed for that

Dependence not homogeneous



Simple dependence:

- Tolerance the norm.
- Withdrawal is expected but not protracted or destabilizing

"Complex persistent dependence":

- Pain and affect more volatile (due to CPD)
- Dose escalation not helpful
- Dose reduction worse
- Some overlap with OUD, but all of it is attributable to the pain and being in care

Warning: CPD reflects a **patient**, not a **taper policy**

Source: Manhapra, Arias & Ballantyne (2017)

Standards

A caveat on evidence

- Most recommendations in the CDC Guideline are
  - Based on type 4 evidence
  - "clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations"

CDC Guideline

Dowell D et al. *MMWR* 2016

When to initiate/ continue opioids	Opioid management	Assess risks/ address harms
1. Do not use opioids as 1st-line therapy. If used, combine w/ other therapies	4. When starting use immediate-release opioids	8. Use strategies to mitigate risk (eg, naloxone)
2. Before starting opioids establish realistic goals. Continue opioids only if meaningful improvements outweighs risks	5. Prescribe the lowest effective opioid dose. Use caution with any dose, if possible avoid doses ≥90 mg morphine mg equivalents	9. Review PDMP data
3. Before starting and then periodically discuss risks and benefits of opioids	6. Prescribe short durations for acute pain. ≤3 days often sufficient; >7 days rarely needed	10. Use urine drug testing
	7. Evaluate benefits and harms within 4 weeks of starting and at least every 3 months thereafter	11. Avoid concurrent benzodiazepines
		12. Offer/arrange treatment for patients with an OUD

I am prescribing opioids. What must I do?

- "Must do" combines
  - Obligations to safety of the patient
  - Obligations derived from regulation

- I mention both
  - "There are things that will help us to assure you are safe and benefitting"
  - "It's important to know that society considers these prescriptions sensitive. This means that for me to prescribe them, we have mutual obligations.."

- Why mention both? Honesty & clarity with an adult
- Sets stage for later discussions

Initiation

- Establish goals for pain and function
  - Refer to a model focused on rehabilitative gain
- Ask if there is another professional needed (eg. rehab, mental)
- Informed consent
  - I speak of "mutual responsibility"
  - Risk of addiction
- Frame as a **trial** of opioid therapy with option to stop
- Clinicians should continue therapy only if there is clinically meaningful improvement in pain and function that outweighs risks

https://www.cdc.gov/drugoverdose/pdf/prescribing/Guidelines_Factsheet-a.pdf

Questions I do ask in pain care

- What do you do each day?
- Are you working?
- Are you taking care of others?
- Are there groups are part in your week?
- Do you walk? Play an instrument?

The activities should play a role in your chart note regarding Benefit vs Harm

PDMP Requirements for AL

- For ≤30 MME per day, "consistent with good clinical practice"
- For >30 MME per day "at least two times per year and document use'
- For >90 MME per day*, "every time prescriptions are written, on the same day"
  - 25 mcg fent patch
  - buprenorphine off label for pain 2 mg bid (but 1 bid is < 90)

- Evidence? No patient-level outcome has been shown to be improved. State-level analyses suggest prescriptions fall and illicit opioid overdose rises

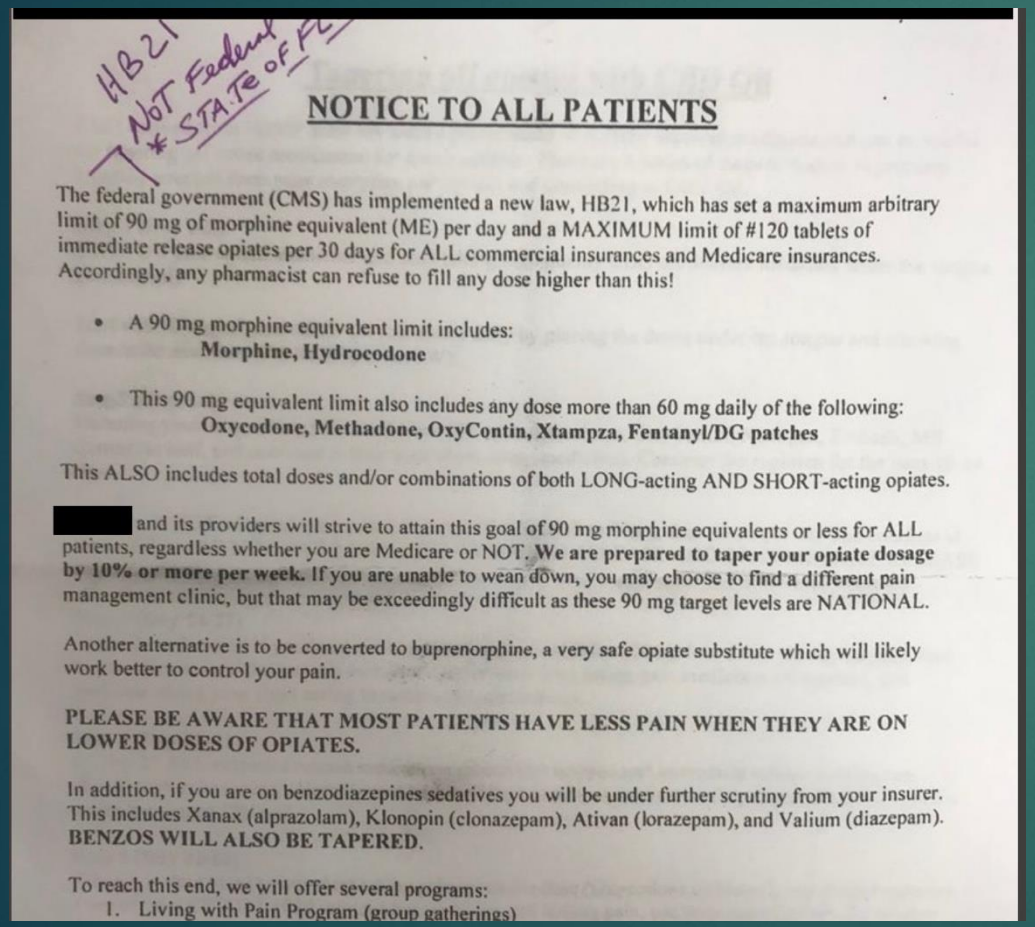
Conversions are based on CMS

Urine drug tests

- Frequency ? (q6 months for Veterans Administration)
- Note:
  - A standard "screen" is an immunoassay. Use that
  - Less sensitive, and subject to false +ve (esp with amphetamines)
  - www.mytopcare.org
- "Negative urine" is common
- Low doss hydrocodone: one situtation
  - Ask about it
- Confirmatory GC/MS if concern is high
- UDS is a test, not an oracle
- Evidence that this improves outcomes? None really

Taper

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

Governmental

- Congress
- Medicaid
- HHS FDA
- Dept of Justice
- Medicare D
- State laws & regs
- Medical boards

Framing Voices

- Leading Journalists
- Advocates
- Government speakers
- Litigation language
- Medical journals

POLICY ACTORS

Guidances & Metrics

- CDC
- VA/DoD & Canadian Guidelines
- NCQA, National Quality Forum

Payors & Other Entities

- Pharmacy chains
- Pharmacy Benefit Managers
- Hospital Administration (and VA)
- Any hospital or chain
- Malpractice policy

40 studies with patient outcomes

- 5/40 were RCTs. Most observational
- None rated as "good quality"
- Improvements in "fair" quality studies
  - Pain: 8/8
  - Pain related function: 5/5

- These are voluntary
- They entail (often) weekly follow-up and multidisciplinary support
- Mostly short-term follow-up
- No studies of mandates
- Insufficient evidence on adverse events

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

Frank et al cautioned:

- no prospective studies of mandatory, involuntary opioid dose reduction among otherwise stable patients
- insufficient evidence on adverse events related to opioid tapering, such as accidental overdose …or suicidality or other mental health symptoms
- Public health surveillance and large-scale observational studies are needed to assess outcomes …such as overdose and suicide

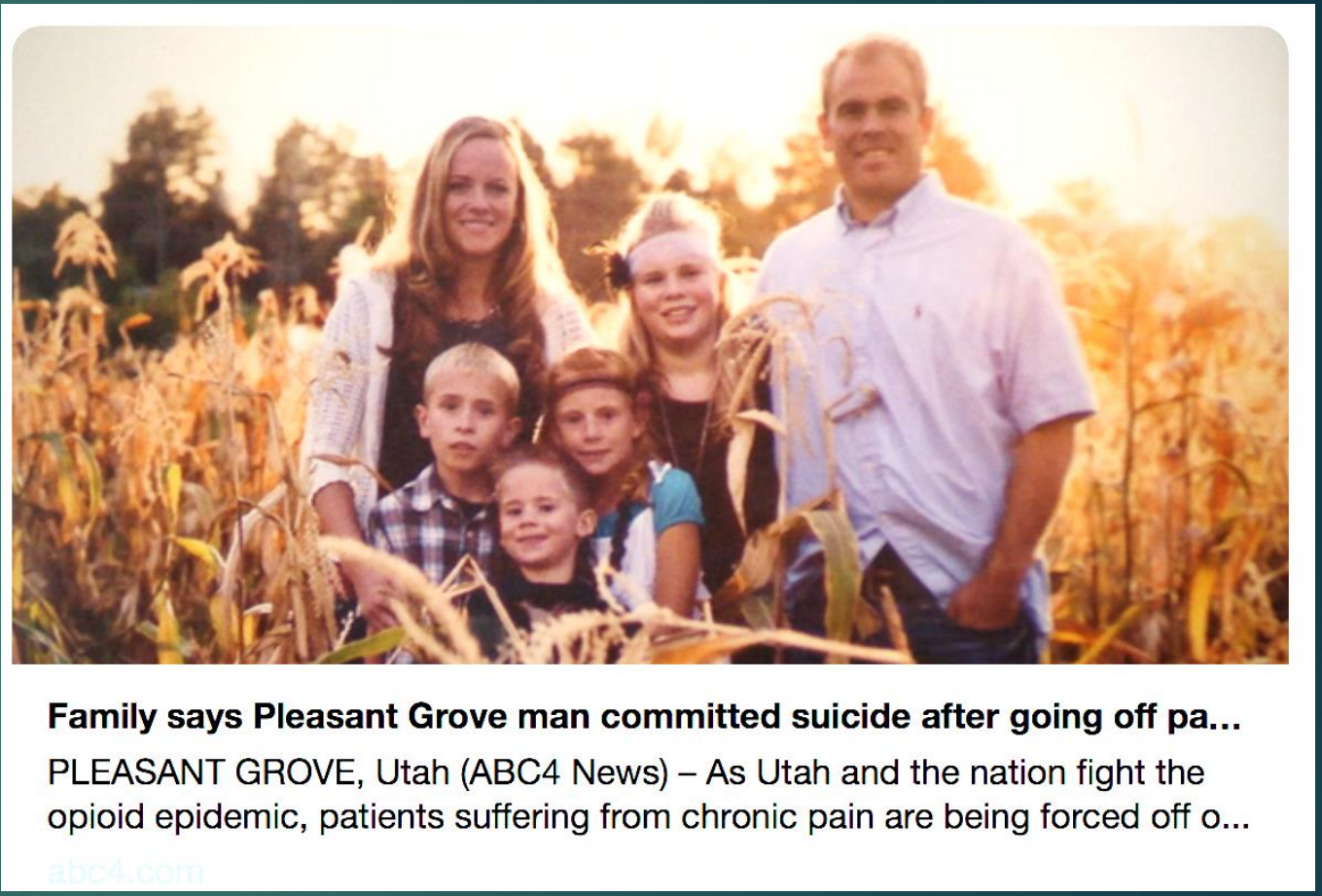
- An updated lit review by Mackey et al (Evidence Synthesis Program, 2019)

This happens, ***a lot***

- *"Due to insurance and dosage changes…Adam no longer had regular access to the pain medication he needed" (ABC News)*

- "The night before he left, he gave us all hugs and told us how much he loved us…I'm glad he's not in pain anymore, even though we do miss him." Kelcee Palmer, age 19

- This has affected our community too



Opioid reduction, in the real world

- Stoppage a/w suicidal ideation and action (11.4%) *(Demidenko, 2017)*
- Dose variation associated with increased OD risk *(Glanz, 2019)*
- Cessation from high dose (>120 MME) typically rapid and followed by emergency care *(Mark, 2019)*
- Cessation associated with 3x risk of OD death *(James, 2019)*
- Associated with termination of outpatient care *(Perez, 2019)*

- Observational data
  - don't prove cause and effect, but they are **not reassuring**
  - do show **discrepancy** between what's **typical** and the **ideal**

Pain Medicine, 0(0), 2019, 1–12
doi: 10.1093/pm/pny307
Review Article
OXFORD

Challenges with Implementing the Centers for Disease Control and Prevention Opioid Guideline: A Consensus Panel Report

Kurt Kroenke, MD,* Daniel P. Alford, MD, MPH,† Charles Argoff, MD,‡ Bernard Canlas, MD,§ Edward Covington, MD,¶ Joseph W. Frank, MD, MPH,‖ Karl J. Haake, MD,‖ Steven Hanling, MD,** W. Michael Hooten, MD,†† Stefan G. Kertesz, MD, MSc,‡‡ Richard L. Kravitz, MD, MSPH,§§ Erin E. Krebs, MD, ...an, MD, PhD‖‖

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering

The NEW ENGLAND JOURNAL *of* MEDICINE

No Shortcuts to Safer Opioid Prescribing

Deborah Dowell, M.D., M.P.H., Tamara Haegerich, Ph.D., and Roger Chou, M.D.

HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics

This *HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics* provides advice to clinicians who are contemplating or initiating a reduction in opioid dosage or discontinuation of long-term opioid therapy for chronic pain. In each case the clinician should review the risks and benefits of the current therapy with the patient, and decide if tapering is appropriate based on individual circumstances.

October 2019

Tapering, HHS Guide -10/2019

- Avoid misinterpreting cautionary doses as **mandates** to taper
- Consider **tapering** if
  - Pain improves;
  - Patient asks; pain/function not meaningfully improved
  - Higher dose, no evidence of benefit
  - Overdose toxicity, current misuse
- Go slow
- Taper should be **part of a comprehensive treatment plan** (*)

- "There are serious risks to noncollaborative tapering: acute withdrawal, pain exacerbation, anxiety, depression, suicidal ideation, self-harm, ruptured trust, and patients seeking opioids from high-risk sources"

Taper is successful if

- The probable risk improvement can be balanced with the degree of achievement of goals that are important to patient
- Stability or improvement in pain and function
- Avoiding instability and harm related to medical, psychiatric and psychological conditions
- Patient feels that they are treated with dignity and respect
- Patient involved in decision process and remains engaged in continued treatment

2010 VA/DoD Guideline, cited by Manhapra et al
Subst Abus. 2018; 39(2): 152–161.

Summary

- **Context:** Our crisis includes a proliferation of prescriptions that are in decline. What we have done to correct course has drawn concern from FDA, CDC, HHS, patients and the media

- **Model:** Caring for people with pain requires asking & interpreting the factors that create the pain experience

- **Evidence:** Opioids are not routine first-line therapies
- **Dependence:** Takes multiple forms
- **Standards:** Caution, documented discussions, assess risk vs benefit

- **Taper:** Plausibly ideal practice is odds with what is typical in today's policy environment