Opioid Overcorrection

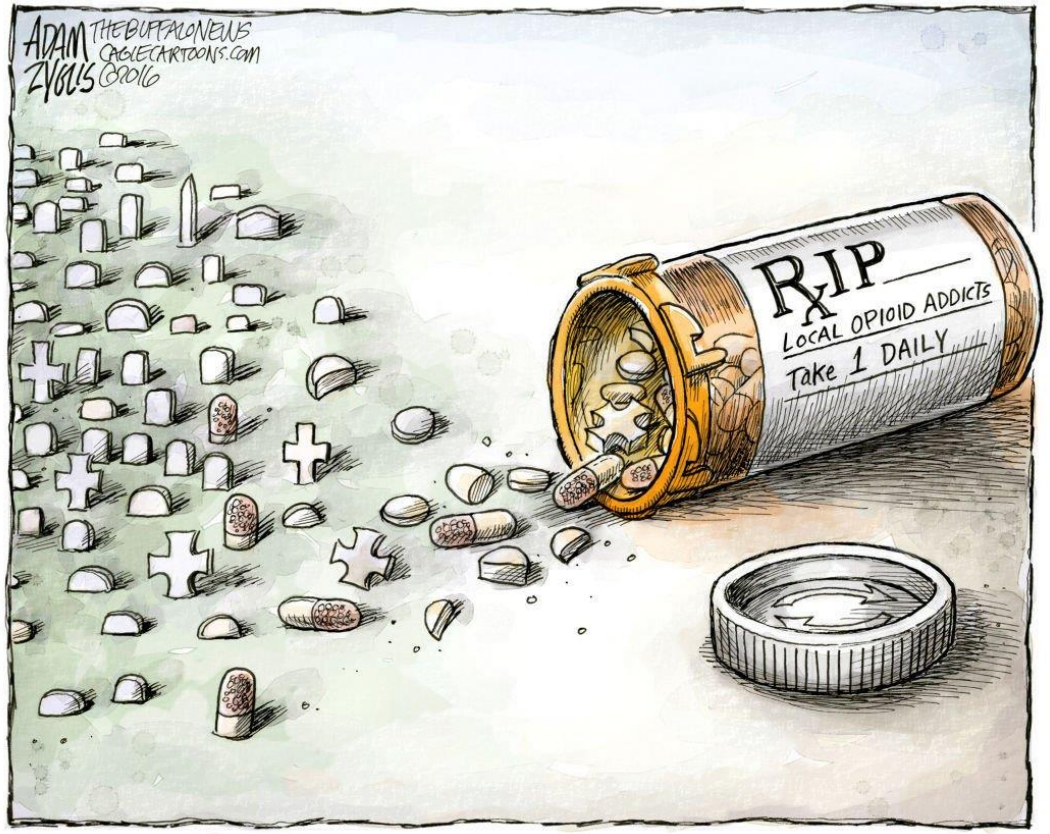
Decreasing harm to patients on long-term opioid therapy

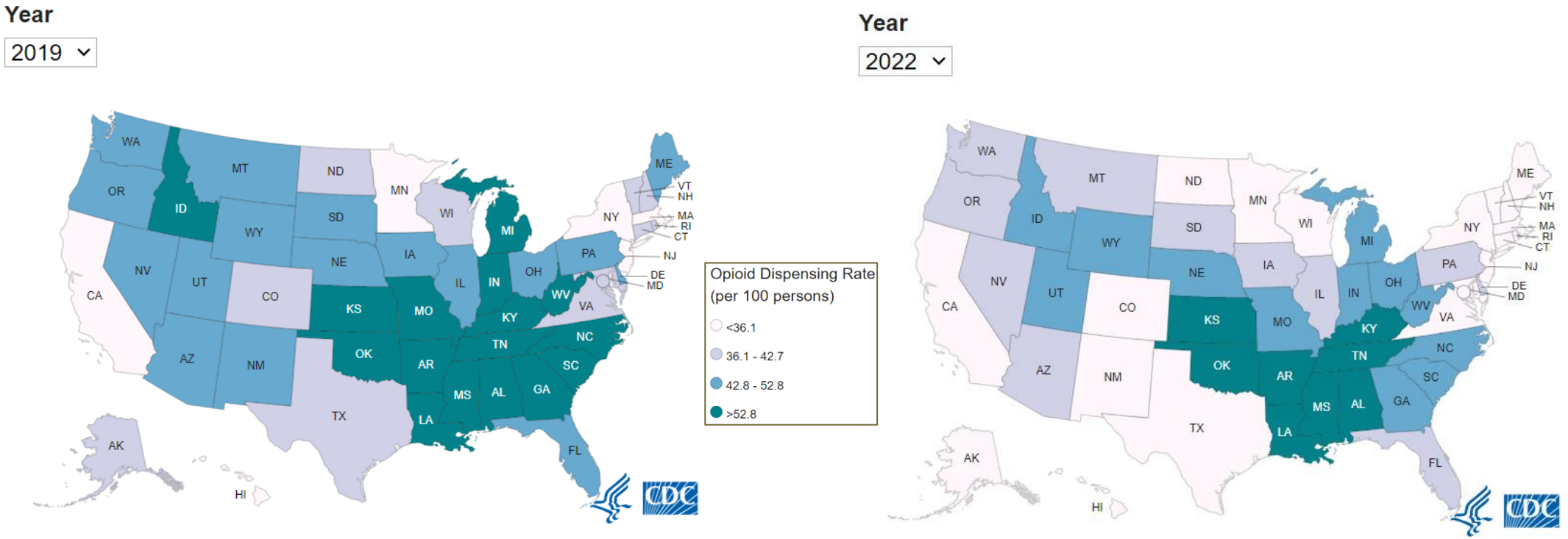
Disclosures

I HAVE NO RELEVANT FINANCIAL DISCLOSURES

Objectives

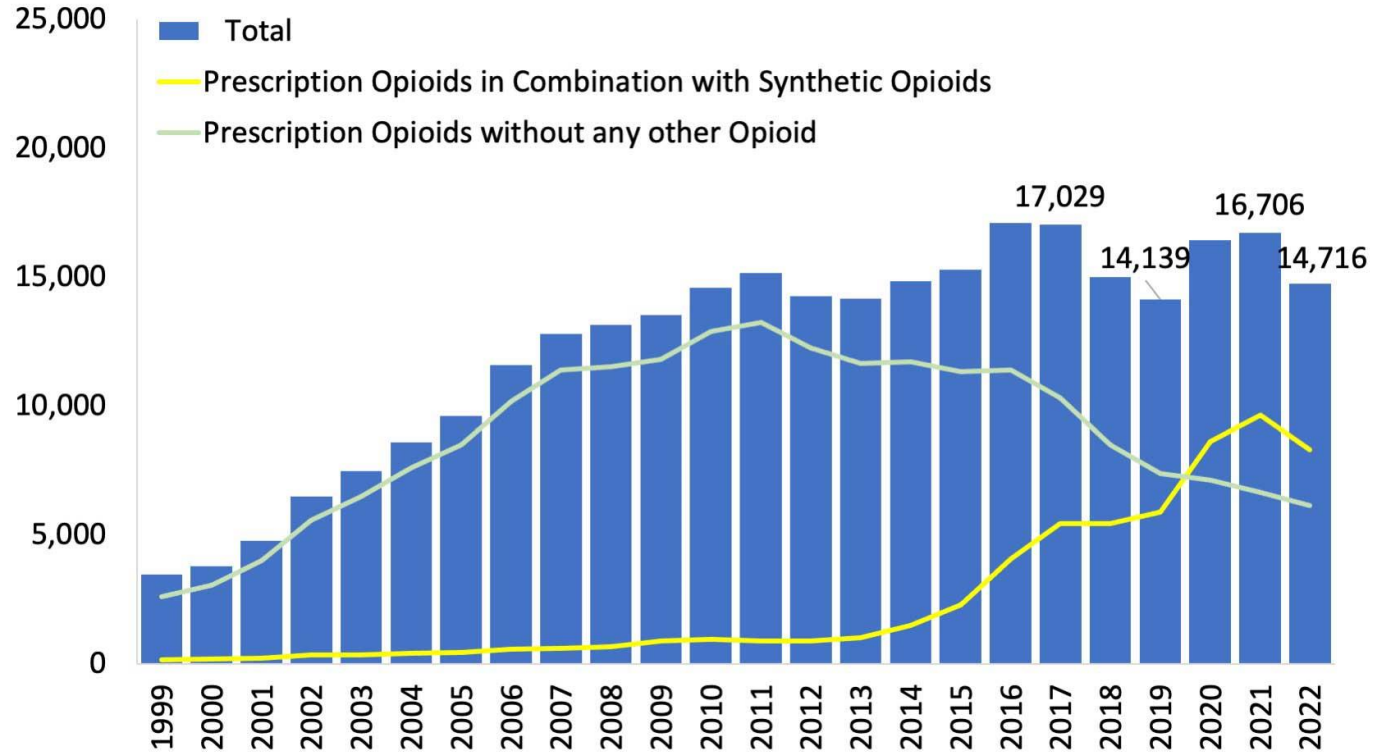
- Identify risks associated with opioid discontinuation
- Balance risks of long-term opioid therapy with risks of discontinuation


ADAM ZYGLIS
THE BUFFALO NEWS
©2016
RIP
LOCAL OPIOID ADDICTS
Take 1 DAILY



https://www.cdc.gov/drugoverdose/rxrate-maps/opioid.html (8/28/24)

Figure 4. U.S. Overdose Deaths Involving Prescription Opioids*, 1999-2022



*Among deaths with drug overdose as the underlying cause, the prescription opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2) or methadone (T40.3). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates#Fig4; 8/24/24

Opioids have risk

+

Opioids are rarely effective for chronic pain

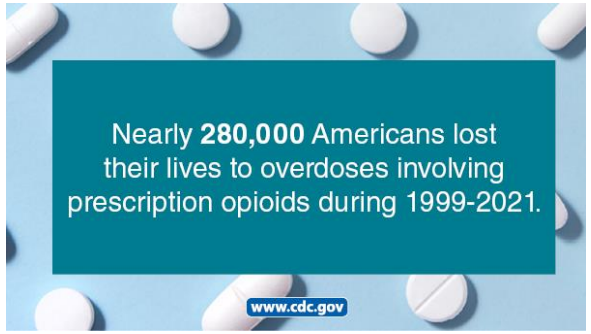
=

If I stop opioids, pain and risk improve

Krebs EE, Gravely A, Nugent S, et al. 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. *JAMA.* 2018;319(9):872–882. doi:10.1001/jama.2018.0899

Opioids Have Risk

TRUE



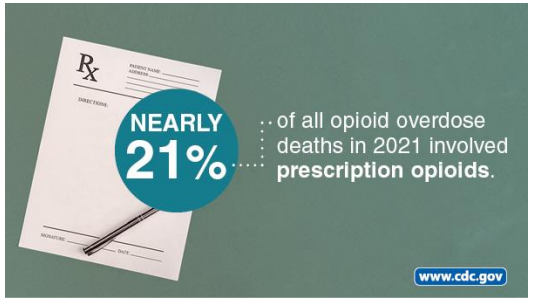


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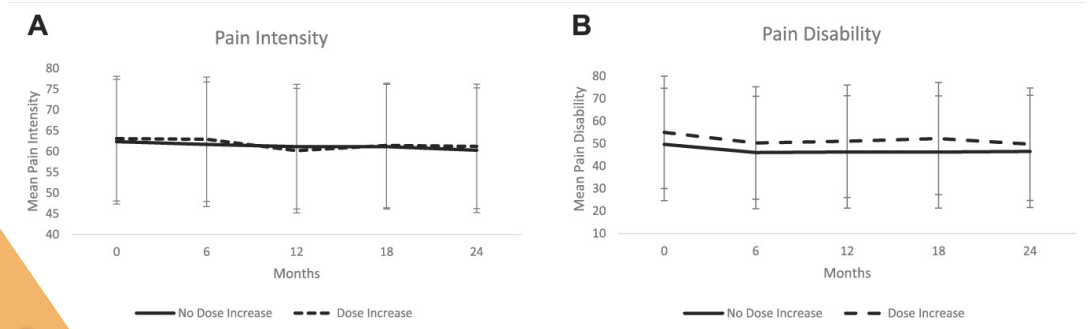
Table 2. Patient-Reported Primary and Secondary Outcomes Among Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication

Outcome	Opioid Group, Mean (SD) (n = 119)	Nonopioid Group, Mean (SD) (n = 119)	Between-Group Difference (95% CI)[a]	Overall *P* Value[b]
Pain-Related Function (Primary Outcome)				
BPI interference scale (range, 0-10; higher score = worse)[c]				
Baseline	5.4 (1.8)	5.5 (2.0)	−0.1 (−0.6 to 0.4)	
3 mo	3.7 (2.1)	3.7 (2.2)	0.0 (−0.6 to 0.6)	.58
6 mo	3.4 (2.1)	3.6 (2.4)	−0.2 (−0.8 to 0.4)	
9 mo	3.6 (2.2)	3.3 (2.4)	0.4 (−0.2 to 1.0)	
12 mo	3.4 (2.5)	3.3 (2.6)	0.1 (−0.5 to 0.7)	
Pain Intensity (Secondary Outcome)				
BPI severity scale (range, 0-10; higher score = worse)[d]				
Baseline	5.4 (1.5)	5.4 (1.2)	0.0 (−0.4 to 0.3)	
3 mo	4.3 (1.8)	4.0 (1.7)	0.3 (−0.2 to	
6 mo	4.1 (1.8)	4.1 (1.9)	0.0 (−	
9 mo	4.2 (1.7)	3.6 (1.7)		
12 mo	4.0 (2.0)	3.5 (1.9)		



TRUE

Opioids Are Rarely Effective for Chronic Pain

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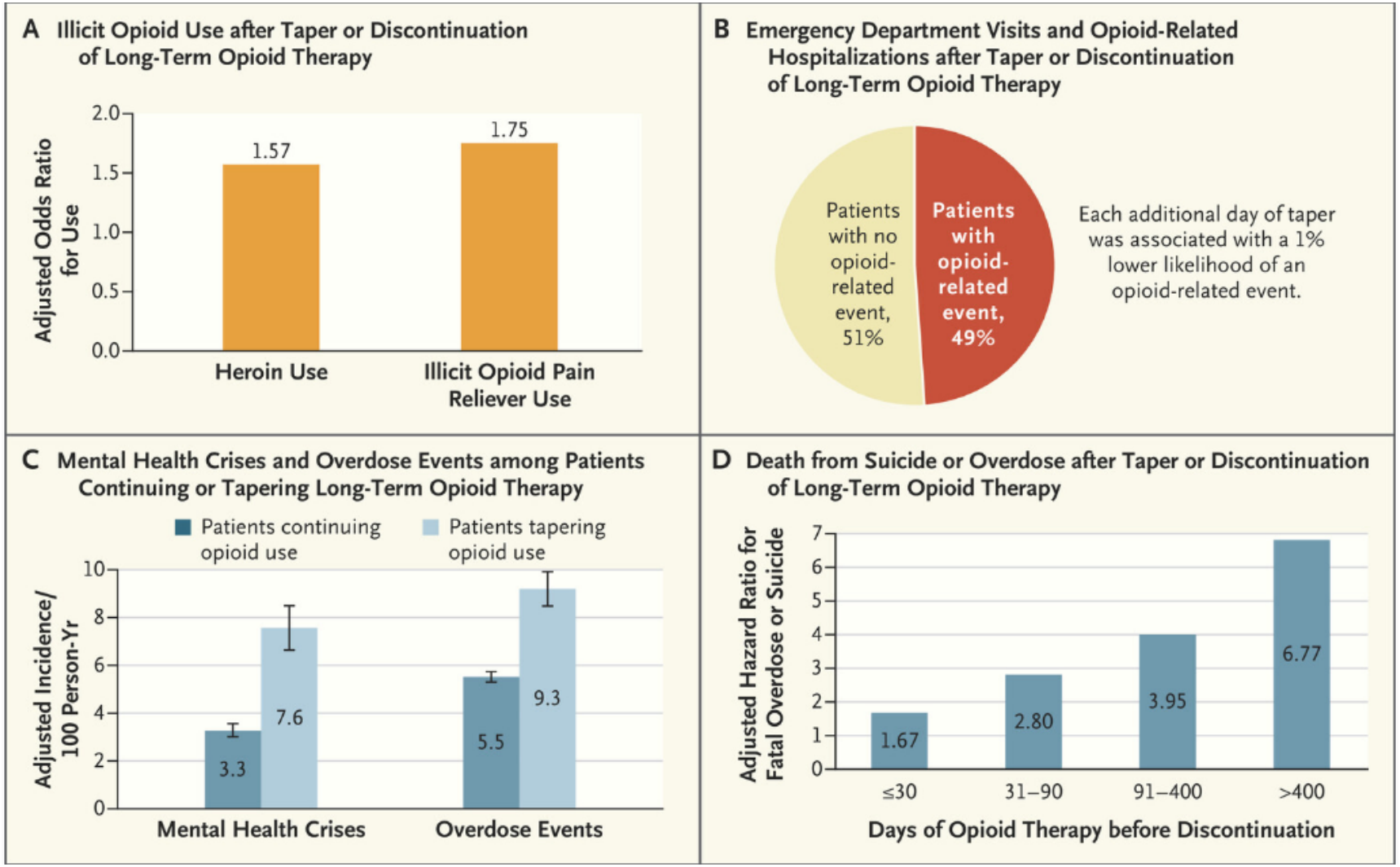
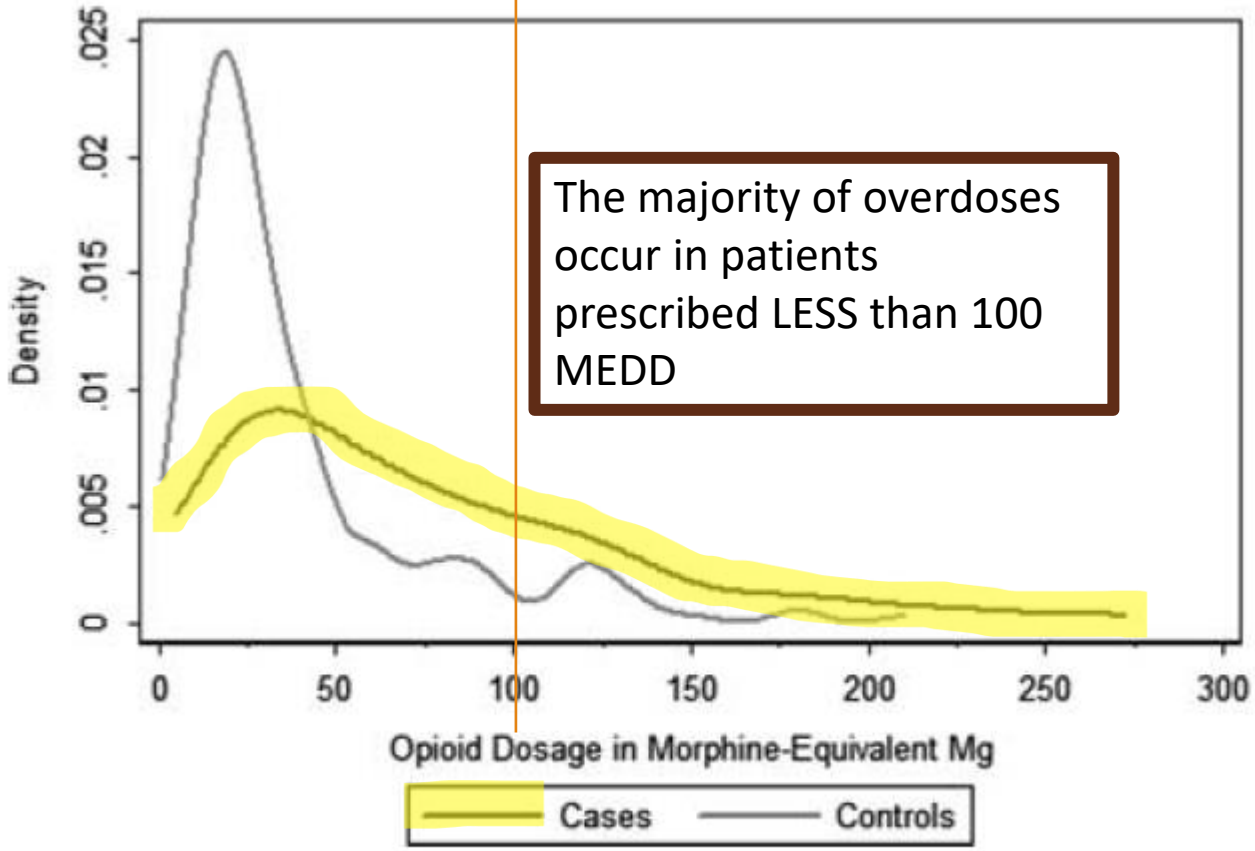
FALSE



Coffin 2022

THE JOURNAL OF LAW, MEDICINE & ETHICS, 48 (2020): 259-267.



The majority of overdoses occur in patients prescribed LESS than 100 MEDD

Mean dose for patients who overdosed: 98 MEDD

Mean dose for controls (no overdose): 48 MEDD

FIGURE 2. Distribution of opioid dosages by group.

Table 3 Unadjusted and Adjusted (final) Cox Regression Models for Predicting 2-Year Overdose Risk for Patients Prescribed Chronic Opioid Therapy at the Derivation Site

Characteristic	Unadjusted model	Adjusted model*	
	Hazard ratio (95 CI†)	β coefficient	Hazard ratio (95 CI†)
Age (per year)	0.93 (0.88–0.98) ‡	−0.06915	0.93 (0.89–0.98)
Age-squared	1.00 (1.00–1.00) ‡	0.0005626	1.00 (1.00–1.00)
Mental health diagnosis§	4.18 (2.88–6.07)	1.22076	3.39 (2.32–4.96)
Psychotropic prescription	2.82 (1.88–4.25)		
Substance abuse/dependence diagnosis‖	6.01 (4.03–8.96)	1.24387	3.47 (2.25–5.36)
Tobacco use or tobacco abuse/dependence diagnosis¶	2.31 (1.60–3.32)	0.42788	1.53 (1.03–2.28)
History of opioid prescriptions in the year prior to initiating chronic opioid therapy	1.43 (1.00–2.05)		
Long-acting or extended-release opioid formulation	2.47 (1.25–4.87)	0.68552	1.99 (1.00–3.93)
Daily opioid dose (per 10 mg morphine equivalents)**	1.01 (0.99–1.03)		
Hepatitis C diagnosis††	2.82 (1.04–7.63)		

The biggest predictive factors for overdose:

- -Mental health diagnosis
- -History of substance use disorders
- -Hepatitis C diagnosis
- -Long-acting or extended-release opioid formulations

Incorrect Conclusions

Higher doses associated with increased risk for overdose, OUD, depression, fracture, motor vehicle accident, suicide.

Decreasing opioid dose does not necessarily decrease risk

Most risk factors for negative outcome are intrinsic to the patient, not the dose

An opioid taper can be only be considered successful if the dose is decreased AND the patient maintains or improves their qualify of life

(PARAPHRASED) THE JOURNAL OF LAW, MEDICINE & ETHICS, 48 (2020): 259-267


This is fine
I'm fine

Insulin: Diabetes ; Opioids: Pain

INSULIN

- (Possibly) indicated when 1st line medications have failed
- High risk
- Low doses, simple regimen generally managed in primary care
- High doses, complex regimen requires specialty care

OPIOIDS

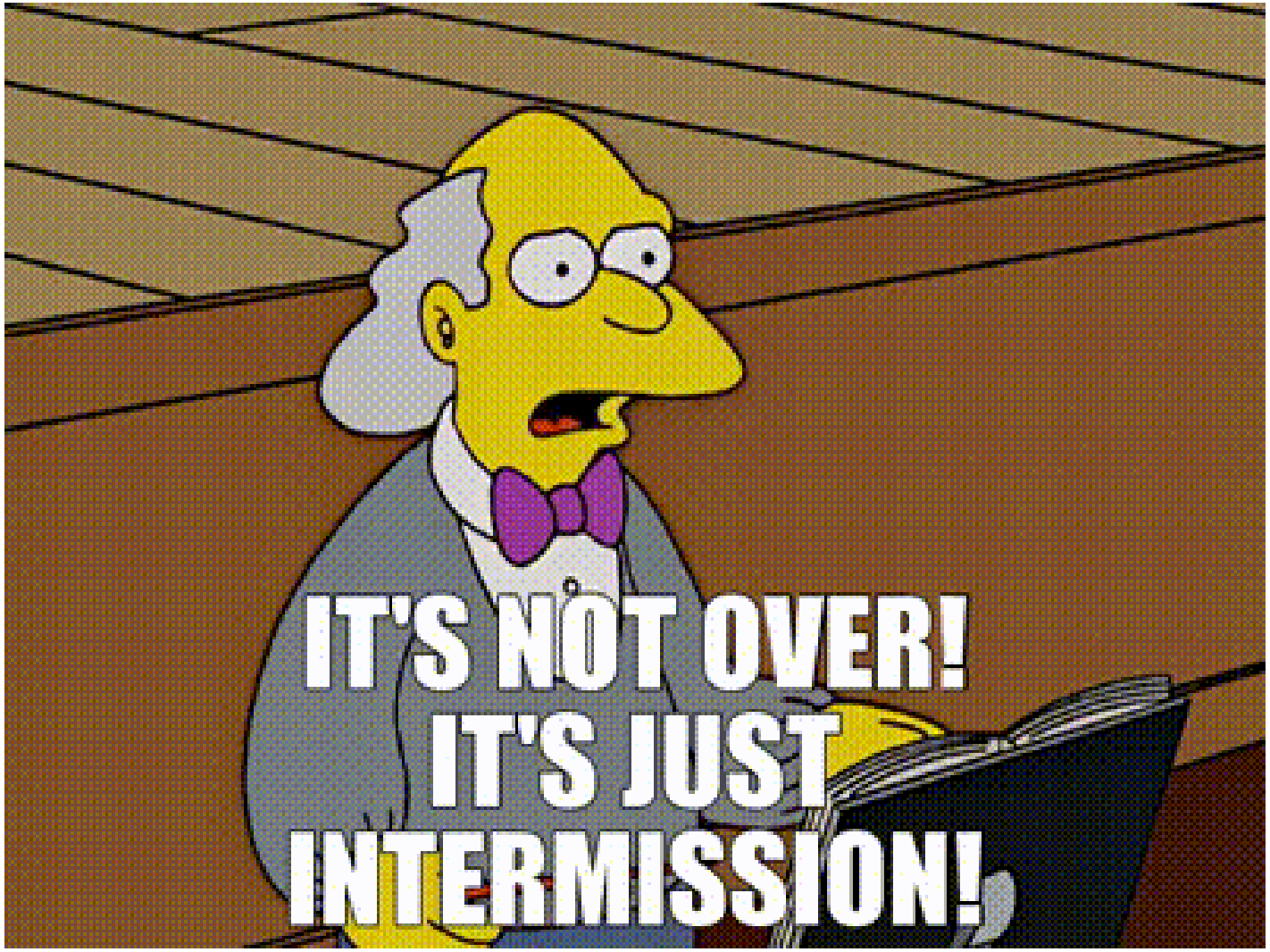
- ✓(Possibly) indicated when 1st line medications have failed
- ✓High risk
- ✓Low doses, simple regimen generally managed in primary care risk
- ✓High doses, complex regimen requires specialty care

Summary

There are risks associated with opioid use AND opioid discontinuation

Opioid tapers should rarely be forced

Decreasing opioid doses does not remove risk


IT'S NOT OVER!
IT'S JUST
INTERMISSION!

Address Concerns

- Acknowledge the situation
- Express empathy
- Ask clarifying questions
- Affirm commitment to patient

Detach Judgment from Observations

- No Assumptions
- No Leading questions
- No Blame
- No Labeling
- No Personal attacks

Universal Precautions

State prescription drug monitoring reports

Urine toxicology screens

Pill counts/ Fill history

Naloxone education/prescription

Risk assessment

- DIRE, ORT, STORM help guide frequency of monitoring

Unexpected UDS

Gather information

- -How/when meds taken
- -Send confirmatory urine toxicology

Reiterate confidence in laboratory results

Responding to Aberrancy

- Misuse ≠ abuse
- Reiterate expectations
- Increase monitoring
- If severe or recurrent, taper or referral

Not-My-Objectives

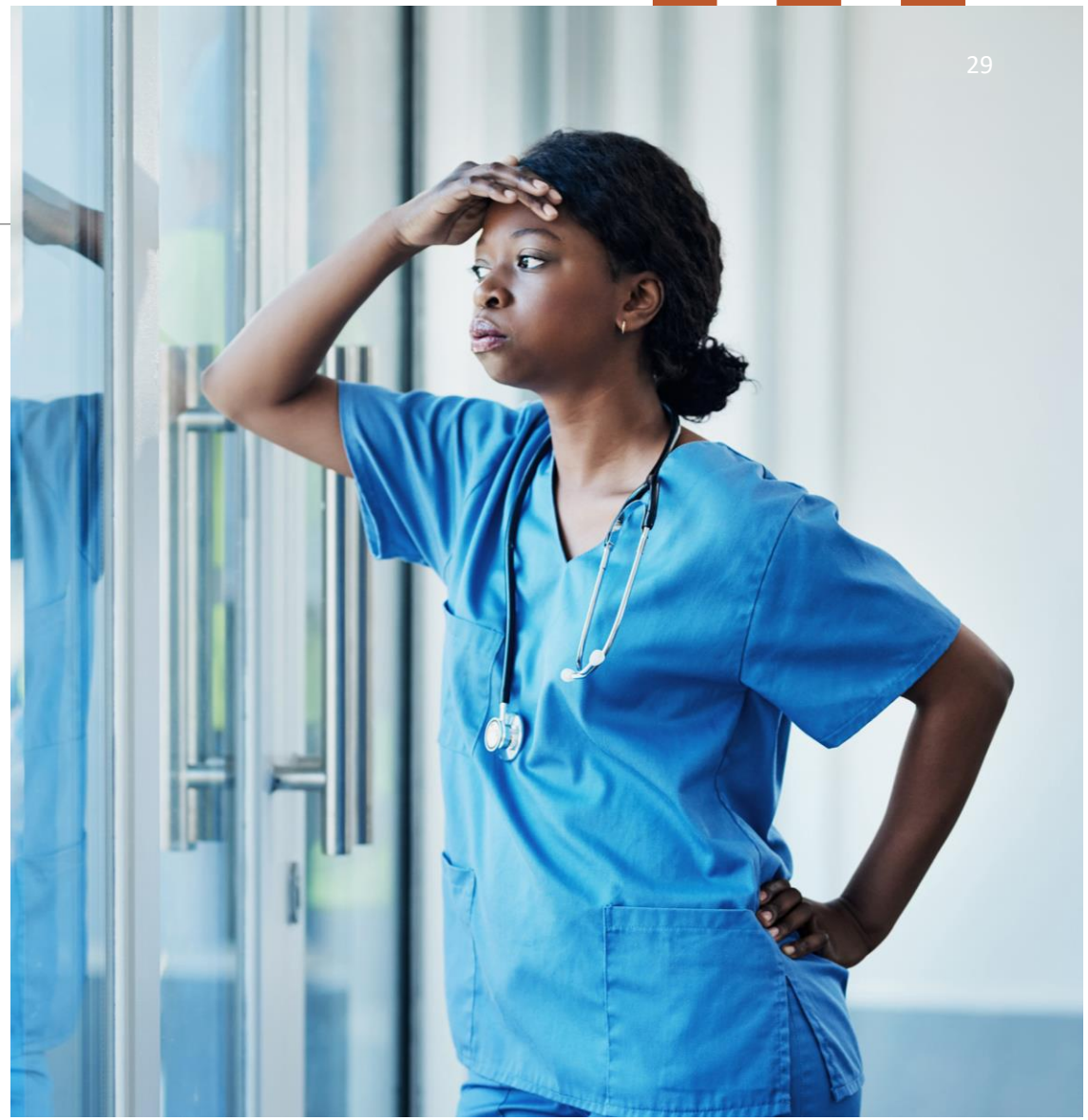
Make opioid prescribing easy and fun

Remove the uncomfortable “gray” area in prescribing

Decrease workload

Objectives

- List pros and cons of opioid tapers
- Accurately interpret results of urine toxicology testing
- Identify patients with chronic pain who may benefit from buprenorphine treatment



The Warden

"I don't make the rules, I just enforce them"

"I'm doing this for your own good"

"It's not my fault you didn't follow the rules"

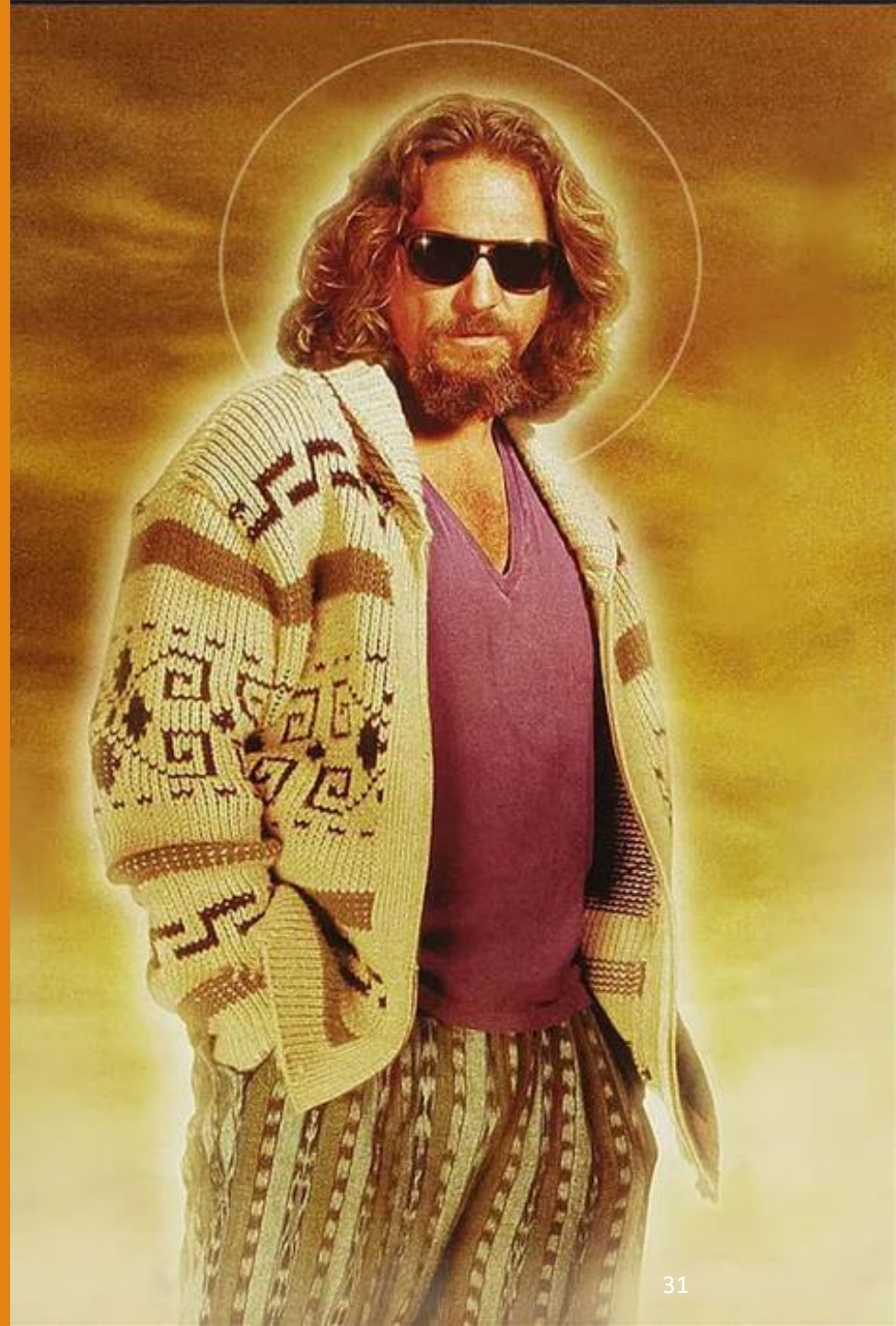
"I don't prescribe opioids for pain"

The Dude

“Of course, I’ll do another early fill—it’s a bummer you’ve been having so much pain.”

“CPAP is uncomfortable-it’s not a big deal if you don’t use it. ”

“Maybe the lab *did* mix up the urine samples”



The Elder

"It seems like the current plan hasn't been working well for you. Let's talk about that"

"I'm concerned about your safety."

"The results of your urine toxicology screen were surprising to me. I'd like to talk more about that."

The Urine Conundrum

- 56 yo patient with chronic low back pain, insomnia and anxiety
- Requesting refill for oxycodone 15mg q6 hours as needed for pain
- PDMP consistent—one provider, on-time fills x 2 years

Urine toxicology screen from prior month:

+Oxycodone
+Opioids
+Amphetamines

What is the next best step?

(A) Refill their oxycodone for another month. They've been on it for years

(B) Discontinue their oxycodone prescription. You don't want to support their meth habit

(C) Refuse to prescribe until you see them in clinic.

(D) Call the patient to gather more information

Medication List

- **Fluoxetine 20mg**
- **Ibuprofen 600mg q6 hours prn pain**
- **Oxycodone 15mg q6 hours prn pain**
- **Trazodone 50mg prn insomnia**

UDS +oxycodone, + opioids, +amphetamines

Urine Toxicology Screens

Type of Test	Logistics	Pearls
Initial Screening Test		
Immunoassay*	• Inexpensive • Fast • Widely available	• High sensitivity, low specificity (higher potential for false positives) • Opiate screen not sensitive for semisynthetic (e.g., oxycodone) or synthetic opioids (e.g., fentanyl)
Confirmatory Test		
Gas Chromatography-Mass Spectrometry (GCMS)**	• Expensive • Time consuming	• High sensitivity, high specificity • Detects medication even if concentration low • Allows detection of a specific drug/metabolite
Liquid Chromatography-Mass Spectrometry (LCMS)	• Less expensive than GCMS • Faster than GCMS	

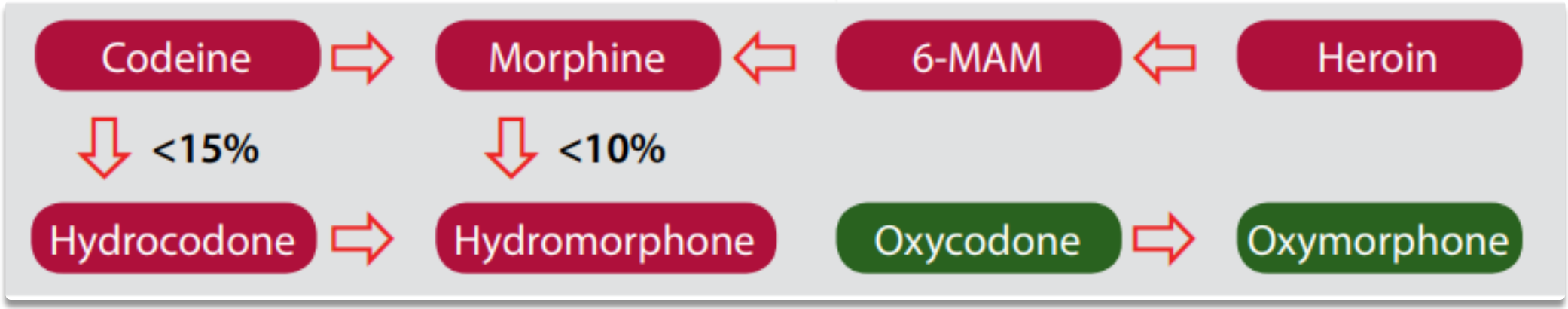
*Immunoassay tests have high predictive values for tetrahydrocannabinol (THC), the testing component of marijuana, and also for cocaine, but lower predictive values for opioids and amphetamines. **GMCS is considered the criterion standard for confirmatory testing.

Inexpensive, fast and generally adequate

Expensive, time-consuming but gold standard for accuracy

Urine Toxicology Interpretations

Items in red result as opioids on screening tests



Oxycodone's metabolic pathway is in green. Usually, it does not trigger opioid screen, but can with high doses or recent intake

Substance	Agents Potentially Causing False Positives			
Marijuana Metabolites	• dronabinol • efavirenzproton	• NSAIDs* • proton pump inhibitors	• hemp foods: tea, oil** • THC/CBD topicals	
Cocaine Metabolites	• coca leaf teas	• topical anesthetics containing cocaine		
Opioid Metabolites	• dextromethorphan • fluoroquinolones	• levofloxacin • ofloxacin	• poppy seeds • poppy oil	• rifampin • quinine
Amphetamines/ Methamphetamine (High Rate of False Positives)	• amantadine • benzphetamine • brompheniramine • bupropion • chlorpromazine • desipramine • dextroamphetamine	• doxepin • ephedrine • fluoxetine • isometheptene • isoxsuprine • labetalol • l-methamphetamine (OTC nasal inhaler)	• methylphenidate • MDMA • phentermine • phenylephrine • phenyl-propanolamine • promethazine • pseudoephedrine	• ranitidine • selegiline • thioridazine • trazodone • trimethobenzamide • trimipramine

Urine Conundrum (continued)

Patient denied any non-prescribed substance use

The Elder wrote for a 2-week prescription pending UDS results

Confirmatory testing revealed presence of oxycodone and oxymorphone *only*

The Dose Dilemma

60 y.o.

PTSD, depression and alcohol use disorder in sustained remission

On 250 MEDD x 3 years

Functional benefit (employed, active)

Yearly urine toxicology screens and PDMP are as expected, no aberrant behavior

What is the best next step?

(A) Offer a taper. If they declines, continue current regimen with more frequent monitoring.

(B) Tell patient you do not prescribe such high doses. Offer a rapid taper to get them down to 100 MEDD.

(C) This patient is too high risk to be on opioids. Offer medications to help with withdrawal, but do not fill additional opioid prescriptions.

(D) Fill as usual. They've been on this for years and has no history of aberrancy.

“Clinicians should **avoid abrupt discontinuation** of opioids, especially for patients receiving high dosages…”

-CDC revised guidelines 2022

Taper Confusions

Higher doses associated with increased risk for overdose, OUD, depression, fracture, motor vehicle accident, suicide.

Decreasing opioid dose does not innately decrease risk

Main risk factors for negative outcome are patient specific

JAMA, APRIL 6, 2011—VOL 305, NO. 13, ADDICTION, 115, 1098–1112

Patients who opt-in for tapers may do better

Low qualify data

Voluntary patients, mostly in supported settings (i.e. pain clinics)

Systematic review suggests pain, function, and quality of life *may* improve during and after opioid dose reduction.

FRANK ET AL. “PATIENT OUTCOMES IN DOSE REDUCTION OR DISCONTINUATION OF LONG-TERM OPIOID THERAPY”

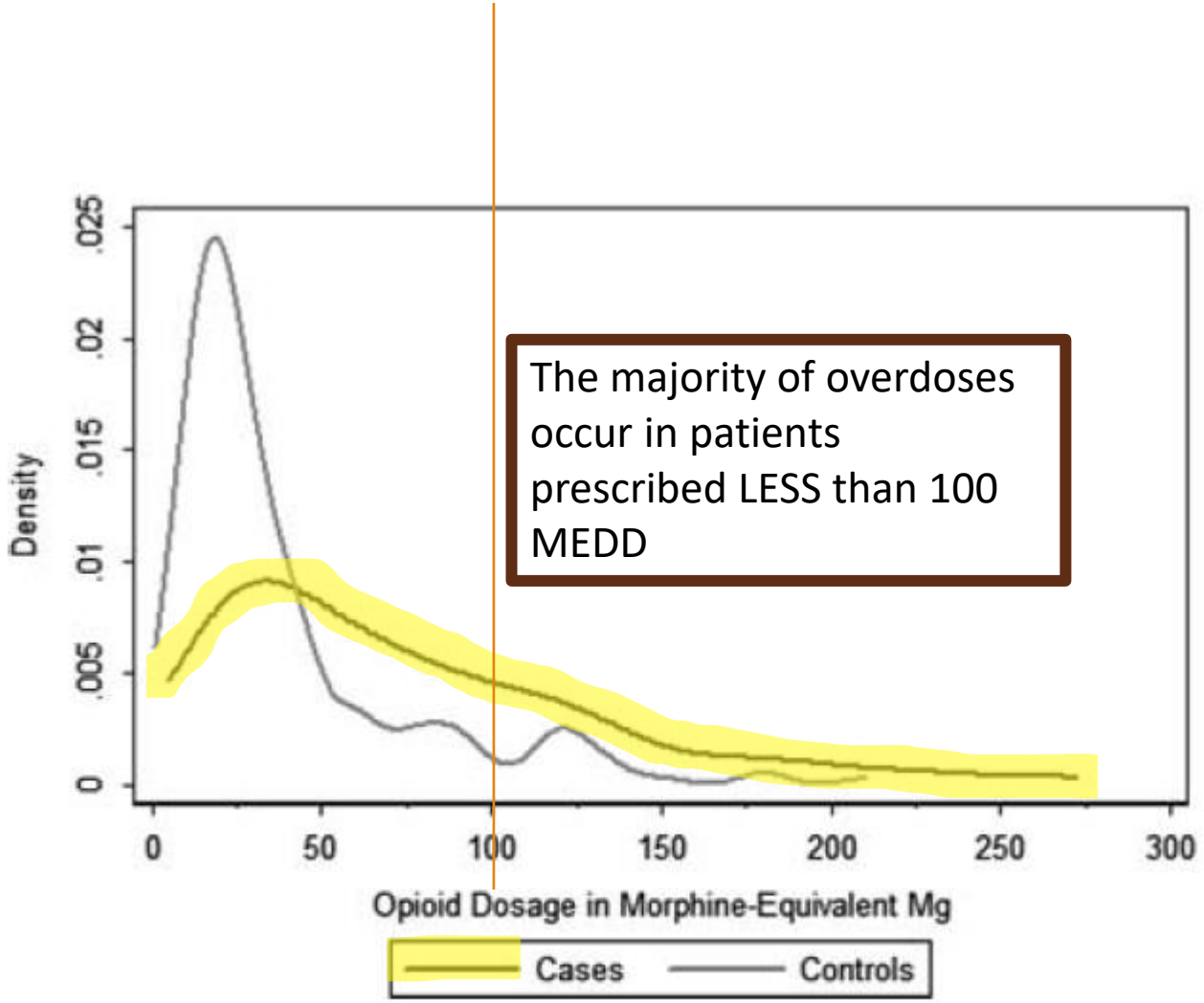
Patients *forced* to taper may do worse

No prospective studies of forced tapers on stable patients

Variable outcomes in observational studies

- Increased risk for overdose
- Increased risk for suicide

Unclear outcomes in function or qualify of life



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(PARAPHRASED) THE JOURNAL OF LAW, MEDICINE & ETHICS, 48 (2020): 259-267

The Dose Dilemma

The Elder discusses concerns about opioid doses

- Overdose risk
- Hypogonadal suppression, bone loss
- Invasive bacterial infections

Patient agrees to attempt a slow taper with Pain Clinic

Opioid Dosing

There is no dose below which there is NO risk

There is no dose above which is an UNACCEPTABLE risk

Dosing/taper decisions should be individualized

Medication Mismanagement

82 year-old, chronic low back pain

On Norco 10-325mg q6 hours prn x 20 years

Variable refill history

- 2 late refill requests, 3 early refill requests

Reports taking medications as prescribed

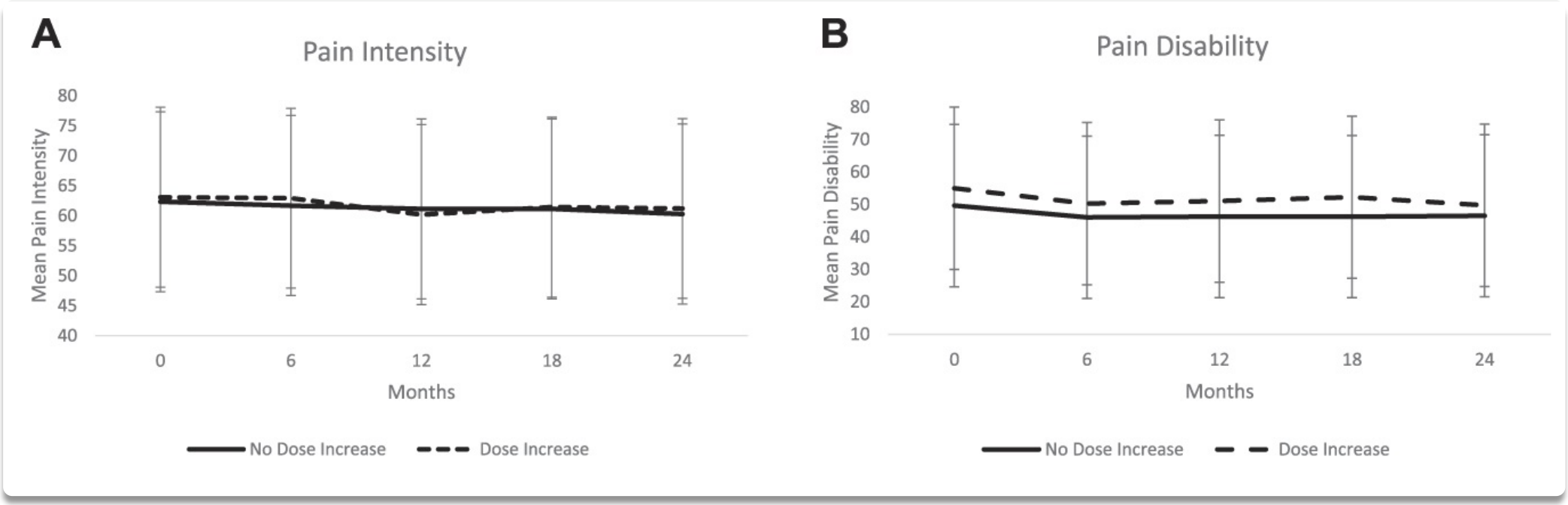
Worsening pain and decreased function

What is the next best step?

(A) Stop their Norco. They seem unable to manage their medications safely.

(B) Work with patient to develop a system to help manage medications.

(C) Go up on his Norco. What he's taking doesn't seem to be cutting it anymore.



Increases in opioid doses do not improve outcome

MORASCO ET AL, PAIN 161(6):P 1332-1340, JUNE 2020

Patient G.G. (continued)

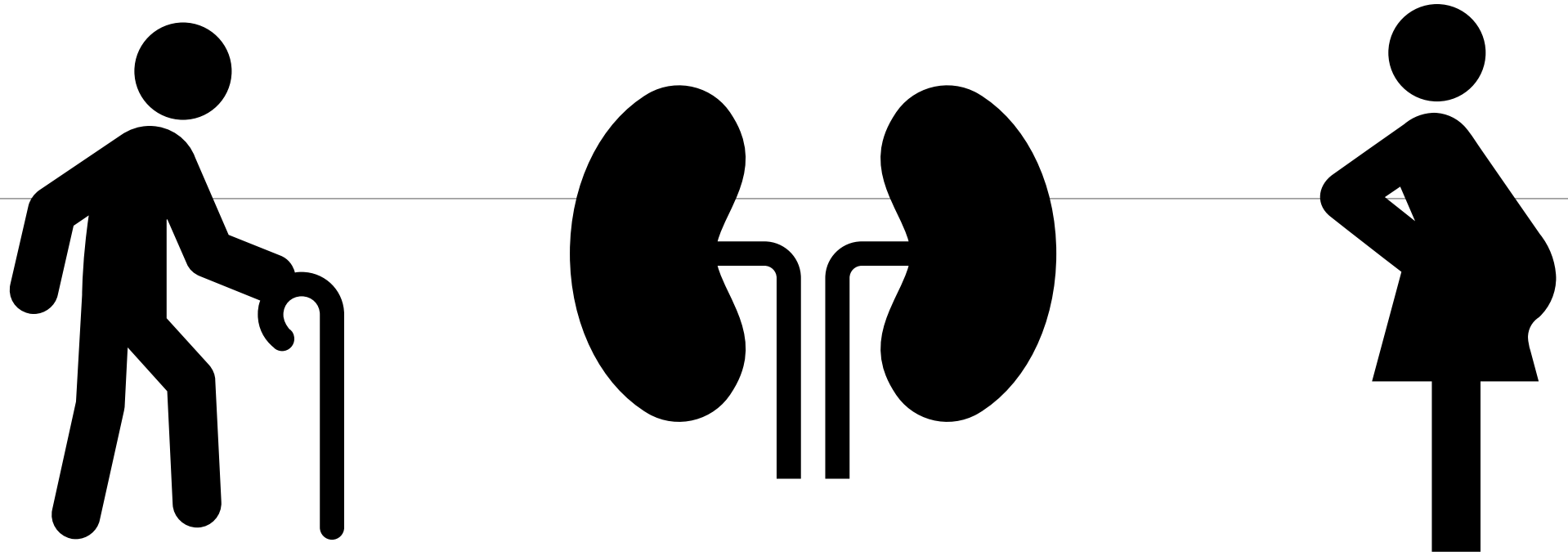
- Mediset helped
- Worsened pain/function on days with missed doses
- Additional attempts to schedule meds ineffective
- Declines taper

What is the next best step?

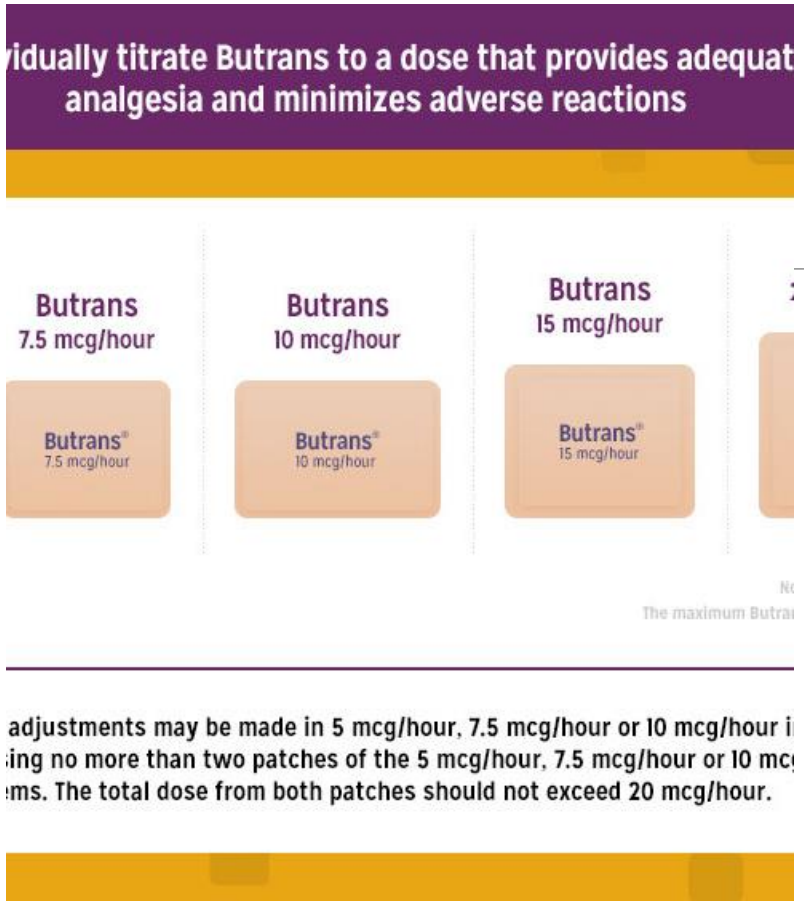
(A) It is against the law to provide more than one month supply at a time, so change your script to reflect what the patient is taking

(B) Change the patient over to an extended-release formulation like MS Contin

(C) Transition to a buprenorphine patch



Safe(r) in Special Populations



Pain Formulations in mcg

Select an opioid medication*:

- Morphine
- Hydrocodone
- Oxycodone
- Tramadol
- Codeine

*Patients using fentanyl transdermal system or extended-release hydromorphone fo
excluded from the pivotal Butrans clinical trial with opioid-experienced patients whos
prior to enrollment was between 30 and 80 mg morphine equivalents.

Select the total daily dose of Hydrocodone:

- <15 mg
- 15–40 mg
- >40 mg

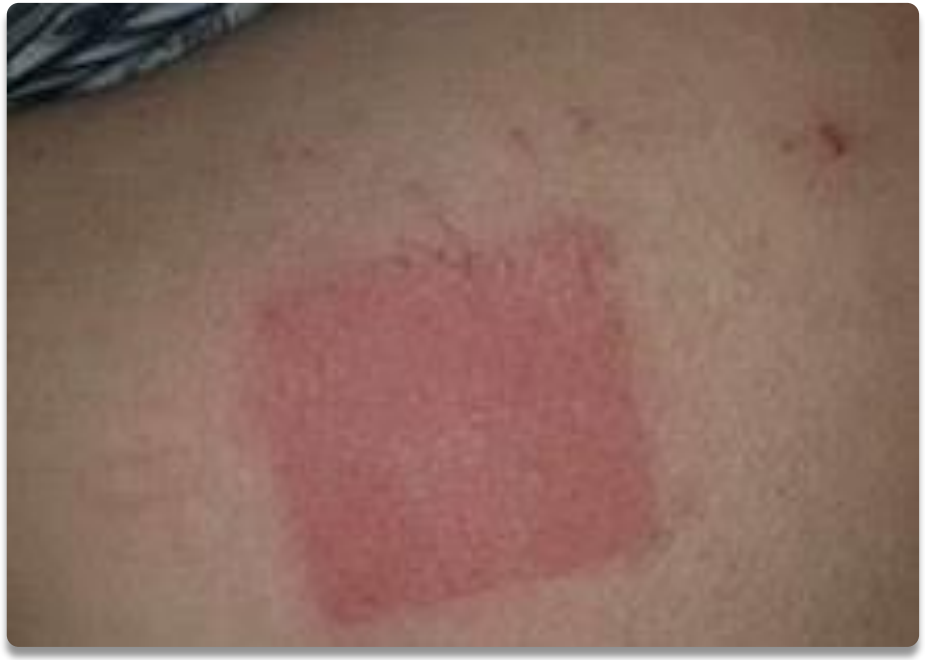
BACK

Butrans
10 mcg/hour

(not shown at actual size)

https://butrans.com/resources/opioid-conversion-tool

Pro Tips



Pain formulations of buprenorphine are unlikely to cause precipitated withdrawal

Apply patch first, then taper opioids over 2-4 days

Local site irritation can be improved with pre and post application hydrocortisone cream.

Transitions to pain formulations of buprenorphine

In *theory* you can transition up to 160 MEDD

In *practice* >80 MEDD generally require OUD formulations

Pain Formulations (mcg) of Buprenorphine

IDEAL CANDIDATES

Opioid naïve AND exhausted non-opioid pain management options

On LTOT and

- Desire transition
- Comorbidities
- Ineffective medications
- Medication burden
- Medication interactions

POOR CANDIDATES

Only intermittent pain flares

Active substance use disorders

Otherwise not candidates for long-term opioid treatments

Opioid use disorder (requires milligram dosing)

Medication Mismanagement (continued)

The Elder discussions options and patient agrees to transition to a 5mcg buprenorphine patch

Tolerates well

Good pain control and function, fewer medications overall

Recap

- Aberrant screening urine toxicology screens require confirmatory testing
- Opioid tapers should be individualized based on individual risk
- Buprenorphine patches are a great option for patients on <80 MEDD

Where do I go from here?

Introspect

- Am I engaging in a power struggle?
- Do I react similarly towards other medical condition?
- Am I avoiding difficult conversations?
- Is an adverse outcome likely?

Advocate

- Against pejorative institutional policies

Teaching Peer Evaluation (TPE) for GIM faculty

Questions? Feedback?

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https://www.cdc.gov/drugoverdose/rxrate-maps/opioid.html (1/

https://www.npr.org/sections/13.7/2015/12/14/459651340/sometimes-confusion-is-a-good-thing; 1/10/249/24)

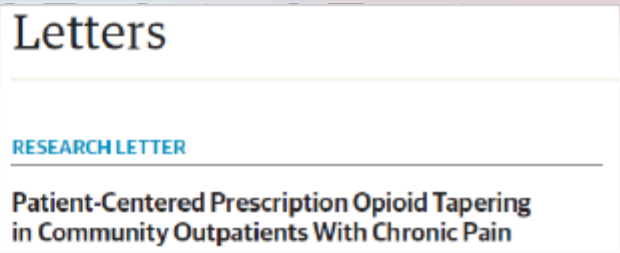
Next best step?

(a) Express condolences—MJ is a deal-breaker. You can not prescribe

(b) Offer two options—quick opioid taper or no prescription

(c) Do a quick safety assessment. If no red flags continue prescription short-term.

Patient-Centered Opioid Tapering


Letters

RESEARCH LETTER

Patient-Centered Prescription Opioid Tapering in Community Outpatients With Chronic Pain

Darnall et al., JAMA Int Med 2018

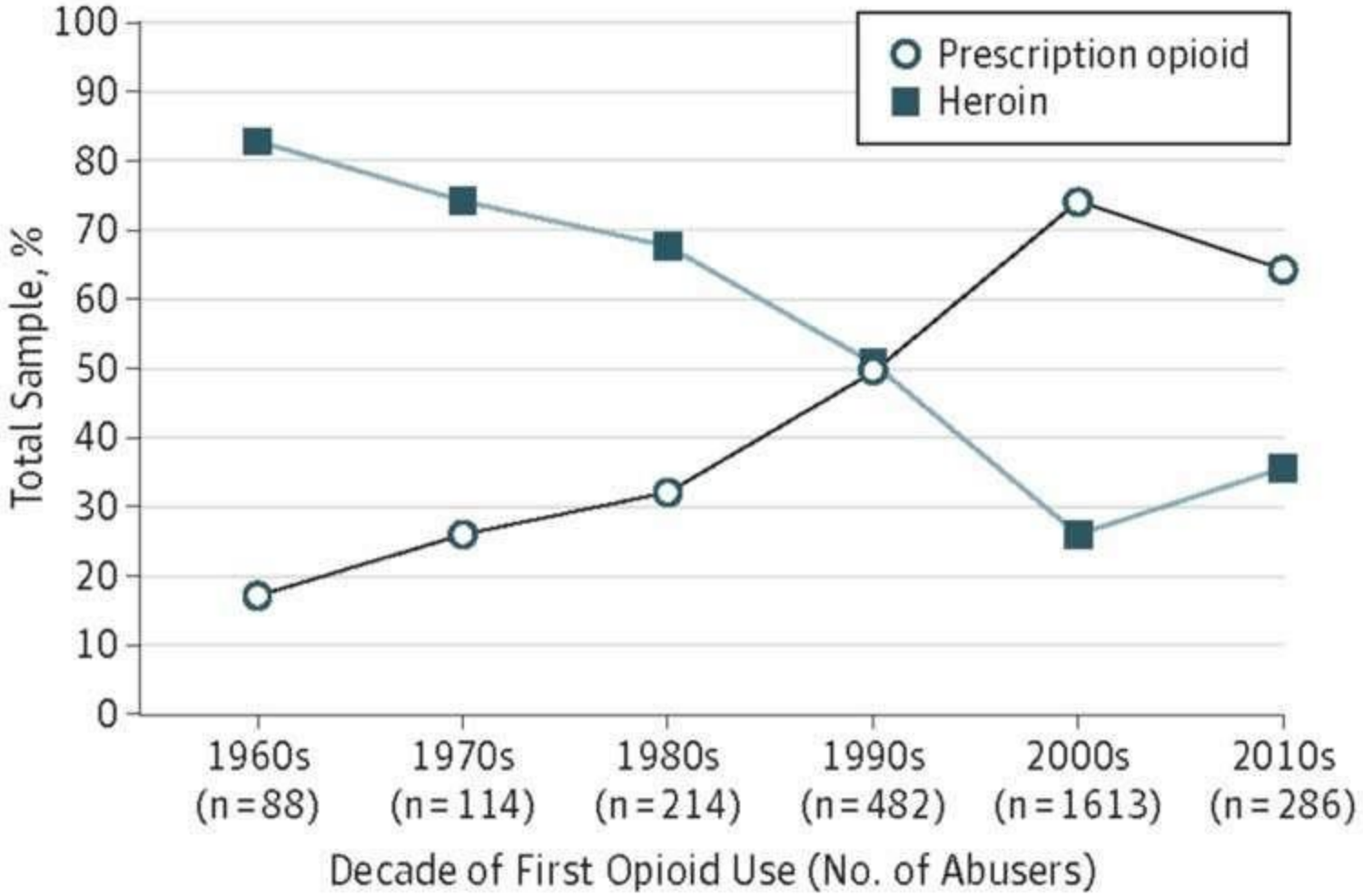
- Community-based outpatient pain specialty clinic
- High dose opioid patients were sent a letter to volunteer for opioid dose reduction with education/support
- 110 eligible, 82 (75%) enrolled; 68 provided baseline data; 51 provided 4-month follow-up
- Baseline MEDD 288 (153-587) mg, median 6 year duration (3-9) of opioid use
- After 4 months: median MEDD 150 (54-248) mg
- Starting dose, baseline pain intensity, years on opioids, or any psychosocial variable did not predict likelihood of >50% dosage reduction
- Pain intensity and pain interference did NOT increase with opioid reduction

TABLE 2. Distribution of Opioid Overdose Cases and Controls at Specific Opioid Dosage Levels

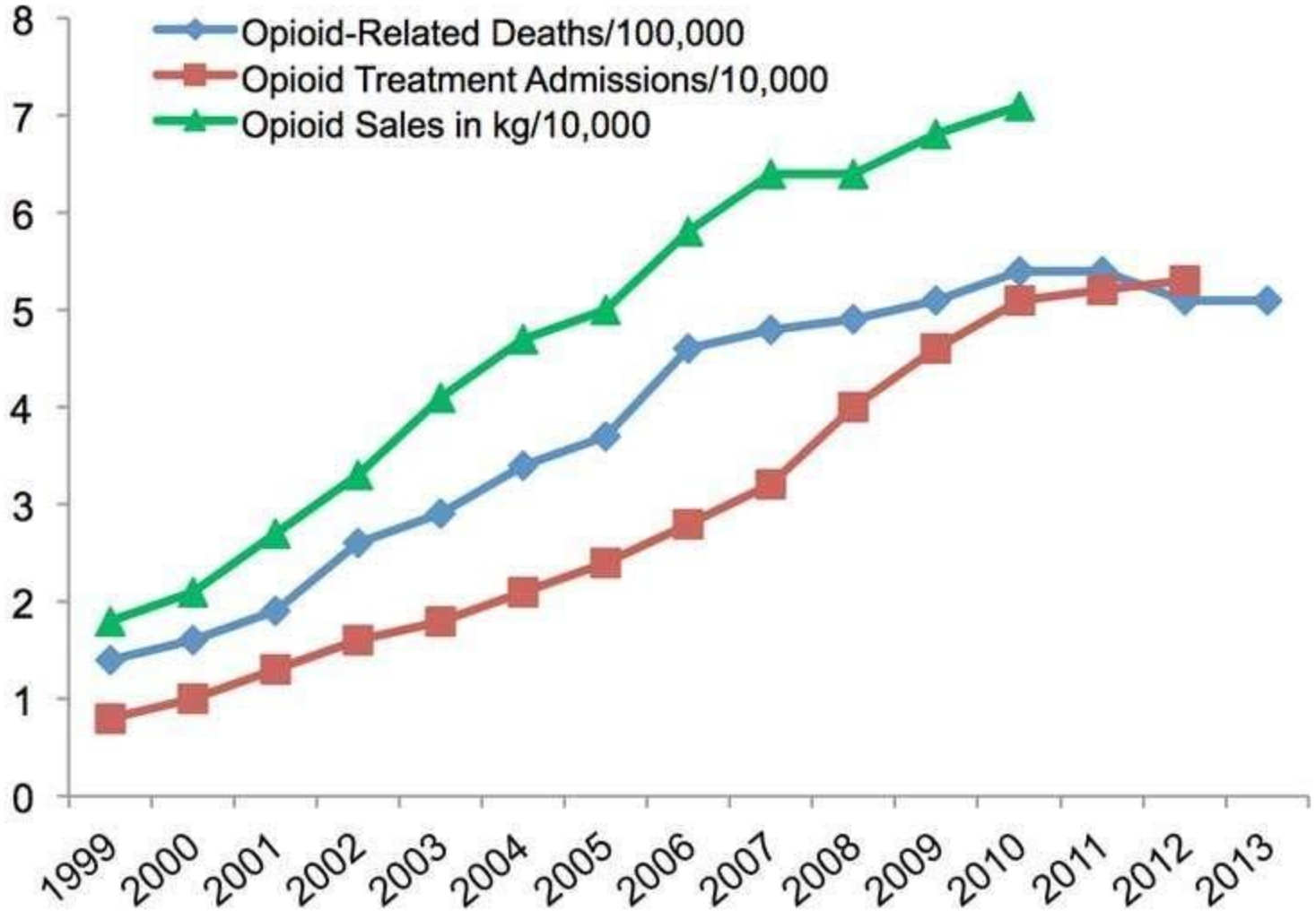
Dose in MEM	Cases Above (Sensitivity) (%)	Controls at or Below (Specificity) (%)	Likelihood Ratio (+)
10	97	14	1.12
20	87	41	1.47
30	71	63	1.94
40	66	71	2.27
50	59	76	2.50
60	48	81	2.50
70	45	82	2.50
80	41	84	2.60
90	33	88	2.67
100	31	89	2.83
110	28	90	2.82
120	21	93	3.06
130	20	95	3.67
140	17	95	3.70
150	15	96	3.67
160	15	96	3.67
170	14	96	3.45
180	12	97	3.71
190	11	97	3.43
200	10	97	3.28

MEM indicates morphine-equivalent mg.

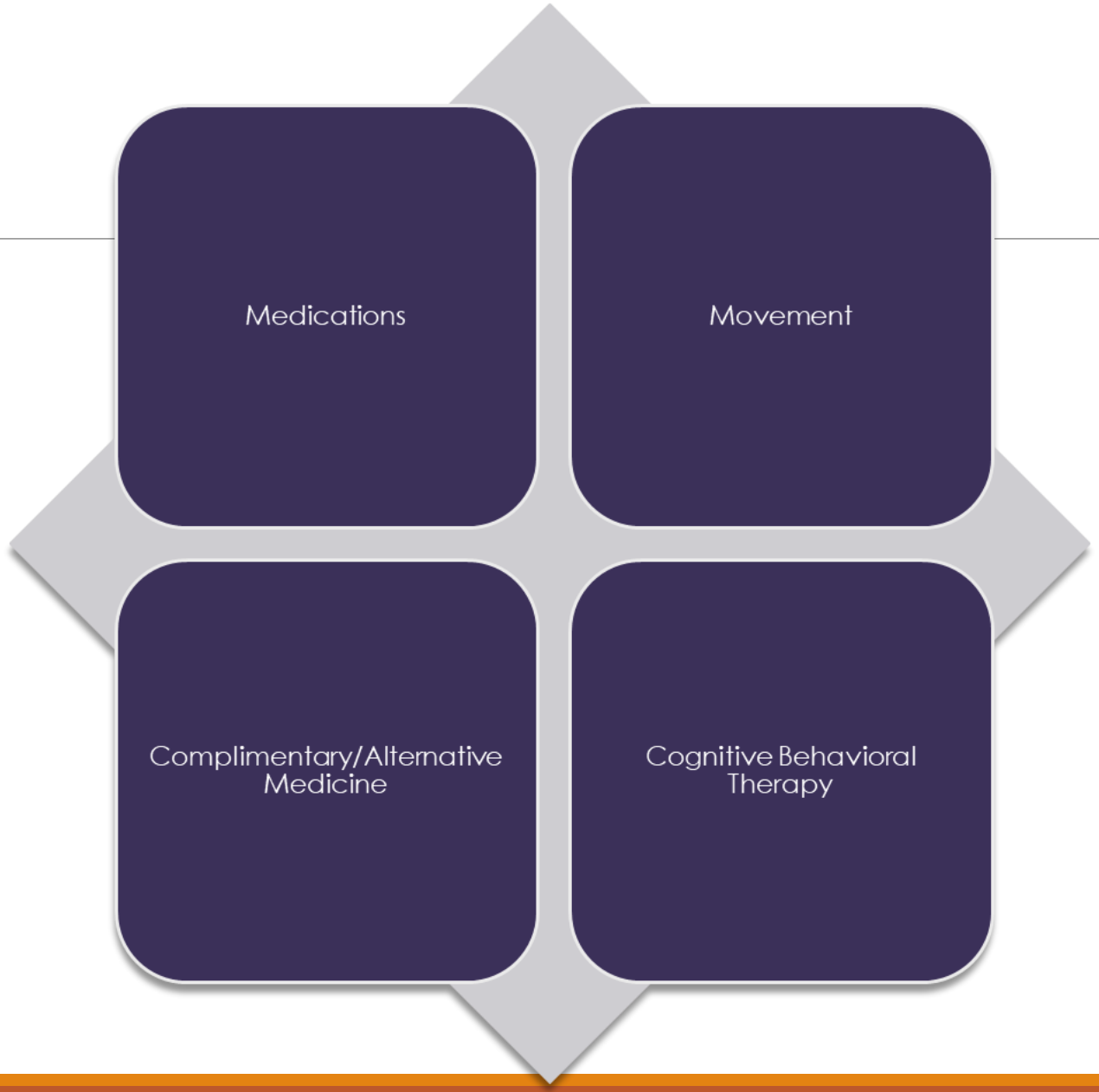
Relative risk of opioid doses



CICERO ET AL., 2014



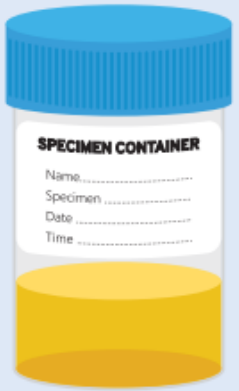
CDC Wonder, 2015; DEA ARCOS, 2015; TEDS, 2015



Chronic Pain Management

Normal characteristics of a urine sample[9,12]

- **Temperature within 4 minutes of voiding:** 90°-100°F (cup will feel warm to the touch)
- **pH:** 4.5-8.0
- **Creatinine*:** ≥ 20 mg/dL
- **Specific gravity*:** > 1.002
- **Volume*:** ≥ 30 mL

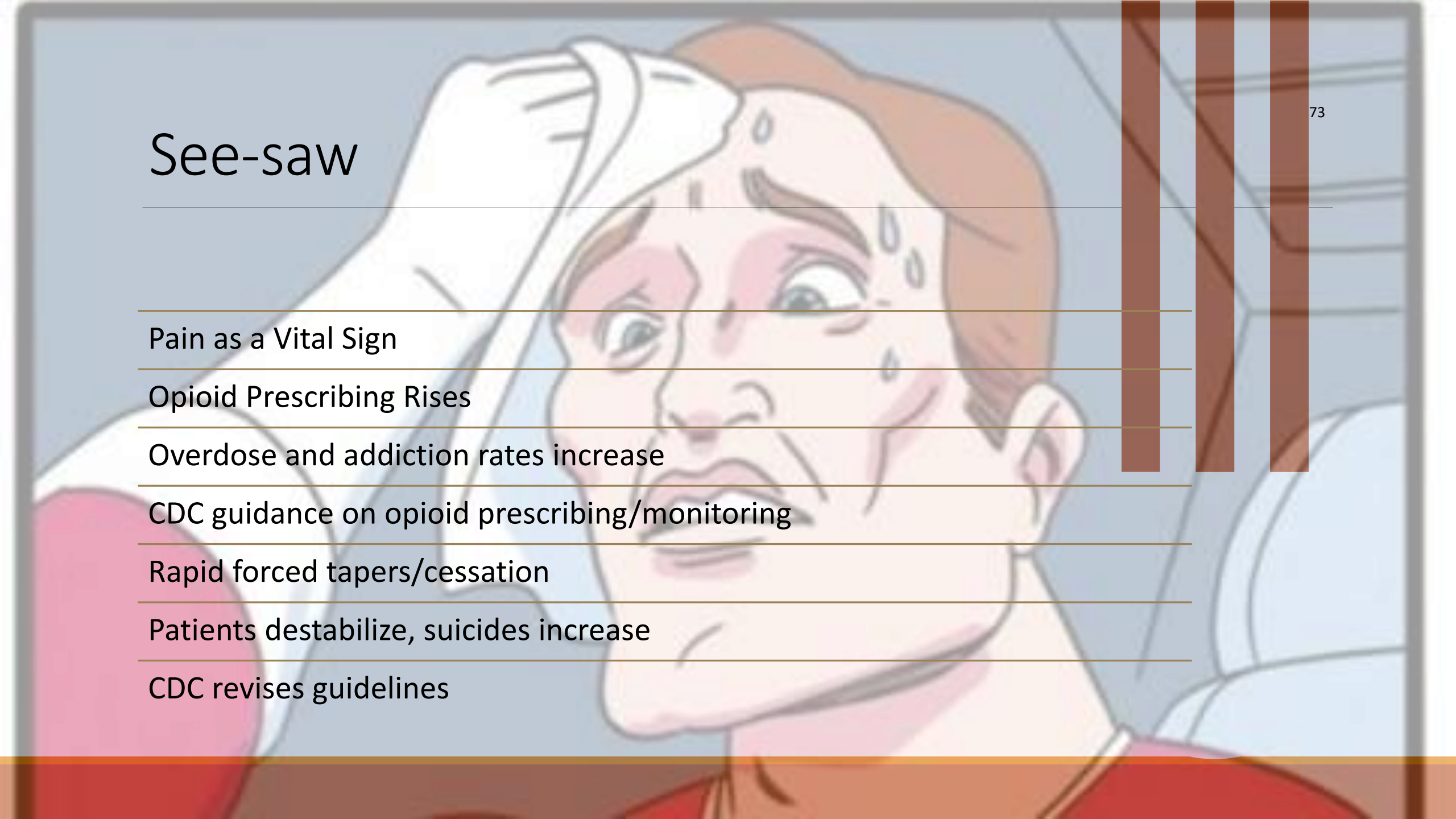


Urine drug testing specimen validity[12,13]

- Urine samples that are adulterated, substituted, or diluted may invalidate test results.
- Urine collected in the early morning is most concentrated and most reliable.
- Excessive water intake and diuretic use can lead to diluted urine samples (creatinine < 20 mg/dL).

*Abnormal creatinine, specific gravity, nitrates, or volume are not necessarily indicative of invalidity. These data should be discussed with the patient.

See-saw



- Pain as a Vital Sign
- Opioid Prescribing Rises
- Overdose and addiction rates increase
- CDC guidance on opioid prescribing/monitoring
- Rapid forced tapers/cessation
- Patients destabilize, suicides increase
- CDC revises guidelines

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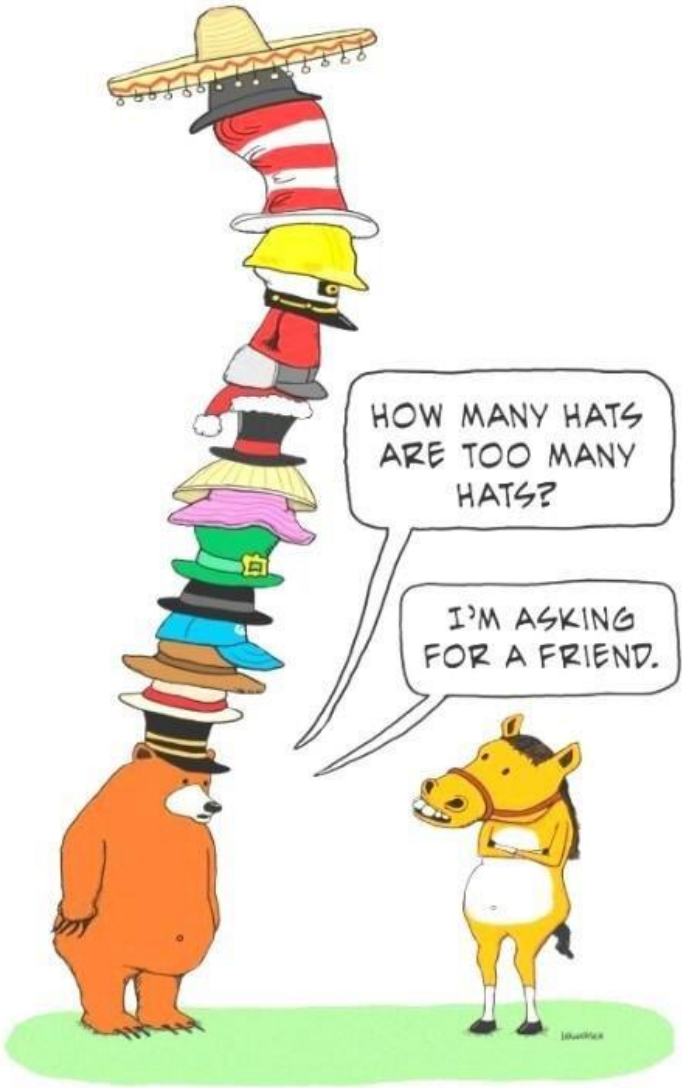
Coffin et al, “Inherited Patients Taking Opioids for Chronic Pain — Considerations for Primary Care” The New England Journal of Medicine 2022-02-17 386(7): 611-613

Monitoring of Low-Risk Patients

- PDMP check with every prescription written (Idaho state law)
- Urine toxicology screen at least yearly
- Assessment (PEG/DVPRS/other) every 3 months
  - Medication use/misuse monitoring
  - Side effect monitoring
  - Can be completed by extended team members



The Power (and curse) of Primary Care

- Dedicated, mission-driven workforce
- Broad scope of practice
- Fill in gaps in medical system
- Demands on our time >> available time

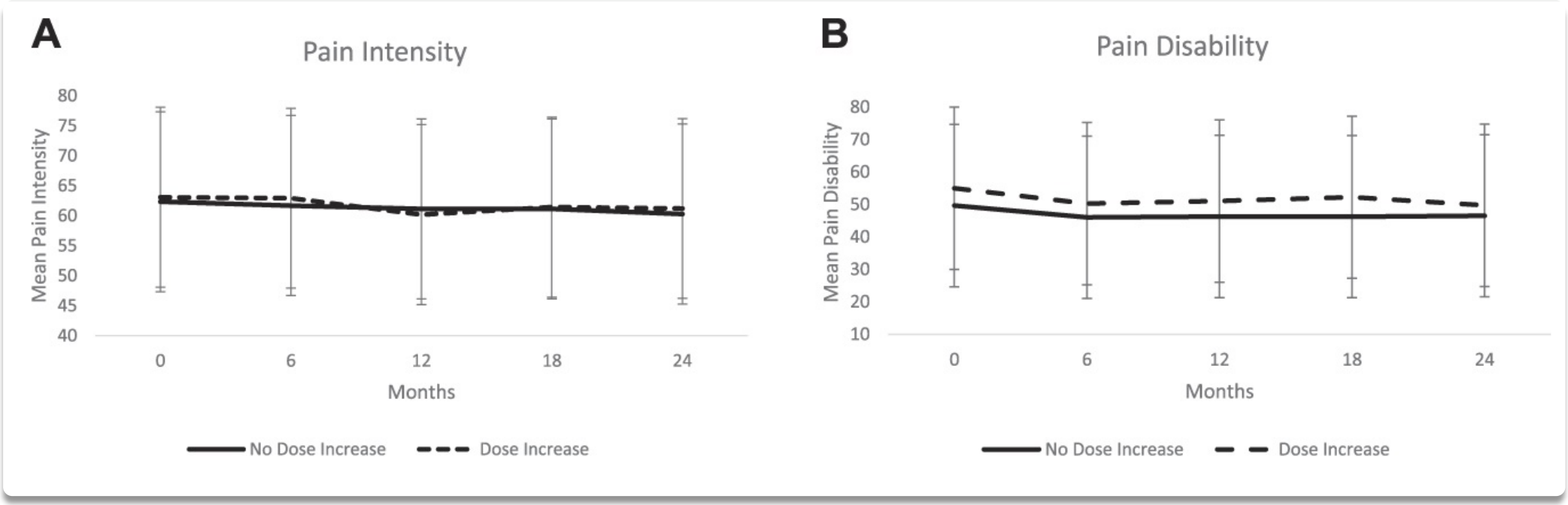
Patients *forced* to taper may do worse

No prospective studies of forced tapers on stable patients

Variable outcomes in observational studies

- Increased risk for overdose
- Increased risk for suicide

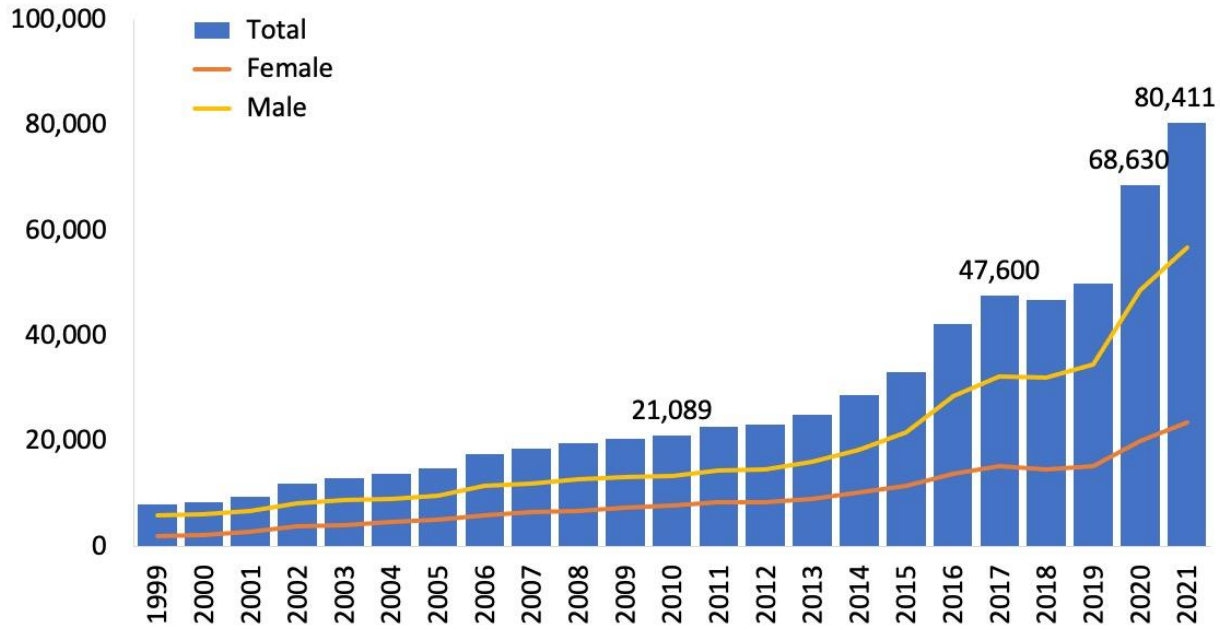
Unclear outcomes in function or qualify of life



Increases in opioid doses do not improve outcome

MORASCO ET AL, PAIN 161(6):P 1332-1340, JUNE 2020

Figure 3. National Overdose Deaths Involving Any Opioid*, Number Among All Ages, by Gender, 1999-2021



*Among deaths with drug overdose as the underlying cause, the "any opioid" subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

New Patient on Opioids: Stages of Grief

- Denial

  "They will do better if I just stop these medications"
  "If I don't write for this, somebody else will"

- Anger

  "Why do I spent my time cleaning up other people's messes?"
  "I don't have time to do anything else in our visits!"
  "Why would anybody have started opioids for this indication in the first place?"

- Bargaining

  "Maybe we can just do a taper?"
  " Can I just defer to pain clinic?"

- Acceptance

“Clinicians should **avoid abrupt discontinuation** of opioids, especially for patients receiving high dosages…”

-CDC revised guidelines 2022

Checklist

I can provide sufficient safety monitoring

Cannot be reasonably met elsewhere

This medication will help my patient function