

Opioid Prescribing: Where Are We? Stuck Between a Rock and a Hard Place



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Conflict of Interest

- ▶ No financial or advisory relationships related to this activity

Learning Objectives



- ▶ Why are we stuck?
- ▶ What do we do?
 - ▶ Ways to mitigate adverse effects and reduce harm
- ▶ What next?

Initial Problem: Inadequate Pain Treatment

- ▶ End-of-life, terminal cancer patients
 - ▶ Inadequate Pain Management: A Suicidogen (“Dr. Jack Kevorkian: Friend or Foe?” Clin Pharm editorial 1997)
- ▶ Nursing home patients with chronic, non-cancer pain
- ▶ Patients with addiction or severe mental illness
- ▶ Health disparities in treatment of pain
 - ▶ Eastern Cooperative Oncology Group Minority Outpatient Pain studies (Cleeland et al, Ann Int Med 1997; VonRoenn et al, Ann Int Med 1993)
 - ▶ Patients with HIV/AIDS
 - ▶ Elderly with fractures

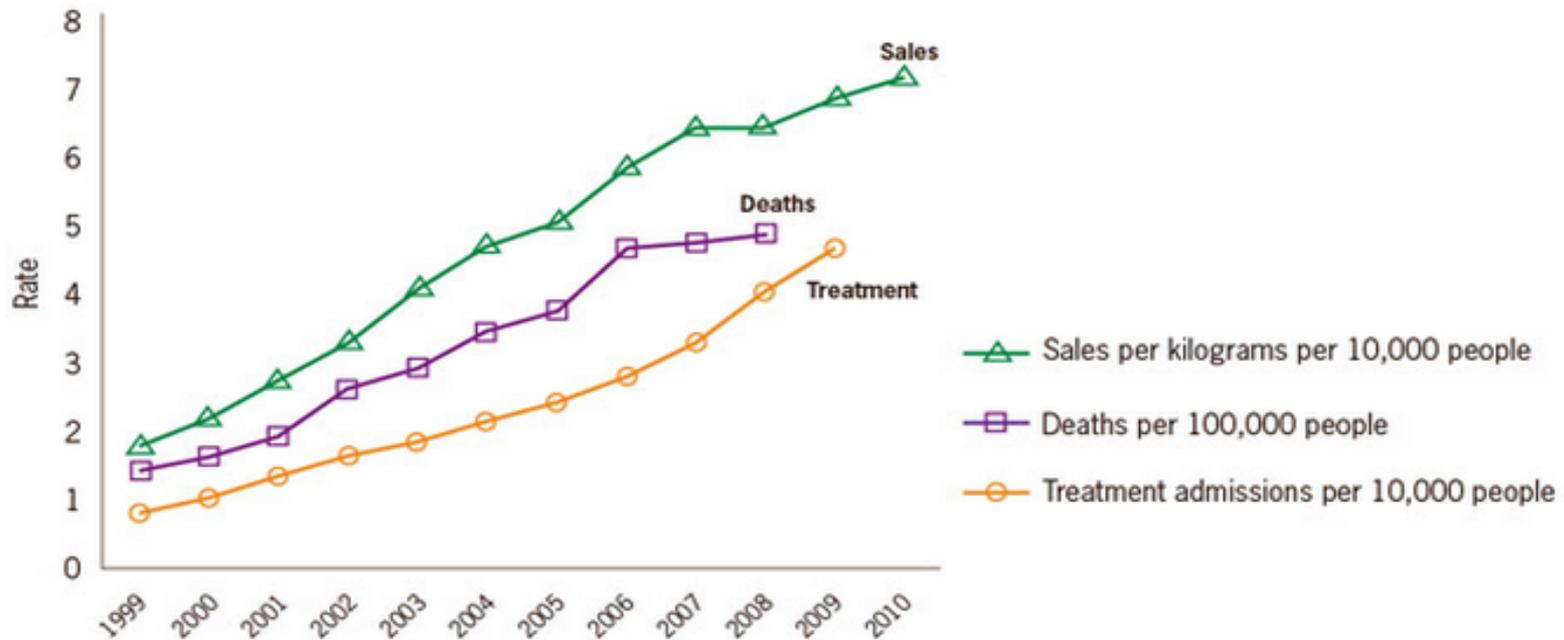
1980's and 1990's Message to Physicians

- ▶ **“American opiophobia: customary underutilization of opioid analgesics.”** Adv Alcohol Subst Abuse. 1985 Fall-1986 Winter;5(1-2):163-73.
 - ▶ “American physicians markedly undertreat severe pain based on an irrational and undocumented fear that appropriate use will lead patients to become addicts.”
- ▶ Legal case of Bergman v Chin, 2001: Doctor found guilty of negligent care for inadequate pain treatment
 - ▶ “Failure to treat pain can now be something that physicians are held accountable for.” (Wash Post, 6/15/01)
- ▶

Fast Forward.....

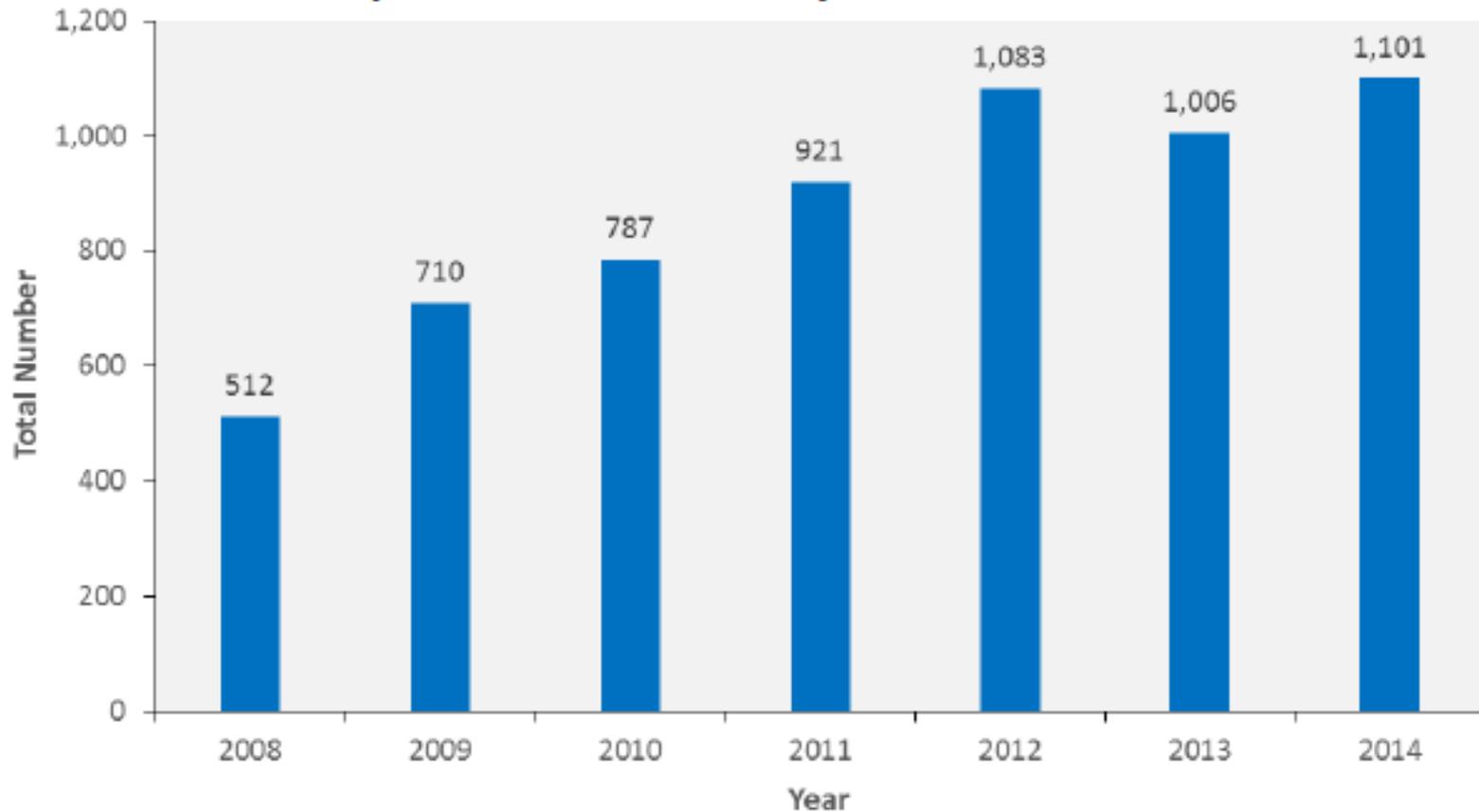
- ▶ **CDC MMWR, January 1, 2016:**
 - ▶ “More persons died from drug overdoses in the United States in 2014 than during any previous year on record.”
- ▶ “Murder trial begins for alleged ‘pill mill’ doctor after string of patients overdose on painkillers” (Miller, Wash Post, 9/1/15)
- ▶ **Maryland Legislature 2016:**
 - ▶ HB 6: Criminal Law - Improper Prescription of Controlled Dangerous Substance Resulting in Death

Rates of prescription painkiller sales, deaths and substance abuse treatment admissions (1999-2010)



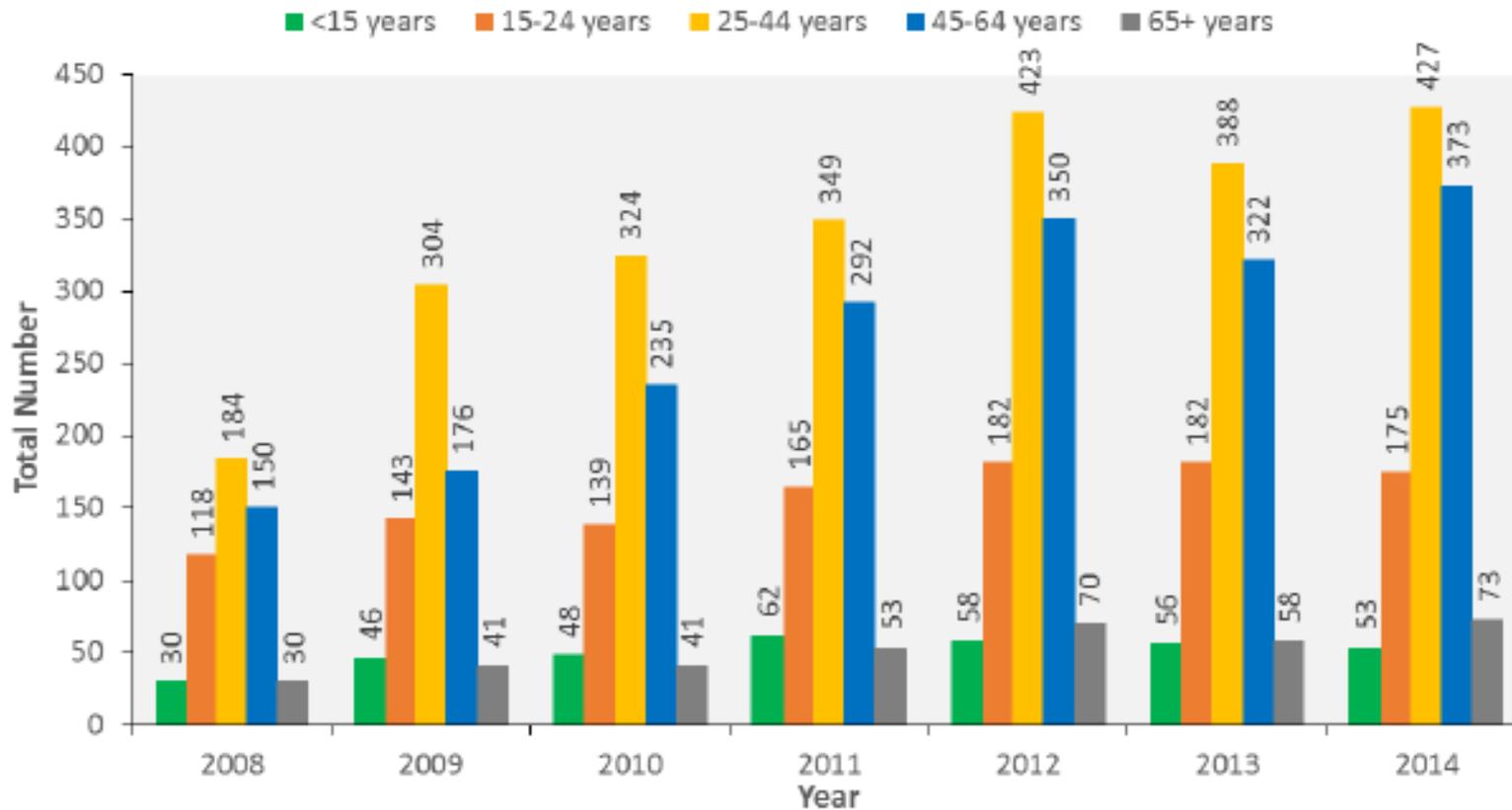
SOURCES: National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009

Figure 63. Total Number of Prescription Opioid-related Emergency Department Visits: Maryland, 2008-2014



DHMH, Data Report: Drug and Alcohol-Related Emergency Department Visits in Maryland 2008-2014, Released 9/15

Figure 69. Number of Prescription Opioid-related Emergency Department Visits by Age Group: Maryland, 2008-2014



DHMH, Data Report: Drug and Alcohol-Related Emergency Department Visits in Maryland 2008-2014, Released 9/15

Reversal of overall mortality rate among 45-54 white Americans

- ▶ Mortality rate in this age group decreased 2% per yr for 20 years since 1978
- ▶ Since 1998, increase in mortality rate per yr (34 per 100,000)
- ▶ Since 1998, decrease in mortality rate for AA and Latino (200 per 100,000 and 60 per 100,000)
- ▶ First increase in mortality rate among mid-life Americans since 1950

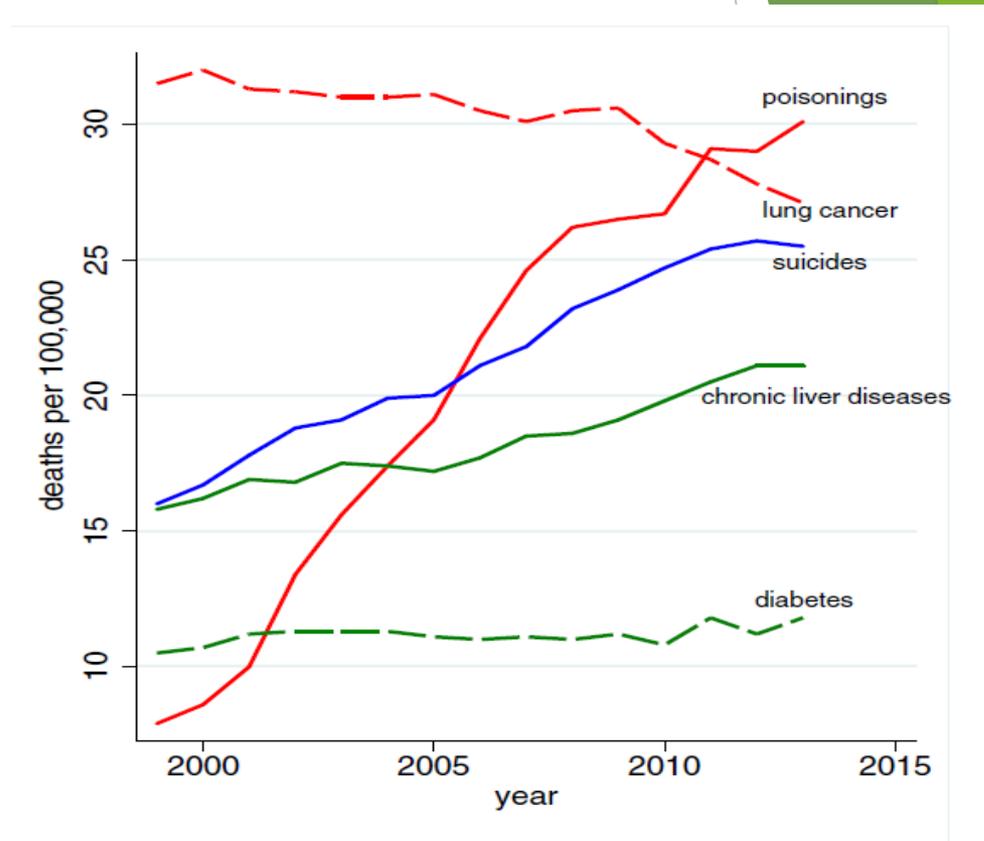
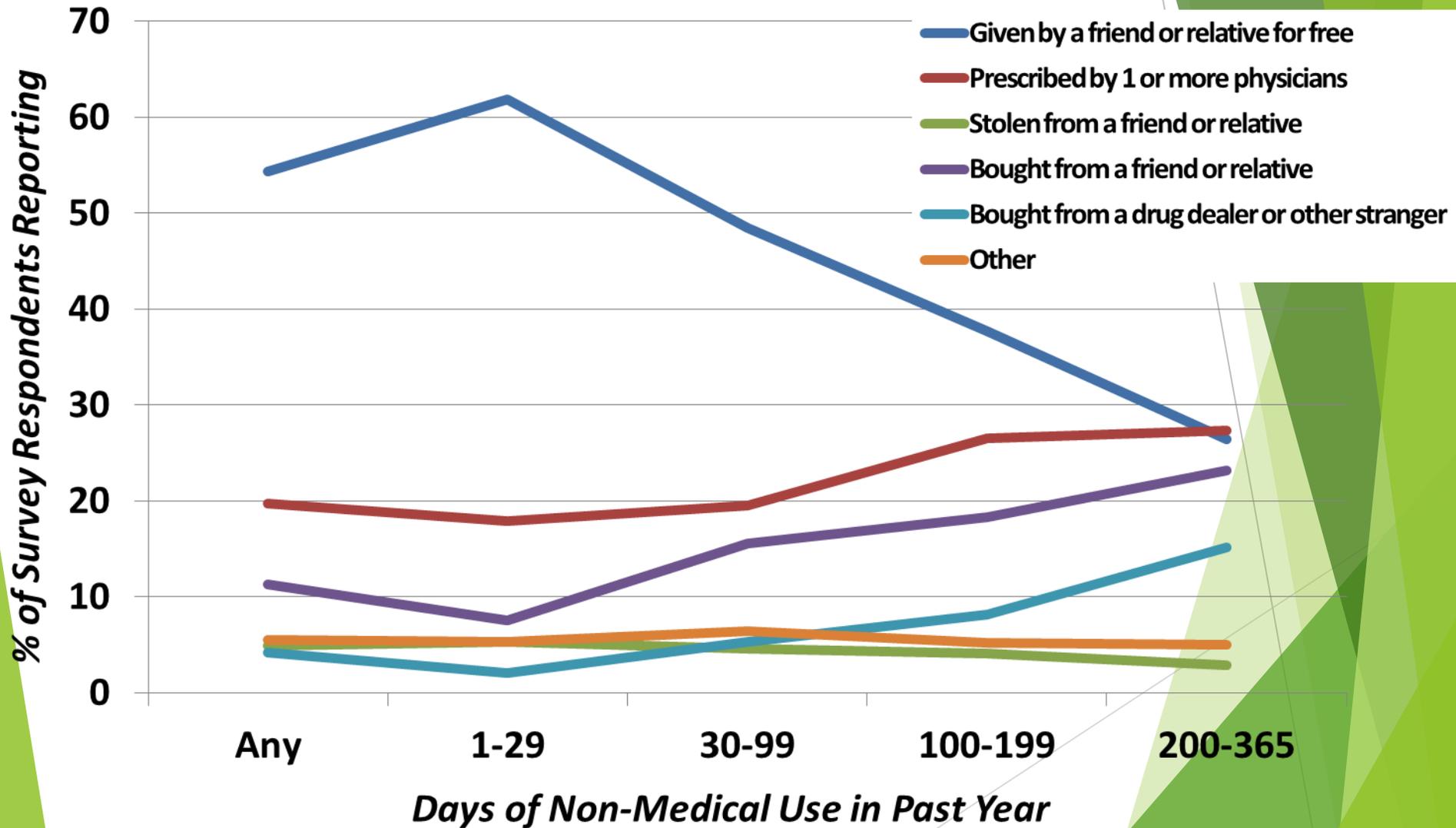


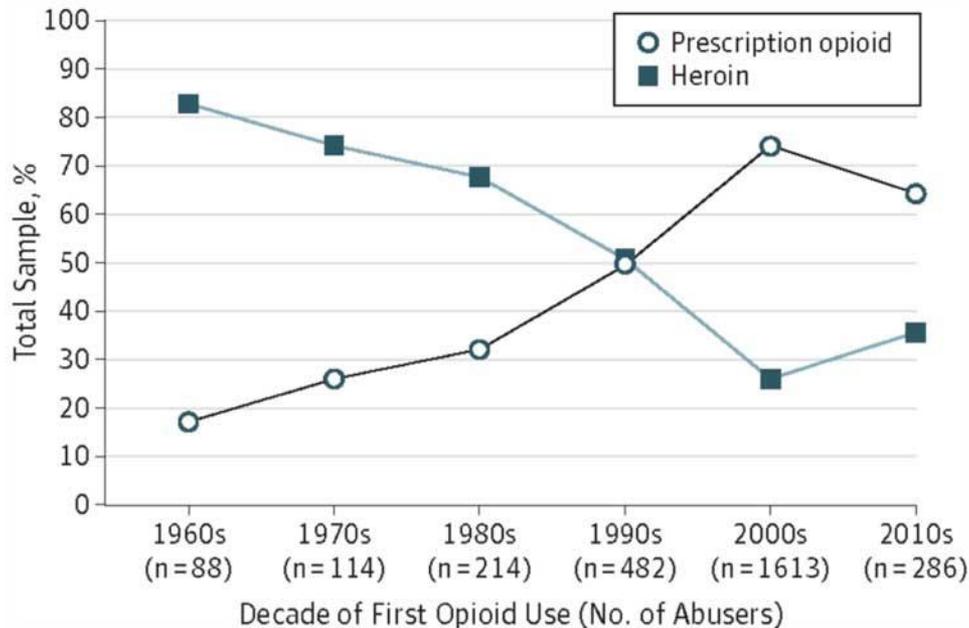
Fig. 2. Mortality by cause, white non-Hispanics ages 45-54.

Source of Opioid Pain Reliever Most Recently Used by Frequency of Past Year Non-Medical Use (NSDUH, 2008-2011)



From Prescription Opioids to Heroin....

- ▶ NSDUH 2002 to 2012 (Muhuri et al, SAMHSA, 2013):
 - ▶ Rate of heroin initiation among prior NMPR users 19 times higher than those who without prior NMPR use (0.39 vs. 0.02 percent).
- ▶ Cicero et al, JAMA Psychiatry 2014



Rock is Still There.....

- ▶ Pain is common
 - ▶ About 100 million adults in US
- ▶ Pain is expensive
 - ▶ Almost \$650 billion annually in medical costs and lost productivity (IOM, 2011)

So what to do?

Federal and State Responses

- ▶ IOM 2011: Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research
- ▶ National Pain Strategy 2015
- ▶ National Drug Control Strategy
- ▶ CDC Draft Opioid Prescribing Guidelines released 12/14/15

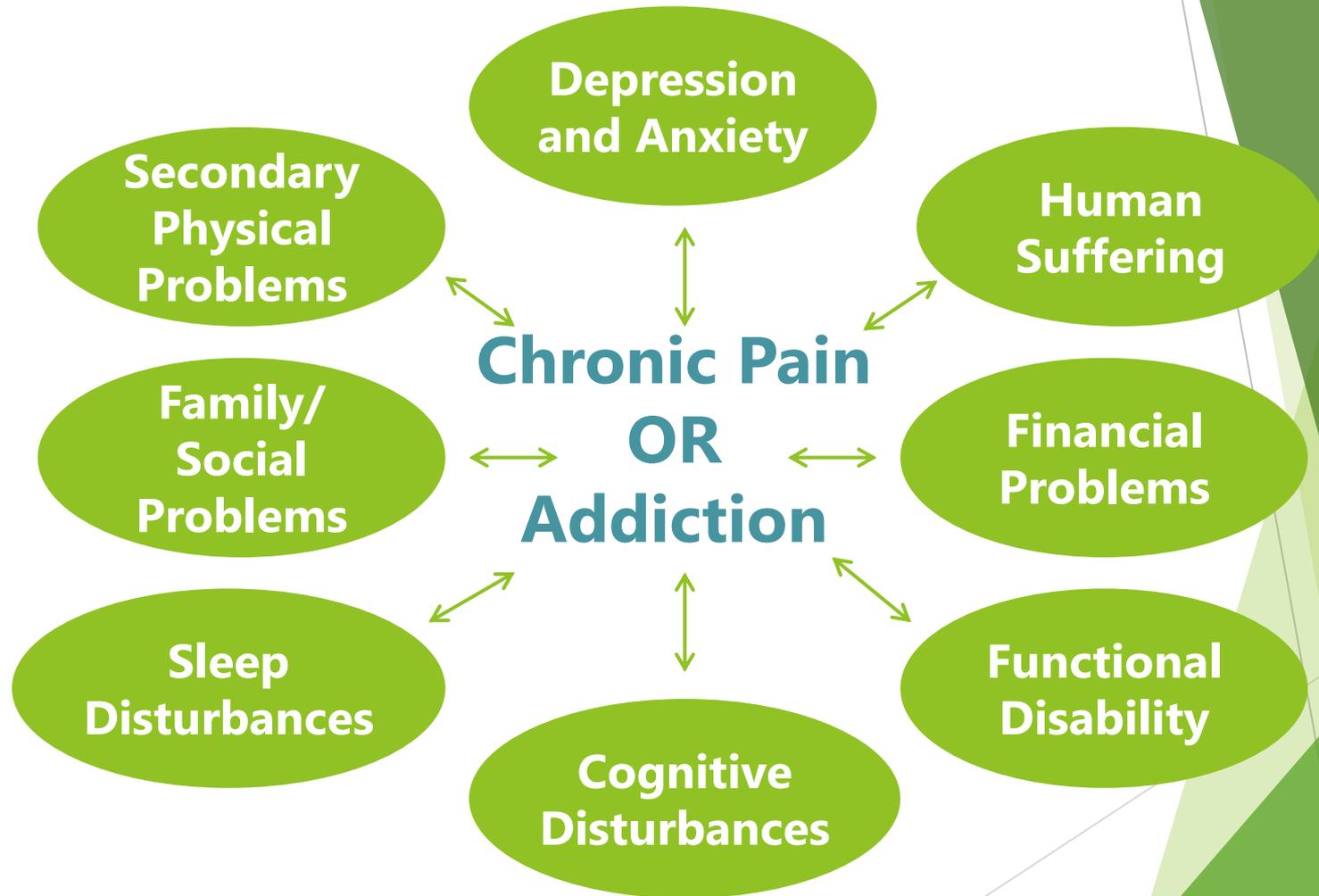
What do clinicians do?

Guiding Principle

“The study of disease and of identity cannot be disjoined. To restore the human subject at the centre—the suffering, afflicted, fighting, human subject— we must deepen a case history to a narrative or tale; only then do we have a ‘who’ as well as a ‘what’, a real person, a patient, in relation to disease—in relation to the physical.”

Oliver Sacks, Preface to *The Man Who Mistook His Wife for a Hat*

Pain and Addiction



Pharmacologic Pain Interventions



Efficacy of Long Term Opioids

- ▶ Cochrane Database Opioid Review:
 - ▶ High discontinuation rates due to adverse events or insufficient pain relief
 - ▶ Weak evidence suggesting clinically significant pain relief for those able to continue
 - ▶ Inconclusive evidence for improvement in quality of life or functioning
 - ▶ Many minor adverse events occurred
 - ▶ Serious adverse events, including iatrogenic opioid addiction, rare
- ▶ CDC draft prescribing guidelines evidence review:
 - ▶ “Evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited”

Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, Schoelles KM. Long termterm opioid management for chronic noncancer pain. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006605.

Proposed 2016 Guideline for Prescribing Opioids for Chronic Pain. **ID:** CDC-2015-0112-0002

Iatrogenic Opioid Addiction

- ▶ Difficult to establish true incidence and prevalence rates
- ▶ Prevalence of addiction in general population around 10%
- ▶ Addictive potential of prescription opioids: National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)
 - ▶ Age-dependent
 - ▶ 25-35% of non-medical users of prescription opioids develop opioid use disorder



Addiction

- ▶ A primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations.*
- ▶ A chronic, relapsing disease characterized by compulsive drug seeking and use despite harmful consequences as well as neurochemical and molecular changes in the brain.**
- ▶ A brain disease that affects behaviour.

*American Society of Addiction Medicine

**National Institute on Drug Abuse (NIDA)

Substance Use Disorder Diagnostic Criteria, DSM-V

More use than intended	Excessive time spent in acquisition
Unsuccessful efforts to cut down	Craving for the substance
Activities given up because of use	Continued use despite consistent social or interpersonal problems
Failure to fulfill major role obligations	Tolerance*
Use despite negative effects	Withdrawal*
Recurrent use in hazardous situations	

Severity measured by number of symptoms; 2-3 mild, 4-6 moderate, 7-11 severe

*** These do not apply if the medication is prescribed**

Disorders of Hedonic Tone

Usual sense of well being,
happiness, pleasure, contentment

Set by mesolimbic system

Range: Euphoria $\leftarrow \rightarrow$ Dysphoria

Altered in those vulnerable to SUDs

Further altered by addiction and
chronic pain

Human Condition



Physical Dependence Vs. Addiction

- ▶ “Physical dependence is neither sufficient nor necessary to diagnose addiction.” Dr. Howard Heit
- ▶ Physical dependence is a neuropharmacological phenomenon while addiction is both a neuropharmacological AND behavioral phenomenon.
- ▶ Patients need to be informed about physical dependence and withdrawal potential

Definitions: Complex Physical Dependence

“Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long term pain treatment that requires consideration when deciding whether to embark on long term opioid pain therapy as well as during the course of such therapy.

Opioid Dependence vs Addiction

A Distinction Without a Difference?

Ballantyne J, Sullivan M, Kolodny A, *Arch Intern Med*, 2012

Aberrant Drug-Related Behaviors

- ▶ The old “drug-seeking” behaviors
- ▶ Not diagnostic for opioid addiction
- ▶ Raises risk level for addiction
- ▶ Cannot be ignored

Aberrant drug-related behaviors

Less Serious

Most serious

Aggressively complaining about need for medication

Asking for specific medications by name

Asking for non-generic medication

Request to have medication dose increased

Taking a few extra, unauthorized doses on occasion

Claiming multiple pain medicine allergies

Visiting multiple doctors for controlled substances prescription

Hoarding medication

Frequent calls to clinic

Using a controlled substance for non-pain relief purposes (e.g. to enhance mood, sleep aid)

Frequent unscheduled clinic visits for early refills

Consistent disruptive behavior when arrives in clinic

Obtaining controlled substances medications from family members

Pattern of lost or stolen prescriptions

Anger or irritability when questioned closely about pain

Unwilling to consider other medications or non-pharmacologic treatments

Frequent unauthorized dose escalations after being told that is inappropriate

Injecting an oral formulation

Forging prescriptions

Unwilling to sign controlled substances agreement

Selling medications

Use of aliases

Refuse diagnostic workup or consultation

More concern about the drug than their medical problem that persists beyond the third clinic visit

Obtaining controlled substance analgesics from illicit sources

Consistently calling outside of clinic hours or when a particular physician is on call who prescribes controlled substances

Deterioration at home or work or reduction of social activities because of medication side effects

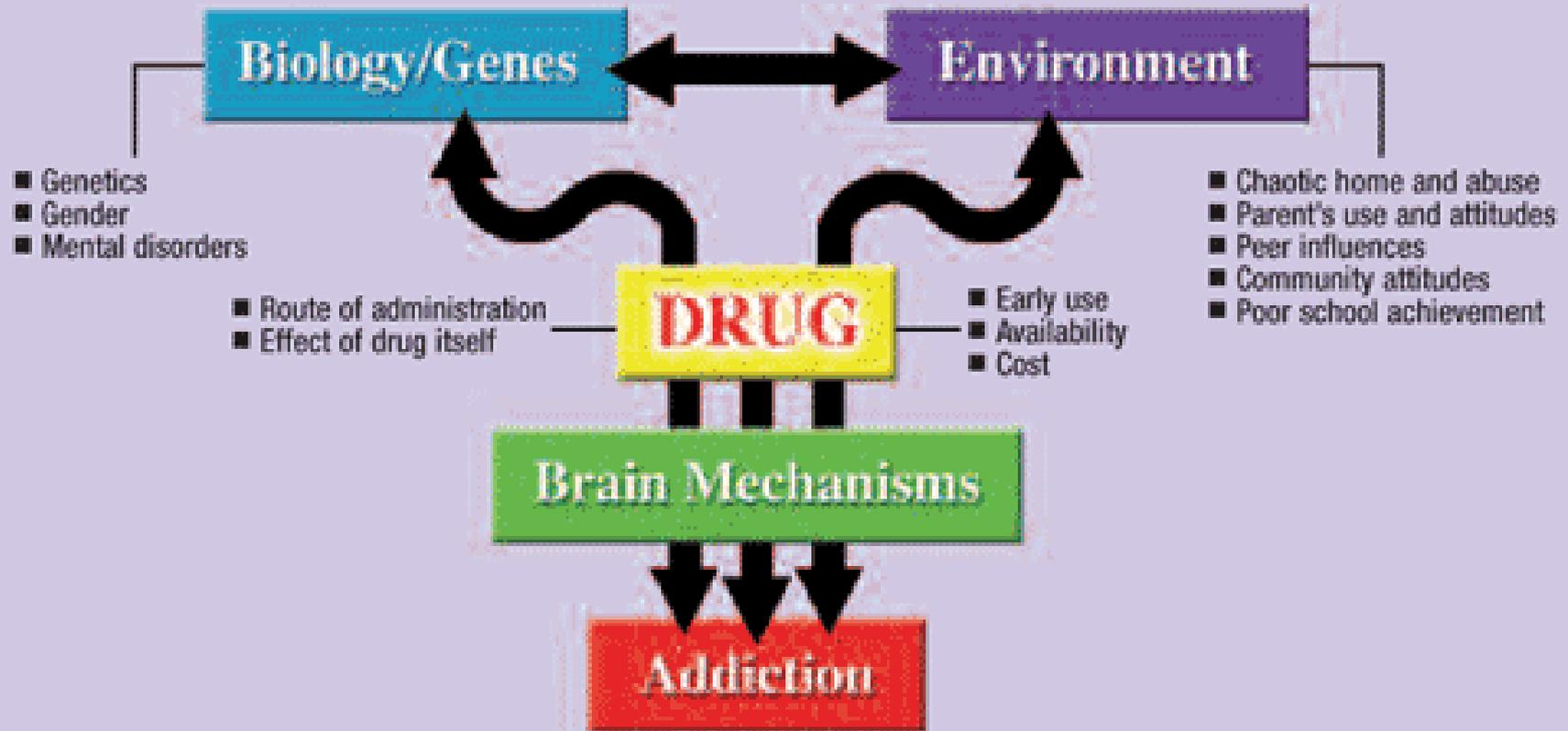
Differential Diagnosis of Aberrant Drug-Related Behaviors

- ▶ Complex physical dependence
- ▶ Opioid use disorder
- ▶ Phenomenon of inadequately treated pain resulting in aberrant drug-taking behaviors
- ▶ Psychiatric disorders
- ▶ Criminal activity

Put in data on opioid prescriptions continuing even after non fatal overdose on them

Addiction: A Perfect Storm

RISK FACTORS



Lifetime Prevalence and Odds Ratios of Mental Disorders by Substance Use Disorder: ECA

Comorbid Disorder	Alcohol		Drug	
	%	O.R.	%	O.R.
Any mental	36.6	2.3	53.1	4.5
Schizophrenia	3.8	3.3	6.8	6.2
Affective	13.4	1.9	26.4	4.7
Anxiety	19.4	1.5	28.3	2.5
Antisocial	14.3	21.0	17.8	13.8

(Regier et al., JAMA 264:2511-2518, 1990)

Pain: Psychiatric Co-Morbidity

**Depression and
Pain Comorbidity-
Bair,et al Arch
Intern Med.
2003;163:2433-
2445**

- **56 Articles(14D > P,
42P > D)**
- **65% with Depression
(Dep.) have significant
Pain**
- **~50% in Pain Clinic
have Dep.**
- **Pain negatively affects
Dep. Outcomes**
- **Dep. associated with
decreased pain mgt.**

Impact of Trauma

- ▶ Adverse Childhood Experiences Study (ACE)
 - ▶ Over 17,000 adults in Kaiser Health Plan
 - ▶ Assessed 8 ACEs
 - ▶ Developed ACE score (0,1,2,3,4, ≥ 5)
 - ▶ Prevalence of number of negative health outcomes associated with increasing ACE scores
 - ▶ Headaches
 - ▶ Substance use disorders
 - ▶ Obesity and DM
 - ▶ Psychiatric disorders

Opioid Addiction Treatment

- ▶ 1974: Narcotic Addict Treatment Act
 - ▶ Recognized use of opioid agonist to treat opioid use disorder - defined “maintenance” treatment
 - ▶ Established NIDA
 - ▶ Separate DEA classification for physicians who dispense opioids for addiction treatment
- ▶ 2000: Drug Addiction Treatment Act (DATA 2000)
- ▶ 2002: Buprenorphine first drug approved by FDA under DATA 2000
- ▶ 2006 and 2010: FDA approval of injectable naltrexone for alcohol use disorder and then opioid use disorder relapse prevention

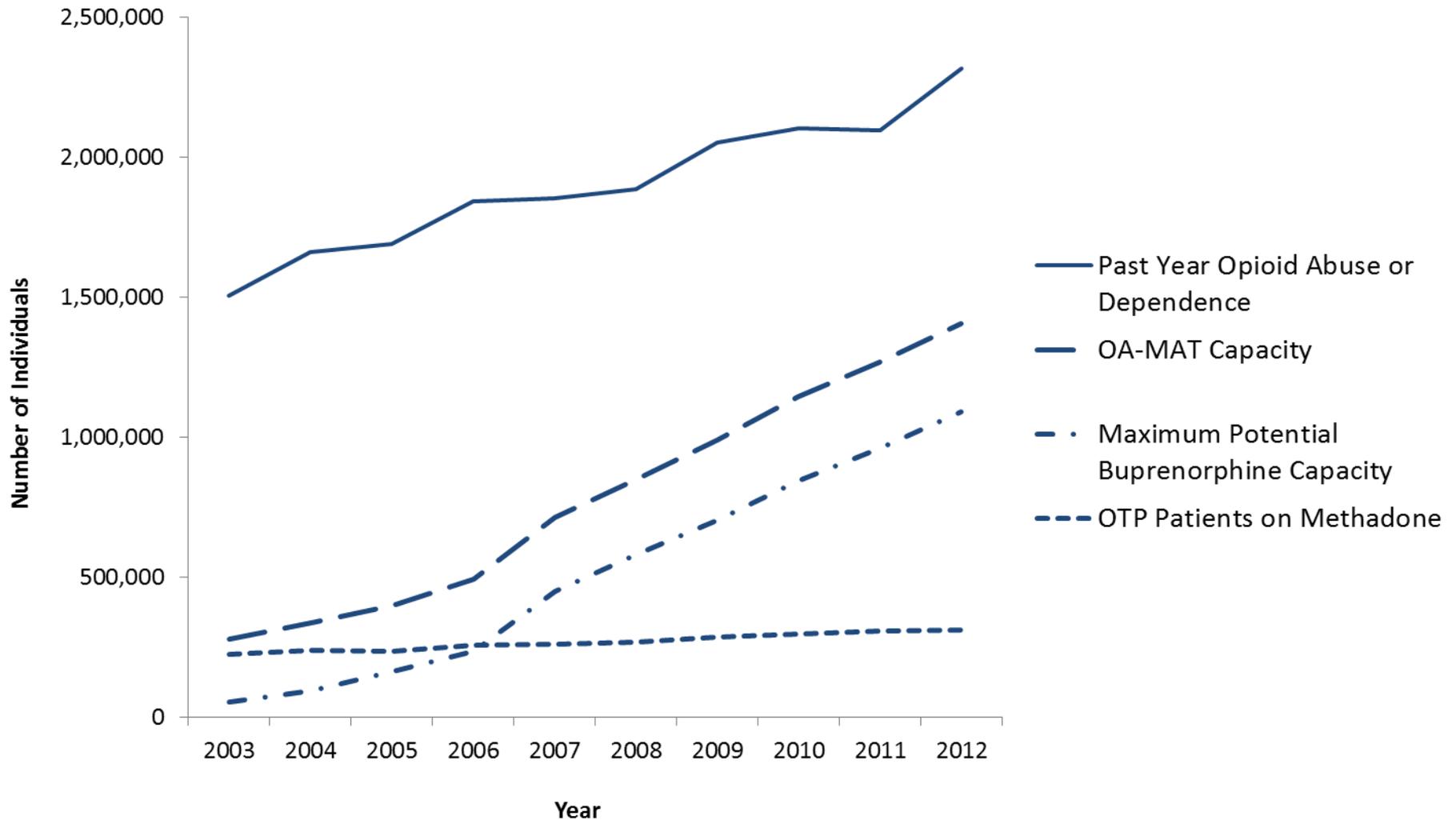
Buprenorphine

- ▶ Partial opioid agonist
- ▶ Only parenteral and transdermal formulations approved for pain
- ▶ Sublingual formulation approved for opioid addiction and used off-label for pain
- ▶ Small studies in Europe and Asia demonstrate analgesic efficacy of SL formulation at low doses (<5mg at q6-8hr dosing) in opioid naïve post-operative patients
- ▶ Ceiling effect for respiratory depression
- ▶ **Analgesic ceiling effect is UNCERTAIN**
 - ▶ Differing data on analgesic ceiling effect in animal models
 - ▶ No published data indicating an analgesic ceiling in humans

Edge WG et al. Anaesthesia. 1979

Moa G et al. Acta Anaesthesiol Scand. 1990

Treatment need for opioid addiction exceeds capacity for opioid agonist medication assisted treatment



Risk Factors for Opioid Overdose

- ▶ Older age
- ▶ Presence of underlying cardiopulmonary conditions
- ▶ History of overdose
- ▶ Dose of prescription opioid

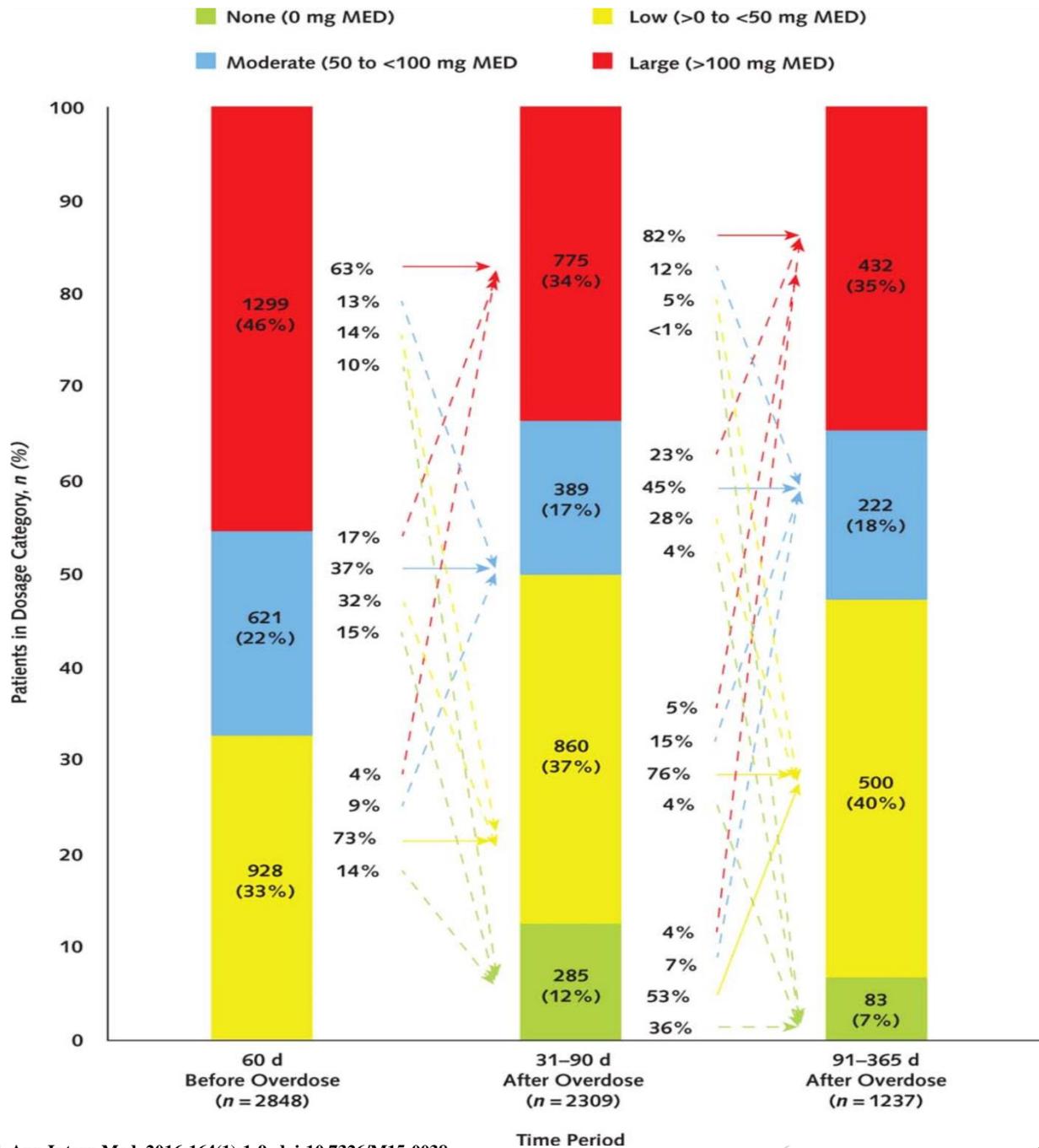
Table 3. Hazard Ratios Between Recent Opioid Doses and Overdose*

Opioid Dose	Patients Who Overdosed, n	Person-Years	Overdose Rate (95% CI) per 100 000 Person-Years	Hazard Ratio for All Overdose Events (95% CI)†	Hazard Ratio for Serious Overdose Events (95% CI)‡
None	6	16 780	36 (13–70)	0.31 (0.12–0.80)	0.19 (0.05–0.68)
1 to <20 mg/d	22	13 770	160 (100–233)	1.00	1.00
20 to <50 mg/d	6	2311	260 (95–505)	1.44 (0.57–3.62)	1.19 (0.40–3.60)
50 to <100 mg/d	6	886	677 (249–1317)	3.73 (1.47–9.50)	3.11 (1.01–9.51)
≥100 mg/d	11	614	1791 (894–2995)	8.87 (3.99–19.72)	11.18 (4.80–26.03)
Any opioid use	45	17 582	256 (187–336)	5.16 (2.14–12.48)	8.39 (2.52–27.98)

* Opioid-related overdose death or nonfatal event.

† Adjusted for smoking, depression, substance abuse, comorbid conditions, pain site, age, sex, recent sedative-hypnotic prescription, and recent initiation of opioid use.

‡ Opioid-related overdose death or serious nonfatal event (n = 40).



Minimize High Risk Combinations

- ▶ Benzodiazepines
- ▶ Muscle relaxants
- ▶ Promethazine
- ▶ Clonidine
- ▶ Quetiapine (Seroquel®)

Naloxone Co-Prescribing

- ▶ Evzio autoinjector
- ▶ Intra-nasal naloxone (Narcan)
- ▶ Intramuscular solution

Rx: Naloxone 0.4 mg/mL or 1mg/mL (IN)

Quantity: 2 single-use vials (IM)/autoinjector (Evzio) or 2 x2 mL as prefilled Luer-lock needleless syringes (IN)

(Add 2x intranasal Mucosal Atomizing Device (MAD 300) for IN)

Sig: For suspected opioid overdose, inject/spray 1 mL in shoulder or thigh/each nostril. Repeat after 3 min if no or minimal response.

Refills: Prescriber preference

Prescription Drug Monitoring Program (PDMP)

- ▶ PDMP in Maryland embedded in Health Information Exchange (HIE)
 - ▶ <https://crisphealth.org/>
- ▶ PDMP Center of Excellence at Brandeis University:
 - ▶ “Evidence continues to accumulate that prescription drug monitoring programs (PDMPs) are effective in improving clinical decision-making, reducing doctor shopping and diversion of controlled substances, and assisting in other efforts to curb the prescription drug abuse epidemic.”

1 Prescription Drug Monitoring Program Center of Excellence at Brandeis, Briefing on PDMP Effectiveness, Updated September 2014.

<http://www.pdmpexcellence.org/sites/all/pdfs/Briefing%20on%20PDMP%20Effectiveness%203rd%20revision.pdf>

PDMP Effectiveness

- ▶ Ohio ED Study:
 - ▶ 41% who reviewed PDMP data altered prescribing for patients receiving multiple simultaneous opioid prescriptions.
 - ▶ Of these, 61% prescribed no opioids or fewer opioids than originally planned, while 39% prescribed more.
- ▶ Prescriber survey in RI / CT:
 - ▶ PDMP users more likely than non-users to take clinically appropriate action in response to suspected cases of prescription drug misuse or diversion
 - ▶ Actions included conducting drug screens or referring them to addiction treatment.

1 Baehren, D. et al., A statewide prescription monitoring program affects emergency department prescribing behaviors.

Annals of Emergency Medicine, 2010 Jul; 56(1):19-23. <http://www.ncbi.nlm.nih.gov/pubmed/20045578>

2 Green, T. et al. How does use of prescription monitoring program change medical practice? Pain Medicine, 2012.

Oct;13(10):1314-23. <http://www.ncbi.nlm.nih.gov/pubmed/22845339>

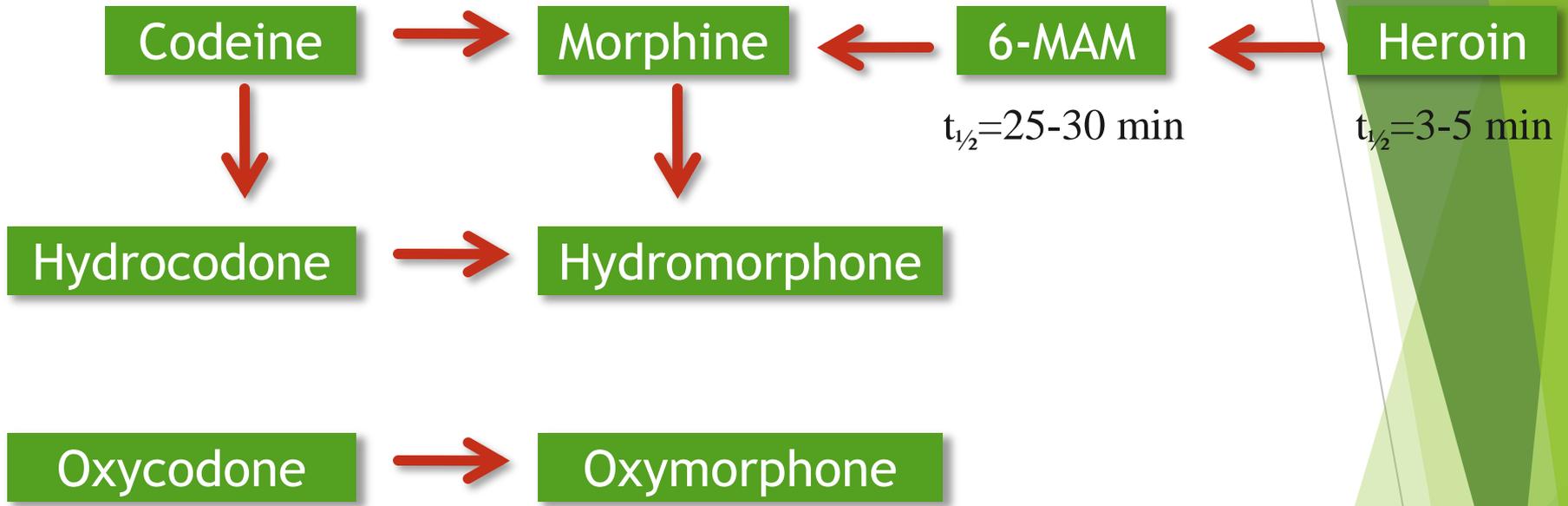
Urine Toxicology Testing

- ▶ Purpose:
 - ▶ Confirm patient history prior to initiating opioids
 - ▶ Monitor adherence to prescribed opioids
 - ▶ Forensic testing
- ▶ Two types of assays
 - ▶ Immunoassay
 - ▶ Specific drug identification (GC/MS or LC/MS)

What should you test for?

- ▶ Opioids
 - ▶ Whichever opiate being prescribed
 - ▶ Include metabolites
- ▶ Test synthetic opioids separately
- ▶ Benzodiazepines
- ▶ Cocaine
- ▶ Marijuana
- ▶ Barbiturates
- ▶ Amphetamines/methamphetamines

Opioid Metabolism



Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care*. Ed 4. 2010.

Slide source: ASAM 2013

Resources

- ▶ Maryland Society of Addiction Medicine (MDSAM)
 - ▶ State chapter of American Society of Addiction Medicine
Mdsam.org
- ▶ MedChi Addiction Committee
- ▶ Local Health Department
 - ▶ For addiction assessment and treatment services information and referrals
- ▶ Maryland Behavioral Health Administration
<http://bha.dhmf.maryland.gov/SitePages/Home.aspx>
- ▶ PCSS-MAT and PCSS-O
<http://pcssmat.org/>
<http://pcss-o.org/>

NARCOTIC ADDICTION — A SYSTEMIC
DISEASE CONDITION

ERNEST S. BISHOP, M.D.

VOLUME LX
NUMBER 6

I realized that the patients were people sick of a definite disease condition, and that until we recognized, understood and treated this condition, and removed the stigma of mental and moral taint from those cases in which it did not exist, we should make little headway toward the solution of our problem.

JAMA. 1913;60(6):431-434.

Summary

- ▶ At another turning point in medicine and public health
- ▶ Chronic pain and addiction are both complex, multifaceted diseases with overlapping features
- ▶ Physicians play a significant role in both: weighing benefits with safety/side effects
- ▶ Mitigating risks and side effects from opioids is possible
 - ▶ Knowing our patients
 - ▶ Using available tools
- ▶ Advocating for patients and ourselves

Questions?

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