Adventures
In Pain Management!

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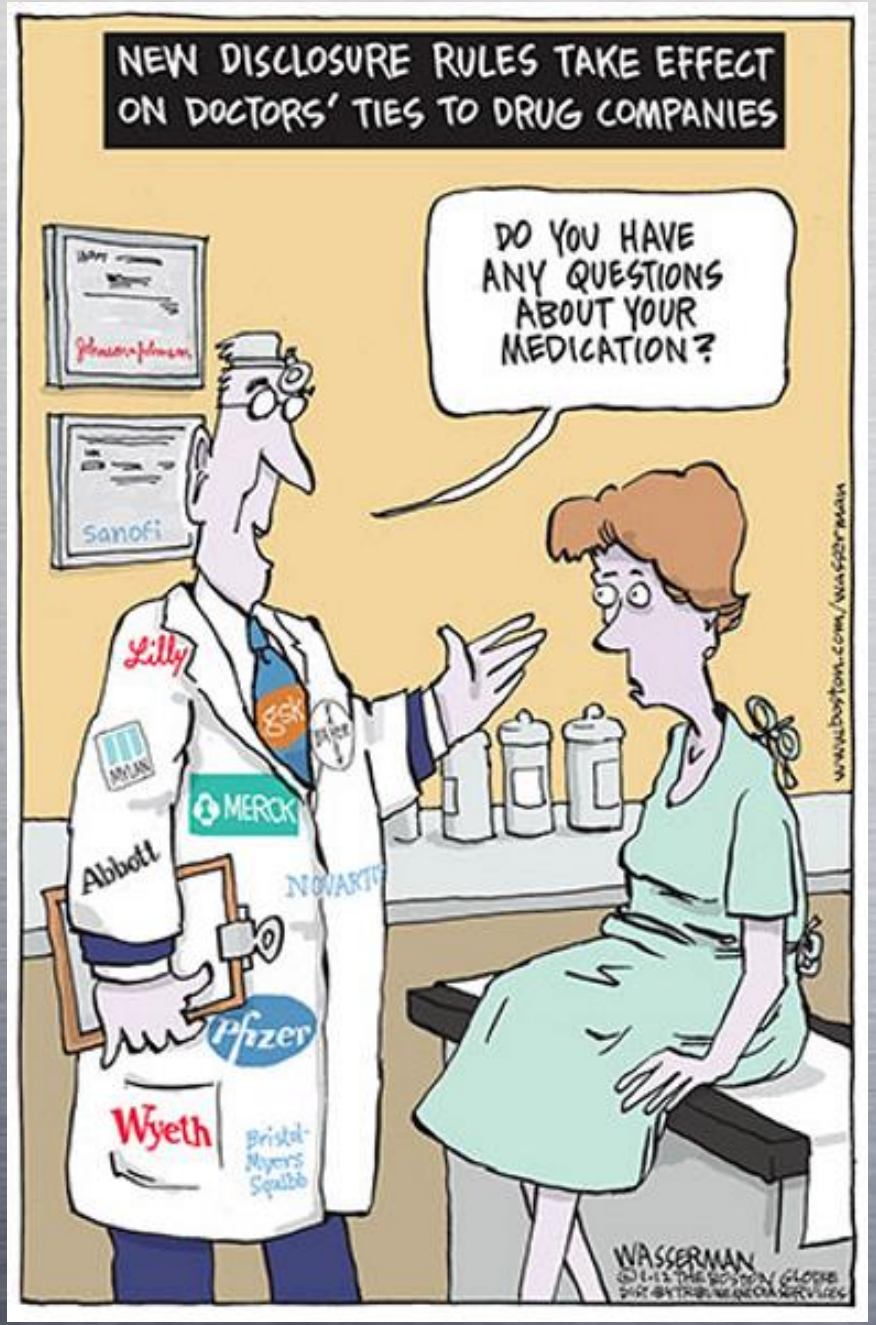
Knowledge that will change your world



Disclosures

Dr. Bailey has no relevant financial conflicts of interest or disclosures.

Objectives

- **Review current issues in pain management**
- **Consider how regulations impact how we practice**
- **Consider current pain management guidelines and how well are they achieving the goal of reducing overdose deaths**
- **Ponder future directions and how we need to adapt**

Pain Epidemiology

Prevalence

Heart Disease	**25.8 million**
Stroke	**16.3 million**
Cancer	**7 million**
Diabetes	**11.7 million**
Total	**60.8 million**
Chronic Pain	**116 million**

http://www.painmed.org/patient/facts.html#incidence

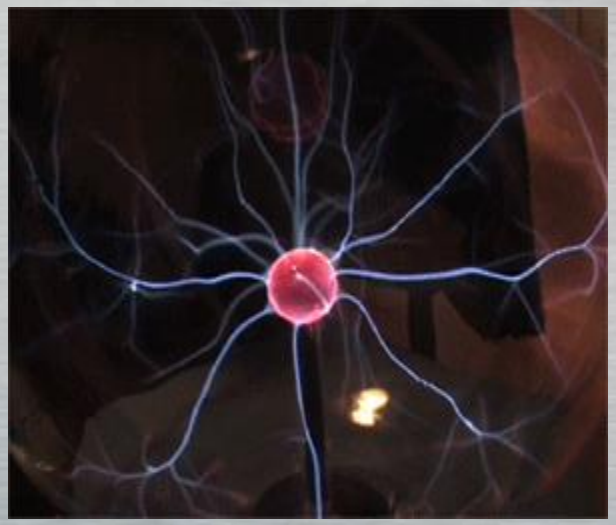
Costs of Chronic Pain

The total annual cost of health care due to chronic pain ranges from $560 billion to $635 billion which combines the medical costs of pain care and the economic costs related to disability days and lost wages and productivity.

Institute of Medicine Report from the Committee on Advancing Pain Research, Care, and Education: Relieving Pain in America, A Blueprint for Transforming Prevention, Care, Education and Research. The National Academies Press, 2011.

Pain

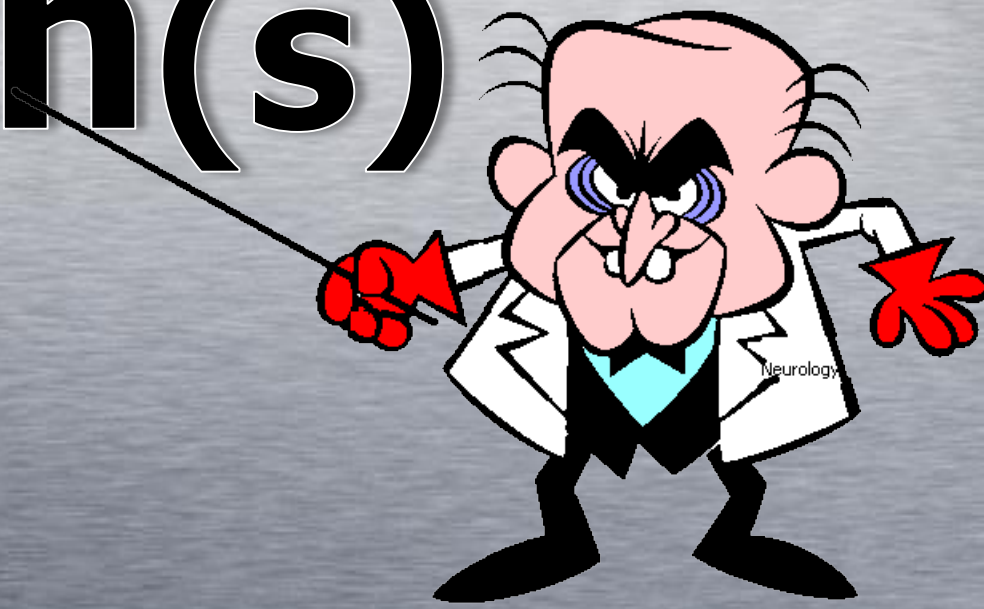
- **#1 reason people seek medical attention**
- **Is an Experience**
- **Multifactorial**
  - Nociceptive / physical
  - Psychological / mood



Definitions

- Chronic pain – lasting over one month
- Acute pain – lasting less than a week
- Morphine Equivalent Dosage (MEQ) – the mg of drug your patient takes / day converted to equianalgesic morphine dosage
- Opioid Risk – how likely your patient is to use opioids in a non-prescribed manner or for a non-medical purpose.

The Harsh Truth(s)



It's a bad time to be a Chronic Pain Patient

- Many physicians don't want to (or are afraid to) write pain medications.
- It's very hard to see a pain specialist.
- Pharmacies often don't want to carry opioids – especially the higher dosages
- You could be robbed for your pain meds
- Less pain medications available in 2017
- Treatment options are often not covered by insurance

It's a bad time to be a Physician with chronic pain patients

- There are many guidelines, recommendations, and laws
- Proper documentation and PDMP use is time-consuming
- You don't want to be seen as the 'candyman' in your community
- You see in the news almost daily about a physician being jailed or fined for improper prescribing
- Naloxone, abuse-deterrent opioids, and many non-opioid choices are often not covered by insurance (while most opioids are)

DEA Ratchets Down Opioid Production

The supply of almost every Schedule II opioid manufactured in the United States will be reduced 25% or more in 2017, as required by the Drug Enforcement Administration (DEA).

The new quota will be sufficient to meet the estimated medical, scientific, research, industrial and export needs for the year, and for the maintenance of reserve stocks, said Demetra Ashley, associate deputy administrator of the DEA Diversion Control Division. Affected drugs include oxycodone, hydrocodone (reduced to 66% of this year's quota), fentanyl, hydromorphone, morphine and other similar opioids.

"DEA must balance the production of controlled substances needed for legitimate use

Pain Medicine News
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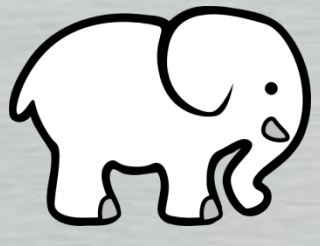
On the front page...

More Harsh Truths

- We have an opioid overdose epidemic in the USA with a 33% overall increase in the last 5 years (per CDC)
- Deaths from synthetic opioids like illicit fentanyl are up 73% while oxycodone and hydrocodone are up 4%.
- Heroin related deaths are up 50%
- US citizens are about 5% of the worlds population, yet use 80% of the global supply of opioids
- Our patients want a pill for everything and seem minimally willing to participate in their own health care – other than take pills

Guidelines

- **CDC**
  - March 18th, 2016
  - Excludes Palliative / End-of-Life / CA pts



- **Federation of State Medical Boards**
  - Revised Spring 2017
- **State level recommendations and laws**
- **Most professional pain organizations**
- **“Standards of Care”**

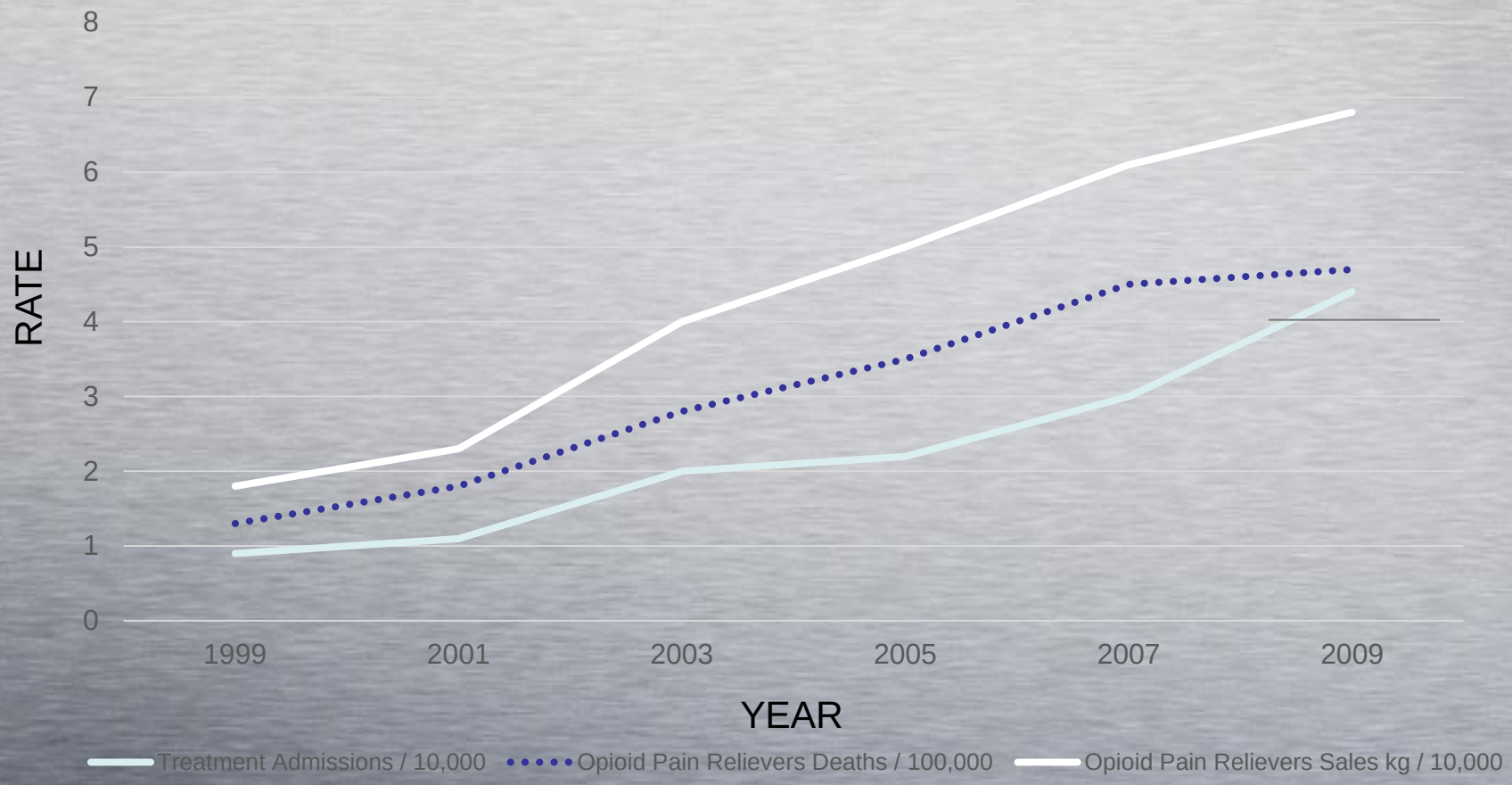
Changes in Rates of Opioid Prescribing

On July 6, 2017, the US Centers for Disease Control and Prevention reported that between 2006 and 2015 the amount of opioids prescribed in the United States peaked in 2010 at 782 morphine milligram equivalents (MME) per capita and then decreased each year through 2015 to 640 MME per capita. Prescribing rates increased from 72.4 to 81.2 prescriptions per 100 persons between 2006 and 2010, were constant between 2010 and 2012, and then declined to 70.6 per 100 persons from 2012 to 2015, a 13.1% decline.[1] Yet the amount of opioids prescribed in 2015 remains more than 3 times higher than in 1999, when the amount prescribed was 180 MME per capita

Additional data from the report include that high-dose opioid prescribing, defined as a daily dose of 90 MME or higher, was stable between 2006 and 2010, and then declined from 11.4 per 100 persons in 2010 to 6.7 in 2015. Also reported was substantial variation in 2015 at the county level from an average of 203 MME per capita in the lowest quartile of counties to 1319 MME per capita in the highest quartile.

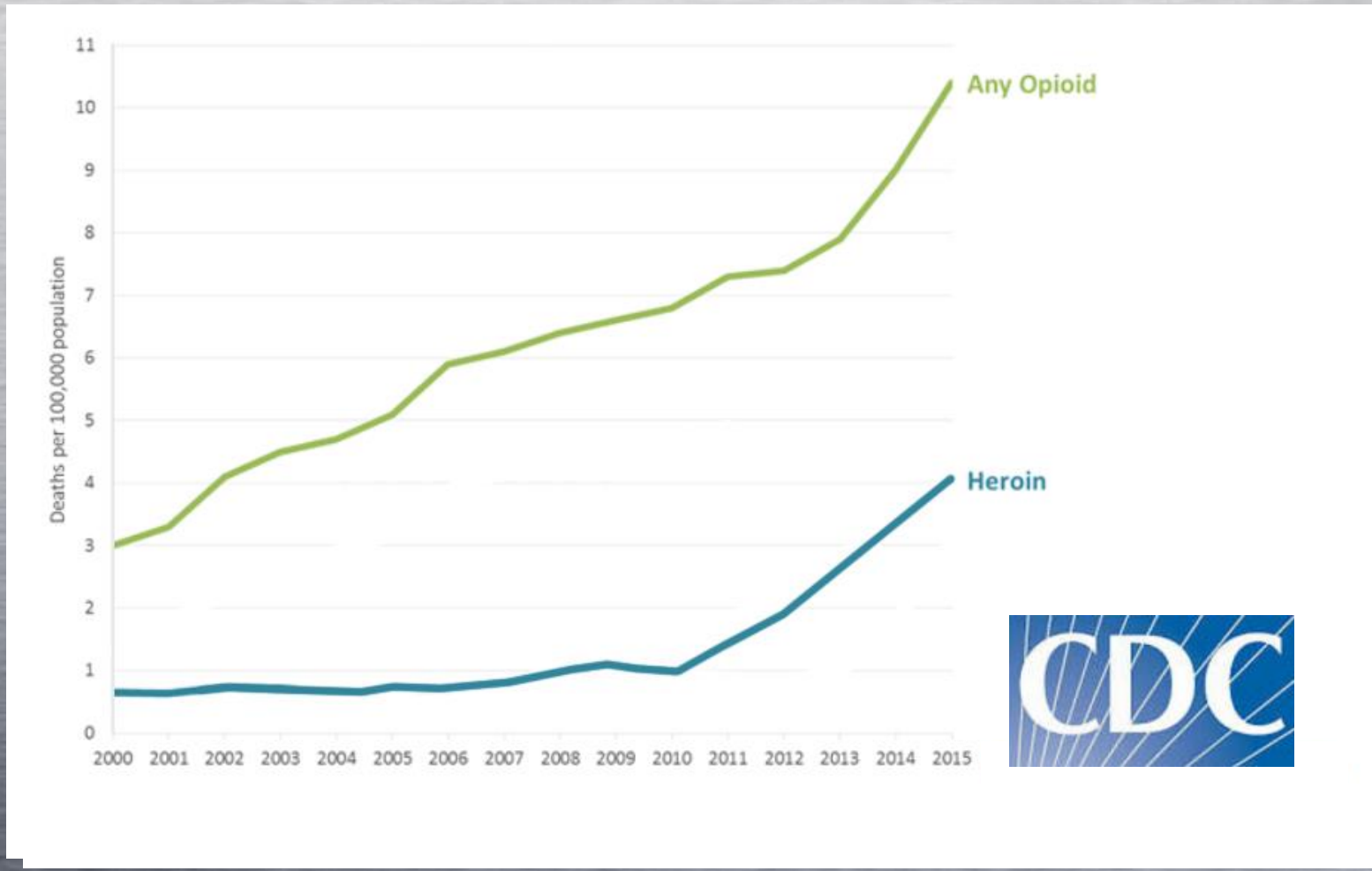
Schuchat A, Houry D, Guy GP. New Data on Opioid Use and Prescribing in the United States. *JAMA*.2017;318(5):425-426. doi:10.1001/jama.2017.8913

OPIOID DEATHS, TREATMENT ADMISSIONS AND PRESCRIBING

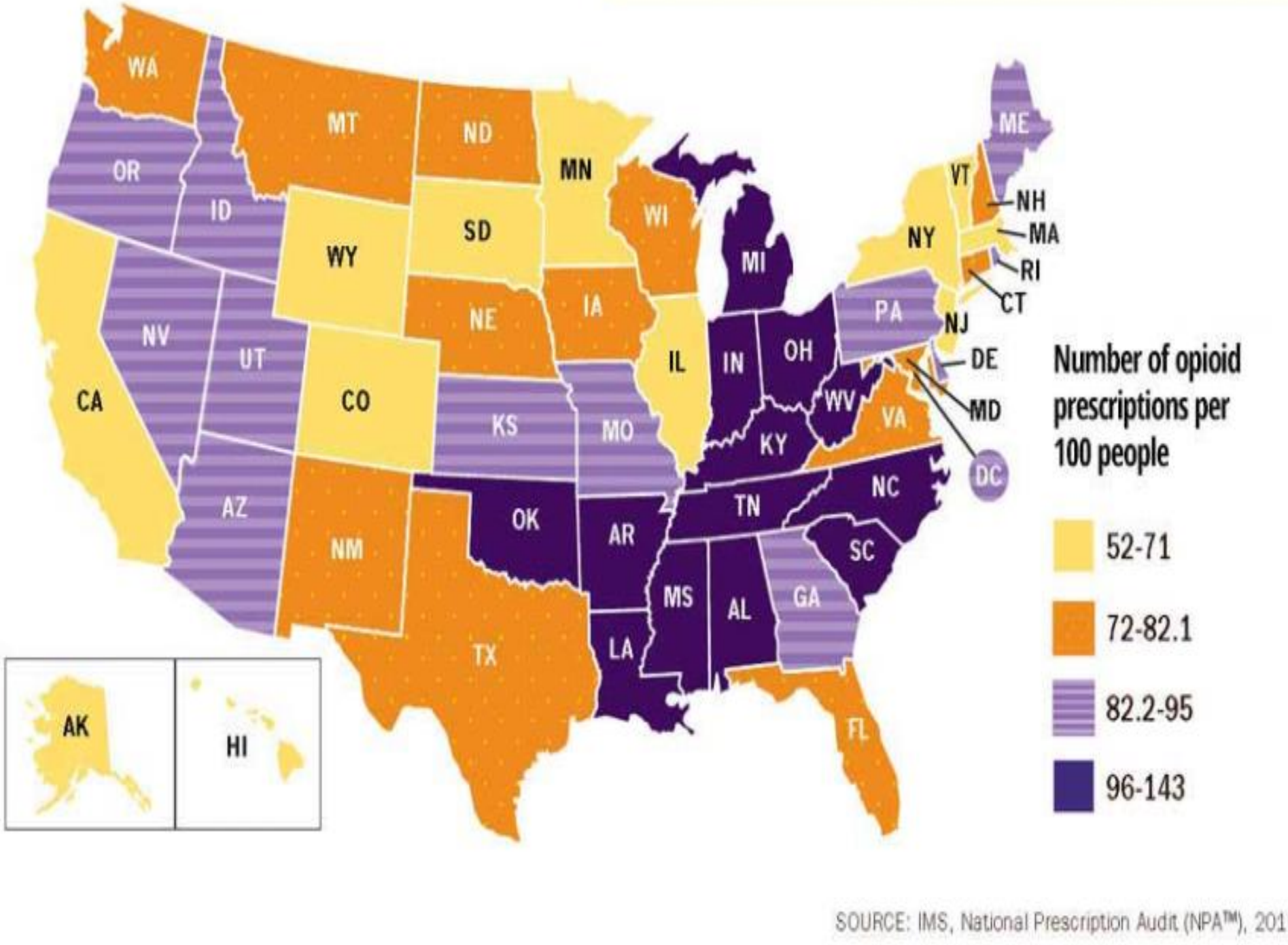


SOURCE: MMWR, November 2, 2011/60(43); 1487-1492
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6043a4.htm

OVERDOSE DEATHS INVOLVING OPIOIDS, U.S, 2000-2015



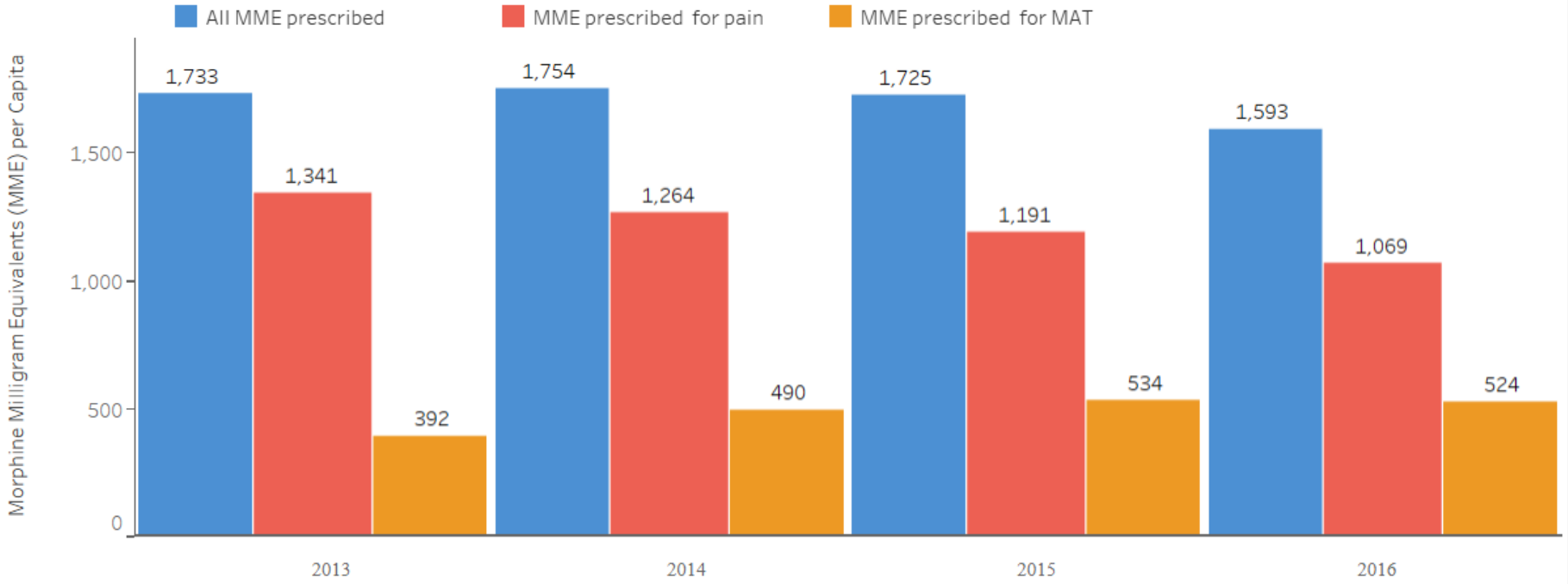
SOURCE: MMWR, January 1, 2016/64(50);1378-82
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm



SOURCE: IMS, National Prescription Audit (NPA™), 2012

(click here for Main page)

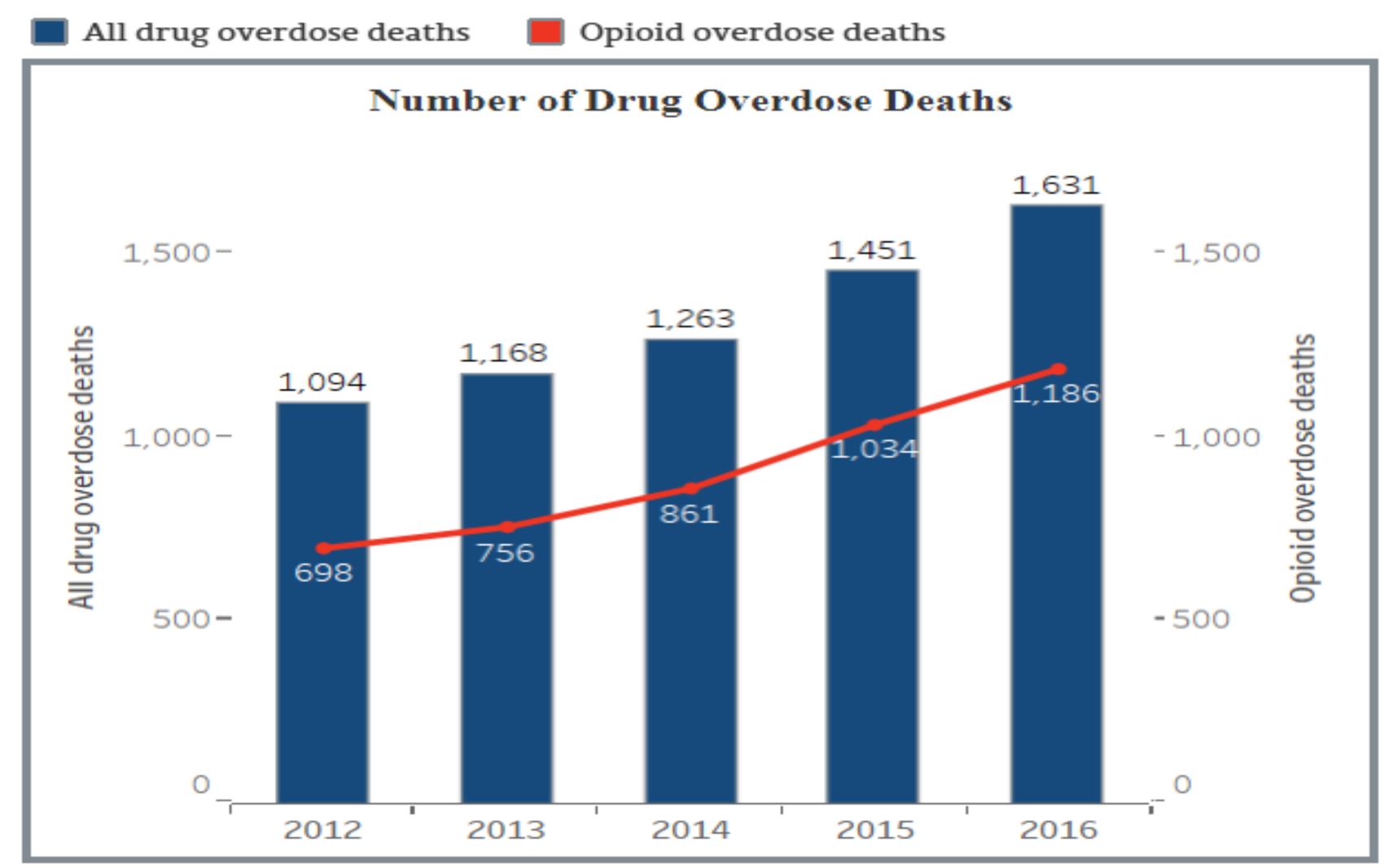
Painkiller Prescriptions: Tennessee



	2013	2014	2015	2016	
All MME prescribed	1,733	1,754	1,725	1,593	⬇ -8.08 %
MME prescribed for MAT	392	490	534	524	⬆ 33.60 %
MME prescribed for pain	1,341	1,264	1,191	1,069	⬇ -20.28 %

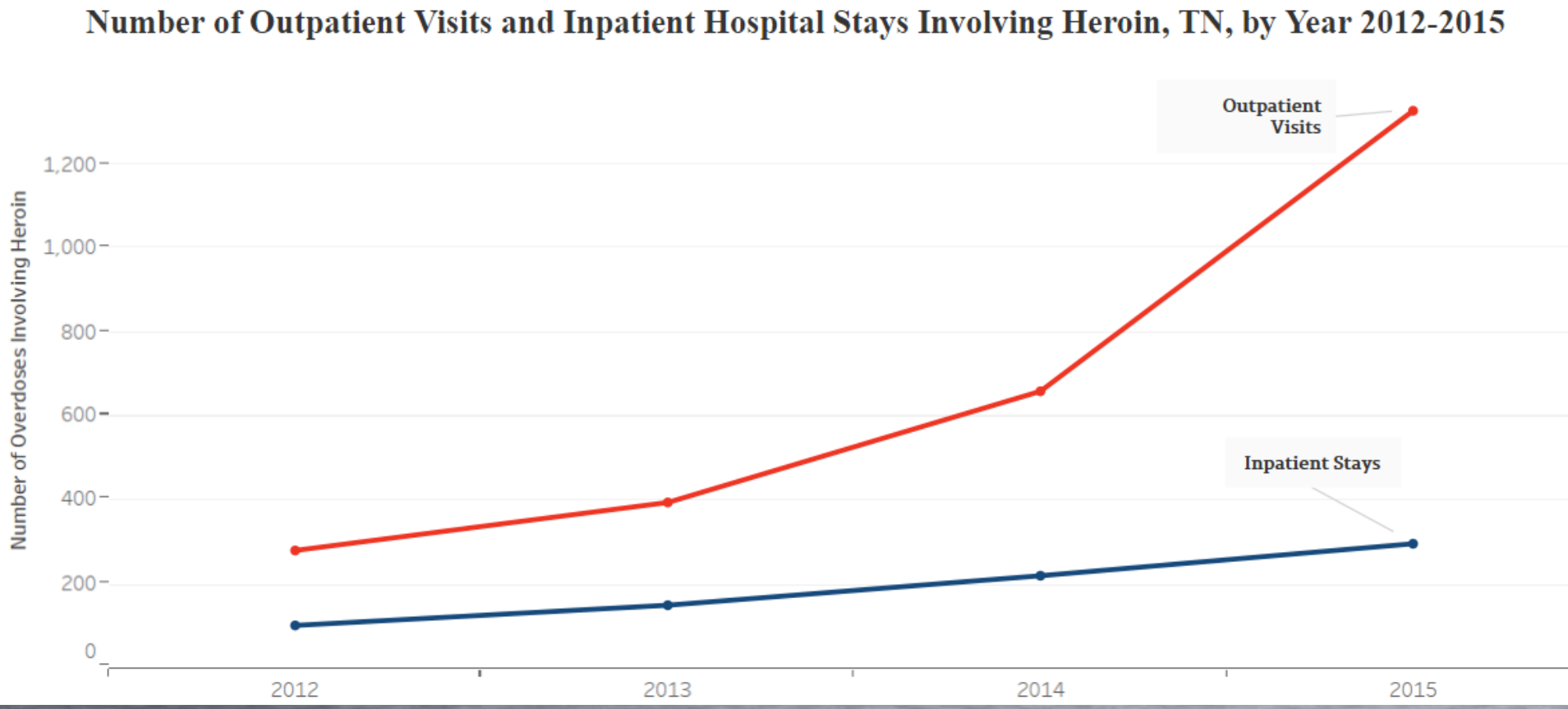
http://tn.gov/health/topic/pdo-data-dashboard

TN Overdose Deaths



http://tn.gov/health/topic/pdo-data-dashboard

Heroin in TN



http://tn.gov/health/topic/pdo-data-dashboard

PDMP: Prescription Drug Monitoring Program

General	• **TN Controlled Substances Monitoring Database Program** www.tncsmd.com • Administered by **Department of Health** • **Schedule II-V** are monitored • **Dispensers and Prescribers are required** to register and input data • Before prescribing, there is **an obligation** to review under certain circumstances
Access	• **Prescribers, dispensers; county medical examiner; law enforcement/judicial; licensing boards; inspector general, the Medicaid fraud control unit, and the bureau of TennCare related to participants in TennCare; chief pharmacist, the state opioid treatment authority, and the medical director of the department of mental health and substance abuse services; quality improvement committee of hospital; patient; third party with signed consent form** • Prescribers **can authorize** a registered delegate
Reporting	• Must be entered into PDMP **24 hours** after dispensing • Unsolicited reports/alerts **are sent** to prescribers, dispensers, licensing boards, law enforcement • Tennessee **does share** data with other states' PDMP • Out-of-state pharmacies **are required** to report to the patient's home state • Patient **will not be notified** if their record has been accessed

http://www.namsdl.org/prescription-drug-monitoring-programs-maps.cfm June 2017

Medical and Recreational Marijuana Status

- It **is not legal** to prescribe
- It **is not legal** for recreational use
  http://lawatlas.org/query?dataset=medical-marijuana-patient-related-laws
  http://www.namsdl.org/controlled-substances-and-prescription-drugs-maps.cfm Jan. 2017

Patient Prescriber Agreement and Treatment Programs

- A Patient Prescriber Agreement (PPA) **is recommended or required**
  http://www.namsdl.org/library/7440DB2D-FE8C-5D71-83963097CEEE4A1F/ Jan. 2016
- For a list of treatment programs in this state:
  https://findtreatment.samhsa.gov/locator/home

Success with Regulations

Less Doctor Shopping

Less Oxycodone Overdose Deaths

Less Doctor Shopping

Opioid Risk Tool (ORT)

Mark each box that applies	Female	Male
1. Family history of substance abuse		
• Alcohol	❑ 1	❑ 3
• Illegal drugs	❑ 2	❑ 3
• Prescription drugs	❑ 4	❑ 4
2. Personal history of substance abuse	❑ 3	❑ 3
• Alcohol	❑ 4	❑ 4
• Illegal drugs	❑ 5	❑ 5
• Prescription drugs		
3. Age (mark box if 16-45 years)	❑ 1	❑ 1
4. History of preadolescent sexual abuse	❑ 3	❑ 0
5. Psychological disease		
• ADD, OCD, bipolar, schizophrenia	❑ 2	❑ 2
• Depression	❑ 1	❑ 1

- Exhibits high degree of sensitivity and specificity
- 94% of low-risk patients did not display an aberrant behavior
- 91% of high-risk patients did display an aberrant behavior

Risk Level Scoring	
0 - 3	Low
4 - 7	Moderate
> 8	High

Webster LR, Webster RM. *Pain Med*. 2005;6:432-442.

Risk Assessment, Office visits, and Drug Screens – per Bailey

- **Risk Assessment - ORT for baseline risk**
- **Adjusted upwards by one risk factor category for each of the following:**
  - Concurrent benzodiazepine use
  - MME > 90
  - Respiratory compromise (OSA / COPD)
  - Concurrent use of hypnotics
  - Concurrent use of carisoprodol
  - Methadone as analgesic
  - History of aberrant behaviors
  - Drug screens positive for marijuana or alcohol in the past
  - Physician Discretion

How often RTC?
(per Bailey)

- **High Risk**
  - Drug screen - Q3 months
  - Office visit – Q month
  - Must have Rx for Narcan Nose Spray and Instructions documented
- **Moderate Risk**
  - Drug screen Q 6 months
  - Office visit – Q 3 months (if stable)
- **Low Risk**
  - Drug screen Q 12 months
  - Office visit – Q 3 months (if stable)

ALL patients:

- **Drug screened on their initial visit and after change in analgesic**
- **Sign all consents / medication management agreements**
- **Have current ORT in chart**
- **PDMP checked on each office visit**
- **Must have current / working contact information in chart**

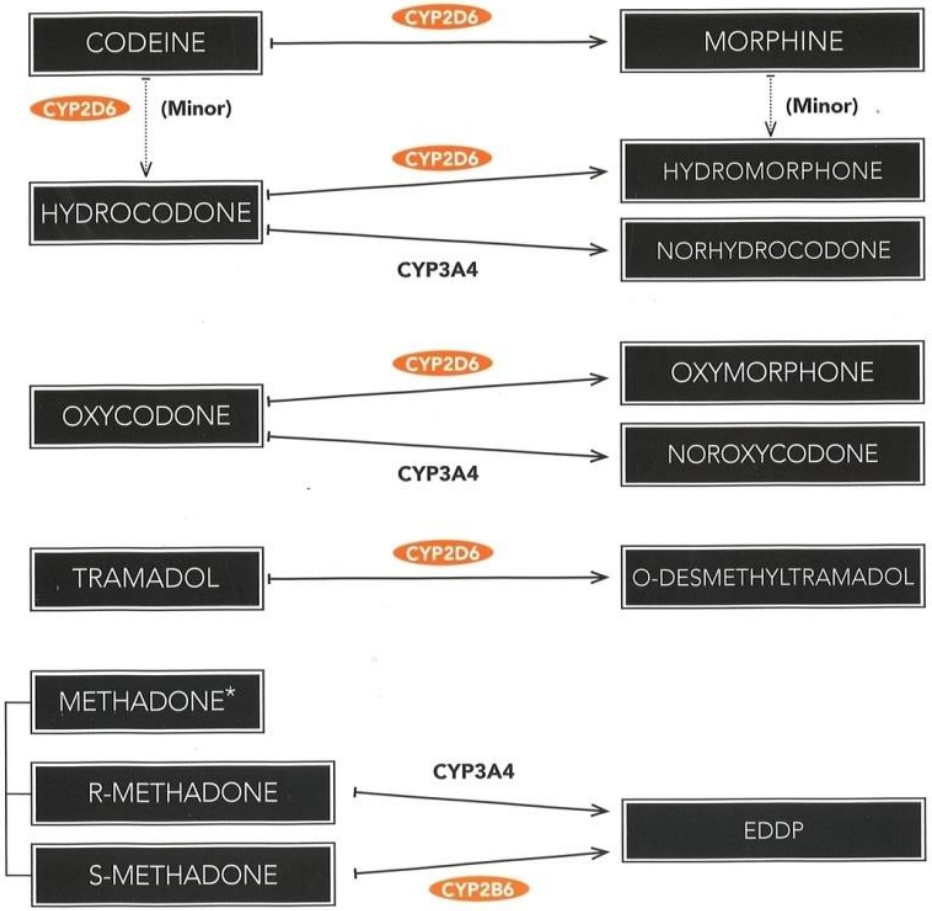
Drug Screen Detection Times

Amphetamines	• **48 hours**
Barbiturates	• **Short-acting (eg, secobarbital), 24 hours** • **Long-acting (eg, phenobarbital), 2–3 weeks**
Benzodiazepines	• **3 days if therapeutic dose is ingested** • **Up to 4–6 weeks after extended dosage (≥ 1 year)**
Cannabinoids	• **Moderate smoker (4 times/week), 5 days** • **Heavy smoker (daily), 10 days** • **Retention time for chronic smokers may be 20–28 days**
Cocaine	• **2–4 days, metabolized**
Ethanol	• **2–4 hours**
Methadone	• **Approximately 30 days**
Opiates	• **2 days**
Phencyclidine	• **Approximately 8 days** • **Up to 30 days in chronic users (mean value = 14 days)**
Propoxyphene	• **6–48 hours**

Gourlay DL, Heit HA. *Pain Med*. 2009;10 Suppl 2:S115-123.

Opioid Metabolism

PRIMARY OPIOID METABOLIC PATHWAYS[2,3]



*Lesser metabolic pathways for methadone also mediated by 2D6, 2C9, 2C19 to varying degrees

→ Major metabolic pathway
⇢ Minor metabolic pathway
⬭ = Tested by Millennium PGT

CYP = cytochrome P450
EDDP = 2-Ethylidene-1, 5-Dimethyl-3, 3-Diphenylpyrrolidine

PARENT DRUG	PRIMARY METABOLITES
CODEINE	Morphine, Hydrocodone (minor)
HYDROCODONE	Hydromorphone; Norhydrocodone
OXYCODONE	Oxymorphone, Noroxycodone
TRAMADOL	O-Desmethyltramadol
METHADONE (R- AND S-ISOMERS)	EDDP

(2) Adapted from Smith HS. Opioid Metabolism. *Mayo Clin Proc.* 2009; 84(7):613-624.
(3) Adapted from Trescot AM, et al. Opioid Pharmacology. *Pain Physician.* 2008;11(suppl):135S-153S.

SUBSTANCE FALSELY IDENTIFIED ON TEST	ACTUAL SUBSTANCE	TYPE OF STUDY	NOTES
Amphetamine and methamphetamine	Selegiline	Single case report[1,2]	L-stereoisomer only detected (D-stereoisomer present in illicit drugs)
Amphetamine and methamphetamine	Vicks Inhaler	Several case reports, controlled-exposure studies[1-3]	L-stereoisomer only detected; most positives noted with twice recommended dosage
Barbiturate	NSAIDs (ibuprofen, naproxen)	Controlled-exposure study of 60 subjects (510 specimens)[4]	0.4% false-positive rate
Benzodiazepine	Oxaprozin	Controlled-exposure study of 12 patients (36 specimens)[5]	100% false-positive rate, some cases lack controls
Cannabinoid	NSAIDs (ibuprofen, naproxen)	Controlled-exposure study of 60 subjects (510 specimens)[4]	0.4% false-positive rate
Opiate	Fluoroquinolone*	Controlled-exposure studies (8 subjects) and case series (9 subjects)[6]	Most levels detected were below new 1998 threshold (2000 ng/mL)
Opiate	Rifampin	3 case reports[7]	
Phencyclidine	Venlafaxine	1case report[8]	Confirmed by GC-MS (7200 mg intentionally ingested)
Phencyclidine	Dextromethorphan	1case report[9]	(500 mg ingested)

*Ofloxacin and levofloxacin most likely to cause false positive.

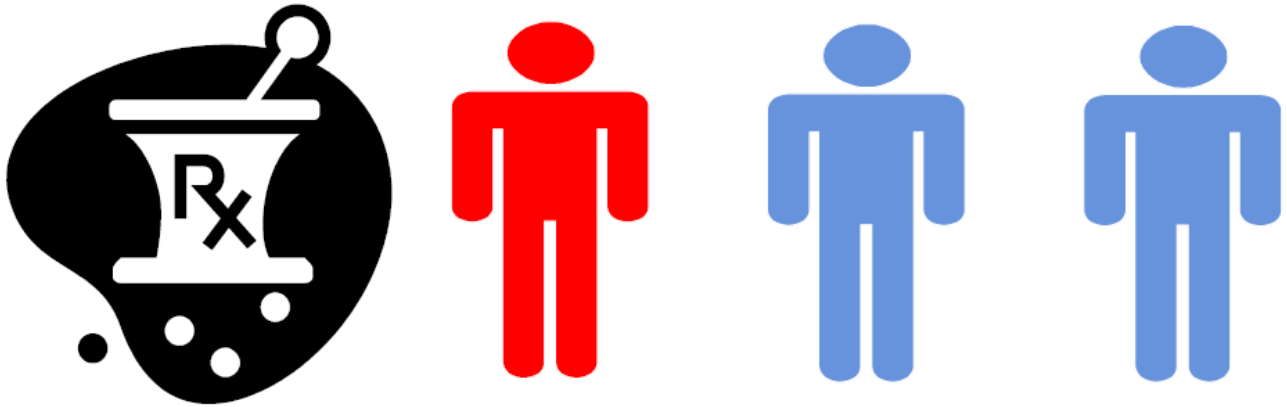
TIRF Products

(Transmucosal Immediate Release Fentanyl)

- **Only approved for use for breakthrough pain in cancer patients who are opioid-tolerant.**
- **Must be registered with TIRF Program**
  - www.tirfremsaccess.com
- **Doctor / Patient / Pharmacist must all document its use**
- **Recent crackdown on ‘off-label’ use**

Methadone-Associated Deaths

- 5,000 people die every year of overdose related to methadone
- Methadone contributed to nearly 1 in 3 prescription opioid deaths in 2009



- Only 2% of opioid analgesic prescriptions were for methadone

CDC. *Prescription Painkiller Overdoses. Use and Abuse of Methadone as a Painkiller.* CDC Vital Signs. July 2012.

PCSS TRAINING
PROVIDERS' CLINICAL SUPPORT SYSTEM
For Opioid Therapies

Oxymorphone (Opana) ER

Today, the U.S. Food and Drug Administration requested that Endo Pharmaceuticals remove its opioid pain medication, reformulated Opana ER (oxymorphone hydrochloride), from the market. After careful consideration, the agency is seeking removal based on its concern that the benefits of the drug may no longer outweigh its risks. This is the first time the agency has taken steps to remove a currently marketed opioid pain medication from sale due to the public health consequences of abuse. - June 8, 2017

The opioid medication Opana ER is being voluntarily withdrawn from the market, its manufacturer Endo Pharmceuticals said in a statement Thursday. The decision comes less than a month after the U.S. Food and Drug Administration (FDA) requested that drug sales be halted, due to concerns over its potential for misuse and abuse. - Jul 07, 2017

There are generic versions of oxymorphone ER available but are sometimes difficult to find / get.

OPIOID TOLERANT / NAIVE

Tolerance to sedating & respiratory-depressant effects is critical to safe use of certain ER/LA opioid products, dosage unit strengths, or doses

Patients must be opioid tolerant before using:

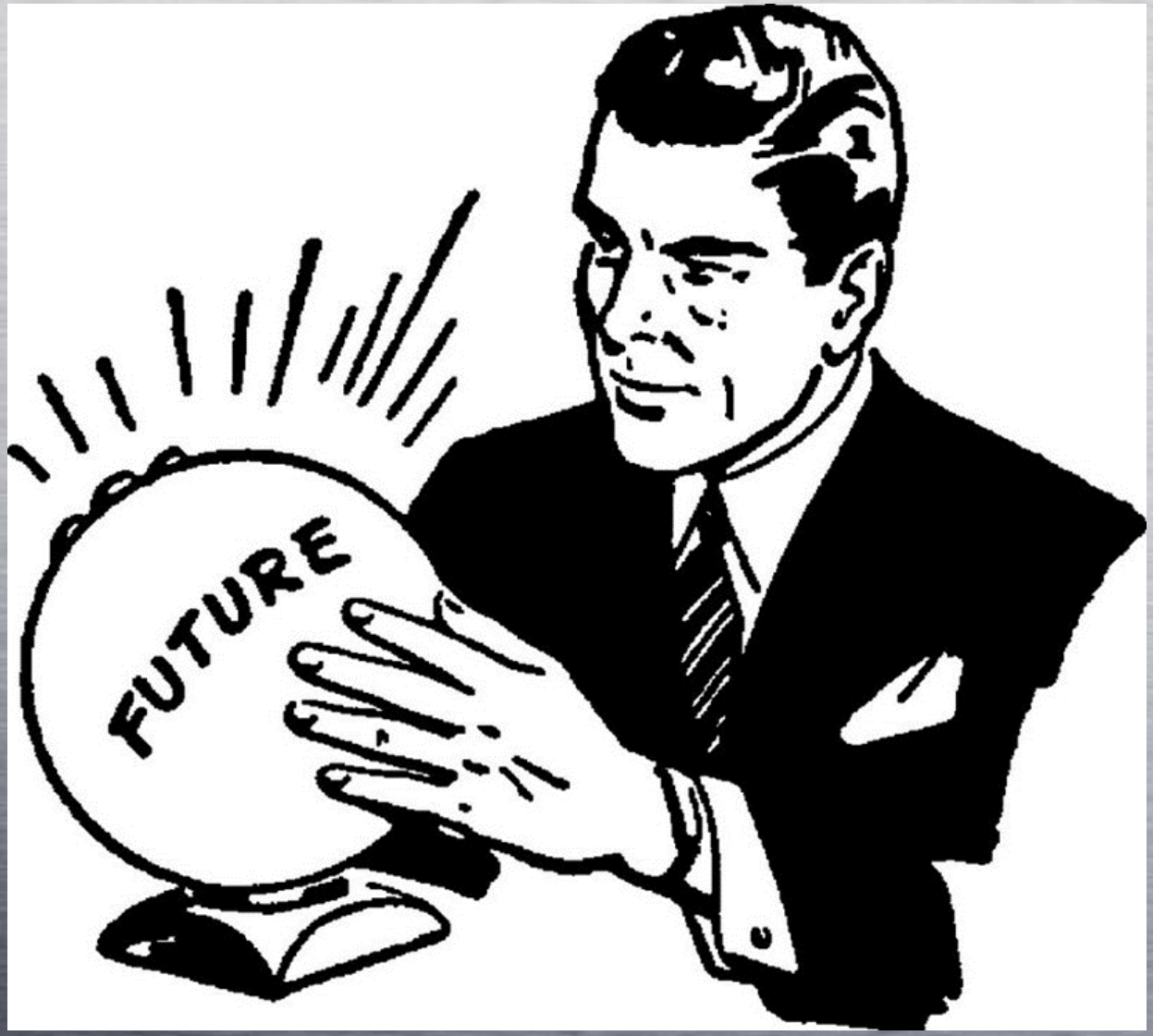
- Any strength of transdermal fentanyl or hydromorphone ER
- Certain strengths or daily doses of other ER products

Opioid-tolerant patients are those taking at least

- **60 mg oral morphine/day**
- **25 mcg transdermal fentanyl/hr**
- **30 mg oral oxycodone/day**
- **8 mg oral hydromorphone/day**
- **25 mg oral oxymorphone/day**
- **An equianalgesic dose of another opioid**

FOR 1 WK OR LONGER

Prognostications



In My Opinion

- **Pain management is hard now and is going to get harder.**
- **Non-opioid treatment is going to have to assume a much more prominent role in chronic pain management – and our patients are going to have to buy into this.**
- **Both patients and physicians are going to have to get past the 'pill for every symptom' mentality**
- **Patients are going to have to become more active participants in their own health care**
- **Naloxone rescue is standard of care**
- **Methadone use in the treatment of chronic pain will diminish markedly**

My Advice

- Apply the concept of risk assessment to your pain patients
- Avoid use of high-dose opioids (whatever that is) and document an effort to decrease dosage whenever possible
- Extreme caution with:
  - Prescribing opioids and benzos
  - Prescribing opioids to anyone who is compromised from a respiratory standpoint (COPD…)
- Encourage the use of Narcan Nasal Spray and abuse-deterrent formulations of opioids
- See your pain patients at no less than 90 day intervals
- Refer for addiction evaluation at the first concern
- Pressure carriers to pay for the non-opioid treatments that our guidelines advise (but presently don't cover)
- Know at least the basics of your own state's laws concerning pain management
- Be willing to work with your pharmacist colleagues

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