Opioids and controlled substances

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Disclosure

- No financial or other material conflicts of interest
- Not representative of any institution or organization

Outline-1

- Pharmacology of opiates
- Epidemiology of opioid crisis
- Current Florida statistics regarding M&M of controlled substance-related deaths
- Current standards, laws and rules on prescribing controlled substances*
- Proper prescribing of opiates

Outline-2

- Risks, diagnosis and treatment of opioid addiction*
- Prescribing emergency opioid antagonists*
- Alternatives to controlled substance prescribing*
  - Nonpharmacological therapies*
- Controlled substance disposal

- Pharmacology of opiates
- Epidemiology of opioid crisis
- Current Florida statistics regarding M&M of controlled substance-related deaths
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- Proper prescribing of opiates

Definitions

- Opiate
- Opioid
- Narcotic
- Controlled substance

https://crsreports.congress.gov/product/pdf/r/r45948

https://www.dea.gov/drug-information/csa

https://uscode.house.gov/view.xhtml?req=granuleid:USC-prelim-title21-section811&num=0&edition=prelim

Receptor activity

Mu	Delta	Kappa
Analgesia	Analgesia with fewer adverse effects	Mild analgesia
Sedation		
Euphoria		Dysphoria
Respiratory depression		Less respiratory depression
Constipation		
Physical dependence		Decreased dependence

Opioid classification

Full agonist	Partial agonist	Agonist-antagonist	Antagonist
Morphine	Buprenorphine	Pentazocine	Naloxone
Fentanyl		Butorphanol	Naltrexone
Oxycodone		Nalbuphine	
Hydrocodone			
Methadone			

Opioid comparison

Medication	Onset (po)	Duration (po)	Equianalgesic dose
Fentanyl patch	12-24 hrs	72 hrs/patch	12.5mcg/hr; 0.1mg IV
Hydromorphone	15-30 mins	4-6 hrs	6 - 7.5mg po/1.5mg IV
Tapentadol	1.5 hrs (IR)	4 hrs	100mg po
Morphine IR	30-60 mins	3-6 hrs	30mg po/10mg IV
MS Contin®	30-90 mins	8-12 hrs	30mg po
Oxycodone IR	15-30 mins	4-6 hrs	20mg po
OxyContin®	1 hr	12 hrs	20mg po
Hydrocodone	30-60 mins	4-6 hrs	30mg po
Codeine	30-60 mins	4-6 hrs	200mg po/100–120mg IV
Meperidine	10-15 mins	2-4 hrs	300mg po/75-100mg IV

Opioid allergy

Phen-anthrenes	Phenyl-piperidines	Diphenyl-heptanes	Phenylpropyl amines
Buprenorphine	Fentanyl*	Methadone*	Tapentadol
Codeine	Meperidine	Propoxyphene	Tramadol
Hydrocodone			
Hydromorphone*			
Morphine			
Oxycodone*			
Oxymorphone*			

Controlled substance examples

C-II	C-III	C-IV	C-V
Higher dose of codeine, >90mg	Lower dose of codeine, <90mg	Tramadol	Lowest dose of codeine, <2mg/mL
Fentanyl	Anabolic steroids	Chloral hydrate	Robitussin-AC®
Hydrocodone	~~Lower dose of hydrocodone~~	Chlordiazepoxide	Lomotil®
Morphine	Ketamine	Clorazepate	Phenergan with codeine®
Oxycodone	Dronabinol	Carisoprodol	~~CBD oil (Epidiolex®)~~
Methadone	GHB	Meprobamate	
Amphetamine	Buprenorphine	Phentermine	
Pentobarbital		Phenobarbital	

https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf

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History

- 1803: scientist discovers morphine
- 1874: chemist synthesizes diacetylmorphine
- 1898: pharmaceutical commercialization
- 1914: Harrison Narcotics Tax Act
- 1924: Anti-Heroin Act
- 1973: graduate student discovers opioid receptor

https://www.history.com/topics/crime/history-of-heroin-morphine-and-opiates

https://www.washingtonpost.com/national/health-science/candace-b-pert-neuroscientist-who-discovered-opiate-receptor-dies-at-67/2013/09/18/c84ef128-1eda-11e3-8459-657e0c72fec8_story.html?utm_term=.54b42d75de3f

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

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1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

N Engl J Med. 1980 Jan 10;302(2):123.

Pain, 25 (1986) 171–186
Elsevier

PAI 00878

Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases

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(Received 10 June 1985, accepted 28 October 1985)

Summary

Thirty-eight patients maintained on opioid analgesics for non-malignant pain were retrospectively evaluated to determine the indications, course, safety and efficacy of this therapy. Oxycodone was used by 12 patients, methadone by 7, and levorphanol by 5; others were treated with propoxyphene, meperidine, codeine, pentazocine, or some combination of these drugs. Nineteen patients were treated for four or more years at the time of evaluation, while 6 were maintained for more than 7 years. Two-thirds required less than 20 morphine equivalent mg/day and only 4 took more than 40 mg/day. Patients occasionally required escalation of dose and/or hospitalization for exacerbation of pain; doses usually returned to a stable baseline afterward. Twenty-four patients described partial but acceptable or fully adequate relief of pain, while 14 reported inadequate relief. No patient underwent a surgical procedure for pain management while receiving therapy. Few substantial gains in employment or social function could be attributed to the institution of opioid therapy. No toxicity was reported and management became a problem in only 2 patients, both with a history of prior drug abuse. A critical review of patient characteristics, including data from the 16 Personality Factor Questionnaire in 24 patients, the Minnesota Multiphasic Personality Inventory in 23, and detailed psychiatric evaluation in 6, failed to disclose psychological or social variables capable of explaining the success of long-term management. We conclude that opioid maintenance therapy can be a safe, salutary and more humane alternative to the options of surgery or no treatment in those patients with intractable non-malignant pain and no history of drug abuse.

How did we get here?

- 1980s: opioids for non-malignant pain
- 1996: the 5th vital sign; OxyContin released
- 2001: TJC weighs in
- 2006: HCAHPS pain questions
- 2021: 207 opioid-related OD deaths/day, US

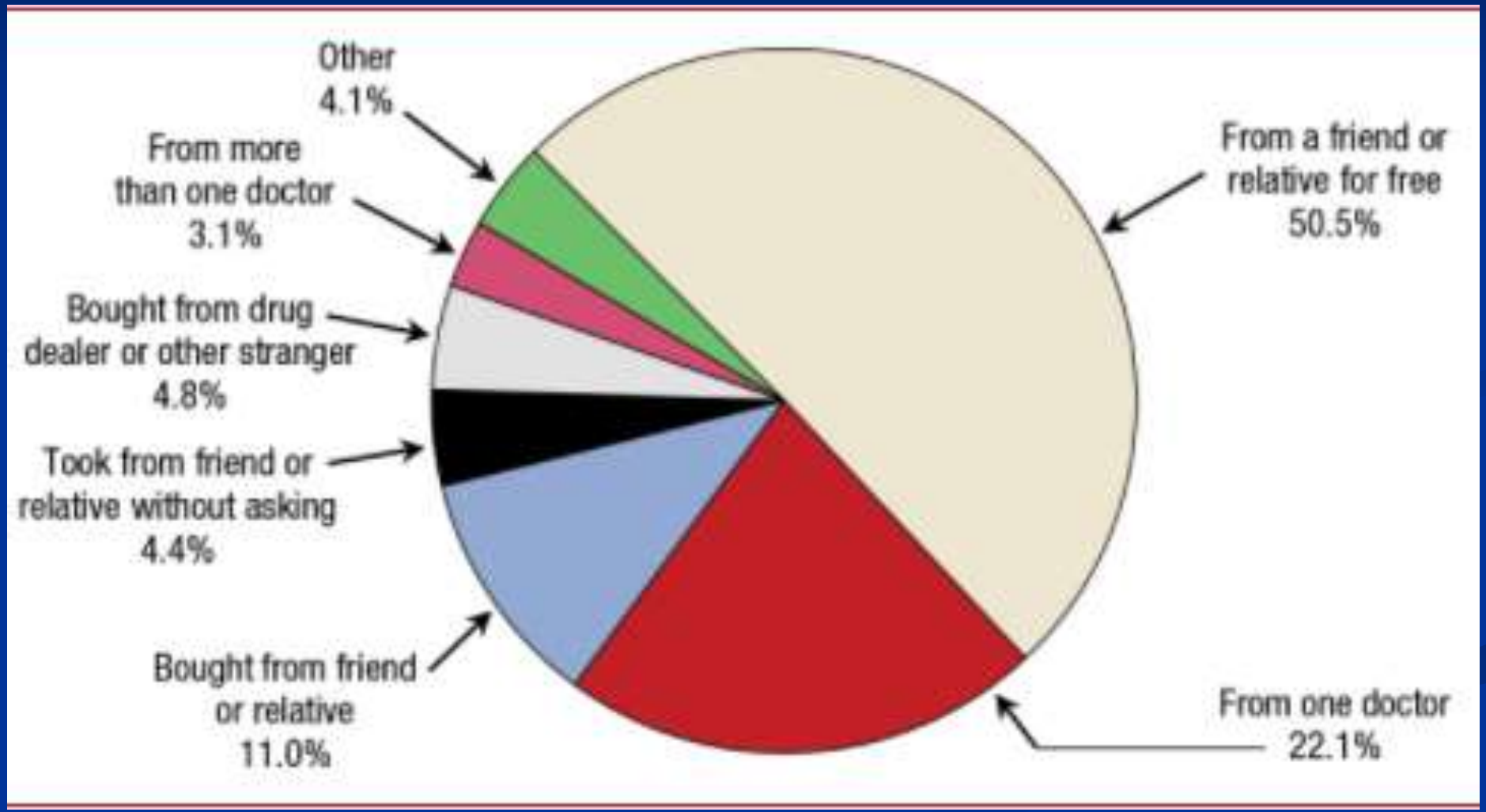
https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/20211117.htm

CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://wonder.cdc.gov.

http://www.nytimes.com/2007/05/10/business/11drug-web.html

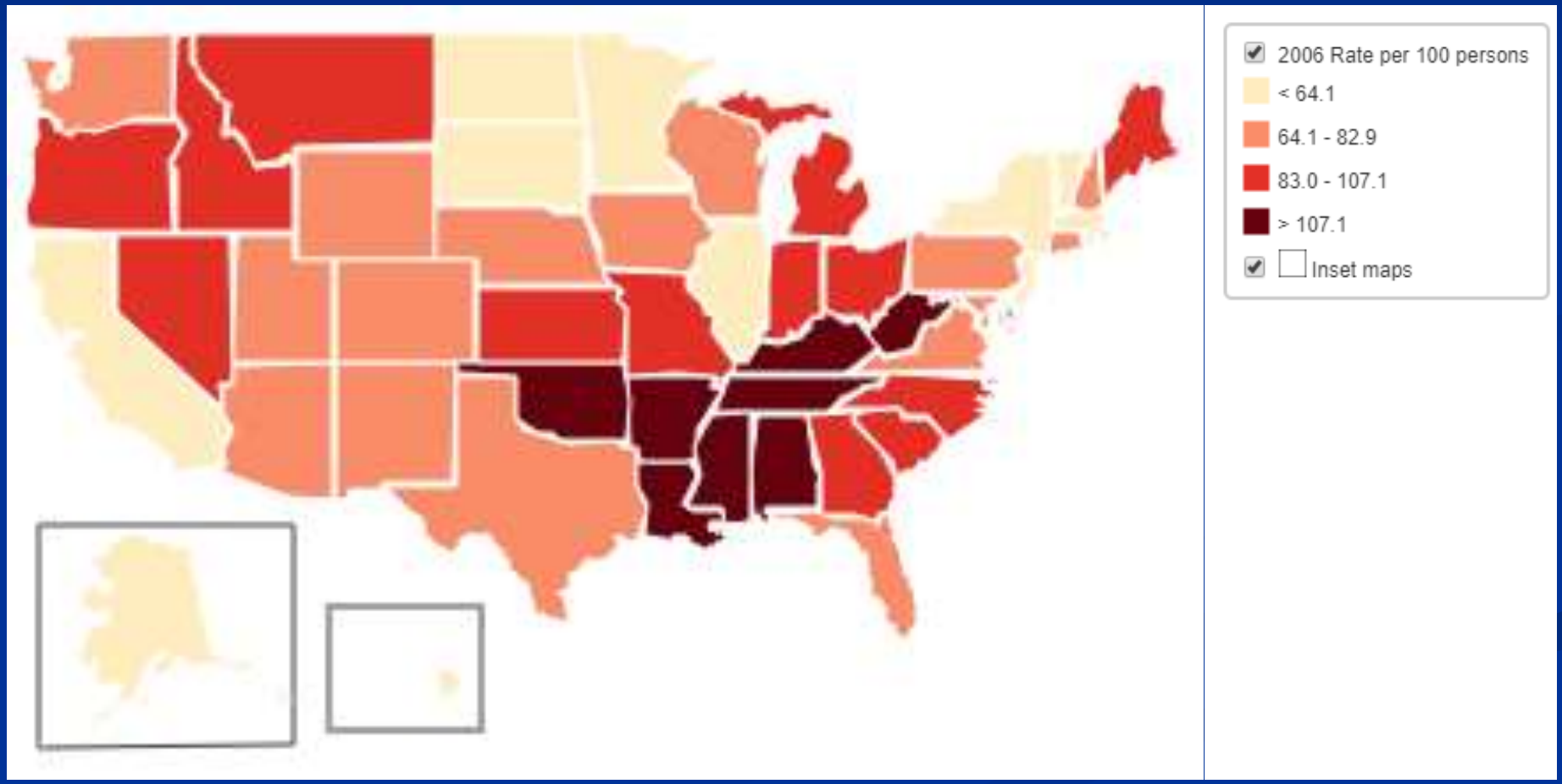
https://www.cdc.gov/drugoverdose/deaths/prescription/maps.html

Source of Rx pain relievers for nonmedical use among users 12yoa+, 2013 and 2014



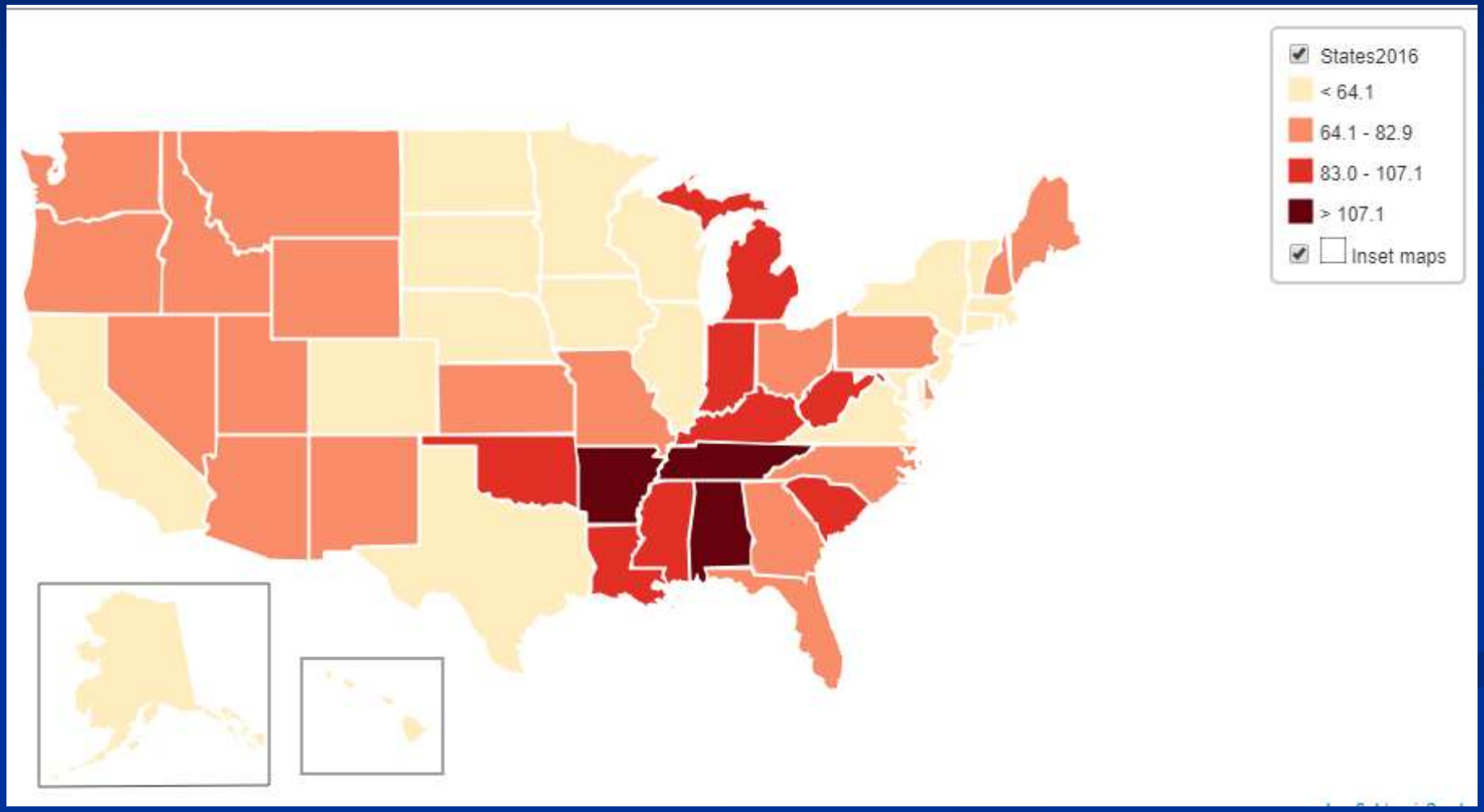
SAMHSA, Center for Behavioral Health Statistics and Quality, National Surveys on Drug Use and Health (NSDUHs), 2013 and 2014.
https://www.samhsa.gov/data/sites/default/files/report_2686/ShortReport-2686.html

U.S. State Prescribing Rates, 2012



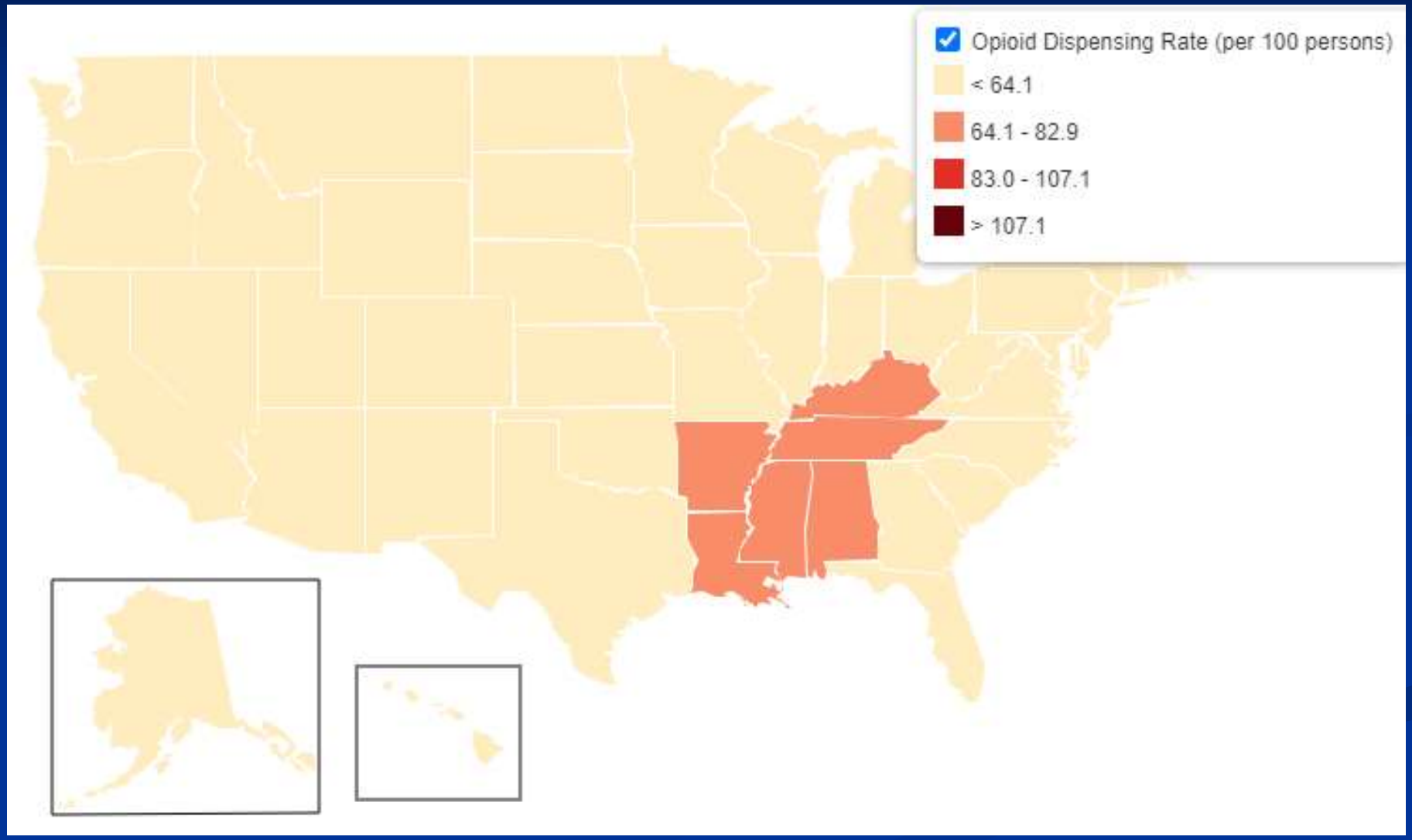
https://www.cdc.gov/drugoverdose/maps/rxstate2006.html

U.S. State Prescribing Rates, 2016



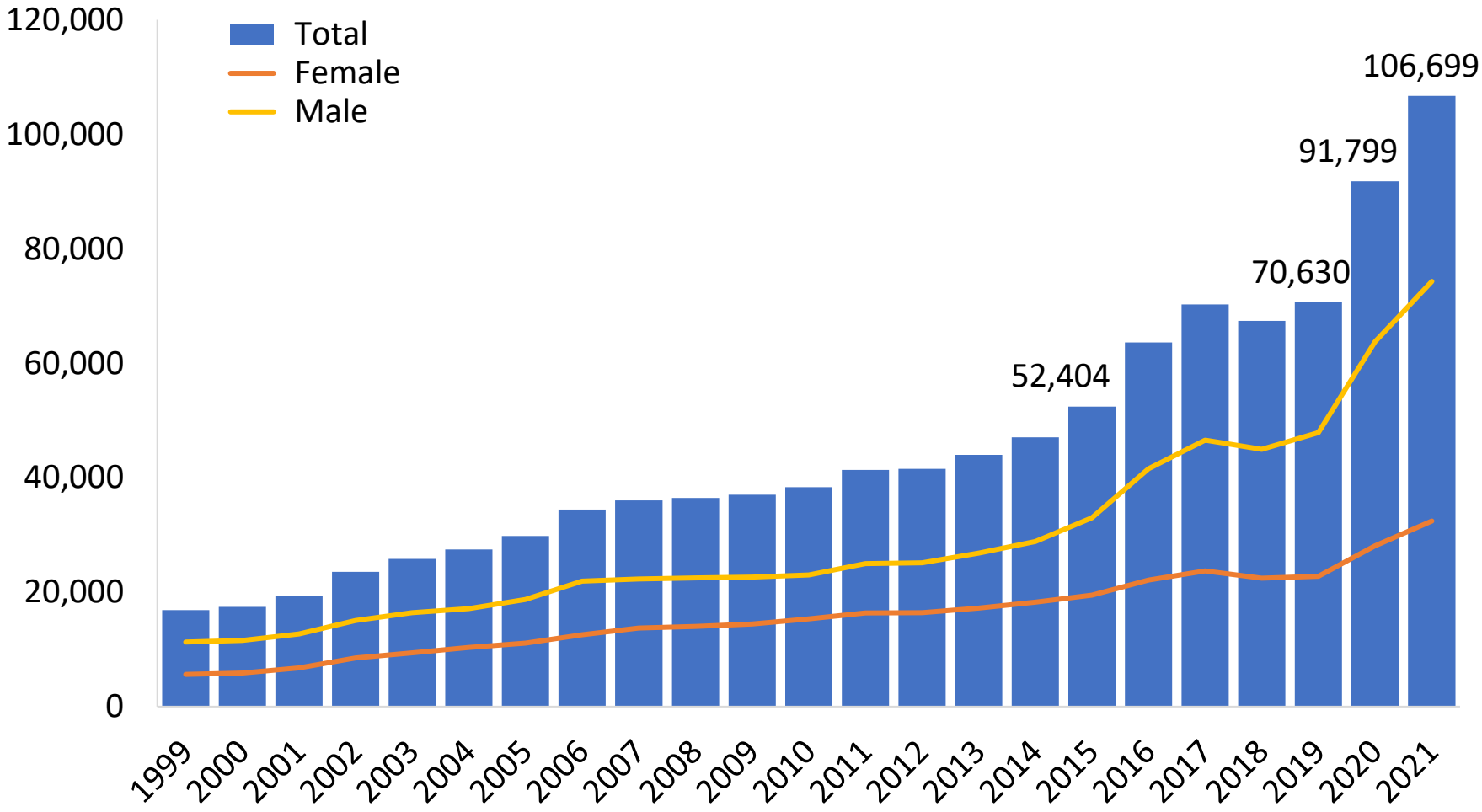
https://www.cdc.gov/drugoverdose/maps/rxstate2016.html

U.S. State Prescribing Rates, 2020



https://www.cdc.gov/drugoverdose/rxrate-maps/state2020.html

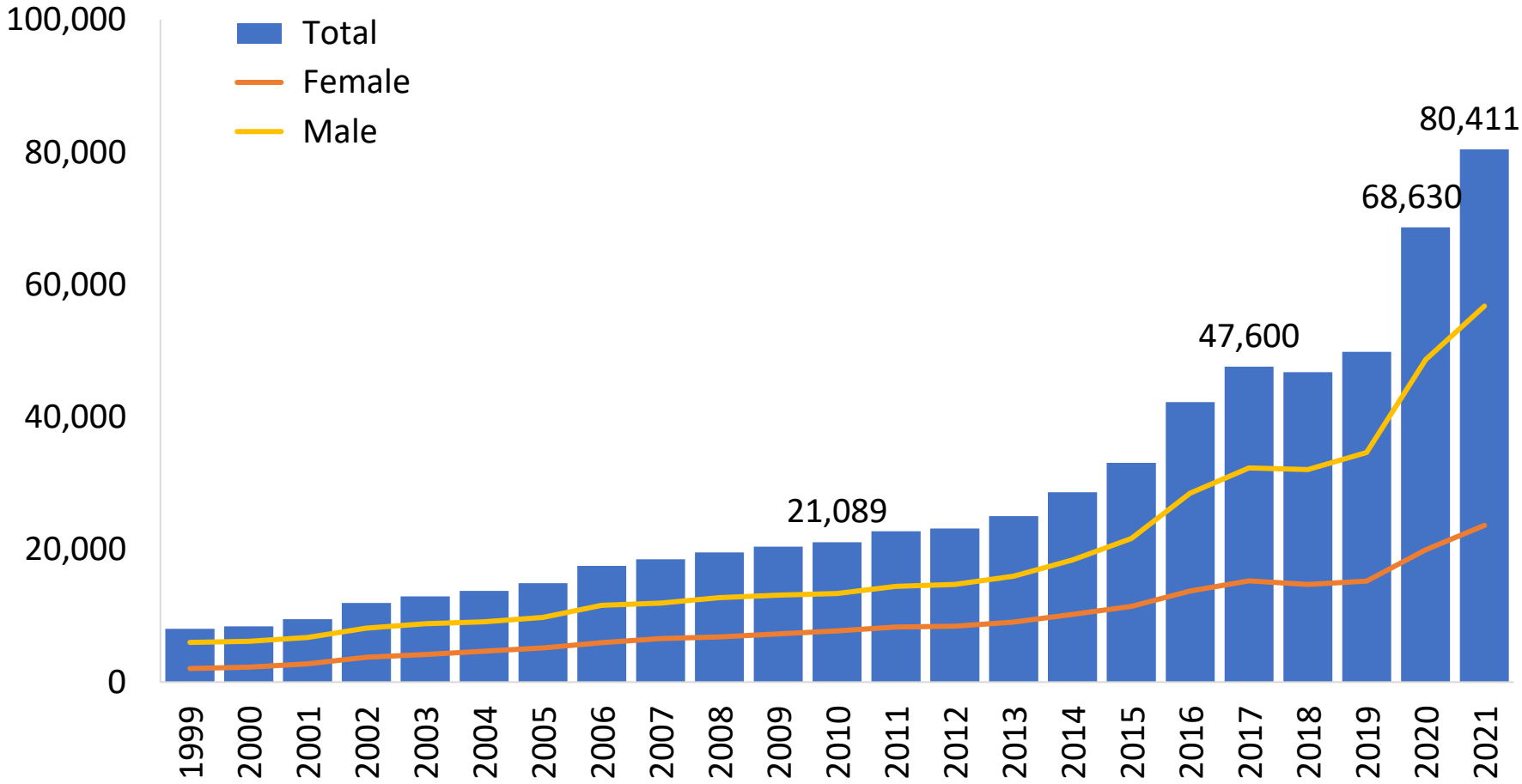
Figure 1. National Drug-Involved Overdose Deaths*, Number Among All Ages, by Gender, 1999-2021



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. 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.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

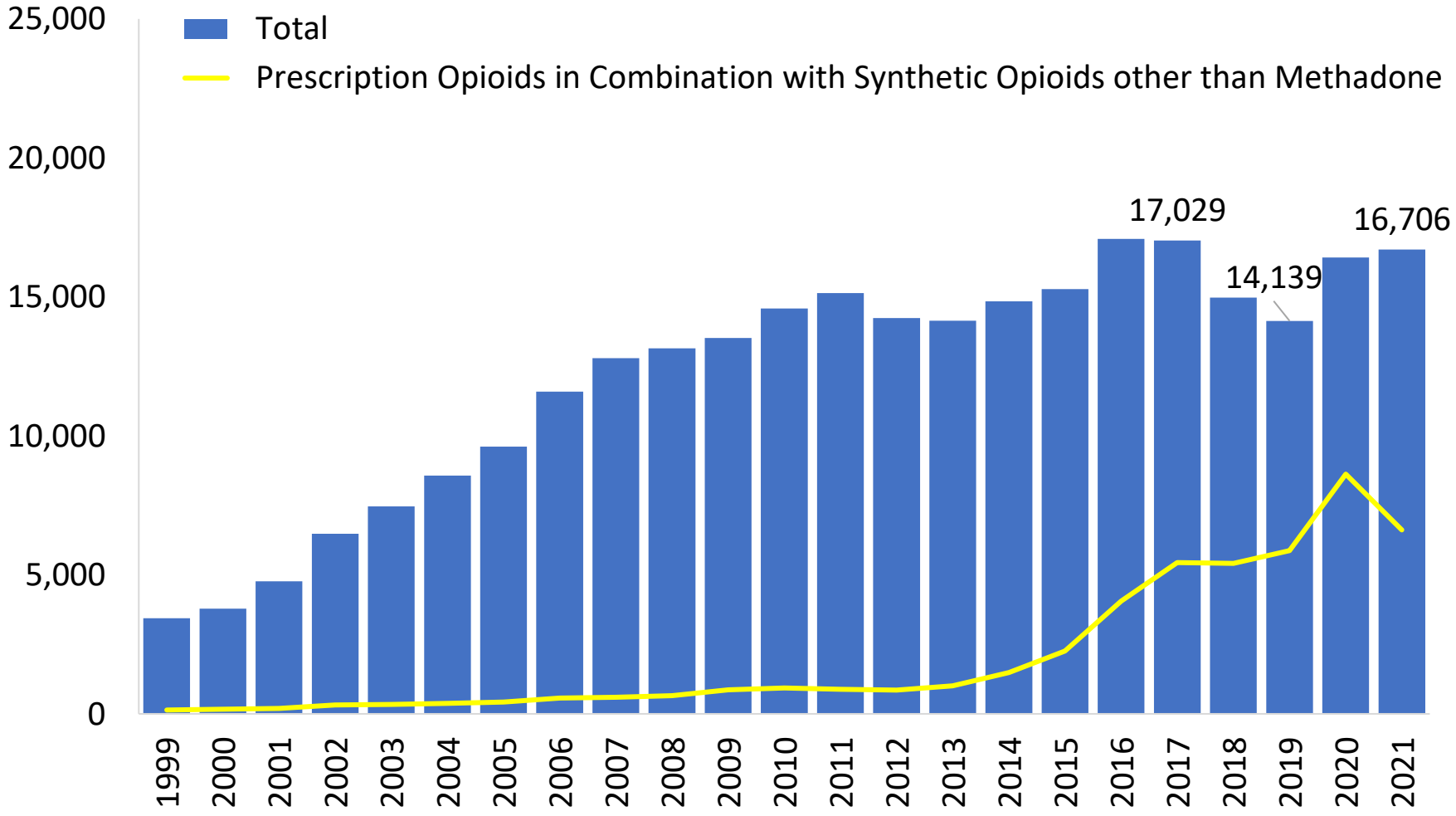
Figure 3. National Overdose Deaths Involving Any Opioid*, Number Among All Ages, by Gender, 1999-2021



https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

*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.

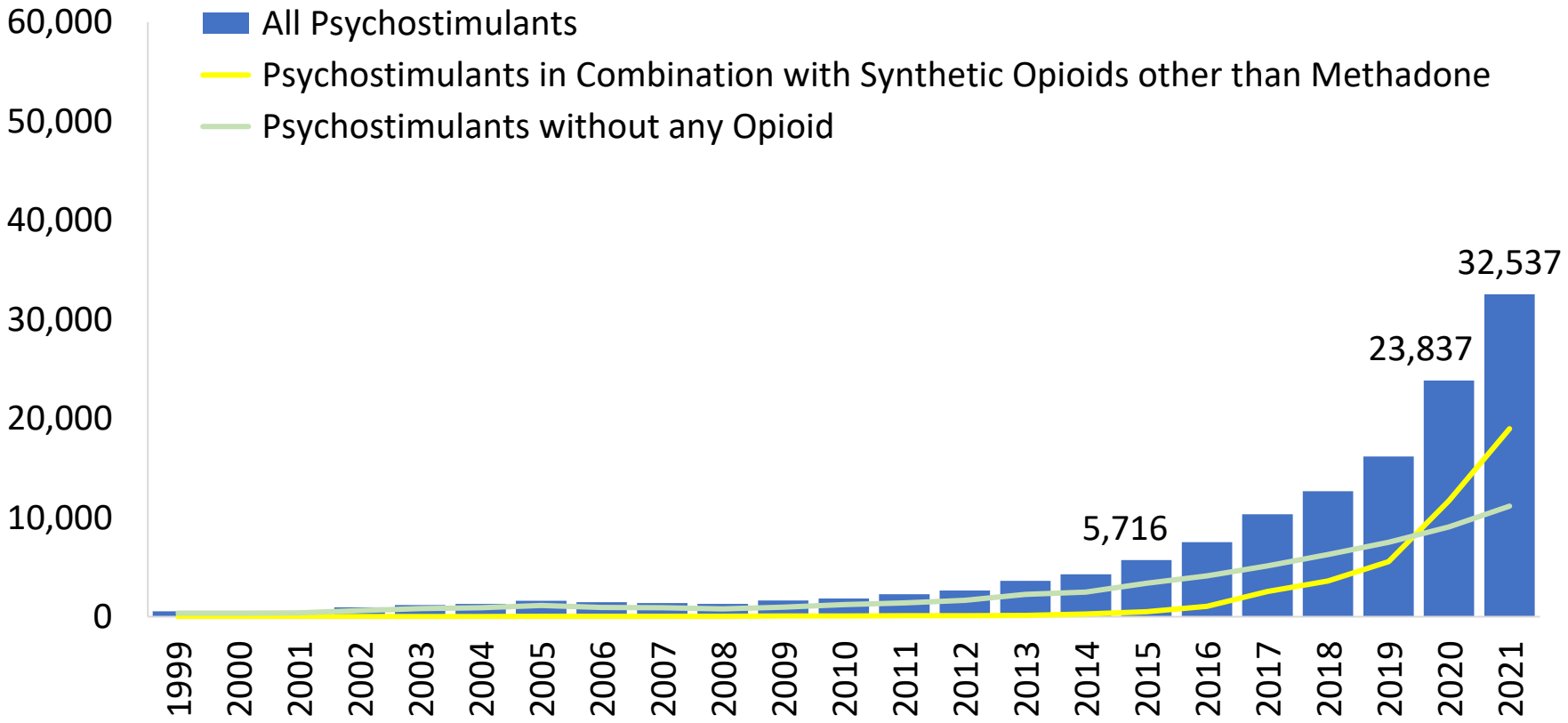
Figure 4. National Overdose Deaths Involving Prescription Opioids*, Number Among All Ages, 1999-2021



*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 1999-2021 on CDC WONDER Online Database, released 1/2023.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

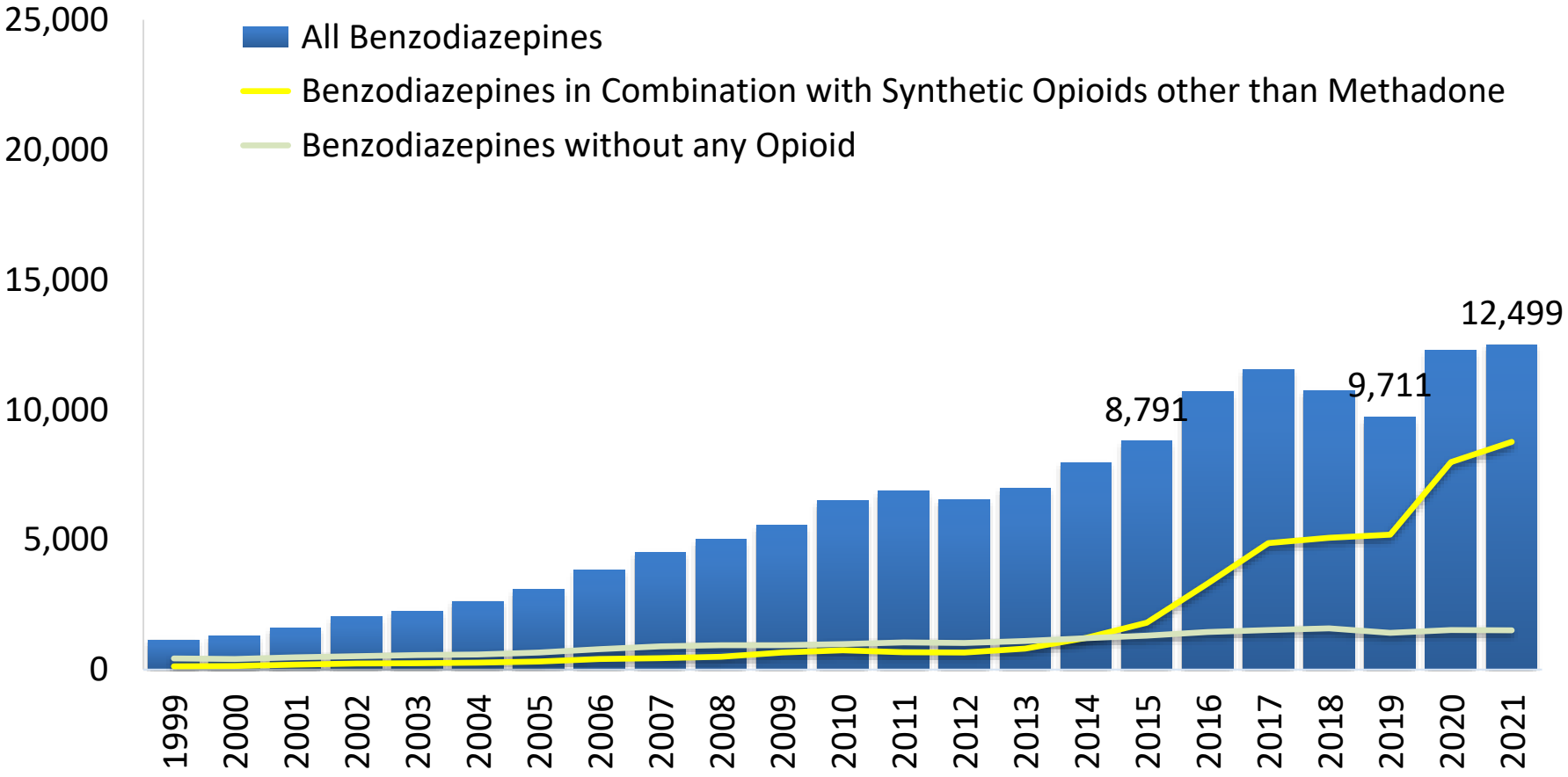
Figure 7. National Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)*, by Opioid Involvement, Number Among All Ages, 1999-2021



*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above.
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.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

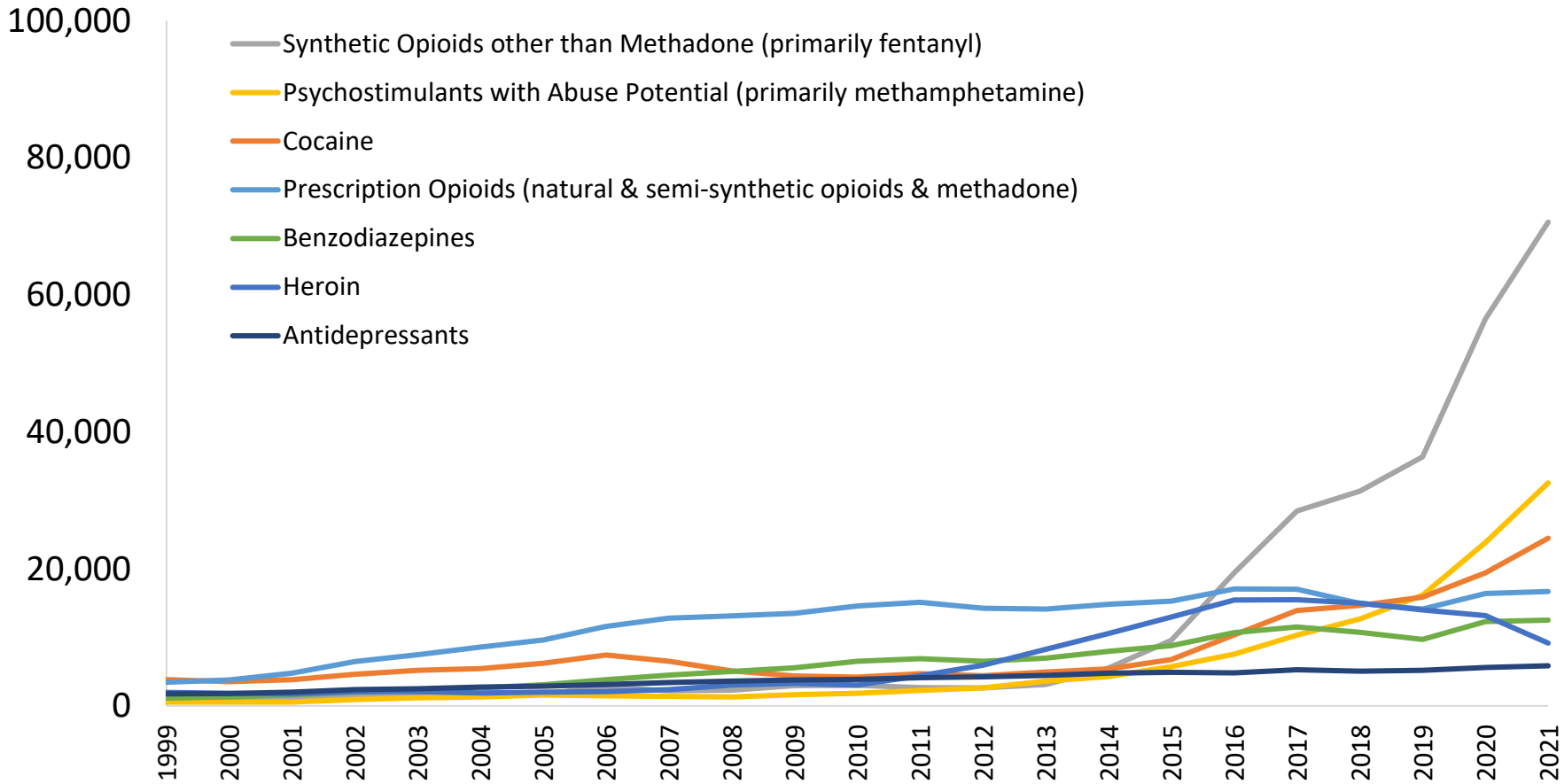
Figure 9. National Drug Overdose Deaths Involving Benzodiazepines*, by Opioid Involvement, Number Among All Ages, 1999-2021



https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

*Among deaths with drug overdose as the underlying cause, the benzodiazepine category was determined by the T42.4 ICD-10 multiple cause-of-death code. 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.

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2021



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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.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates

Newest agent of death: xylazine

- α_2 agonist
- Not for human use
- Fentanyl adulterated or associated with xylazine (FAAX)
- Apr 2023: "Emerging threat to the US"
- Death by respiratory depression
- Naloxone-resistant
- Tranq, Zombie drug

Rubin R. *JAMA* 329;22:1904-6.
Gupta R, et al. *N Engl J Med* 388;24:2209-12.
https://www.whitehouse.gov/wp-content/uploads/2023/07/FENTANYL-ADULTERATED-OR-ASSOCIATED-WITH-XYLAZINE-EMERGING-THREAT-RESPONSE-PLAN-Report-July-2023.pdf

Sobering statistics

- 21 – 29% of those Rx opioids misuse them
- 8 – 12% develop OUD
- 4 – 6% who misuse Rx opioids => heroin
- ~80% of heroin users first misused Rx opioids

- 80% post-op opioids go unused
- 3 – 10% chronic users post-op

- $78.5B/yr in economic cost, 2018

https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis

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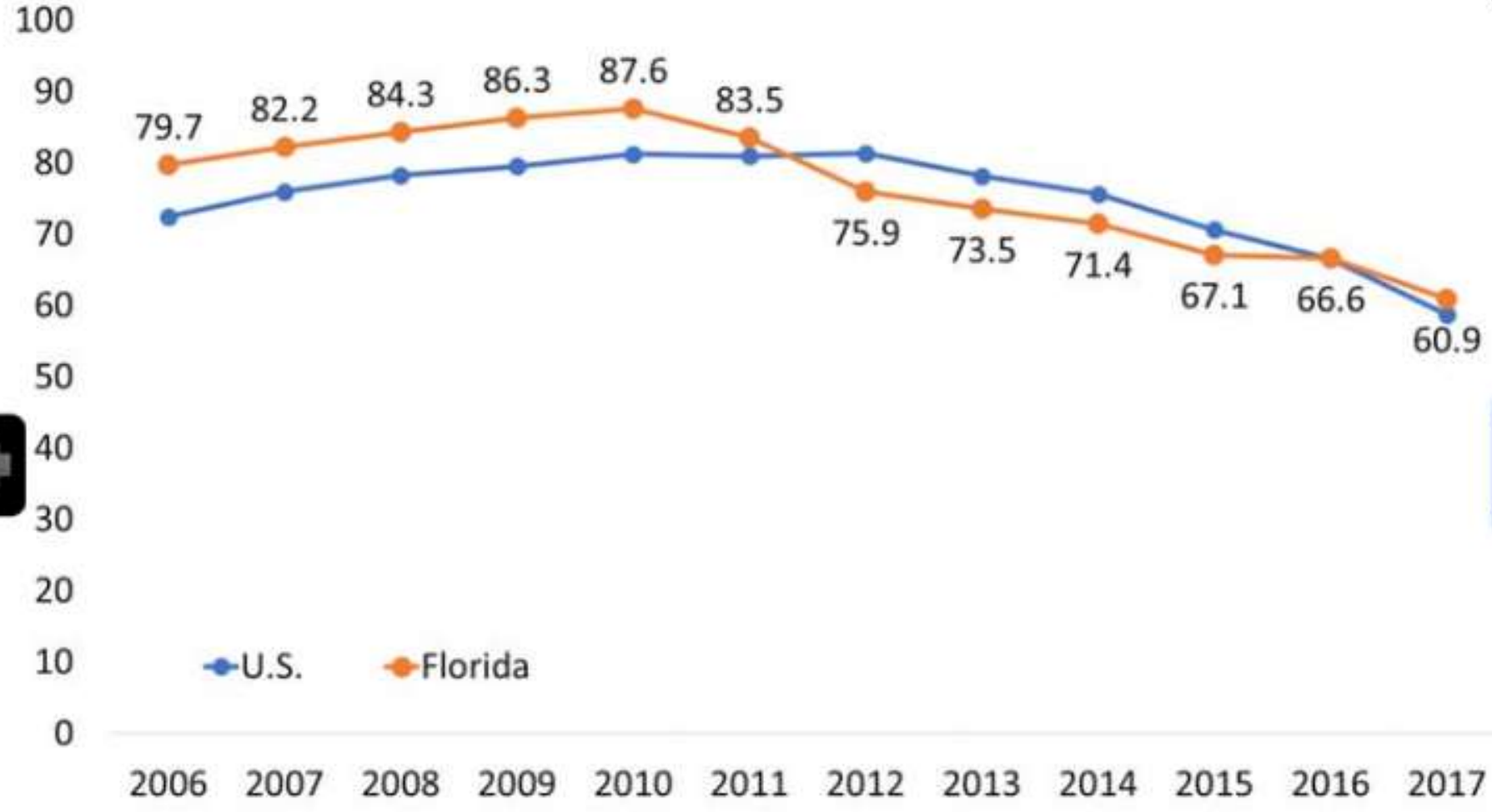
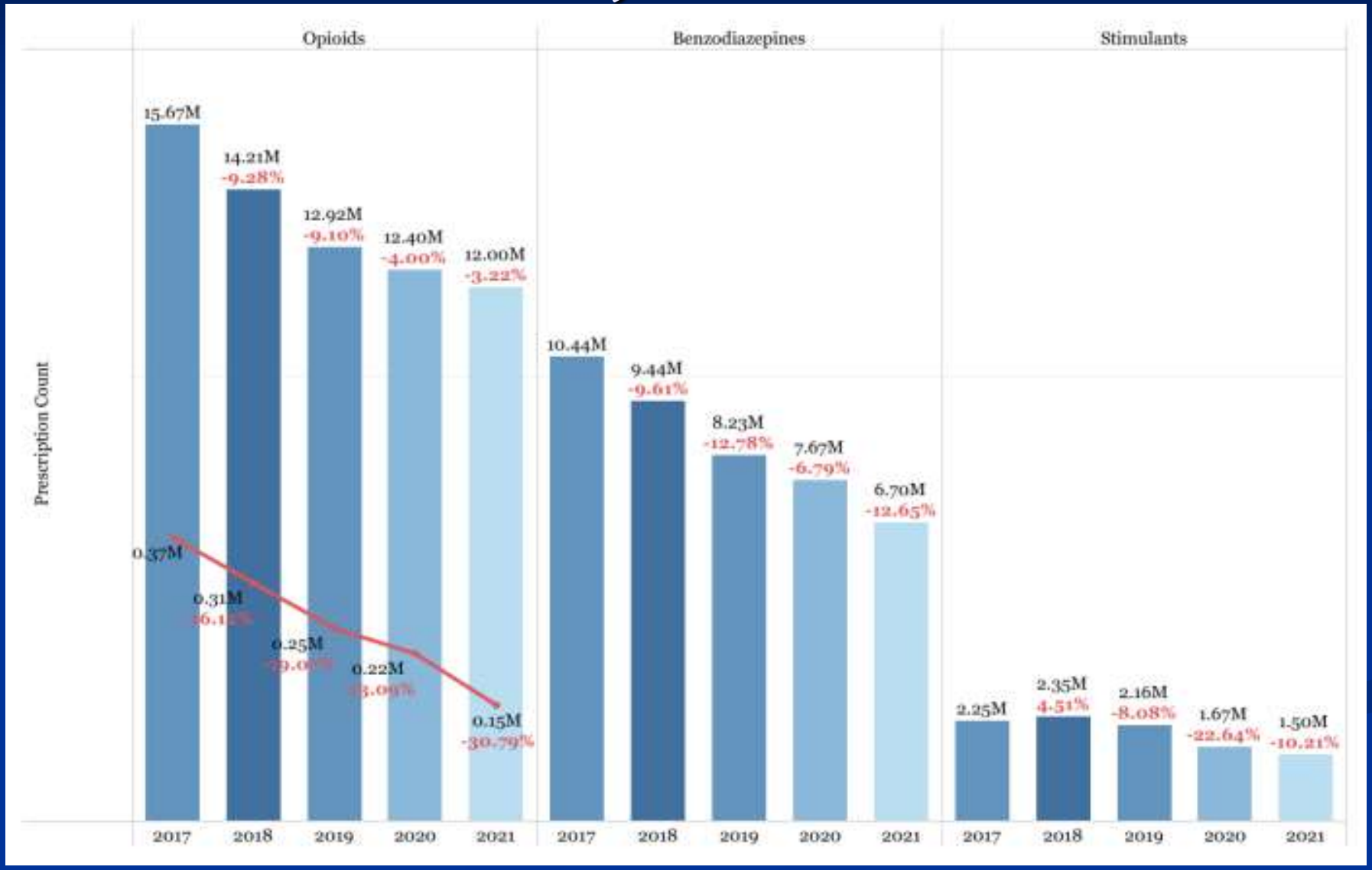


Figure 2. The U.S. and Florida opioid prescribing rate per 100 persons. Source: CDC and IQVIA Xponent 2006–2017.

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

https://www.drugabuse.gov/drugs-abuse/opioids/opioid-summaries-by-state/florida-opioid-summary

Prescriptions by Drug Type & Year, Florida, 2017 - 2021



https://www.floridahealth.gov/statistics-and-data/e-forcse/_documents/monthly-report-november-2022.pdf

- Pharmacology of opiates
- Epidemiology of opioid crisis
- Current Florida statistics regarding M&M of controlled substance-related deaths
- Current standards, laws and rules on prescribing controlled substances
- Proper prescribing of opiates

- C-II prescriptions do not have an expiration
  - Florida Rx must be filled within 1yr
  - No refills allowed
- C-III–V prescriptions expire 6mos post date written
  - Max of 5 refills within 6mos
- Physicians who write or dispense controlled substances for detoxification must be separately registered for that purpose
- Emergencies
- Partial fills

http://www.leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0800-0899/0893/Sections/0893.04.html

“Chronic nonmalignant pain”

The 2016 Florida Statutes

Title XXXII	Chapter 456	View Entire Chapter
REGULATION OF PROFESSIONS AND OCCUPATIONS	HEALTH PROFESSIONS AND OCCUPATIONS: GENERAL PROVISIONS	

456.44 Controlled substance prescribing.–

(1) DEFINITIONS.–As used in this section, the term:

(e) “Chronic nonmalignant pain” means pain unrelated to cancer which persists beyond the usual course of disease or the injury that is the cause of the pain or more than 90 days after surgery.

http://www.leg.state.fl.us/Statutes/index.cfm?App_mode=Display_Statute&Search_String=&URL=0400-0499/0456/Sections/0456.44.html

Florida HB 21: 2018

- Signed by Gov. Scott on March 19, 2018
- Presently in full effect (mostly as of July 1, 2018)

- Impact on key areas
  - Prescription Drug Monitoring Program (PDMP)
  - Controlled substance prescribing
  - Pain management clinic registration
  - Continuing medical education

E-FORCSE

- Electronic - Florida Online Reporting of Controlled Substances Evaluation program: Florida's Prescription Drug Monitoring Program (PDMP)
- Created by the 2009 legislature, an initiative to encourage safer prescribing of controlled substances and to reduce drug abuse and diversion within the State
- Operational 9/1/11; Health care practitioner (HCP) access 10/17/11; law enforcement access 11/14/11
- Health Information Designs, Inc. developed a database that collects and stores prescribing and dispensing data for controlled substances in Schedules II, III, and IV
- PDMP purpose: to provide information to HCPs to guide their decisions in prescribing and dispensing controlled substances

Florida's PDMP: https://florida.pmpaware.net

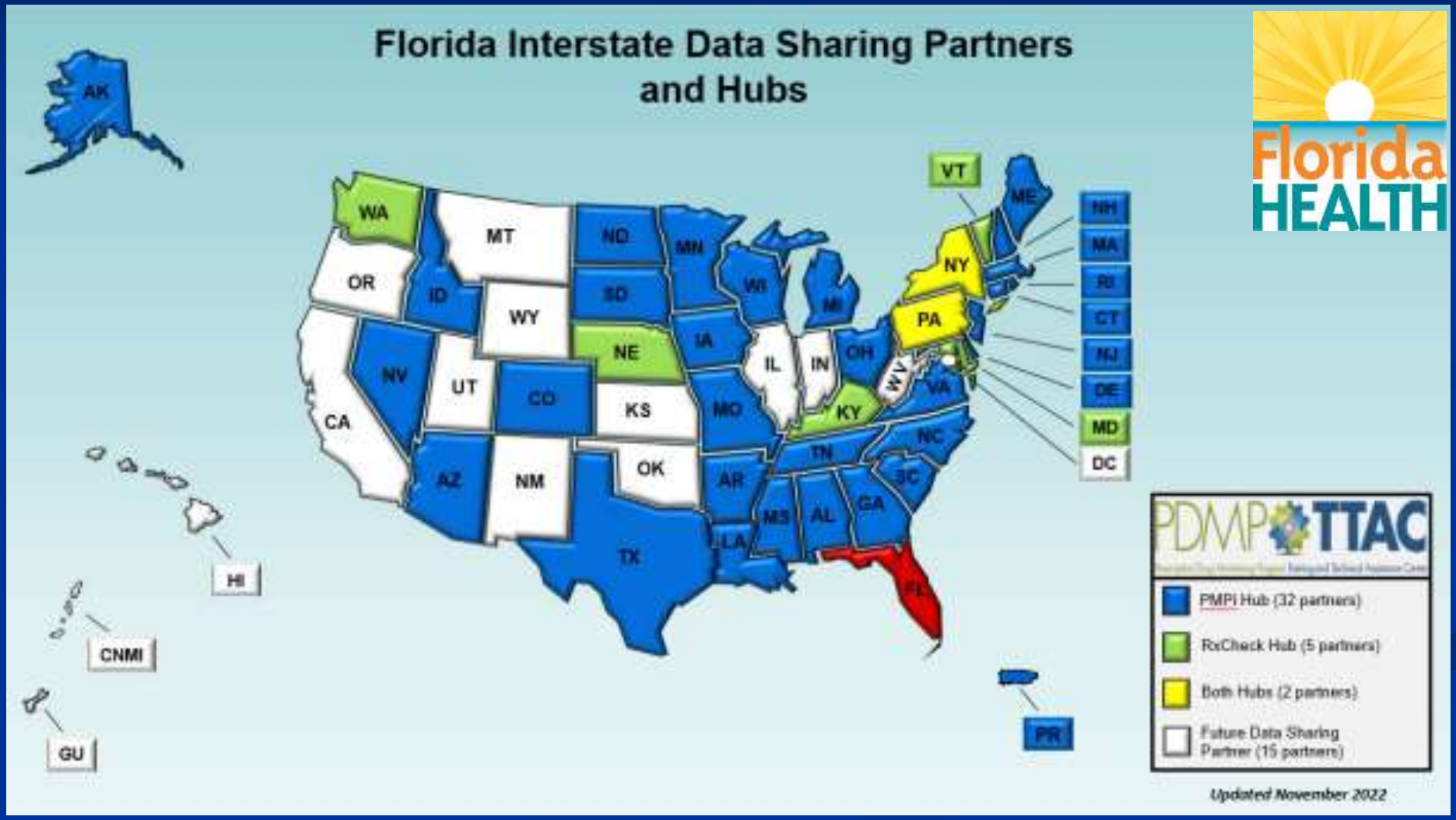
As of July 31, 2023 –

- Dispensing records uploaded: ~ 500M
- Total registrants: > 150K
- Total reports requested: ~ 250M

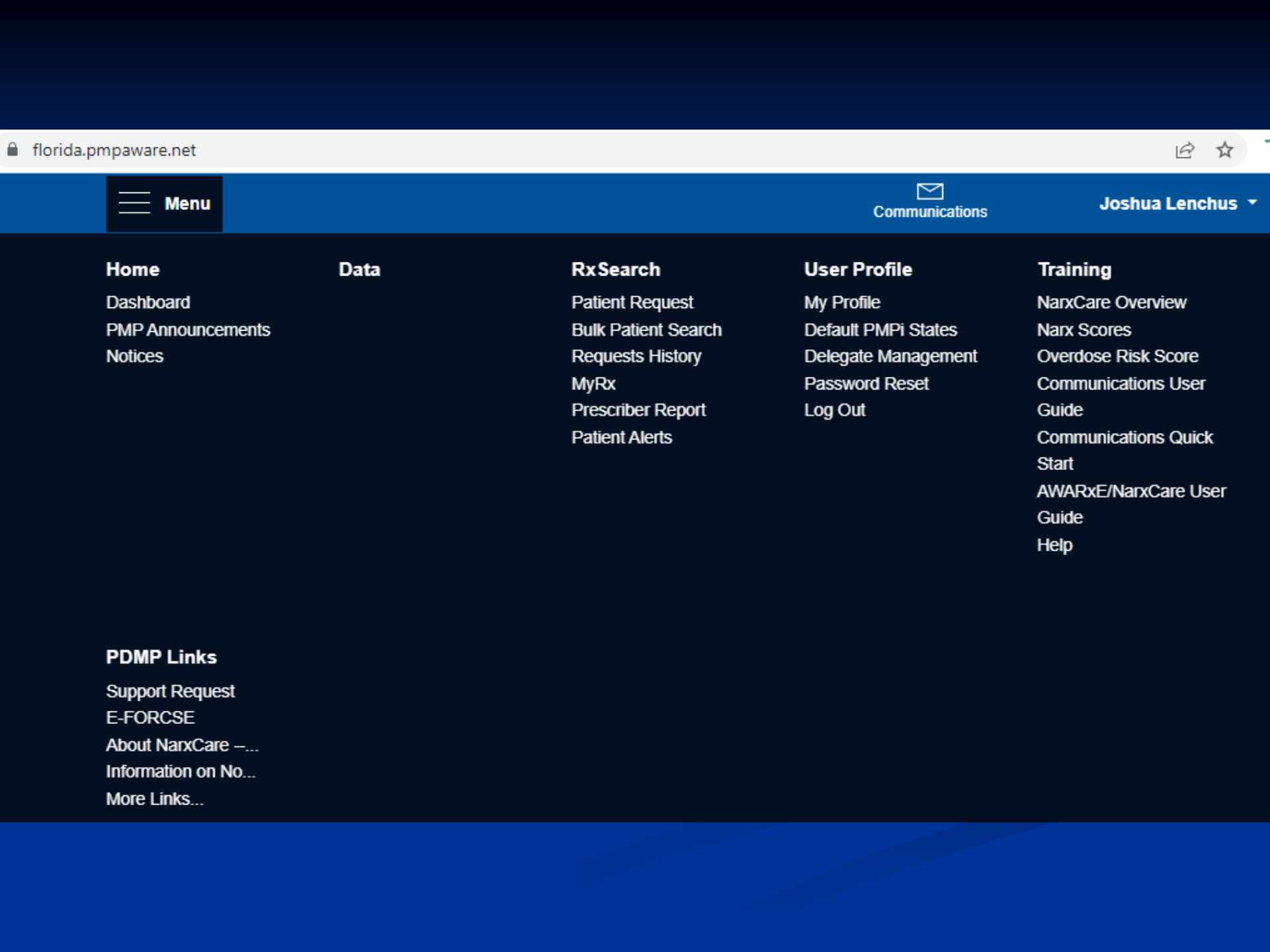
https://www.floridahealth.gov/statistics-and-data/e-forcse/news-reports/2022-pdmp-annual-report.pdf

PDMP Compatibility

https://florida.pmpaware.net



https://www.floridahealth.gov/statistics-and-data/e-forcse/news-reports/2022-pdmp-annual-report.pdf


florida.pmpaware.net
Menu
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Joshua Lenchus
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Patient Request
Bulk Patient Search
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User Profile
My Profile
Default PMPi States
Delegate Management
Password Reset
Log Out
Training
NarxCare Overview
Narx Scores
Overdose Risk Score
Communications User Guide
Communications Quick Start
AWARxE/NarxCare User Guide
Help
PDMP Links
Support Request
E-FORCSE
About NarxCare –...
Information on No...
More Links...

Registration, 07-31-23

License type	Total licensees (no.)	Registered users (no.)	Registered users (%)
ARNP	47,615	23,046	48
DN	16,462	9,376	57
ME	89,837	63,156	70
OPC	3,734	101	3
OS	12,289	11,409	93
PA	12,060	9,129	76
PO	1,999	1,519	76
PS	34,866	32,457	93

http://www.floridahealth.gov/statistics-and-data/e-forcse/health_care_practitioners/_documents/quarterly-dashboard2018Sept30.pdf

PDMP: 7/1/2018

- Prescribers and dispensers, or their designees, must access and consult the PDMP before each time a controlled substance, other than a C-V nonopioid, is prescribed or dispensed, but not ordered, for a patient 16 years or older, *except hospice* (7-1-19)
- Applies to **ALL** controlled substances
- Document reason for not consulting (cannot dispense more than 3d supply)
- Dispensing must be reported by next day's EOB

http://www.leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0800-0899/0893/Sections/0893.055.html

http://www.hidesigns.com/assets/files/flpdms/2016/Training_Guide_for_Florida_Practitioners_and_Pharmacists_-_Designee_Update_Final.pdf

http://www.flsenate.gov/Session/Bill/2018/21/BillText/er/PDF

https://flpdm-ph.hidinc.com/fllogappl/bdflpdmqlog/pmqhome.html

https://www.drugs.com/schedule-5-drugs.html

Florida Medical Association brief on HB 21

Controlled substance Rx: 7/1/2018

- Added treatment of acute pain to F.S.456.44
- Board authority: Rule 64B8-9.013 (2/21/19)
- Acute pain: "the normal, predicted, physiological, and time-limited response to an adverse chemical, thermal, or mechanical stimulus associated with surgery, trauma, or acute illness."

https://www.flrules.org/gateway/RuleNo.asp?ID=64B8-9.013

http://www.flsenate.gov/Session/Bill/2018/21/BillText/er/PDF

Injury Severity Score

Body system
Head and neck
Face
Chest
Abdomen
Extremity, inc pelvis
External

Injury severity	Points
No injury	0
Minor	1
Moderate	2
Serious	3
Severe	4
Critical	5
Unsurvivable	6

http://www.trauma.org/archive/scores/iss.html

- 3-day limit on C-II opioid
- Up to 7-day supply IF…
  - Medically necessary
  - "Acute pain exception" is written on Rx
  - Documents acute condition and lack of alternatives

Note that all 3 criteria must be met

- Emergency opioid antagonist
- "Nonacute pain"

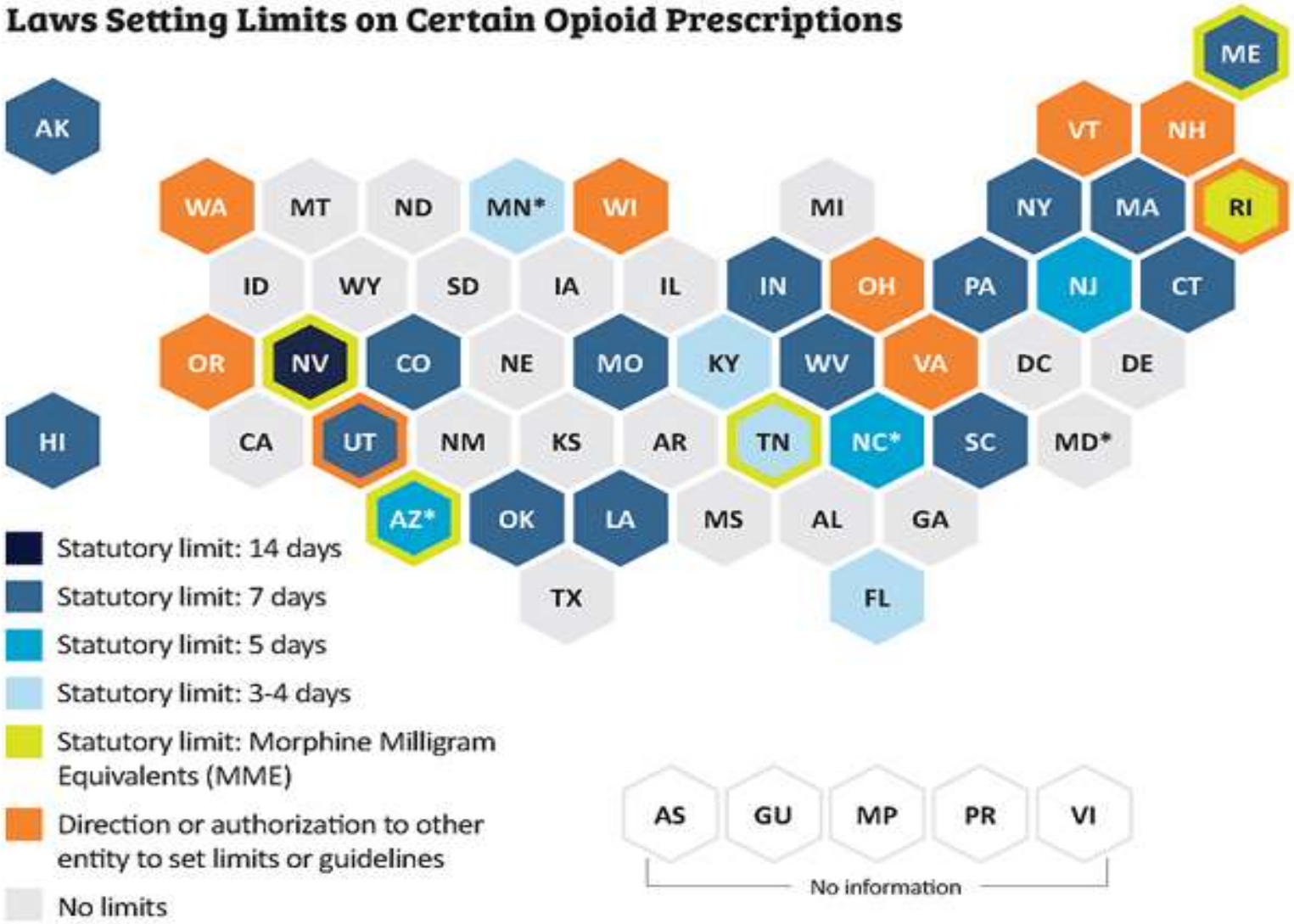
http://www.flsenate.gov/Session/Bill/2018/21/BillText/er/PDF

- Jan 1, 2019: CMS addresses opioid crisis
  - Hard safety edit at pharmacy
  - 90 MME threshold
  - Encourage drug management program

Medicare Prescription Drug Coverage

- Also called Part D
- Provides outpatient prescription drugs
- All Medicare beneficiaries are eligible
  - Can have Part A ***and/or*** Part B
- Coverage for Part D is provided by:
  - Prescription Drug plans (PDP's), also known as stand alone plans
  - Medicare Advantage Prescription Drug Plans (MAPD's)

Laws Setting Limits on Certain Opioid Prescriptions

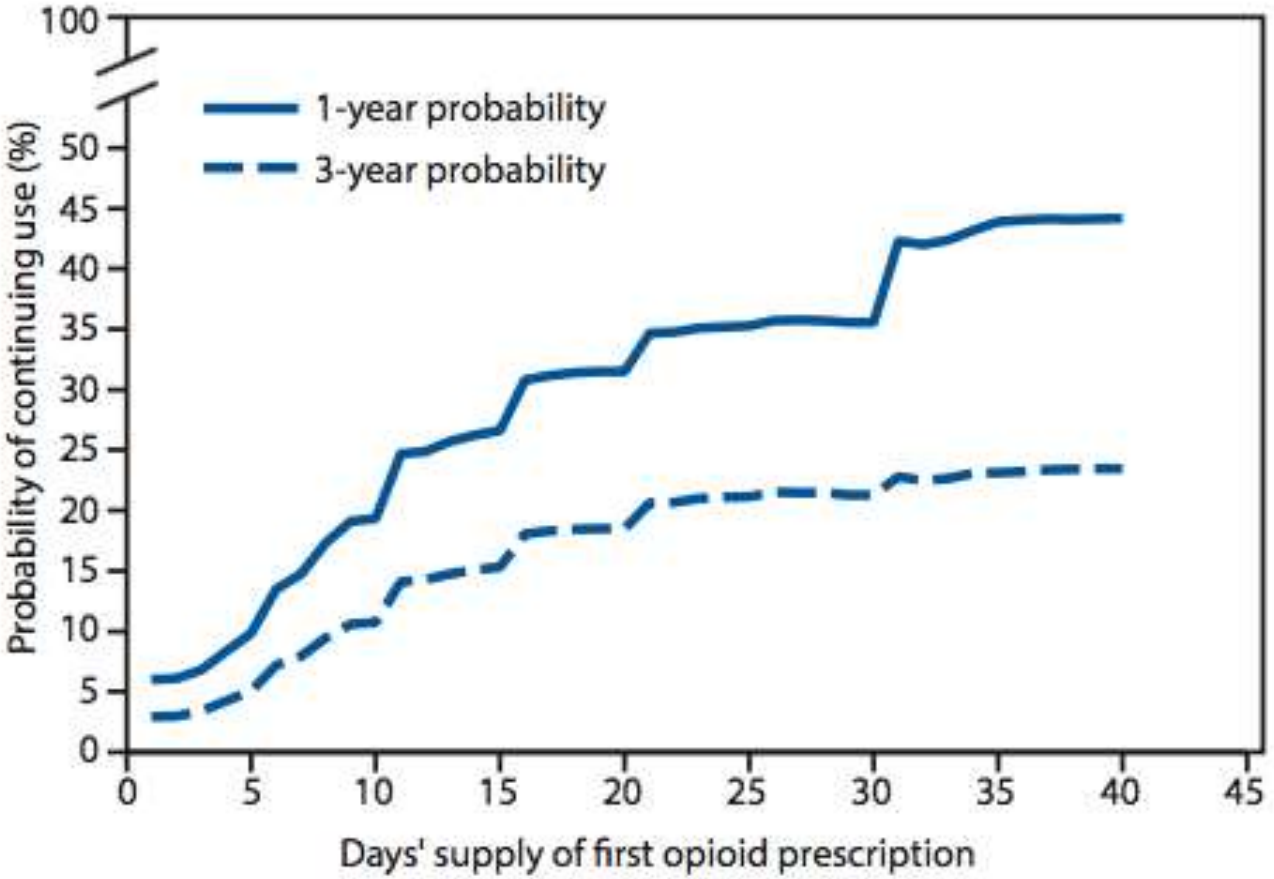


*** Note:** The map displays the state's primary opioid prescription limit and does not include additional limits on certain providers or in certain settings. Arizona allows prescriptions up to 14 days following surgical procedures and North Carolina allows up to seven days for post-operative relief. Maryland requires the "lowest effective dose." Minnesota's limit is for acute dental or ophthalmic pain. The map also does not reflect limits for minors that exist in at least eight states.

Source: NCSL, StateNet

http://www.ncsl.org/research/health/prescribing-policies-states-confront-opioid-overdose-epidemic.aspx

When does dependence begin?



* Days' supply of the first prescription is expressed in days (1–40) in 1-day increments. If a patient had multiple prescriptions on the first day, the prescription with the longest days' supply was considered the first prescription.

http://www.newsweek.com/cdc-opiate-addiction-572498

https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm

Pain management clinic: 1/1/2019

- Pain management clinic registration
- Exempt entities
  - Clinic in which the majority of physicians there primarily provide surgical services
  - Clinic held by a publicly traded company whose most recent total quarterly assets exceed $50M
  - Clinic affiliated with a medical school at which training is provided
- Certificate of exemption

http://www.floridahealth.gov/licensing-and-regulation/pain-management-clinics/applications-and-forms/index.html

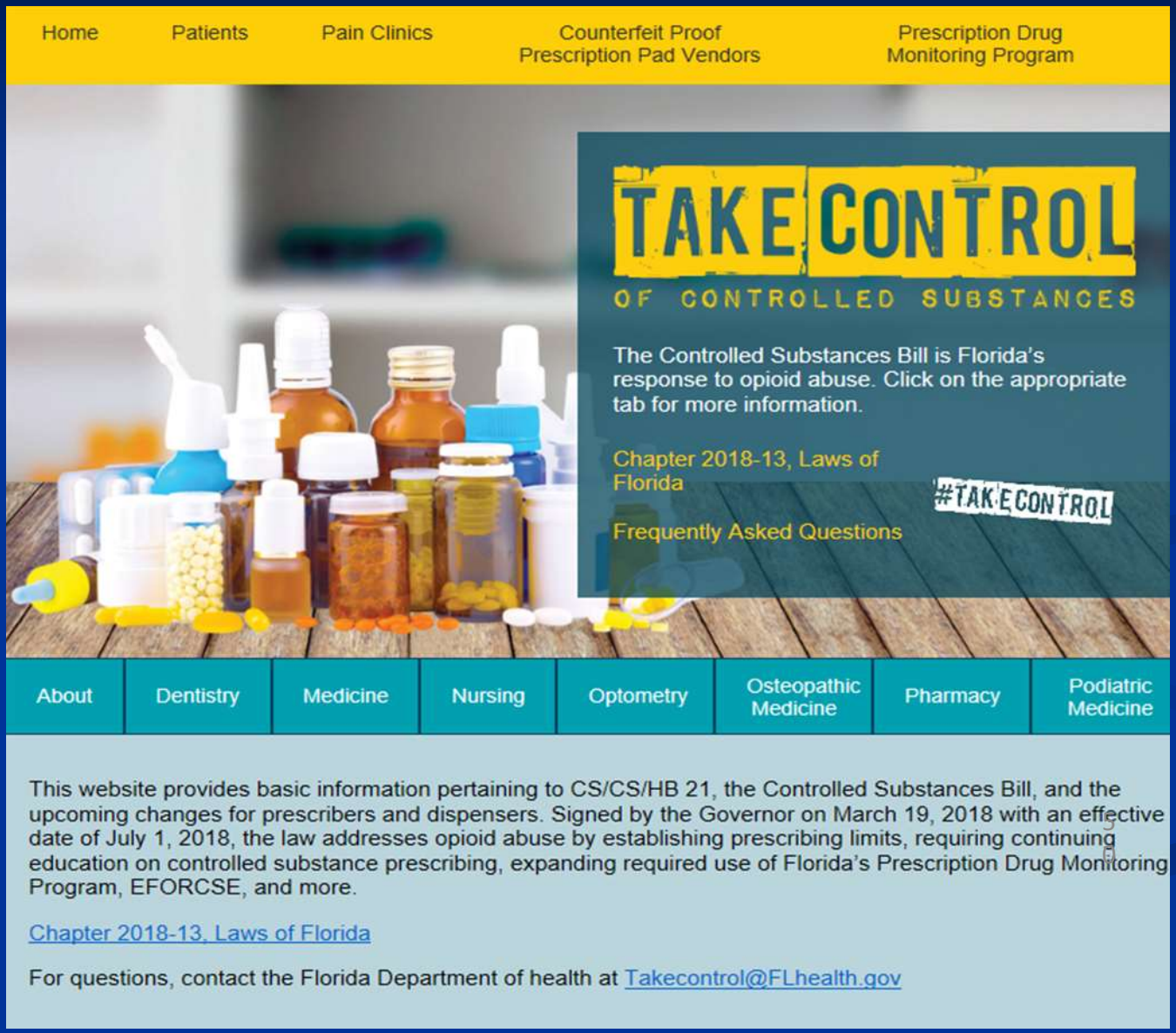
http://www.flsenate.gov/Session/Bill/2018/21/BillText/er/PDF

CME: 1/31/2019

- DEA registrants
- Controlled substance prescribers
- 2-hour, board-approved, CME
- Part of biennial license renewal
- Within the number of CE hours required by law
- Failure to complete course = no license renewal
- During each license renewal cycle since 1/31/19
- Submit confirmation of course completion
- All dentists (HB549, 7-1-19)

http://www.flsenate.gov/Session/Bill/2018/21/BillText/er/PDF

www.flhealthsource.gov/FloridaTakeControl



- Pharmacology of opiates
- Epidemiology of opioid crisis
- Current Florida statistics regarding M&M of controlled substance-related deaths
- Current standards, laws and rules on prescribing controlled substances
- Proper prescribing of opiates

Purpose of issue of prescription

- Legitimate medical purpose
- Practitioner
- Usual course of practice

- Corresponding responsibility

https://www.ecfr.gov/current/title-21/chapter-II/part-1306

465.035: Dispensing of medicinal drugs pursuant to facsimile of prescription

- (1) It is lawful for a pharmacy to dispense medicinal drugs, inc CS authorized under subsection (2), based on receipt of an electronic facsimile of the original Rx if all of the following conditions are met:
  - In the course of the transaction the pharmacy complies with laws and administrative rules relating to pharmacies and pharmacists.
  - Exc in the case of the transmission of a Rx by a person authorized by law to Rx medicinal drugs:
    - The facsimile system making the transmission provides the pharmacy receiving the transmission with audio communication via telephonic, electronic, or similar means with the person presenting the prescription.
    - At the time of the delivery of the medicinal drugs, the pharmacy has in its possession the original Rx for the medicinal drug involved.
    - The recipient of the Rx shall sign a log and shall indicate the name and address of both the recipient and the pt for whom the medicinal drug was prescribed.
- (2) C-II as defined in s. 893.03(2) may be dispensed as provided in this section to the extent allowed by 21 C.F.R. s. 1306.11.

http://www.leg.state.fl.us/Statutes/index.cfm?App_mode=Display_Statute&Search_String=&URL=0400-0499/0465/Sections/0465.035.html

Counterfeit-proof Rx pads

- Controlled substance Rx must be written on a counterfeit-resistant pad produced by an approved vendor, or electronically prescribed
- Otherwise, risk of Rx rejection and confiscation

http://www.floridashealth.com/mqu/counterfeit-proof.html

http://www.deadiversion.usdoj.gov/ecomm/e_rx/faq/faq.html

https://www.floridahealth.gov/licensing-and-regulation/counterfeit-proof-prescription-pad-vendors/faq.html

http://www.leg.state.fl.us/Statutes/index.cfm?App_mode=Display_Statute&URL=0400-0499/0465/Sections/0465.035.html

Example

Dr. Ali Ababwa
1234 Main Street
Anytown, Florida 33312
867-555-5309

Date: August 1, 2023

Patient Name: Jasmine Akrabah DOB: 08/27/1992

Address: 1111 Center Lane, Anytown, Florida 33312

Percocet (5/325)

Disp. # 10 (Ten)

Sig: Take one tab by mouth every 6 hours PRN post-op pain

No Refills

DEA # BA1222103

Signature 

DEA 2010

- EPCS is born
- Dual factor authentication is required
  - Something you know: a knowledge factor
  - Something you have: a hard token
  - Something you are: biometric information
- Confirm identity
- Two-factor authentication issued
- Setting access control

https://www.cms.gov/Medicare/E-Health/Eprescribing/index.html

https://www.deadiversion.usdoj.gov/ecomm/e_rx/index.html

https://www.deadiversion.usdoj.gov/ecomm/e_rx/faq/practitioners.htm

SUPPORT Act of 2018

- Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act
  - Section 2003
  - EPCS under Medicare Part D
  - Jan 1, 2021

https://www.congress.gov/bill/115th-congress/house-bill/6/text

https://www.cms.gov/newsroom/fact-sheets/calendar-year-cy-2022-medicare-physician-fee-schedule-final-rule

Opioid Prescribing Recommendations: Summary of 2016 CDC Guidelines

Determining when to initiate or continue opioids for chronic pain

- Opioids are not first-line or routine therapy
- Establish treatment goals before starting opioid therapy and a plan if therapy is discontinued
- Only continue opioid if there is clinically meaningful improvement in pain and function
- Discuss risks, benefits and responsibilities for managing therapy before starting and during treatment

Opioid selection, dosage, duration, follow-up and discontinuation

- Use immediate-release (IR) opioids when starting therapy
- Prescribe the lowest effective dose
- When using opioids for acute pain, provide no more than needed for the condition
- Follow up and review benefits and risks before starting *and* during therapy
- If benefits do not outweigh harms, consider tapering opioids to lower doses or taper and discontinue

Assessing risk and addressing harms of opioid use

- Offer risk mitigation strategies, including naloxone for patients at risk for overdose
- Review PDMP* data at least every 3 months and perform UDT** at least annually***
- Avoid prescribing opioid and benzodiazepines concurrently when possible
- Clinicians should offer or arrange MAT**** for patients with OUD†

*Prescription drug monitoring program
**Urine drug testing
***Some VA facilities may require more frequent testing
****Medication-assisted treatment
†Opioid use disorder

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

2022 updated guidelines, >18yoa

1. Determining whether or not to initiate opioids for pain
2. Selecting opioids and determining opioid dosages
3. Deciding duration of initial opioid prescription and conducting follow-up
4. Assessing risk and addressing potential harms of opioid use

https://www.cdc.gov/opioids/healthcare-professionals/prescribing/guideline/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fopioids%2Fhealthcare-professionals%2Fprescribing%2Fapp.html

https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm#B1_down

Clinically meaningful improvement

- 30%+ improvement
- Assess and document
- Validated tools

- What is not CMI?

- Rx – CMI = inappropriate care

https://www.medscape.com/viewarticle/813875_2

Appropriate opioid use

1. Limit use for acute pain
2. May be used for moderate – severe refractory pain
3. Identify patients at risk of misuse
4. Reduce risk of overdose
5. Start low, go slow with short-acting meds
6. Co-prescribe naloxone
7. Discuss expectations
   - "Opioids are a time-limited trial"

Clinical Resource, *Appropriate Opioid Use. Pharmacist's Letter/Prescriber's Letter.* January 2023. [390105]

Appropriate opioid use

8. Educate about opioid safety
9. Assess for misuse
10. Regular follow up
11. Consider non-opioids +/- adjunctive therapies
12. Taper or discontinue, when appropriate
13. Opioid disposal
14. OUD treatment, as relevant

Clinical Resource, *Appropriate Opioid Use. Pharmacist's Letter/Prescriber's Letter.* January 2023. [390105]
https://www.cdc.gov/drugoverdose/pdf/guidelines_factsheet-patients-a.pdf
https://www.fda.gov/consumers/consumer-updates/where-and-how-dispose-unused-medicines

- Risks, diagnosis and treatment of opioid addiction
- Prescribing emergency opioid antagonists
- Alternatives to controlled substance prescribing
  - Nonpharmacological therapies
- Controlled substance disposal

Consequences

- Opioid use disorder
- Addiction
- Addiction treatment
- Withdrawal
- Toxicity/overdose
- Overdose treatment

Risks of Opioid Therapy

- Mortality (of all-causes)
  - **Hazard ratio (HR) 1.64** for long acting opioids for non-cancer pain
- Overdose deaths (unintentional)
  - **HR 7.18-8.9** for MED > 100 mg/d
- Opioid use disorder

  For patients on long-term opioids (> 90 days)
  - **HR 15** for 1-36 mg/d MED
  - **HR 29** for 36-120 mg/d MED
  - **HR 122** for > 120 mg/d MED

*MED=Morphine Equivalent Daily Dose (in mg/d)

DSM-5 Criteria for OUD (Rx opioids)

(2 or more criteria)

DSM-5 Criteria	Example behaviors
Craving or strong desire to use opioids	Describes constantly thinking about opioids
Recurrent use in hazardous situations	Repeatedly driving under the influence
Using more opioids than intended	Repeated requests for early refills
Persistent desire/unable to cut down or control opioid use	Unable to taper opioids despite safety concern or family's concern
Great deal of time spent obtaining, using or recovering from the effects	Spending time going to different doctor's offices and pharmacies to obtain opioids
Continued opioid use despite persistent opioid-related social problems	Marital/family problems or divorce due to concern about opioid use
Continued opioid use despite opioid-related medical/psychological problem	Insistence on continuing opioids despite significant sedation
Failure to fulfill role obligations	Poor job/school performance; declining home/social function
Important activities given up	No longer active in sports/leisure activities

National Drug Control Strategy

"Saving Lives is Our North Star"

1. Harm reduction practices
2. Medications for treating OUD
3. Criminal justice reform

The White House. National drug control strategy. www.whitehouse.gov/wp-content/uploads/2022/04/National-Drug-Control-2022Strategy.pdf

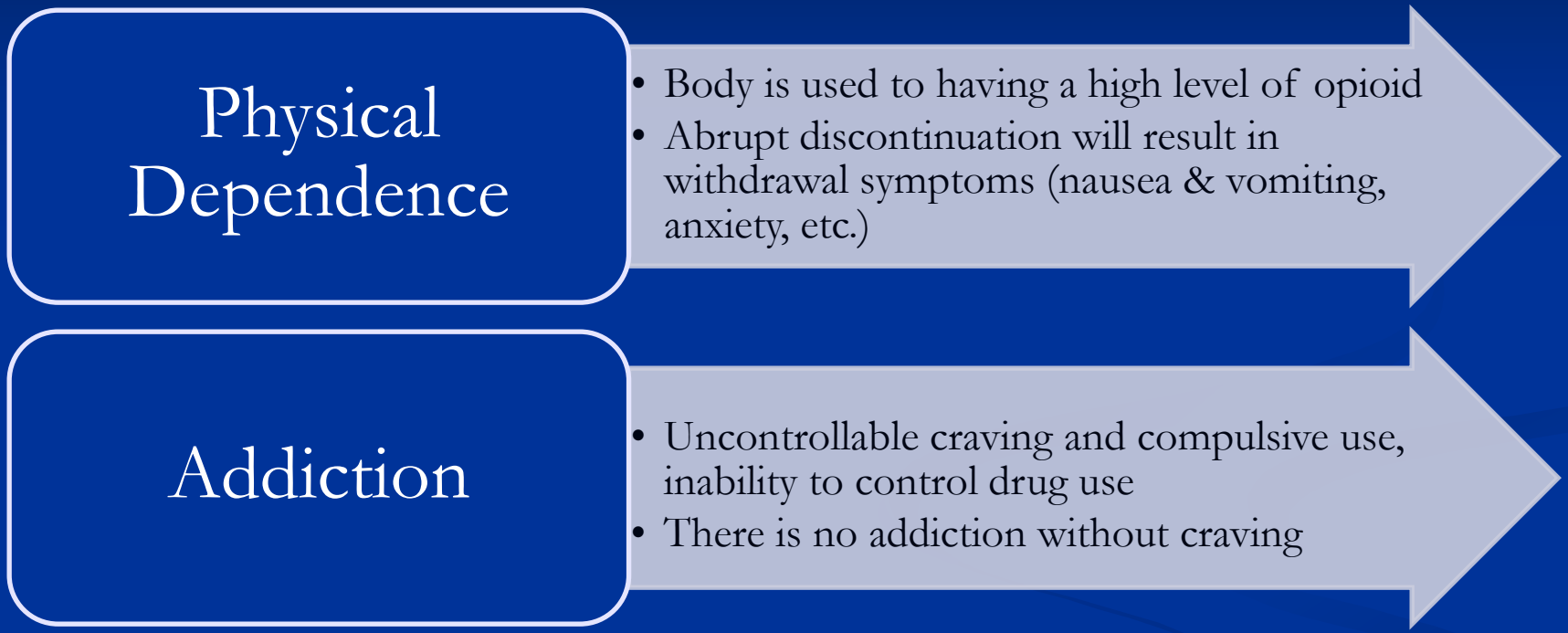
Opioid Risk Tool

This tool should be administered to patients upon an initial visit prior to beginning opioid therapy for pain management. A score of 3 or lower indicates low risk for future opioid abuse, a score of 4 to 7 indicates moderate risk for opioid abuse, and a score of 8 or higher indicates a high risk for opioid abuse.

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Rx drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Rx drugs	5	5
Age between 16—45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	2	2
Depression	1	1
Scoring totals		

https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf

Physical dependence vs. addiction



Addiction is a chronic, progressive brain disease due to altered brain structure and function

Kosten, T. R., & George, T. P. (2002). The Neurobiology of Opioid Dependence: Implications for Treatment. *Science & Practice Perspectives*, *1*(1), 13–20.

Addiction

- Definition
  1. Tolerance
  2. Withdrawal
  3. Abuse
  4. Helplessness
  5. Compulsion
  6. Isolation
  7. Vicious circle of devastation
- Dependence
- Hyperalgesia

http://www.medscape.com/viewarticle/562216_4

American Society of Addiction Medicine. (2011). Public Policy Statement: Definition of Addiction. Chevy Chase, MD.

Addiction treatment

- Inpatient
  - Short term
  - Long term
  - Partial hospitalization
- Outpatient
  - Intensive programs
  - Clinics
- Medication-assisted treatment programs

http://www.samhsa.gov/medication-assisted-treatment

MAT

- Component of comprehensive treatment

- Methadone
- Buprenorphine

- Naltrexone/naloxone?

http://store.samhsa.gov/product/Cl inical-Use-of-Extended-ReleaseInjectable-Naltrexone-in-theTreatment-of-Opioid-UseDisorder-A-Brief-Guide/SMA14- 4892R

Buprenorphine today: X the X-waiver

- MAT Act of 2021
- MATE Act of 2021
  1. All DEA-certificate holders
  2. > 6/27/2023
  3. One time only
  4. ≥ 8 hours training
  5. Self-attestation
  6. Training exceptions
- ➢ HB21 requirement?

https://www.congress.gov/117/bills/hr2617/BILLS-117hr2617enr.pdf
https://www.congress.gov/bill/117th-congress/senate-bill/445
https://www.deadiversion.usdoj.gov/pubs/docs/MATE_Training_Letter_Final.pdf
https://www.samhsa.gov/medications-substance-use-disorders/waiver-elimination-mat-act
https://www.deadiversion.usdoj.gov/drug_chem_info/buprenorphine.pdf

Withdrawal

- Rhinorrhea
- Diarrhea
- Yawning
- Anxiety
- Mydriasis
- Sneezing
- Lacrimation
- Vomiting
- Hyperventilation
- Hostility
- Piloerection

Clinical Opiate Withdrawal Scale

Clonidine v lofexidine

https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf

Opiate-induced constipation (OIC)

- Dietary and lifestyle interventions
- OTC medications
  - Stimulant laxatives: bisacodyl, senna
  - Stool softeners: docusate, mineral oil, Mg citrate
  - Enemas
- Prescription medications
  1. Naldemedine (Symproic)
  2. Naloxegol (Movantik)/Alvimopan (Entereg)
  3. Methylnaltrexone (Relistor)

  Lubiprostone (Amitiza)/Prucalopride (Motegrity)

https://www.uspharmacist.com/article/opioidinduced-constipation-clinical-guidance-and-approved-therapies

Ouyang R, Li Z, Huang S, et al. *Efficacy and Safety of Peripherally Acting Mu-Opioid Receptor Antagonists for the Treatment of Opioid-Induced Constipation: A Bayesian Network Meta-analysis.* Pain Med. 2020 Jun 3. pii: 5850638. doi: 10.1093/pm/pnaa152.

- Risks, diagnosis and treatment of opioid addiction
- Prescribing emergency opioid antagonists
- Alternatives to controlled substance prescribing
  - Nonpharmacological therapies
- Controlled substance disposal

Overdose treatment

- Assess risk proactively
- Pale, clammy skin, miosis, vomiting, bradypnea, hypoventilation, limp, unarousable, coma
- BLS

Opioid antagonist

- Naloxone
- Pharmacokinetics
- Federal government guidelines

- SB 544, effective *7/1/2022*

https://www.flsenate.gov/Session/Bill/2022/544/BillText/er/PDF

https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio

https://www.hhs.gov/about/news/2018/12/19/hhs-recommends-prescribing-or-co-prescribing-naloxone-to-patients-at-high-risk-for-an-opioid-overdose.html

Co-Rx opioid antagonist

Patients who:

- Are receiving opioids at a dosage of ≥ 50 MME/d;
- Have respiratory conditions (i.e., COPD, OSA), regardless of opioid dose;
- Have been prescribed BZDs, regardless of opioid dose; OR
- Have a non-opioid substance use disorder, report excessive alcohol use, or have a mental health disorder, regardless of opioid dose.

https://www.cdc.gov/stopoverdose/naloxone/index.html

https://www.hhs.gov/about/news/2018/12/19/hhs-recommends-prescribing-or-co-prescribing-naloxone-to-patients-at-high-risk-for-an-opioid-overdose.html

https://www.hhs.gov/opioids/sites/default/files/2018-12/naloxone-coprescribing-guidance.pdf

Naloxone +

- Injectable (Narcan)
- Autoinjectable (Evzio, Kaleo*)
- Nasal spray (Narcan, naloxone, Kloxxado)

- Nalmefene (Revex)

- Active monitoring

https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio

https://www.purduepharma.com/news/2022/02/23/fda-approves-nalmefene-hcl-injection-2mg-2ml-1mg-1ml-for-the-treatment-of-known-or-suspected-opioid-overdose-with-natural-or-synthetic-opioids/

https://kaleo.com/fda-approves-kaleos-naloxone-auto-injector-10-mg-for-the-treatment-of-known-or-potential-exposure-to-ultra-potent-weaponized-opioids/#:~:text=Kal%C3%A9o%20is%20headquartered%20in%20Richmond%2C%20Virginia%20in%20the,by%20military%20personnel%20and%20chemical%20incident%20responders%20for%3A

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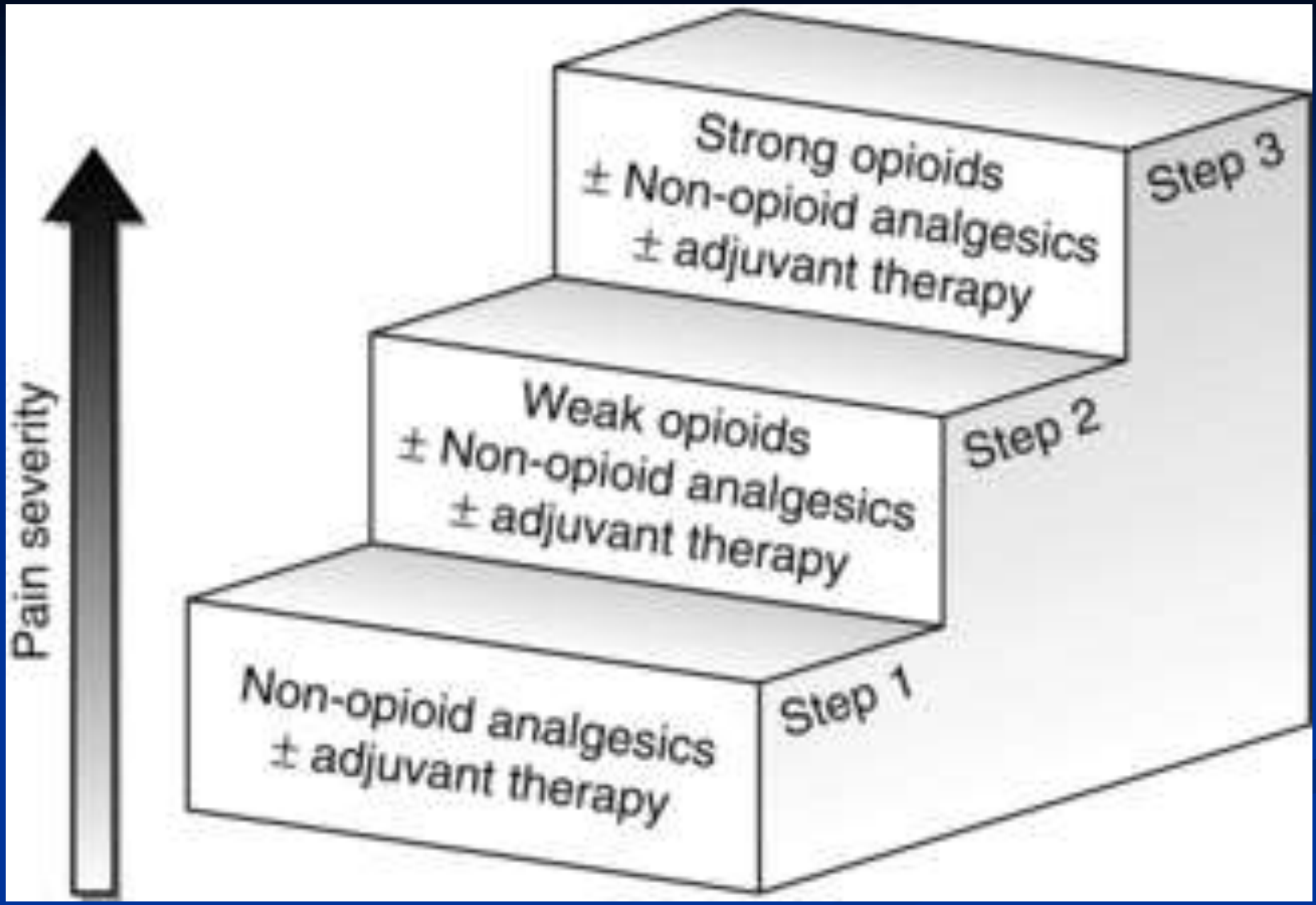
Pain severity
Strong opioids
± Non-opioid analgesics
± adjuvant therapy
Step 3
Weak opioids
± Non-opioid analgesics
± adjuvant therapy
Step 2
Non-opioid analgesics
± adjuvant therapy
Step 1

Abuse-deterrent opioids

- Hydrocodone: Hysingla ER; Vantrela ER; Zohydro ER
- Hydromorphone: Exalgo
- Morphine ER: Morphabond; Arymo ER
- Morphine ER/Naltrexone: Embeda
- Oxycodone IR: Oxaydo; Roxybond
- Oxycodone ER: Oxycontin; Xtampza ER
- Oxycodone ER/Naltrexone: Targiniq ER; Troxyca ER

JAMA. May 15, 2018;319(19):2036-2037.

Tapering opioids: initiation

- Individualize
- Monitor and adjust
- Consolidate

- Regimens
  - 5 – 20% every 4wks
  - 10% weekly
  - 10% each month (chronic)
- Dose before frequency

https://www.agencymeddirectors.wa.gov/Calculator/TaperDoseCalculator.html

https://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Taper-Template.pdf

Clinical Resource, Opioid Tapering: Tips for Success. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber's Letter. February 2023. [390202]

Tapering opioids: monitoring

- Weekly – monthly check
- CMI assessment – pain & function
- Non-opioids for pain
- Evaluate behavioral health conditions
- Monitor for withdrawal – treat prn
- Risk of overdose counseling
- Naloxone

Clinical Resource, Opioid Tapering: Tips for Success. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber's Letter. February 2023. [390202]

Non-opioid alternatives

- Antidepressants
- Anticonvulsants
- Acetaminophen
- NSAIDs
  - Preop IV ketorolac: lap chole
- Anesthetics
- Corticosteroids
- Non-BZD muscle relaxers

JAMA. 2018;320(23):2448-2460.

Lee et al. *Ann Hepatobiliary Pancreat Surg.* Published online Mar 10, 2022. doi:10.14701/ahbps.21-151.

Table 2. Recommendations for the pharmacologic management of osteoarthritis of the hand, knee, and hip

Intervention	Joint		
	Hand	Knee	Hip
Topical nonsteroidal antiinflammatory drugs			
Topical capsaicin			
Oral nonsteroidal antiinflammatory drugs			
Intraarticular glucocorticoid injection			
Ultrasound-guided intraarticular glucocorticoid injection			
Intraarticular glucocorticoid injection compared to other injections			
Acetaminophen			
Duloxetine			
Tramadol			
Non-tramadol opioids			
Colchicine			
Fish oil			
Vitamin D			
Bisphosphonates			
Glucosamine			
Chondroitin sulfate			
Hydroxychloroquine			
Methotrexate			
Intraarticular hyaluronic acid injection	(First carpometacarpal)		
Intraarticular botulinum toxin			
Prolotherapy			
Platelet-rich plasma			
Stem cell injection			
Biologics (tumor necrosis factor inhibitors, interleukin-1 receptor antagonists)			

Strongly recommended
Conditionally recommended
Strongly recommended against
Conditionally recommended against
No recommendation

https://www.rheumatology.org/Portals/0/Files/Osteoarthritis-Guideline-Early-View-2019.pdf

Next generation

- ERAS /pre-operative Rx
- IV acetaminophen
- Slow-release bupivacaine
- Different targets than opioid receptors
- Longer acting agents
- Nerve fiber inactivation
- Novel combinations
- Sodium channel blockers
- Potassium channel blockers

- Nonpharmacological

Hot/cold	Osteopathic manipulation
Physical therapy	Chiropractic medicine
Accupuncture	TENS
Biofeedback	Cognitive behavioral therapy
Exercise	Yoga
Music	Moxibustion
Pulsed radiofrequency	

Colebaugh CA, et al. *J Pain,* published online Jan 13, 2023. doi:10.1016/j.jpain.2023.01.006.

Nielsen A, et al. *Pain Med.* 2022;pnac056. doi:10.1093/pm/pnac056.

Nadlinda PG, et al. *Pain*, published online Oct 26, 2021, doi:10.1097/j.pain.0000000000002521.

Table 1. Recommendations for physical, psychosocial, and mind-body approaches for the management of osteoarthritis of the hand, knee, and hip

Intervention	Joint		
	Hand	Knee	Hip
Exercise			
Balance training			
Weight loss			
Self-efficacy and self-management programs			
Tai chi			
Yoga			
Cognitive behavioral therapy			
Cane			
Tibiofemoral knee braces		(Tibiofemoral)	
Patellofemoral braces		(Patellofemoral)	
Kinesiotaping	(First carpometacarpal)		
Hand orthosis	(First carpometacarpal)		
Hand orthosis	(Other joints)		
Modified shoes			
Lateral and medial wedged insoles			
Acupuncture			
Thermal interventions			
Paraffin			
Radiofrequency ablation			
Massage therapy			
Manual therapy with/without exercise			
Iontophoresis	(First carpometacarpal)		
Pulsed vibration therapy			
Transcutaneous electrical nerve stimulation			

Strongly recommended
Conditionally recommended
Strongly recommended against
Conditionally recommended against
No recommendation

https://www.rheumatology.org/Portals/0/Files/Osteoarthritis-Guideline-Early-View-2019.pdf

Timing is everything

- Low back pain
  - 40%-60% less likely to use opioids over 2 years if PT seen within 2 weeks of onset
    - Childs et al 2015; Fritz et al 2013
- Neck pain
  - 41% less likely to receive opioid therapy for neck pain in the next 12 months
    - Horn et al, 2018
- Knee pain
  - 33% less likely over 12 months
    - Stevans et al 2017

Bottom Line

- Individualized approach to patient and pain type
  - Review PDMP
  - Evaluate those at higher risk of misuse/abuse
- Discuss realistic analgesic expectations
- Multimodal analgesia + non-pharmacological tx
- Educate about storage, tapering, and disposal
- Monitor for efficacy and adverse effects
- Consider referral to pain management

- Risks, diagnosis and treatment of opioid addiction
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- Controlled substance disposal

Controlled substance disposal

- Small amounts
- Secure safely
- Safe disposal options

- Household trash (***not for controlled substances***)

- National Prescription Drug Take-Back Day
  - April and October annually
  - https://www.deadiversion.usdoj.gov/drug_disposal/takeback/

- DEA-authorized collectors
  - https://apps.deadiversion.usdoj.gov/pubdispsearch/spring/main?execution=e1s1
  - DEA Office of Diversion Control's Registration Call Center: 1-800-882-9539

- Flushing: https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm588196.pdf

https://takebackday.dea.gov/sites/default/files/NTBI%20XVI%20Totals.pdf
Khan, et al. Risks associated with the environmental release of pharmaceuticals on the U.S. Food and Drug Administration "flush list". Sci Total Environ 2017 Dec 31;609:1023-1040.
https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/ensuringsafeuseofmedicine/safedisposalofmedicines/ucm186188.htm

Thank you

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954-817-5684 (cel)

Additional references

- American Society of Addiction Medicine Opioid Addiction 2016 Facts & Figures http://www.asam.org/docs/default-source/advocacy/opioid-addiction-disease-facts-figures.pdf
- Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1
- Medication Assisted Treatment http://www.samhsa.gov/medication-assisted-treatment, http://pcssmat.org/
- National Institute on Drug Abuse (NIDA) https://www.drugabuse.gov/
- Schuckit MA. Treatment of Opioid Use Disorders. *NEJM* (07/28/16) Vol. 375, No. 4, P. 357 http://www.nejm.org/doi/full/10.1056/NEJMra1604339#t=article
- Substance Abuse and Mental Health Services Administration. *Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders.* Treatment Improvement Protocol (TIP) Series 54. HHS Publication No. (SMA) 12-4671. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011
- Drug disposal: https://www.deadiversion.usdoj.gov/drug_disposal/index.html
- National Academy of Medicine: https://nam.edu/wp-content/uploads/2017/09/First-Do-No-Harm-Marshaling-Clinician-Leadership-to-Counter-the-Opioid-Epidemic.pdf

Additional references

- https://www.citizen.org/news/dangerously-overprescribed-gabapentin-should-be-classified-as-a-controlled-substance/
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