Opioids and controlled substances

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Disclosure

- Aetna/CVS Health Medical Director, Medicare Advantage, Florida Market
- 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 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
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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

https://pharmacy.ufl.edu/2025/04/07/uf-researchers-identify-safer-pathway-for-pain-relief/

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*	Alfentanil		
Morphine	Remifentanil		
Oxycodone*	Sufentanil		
Oxymorphone*			

FENTANYL > HYDROMORPHONE > OXYMORPHONE > OXYCODONE > TRAMADOL

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	Fiorinal	Meprobamate	
Amphetamine	Buprenorphine	Phentermine	
Pentobarbital	Cannabis???	Phenobarbital	

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

Marijuana

- CSA of 1970
  - Rescheduling efforts
    - 8-FA
    - Relative abuse potential
    - CAMU
    - Relative safety or ability to produce physical dependence
- Agriculture Improvement Act of 2018
- Rescheduling = regulations

https://www.federalregister.gov/documents/2024/05/21/2024-11137/schedules-of-controlled-substances-rescheduling-of-marijuana
https://www.dea.gov/sites/default/files/2024-05/2016-17954-HHS.pdf

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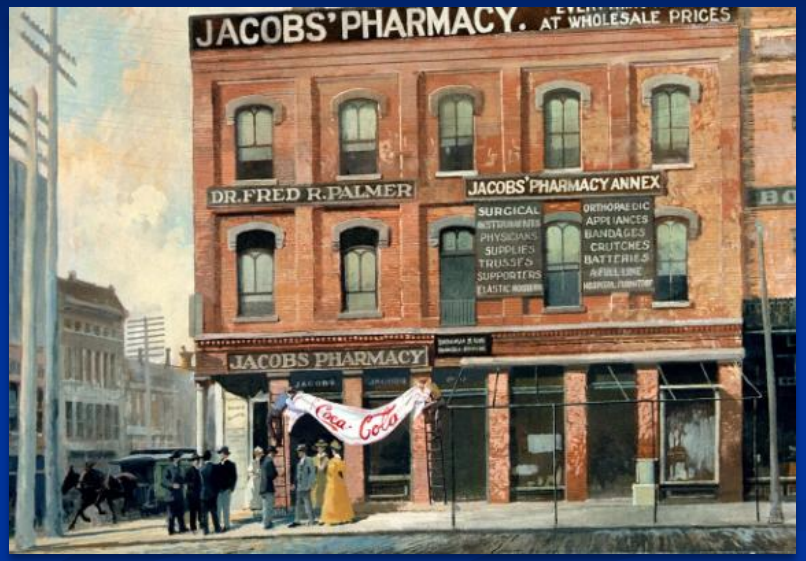
19th Century

- 1886: Coca-Cola™
- 1898: diacetylmorphine
- 1899: acetylsalicylic acid



20th Century

- 1906: Pure Food and Drug Law
- 1909: Opium Exclusion Act
- 1914: Harrison Narcotics Tax Act
- 1914 – 1918: WWI
- 1920 – 1970

YORKSHIRE
Telegraph & Star
WAR SPECIAL

No. 10,018. SHEFFIELD, MONDAY, NOVEMBER 11, 1918. ONE PENNY

THE WORLD WAR AT AN END.

STATEMENT by the PREMIER

Historic Document Signed at 5 o'clock This Morning.

HOSTILITIES ENDED AT 11 a.m. TO-DAY

OVERTHROW.

German Republics Proclaimed.

PEOPLE CONTROL.

Troops Go Over to the New Authority.

FIGHTING IN BERLIN.

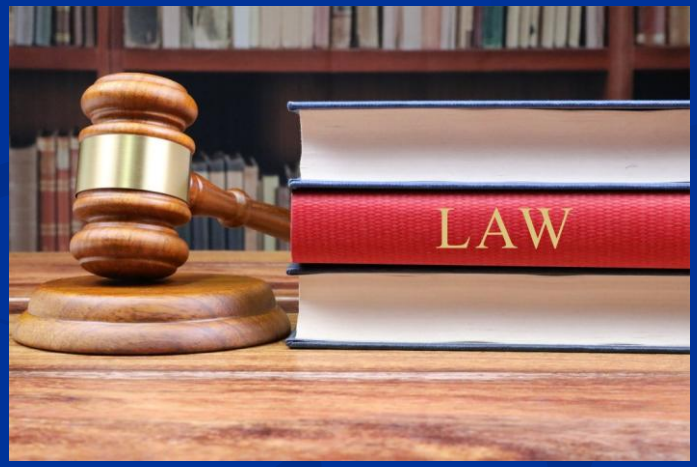
Soviets Formed Everywhere.

This Photo by Unknown Author is licensed under CC BY-SA-NC

https://www.encyclopedia.com/law/encyclopedias-almanacs-transcripts-and-maps/harrison-act

20th Century

- 1970: Controlled Substance Act (CSA)
- 1974: Narcotic Addict Treatment Act



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

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

https://www.govtrack.us/congress/bills/93/hr12503

https://www.buprenorphine-doctors.com/opioid-articles/what-is-data-2000/.

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
- 2024: 220 opioid-related OD deaths/day, US

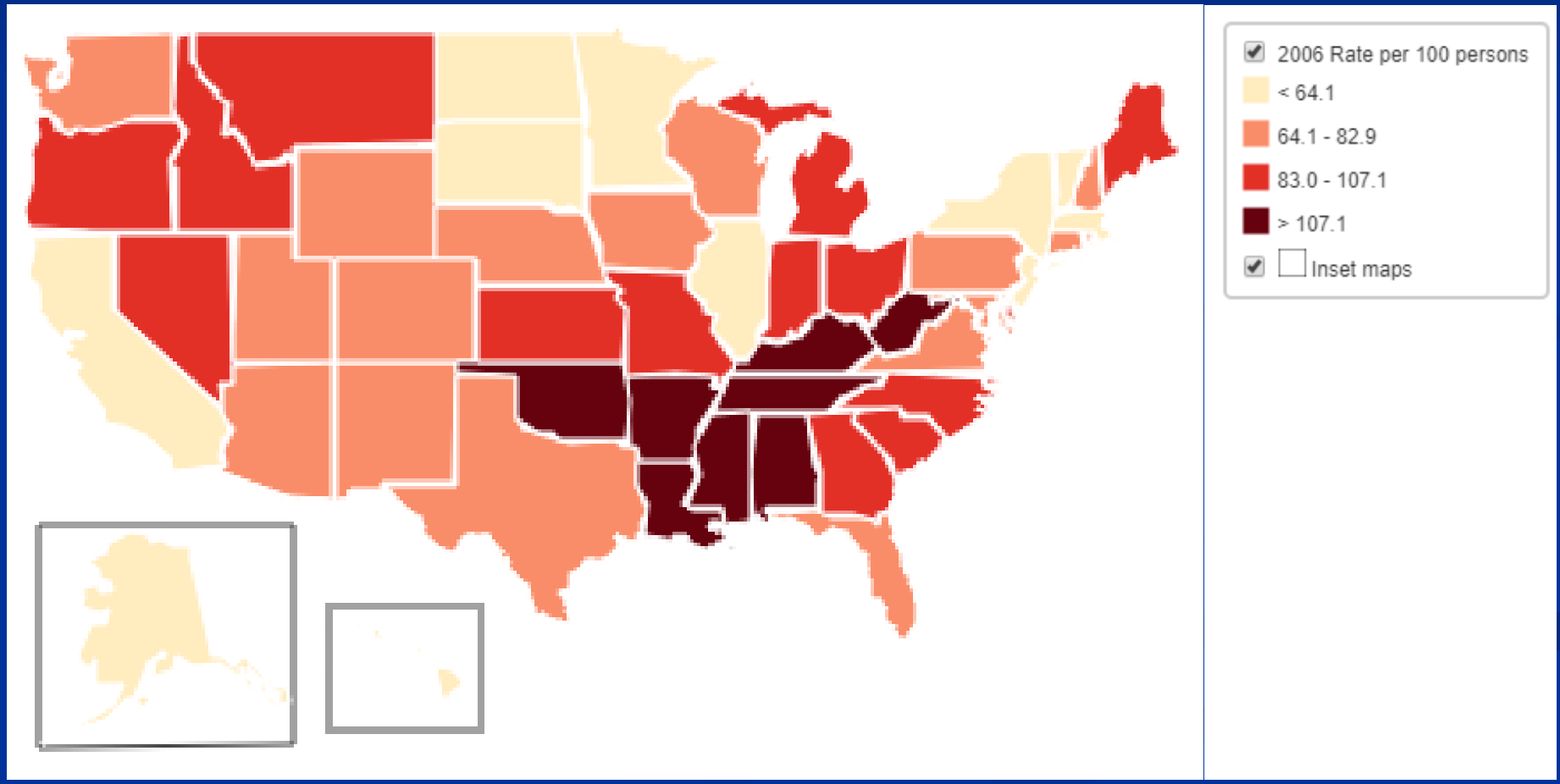
https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2021/20211117.htm

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

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

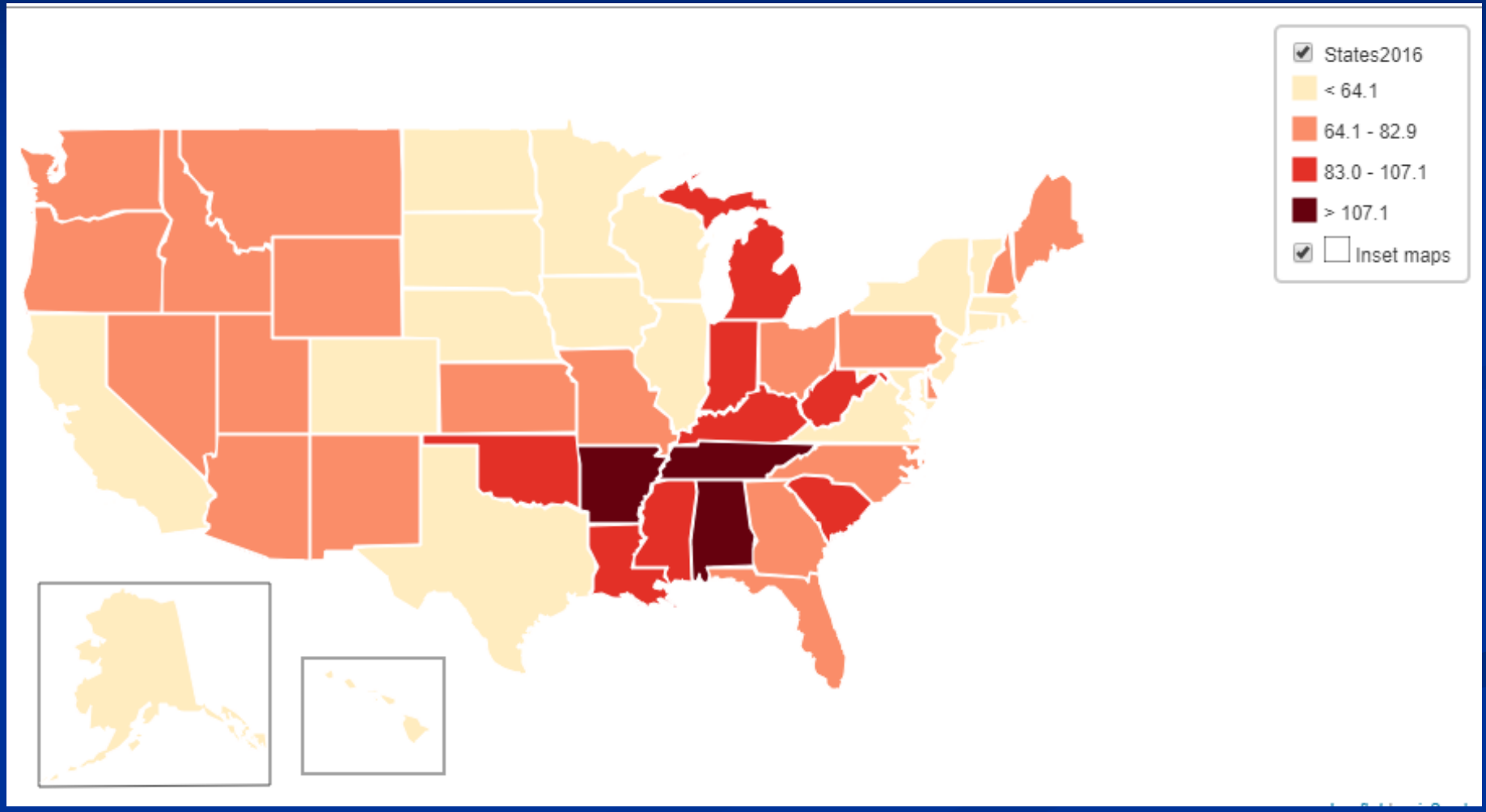
https://www.cdc.gov/drugoverdose/deaths/prescription/maps.html

U.S. State Prescribing Rates, 2012



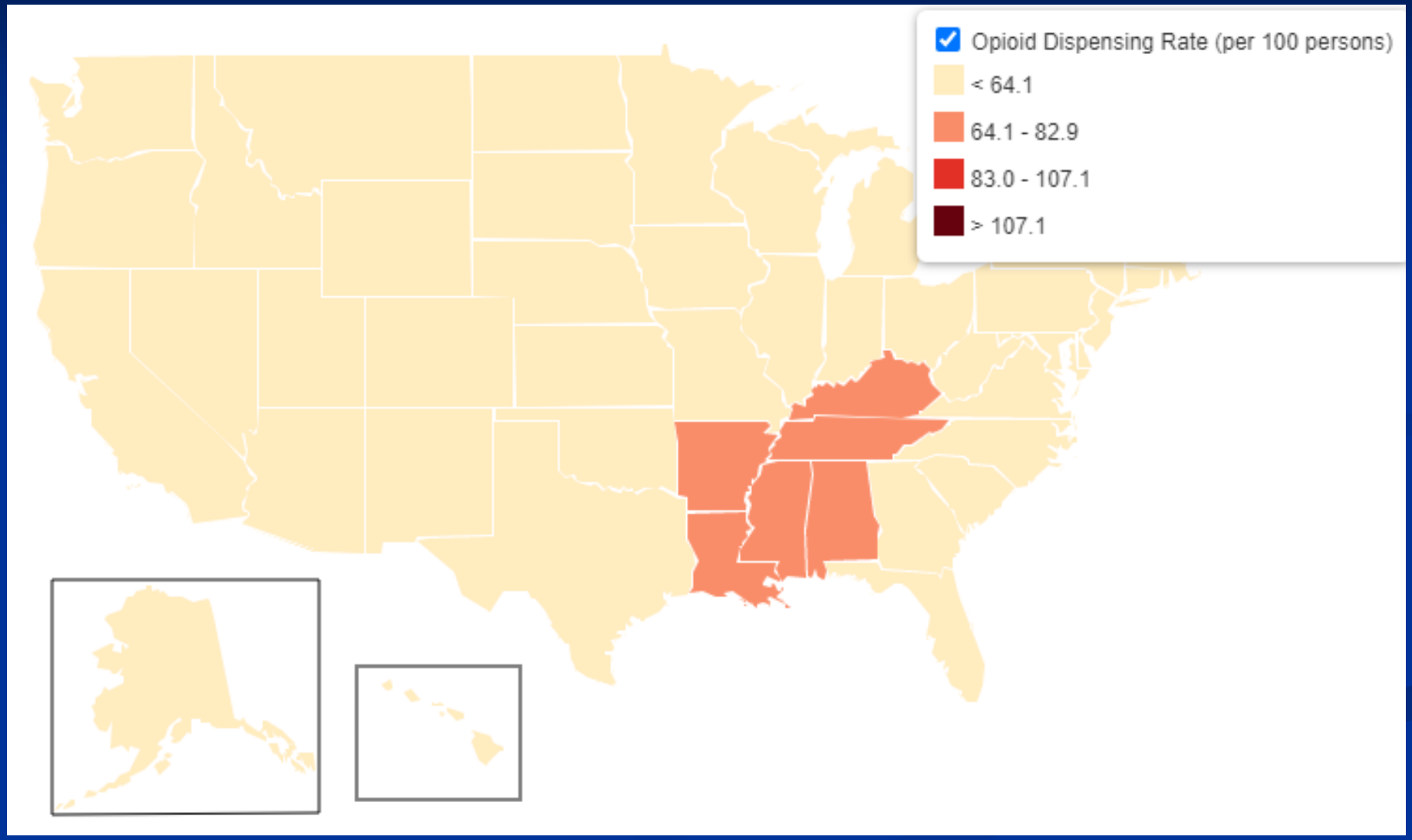
https://www.cdc.gov/drugoverdose/maps/rxstate2006.html

U.S. State Prescribing Rates, 2016



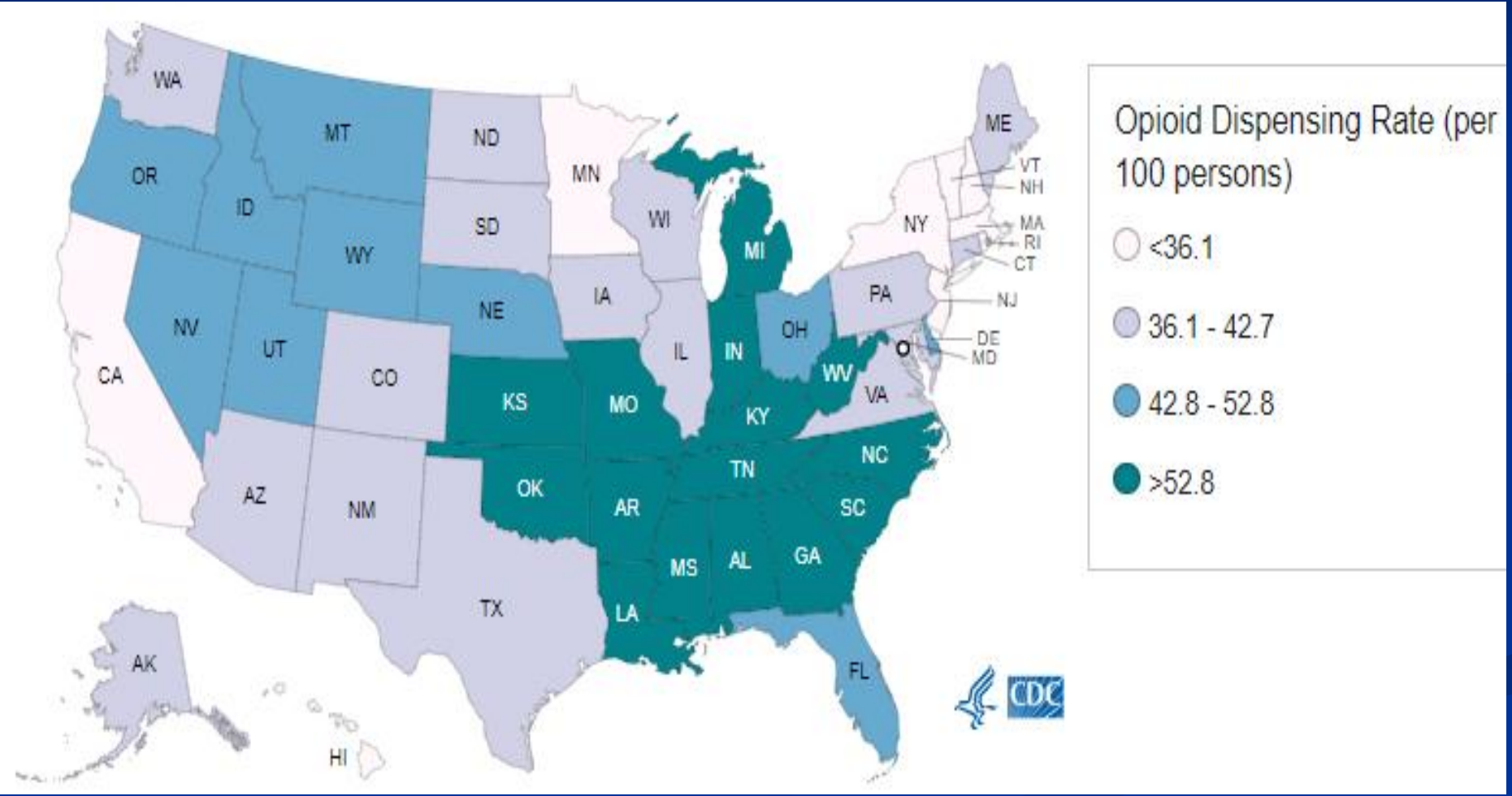
https://www.cdc.gov/drugoverdose/maps/rxstate2016.html

U.S. State Prescribing Rates, 2020



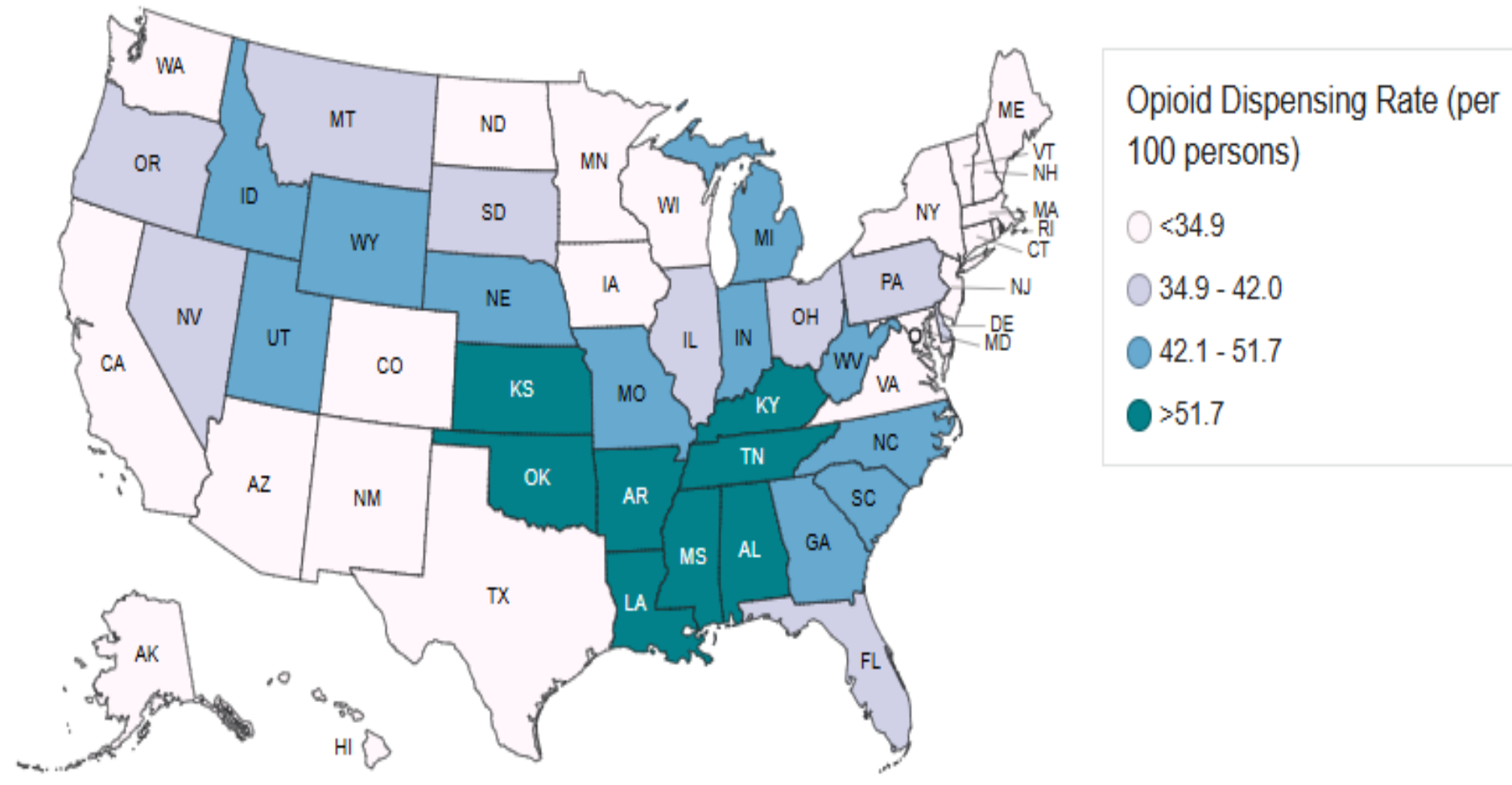
https://www.cdc.gov/drugoverdose/rxrate-maps/state2020.html

U.S. State Prescribing Rates, 2020



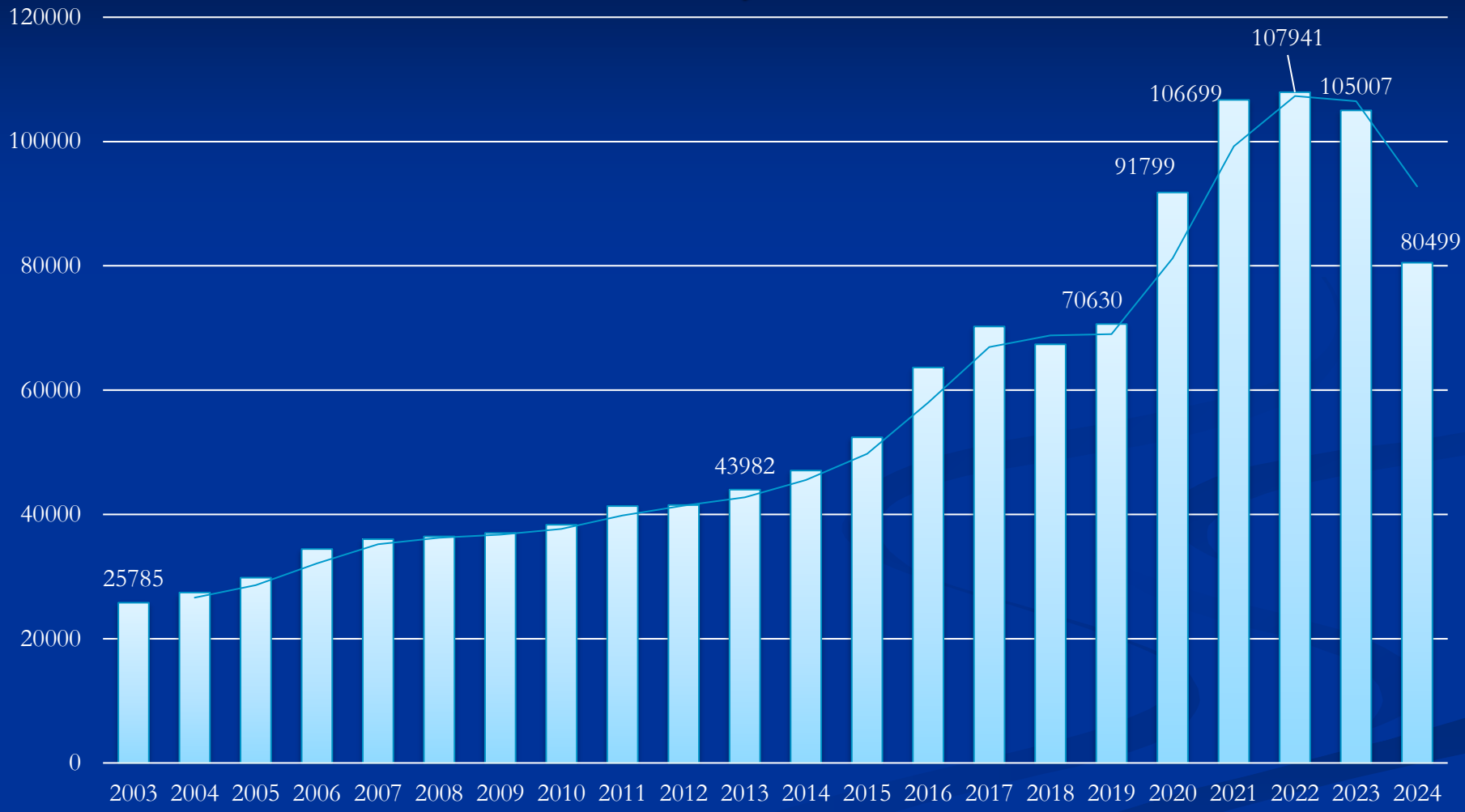
https://www.cdc.gov/overdose-prevention/data-research/facts-stats/opioid-dispensing-rate-maps.html

U.S. State Prescribing Rates, 2023



https://www.cdc.gov/overdose-prevention/data-research/facts-stats/opioid-dispensing-rate-maps.html

Age-adjusted drug overdose death rate: United States, 2003–2024

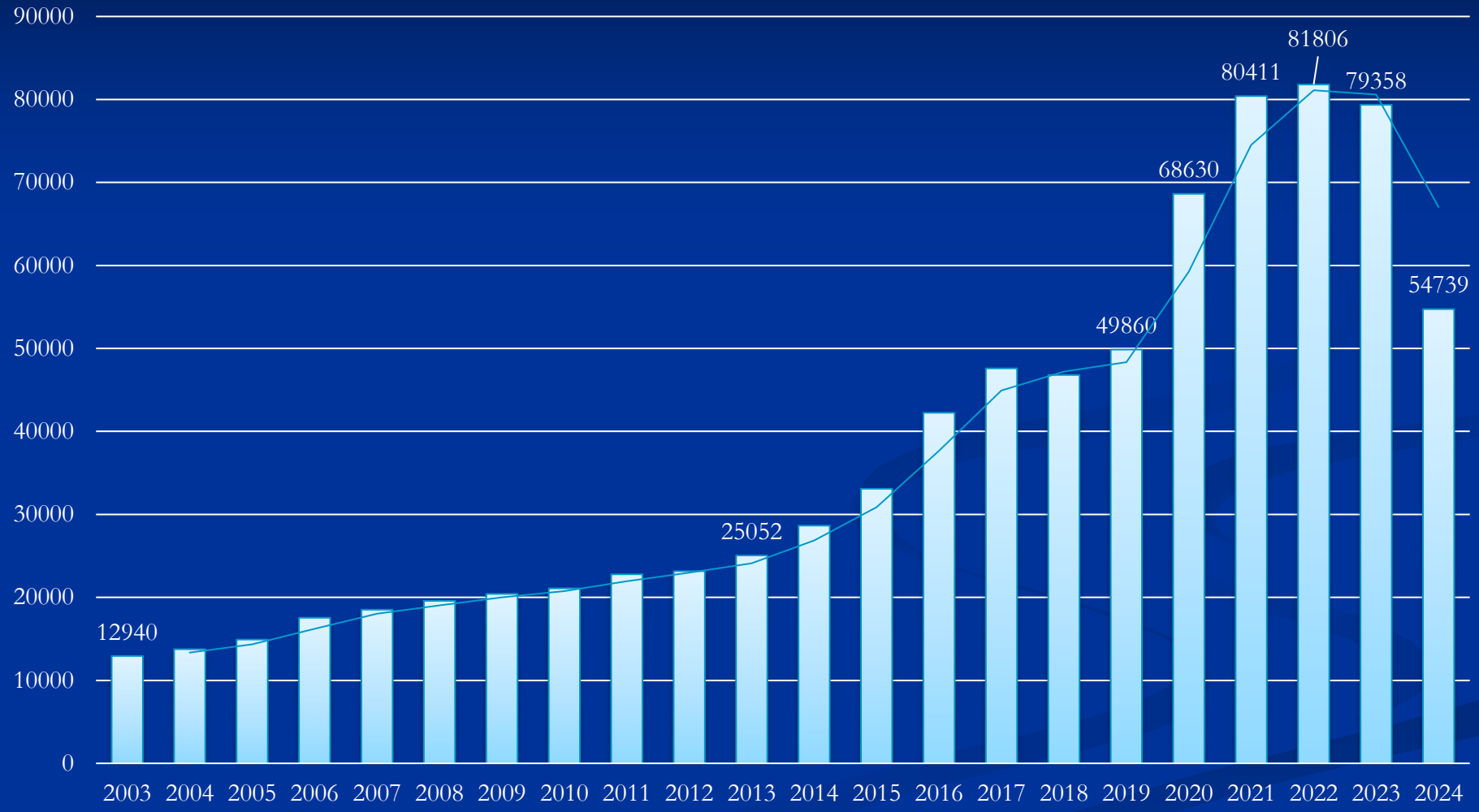


https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates#Fig1

https://www.overdoselifeline.org/news/2024-opioid-overdose-data-report-key-trends-and-insights/

Garnett MF, Miniño AM. Drug overdose deaths in the United States, 2003–2023. NCHS Data Brief, no 522. Hyattsville, MD: National Center for Health Statistics. 2024. DOI: https://dx.doi. org/10.15620/cdc/170565.

Age-adjusted rate of drug overdose deaths involving opioids: United States, 2003–2024

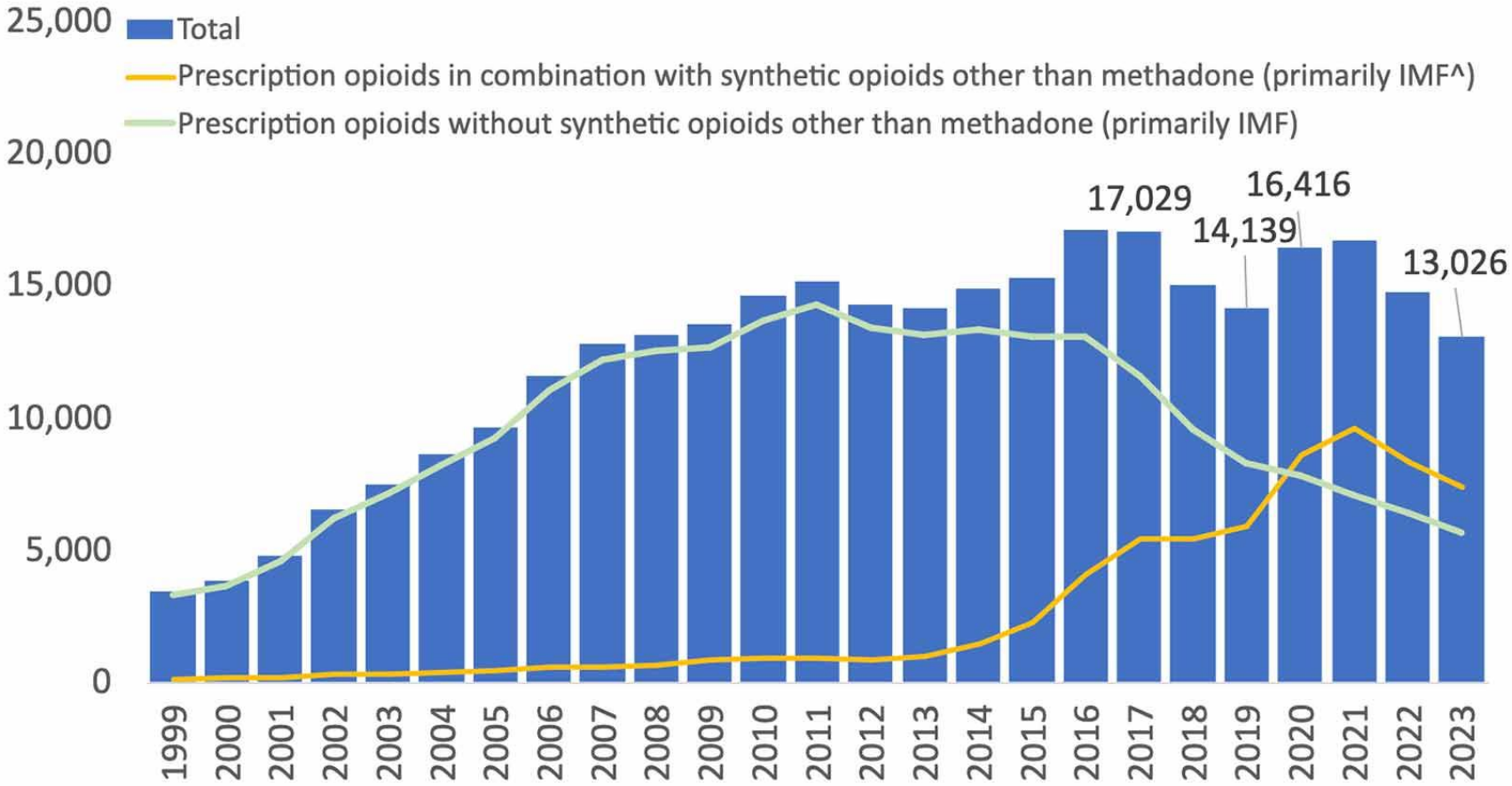


https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates#Fig3

https://www.overdoselifeline.org/news/2024-opioid-overdose-data-report-key-trends-and-insights/

Garnett MF, Miniño AM. Drug overdose deaths in the United States, 2003–2023. NCHS Data Brief, no 522. Hyattsville, MD: National Center for Health Statistics. 2024. DOI: https://dx.doi. org/10.15620/cdc/170565.

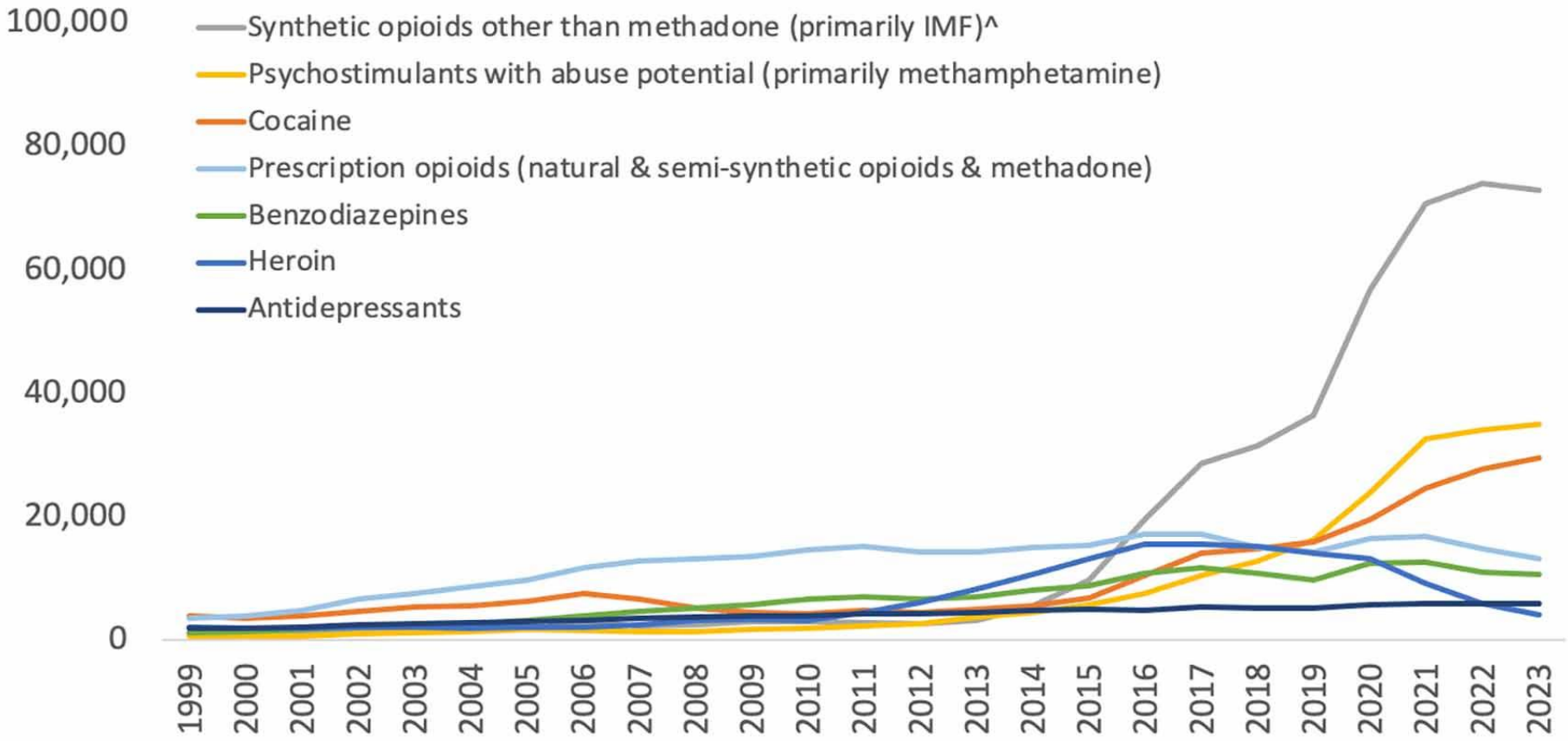
Figure 4. U.S. Overdose Deaths Involving Prescription Opioids*, 1999-2023



*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). ^illicitly manufactured fentanyl. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2023 on CDC WONDER Online Database, released 1/2025.

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

Figure 2. U.S. Overdose Deaths*, Select Drugs or Drug Categories, 1999-2023



*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. ^Illicitly manufactured fentanyl. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2023 on CDC WONDER Online Database, released 1/2025.

https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates#Fig2

DEA

Popular Emoji Drug Codes

Additional Threat: Access

Monitoring for suspicious text messages on social media or cash app posts could spark an important, and potentially life-saving, conversation.

ONE PILL CAN KILL

https://www.dea.gov/onepill

https://www.dea.gov/sites/default/files/2025-06/DEA_OPCK-PPT-5-6-2025%20%28ROPP%29.pdf

https://www.dea.gov/sites/default/files/2025-06/DEA_OPCK-PPT-5-6-2025%20%28ROPP%29.pdf

- Pharmacology of opiates
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- 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
REGULATION OF PROFESSIONS AND OCCUPATIONS

Chapter 456
HEALTH PROFESSIONS AND OCCUPATIONS: GENERAL PROVISIONS

View Entire Chapter

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

- 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

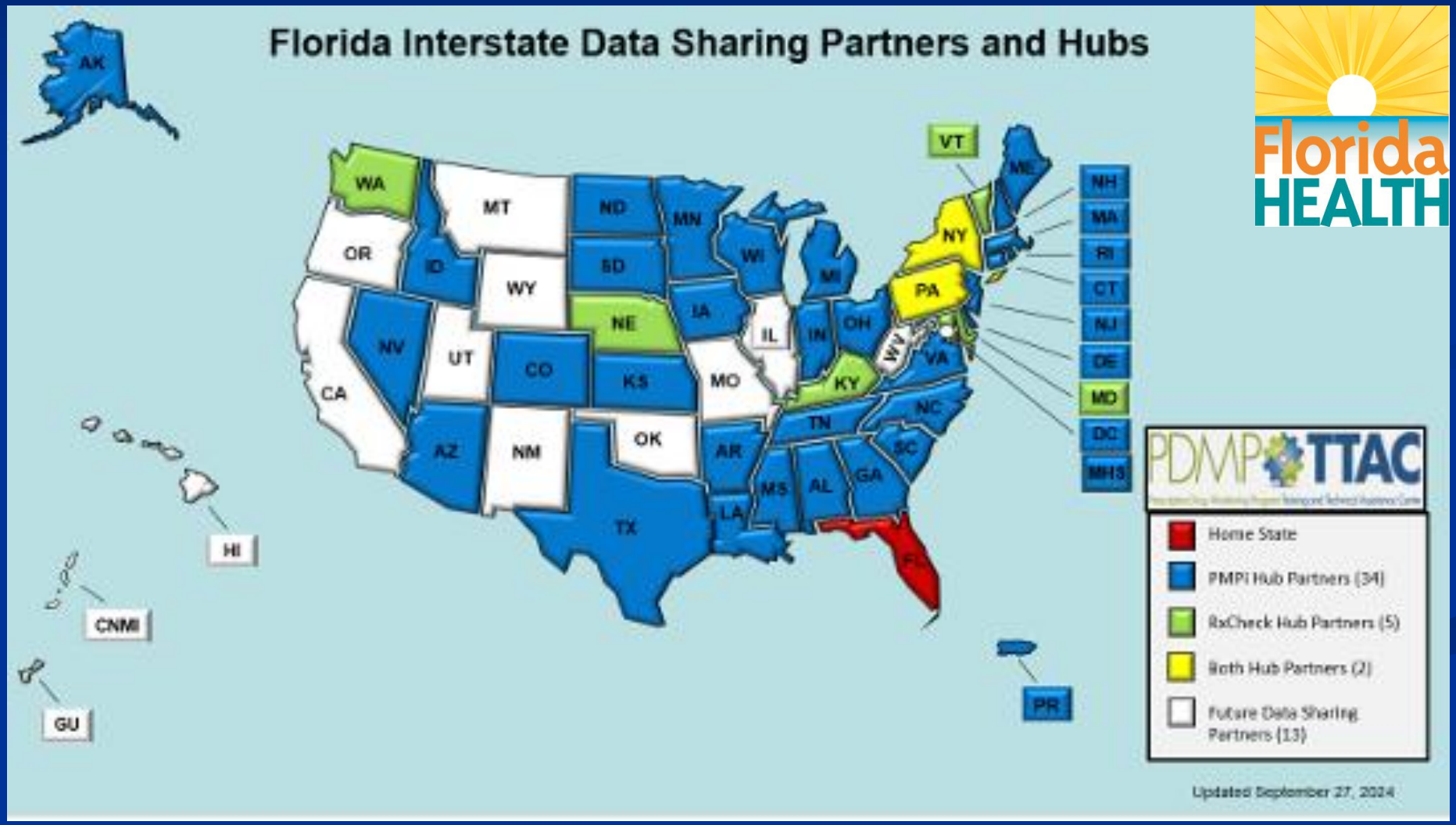
Impact, 06-30-24

License type	Total licensees (no.)	Registered users (no.)	Registered users (%)
APRN	57,467	22,595	39
DN	17,632	9,379	53
ME	96,224	62,162	65
OPC	3,928	105	3
OS	13,370	11,117	83
PA	13,781	8,982	65
PO	2,001	1,523	76
PS	36,116	33,410	93

https://www.floridahealth.gov/licensing-and-regulation/reports-and-publications/2024.10.28.FY23-24AR-FINAL.pdf

PDMP Compatibility

https://florida.pmpaware.net



https://www.floridahealth.gov/statistics-and-data/e-forcse/news-reports/index.html

PDMP: 7/1/18 – s. 893.055(8)

- Prescribers and dispensers, or their designees, must consult the PDMP before each time a CS, other than a C-V nonopioid, is prescribed or dispensed, 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

*****Avoid downloading & printing information*****

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

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

Florida Medical Association brief on HB 21

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

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

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

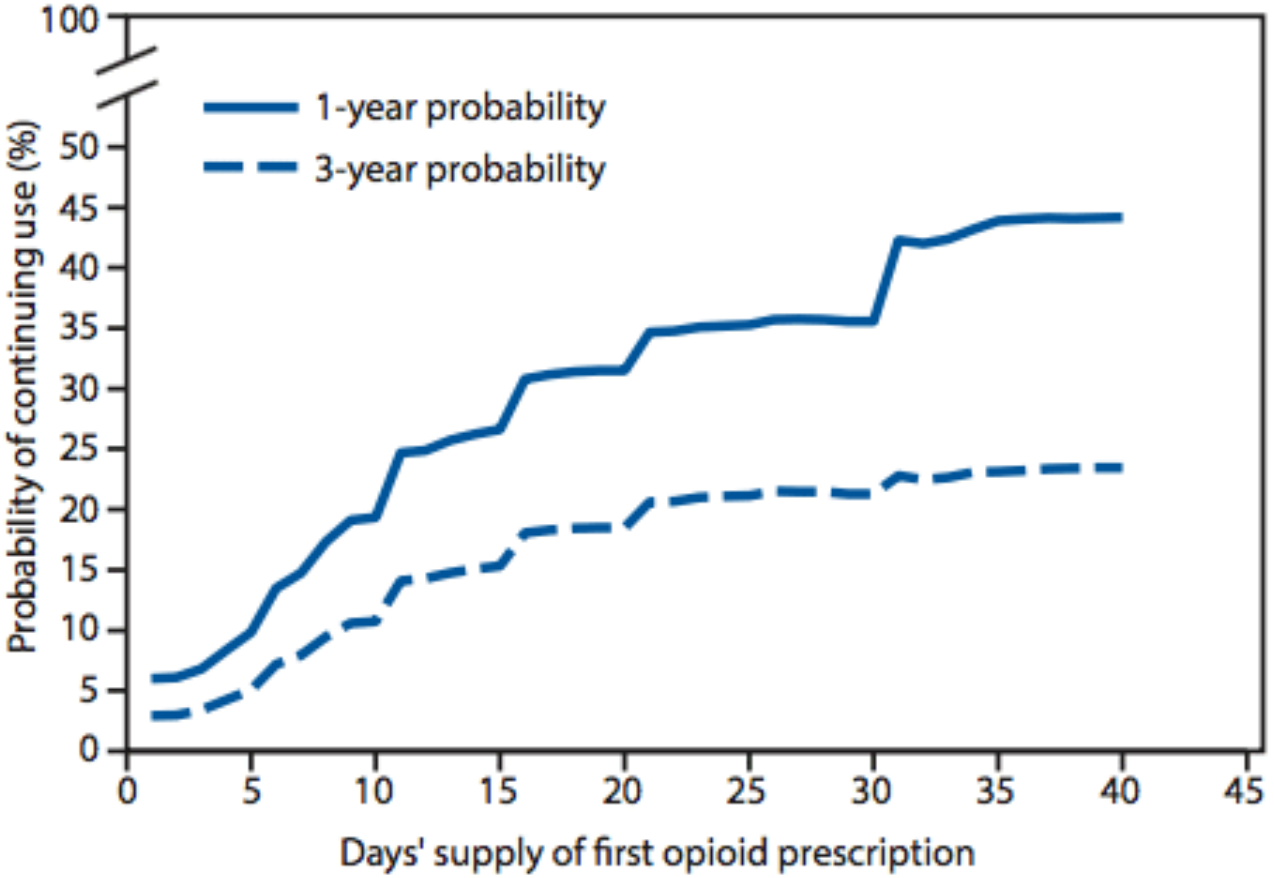
- 3-day limit on C-II opioid
- Up to 7-day supply IF…
  - Medically necessary
  - "Acute pain exception" is written on Rx
  - Documents acute condition and lack of alternatives

Note that all 3 criteria must be met

- Emergency opioid antagonist
- "Nonacute pain"

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

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/CS prescribers
- 2-hour, board-approved, CME
- Part of total required CME hours
- For licensure renewal, since 1/31/2019
- CE Broker

- All dentists (HB549, 7-1-19)
- All podiatrists (HB17, 7-1-21)

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

- Pharmacology of opiates
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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

s. 465.035: Dispensing of medicinal drugs pursuant to facsimile of prescription

- (1) It is lawful for a pharmacy to dispense medicinal drugs, including controlled substances 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.
  - Except in the case of the transmission of a prescription by a person authorized by law to prescribe 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 prescription for the medicinal drug involved.
    - The recipient of the prescription shall sign a log and shall indicate the name and address of both the recipient and the patient 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

Telehealth Extension of COVID-19 PHE

(c) During the period May 12, 2023, through December 31, 2024, a Drug Enforcement Administration (DEA)-registered practitioner is authorized to prescribe schedule II–V controlled substances via telemedicine, as defined in 21 CFR 1300.04(i), to a patient without having conducted an in-person medical evaluation of the patient if all of the conditions listed in paragraph (e) of this section are met.

(e) A practitioner is only authorized to issue prescriptions for controlled substances pursuant to paragraphs (c) or (d) of this section if all of the following conditions are met:

(1) The prescription is issued for a legitimate medical purpose by a practitioner acting in the usual course of professional practice;

(2) The prescription is issued pursuant to a communication between a practitioner and a patient using an interactive telecommunications system referred to in 42 CFR 410.78(a)(3);

(3) The practitioner is:

(i) Authorized under their registration under 21 CFR 1301.13(e)(1)(iv) to prescribe the basic class of controlled substance specified on the prescription; or

(ii) Exempt from obtaining a registration to dispense controlled substances under 21 U.S.C. 822(d); and

(4) The prescription is consistent with all other requirements of 21 CFR part 1306.

https://www.federalregister.gov/documents/2023/05/10/2023-09936/temporary-extension-of-covid-19-telemedicine-flexibilities-for-prescription-of-controlled
https://www.federalregister.gov/documents/2023/10/10/2023-22406/second-temporary-extension-of-covid-19-telemedicine-flexibilities-for-prescription-of-controlled
https://www.ecfr.gov/current/title-42/chapter-I/subchapter-A/part-12

s. 456.47: Use of telehealth to provide services

(2) PRACTICE STANDARDS.—

(b) A telehealth provider may use telehealth to perform a patient evaluation. If a telehealth provider conducts a patient evaluation sufficient to diagnose and treat the patient, the telehealth provider is not required to research a patient's medical history or conduct a physical examination of the patient before using telehealth to provide health care services to the patient.

(c) A telehealth provider may not use telehealth to prescribe a controlled substance listed in Schedule II of s. 893.03 unless the controlled substance is prescribed for the following:

- 1. The treatment of a psychiatric disorder;
- 2. Inpatient treatment at a hospital licensed under chapter 395;
- 3. The treatment of a patient receiving hospice services as defined in s. 400.601; or
- 4. The treatment of a resident of a nursing home facility as defined in s. 400.021.

(d) A telehealth provider and a patient may be in separate locations when telehealth is used to provide health care services to a patient.

(e) A nonphysician telehealth provider using telehealth and acting within his or her relevant scope of practice, as established by Florida law or rule, is not in violation of s. 458.327(1)(a) or s. 459.013(1)(a).

https://www.flsenate.gov/Laws/Statutes/2023/Chapter456/All

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. Stephen Strange, DO
177A Bleecker Street
New York City, Florida 33313
954-867-5309

Date: October 20, 2025

Patient Name: Peter Parker DOB: 08/27/1992

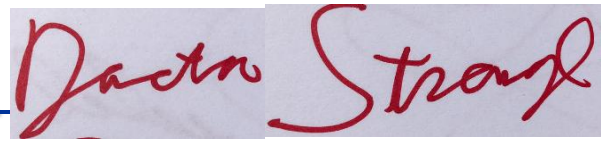
Address: 1111 Center Lane, London, Florida 33312

Percocet (5/325)

Disp. # 10 (Ten)

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

No Refills

DEA # BS1838616 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

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

- 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
- Hyperalgesia/allodynia
- Addiction
- 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)

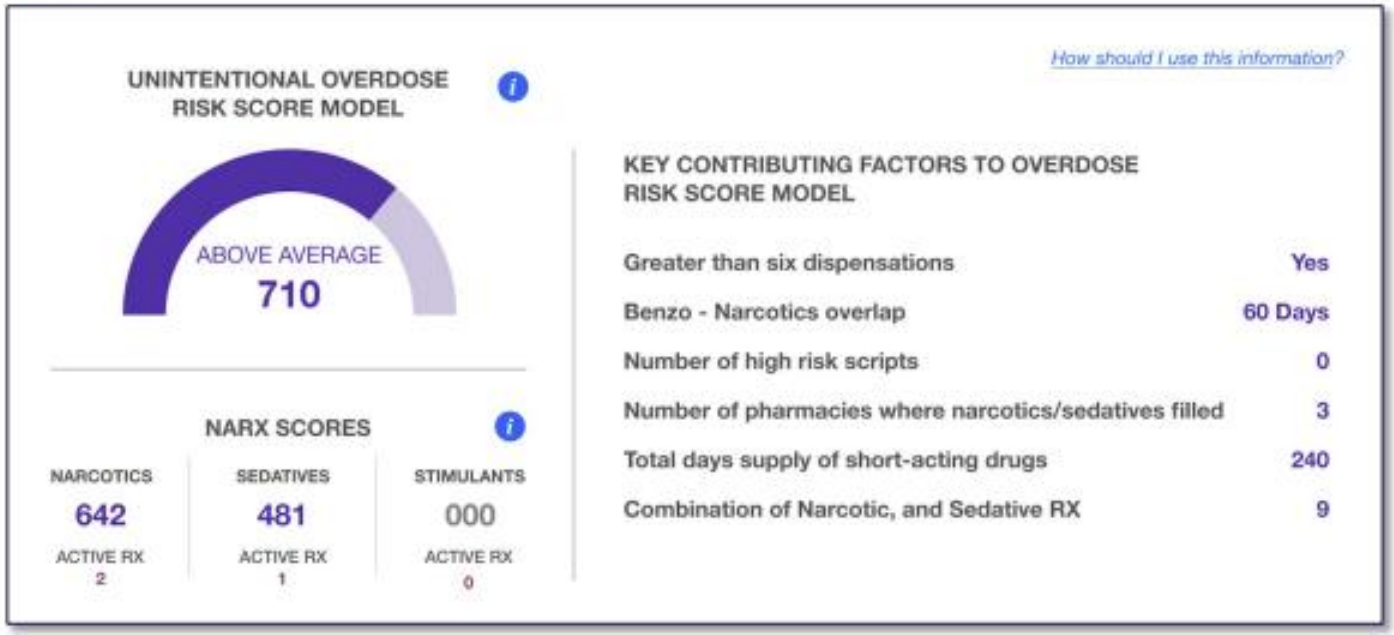
(2 or more criteria)

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

Bamboo Health

Original ORS

Updated ORS



https://go.bamboohealth.com/rs/228-ZPQ-393/images/Bamboo-Health-NarxCare-ORS-Overview_FINAL.pdf?version=1&mkt_tok=MjI4LVpQUS0zOTMAAAGPr9vDcixDj_ETHc3g3JvUHfLHkjShloyT6ts82hxY935lmRDWOfQqM6i38aR1CTJsJBOTxoC0haG3hbDAQIWrA1XzEdhKs2OTcRvfdDDYCA

Bamboo Health

https://go.bamboohealth.com/rs/228-ZPQ-393/images/Bamboo-Health-NarxCare-ORS-Overview_FINAL.pdf?version=1&mkt_tok=MjI4LVpQUS0zOTMAAAGPr9vDcixDj_ETHc3g3JvUHfLHkjShloyT6ts82hxY935lmRDWOfQqM6i38aR1CTJsJBOTxoC0haG3hbDAQIWrA1XzEdhKs2OTcRvfdDDYCA

Physical dependence vs. addiction

Physical Dependence	• Body is used to having a high level of opioid • Abrupt discontinuation will result in withdrawal symptoms (nausea & vomiting, anxiety, etc.)
Addiction	• Uncontrollable craving and compulsive use, inability to control drug use • There is no addiction without craving

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

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 Sx

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

https://www.asam.org/docs/default-source/education-docs/cows_induction_flow_sheet.pdf?sfvrsn=b577fc2_2

Clinical Opiate Withdrawal Scale

- Resting HR
- GI upset
- Sweating
- Tremor
- Restlessness
- Yawning
- Pupil size
- Anxiety/irritability
- Bone/joint aches
- Gooseflesh skin
- Runny nose/tearing

Score: 5-12 = mild; 13-24 = moderate;
25-36 = moderately severe; > 36 = severe

https://nida.nih.gov/sites/default/files/ClinicalOpiateWithdrawalScale.pdf

Withdrawal treatment

	Symptoms	OUD
Clonidine, lofexidine	X	
Naltrexone		X
Buprenorphine, methadone	X	X

- Clondine, lofexidine: α2-agonists
- Naltrexone: mu receptor antagonist
- Buprenorphine: partial mu receptor agonist
- Methadone: mu receptor agonist
  - Opioid treatment program (OTP)

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

Opiate-induced constipation (OIC)

- At least 2 of the following criteria = Dx
  - < 3 BMs/wk
  - Hard/lumpy stools
  - Sensation of incomplete evacuation
  - Small stools
  - Sensation of anorectal obstruction
  - Straining with defecation
  - Bloating + abdominal pain relieved by BM
  - GERD

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.

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Overdose treatment

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

Opioid antagonist

- Naloxone
- Pharmacokinetics

- Federal government guidelines
- Naloxone access law

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

Highest risk population

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

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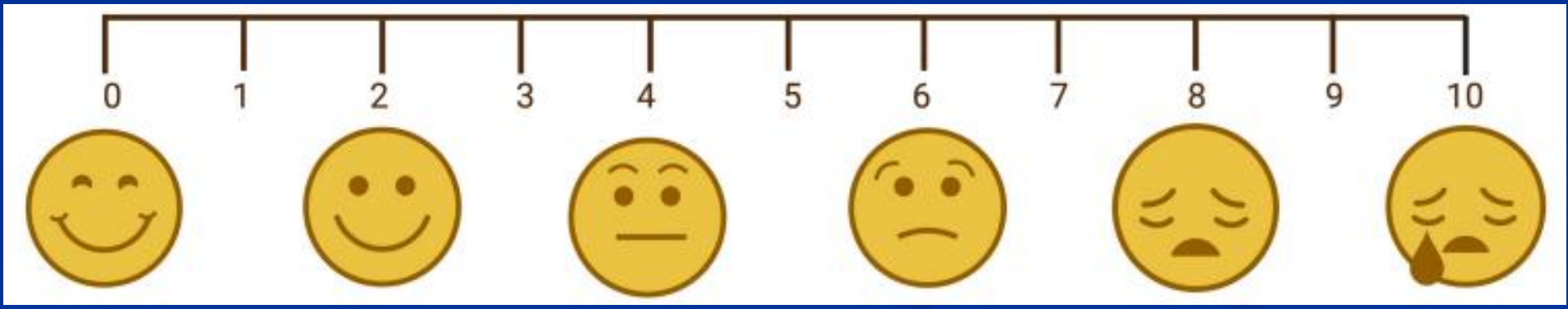
Wong–Baker FACES scale



Sansone L, Gentile C, Grasso EA, Di Ludovico A, La Bella S, Chiarelli F, Breda L. Pain Evaluation and Treatment in Children: A Practical Approach. Children (Basel). 2023 Jul 13;10(7):1212. doi: 10.3390/children10071212. PMID: 37508709; PMCID: PMC10378137.

Pain characteristics

	Nociceptive Pain		Neuropathic Pain
	Somatic Pain	**Visceral Pain**	
Origin	Superficial receptors	Visceral receptors	Nerves
Location and distribution	• Superficial (skin and subcutaneous tissue) • Well-localized • Not referred	• Deep (e.g., from muscle/bone/fascia/periosteum) • Poorly localized • Often referred	• Nerve structures (e.g., trigeminal nerve) • Radiating or specific
Transmission	A-delta-fibers	C-fibers	Dermatomal (periphery) or non-dermatomal (central)
Type of pain reported	Pinprick, sharp or stabbing	Pressure, sharp or ache	Tingling, prickling, lancinating or burning

Sansone L, Gentile C, Grasso EA, Di Ludovico A, La Bella S, Chiarelli F, Breda L. Pain Evaluation and Treatment in Children: A Practical Approach. Children (Basel). 2023 Jul 13;10(7):1212. doi: 10.3390/children10071212. PMID: 37508709; PMCID: PMC10378137.

Common podiatric pain causes

Achilles tendinitis	Bursitis	Broken ankle/foot/toe
Bunions	Corn/callus	Diabetic neuropathy
Gout	Ingrown toenail	Morton's neuroma
Osteomyelitis	Plantar fasciitis	Plantar warts
Psoriatic arthritis	Stress fractures	Venous thromboembolism

https://www.mayoclinic.org/symptoms/foot-pain/basics/causes/sym-20050792#:~:text=Arthritis%20is%20a%20common%20cause%20of%20foot%20pain.,rupture.%20Avulsion%20fracture.%20Bone%20spurs.%20Broken%20ankle%2Fbroken%20foot.

Nonpharmacological

Hot/cold	Osteopathic manipulation
Physical therapy	Chiropractic medicine
Acupuncture	TENS
Biofeedback	Cognitive behavioral therapy
Exercise	Yoga
Music	Moxibustion
Pulsed radiofrequency	Mindfulness
Tai-chi	Laughter/humor

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.

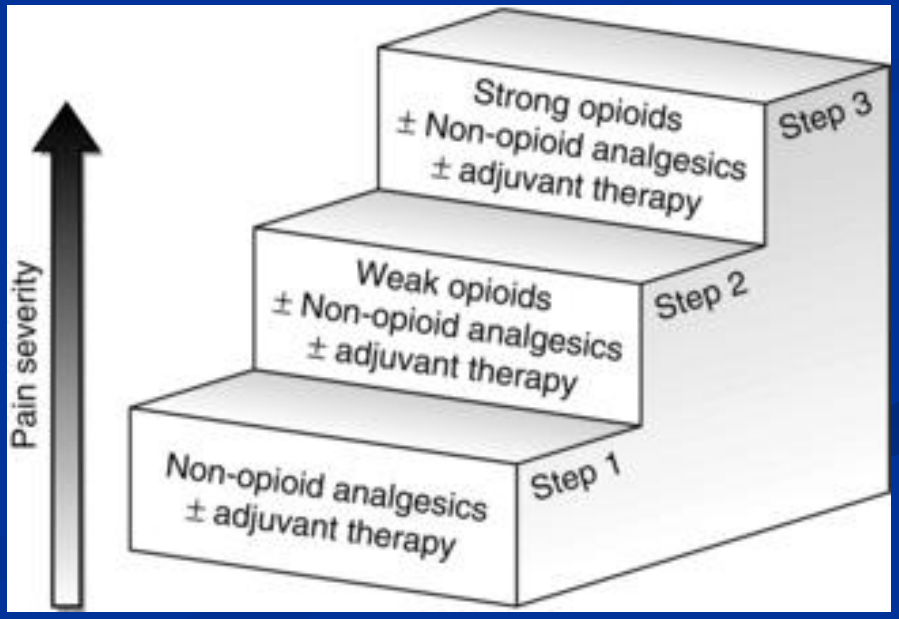
Nadlinda PG, et al. *Pain*, published online Oct 26, 2021, doi:10.1097/j.pain.0000000000002521.

Phased approach to analgesia

- Medications

- Mild (1 – 4): acetaminophen or NSAIDs
- Moderate (5 – 6): acetaminophen +/- NSAIDs +/- oral opioids
- Severe (7 – 10): IV opioids

- Non-pharmacological interventions



Sansone L, Gentile C, Grasso EA, Di Ludovico A, La Bella S, Chiarelli F, Breda L. Pain Evaluation and Treatment in Children: A Practical Approach. Children (Basel). 2023 Jul 13;10(7):1212. doi: 10.3390/children10071212. PMID: 37508709; PMCID: PMC10378137.

Non-opioid alternatives

- Acetaminophen
- NSAIDs
- Antidepressants
- Anticonvulsants
- 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.

Non-opioids

- Acetaminophen
  - 325-1000mg q4-6h (max 4g/d)
- NSAIDs
  - Diclofenac
    - 50mg q6-12h (max 150mg/d)
  - Ibuprofen
    - 600-800mg q6-8h (max 3.2g/d)
  - Naproxen (base)
    - 500mg q12h

Non-opioids

- Gabapentinoids
  - Pregabalin
    - 75-150mg q12h or 50-100mg q8h (max 300mg/d)
  - Gabapentin (IR)
    - 300mg qd (d.1) – 300mg BID (d.2) – 300mg TID (d.3)
    - Titrate up to max of 600mg q8h (1800mg/d)
- Dexamethasone
  - 4-8mg q8h

Analgesics for comorbidities

- Renal impairment

Preferred	Caution	Avoid
Acetaminophen, fentanyl, buprenorphine	Hydromorphone, oxycodone, gabapentinoids, SNRIs	Morphine, codeine, tramadol, meperidine

- NSAIDs – short-term, close monitoring
- Altered pharmacokinetics
- Lipophilic agents
- Topicals

Odoma VA, Pitliya A, AlEdani E, Bhangu J, Javed K, Manshahia PK, Nahar S, Kanda S, Chatha U, Mohammed L. Opioid Prescription in Patients With Chronic Kidney Disease: A Systematic Review of Comparing Safety and Efficacy of Opioid Use in Chronic Kidney Disease Patients. Cureus. 2023 Sep 18;15(9):e45485. doi: 10.7759/cureus.45485. PMID: 37727840; PMCID: PMC10506738.

Analgesics for comorbidities

- Hepatic dysfunction

Preferred	Caution	Avoid
Acetaminophen	Hydromorphone, oxycodone, fentanyl, gabapentinoids	Morphine, codeine, tramadol, meperidine, SNRIs

- NSAIDs – no
- Decrease dose, longer frequency intervals
- Topicals (NSAIDs, lidocaine, capsaicin)

Odoma VA, Pitliya A, AlEdani E, Bhangu J, Javed K, Manshahia PK, Nahar S, Kanda S, Chatha U, Mohammed L. Opioid Prescription in Patients With Chronic Kidney Disease: A Systematic Review of Comparing Safety and Efficacy of Opioid Use in Chronic Kidney Disease Patients. Cureus. 2023 Sep 18;15(9):e45485. doi: 10.7759/cureus.45485. PMID: 37727840; PMCID: PMC10506738.

Soleimanpour H, Safari S, Shahsavari Nia K, Sanaie S, Alavian SM. Opioid Drugs in Patients With Liver Disease: A Systematic Review. Hepat Mon. 2016 Mar 6;16(4):e32636. doi: 10.5812/hepatmon.32636. PMID: 27257423; PMCID: PMC4887963.

Past, present, and future

- ERAS /pre-operative Rx
- IV acetaminophen (e.g., Ofirmev)
- Slow-release bupivacaine (e.g., Exparel)
- Different targets than opioid receptors
- Longer acting agents (i.e, Zilretta)
- Nerve fiber inactivation
- Novel combinations (i.e., Zynrelef)
- Sodium channel blockers (i.e., Journavx)
- Potassium channel blockers

https://centrexion.com/science/pipeline/

https://post.health.ufl.edu/2023/08/17/uf-scientists-on-team-working-to-tame-dangerous-fentanyl/

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

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.

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
- Prescribing emergency opioid antagonists
- Alternatives to controlled substance prescribing
  - Nonpharmacological therapies
- 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
  - www.DEATakeBack.com

- 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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Select additional references

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- 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
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- 2022 CDC guidelines for prescribing opioids for the treatment of pain - https://www.cdc.gov/opioids/patients/guideline.html
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- https://public-inspection.federalregister.gov/2024-27018.pdf
- Lim JK, Ramgopal S, Hoffmann JA, Lorenz D, Toce MS. Characteristics and Trends of Prehospital Encounters for Opioid Overdoses Among US Youth, 2018-2022. *JAMA*. 2024;332(15):1299–1302. doi:10.1001/jama.2024.17341.