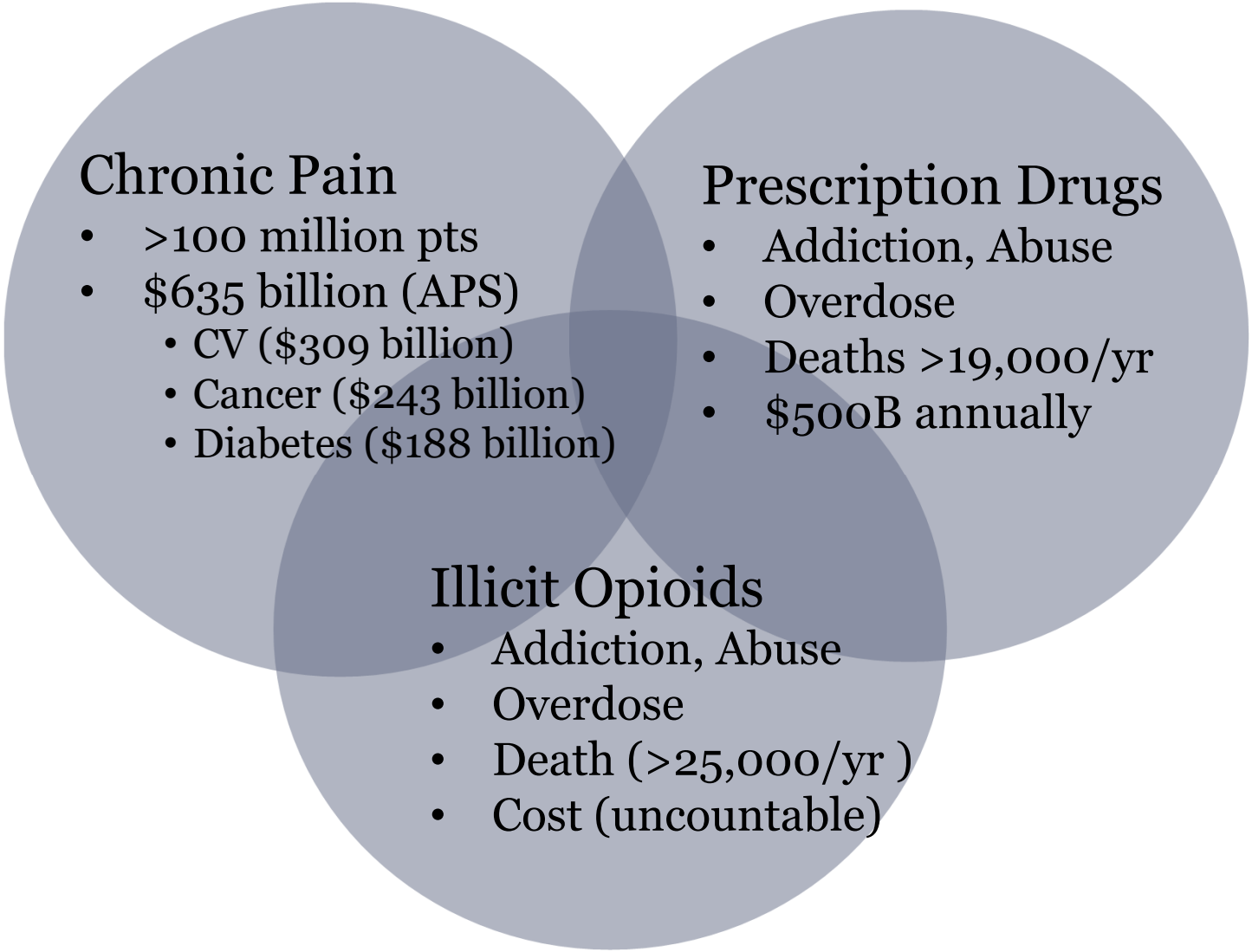
The Newest Opium War: Insights into the Current Opioid Epidemic

Lewis S. Nelson, MD
Rutgers New Jersey Medical School

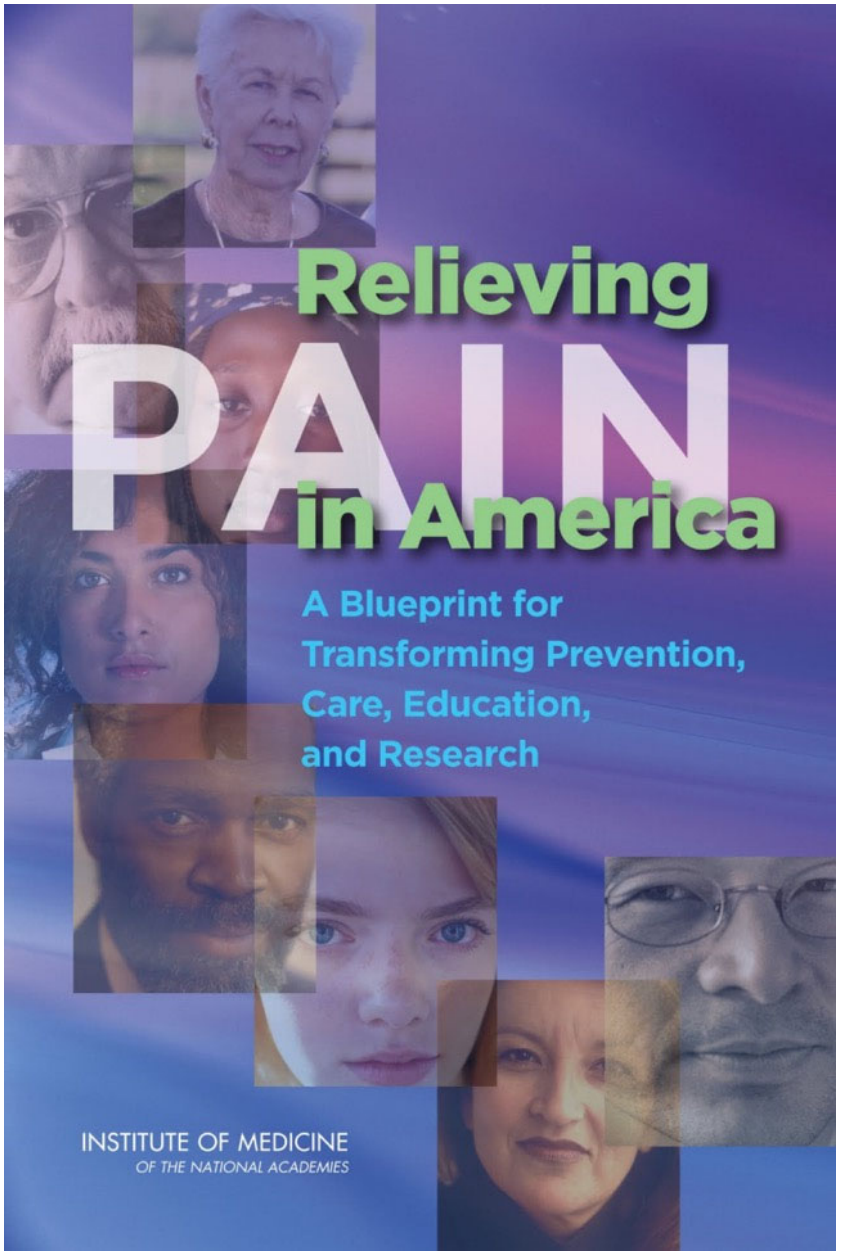
Three Inextricable Concurrent Epidemics



Chronic pain affects 116 million people in the US

- 37% of the US population
- 47% if children are removed from the calculation

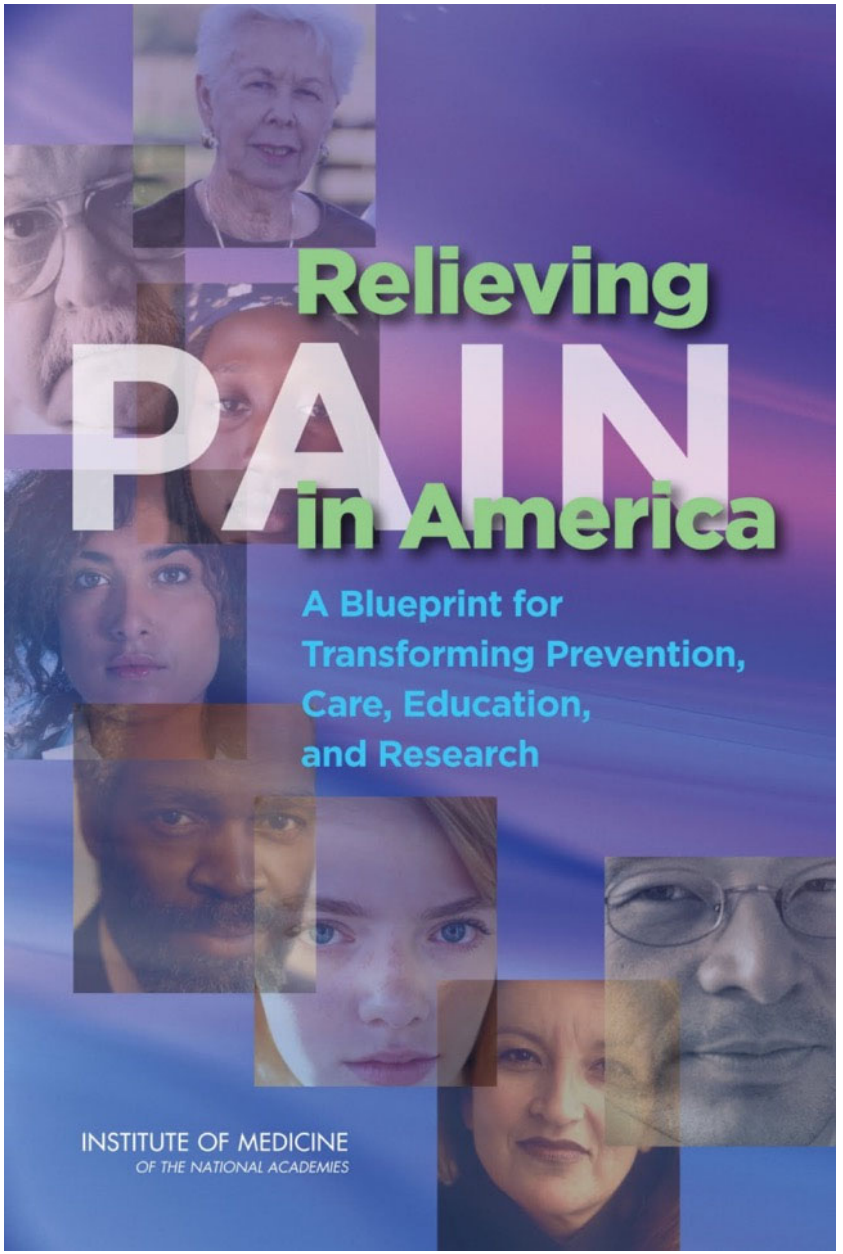
- Not end of life/palliative care



IOM April 2011

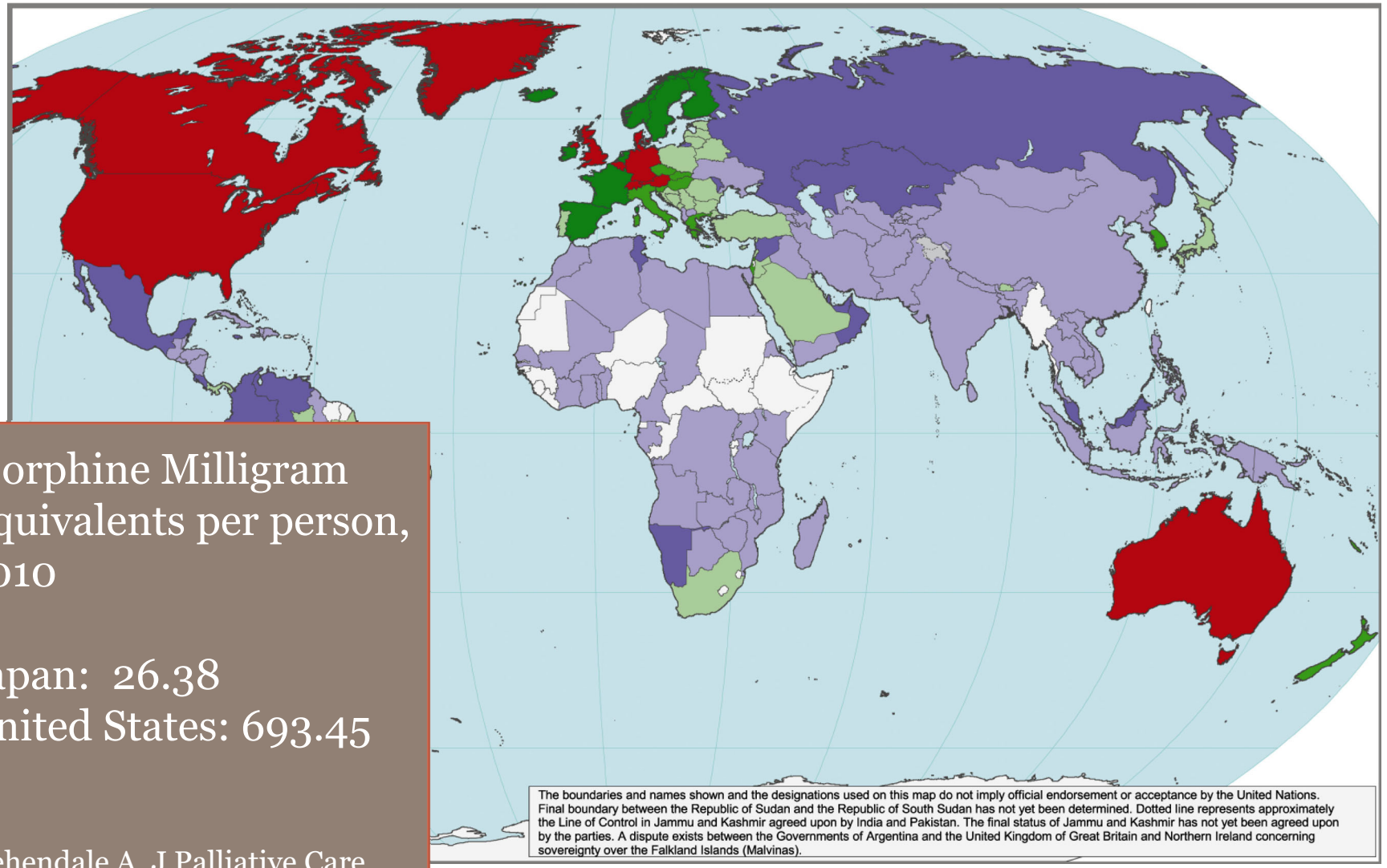
Pain is woefully undertreated, despite…

- Dozens of approved medications
- The 5th vital sign (Joint Commission)
- Patient satisfaction scores (Centers for Medicare & Medicaid Services)



IOM April 2011

"The US accounts for 4% of the world's population but uses 80% of its prescription opioid"



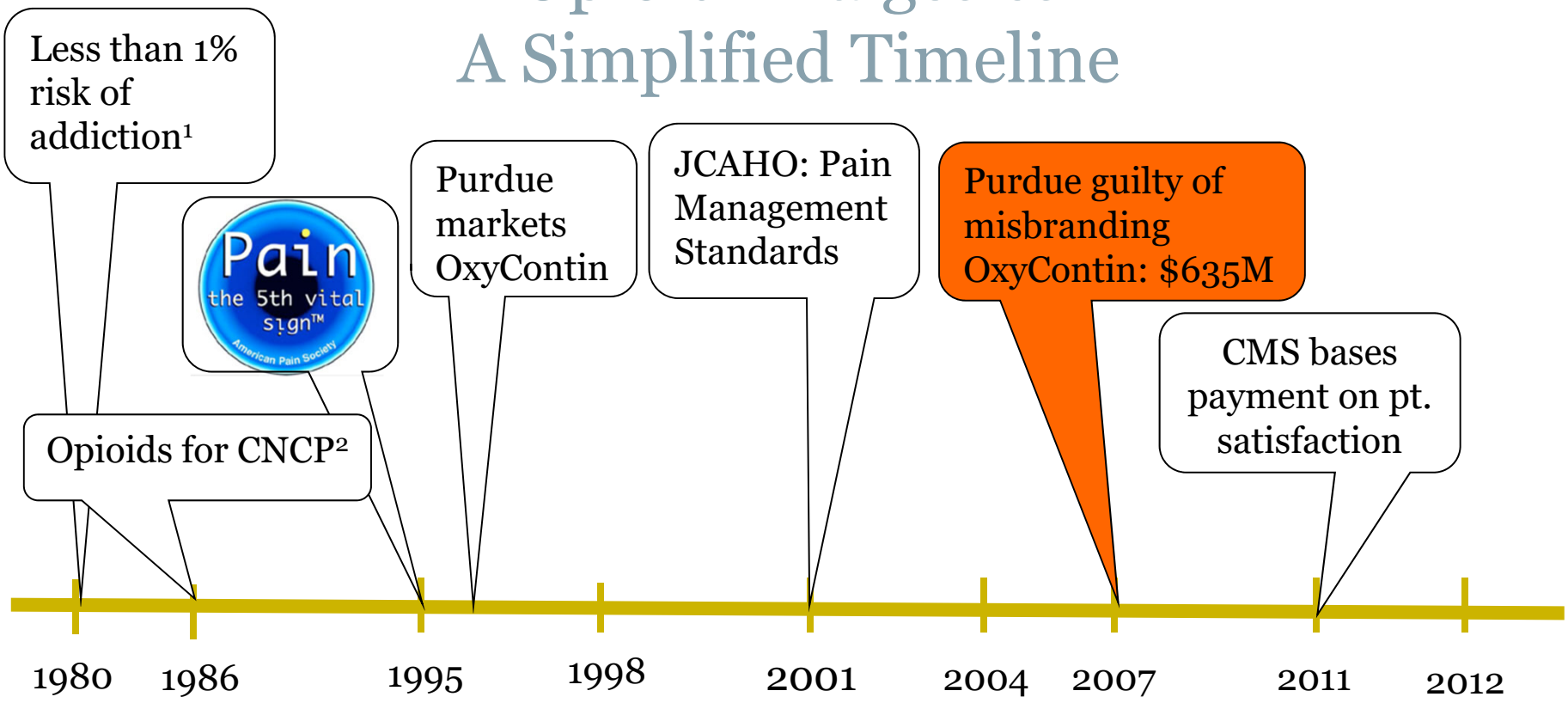
Morphine Milligram Equivalents per person, 2010

Japan: 26.38
United States: 693.45

Mehendale A. J Palliative Care Med 2013:3: 151-3

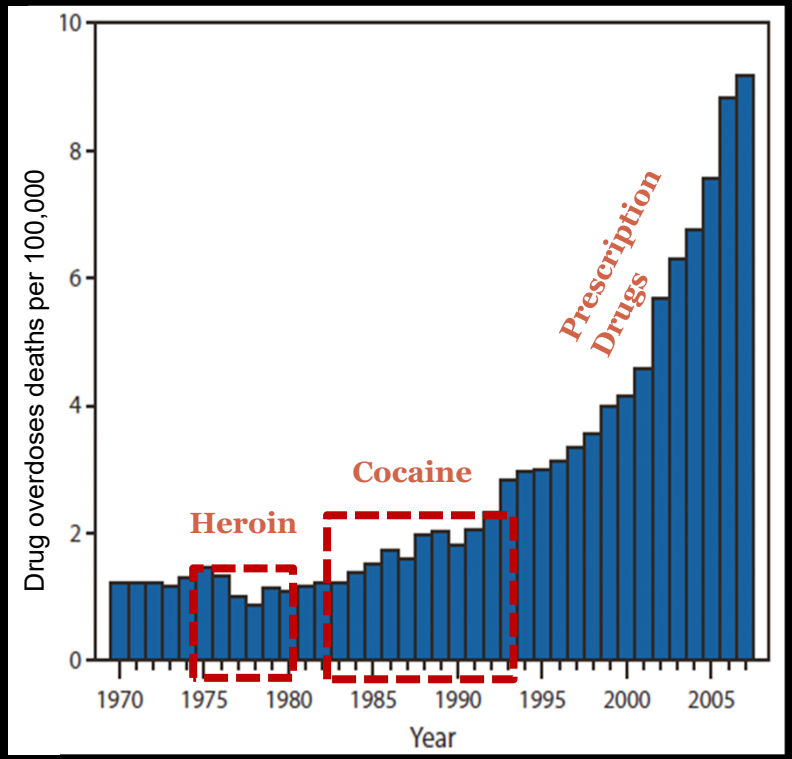
International Narcotics Control Board for the UN; 2014

Opioid Analgesics
A Simplified Timeline



[1]Porter J, Jick H. Addiction rare in patients treated with narcotics. N Engl J Med 1980;302:123.

[2] Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. Pain. 1986;25(2):171-86


Drug overdoses deaths per 100,000
10
8
6
4
2
0
1970
1975
1980
1985
1990
1995
2000
2005
Year
Heroin
Cocaine
Prescription Drugs

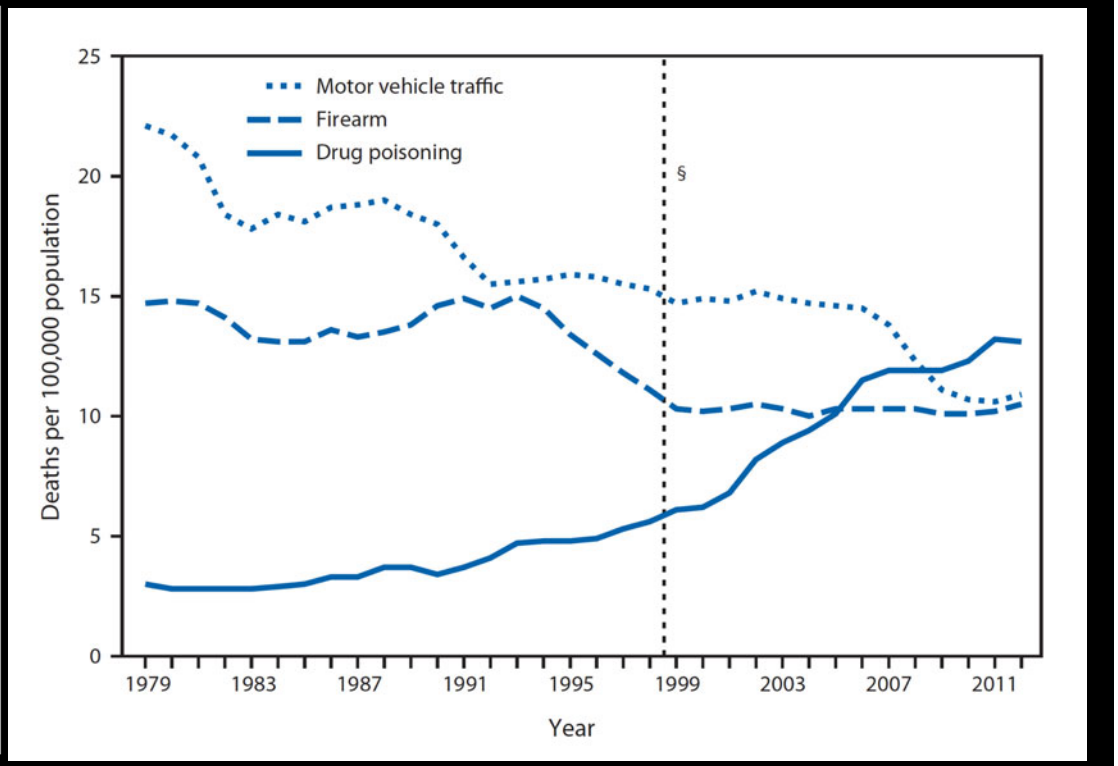
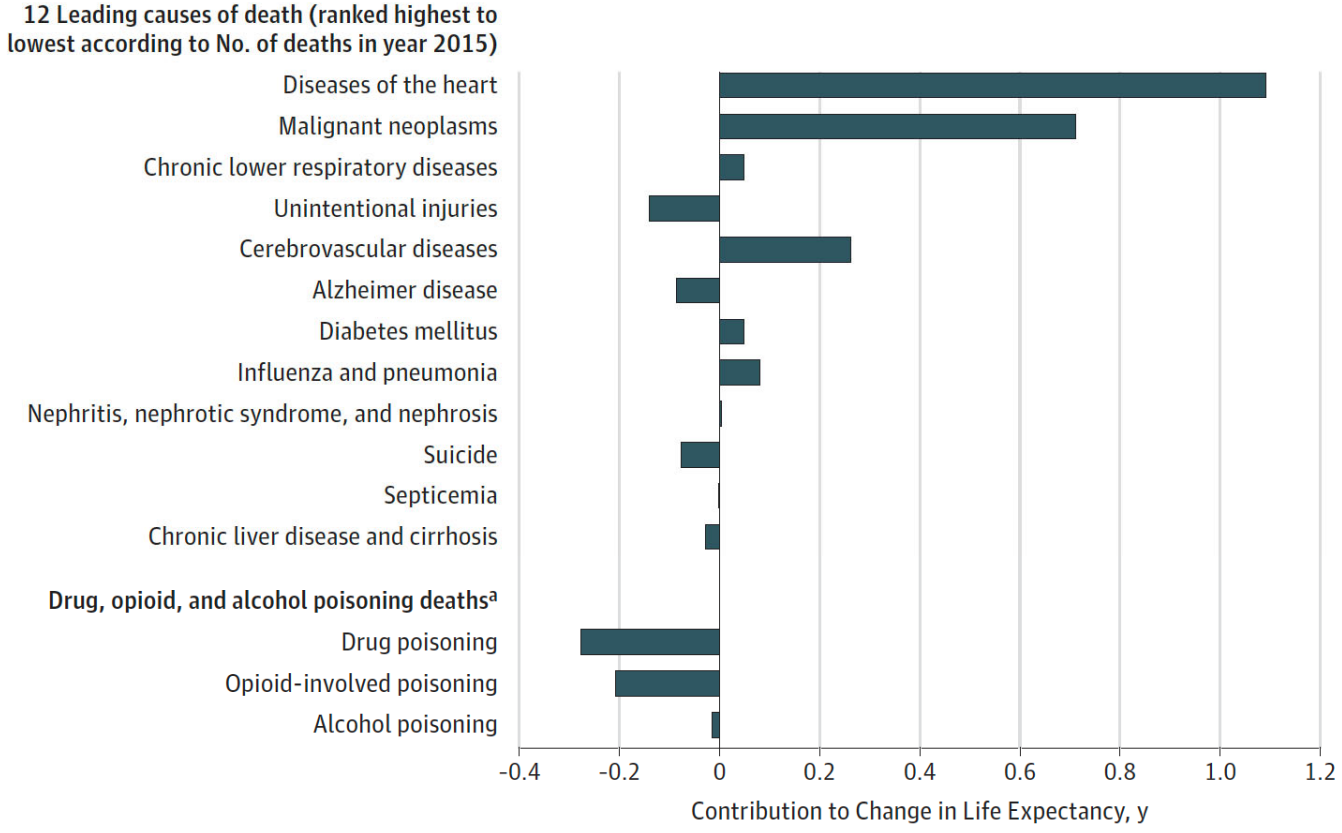

Deaths per 100,000 population
25
20
15
10
5
0
1979
1983
1987
1991
1995
1999
2003
2007
2011
Year
Motor vehicle traffic
Firearm
Drug poisoning
§

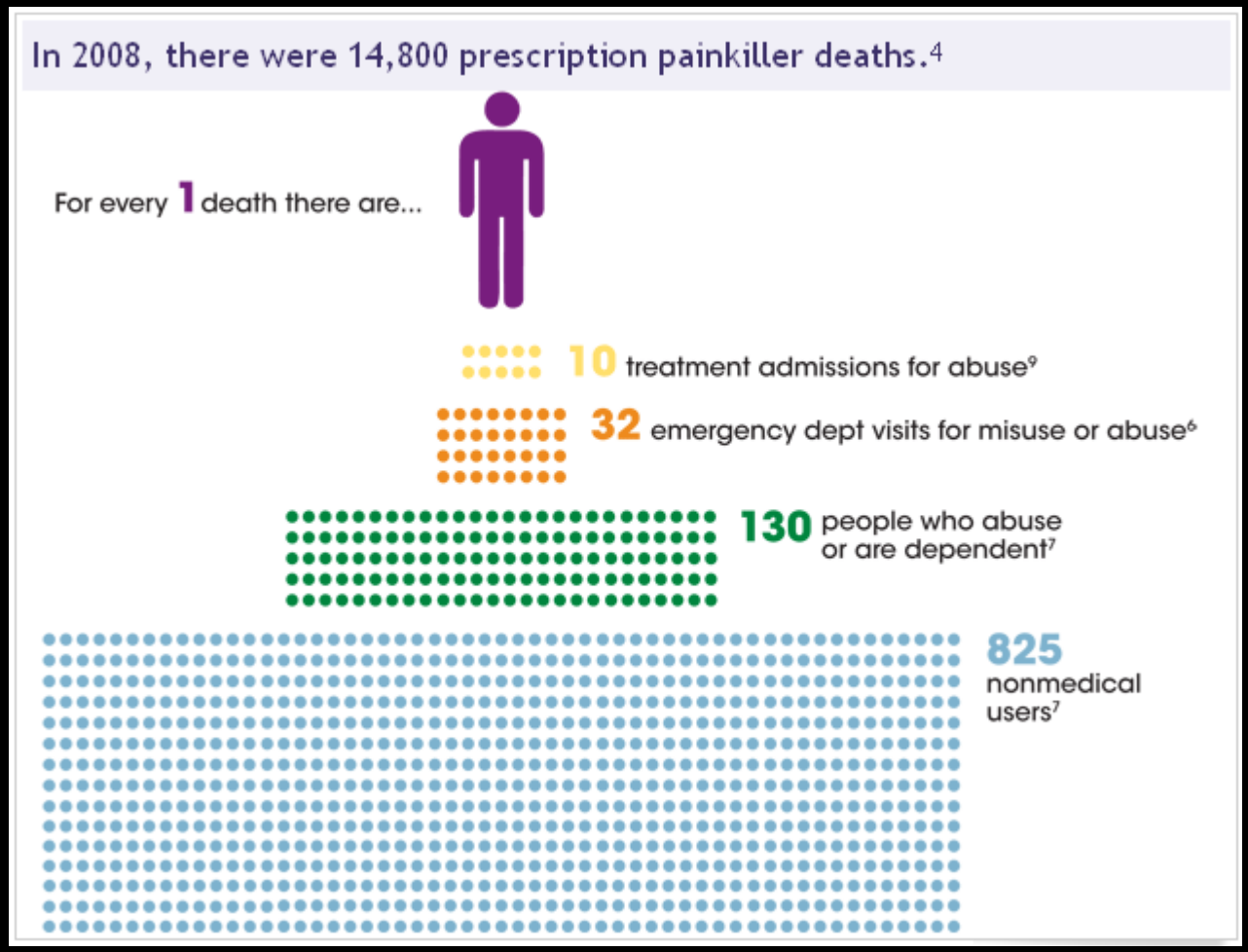
Figure. Contributions of Selected Causes of Death to the Change in Life Expectancy in the United States, 2000-2015



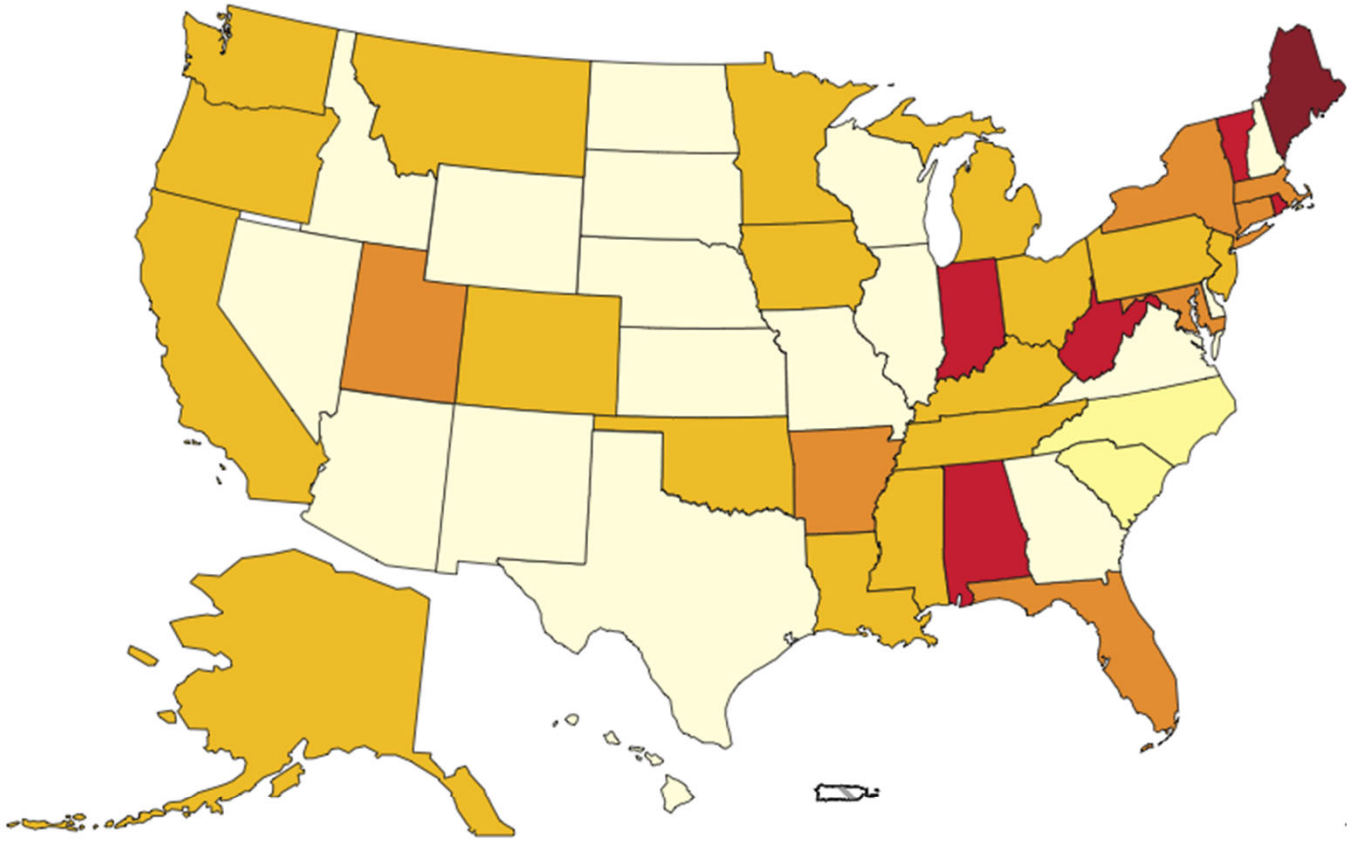
[a] In ranked cause-of-death classification, drug, opioid, and alcohol poisoning are not considered to be unique cause-of-death categories. Instead, poisoning deaths are classified as either accidental poisonings (which contribute to unintentional injuries), suicides, or homicides (ranked 16th in leading causes of death). Contributions from drug, opioid, and alcohol poisoning deaths overlap with both unintentional injury deaths and suicides and cannot be summed with these leading ranked causes of death.

Dowell D, et al. JAMA. 2017 Sep 19;318(11):1065-7

Public Health Impact
Death Is The Tip Of The iceberg



Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



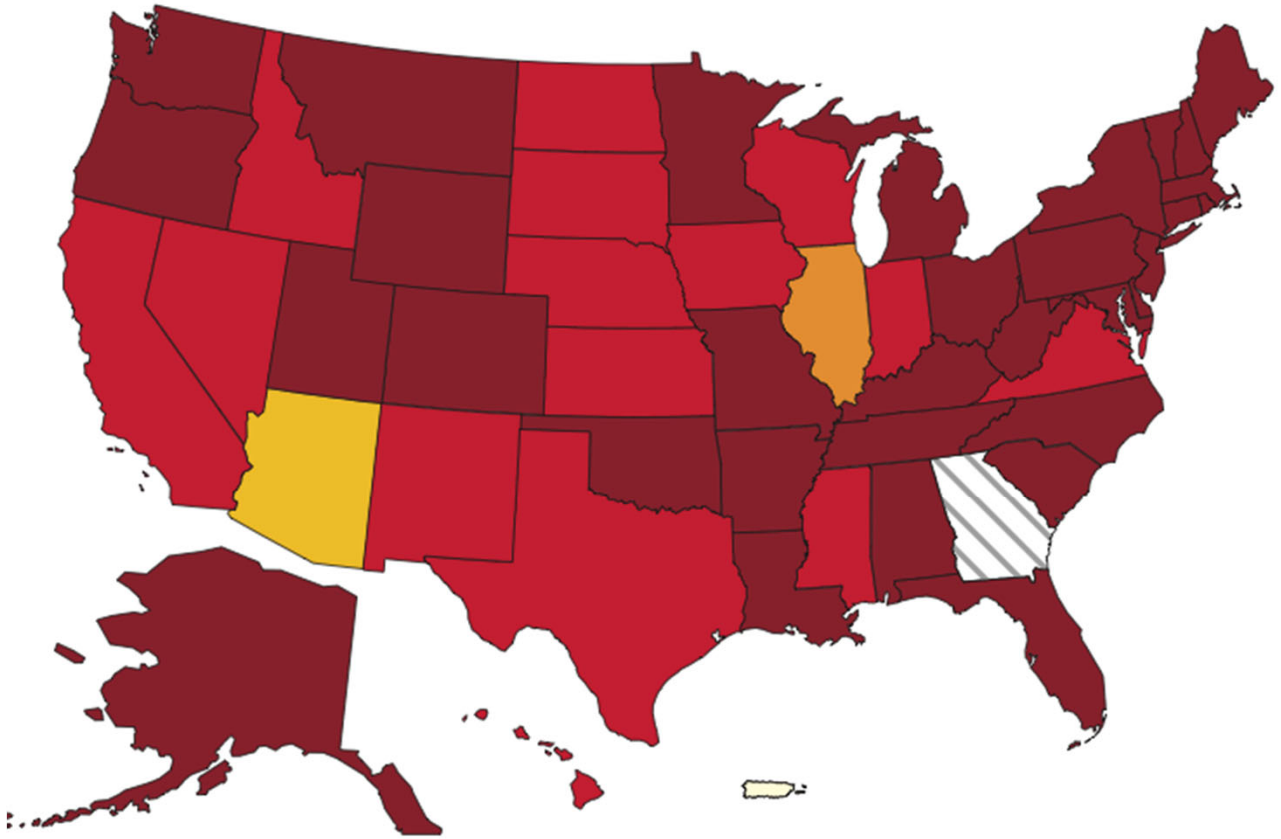
1999

(range 1 - 50)

< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



2009

(range 1 – 379)

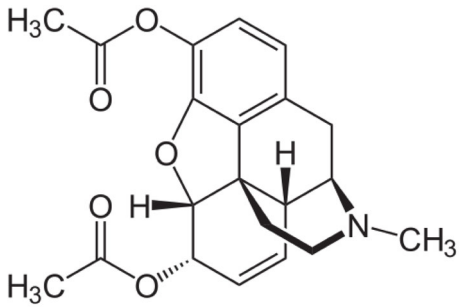
< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

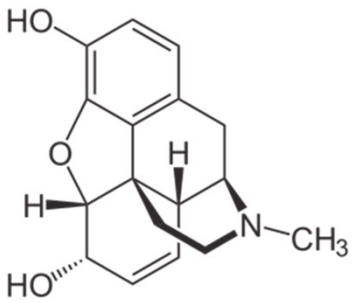
"Oxy" euphoria

- Oxycodone, fentanyl, hydromorphone, and morphine bind the mu-1 opioid receptor
  - Pain relief, but also euphoria
- Lipid solubility, receptor specificity, binding affinity

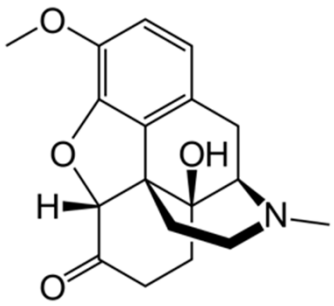
Why isn't heroin legal?
or
Is oxy just legal heroin?*



Heroin
(diacetyl morphine)



Morphine



Oxycodone

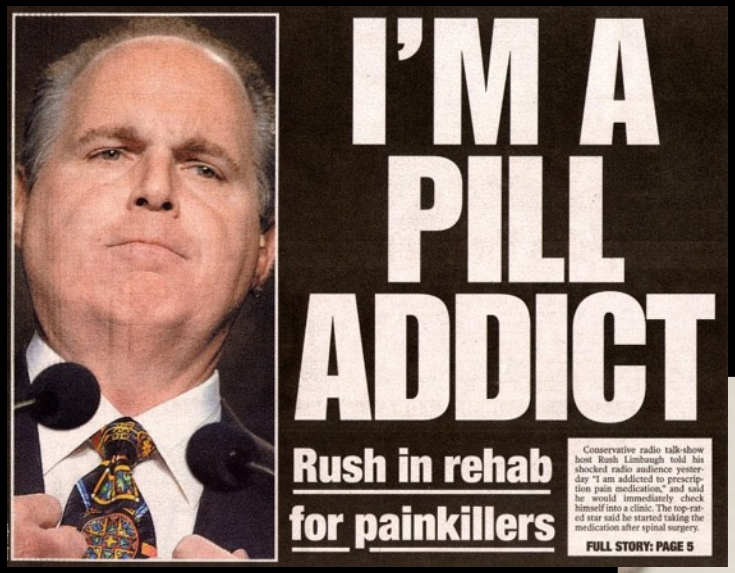
*Okie S. N Engl J Med 2010; 363:1981-1985

Would you give your child HEROIN for a sports injury?

Ask Your Doctor How Prescription Drugs Can Lead to Heroin Abuse.

BEFORE THEY PRESCRIBE - YOU DECIDE.

Prescription for Addiction



I'M A PILL ADDICT

Rush in rehab for painkillers

Conservative radio talk-show host Rush Limbaugh told his shocked radio audience yesterday "I am addicted to prescription pain medication," and said he would immediately check himself into a clinic. The top-rated star said he started taking the medication after spinal surgery.

FULL STORY: PAGE 5

Bad tooth, dental visit, addict

Legal script changes life

Jul. 27, 2013 | Comments

Clement works on a fence at a home in Byram. Clement, who was hooked on the painkiller being prescribed the medication because of a dental issue, is now able to cope with the issue with edication. / Rick Guy/The Clarion-Ledger

tchell

Somehow, Scott Clement survived.

On Labor Day weekend in 1997, the 35-year-old insurance agent throbbed with pain from an abscessed tooth and called a dentist for medicine.

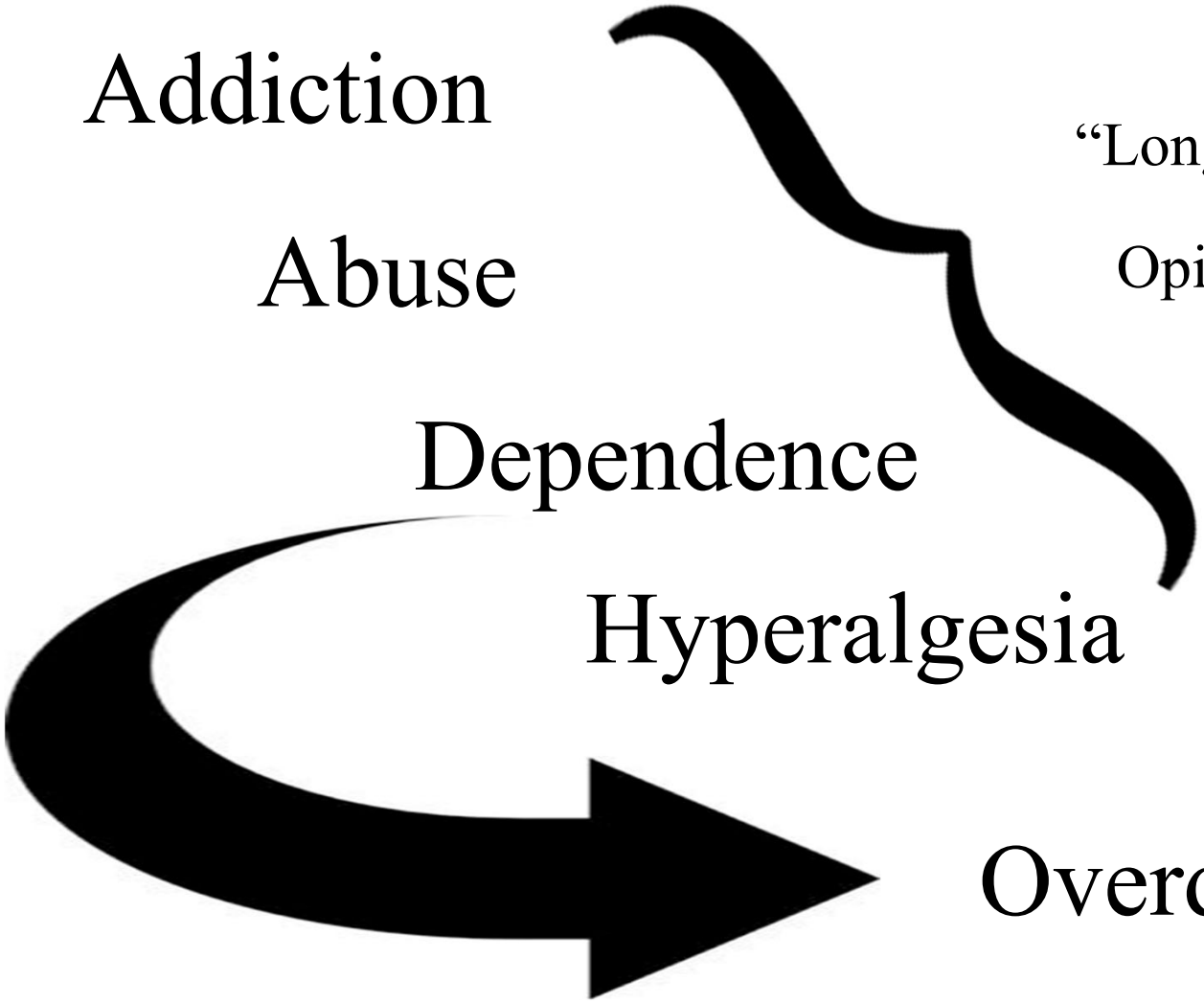
Days later, struggling to sleep, he took a couple of the oxycodone painkillers and found himself overwhelmed by "a ridiculous sense of well-being," he said.

It began his descent into addiction.

Going through the rest of the oxycodone, Clement returned to the dentist, who refused to prescribe more. He went online instead, ordering as many as he could.

UPS made regular deliveries to his insurance agency, and he was gulping 40 pills a day.

Consequences of opioid use



"Long term use"

Opioid use disorder

What are we going to do about it?

- Limit opioid initiation
  - Pain management guidelines
    - Alternatives to opioids
    - Prescribing guidelines
- Safe opioid use
  - Default prescribing EHR
    - Regulatory limits
    - Order sets
  - Nudge prescribers
  - Patient education
- Prescription Monitoring Program

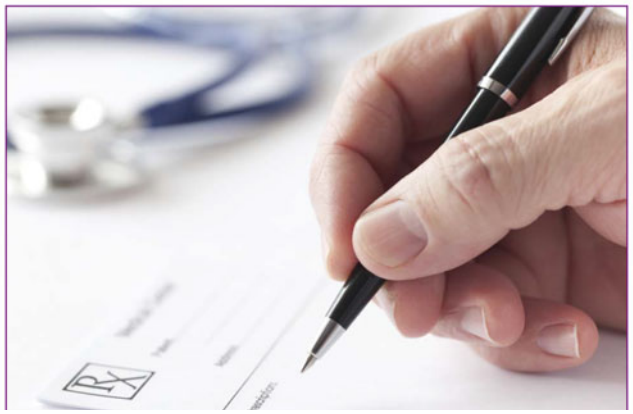
- Harm reduction
  - Naloxone distribution/prescribing
  - Recovery coaches
  - Family engagement
  - Public health interventions
- Addiction management
  - Screening
  - Reduce barriers to treatment
  - Linkage to care/warm handoff
  - Mediation-assisted therapy

Strategies to Curb the Prescription Opioid Problem

Pain Guidelines

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
March 15, 2016

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016



Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

UNIVERSITY HOSPITAL
Newark, New Jersey

University Hospital Adult Emergency Medicine Treatment of Acute Pain Guideline

- Alternative therapies should be considered if there are contraindications to first line recommendations
- Consider next line therapies in a stepwise manner if pain persists 30 minutes after an IV dose **OR** 60 minutes after a PO dose
- Other than in the treatment of severe acute pain, the oral route is the preferred route of administration of most analgesic drugs

Abdominal Pain

First Line	Second Line	Third Line	Adjunctive Therapy	Discharge
Undifferentiated abdominal pain Acetaminophen 975 mg PO **AND/OR** Ibuprofen 400 – 600 mg PO (If patient cannot tolerate PO, ketorolac 15 mg IV) *Spasmodic pain* Dicyclomine 20 mg PO (If patient cannot tolerate PO, dicyclomine 10 mg IV) *Gastroparesis* Metoclopramide 10 mg IV	*Undifferentiated abdominal pain* Ketamine 0.3 mg/kg IV over 15 minutes *Gastroparesis* Haloperidol 5 mg IV **OR** Haloperidol 5 mg IM	Opioid rescue*	*Anti-emetics* Ondansetron 4 mg IV **OR** Ondansetron ODT 4 mg PO **OR** Metoclopramide 10 mg IV *Antacids* Mag hydroxide/aluminum hydroxide/simethicone 1200 mg/1200 mg/120 mg PO **AND/OR** Famotidine 20 mg IV	*Undifferentiated abdominal pain* Acetaminophen 975 mg PO q6H PRN **AND/OR** Ibuprofen 400 mg PO q6H PRN *Spasmodic pain* Dicyclomine 20 mg PO q6H PRN *Gastroparesis* Metoclopramide 10 mg PO q6H PRN

Clinical Pearls:

- Consider underlying etiology of abdominal pain before selecting treatment option (e.g. anticholinergics and opioids counterintuitive in gastroparesis)
- Ketamine: avoid use in patients with severe hypertension or history of psychosis
- NSAIDs: avoid use in third trimester of pregnancy, peptic ulcer disease, history of GI bleed, or active major bleeding
- Provide patient education regarding type of pain, medication choices, and what to expect
- Consider distractions such as music, talking to patient

Dental Pain

First Line	Second Line	Third Line	Adjunctive Therapy	Discharge
Acetaminophen 975 mg PO **AND/OR** Ibuprofen 400 – 600 mg PO (If patient cannot tolerate PO, ketorolac 15 mg IV)	Lidocaine 2% viscous solution – swish and spit	Lidocaine 1% dental block	Apply ice pack to painful area	Acetaminophen 975 mg PO q6H PRN **AND/OR** Ibuprofen 400 – 600 mg PO q6H PRN **AND/OR** Lidocaine 2% viscous solution – swish and spit q3 hours PRN

Clinical Pearls:

- Provide patient education regarding type of pain, medication choices, and what to expect
- Analgesia is a temporizing measure for more definitive treatment
- NSAIDs: avoid use in third trimester of pregnancy, peptic ulcer disease, history of GI bleed, or active major bleeding


NJ PMP
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Alerts
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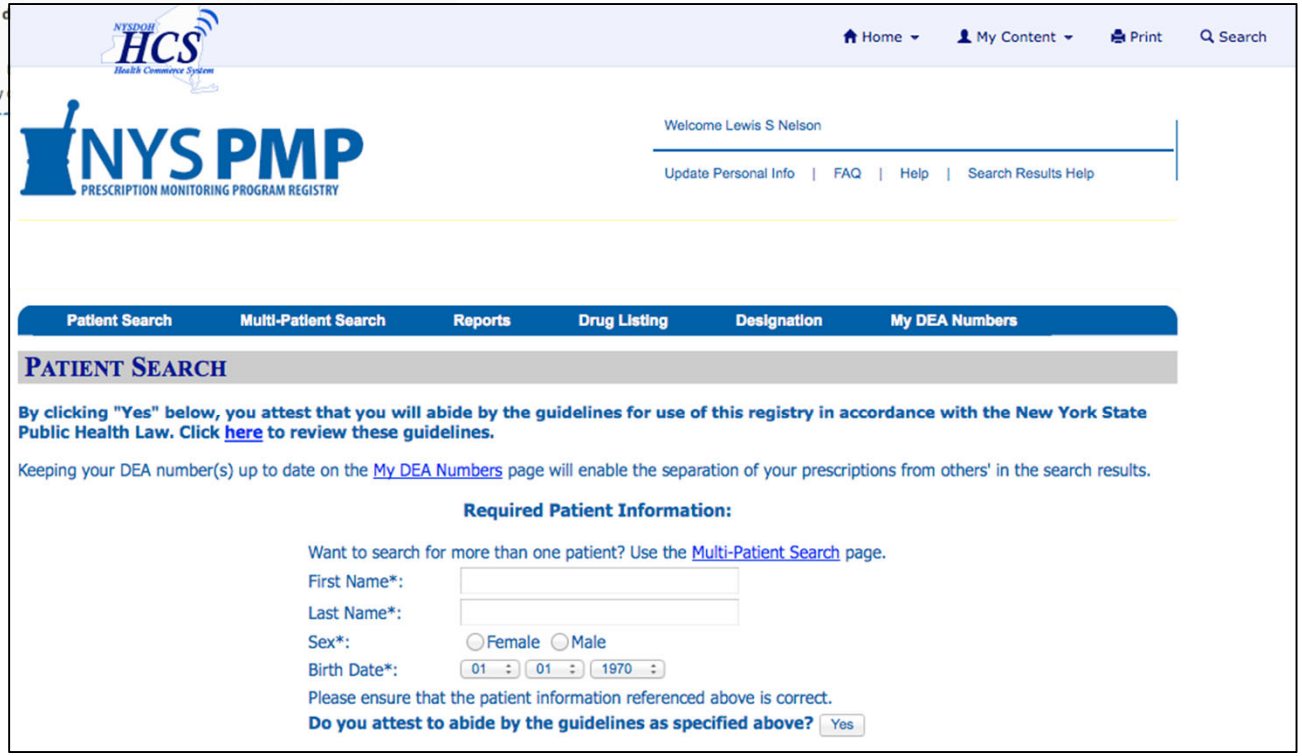
Pharmacy Reporting Requirements
Frequently Asked Questions
Suspicious Activity Report
Useful Links
Law Enforcement
Treatment
Media
Project Medicine Drop
NJ Prescription Monitoring Program
For Too Many New Jerseyans, Addiction Begins in the Medicine Cabinet
The New Jersey Prescription Monitoring Program (NJPMP) is an important component of the New Jersey Division of Consumer Affairs' initiative to halt the abuse and diversion of prescription drugs.
Established pursuant to N.J.S.A. 45:1-45 et. seq., the NJPMP is a statewide database that collects prescription data on Controlled Dangerous Substances (CDS) and Human Growth Hormone (HGH) dispensed in outpatient settings in New Jersey, and by out-of-State pharmacies dispensing into New Jersey.
Pharmacies are required to report information to the NJPMP on a daily basis to the PMP Clearinghouse using the ASAP 4.2 format. Prescriptions must be reported to the database no more than one (1) business
date the prescription was dispensed.
The Division of Consumer Affairs and
Administrator keep patient information strictly
Email
NJ Prescription Monitoring Program
Call
(973) 273-8010
Inquiries about the NJPMP may be forwarded to
Jeffrey D. Laszczyk, Jr., PharmD
NJPMP Administrator
P.O. Box 47014
Newark, New Jersey 07101


NYSDOH HCS Health Commerce System
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PRESCRIPTION MONITORING PROGRAM REGISTRY
Welcome Lewis S Nelson
Update Personal Info | FAQ | Help | Search Results Help
Patient Search
Multi-Patient Search
Reports
Drug Listing
Designation
My DEA Numbers
PATIENT SEARCH
By clicking "Yes" below, you attest that you will abide by the guidelines for use of this registry in accordance with the New York State Public Health Law. Click here to review these guidelines.
Keeping your DEA number(s) up to date on the My DEA Numbers page will enable the separation of your prescriptions from others' in the search results.
Required Patient Information:
Want to search for more than one patient? Use the Multi-Patient Search page.
First Name*:
Last Name*:
Sex*: Female Male
Birth Date*: 01 01 1970
Please ensure that the patient information referenced above is correct.
Do you attest to abide by the guidelines as specified above? Yes

What are we going to do about it?

- Limit opioid initiation
  - Pain management guidelines
    - Alternatives to opioids
    - Prescribing guidelines
- Safe opioid use
  - Default prescribing EHR
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Home > Priorities > Opioid Overdose Prevention > Surgeon General's Advisory on Naloxone and Opioid Overdose

Text Size: A A A Share

Surgeon General's Advisory on Naloxone and Opioid Overdose

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, ***knowing how to use naloxone and keeping it within reach can save a life.***

BE PREPARED. GET NALOXONE. SAVE A LIFE.

The Opioid Epidemic

Over the past 15 years, individuals, families, and communities across our Nation have been tragically affected by the opioid epidemic, with the number of overdose deaths from prescription and illicit opioids doubling from 21,089 in 2010 to 42,249 in 2016.[1] This steep increase is attributed to the rapid proliferation of illicitly made fentanyl and other highly potent synthetic opioids. These highly potent opioids are being mixed with heroin, sold alone as super-potent heroin, pressed into counterfeit tablets to look like commonly misused prescription opioids or sedatives (e.g., Xanax), and being mixed (often unknowingly) with other illicit drugs like cocaine or methamphetamine. The resulting unpredictability in illegal drug products is dramatically increasing the risk of a fatal overdose. Another contributing factor to the rise in opioid overdose deaths is an increasing number of individuals receiving higher doses of prescription opioids for long-term management of chronic pain. Even when taking their pain medications as prescribed, these patients are at increased risk of accidental overdose as well as drug-alcohol or drug-drug interactions with sedating medications, such as benzodiazepines (anxiety or sleep medications).

NALOXONE

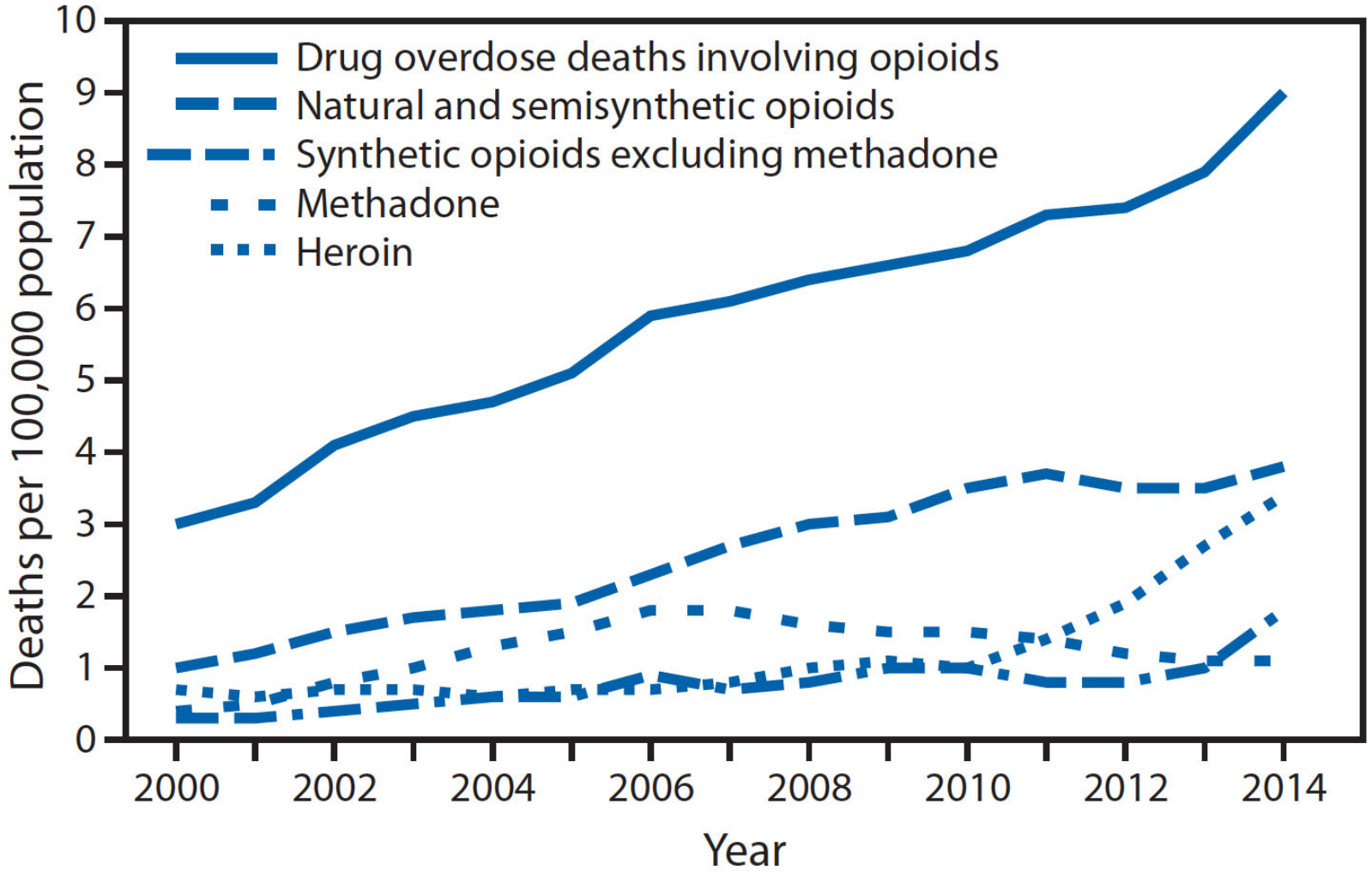
10 percent revived by Narcan in Mass. died within year, study says

JESSICA RINALDI/GLOBE STAFF/FILE

Doses of Narcan have proven to be effective in reversing overdoses, but doctors say follow-up medication is needed.

By Felice J. Freyer | GLOBE STAFF OCTOBER 30, 2017

FIGURE 2. Drug overdose deaths* involving opioids,[†,§] by type of opioid[¶] — United States, 2000–2014



The Newest Opium War

Fentanyl(s)

- Mu opioid receptor full agonist
  - Variable effect at other opioid receptor subtypes
- High potency
- Highly lipophilic
  - Rapid onset IV
  - Generally rapid offset
    - Slow redistribution
- Apnea
  - At high doses
- Rigidity
  - At high infusion rates

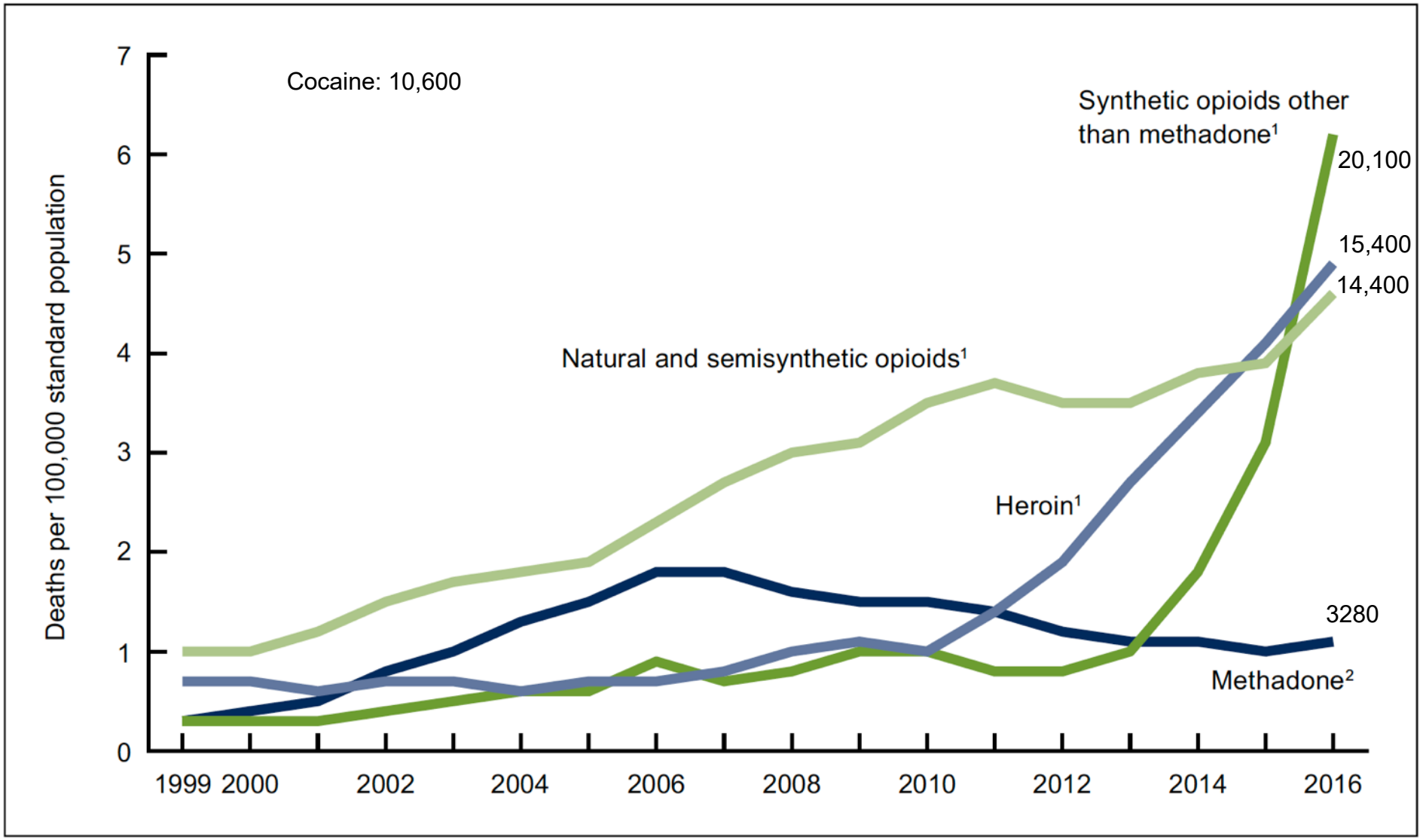
Table.
Characteristics of opioids including fentanyl derivatives.[25,34-36]

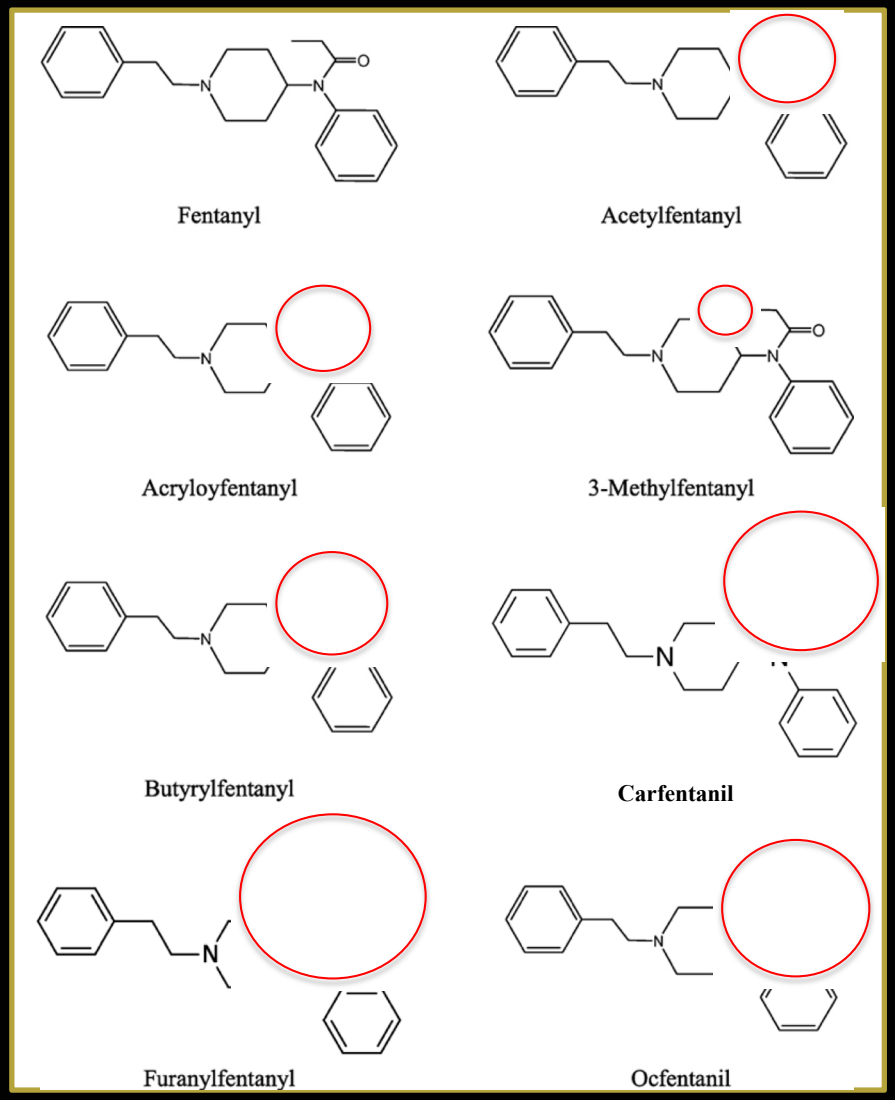
Opioid	Potency (Compared With Morphine)	Lipid Solubility*	Therapeutic Index†
Morphine	1	1.4	70
Meperidine	0.5	40	5
Methadone	4	120	12
Fentanyl	300	800	300
Sufentanil	4500	1800	25,000
Alfentanil	75	150	1100
Remifentanil	220	18	33,000
Carfentanil	10,000		10,600

*Lipid solubility=octanol/water distribution coefficient.
†Therapeutic index=median lethal dose (LD_{50})/lowest median effective dose (ED_{50}).

Wax, P. Ann Emerg Med 2003; 41: 700–705.

Figure 4. Age-adjusted drug overdose death rates, by opioid category: United States, 1999–2016




Fentanyl
Acetylfentanyl
Acryloyfentanyl
3-Methylfentanyl
Butyrylfentanyl
Carfentanil
Furanylfentanyl
Ocfentanil

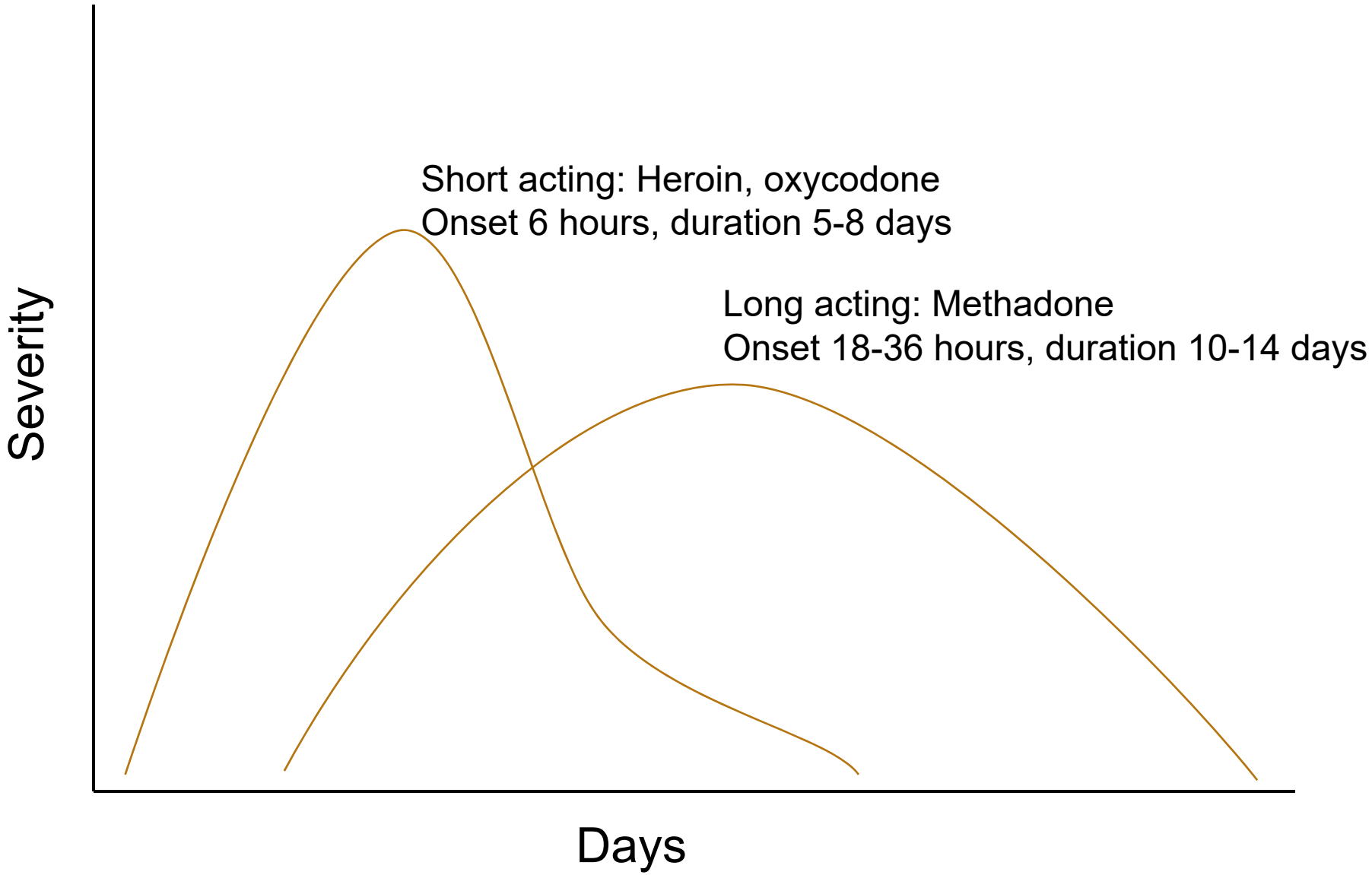

Home
The New York Times
ARTS
Prince's Addiction and an Intervention Too Late

Equi-effective "safe" doses

Equi-effective "safe" doses

Dangerous doses

Deadly doses


Short acting: Heroin, oxycodone
Onset 6 hours, duration 5-8 days
Long acting: Methadone
Onset 18-36 hours, duration 10-14 days
Severity
Days

ABSTINENCE-INDUCED OPIOID WITHDRAWAL

Naturally occurring opioid withdrawal is not life-threatening.

ABSTINENCE-INDUCED OPIOID WITHDRAWAL

Naturally occurring opioid withdrawal is not life-threatening.

PRECIPTATED OPIOID WITHDRAWAL

Altered mental status

Autonomic instability

Pulmonary edema

Appendix 6. Clinical Opiate Withdrawal Scale[1]

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

Patient's Name: _____ **Date and Time:** _____/_____/____:____

Reason for this assessment: _____

Resting Pulse Rate _____ beats/minute
Measured after patient is sitting or lying for one minute
0 pulse rate 80 or below
1 pulse rate 81–100
2 pulse rate 101–120
4 pulse rate greater than 120

GI Upset *over last ½ hour*
0 no GI symptoms
1 stomach cramps
2 nausea or loose stool
3 vomiting or diarrhea
5 multiple episodes of diarrhea or vomiting

Sweating *over past ½ hour not accounted for by room temperature or patient activity*
0 no report of chills or flushing
1 subjective report of chills or flushing
2 flushed or observable moistness on face
3 beads of sweat on brow or face
4 sweat streaming off face

Tremor *observation of outstretched hands*
0 no tremor
1 tremor can be felt, but not observed
2 slight tremor observable
4 gross tremor or muscle twitching

Restlessness *observation during assessment*
0 able to sit still
1 reports difficulty sitting still, but is able to do so
3 frequent shifting or extraneous movements of legs/arms
5 unable to sit still for more than a few seconds

Yawning *observation during assessment*
0 no yawning
1 yawning once or twice during assessment
2 yawning three or more times during assessment
4 yawning several times/minute

Pupil Size
0 pupils pinned or normal size for room light
1 pupils possibly larger than normal for room light
2 pupils moderately dilated
5 pupils so dilated that only the rim of the iris is visible

Anxiety or Irritability
0 none
1 patient reports increasing irritability or anxiousness
2 patient obviously irritable anxious
4 patient so irritable or anxious that participation in the assessment is difficult

Bone or Joint Aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored*
0 not present
1 mild diffuse discomfort
2 patient reports severe diffuse aching of joints/muscles
4 patient is rubbing joints or muscles and is unable to sit still because of discomfort

Gooseflesh Skin
0 skin is smooth
3 piloerrection of skin can be felt or hairs standing up on arms
5 prominent piloerrection

Runny Nose or Tearing
Not accounted for by cold symptoms or allergies
0 not present
1 nasal stuffiness or unusually moist eyes
2 nose running or tearing
4 nose constantly running or tears streaming down cheeks

Total Score _____
The total score is the sum of all 11 items.

Initials of person completing assessment: _____

Score: 5–12 = mild; 13–24: moderate; 25–36 = moderately severe; more than 36 = severe withdrawal

Reference:
1. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs. 2003;35(2):253–259.

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Appendix 7. Subjective Opiate Withdrawal Scale (SOWS)[1]

The SOWS is a self-administered scale for grading opioid withdrawal symptoms. It contains 16 symptoms whose intensity the patient rates on a scale of 0 (not at all) to 4 (extremely), and takes less than 10 minutes to complete.

Patient Instructions: please score each of the 16 items below according to how you feel right now. Circle one number only.

Item	Symptom	Not at all	A little	Moderately	Quite a bit	Extremely
1	I feel anxious	0	1	2	3	4
2	I feel like yawning	0	1	2	3	4
3	I am perspiring	0	1	2	3	4
4	My eyes are teary	0	1	2	3	4
5	My nose is running	0	1	2	3	4
6	I have goosebumps	0	1	2	3	4
7	I am shaking	0	1	2	3	4
8	I have hot flushes	0	1	2	3	4
9	I have cold flushes	0	1	2	3	4
10	My bones and muscles ache	0	1	2	3	4
11	I feel restless	0	1	2	3	4
12	I feel nauseous	0	1	2	3	4
13	I feel like vomiting	0	1	2	3	4
14	My muscles twitch	0	1	2	3	4
15	I have stomach cramps	0	1	2	3	4
16	I feel like using now	0	1	2	3	4

Total Score: _____

Reference:
1. Handelsman L, Cochrane KJ, Aronson MJ, Ness R, Rubinstein KJ, Kanof PD. Two New Rating Scales for Opiate Withdrawal. 1987. American Journal of Alcohol Abuse 13, 293-308.


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Loperamide hydrochloride
Can relieve diarrhoea
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Serving Size: 2 capsule
Servings per Container: 30
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Theobromine
Huperzine A
* % Daily Value (DV) not established
100% GMP


MITADONE
Anti-Opiate Aid Plus
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• MOOD SUPPORT†
DIETARY SUPPLEMENT
120 TABLETS

MANAGEMENT OF OPIOID WITHDRAWAL

- Methadone
  - 10 mg IM (or the equivalent 20 mg PO)
    - Blocks withdrawal in virtually all patients regardless ofbuse pattern
  - Suppresses craving

Su MK, et al. AmJEM 2018

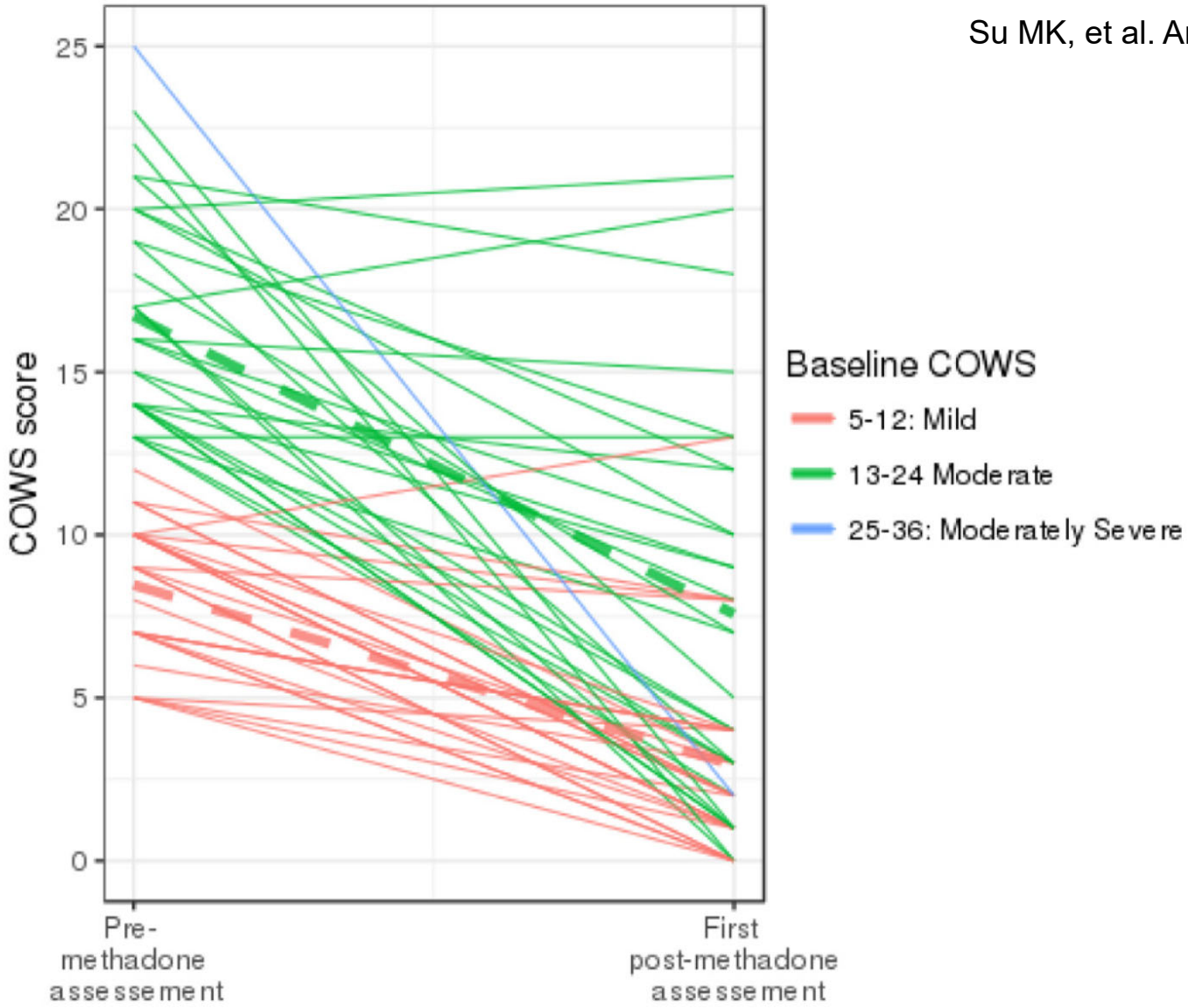
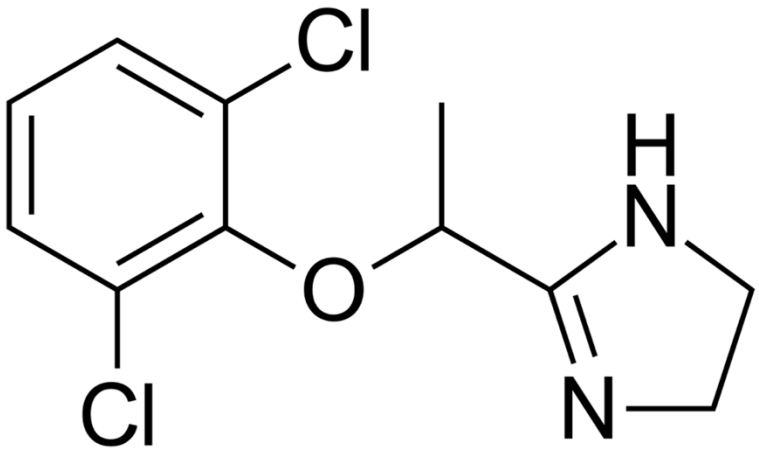


Fig. 2. Change in COWS score from baseline (prior to methadone administration) to first assessment post-methadone administration. Each one of the solid lines represents the change for one patient. Lines are colored according to symptom severity at baseline. The thick dotted lines represent the average change for each of the severity categories.

MANAGEMENT OF OPIOID WITHDRAWAL

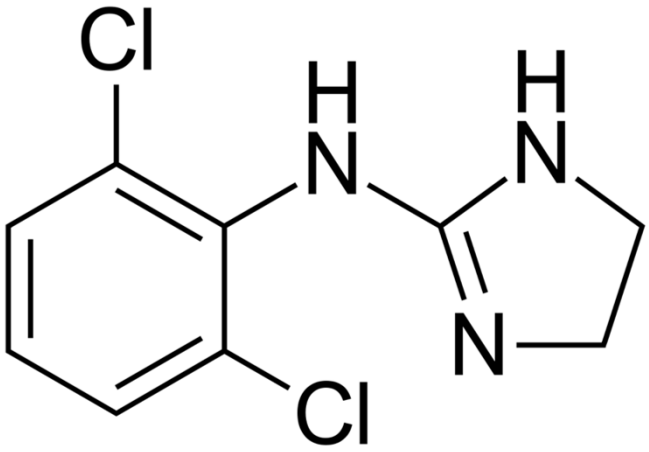
- Methadone
  - 10 mg IM (or the equivalent 20 mg PO)
    - Blocks withdrawal in virtually all patients regardless of use pattern
  - Suppresses craving
- Centrally acting alpha agonist
  - Reduces autonomic activity
  - Does not suppress craving

Lofexidine



Brand: $1738.00/mo

Clonidine



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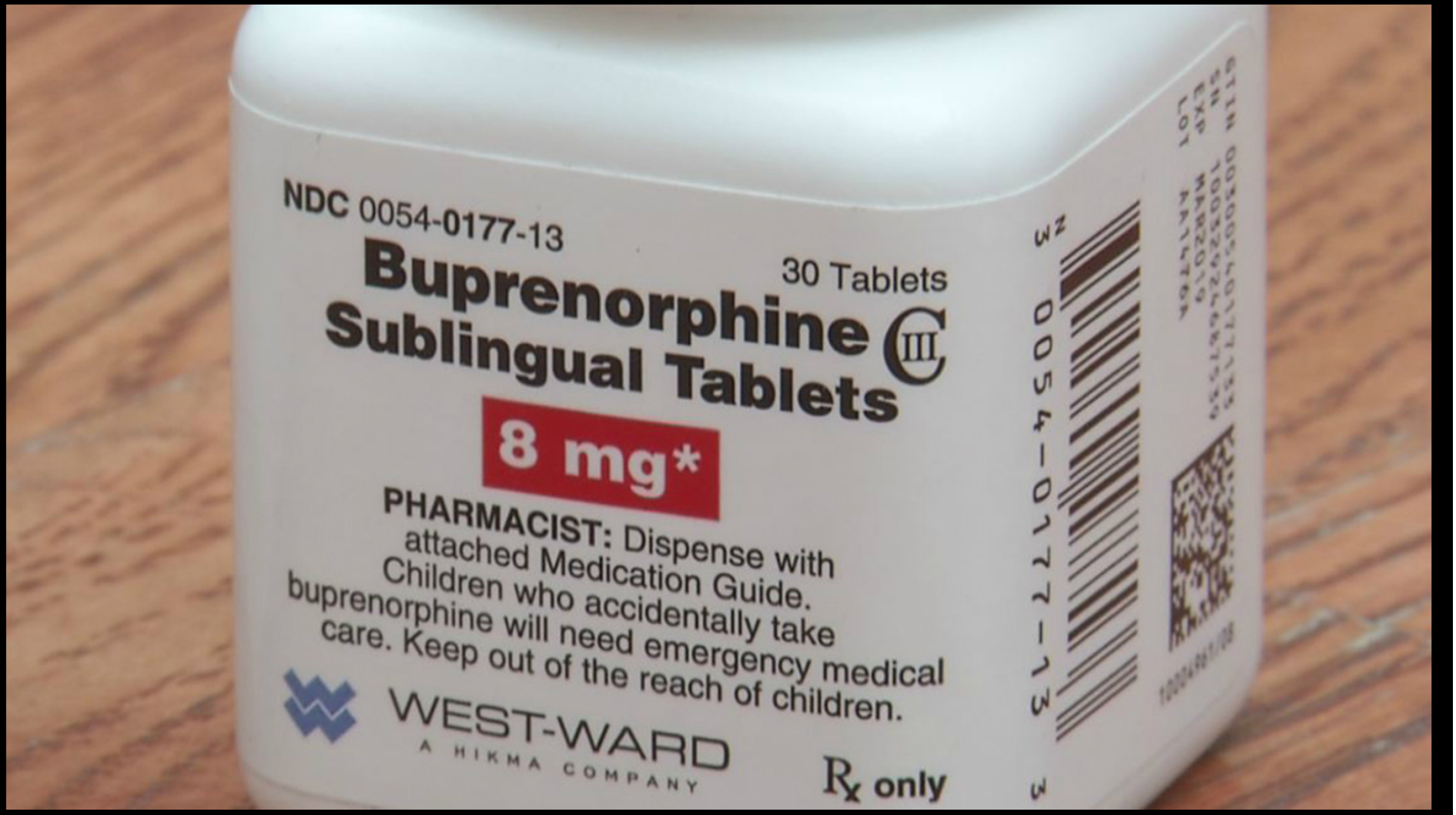
MANAGEMENT OF OPIOID WITHDRAWAL

- Methadone
  - 10 mg IM (or the equivalent 20 mg PO)
    - Blocks withdrawal in virtually all patients regardless ofbuse pattern
  - Suppresses craving
- Centrally acting alpha agonist
  - Reduces autonomic activity
  - Does not suppress craving
- Buprenorphine
  - Partial agonist that may worsen withdrawal


NDC 0054-0177-13
30 Tablets
Buprenorphine
Sublingual Tablets
CIII
8 mg*
PHARMACIST: Dispense with attached Medication Guide. Children who accidentally take buprenorphine will need emergency medical care. Keep out of the reach of children.
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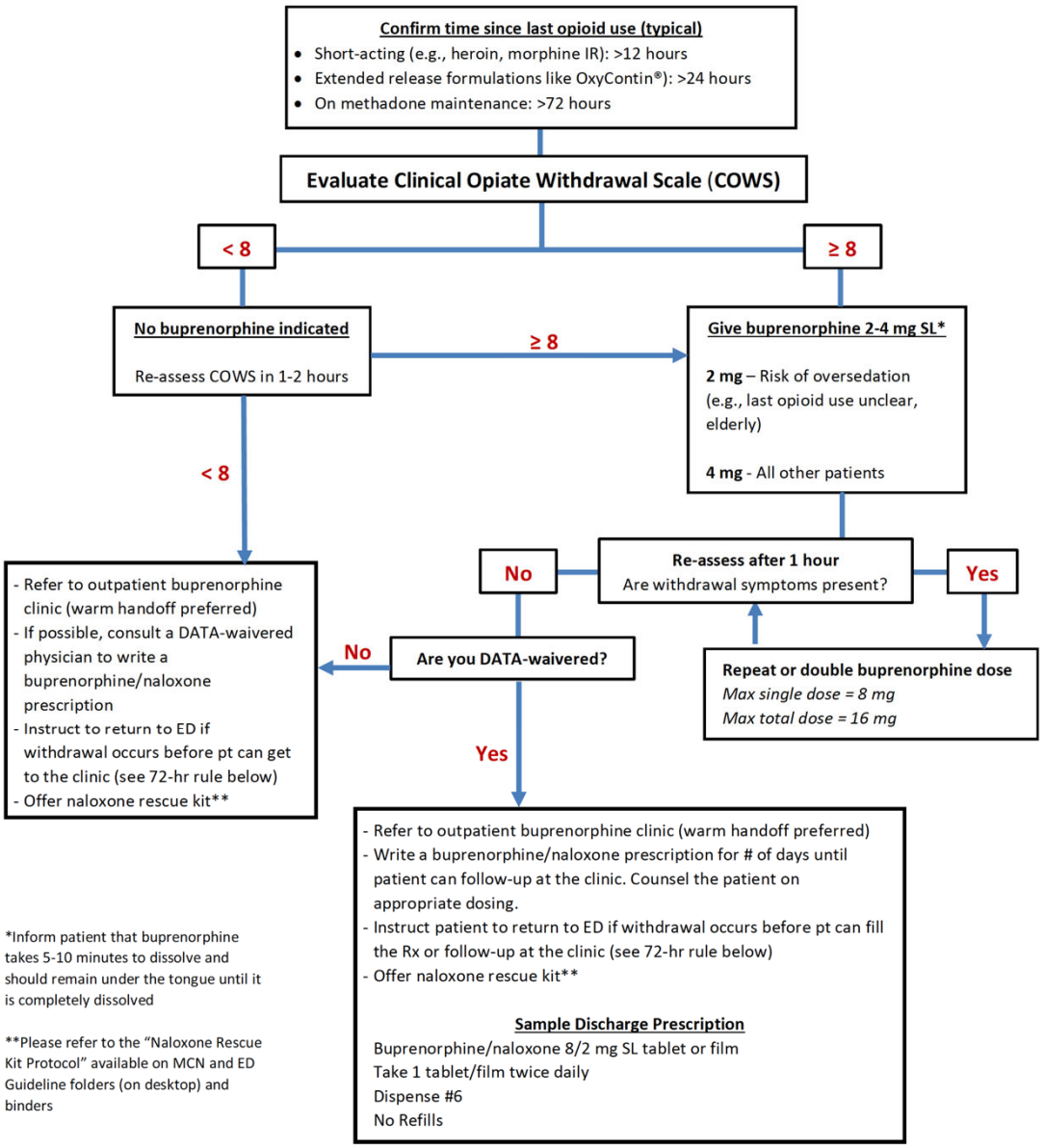
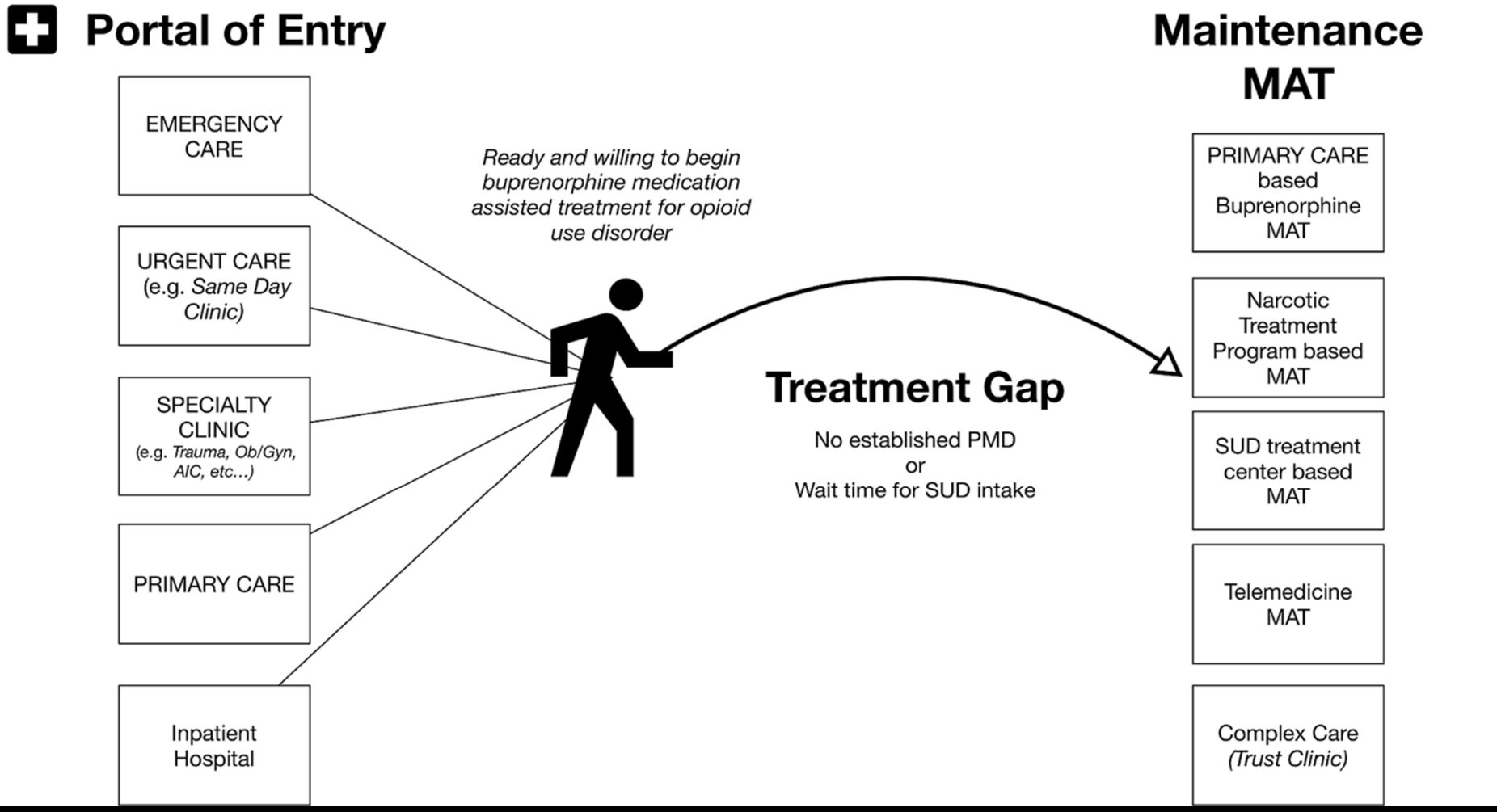
Buprenorphine Dosing Guideline for Acute Opioid Withdrawal



*Inform patient that buprenorphine takes 5-10 minutes to dissolve and should remain under the tongue until it is completely dissolved

**Please refer to the "Naloxone Rescue Kit Protocol" available on MCN and ED Guideline folders (on desktop) and binders

Bridge Program



MADDIE MCGARVEY/FOR CNN

ORIGINAL ARTICLE

Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, Ph.D., Kevin E. O'Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D.

Jones HE, et al. NEJM 2010;363:2320

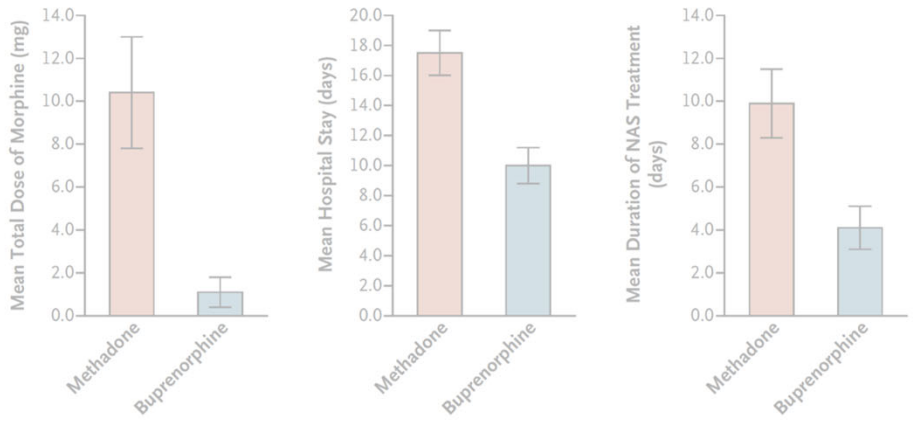


Figure 2. Mean Neonatal Morphine Dose, Length of Neonatal Hospital Stay, and Duration of Treatment for Neonatal Abstinence Syndrome.

Kraft WK, et al. NEJM 2017;376:2341

ORIGINAL ARTICLE

Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome

Walter K. Kraft, M.D., Susan C. Adeniyi-Jones, M.D., Inna Chervoneva, Ph.D., Jay S. Greenspan, M.D., Diane Abatemarco, Ph.D., Karol Kaltenbach, Ph.D., and Michelle E. Ehrlich, M.D.

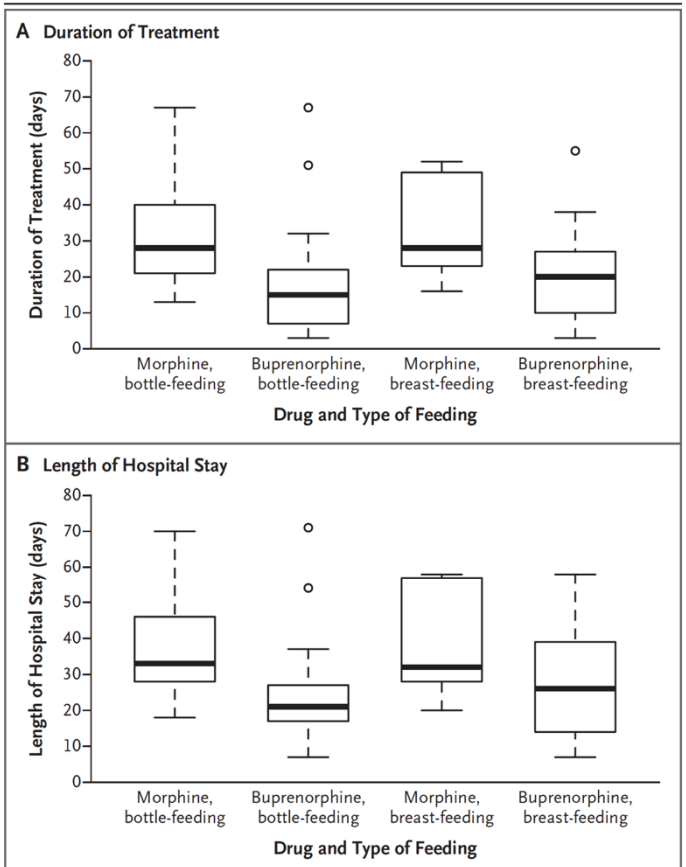


Figure 2. Duration of Treatment and Length of Hospital Stay.

The duration of treatment (Panel A) and length of hospital stay (Panel B) were shorter in the buprenorphine group than in the morphine group ($P<0.001$ for both comparisons). Randomization was stratified according to the type of intended feeding method (bottle-feeding or breast-feeding). The box-and-whisker plots represent medians (horizontal lines) and interquartile ranges (top and bottom of the boxes); the I bars represent the maximum or minimum value or 1.5 times the interquartile range. Outliers are indicated by circles.

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