# PHARMACOLOGICAL TREATMENT of PAIN:
# o what are we going to give grandma?

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# Disclosures

- **Nothing to disclose**

# Denis Leary "Quote"

- I did not bother to look everything up and reference it, because frankly it would take too much time.  If you truly feel the need, just google it.

# Goal

- To educate
- To be upsetting
- I have earned this podium

# More Questions than Answers

- The more I research and study this topic, the less I realize I know.
- I dug deep into opioid pharmacology/receptors/etc.
- Lots of new knowledge, more questions than answers.
  - which receptors
  - clinical data
  - we have to keep it real with good science vs. opinion

# Motivation to present today

- 1) Thank you for indulging me with the opportunity to speak today
- 2) Officer's lecture was flashback to my college years with some updates (crack) minus the barbs/ludes. Do not underscore booze.
- 3) What do I teach my students?
  - Ph.D. from Harvard in anecdotal medicine
  - Heavy on statistics, quality of data, bias, confidence intervals, p values.
  - Approach problems in a epidemiologic way (50,000 ft) vs the individual patient
  - Booze & Nicotine a problem

# Why am I interested in pain? QOL is important to me.

- 40 year old pet peeve concerning confusion of health care professionals between addiction and physical dependence (even hospice)
- 15 year history of multiple myeloma
- Two stem cell transplants
- Epididymitis/urethritis x3 prior to Dx
- Inflamed necrotic lesion size/shape of Africa on left thigh (2 yrs to heal) led to Dx. oF MM
- Shingles
- Post herpetic neuralgia
- Grade IV peripheral neuropathy x 13 years (thalidomide)
- Open fracture of radius and ulna (5 surgeries)
- 18 year Hx of 6 DVT's (5/2000 – 5/2018)
- Meds : acetaminophen, Celebrex, Lyrica 300mg bid, oxycodone 5 mg prn, warfarin/Eliquis, Revlimid, pain cocktail

# Key Questions

- **Is the “patient” treating true pain?**
- **Is the ‘individual” taking the medication to get high?**
- **Do Physicians believe they have a moral and ethical responsibility to treat pain and suffering?**
- **Quality of life, living in pain**
- **Functionality of a patient in pain vs on medications?**
- **Can a pharmacist talk about the treatment of pain without it being a MAPS talk?**

# Goodman and Gilman

Pain is a component of virtually all clinical pathologies, and management of pain is a primary clinical imperative.

# Axioms/Comments

- Often based more on opinion than facts
- More expert opinions than experts
- **Lots of well intended motives/emotions**
- Can we use broad strokes to address opioid use? Or is it an extremely complicated problem?
- So how do we treat grandma?

# Patient grandpa

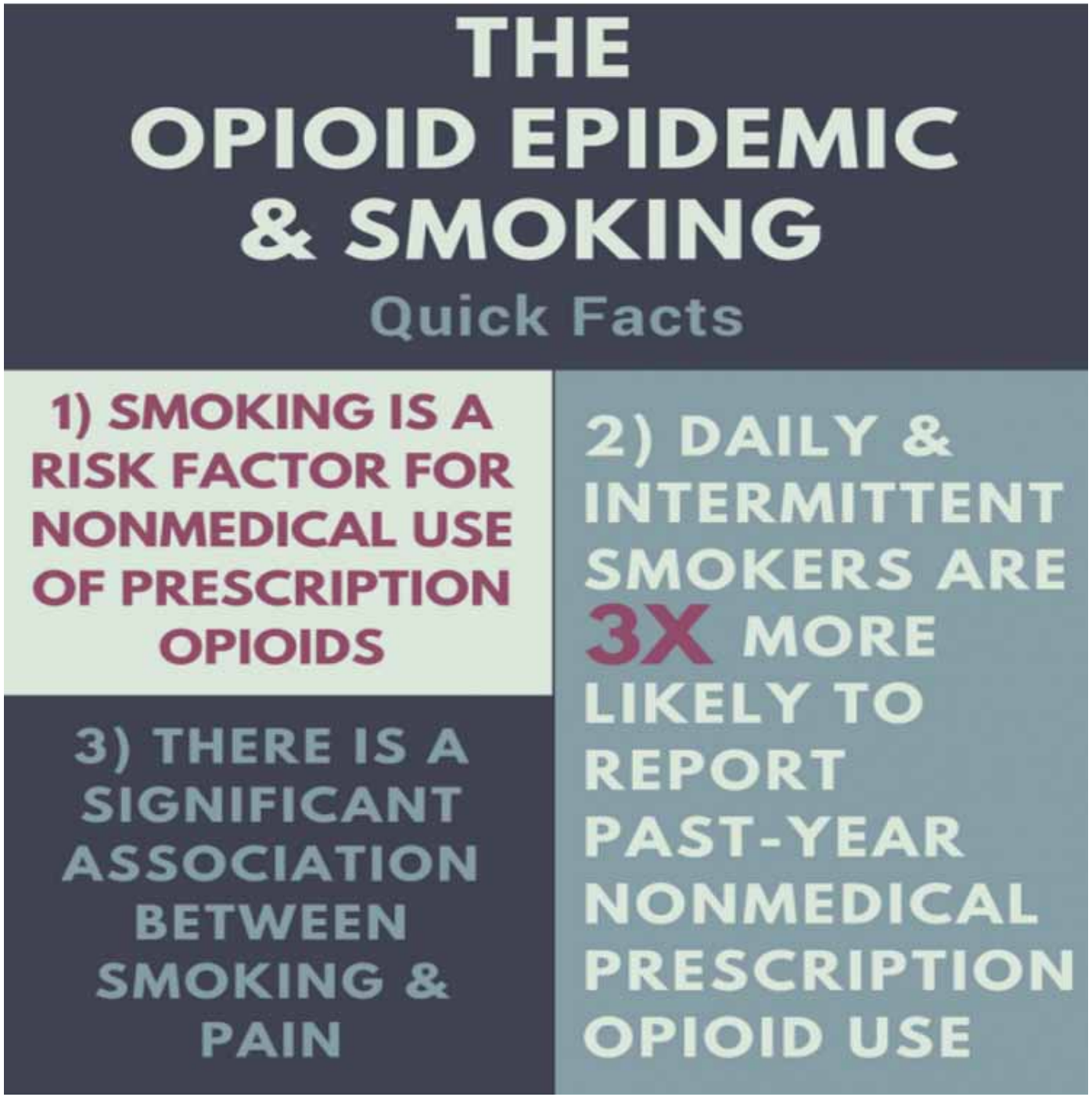
- 70 year old male QAL issues with hip and back pain
- Home dialysis
- Chronic liver disease
- Hx PUD/HTN
- Not a surgical candidate for hip replacement
- Severe osteoarthritis of neck and right hip
- Told not to take more than 1 gram of Tylenol/day
- Told not to take NSAIDs
- Taking 30-40 Norco/month for 10+ years (bedtime to help sleep) - effective
- Cut off, cold turkey, now in pain, difficulty sleeping

# hould we minimize vs. eliminate the use of opioids?

- Intuitively obvious to the most casual observer – need to dramatically minimize opioids.
- Sometimes : Not always as easy as you think
- Lot's of folks out there in true pain

ddiction

- How many individuals (not patients) die per year of tobac use?(>500,000)
- $10 billion on promotion of smoking annually. Of opioid us
- How many individuals die per year of opioid use? 40,000 -
- How many individuals die of "pure" opioids?
- Why do we use tobacco?
- Why do we use opioids in our patients?
- Wouldn't it be nice if there was a mobilization to combat "tobacco crisis"?

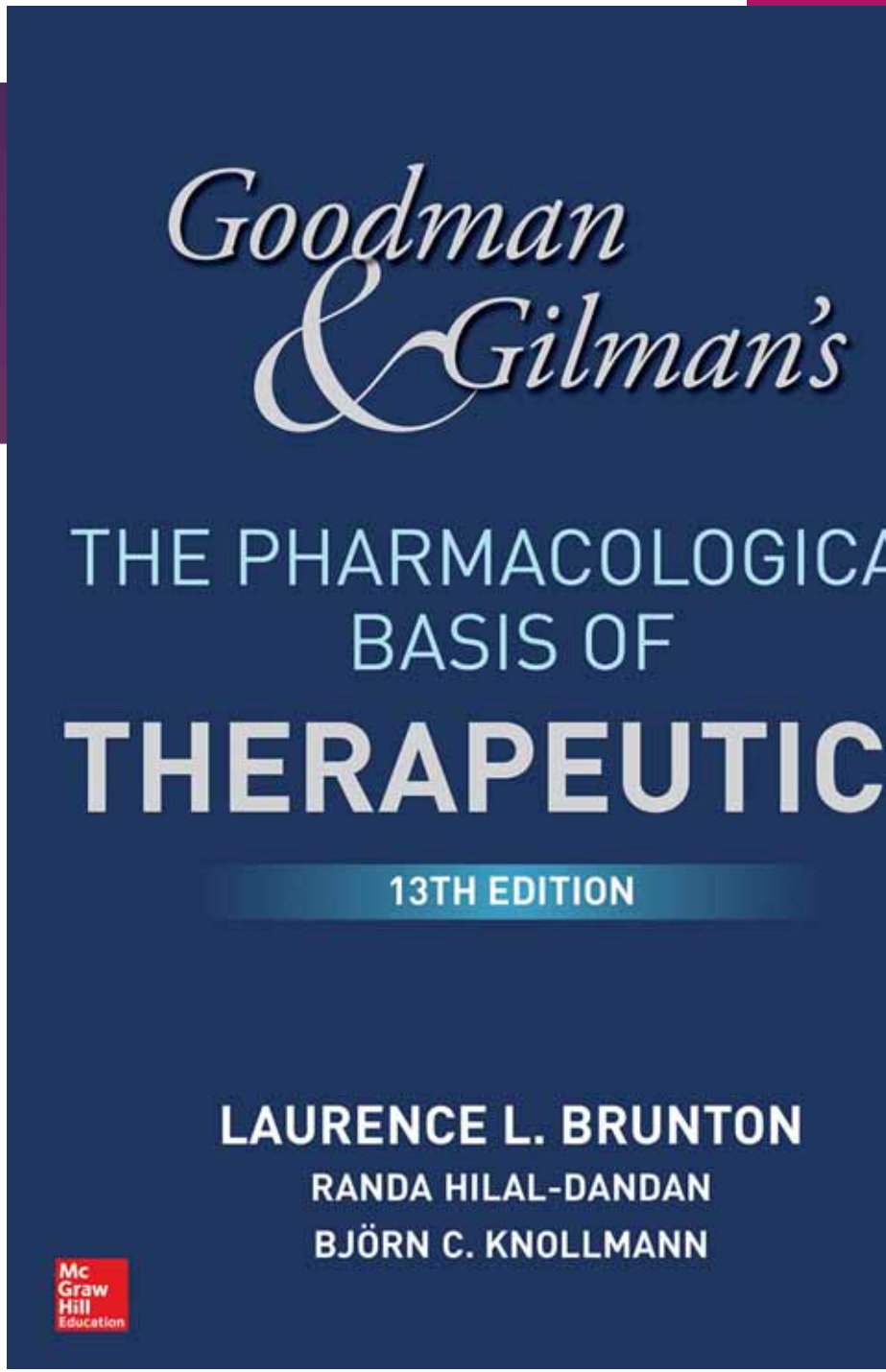

THE
OPIOID EPIDEMIC
& SMOKING
Quick Facts
1) SMOKING IS A RISK FACTOR FOR NONMEDICAL USE OF PRESCRIPTION OPIOIDS
2) DAILY & INTERMITTENT SMOKERS ARE 3X MORE LIKELY TO REPORT PAST-YEAR NONMEDICAL PRESCRIPTION OPIOID USE
3) THERE IS A SIGNIFICANT ASSOCIATION BETWEEN SMOKING & PAIN


85%
4) OF PATIENTS IN TREATMENT FOR OPIOID ADDICTION SMOKE
(HIGHER THAN ALCOHOL USE DISORDER)
5) NICOTINE MAY ENHANCE THE REWARDING PROPERTIES OF OPIOID MEDICATIONS TO THE NEURAL SYSTEM
6) PAIN CAN INCREASE SMOKING AND THE MAINTENANCE OF TOBACCO ADDICTION CREATING A POSITIVE FEEDBACK LOOP
7) ACTION STEP:
ALWAYS TAKE INTO ACCOUNT TOBACCO USE WHEN ASSESSING THE ABUSE POTENTIAL OF PRESCRIBING OPIOIDS
Smoking Cessation Leadership Center

# Since this is an Opioid Conference, let's dissect the opioids

- **Pharmacology (pharmacokinetics/pharmacodynamics)**
- **Statistics**
- **Use in acute and chronic pain**

# The bible, the holy grail of pharmacology



# What is an Opioid?
# What is a Narcotic?

- **Opioid**
  - refers to compounds structurally related to products found in opium, a wor
  derived from *opos*, the Greek word for "juice," natural opiates being derived
  from the resin of the opium poppy, *Papaver somniferum*. Opiates include the
  natural plant alkaloids, such as morphine, codeine, thebaine, and many
  semisynthetic derivatives. An *opioid* is any agent that has the functional and
  pharmacological properties of an opiate.
- **Narcotic**
  - has an imprecise legal connotation
  - derived from the Greek word narko – narcosis
  - over the years became associated with opioids

# Pharmacodynamics

## P-COL ACTION – DRUG AT THE RECEPTOR

# Opioids are part of human evolution: Humans have been using opioids since recorded history

- Endogenous opioids are naturally occurring ligands for opioid receptors found in animals. The term *endorphin* not only is used synonymously with *endogenous opioid peptides* but also refers to a specific endogenous opioid, *β-endorphin*.

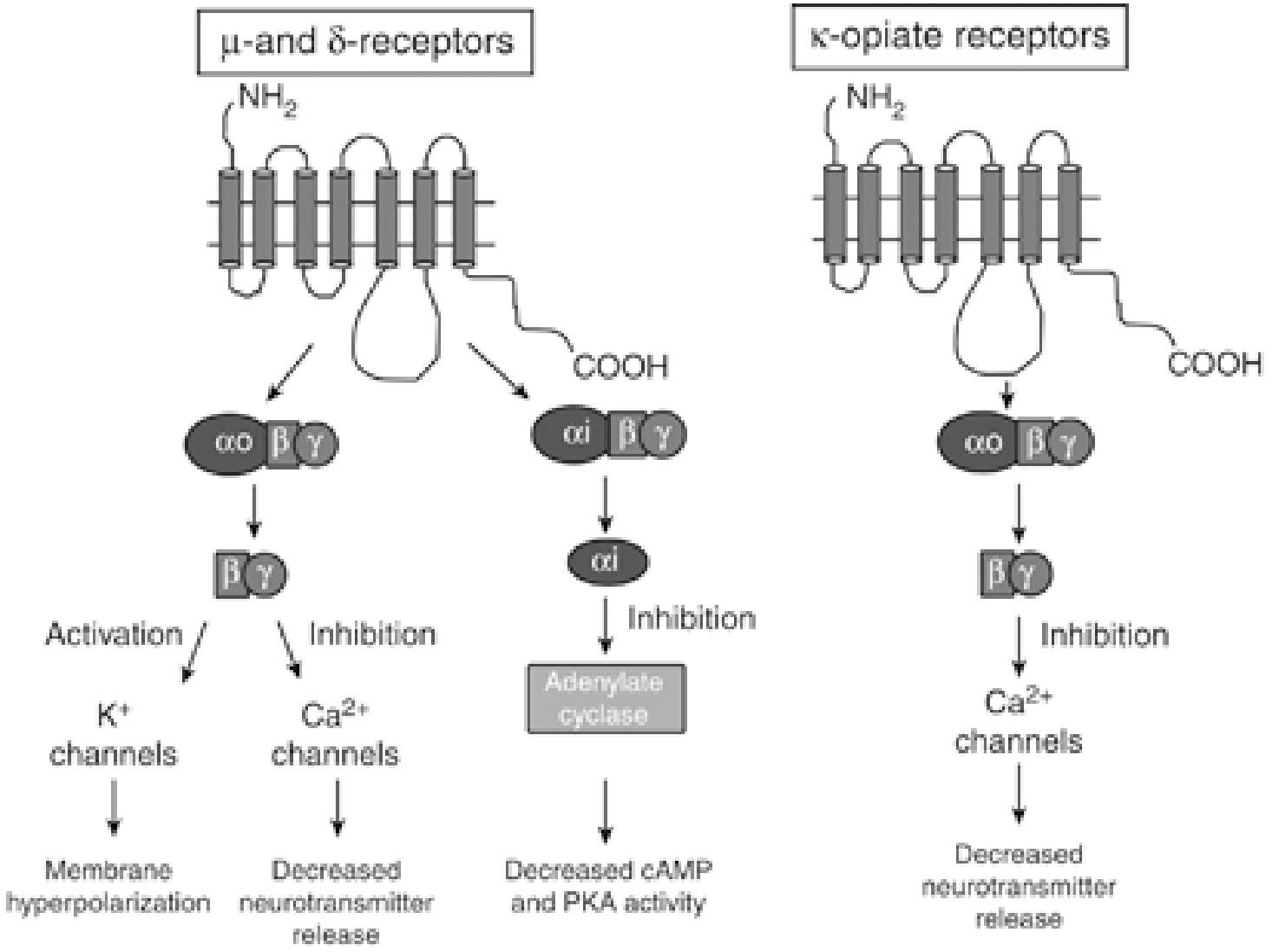
# Opioid Receptors

- The body produces peptides that activate opioid receptors to reduce pain (endogenous opioids)
- 4 identified opioid receptors:
  - μ (mu opioid receptor, MOR)
  - δ (delta opioid receptor, DOR)
  - κ (kappa opioid receptor, KOR)
  - nociceptin/orphanin FQ (NOP, ORL1)

# Opioid Receptors

- Exogenous opioids (i.e. drugs) also activate opioid receptors
- Most opioids modulate pain primarily through actions on MOR
- Activation of MOR is responsible for euphoria and sedation
- Also responsible for unwanted effects like constipation and respiratory depression

# Opioid Receptors



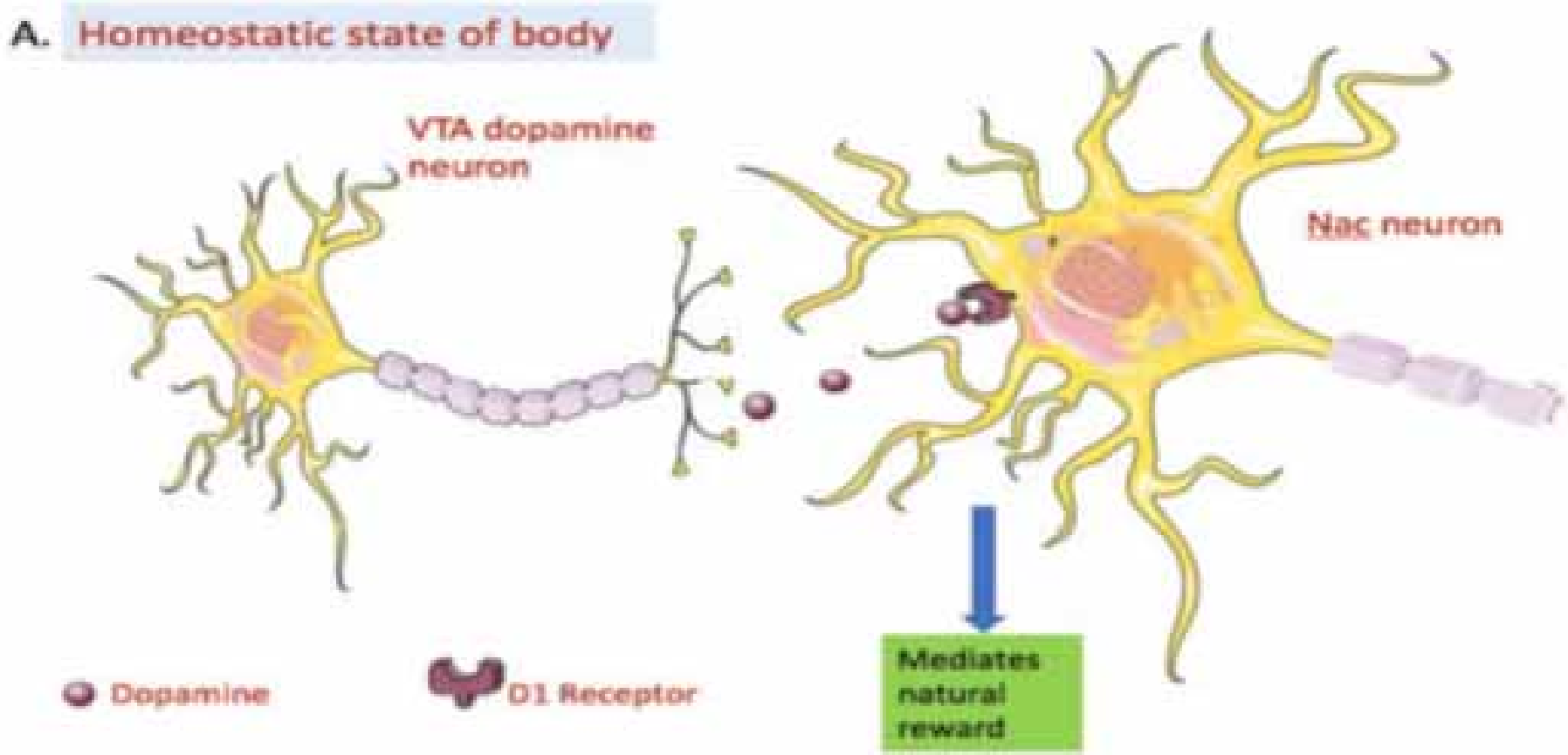
# What's the Deal With Dopamine?

- Dopamine is a neurotransmitter released during pleasurable activities:
  - Eating, gambling, sexual intercourse, drugs
- Activation of MOR causes release of dopamine
- This can cause extreme pleasure and euphoria, which may reinforce patterns of abuse

# Dopamine/Dopamine/Dopamine Buzz - the neurotransmitter of addiction

- Methamphetamine
- Cocaine
- Nicotine
- Yup and now heroin/opioids

# Opioids and Dopamine



# Pharmacology Definitions

- Agonist
- Antagonist
- Partial Agonist
- Half- life
- Steady State
- Time to Steady State

# Pharmacology Definitions

- **Agonist**
  - a chemical that binds to a receptor, and activates the receptor to produce a biological response

# Pharmacology Definitions: Agonists Examples

- Heroin
- Oxycodone
- Fentanyl
- Hydrocodone
- Morphine
- Methadone
- Hydromorphone

# Pharmacology Definitions

- Antagonist
  - a chemical that binds to a receptor and blocks or reduces the effect of an agonist
  - Opioids antagonist examples:
    - naloxone
    - naltrexone

# Pharmacology Definitions

- Partial agonist
  - a chemical that binds to and activates a receptor with reduced efficacy relative to a full agonist. Will behave as an antagonist in the presence of an agonist
  - Opioid partial agonist examples:
    - Buprenorphine
    - Tramadol
    - Pentazocine

# Suboxone

- Partial agonist/antagonist combination:
  - buprenorphine/naloxone
  - buprenorphine partially activates MOR to produce analgesia and prevent withdrawal symptoms
  - Naloxone is poorly absorbed orally, but if injected or snorted it will block the action of buprenorphine and precipitate withdrawal

# Pharmacokinetics

## WHAT THE BODY DOES TO THE DRUG

## ( ELIMINATION/WHERE IT GOES IN THE BODY)

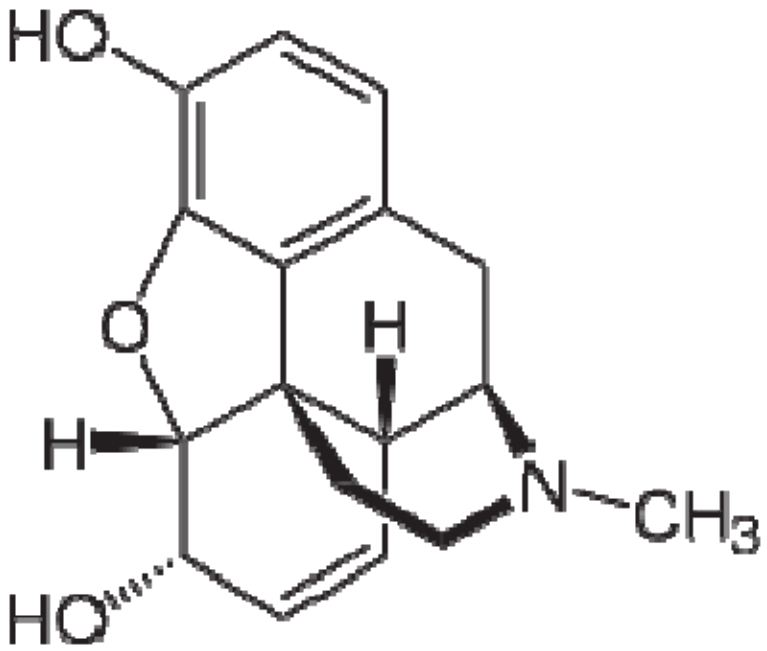
# Pharmacology 101
## Goodman and Gilman

*The abuse liability of a drug is enhanced by rapidity of onset*. (Delivery)

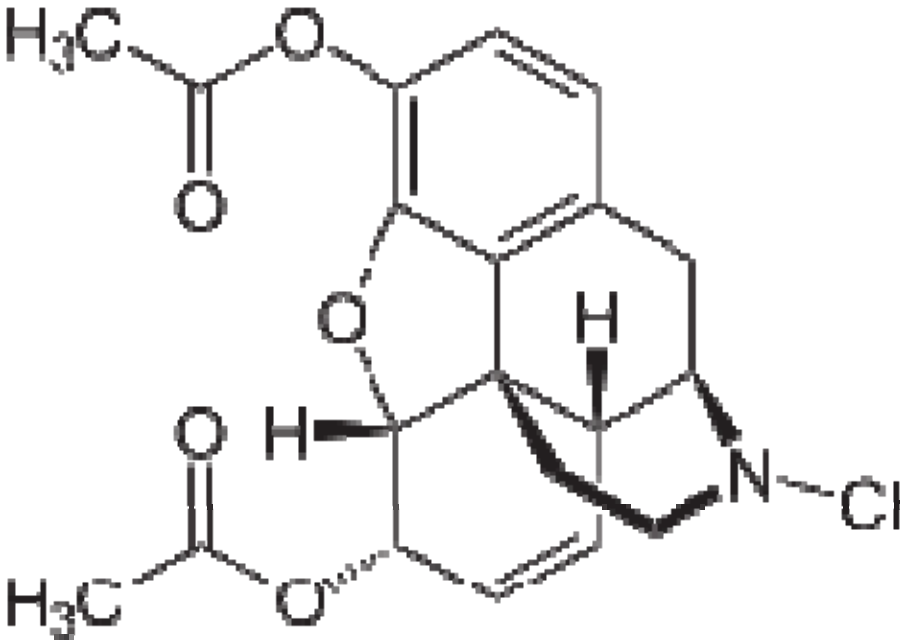
# Fundamentals of CNS Pharmacology (P-dynamics/P-kinetics)

- Dose
- Delivery
- Lipophilicity

# Morphine




# Heroin



# THE CONFUSING TERMINOLOGY OF DRUG USE DISORDERS

- The **terminology** of **drug dependence**, **abuse**, and **addiction** has long elicited **confusion** that stems from the fact that repeated use of certain prescribed medications can produce neuroplastic changes resulting in two distinctly abnormal states. **The first state is *dependence*, or "physical" dependence**, produced when there is **progressive pharmacological adaptation to the drug resulting in tolerance.**

# DSM-5 Definitions

**Substance Use Disorder**

- A cluster of cognitive, behavioral, and physiological symptoms indicating that an individual will continue using a substance despite significant substance-related problems

# Addiction vs. Physical Dependence (career pet peeve)

- What's the difference?
- Hospice nurse?

# THE CONFUSING TERMINOLOGY OF DRUG USE DISORDERS

- ***Addiction*,** the second abnormal state produced by repeated drug use, occurs in only a minority of those who initiate drug use; addiction leads progressively to compulsive, out-of-control drug use.

# Addiction

- The individual becomes drawn into **compulsive repetition of the experience, focusing on the immediate pleasure despite negative long-term consequences and neglect of important social responsibilities.**

# THE CONFUSING TERMINOLOGY OF DRUG USE DISORDERS

- **Tolerance is** a normal reaction that is **often mistaken for a sign of "addiction."** In the tolerant state, repeating the same dose of a drug produces a smaller effect. If the drug is abruptly stopped, a **withdrawal syndrome** ensues in which the adaptive responses are now unopposed by the drug. The appearance of **withdrawal symptoms is the cardinal sign of "physical" dependence**.

# Tolerance -- types
# P-kinetic / P-dynamic

- These issues of tolerance, while straightforward, seem to produce a dangerous misunderstanding among self-medicating opioid users**. Degrees of tolerance depend on the type of opioid, its half-life, and the route of administration.** The typical addicted user is craving the "high" and seems willing to risk overdose by going beyond the safe level.

# Dependence (physical dependence)

**Dependence** represents a state of adaptation manifested by a withdrawal syndrome produced by cessation of drug exposure (e.g., by drug abstinence) or administration of an antagonist (e.g., naloxone). **Dependence** is specific to the drug class and receptor involved. At the organ system leve **opiate withdrawal** is manifested by significant somatomoto and autonomic outflow (reflected by agitation, hyperalgesia, hyperthermia, hypertension, diarrhea, pupillary dilation, and release of virtually all pituitary and adrenomedullary hormones) and by affective symptoms (dysphoria, anxiety, and depression).

# Dependence vs. Addiction

- The **distinction between dependence and addiction is important** because patients with pain sometimes are deprived of adequate opioid medication by their physician simply because they have shown evidence of tolerance or they exhibit withdrawal symptoms if the analgesic medication is stopped or reduced abruptly.

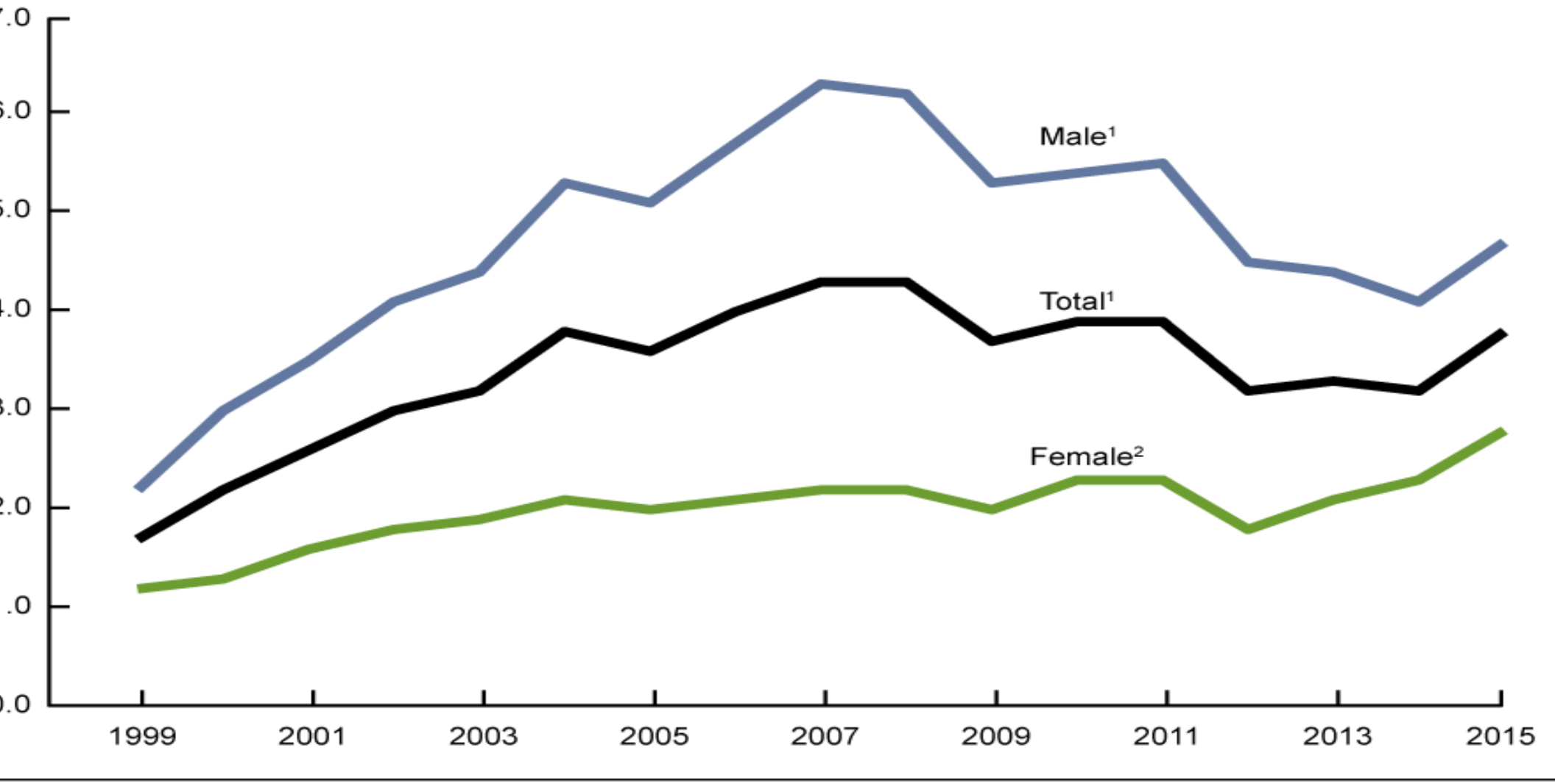
# What are the statistics?

- Statistics are only as good as the data
- The best data can be incorrect or incomplete
- Bad data or incomplete date = NOISE

# Who is dying from opioids? Which agent? Can we generalize?

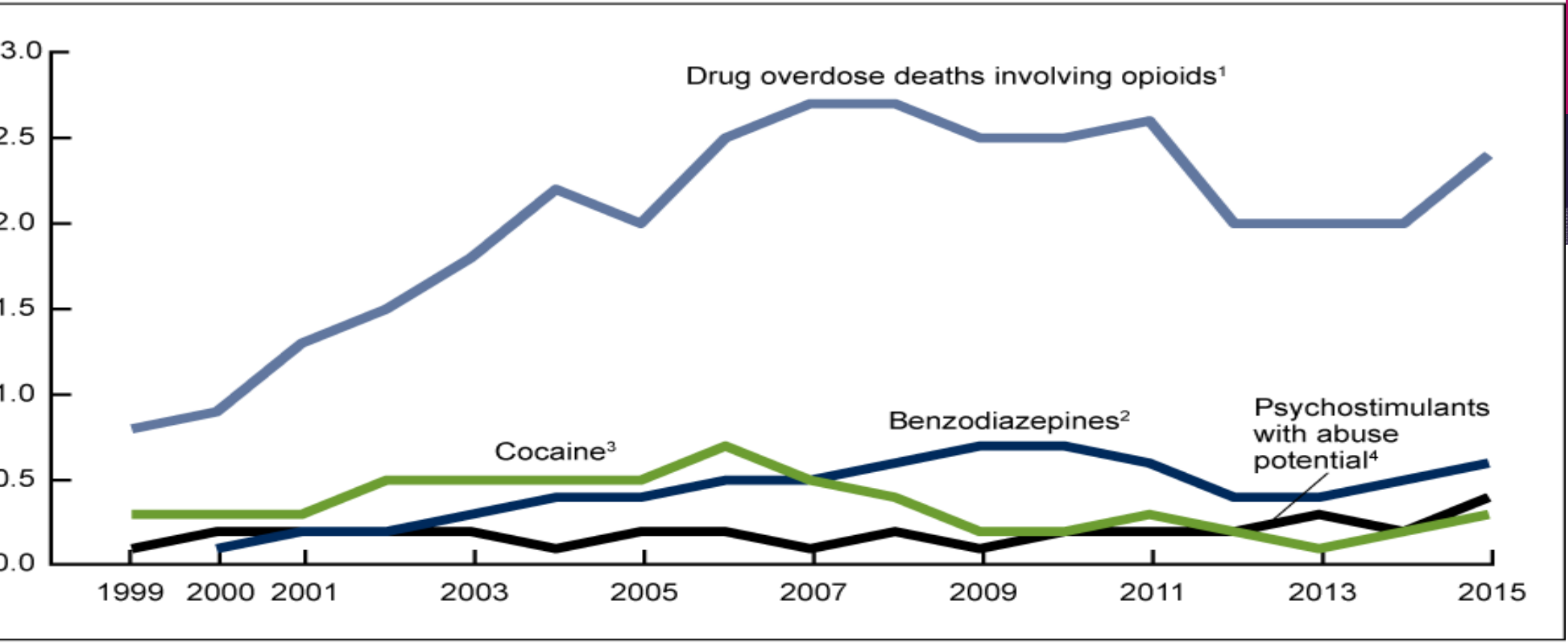
2015, the percentage of drug overdose deaths involving heroin was triple the
centage in 2010.
eaths from drug overdose involving heroin tripled from 8% in 2010 to 25% in
5.
r drug overdose deaths involving natural and semisynthetic opioid analgesics,
ch include drugs such as oxycodone and hydrocodone, the percentage
creased from 29% in 2010 to 24% in 2015.
e percentage of drug overdose deaths involving methadone also decreased,
m 12% in 2010 to 6% in 2015.
r drug overdose deaths involving synthetic opioids other than methadone,
ch include drugs such as fentanyl and tramadol, the percentage increased
m 8% in 2010 to 18% in 2015.
e percentage of drug overdose deaths involving cocaine increased from 11%
2010 to 13% in 2015.
ug overdose deaths involving psychostimulants with abuse potential, which
ude drugs such as methamphetamine, increased from 5% in 2010 to 11% in
5.

. Drug overdose death rates for adolescents aged 15–19, by sex: United States, 1999–2015



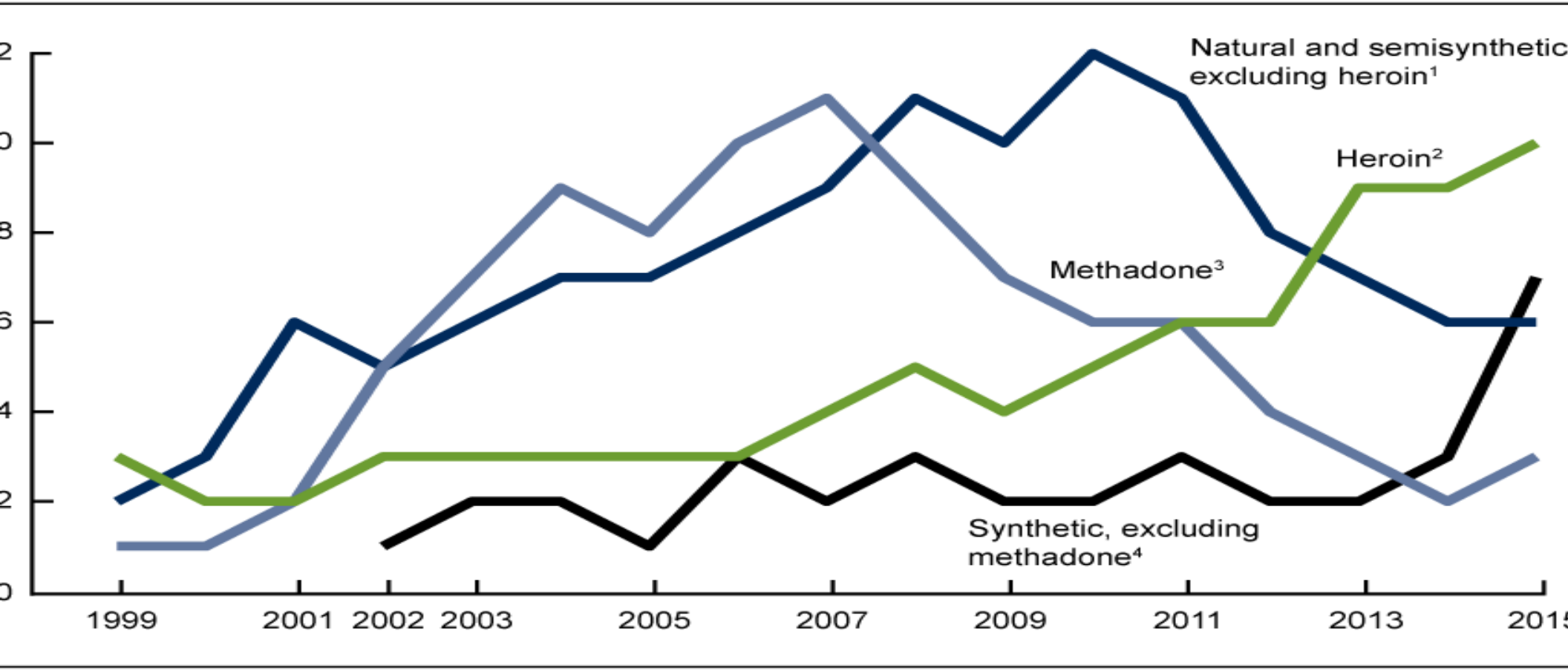

nt increasing trend for 1999–2007; significant decreasing trend for 2007–2014; rate for 2015 significantly higher than for 2014; $p < 0.05$.
nt increasing trend for 1999–2004; stable trend for 2004–2013; significant increasing trend for 2013–2015; $p < 0.05$.
Drug overdose deaths are identified with *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X40–X44,
X85, and Y10–Y14. In 2015, there were 772 total drug overdose deaths: 494 for males and 278 for females. Access data table for Figure 1 at:
w.cdc.gov/nchs/data/databriefs/db282_table.pdf#1.
: NCHS, National Vital Statistics System, Mortality.

3. Drug overdose death rates for adolescents aged 15–19, by type of drug involved: United States, 1999–2015




nt increasing trend for 1999–2007; fluctuations, but significant decreasing trend for 2007–2014; rate for 2015 significantly higher than for 2014; $p < 0.05$.
nt increasing trend for 1999–2009; significant decreasing trend for 2009–2012; significant increasing trend for 2012–2015; $p < 0.05$; too few cases in
ompute a reliable rate.
nt increasing trend for 1999–2006; significant decreasing trend for 2006–2009; stable trend for 2009–2013; rate for 2015 significantly higher than for
0.05.
nt increasing trend for 1999–2015; $p < 0.01$.
Drug overdose deaths are identified with *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X40–X44, X60–X64,
Y10–Y14. Drug overdose deaths involving opioid analgesics include drug poisoning deaths with multiple cause-of-death codes, including T40.0, T40.1,
0.3, T40.4, or T40.6 (2015 $N = 506$). Drug overdose deaths involving cocaine include code T40.5 (2015 $N = 70$); benzodiazepines include code T42.4
126); and psychostimulants with abuse potential include code T43.6 (2015 $N = 82$). Deaths might involve more than one drug, so categories are not
Trends may have been affected by improvement in the reporting of specific drugs for drug overdose deaths during the reporting period; see Data source
ods. Access data table for Figure 3 at: https://www.cdc.gov/nchs/data/databriefs/db282_table.pdf#3.
: NCHS, National Vital Statistics System, Mortality.

Drug overdose death rates for adolescents aged 15–19, by type of opioid drug involved: United States, 15




ncreasing trend for 1999–2010; significant decreasing trend for 2010–2015; $p < 0.05$.
ncreasing trend for 1999–2015; $p < 0.0001$.
ncreasing trend for 1999–2007; significant decreasing trend for 2007–2014; rate for 2015 significantly higher than for 2014; $p < 0.05$.
ncreasing trend for 2002–2015; $p < 0.05$; too few cases in 1999–2001 to compute a reliable rate.
g overdose deaths are identified with *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X40–X44, X60–X
0–Y14. Drug overdose deaths involving heroin include code T40.1 (2015 $N = 208$); natural and semisynthetic opioids, excluding heroin include c
$N = 136$); methadone include code T40.3 (2015 $N = 53$); and synthetic opioids, excluding methadone include code T40.4 (2015 $N = 143$). Deaths
e more than one drug, so categories are not exclusive. Trends may have been affected by improvement in the reporting of specific drugs for drug
aths during the reporting period; see Data source and methods. Access data table for Figure 4 at:
cdc.gov/nchs/data/databriefs/db282_table.pdf#4.
CHS, National Vital Statistics System, Mortality.

Percentage of deaths with concomitant drug involvement and average number of concomitant drugs for drug
e deaths involving the top 10 drugs: United States, 2014

| Referent drug | Number of drug overdose deaths involving referent drug | Percentage of drug overdose deaths involving referent drug and concomitant drugs | Averag concomitant |
|---|---|---|---|
| Opioids | | | |
| tanyl | 4,200 | 63.9 | |
| oin | 10,863 | 51.6 | |
| drocodone | 3,274 | 80.4 | |
| thadone | 3,495 | 63.5 | |
| phine | 4,022 | 72.2 | |
| ycodone | 5,417 | 76.2 | |
| Benzodiazepines | | | |
| prazolam | 4,217 | 95.5 | |
| azepam | 1,729 | 96.7 | |
| Stimulants | | | |
| ocaine | 5,856 | 66.1 | |
| ethamphetamine | 3,728 | 45.0 | |

st frequent concomitant drugs for drug overdose deaths involving the top 10 drugs: United States, 2014

| drug | Number of deaths involving referent drug | Most frequent concomitant drug | | | Second most frequent concomitant drug | | |
|---|---|---|---|---|---|---|---|
| | | Concomitant drug | Deaths involving both drugs | | Concomitant drug | Deaths involving both drugs | |
| | | | Number | Percentage[1] | | Number | P |
| ds | | | | | | | |
| ..... | 4,200 | Heroin | 954 | 22.7 | Cocaine | 614 | |
| ..... | 10,863 | Cocaine | 2,181 | 20.0 | Fentanyl | 954 | |
| ..... | 3,274 | Alprazolam | 836 | 25.5 | Oxycodone | 520 | |
| ..... | 3,495 | Alprazolam | 634 | 18.1 | Oxycodone | 352 | |
| ..... | 4,022 | Oxycodone | 572 | 14.2 | Heroin | 518 | |
| ..... | 5,417 | Alprazolam | 1,252 | 23.1 | Morphine | 572 | |
| epines | | | | | | | |
| ..... | 4,217 | Oxycodone | 1,252 | 29.6 | Heroin | 839 | |
| ..... | 1,729 | Oxycodone | 566 | 32.7 | Hydrocodone | 324 | |
| nts | | | | | | | |
| ..... | 5,856 | Heroin | 2,181 | 37.2 | Fentanyl | 614 | |
| e..... | 3,728 | Heroin | 734 | 19.6 | Morphine | 300 | |

# Crude and age-adjusted rates for drug overdose deaths involving selected opioids: United States, 2010–2014

| Opioid | Crude death rate | | | | | Age-adjusted death rate | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2010 | 2011 | 2012 | 2013 | 2014 | 2010 | 2011 | 2012 | 2013 |
| . . . . . | 0.5 | 0.5 | 0.5 | 0.6 | 1.3 | 0.5 | 0.5 | 0.5 | 0.6 |
| . . . . . | 1.0 | 1.5 | 2.0 | 2.7 | 3.4 | 1.0 | 1.5 | 2.0 | 2.7 |
| one . . . . . | 0.9 | 1.0 | 1.0 | 1.0 | 1.0 | 0.9 | 1.0 | 0.9 | 1.0 |
| ne . . . . . | 1.4 | 1.5 | 1.3 | 1.2 | 1.1 | 1.4 | 1.5 | 1.3 | 1.2 |
| . . . . . | 1.0 | 1.1 | 1.1 | 1.2 | 1.3 | 0.9 | 1.0 | 1.1 | 1.2 |
| ne . . . . . | 1.7 | 1.8 | 1.6 | 1.6 | 1.7 | 1.7 | 1.8 | 1.7 | 1.6 |

g-poisoning deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the
ving more than one drug (e.g., a death involving both heroin and cocaine) are counted in both rates. Caution should be used when comparing numbers across years
ne specific drug in the literal text improved, from 67% of drug overdose deaths in 2010 to 78% of drug overdose deaths in 2014.

CHS, National Vital Statistics System, Mortality files linked with death certificate literal text.

## Table E. Percentage of deaths with concomitant alcohol involvement for drug overdose deaths involving the top 10 drugs States, 2014

| Referent drug | Number of drug overdose deaths involving referent drug | Drug overdose deaths with concomitant alcohol involvement | |
|---|---|---|---|
| | | Number | Percentage |
| **Opioids** | | | |
| Fentanyl | 4,200 | 513 | 12.2 |
| Heroin | 10,863 | 2,252 | 20.7 |
| Hydrocodone | 3,274 | 562 | 17.2 |
| Methadone | 3,495 | 342 | 9.8 |
| Morphine | 4,022 | 522 | 13.0 |
| Oxycodone | 5,417 | 905 | 16.7 |
| **Benzodiazepines** | | | |
| Alprazolam | 4,217 | 652 | 15.5 |
| Diazepam | 1,729 | 374 | 21.6 |
| **Stimulants** | | | |
| Cocaine | 5,856 | 1,210 | 20.7 |
| Methamphetamine | 3,728 | 257 | 6.9 |

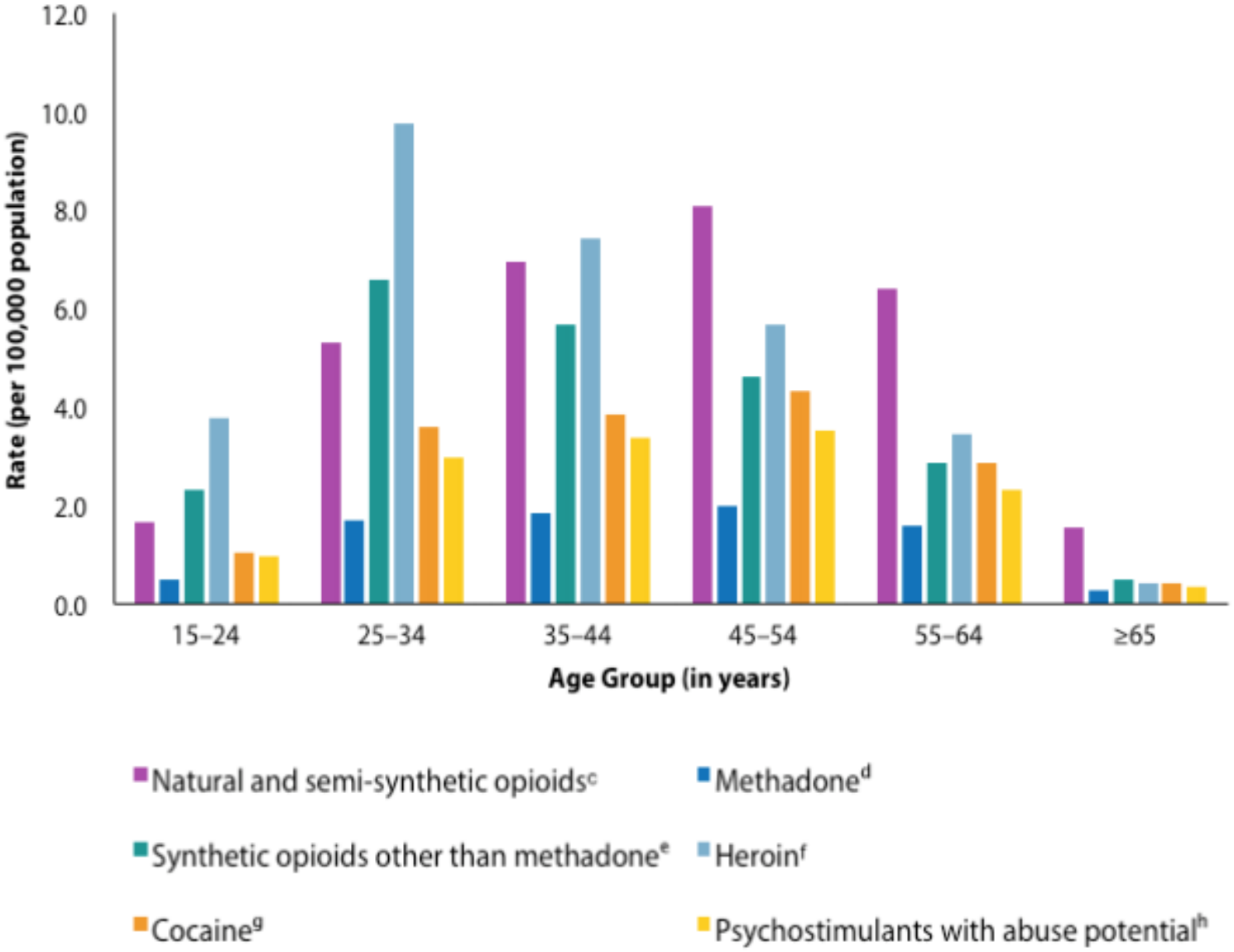
NOTES: Drug overdose deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the (i.e., the one listed). Alcohol involvement included mentions of ethanol, isopropyl alcohol, and a nonspecific reference to alcohol.

SOURCE: NCHS, National Vital Statistics System, Mortality files linked with death certificate literal text.

# Age adjusted death rate: definition

- A "standard" population distribution is used to **adjust death** and hospitalization **rates**. The **age-adjusted rates** are **rates** that would have existed if the population under study had the same **age** distribution as the "standard" population. Therefore, they are summary measures **adjusted** for differences in **age** distributions.

# Age-adjusted rates of drug overdose deaths, by drug or drug class and age category – U.S. 2015




CDC Annual Surveilla
of Drug-Related Risks
Outcomes - 2017

# ates* of self-reported prevalence of illicit and prescription drug suse in past month – U.S. 2015

| group ars) | All illicit/prescription drug misuse | Prescription pain relievers | Heroin |
|---|---|---|---|
| 12-17 | 8.8 | 1.1 | 0 |
| 18-25 | 22.3 | 2.4 | 0.3 |
| 26-34 | 15.4 | 2.1 | 0.3 |
| 35-39 | 10.6 | 1.5 | 0.2 |
| 40-44 | 8.5 | 1.7 | 0.0 |
| 45-49 | 8.6 | 1.9 | NA |
| 50-54 | 8.3 | 1.2 | NA |
| 55-59 | 8.0 | 1.1 | NA |
| 60-64 | 6.2 | 1.0 | NA |
| ≥65 | 1.9 | 0.3 | NA |

* # per 100 persons

CDC Annual Surveillance Report of Drug-Related Risks and Outcomes

Age-adjusted rates* of opioid overdose deaths by age group – U.S. **2014**

| Group s) | Any opioid | Natural and semi-synthetic opioids | Methadone | Synthetic opioids other than methadone | Prescription opioids | Heroin |
|---|---|---|---|---|---|---|
| | 0.1 | 0.1 | NA | NA | 0.1 | NA |
| | 2.0 | 0.6 | 0.2 | 0.3 | 0.8 | 0.9 |
| | 10.0 | 2.6 | 0.8 | 1.9 | 3.3 | 5.6 |
| | 16.2 | 4.9 | 1.8 | 3.4 | 6.4 | 8.0 |
| | 15.6 | 6.5 | 1.9 | 3.1 | 8.0 | 5.9 |
| | 16.1 | 8.0 | 2.0 | 3.1 | 9.5 | 4.7 |
| | 11.1 | 6.1 | 1.6 | 1.9 | 7.3 | 2.7 |
| | 2.3 | 1.5 | 0.2 | 0.4 | 1.7 | 0.3 |

* # per 100,000 persons

CDC Annual Surveillance Report of Drug-Related Risks and Outco

Age-adjusted rates* of opioid overdose deaths by age group – U.S. **2015**

| Group s) | Any opioid | Natural and semi-synthetic opioids | Methadone | Synthetic opioids other than methadone | Prescription opioids | Heroin |
|---|---|---|---|---|---|---|
| | 0.1 | 0.1 | NA | NA | 0.1 | NA |
| | 2.4 | 0.6 | 0.3 | 0.7 | 0.9 | 1.0 |
| | 11.3 | 2.5 | 0.7 | 3.8 | 3.1 | 6.3 |
| | 19.4 | 5.3 | 1.7 | 6.6 | 6.6 | 9.7 |
| | 18.4 | 6.9 | 1.8 | 5.6 | 8.4 | 7.4 |
| | 17.6 | 8.1 | 2.0 | 4.6 | 9.5 | 5.6 |
| | 12.4 | 6.4 | 1.6 | 2.9 | 7.6 | 3.4 |
| | 2.5 | 1.5 | 0.3 | 0.5 | 1.7 | 0.4 |

* # per 100,000 persons

CDC Annual Surveillance Report of Drug-Related Risks and Outco

Don’t forget grandma’s PAIN

# Science vs. Opinion

# Goals

- Improve QOL via minimizing pain
- Minimize opioids
- Minimize adverse effects /death
- Maximize multi-modal analgesia
- To honor our clinical and ethical responsibilities  to the patient by minimizing their pain.
- Not to let your treatment of pain in an individual patient be affected by “drug seekers”
- Discuss the misinterpretation of CDC guidelines on prescribing opioids

# What's going to work to treat grandma's osteoarthritis pain, and what's going to kill grandma?

- Acetaminophen
- NSAID's (no ASA)
- Opioid's
- Topical
- Joint Injections

# What makes a patient non-functional?

a) Significant pain - story
b) Inappropriate dosed opioids
c) Appropriate dosed opioids

# OPINION

- Daniel Alford, a substance use disorder specialist at the Boston University School of Medicine and director of the school's Safe and Competent Opioid Prescribing Education program, **criticizes "blanket regulatory changes that treat everybody the same. Opioids can harm some patients, but they absolutely help some patients"**

# Pain and Suicide Risk

- The most common conditions associated with chronic pain were back pain, cancer, and arthritis. In a random sample of cases with chronic pain in which suicide notes were available, two-thirds of the notes mentioned pain as a contributing factor to the suicide.
- The researchers write, "Providers should be alert to and possibly screen for depression and suicidal behaviors among patients with chronic pain." An editorialist adds, "Suicide prevention involves making effective pain interventions more available, which extends beyond providing access to opioids and should also include, if appropriate, other medications, interventional programs, physical therapy, and psychosocial approaches

# Chronic Pain Tied to Increased Suicide Risk Annals of Internal Medicine

- **Chronic Pain Among Suicide Decedents, 2003 to 2014: Findings From the National Violent Death Reporting System**
- *Emiko Petrosky, MD, MPH; Rafael Harpaz, MD, MPH; Katherine A. Fowler, PhD; Michele K. Bohm, MPH; Charles G. Helmick, MD; Keming Yuan, MS; Carter J. Betz, MS*

# Older Adult Experience with Opioids

- 29% filled an opioid Rx in the last two years
- Reason for pain Rx was arthritis, back, surgery, injury
- Physicians and pharmacists only gave information about Rx concerning how often to take it (90%). Everything else 50-50
- ¾ tried to take medicine less frequently than prescribed. 5% more frequently
- 50% had meds left over
- 86% kept meds in case they had pain again. ($$)

# Opioids in the Elderly: Pharmacotherapeutics 101

- It's about the dose, the dose, the dose ( steady state vs. time to peak)
- Avoid polypharmacy
- What's going to kill grandma??? No brainer.
- NSAIDs
- ASA (low dose bleeding risk)
- CDC – cognitive, constipation

# Interpretation of recommendation categories and evidence type

## Recommendation Categories CDC 2016

- **Category A recommendation**: Applies to all persons; most patients should receive the recommended course of action.
- **Category B recommendation**: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

## Interpretation of recommendation categories and evidence type

## Recommendation Categories

- **Type 1 evidence**: Randomized clinical trials or overwhelming evidence from observational studies.
- **Type 2 evidence**: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.
- **Type 3 evidence**: Observational studies or randomized clinical trials with notable limitations.
- **Type 4 evidence**: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

# The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use

# Determining When to Initiate or Continue Opioids for Chronic Pain - CDC

**Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain**. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If **opioids are used, they should be combined with nonpharmacologic therapy and nonopioid** pharmacologic therapy, as appropriate. (A-3)

Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. **Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety**. (A-4)

Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy. (A-3)

# Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation - CDC

- When starting opioid therapy for chronic pain, clinicians **should prescribe immediate-release opioids** instead of extended-release/long-acting (ER/LA) opioids. (A-4)
- When opioids are started, clinicians should **prescribe the lowest effective dosage**. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to =50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to =90 MME/day or carefully justify a decision to titrate dosage to =90 MME/day. (A-3)
- 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**. (A-4)
- Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids. (A-4)

# Assessing Risk and Addressing Harms of Opioid Use - CDC

- Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone whe factors that increase risk for opioid overdose, such as history of overdose, history of substa use disorder, higher opioid dosages (=50 MME/day), or concurrent benzodiazepine use, a present. (A-4)
- Clinicians should review the patient's history of controlled substance prescriptions using st prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pa and periodically during opioid therapy for chronic pain, ranging from every prescription t every 3 months. (A-4)
- When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for presc medications as well as other controlled prescription drugs and illicit drugs. (B-4)
- Clinicians should **avoid prescribing opioid pain medication and benzodiazepines concurr whenever possible. (A-3)**
- Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) f patients with opioid use disorder. (A-2)

# ALTERNATIVES TO OPIOIDS?

# What's the down side to NSAID's?

- Increased morbidity and mortality with GI bleeding
- DDI with anti-platelets, ASA, anti-coagulants
- Increased mortality and morbidity with CV disease (HF, Stroke, MI,)
- Renal disease, hepatic disease
- Increased intra-cranial bleeds with anti-depressants

# What's the down side of acetaminophen?

- Often first-line, but often doesn't work
- Good for fever, headaches, and multimodal uses
- Dosing issues with liver/ETOH
- Chronic high dose use is not as "clean" as you think

## How effective are different non-invasive interventions for non-radicular low back pain, radicular low back pain, or spinal stenosis, and under what circumstances?

- Acetaminophen:
  - Non-inferior to placebo
  - Inferior to non-inferior to NSAIDS
  - Lower risk than NSAIDS
    - ✓ Increased liver toxicity
    - ✓ May increase HTN, CV events, kidney toxicity

## How effective are different non-invasive interventions for non-radicular low back pain, radicular low back pain, or spinal stenosis, and under what circumstances?

- COX-2 selective NSAIDs
  - Superior to acetaminophen
  - GI bleeds < non-selective
  - Equivalent CV and renal risk to non-selective agents
    - ✓naproxen may be preferred

**Table 2. Pharmacologic recommendations for the initial management of hand OA***

| |
|---|
| We conditionally recommend that health professionals should use one or more of the following: |
| Topical capsaicin |
| Topical NSAIDs, including trolamine salicylate |
| Oral NSAIDs, including COX-2 selective inhibitors |
| Tramadol |
| We conditionally recommend that health professionals should not use the following: |
| Intraarticular therapies |
| Opioid analgesics |
| We conditionally recommend that persons age ≥75 years should use topical rather than oral NSAIDs. In persons age <75 years, the TEP expressed no preference for using topical rather than oral NSAIDs. |

* No strong recommendations were made for the pharmacologic management of hand osteoarthritis (OA). For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs = nonsteroidal antiinflammatory drugs; COX-2 = cyclooxygenase 2; TEP = Technical Expert Panel.

**Table 4. Pharmacologic recommendations for the initial management of knee OA***

| |
|---|
| We conditionally recommend that patients with knee OA should use one of the following: |
| Acetaminophen |
| Oral NSAIDs |
| Topical NSAIDs |
| Tramadol |
| Intraarticular corticosteroid injections |
| We conditionally recommend that patients with knee OA should not use the following: |
| Chondroitin sulfate |
| Glucosamine |
| Topical capsaicin |
| We have no recommendations regarding the use of intraarticular hyaluronates, duloxetine, and opioid analgesics |

* No strong recommendations were made for the initial pharmacologic management of knee osteoarthritis (OA). For patients who have an inadequate response to initial pharmacologic management, please see the Results for alternative strategies. NSAIDs = nonsteroidal antiinflammatory drugs.

# Conclusions

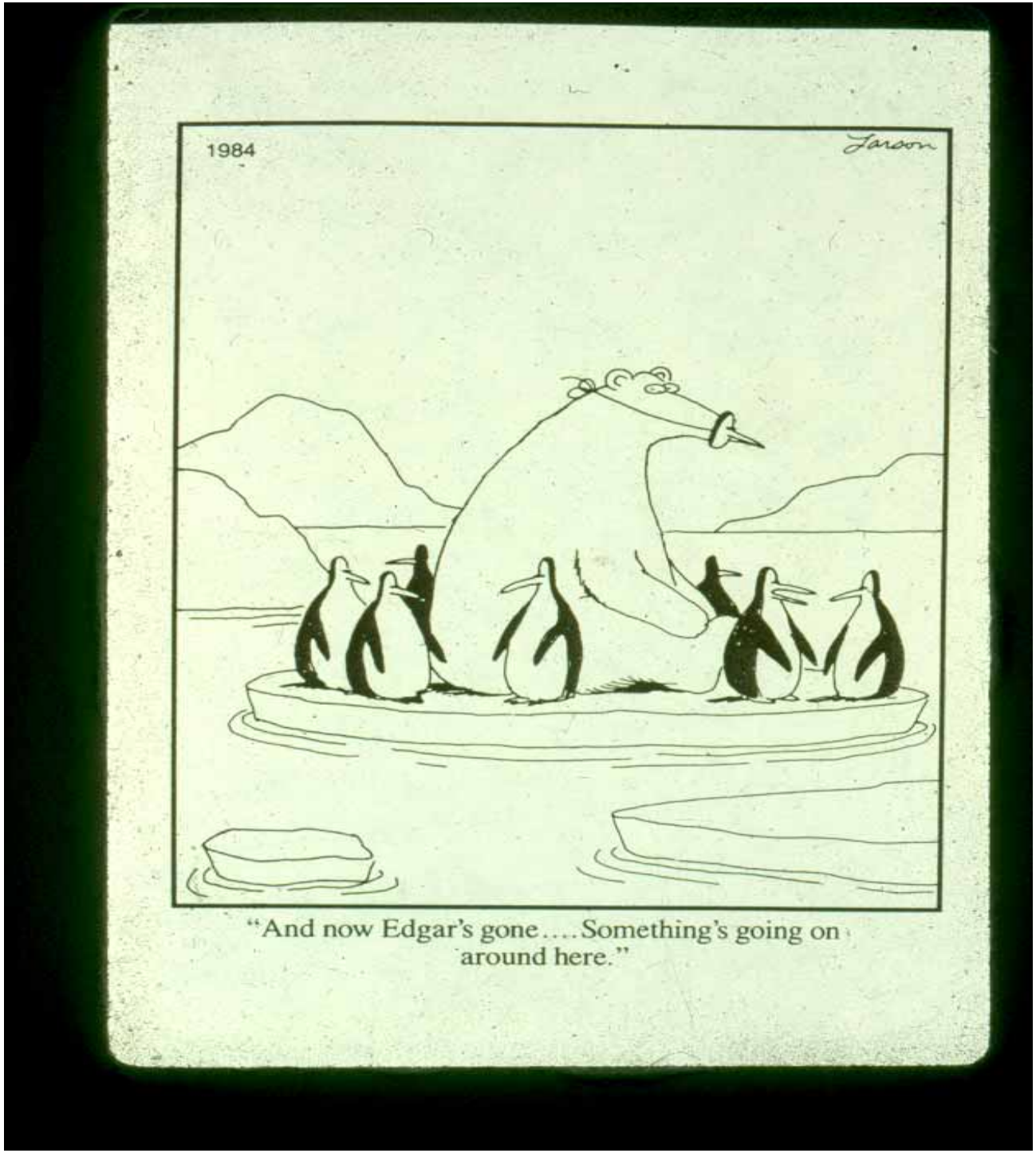
- Don't forget the individual patient – ethical/moral responsibility to treat pain
- Multi-modal philosophy of pain control
- Minimize opioids when possible, both in acute and chronic pain
- Current policies on opioid use have been detrimental to many patients with pain, including grandma
- Long-term opioids are effective pain relievers for many patients… but certainly not all
- We must deal with the fact that current policies leave many of our chronic pain patients in significant pain.

# Conclusion

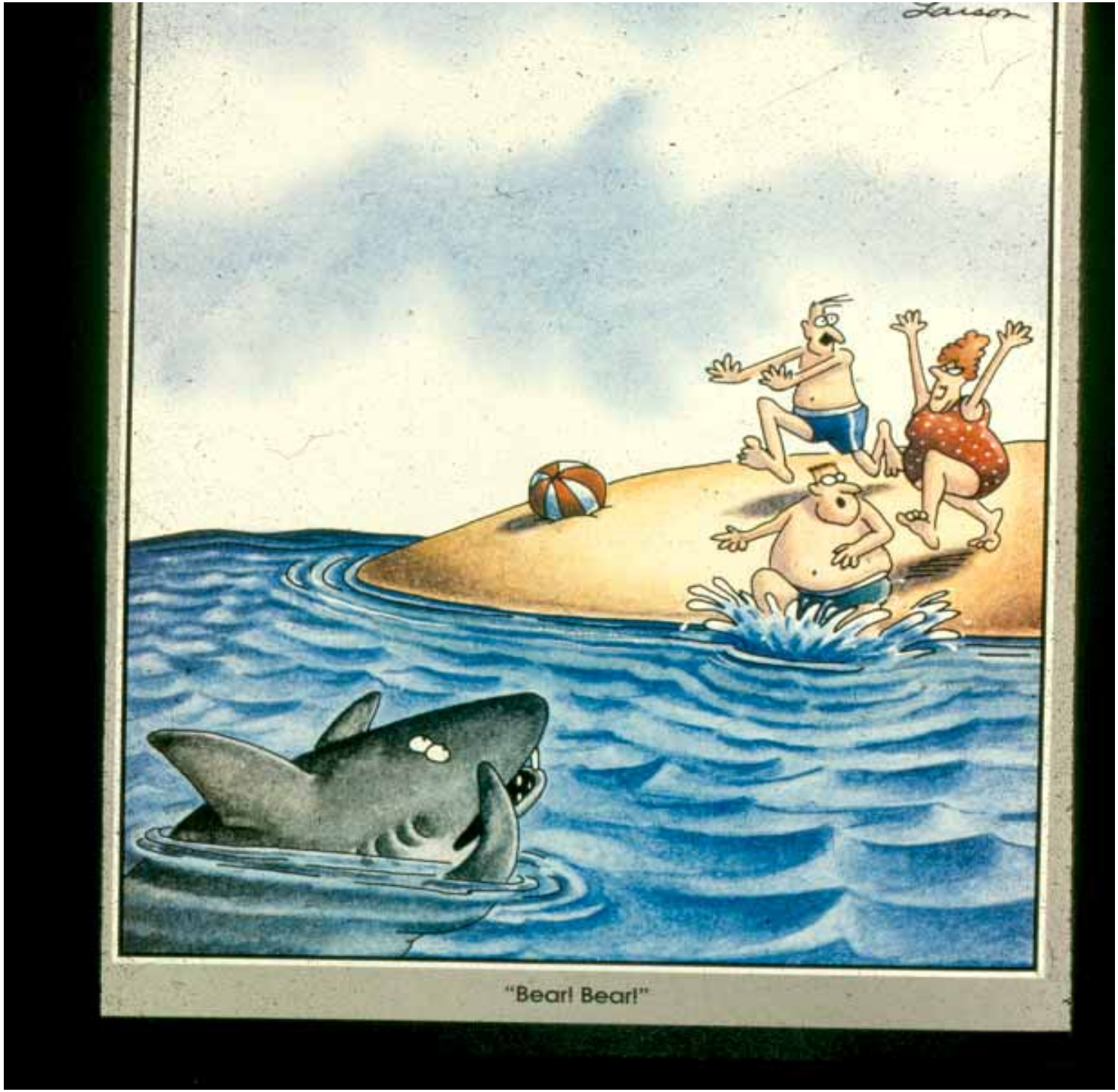
- The CDC's guideline on prescribing opioids has been misconstrued as a blunt mandate rather than a policy to help guide the safe use of opioids
- Stefan G. Kertesz, MD, and Adam J. Gordon, MD, have criticized new policies that they say have "weaponized" the CDC's guidelines and come primarily from individuals and agencies ill-equipped to objectively and responsibly evaluate this complex issue. As a result, they warn that they have, "incentivized involuntary termination of opioids in otherwise stable patients, with resultant reports of harm."

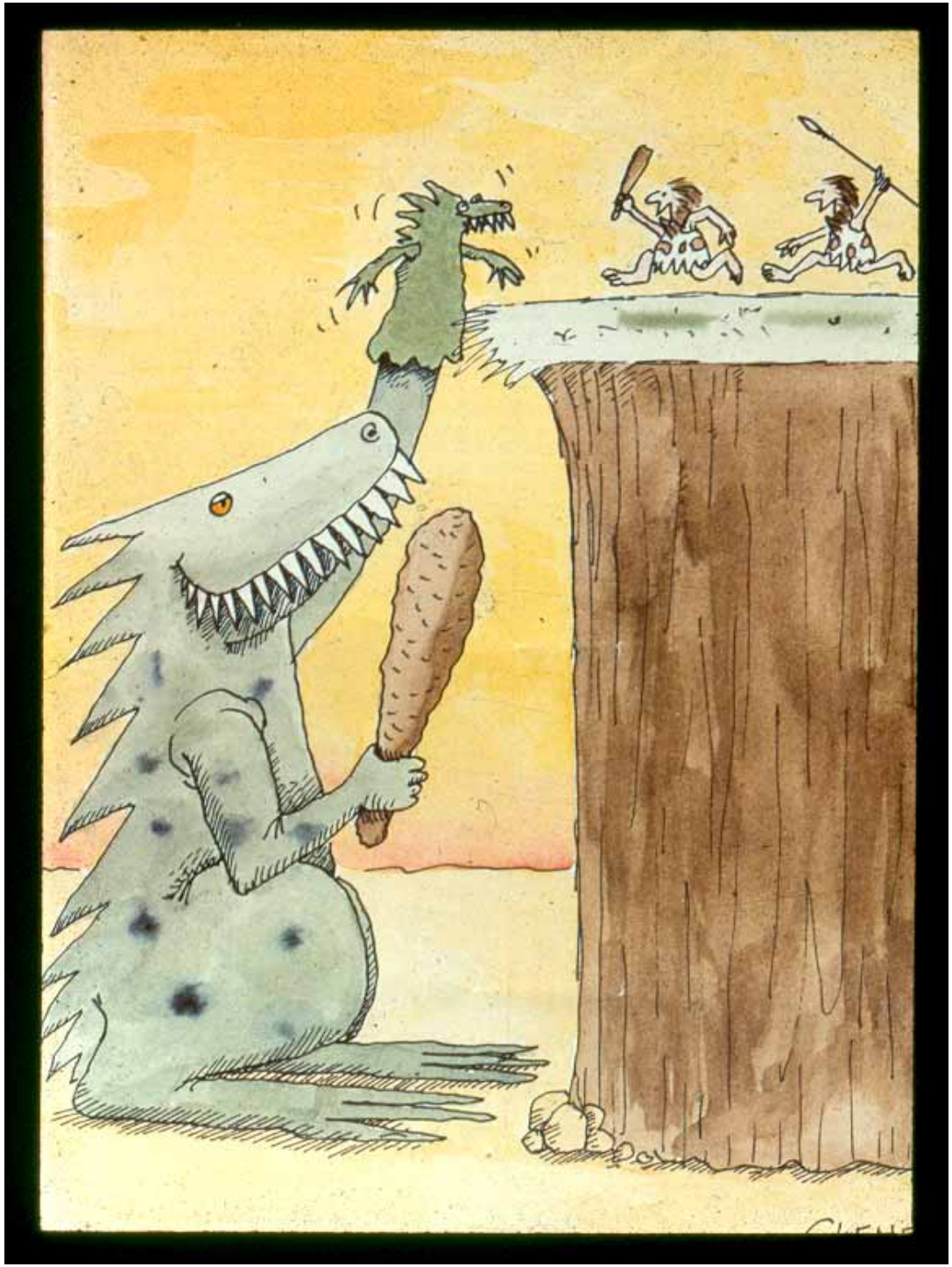
# Conclusion

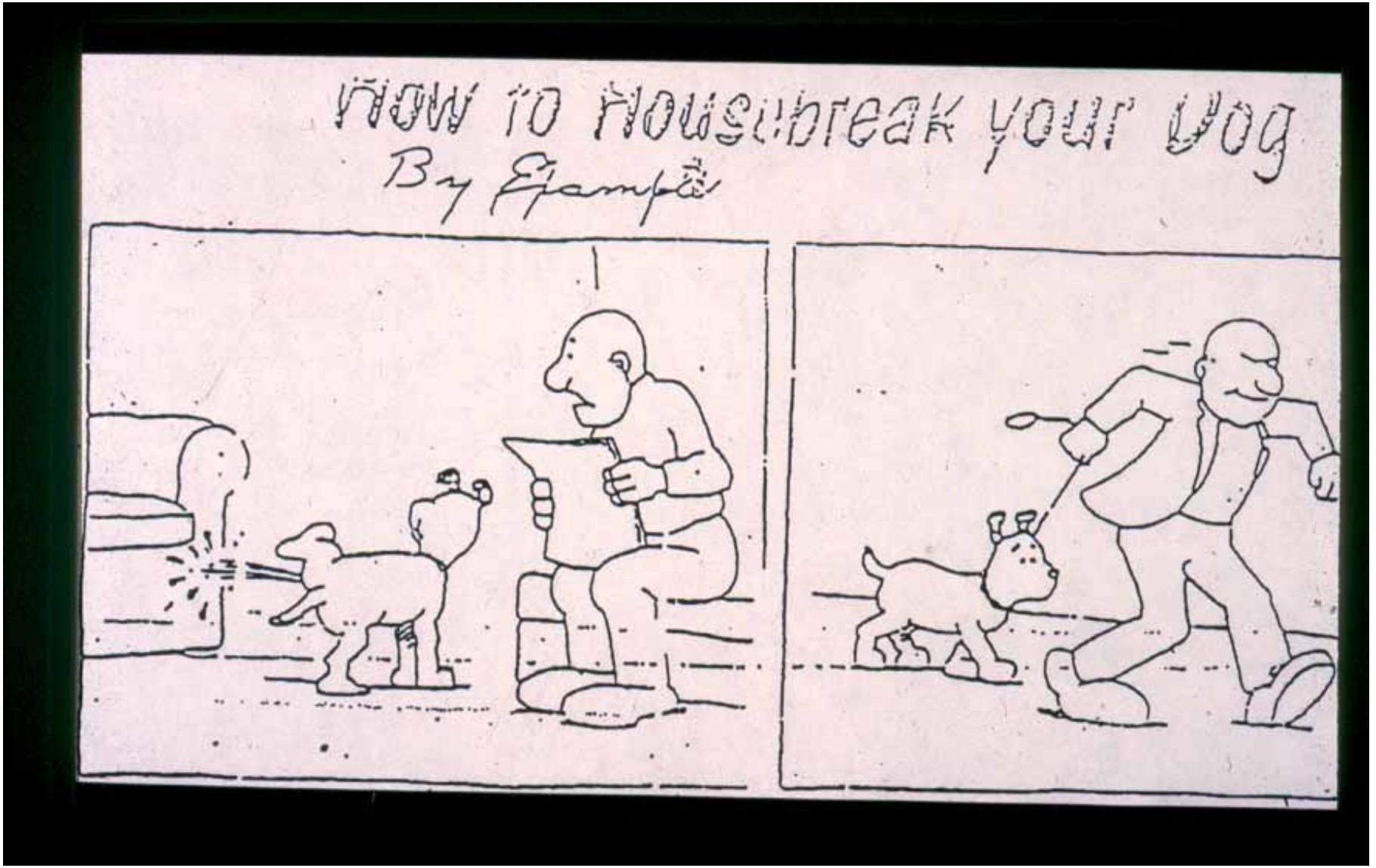
- Gery Guy, M.D. has referred to an editorial from Annals of Internal Medicine, emphasizing that it **“does not support involuntary tapering and discontinuation of opioids, as this practice can precipitate withdrawal symptoms, damage the clinician-patient relationship, and cause patients to obtain opioids from other sources,”** and clinicians should **“not abandon patients in chronic pain”**




"And now Edgar's gone....Something's going on around here."


Larson
"Bear! Bear!"




How to Housebreak your Dog
By Gamps