Using Methadone and Buprenorphine when Treating the Opioid-Dependent Chronic Pain Patient

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No conflicts to disclose

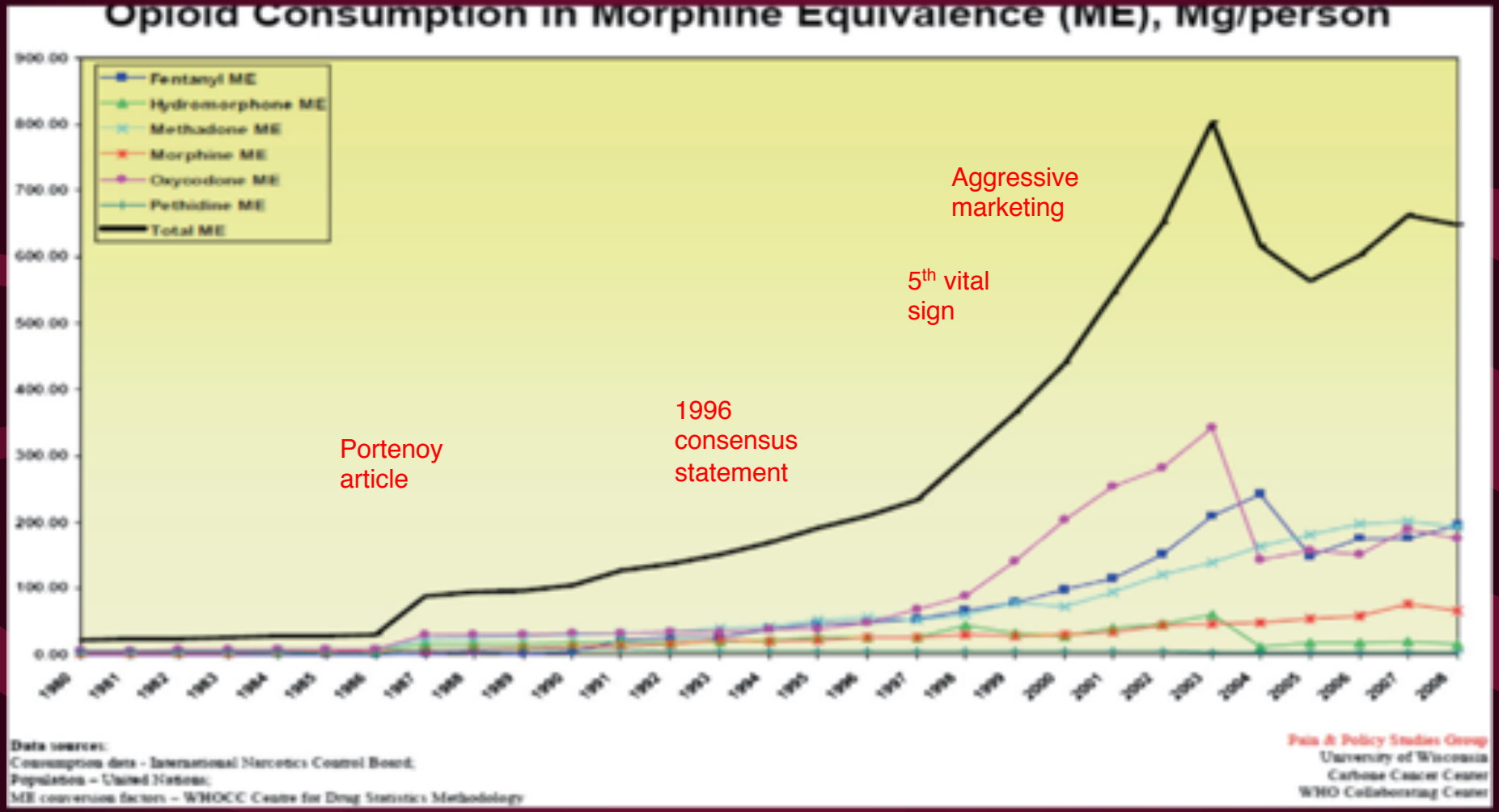
- I have no relationship with any industry or person(s) that could be construed as a conflict of interest in presenting this material

- -No off label therapies or products will be discussed in this presentation.

Learnig Objectives

- To increase understanding of why methadone and buprenorphne can be useful in the management of the opioid-dependent chronic pain patient, and

- to gain comfort in techniques of their use.


Opioid Consumption in Morphine Equivalence (ME), Mg/person
Fentanyl ME
Hydromorphone ME
Methadone ME
Morphine ME
Oxycodone ME
Pethidine ME
Total ME
900.00
800.00
700.00
600.00
500.00
400.00
300.00
200.00
100.00
0.00
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
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1994
1995
1996
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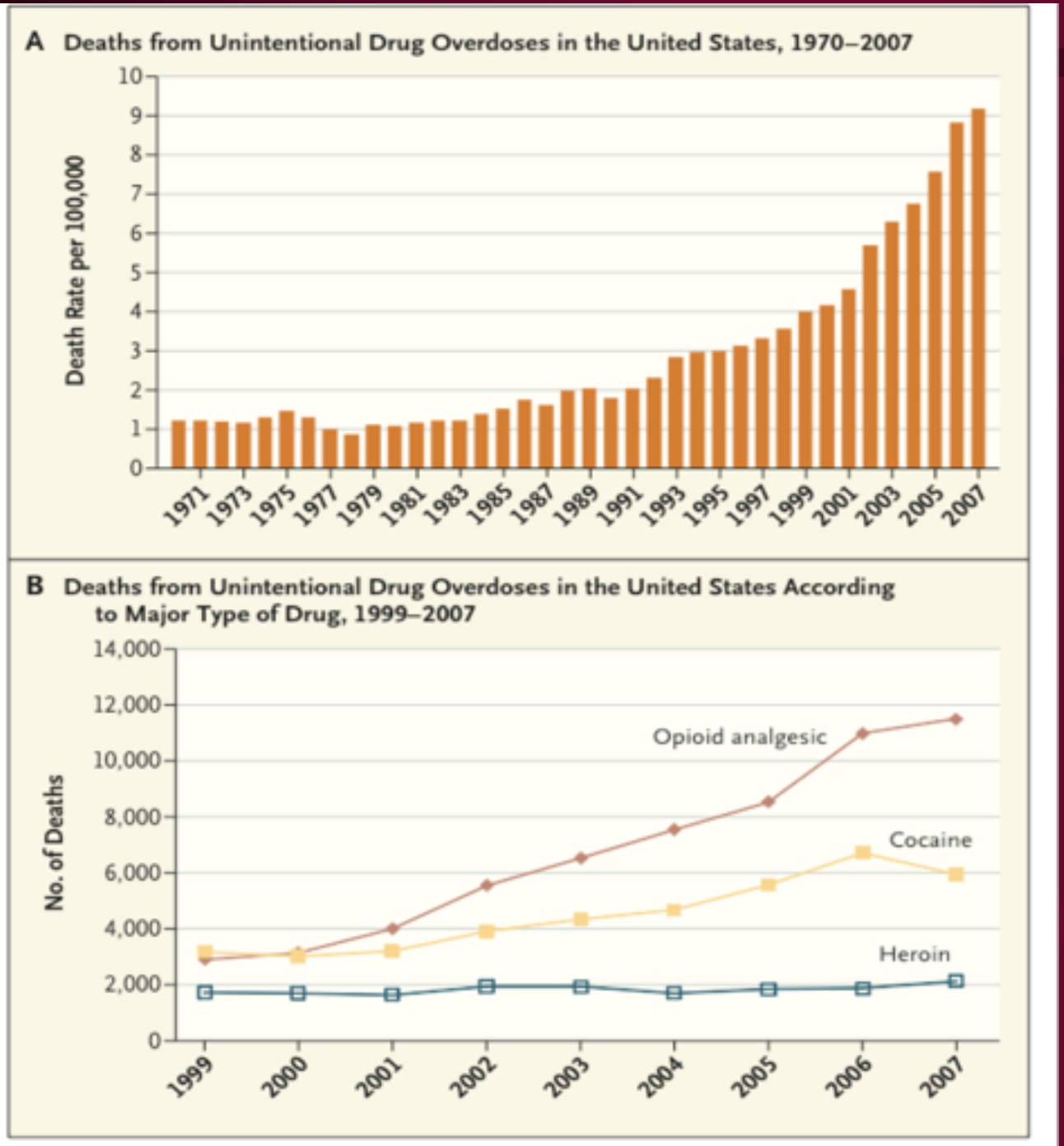
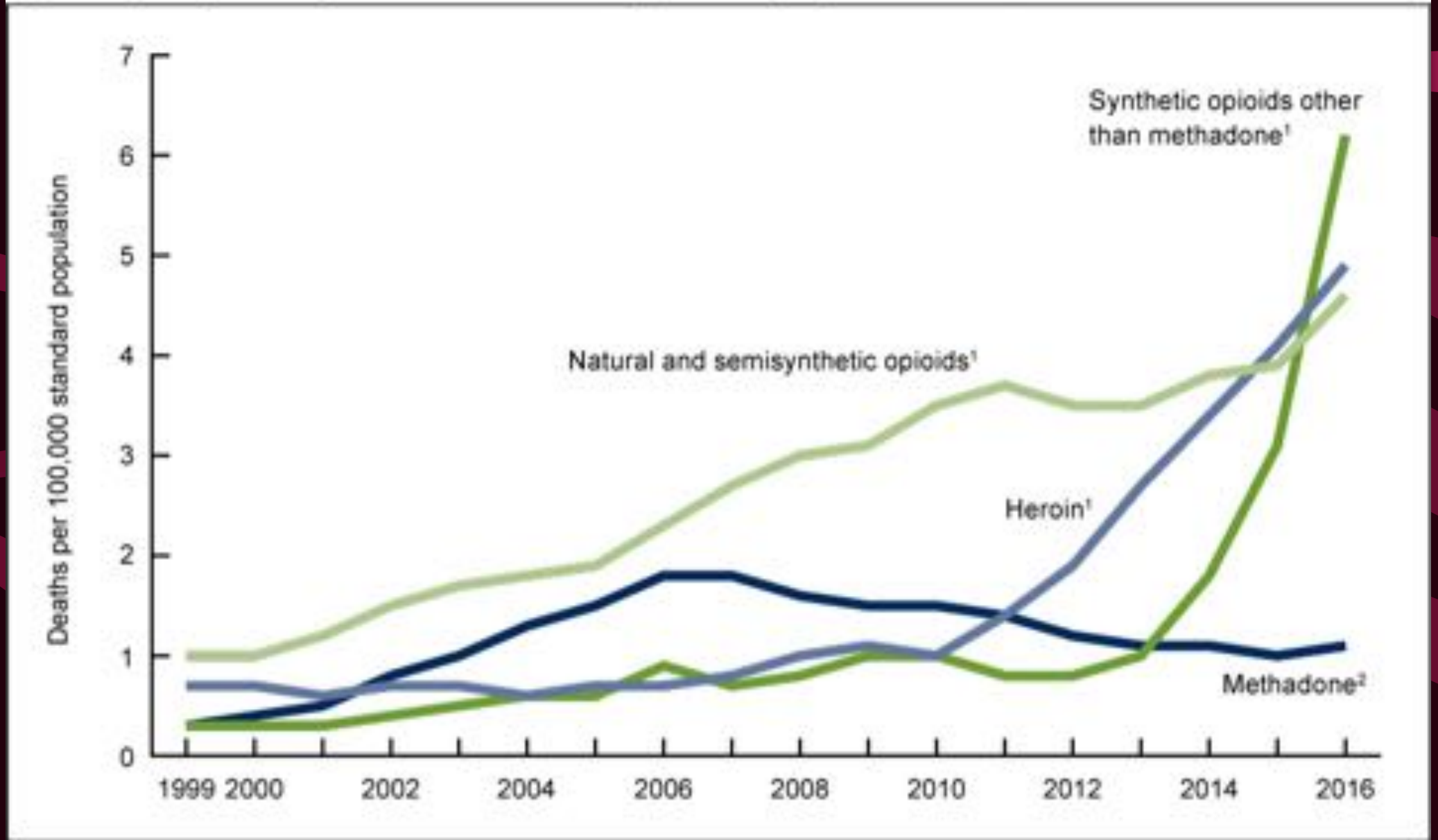
2001
2002
2003
2004
2005
2006
2007
2008
Aggressive marketing
5th vital sign
1996 consensus statement
Portenoy article
Data sources:
Consumption data - International Narcotics Control Board;
Population – United Nations;
ME conversion factors – WHOCC Centre for Drug Statistics Methodology
Pain & Policy Studies Group
University of Wisconsin
Carbone Cancer Center
WHO Collaborating Center



Okie, NEJM:363:1981-4, 2010

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



92 million adults rxed opioids in 2015

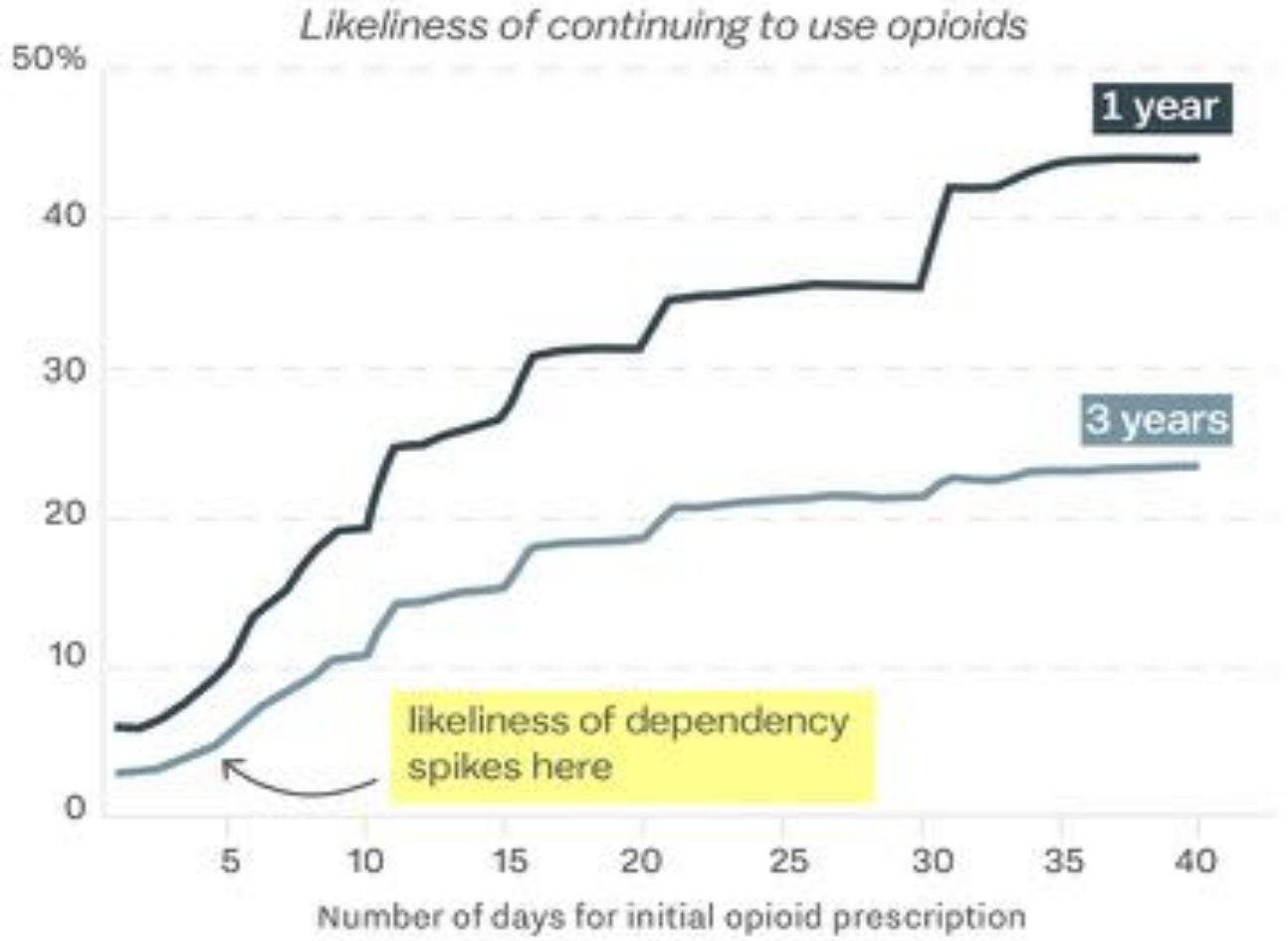
If rxed at least 1 day, 6% still using after 1 year

If rxed 8 days, 13.5% went on to long-term use

If rxed 30 days, 30% went on to long-term use

Ref: Shah et al., MMWR, 66(10):265-9, 2017

Risk of continued opioid use increases at 4-5 days

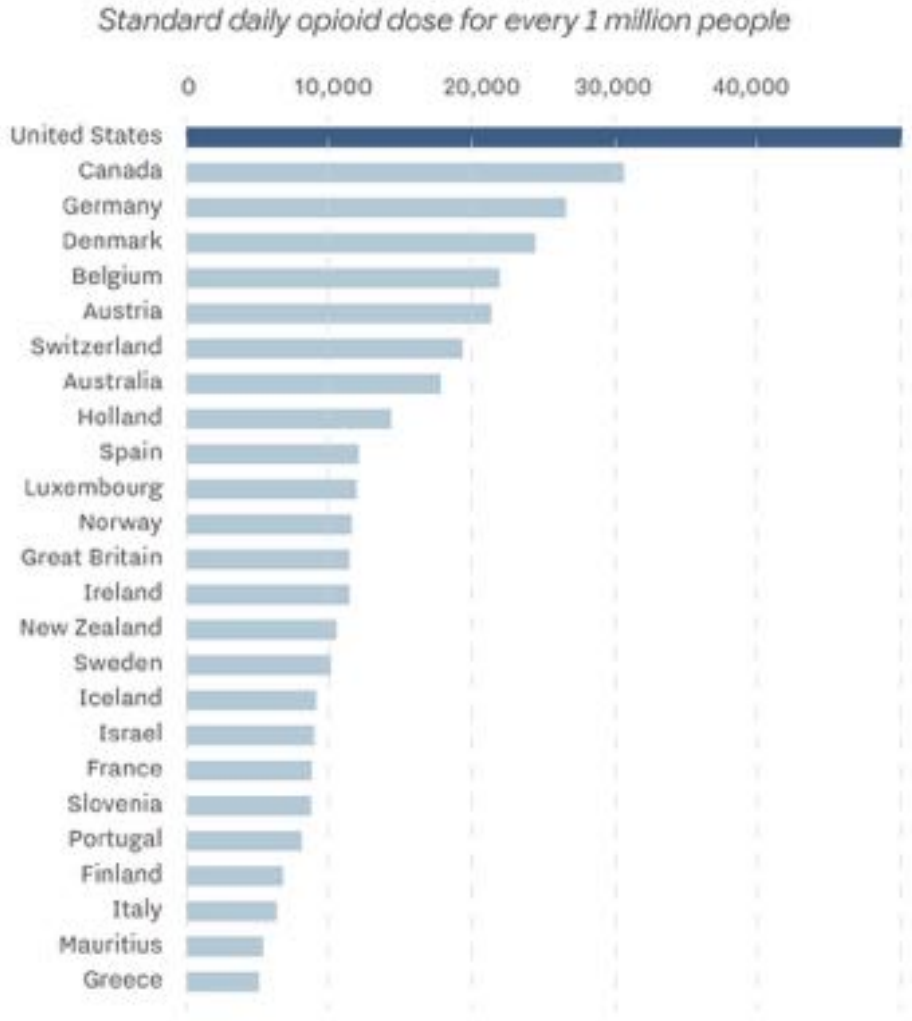


Source: Centers for Disease Control and Prevention

Credit: Sarah Frostenson

Vox

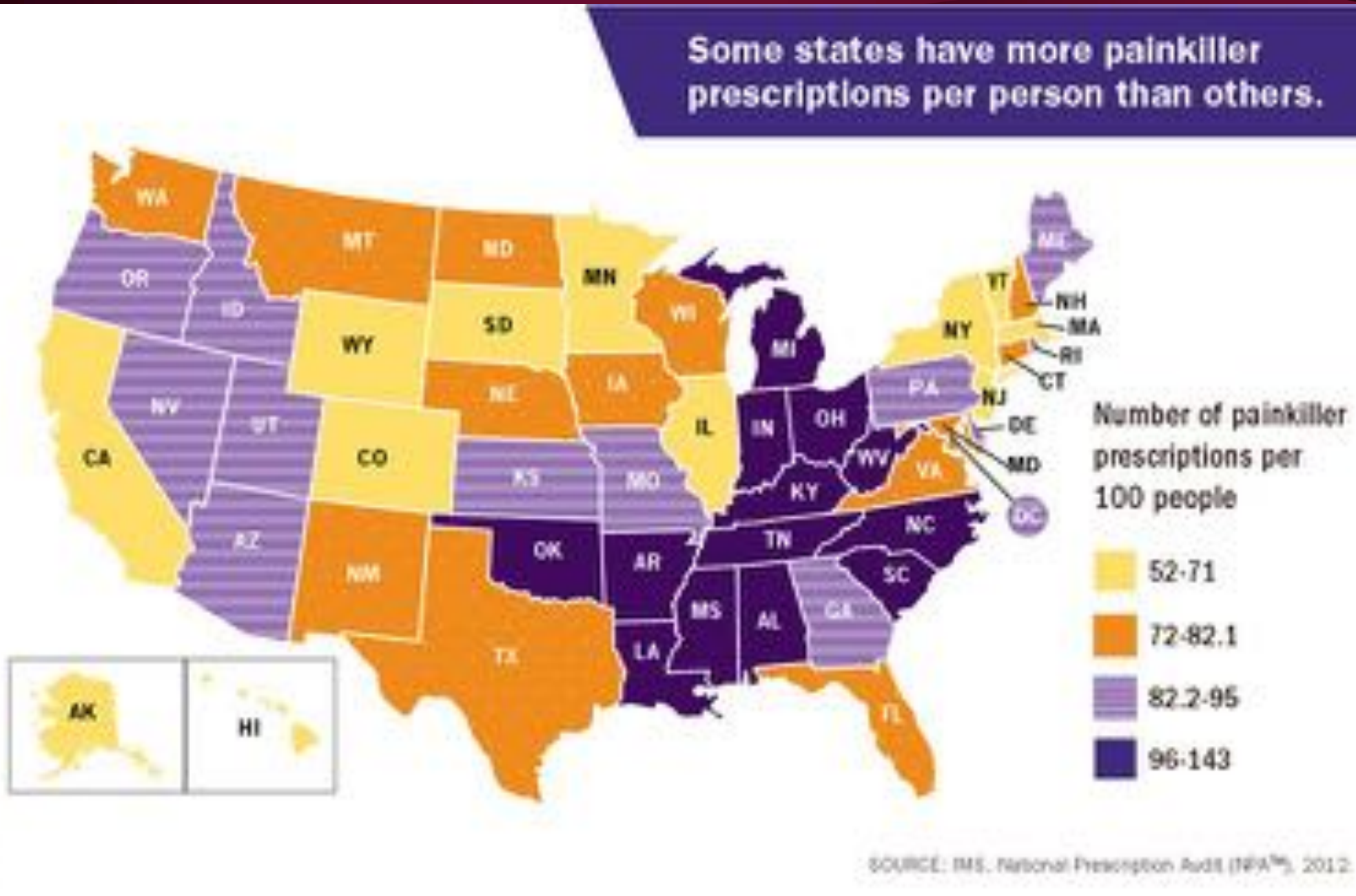
Americans consume more opioids than any other country



Source: United Nations International Narcotics Control Board

Credit: Sarah Frostenson

Vox


Some states have more painkiller prescriptions per person than others.
WA
OR
CA
ID
NV
MT
WY
UT
AZ
CO
NM
ND
SD
NE
KS
OK
TX
MN
IA
MO
AR
LA
WI
IL
MS
MI
IN
OH
KY
TN
AL
WV
GA
FL
SC
NC
VA
PA
NY
VT
ME
NH
MA
RI
CT
NJ
DE
MD
DC
AK
HI
Number of painkiller prescriptions per 100 people
52-71
72-82.1
82.2-95
96-143
SOURCE: IMS, National Prescription Audit (NPA™), 2012

Purdue Pharma, Executives Plead Guilty To Misbranding OxyContin, Fined $634.5M (2007)

- The settlement is one of the largest financial penalties ever imposed on a drug company,
- the company made claims that OxyContin was less addictive than other painkillers and less subject to abuse, "despite warnings to the contrary from doctors, the media and members of its own sales force," the Times reports (Zimmerman, Los Angeles Times, 5/11). The company also claimed that OxyContin could be discontinued without feeling symptoms of withdrawal

Opioid Crisis Cost U.S. Economy $504 Billion in 2015: White House

By Reuters Staff
November 22, 2017

The White House Council of Economic Advisers (CEA) said the toll from the opioid crisis represented 2.8% of gross domestic product that year.

Lack of efficacy of long-term opioids for pain

There are no placebo-RCTs supporting the effectiveness and safety of long-term opioid therapy for treatment of CLBP.

Cochrane Database Syst Rev. 2013 Aug 27;8:CD004959. doi: 10.1002/14651858.CD004959.pub4.

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial.

Krebs et al., JAMA 2018 Mar 6;319(9):872-882

Treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

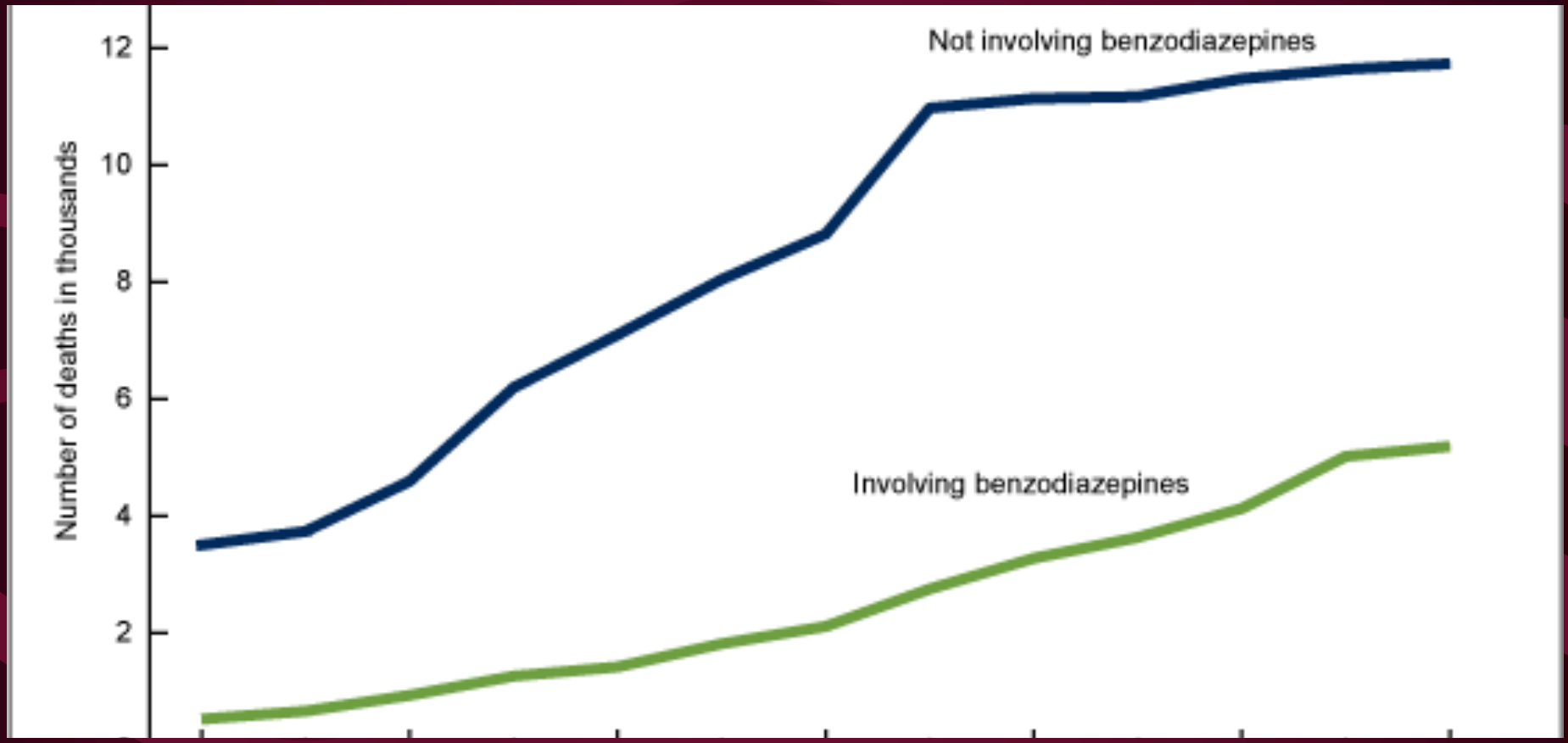
Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department: A Randomized Clinical Trial

Chang, etal *JAMA.* 2017;318(17):1661-1667

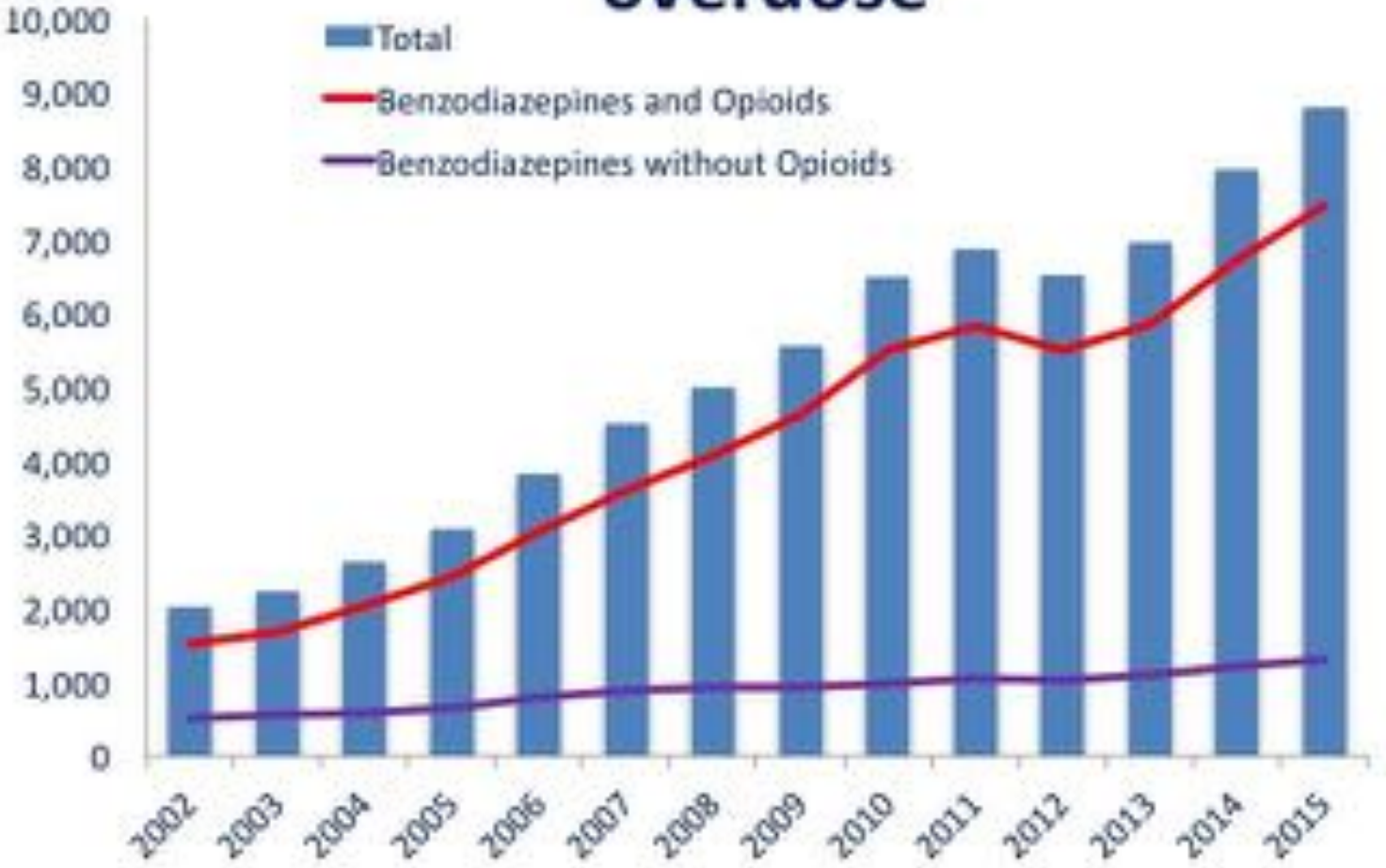
In this randomized clinical trial of 411 ED patients with acute extremity pain (mean score, 8.7 on the 11-point numerical rating scale), there was no significant difference in pain reduction at 2 hours. Mean pain scores decreased by 4.3 with ibuprofen and acetaminophen (paracetamol); 4.4 with oxycodone and acetaminophen; 3.5 with hydrocodone and acetaminophen; and 3.9 with codeine and acetaminophen.

CDC: PUBLICATION # **Number 166, September 2014**

Drug-poisoning Deaths Involving Opioid Analgesics: United States, 1999–2011



Opioid involvement in benzodiazepine overdose



Gabapentin, opioids, and the risk of opioidrelated death: A population-based nested case±control study

Gomes et al. PLOS Medicine I https://doi.org/10.1371/journal.pmed.1002396 October 3, 2017

1. 16 yr, 2.4M subjects rxed opioids
2. 8% rxed gabapentin
3. Death risk increased 50% , double that if high dose gabapentin

Gabapentin, Pregabalin and back pain - not effective

- In a placebo-controlled study of pregabalin (titrated to 600 mg daily for as long as 8 weeks) in patients with sciatica, pregabalin was ineffective (However, in a placebo-controlled study of pregabalin (titrated to 600 mg daily for as long as 8 weeks) in patients with sciatica, pregabalin was ineffective (NEJM Gen Med 2017 and *N Engl J Med* 2017; 376:1111). A meta-analysis that included six studies of gabapentin versus placebo or pregabalin versus another analgesic in patients with LBP (≈500 total patients), revealed no clinically meaningful benefits and substantial side effects for gabapentinoidNNEJM Gen Med 2017 and *PLoS Med* 2017; 14:e1002369).

CDC guidelines 2016

- Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain
- avoid increasing dosage to 90 MME or more per day
- For acute pain, three days or less will often be sufficient; more than 7 days will rarely be needed
- Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible
- Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with **buprenorphine or methadone** in combination with behavioral therapies) for patients with opioid use disorder.

Tapering opioids in pain patients

A convenience sample of 110 adult patients (median age, 52, median daily opioid dose, 288 mg morphine equivalents) ; 82 agreed to participate. 51 patients were available for assessment.

Each patient received educational materials about the benefits of dose reduction and an individualized taper plan that started with a 5% reduction in two steps in the first month. In the next 3 months, a taper of up to 10% weekly was attempted.

The median opioid dosage after 4 months of frequent visits was still 150 mg morphine equivalents, so considerable work remained to get to a safer dose.

Darnall BD et al. Patient-centered prescription opioid tapering in community outpatients with chronic pain. JAMA Intern Med 2018

Treatment of the Opioid Dependent Chronic Pain Patient

- Explain how narcotics maintain pain
- **Detoxification**
- Treat pain independently of detox
- Psychological support during detox and after
- Coordinate care, mobilizing caregivers and family
- Promote healthy behaviors: smoking, diet, exercise, attitude

Methadone - History

- Discovery
- 1st study with double-blind prtocol – 1947
- Complex metabolism – long-acting
- Harm reduction-methadone clinics – 1966
- Pain treatment-cancer

Methadone - Risks

- Dose equivalents
- Overdose deaths
- Qtc

Using Methadone -

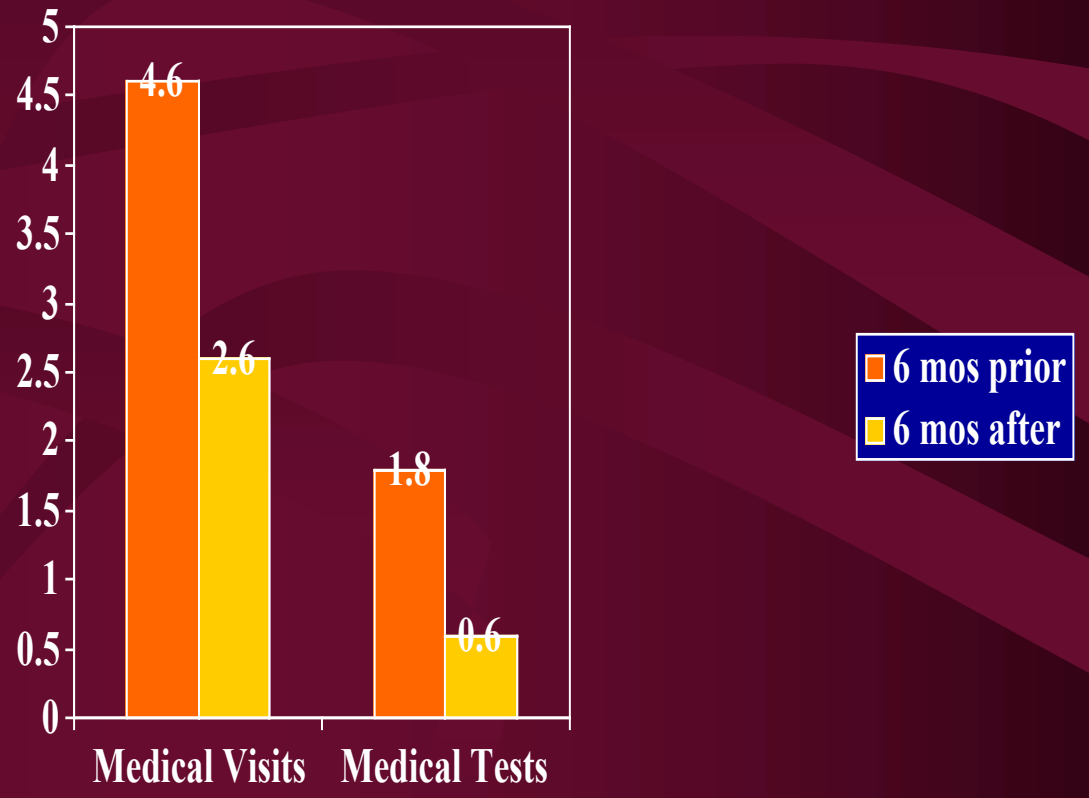
Excellent to detoxify – if contolled environment.

- Keep dose low
- Inpatient – taper strategy. Liquid
- Outpatient Rx must be for pain
- Bridge to buprenorphine

Effectiveness of a Psychiatric Pain Clinic

Anooshian, Streltzer, Goebert, Psychosomatics 1999; 40:226–232

- Followup of 100 pts
- Almost all patients had psychological factors or med management problems
- Rx: support, change meds
- Patient and physician satisfaction.
- Medical costs cut



BUPRENORPHINE
and BUPRENORPHINE/NALOXONE (SUBOXONE)

- Binds tightly to mu opioid receptor
- Partial mu agonist
- Sublingual
-

BUPRENORPHINE
and BUPRENORPHINE/NALOXONE (SUBOXONE)

- DOSING:

- Generally 2 to 16 mg/d
- Check PDMP
- Inpatient vs outpatient – Detox vs Maintennce
- Duration

BUPRENORPHINE
and BUPRENORPHINE/NALOXONE (SUBOXONE)

- Precipitates withdrawal if pt. tolerant to more than 30 mg methadone or equivalent, depending on duration of dependence
- Bridge dosing

- Naloxone protects from IV abuse - ??

BUPRENORPHINE
and BUPRENORPHINE/NALOXONE (SUBOXONE)

Associated Issues;

Dirty Urines, marijuana

Other medications – benzos, gabapentin, antidepressants, SOMA, butalbital

Cost, insurance, PAs

Acute pain pregnancy

Outpatient Experience with Buprenorphine

- Well tolerated
- ~ 12mg/day average
- Maintenance rather than detox is typical
- Multidisciplinary approach to treat pain-?
- Similar concerns about hyperalgesia as with other opioids-?

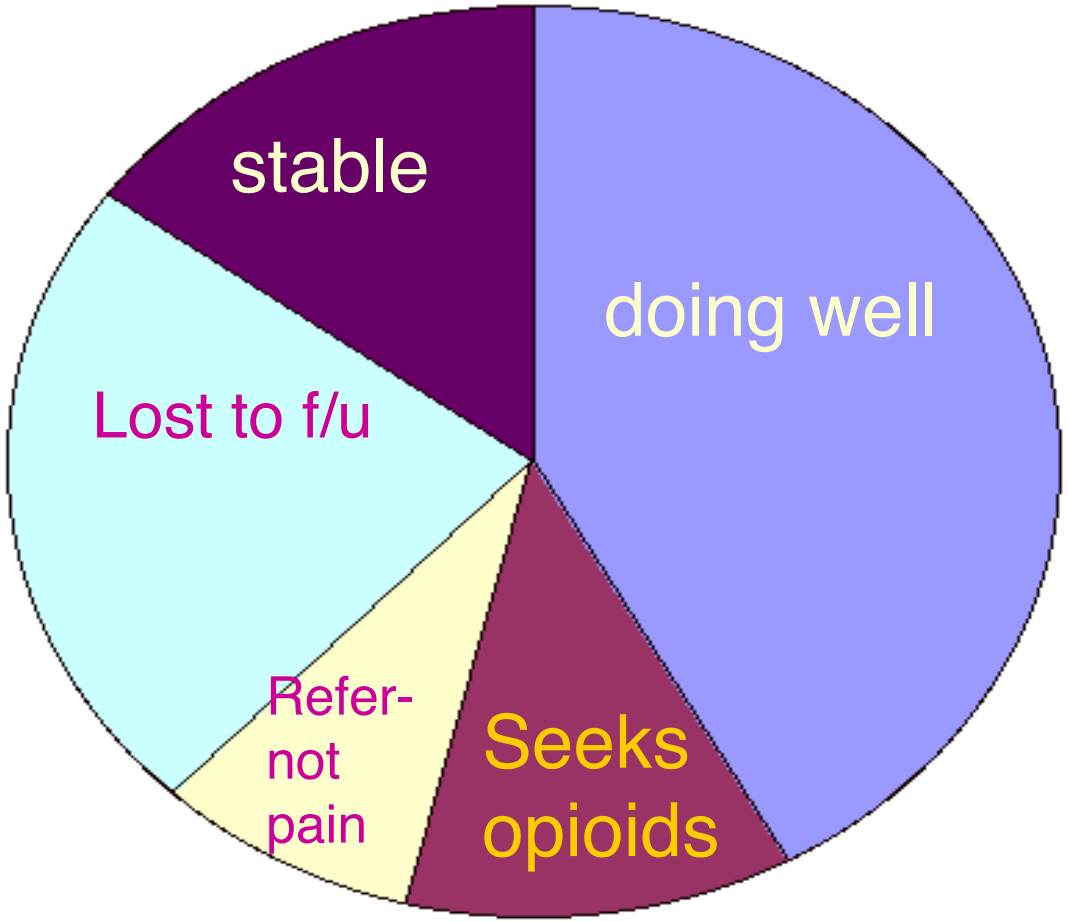
An Observational Study of Buprenorphine Treatment of the Prescription Opioid Dependent Pain Patient

- Jon Streltzer, MD, Raymond Davidson, MD, Deborah Goebert, DrPH
- Department of Psychiatry, University of Hawaii, School of Medicine, Honolulu, Hawaii
- The Queen's Medical Center, Honolulu, Hawaii

- The American Journal on Addictions, 24;357–361, 2015

Rx buprenorphine in pain clinic

Jennifer Farrell, J Streltzer



QUESTIONS?

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