

The Triple Wave Epidemic: Supply and Demand Drivers of the US Opioid Crisis

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DISCLOSURES

- Dr Ciccarone provided one time consulting for Mallinckrodt and Nektar Therapeutics
- No perceived or real conflicts with the content of this presentation

OBJECTIVES

- National data on opioid, heroin and fentanyl overdose
 - The “Triple Wave” crisis
- Structural drivers of the opioid epidemic
 - Opioid, heroin and fentanyl supplies
 - Root causes: economic, social
- How to address the crisis

HEROIN IN TRANSITION (“HIT”) STUDY

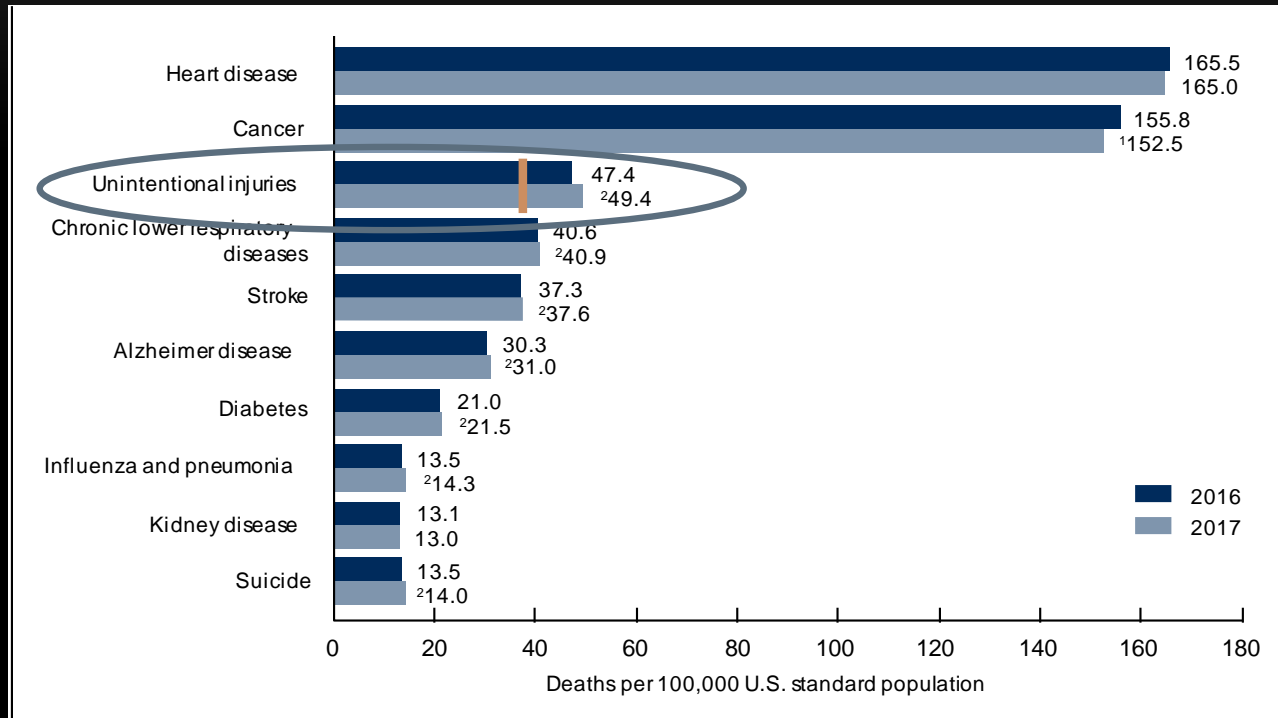
- NIH: National Institute of Drug Abuse
 - DA037820
- Multi-methodological study: quantitative and qualitative aims
 - Supply changes – adulteration – overdose
 - New drug forms and user perceptions, adaptation, etc.

PUBLICALLY AVAILABLE DATA:

- Centers for Disease Control and Prevention, National Center for Health Statistics
- US Drug Enforcement Administration: National Drug Threat Assessment 2016; National Heroin Threat Assessment, 2015

Leading Causes of Death

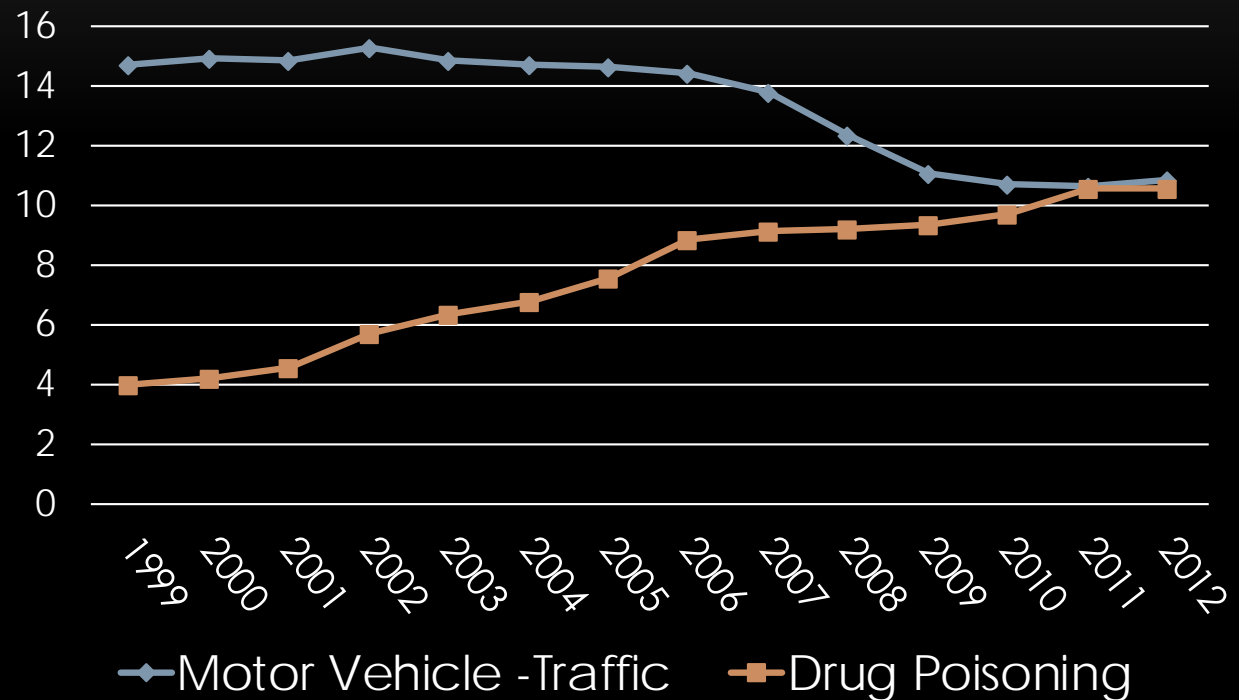
- Age-adjusted death rates for the 10 leading causes of death in 2017



NCHS Data Brief No. 328 November 2018. Mortality in the United States, 2017
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention. National Center for Health Statistics

Unintentional Injury 1999-2012

- Age-adjusted death rates per 100,000 pop.



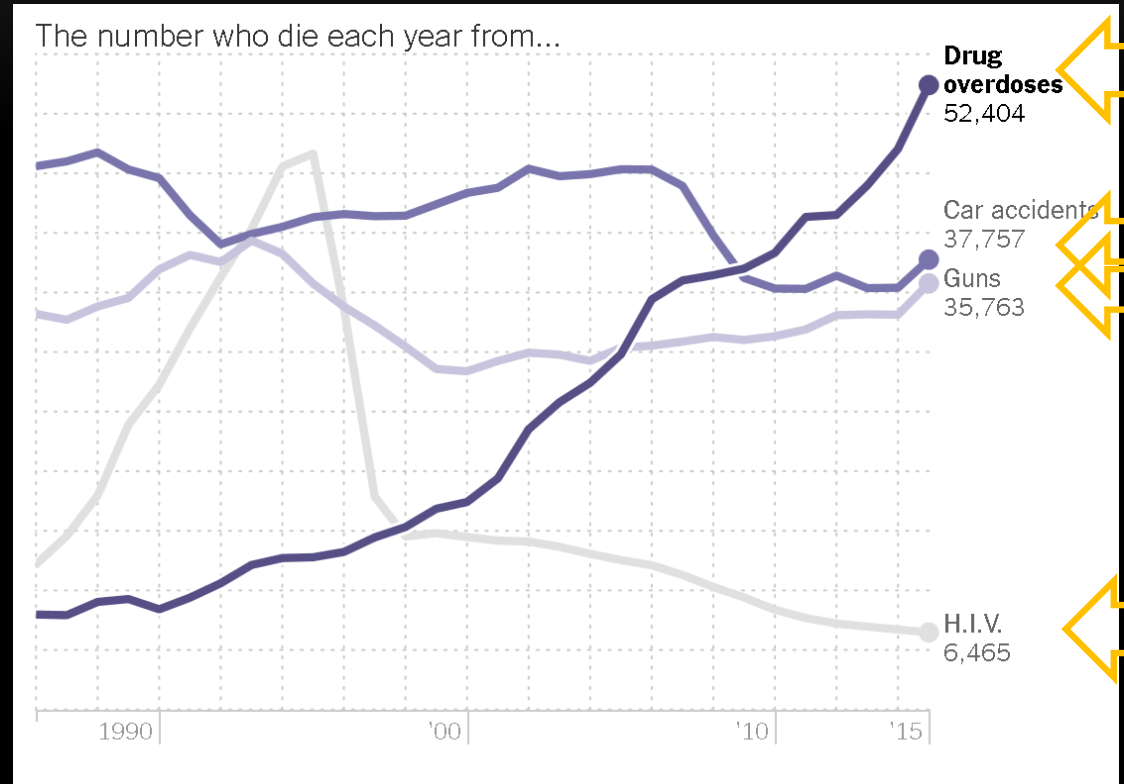
Produced by: National Center for Injury Prevention and Control, CDC

Data Source: NCHS Vital Statistics System for numbers of deaths. Bureau of Census for population estimates. Accessed: 11.5.14

An Epidemic of Crisis Proportion

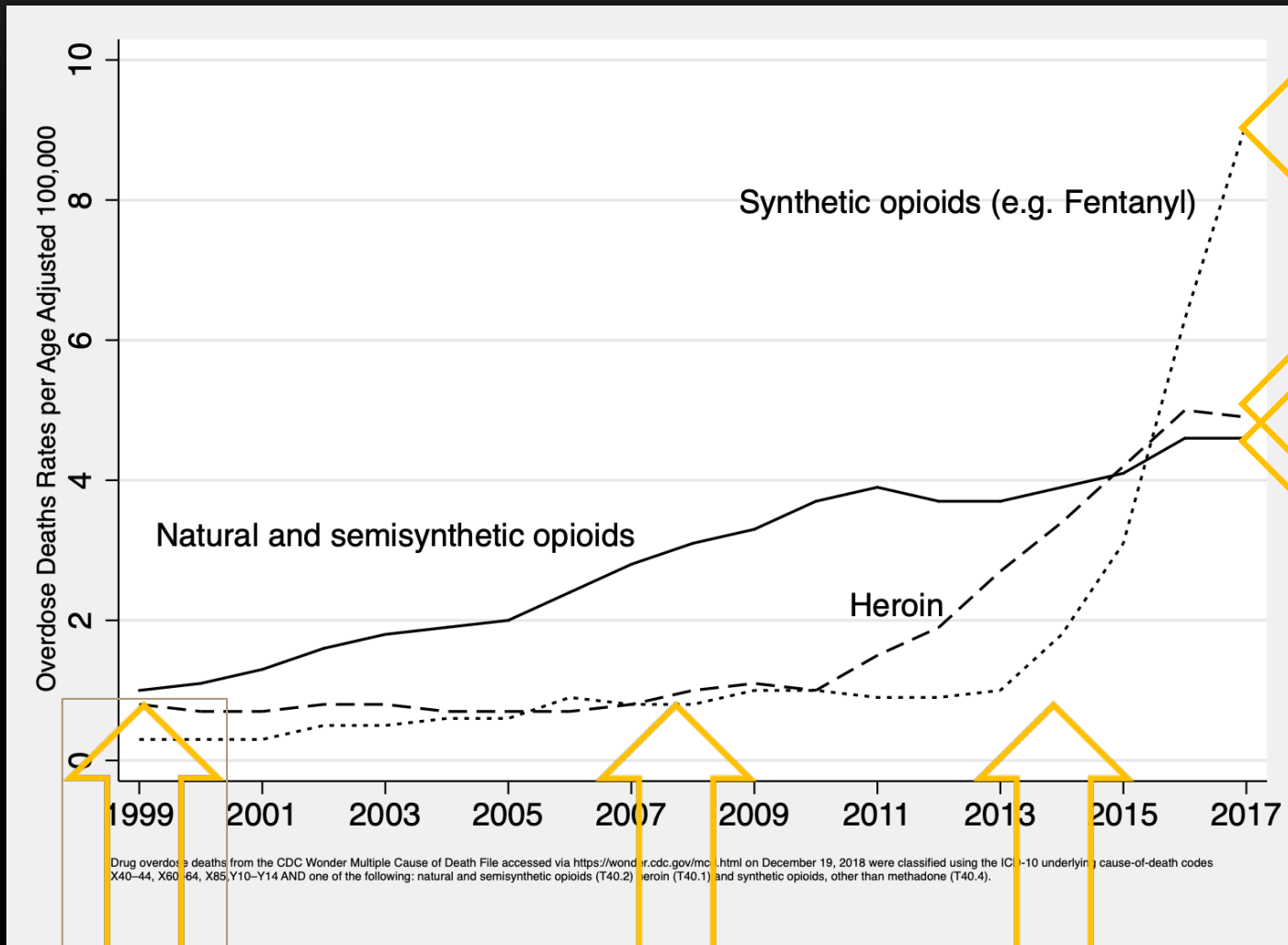
Numbers of deaths:

- Drug overdose >
- Motor vehicle >
- Gun homicide >
- HIV



Source: New York Times, The Upshot; Josh Katz; April 14, 2017. Data from: Centers for Disease Control and Prevention, National Center for Health Statistics

THE TRIPLE WAVE Epidemic



A BRIEF HISTORY OF OPIOID “EPIDEMICS”

- Epidemic

- Morphine & heroin 1880-1900's
- Heroin (wave 2, illicit, 1920 's)
- Heroin (Jazz era)
- Heroin (Vietnam era)
- Heroin (Colombian-sourced, 1990's)
- Opioid pills (2000's)
- Heroin (late 2000's)
- Synthetics eg fentanyl (2013)

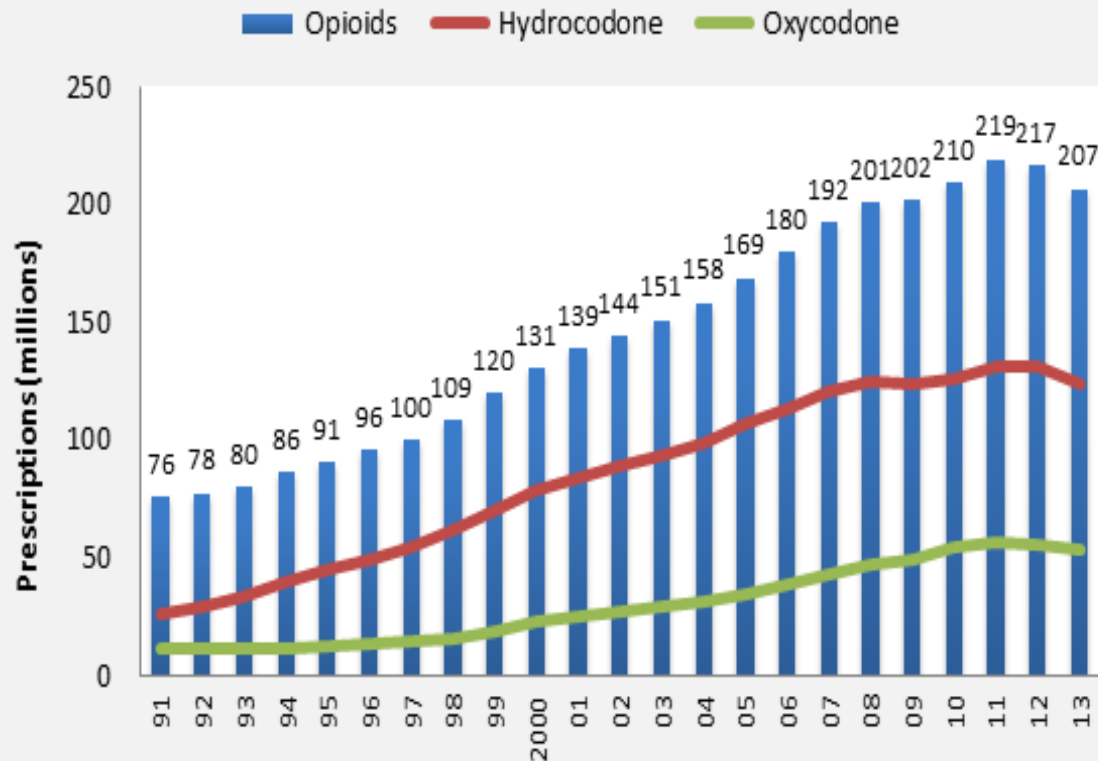
- Trigger

- Novel drug/ Iatrogenic source/ technological
- Harrison Act (restriction)? > illicit
- Cultural?
- New source & cultural
- New source
- Iatrogenic source/ novel form/ technological (ERLA)
- New source-form /restriction
- New source/ novel forms

THE TRIPLE WAVE:

OPIOIDS > HEROIN > FENTANYL

WAVE ONE: TRIPLING OF OPIOID PRESCRIPTIONS



IMS Health, Vector One®: National, 1991-2011

IMS Health, National Prescription Audit, 2012-2013

Thanks: **Wilson Compton**, Deputy Director, NIDA

CONTROL THE “VECTOR”

Supply based:

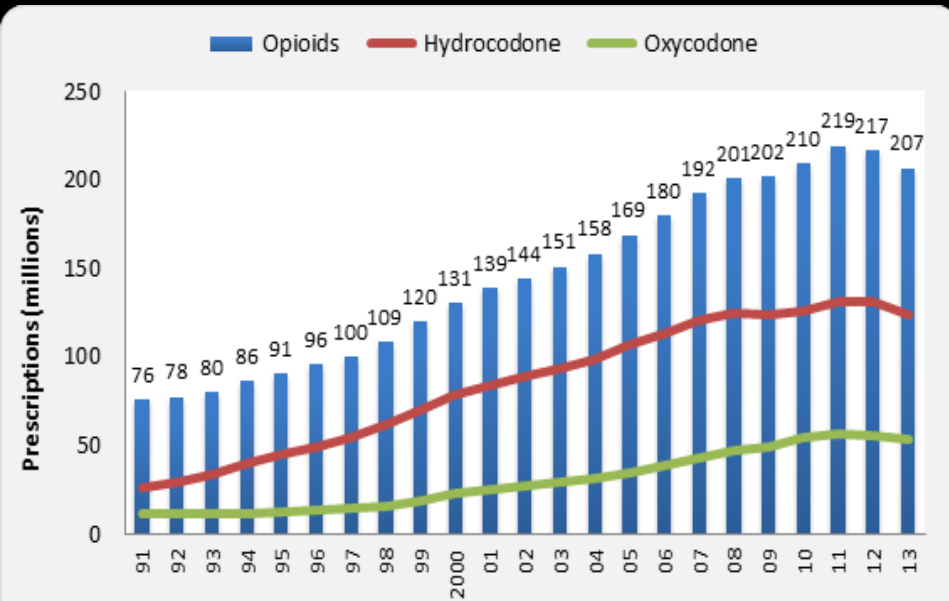
- Prescription
- “Doctor shopping”
- “Pill mills”
- Diversion
- Illicit use (e.g. IN, IV)
- Goal: cut down supply of illicit opioids to reduce illicit flows/use
- Is it working?

Control:

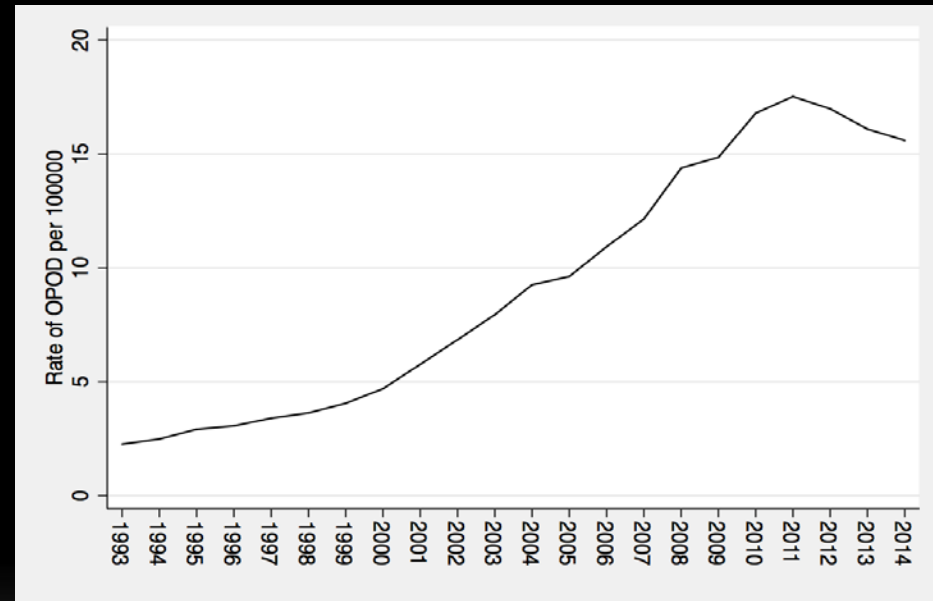
- Prescribing guidelines
- PDMPs
- DEA
- Disposal & above
- Abuse-deterrent (ADF)

OPIOID SUPPLY

Opioid prescriptions



Opioid overdose hospitalizations



IMS Health, Vector One®: National, 1991-2011
IMS Health, National Prescription Audit, 2012-2013
Thanks: Wilson Compton, Deputy Director, NIDA

PUBLIC HEALTH

- Drug epidemics: supply and demand
- “Upstream” or “root causes”
- QUESTION: What brought patients in to see the provider?

Opioid Crisis: No Easy Fix to Its Social and Economic Determinants

The accepted wisdom about the US overdose crisis singles out prescribing as the causative vector. Although drug supply is a key factor, we posit that the crisis is fundamentally fueled by economic and social upheaval, its etiology closely linked to the role of opioids as a refuge from physical and

Nabanun Dasgupta, PhD, MPH, Leo Beletsky, JD, MPH, and Daniel Ciccarone, MD, MPH

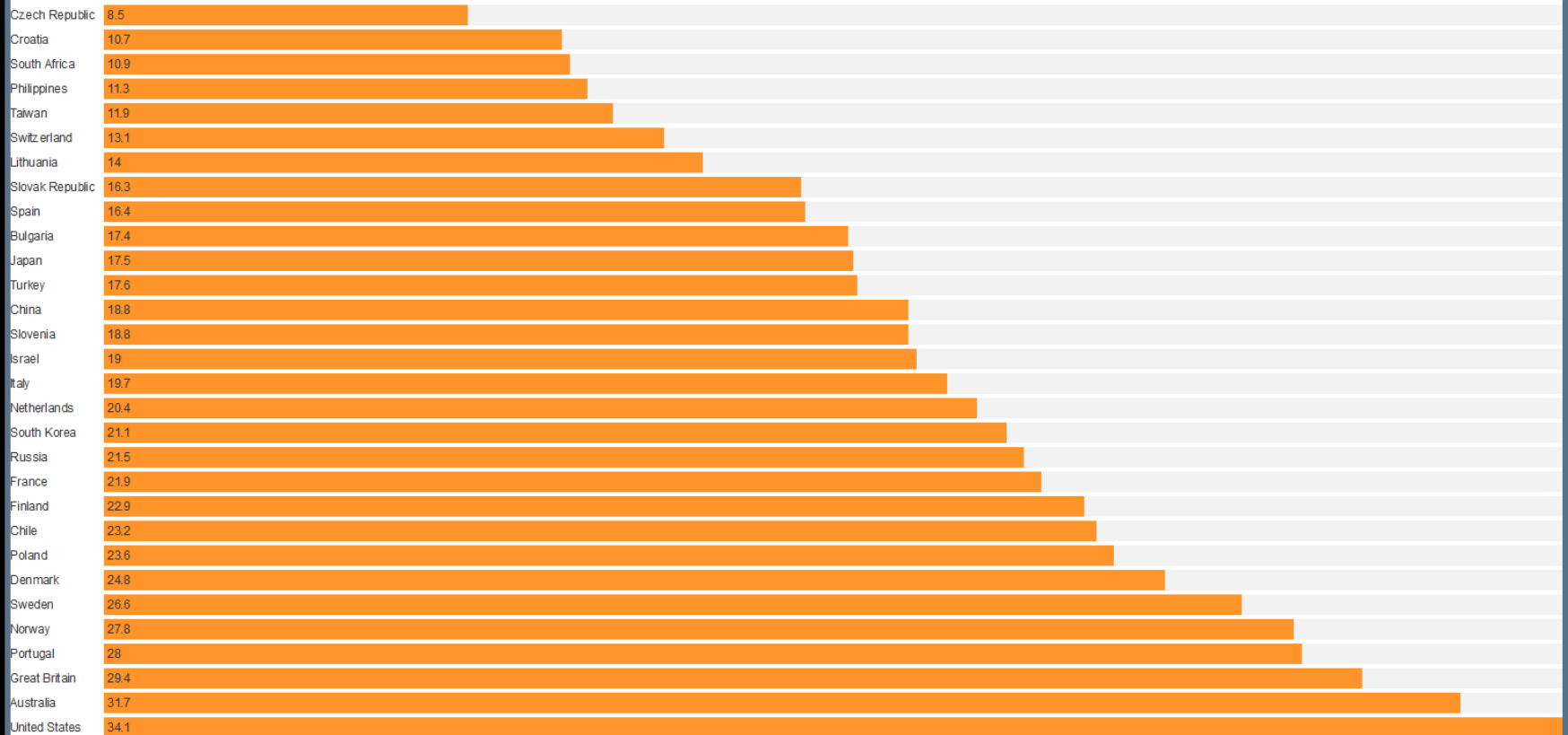
The accepted wisdom about the US opioid crisis singles out opioid analgesics as causative agents of harm, with physicians as unwitting conduits and pharmaceutical companies as selfish promoters.¹ Although invaluable for infection control, this vector

death.”^{7(p301)} A decade later, US medicine was shaken by revelations of undertreated chronic pain, motivating normative practice and policy shifts.⁸ Previously, chronic pain was managed largely with cognitive behavioral therapy, even

chronic pain was big business. Withdrawals from the market of popular nonopioid analgesics because of cardiovascular risk and acetaminophen toxicity raised concerns about nonopioid alternatives.¹⁰ Short lived but indelible, some pharmaceutical

GLOBAL PAIN RANK

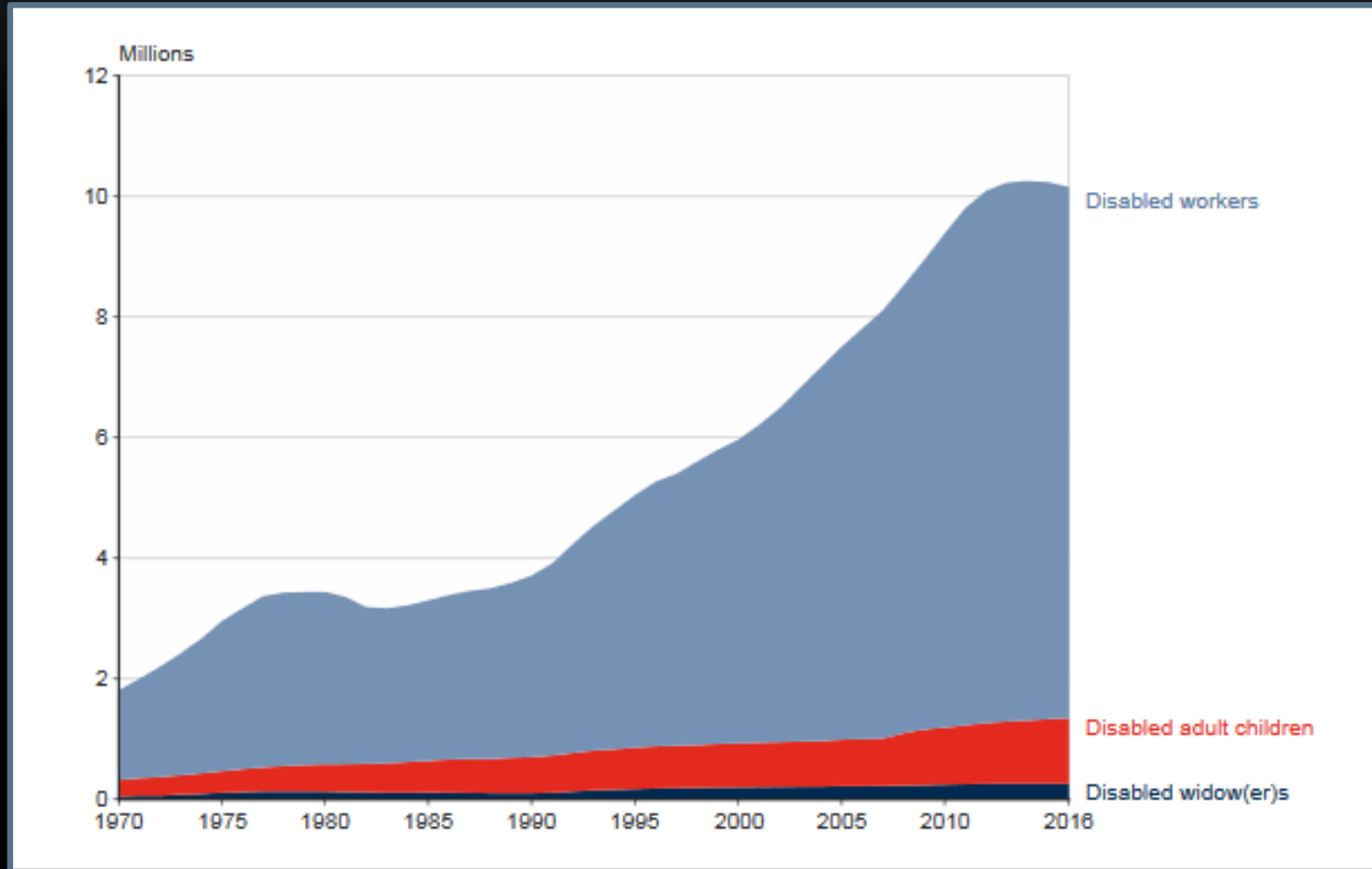
Percent with physical pain "often" or "very often"



Source: International Social Survey Programme • Created with Datawrapper

Source: Unhappiness and Pain in Modern America: A Review Essay, and Further Evidence, on Carol Graham's Happiness for All? David G. Blanchflower, Andrew Oswald, NBER Working Paper No. 24087. Nov, 2017

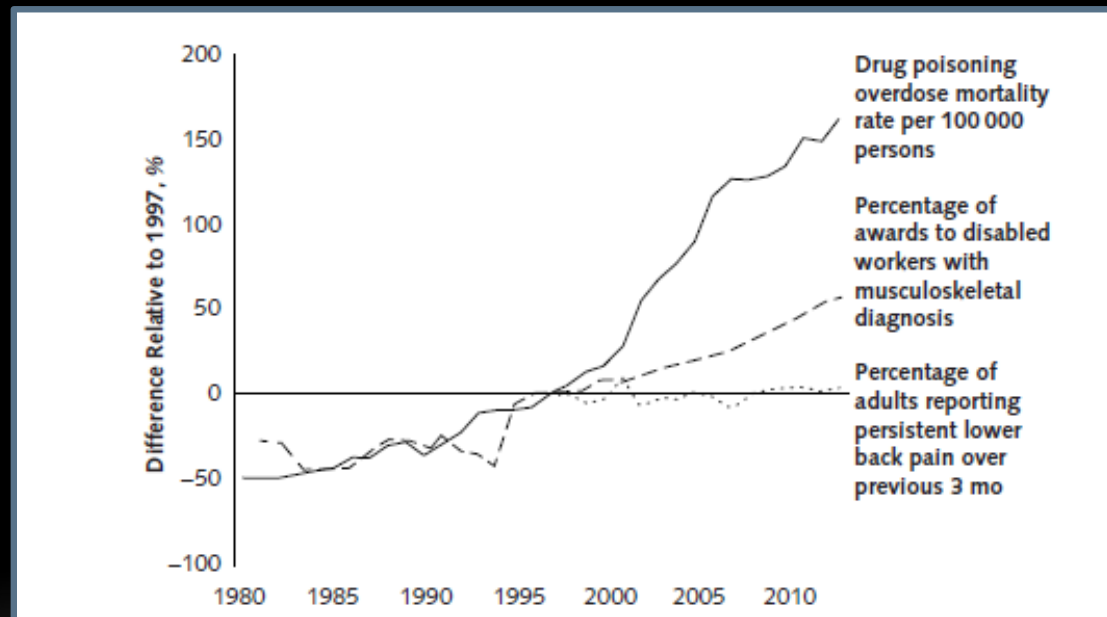
RISE IN SSDI RECIPIENTS



Social Security Administration. Annual Statistical Report on the Social Security Disability Insurance Program, 2016. Washington, DC: Social Security Administration, Office of Retirement and Disability Policy, Office of Research Evaluation and Statistics; 2017.

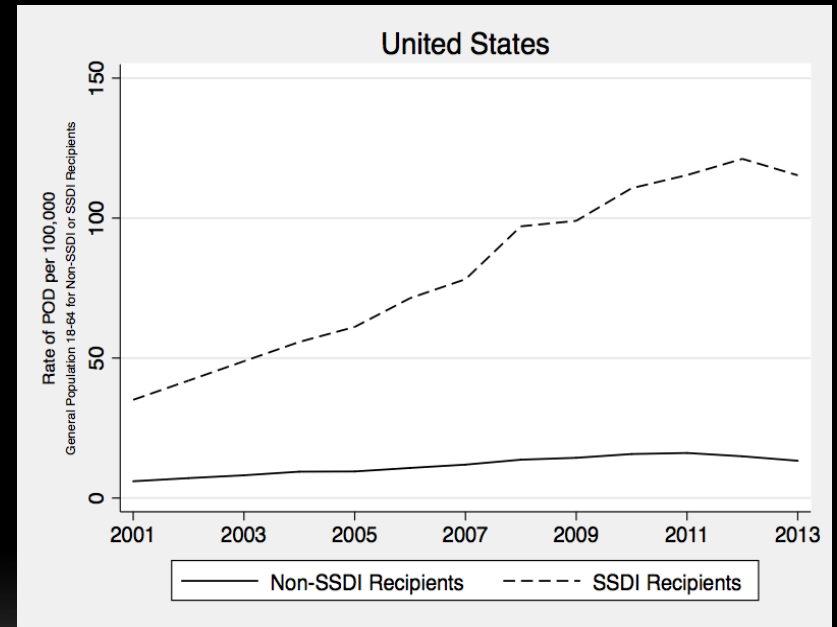
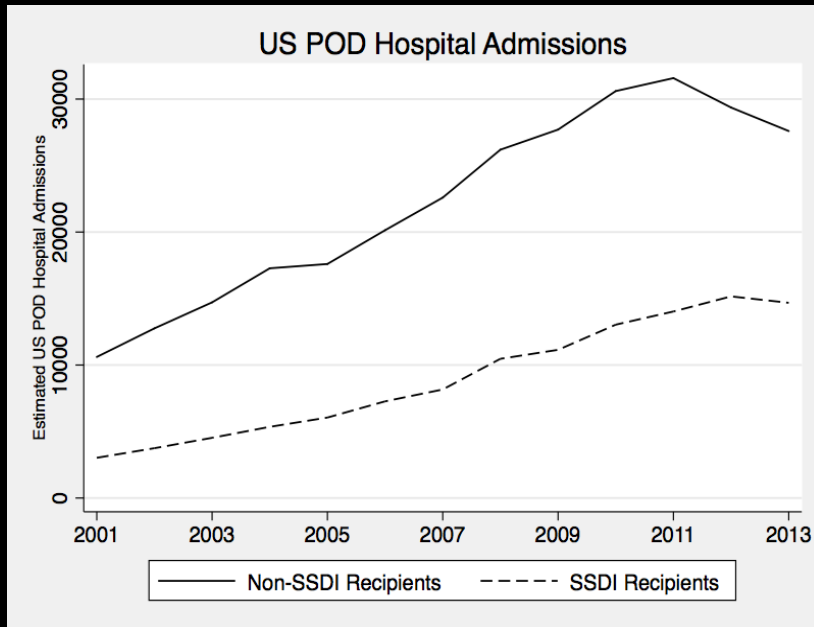
King et al: SSDI & OD

- Rise in disabled workers:
 - Aging
 - Welfare reform:
 - Medicalization of social support
- Rise in MSK-disability



Source: King, Strumpf & Harper. Has the Increase in Disability Insurance Participation Contributed to Increased Opioid-Related Mortality? *Ann Intern Med.* 2016 Nov 15;165(10):729-730.

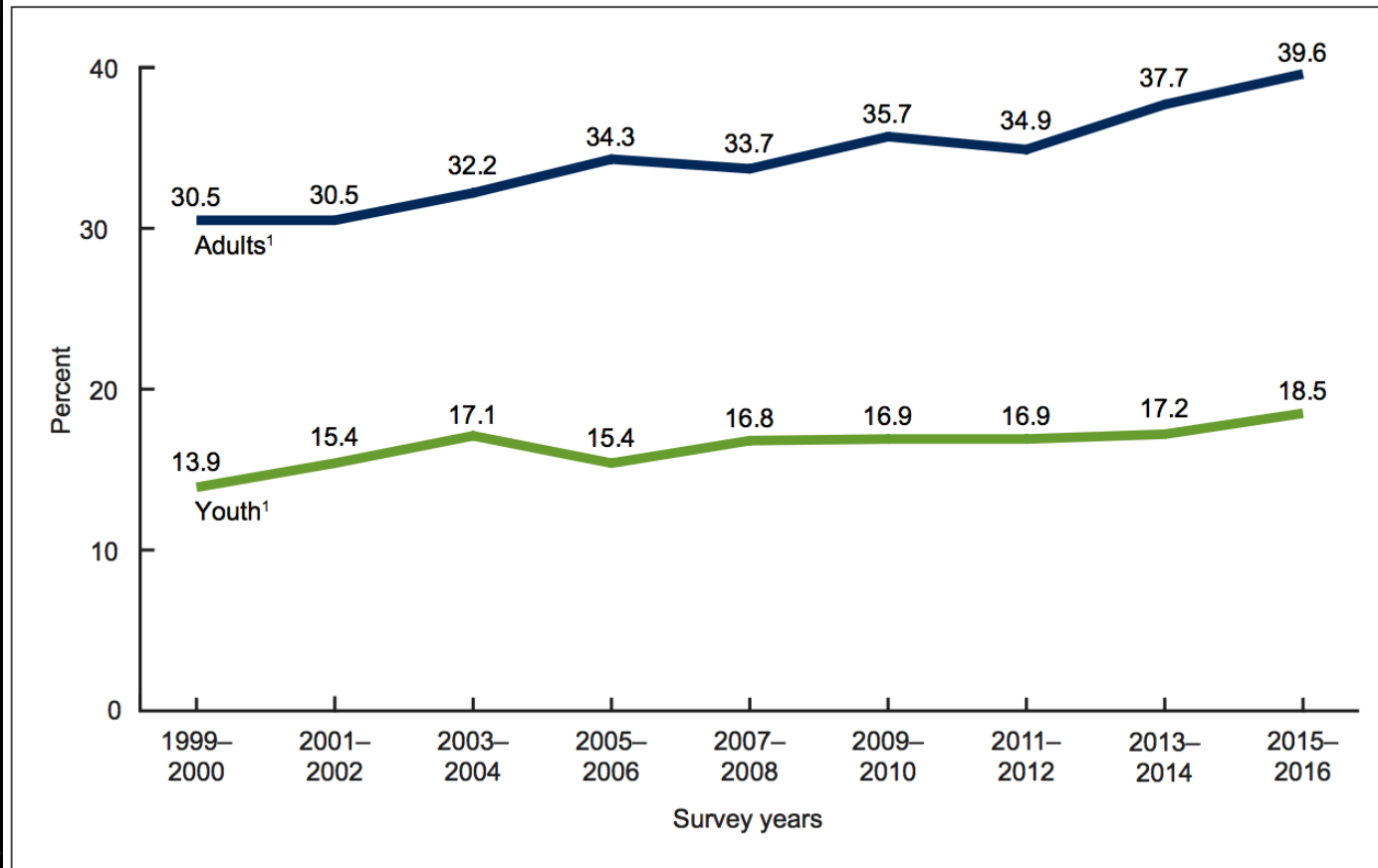
SSDI AND OPIOID OVERDOSE



Source: Unick and Ciccarone; submitted paper

OBESITY PREVALENCE

Figure 5. Trends in obesity prevalence among adults aged 20 and over (age adjusted) and youth aged 2–19 years: United States, 1999–2000 through 2015–2016



¹Significant increasing linear trend from 1999–2000 through 2015–2016.

NOTES: All estimates for adults are age adjusted by the direct method to the 2000 U.S. census population using the age groups 20–39, 40–59, and 60 and over.

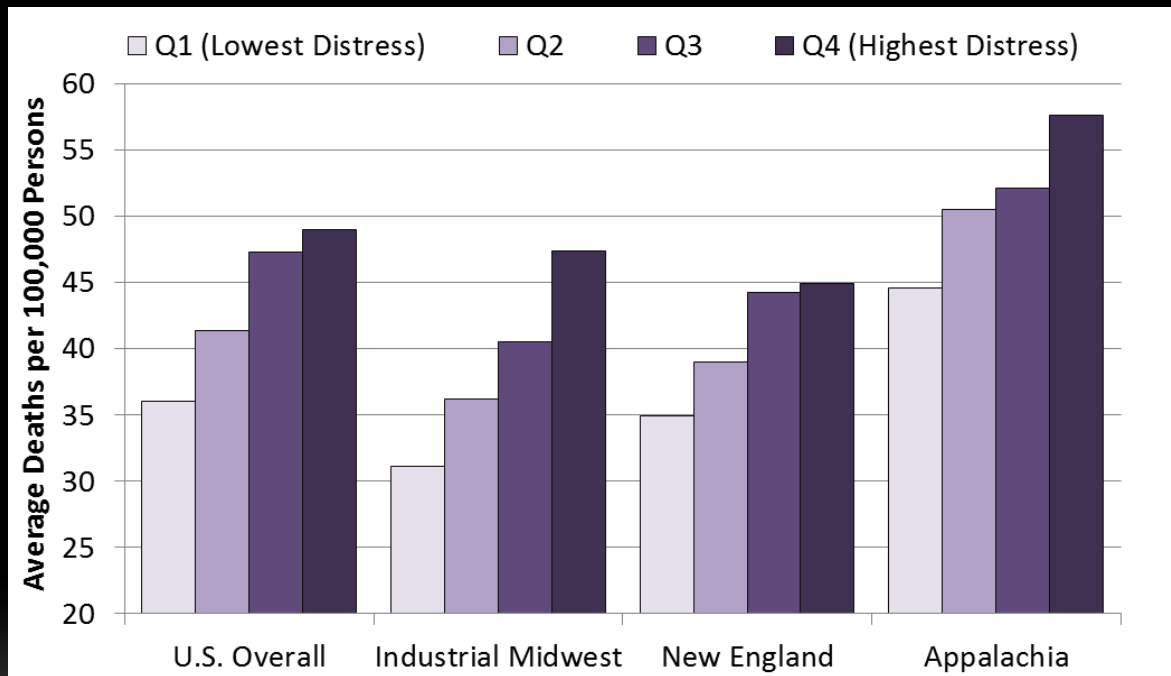
Access data table for Figure 5 at: https://www.cdc.gov/nchs/data/databriefs/db288_table.pdf#5.

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2016.



Monnat: Economic distress and OD

- Decades of wage stagnation, chronic unemployment, disability, and poverty
- Strong disparities at county-level



Source: Monnat, S. Deaths of Despair and Support for Trump in the 2016 Presidential Election. Research Brief, 12/2016

“WE MUST STOP KILLING EACH OTHER”



Photo: D. Ciccarone

SHOOTING GALLERY



Monnat: Economic and Social Factors Contributing to Between-county Differences In U.S. Drug-related Mortality Rates

Risk factors:

- Economic:
 - Economic distress
 - Rental stress
 - Mining dependence
- Social:
 - Family distress

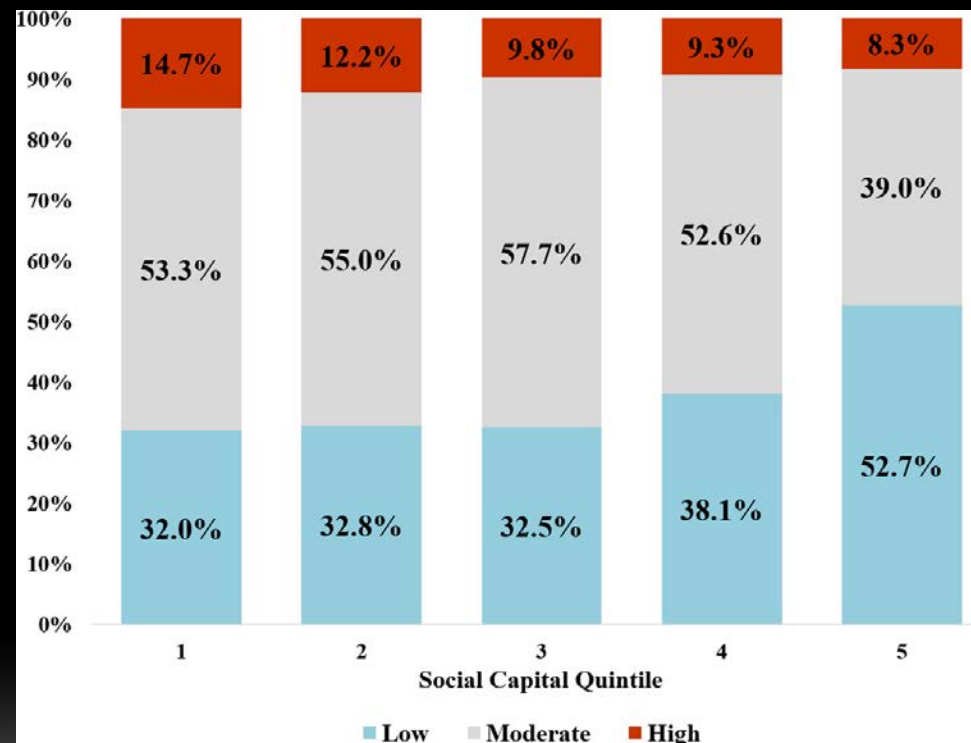
Protective factors:

- Economic:
 - Public-sector dependent
 - Farming dependent (trend)
- Social:
 - In-migration
 - Religious establishments

ZOOROB & SALEMI: "BOWLING ALONE, DYING TOGETHER"

Social capital:

- Density of community and personal networks
- Civic engagement and participation
- Sense of belonging
- Reciprocity and cooperation
- Trust in the community



Zoorob, M. & Salemi, J. Bowling alone, dying together: The role of social capital in mitigating the drug overdose epidemic in the United States. *Drug and Alcohol Dependence*, 173 (2017).

WHAT IF WE DON'T ADDRESS ROOT CAUSES?

- Balloon effects



Photo: D. Ciccarone

WAVE TWO: FUELING HEROIN-RELATED OVERDOSE

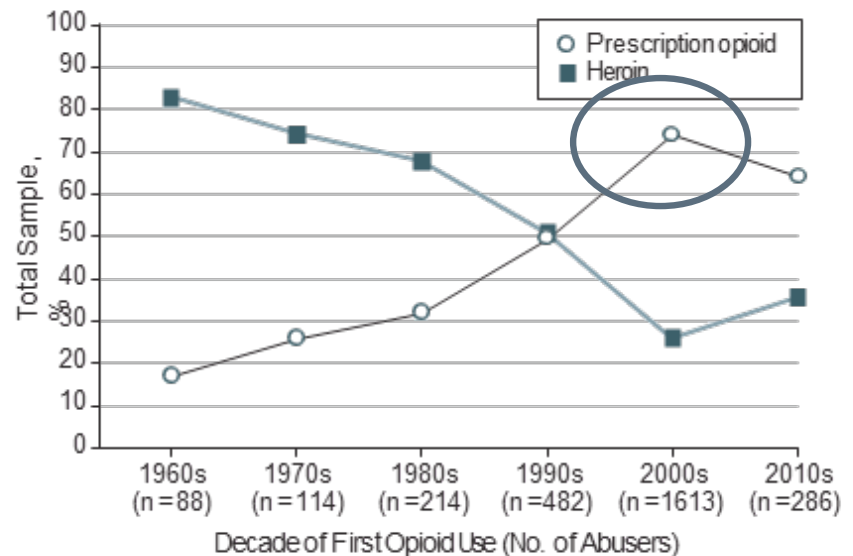
- Rising numbers of heroin users
 - Transitioning from opioid pills:
 - “Intertwined Epidemics”
 - “Every never...”



Photo: F. Montero Castrillo

Heroin treatment: Initial opioid of choice

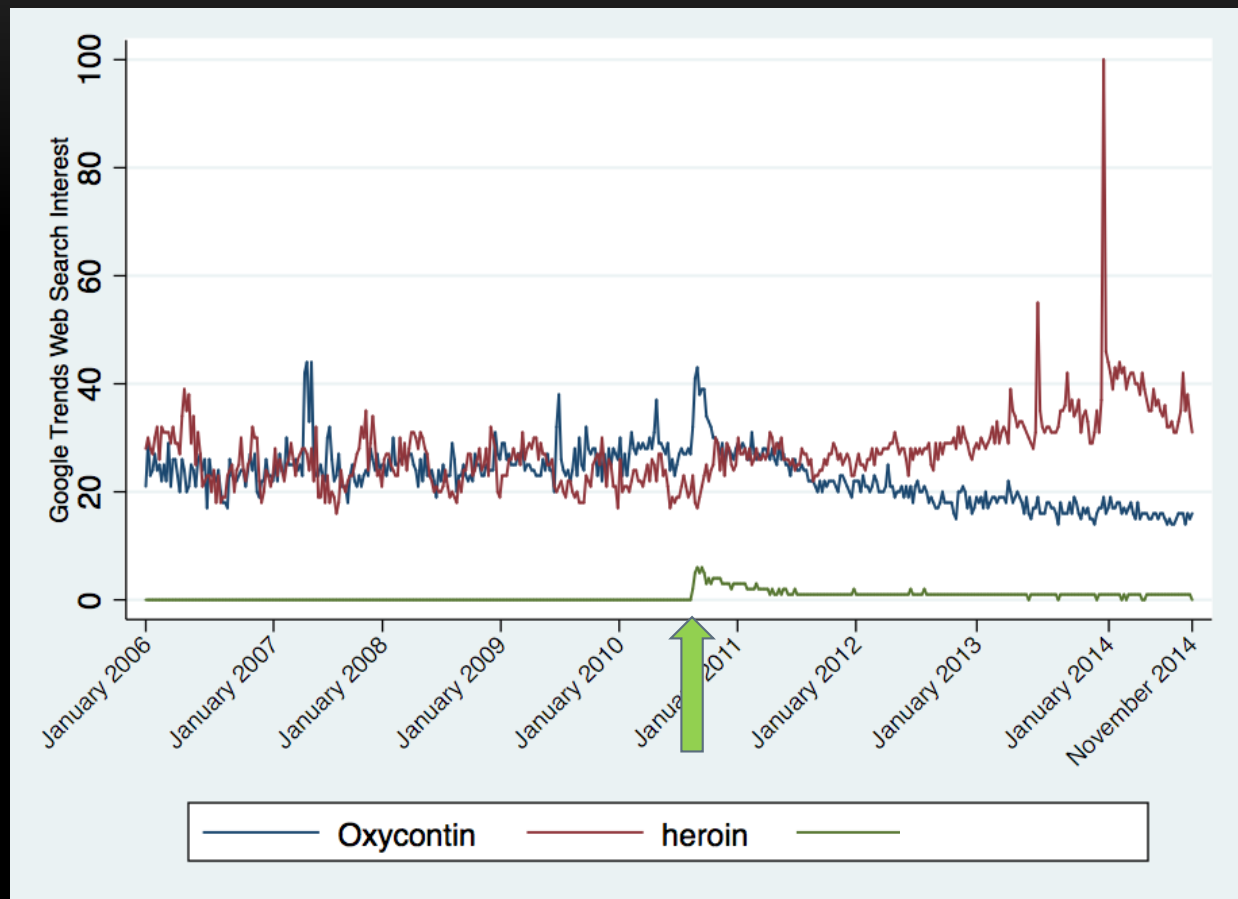
Figure 1. Percentage of the Total Heroin-Dependent Sample That Used Heroin or a Prescription Opioid as Their First Opioid of Abuse



Data are plotted as a function of the decade in which respondents initiated their opioid abuse.

Google trends: interest in OxyContin vs heroin vs _____

- US
- Health category
- Jan. 2006 to Nov. 2014



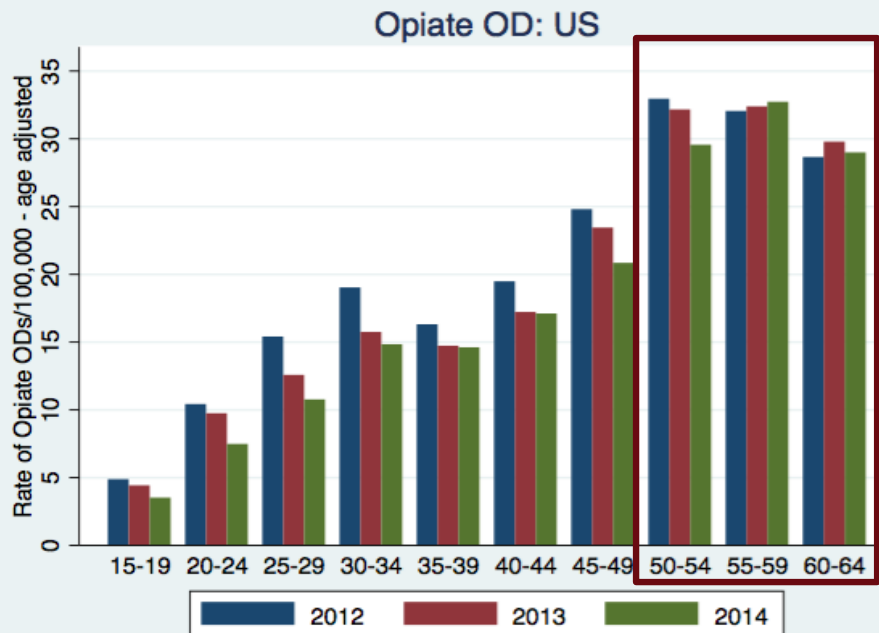
Data Source: Google Trends (www.google.com/trends)

Search: D Ciccarone, 11.3.14

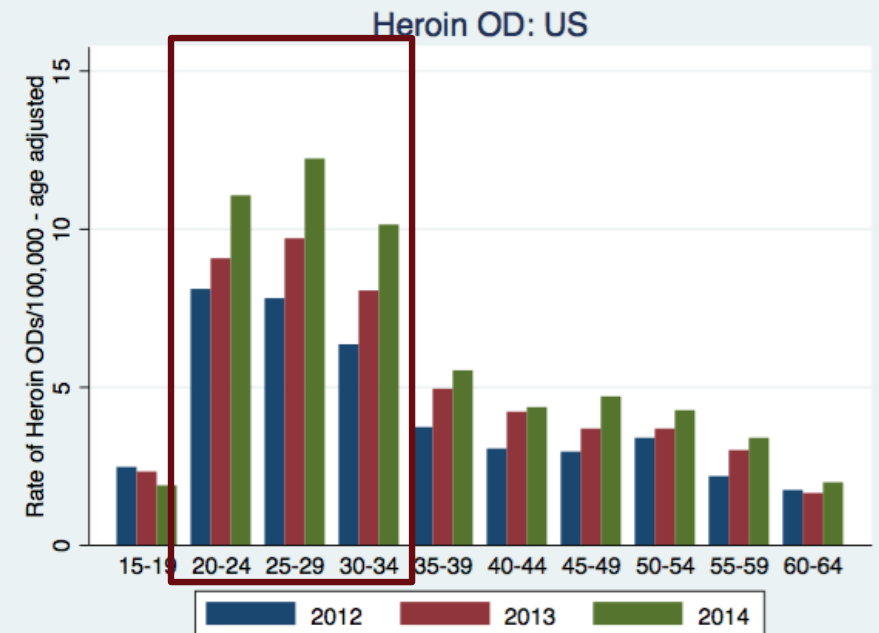
Analysis: J Unick

NIS: US OVERDOSE RATES (2012-2014) BY AGE GROUP:

Opioid overdose

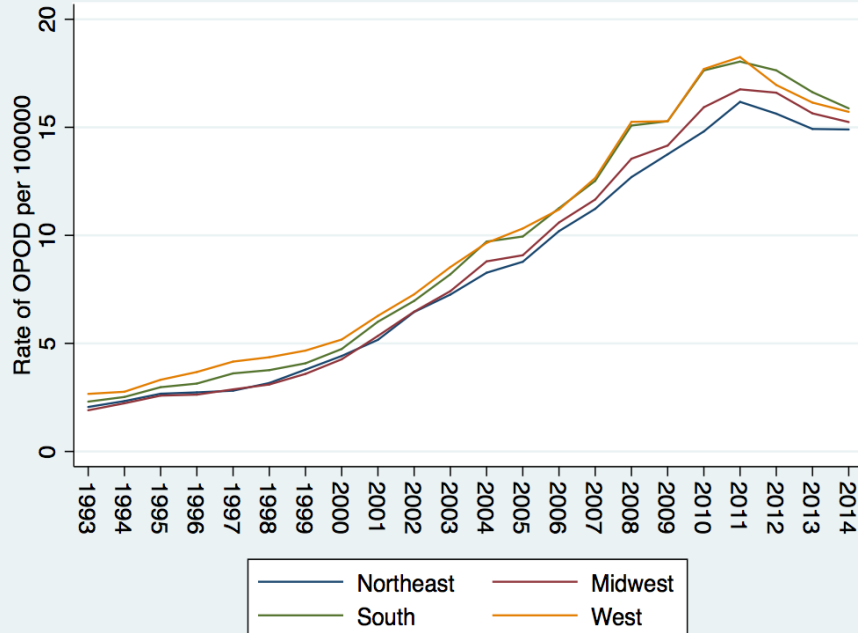


Heroin overdose

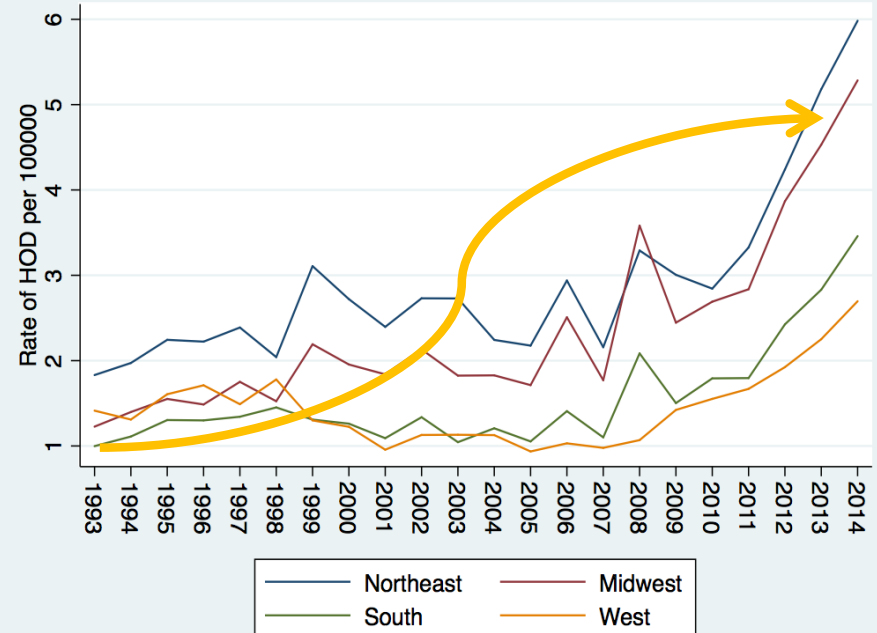


NIS: OVERDOSE RATES (1993-2014) BY GEOGRAPHIC REGION:

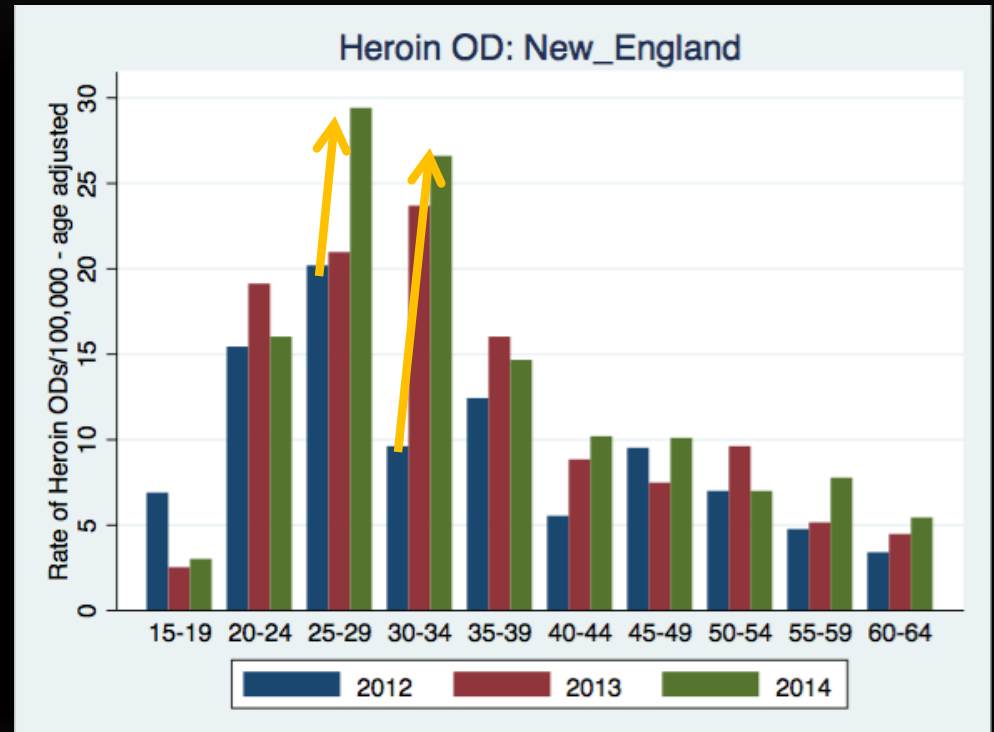
OPOD: Even –



HOD: Northeast and
Midwest!



New England: Large increases in heroin OD hospitalizations for 25-35 yo.



FUELING HEROIN-RELATED OVERDOSE

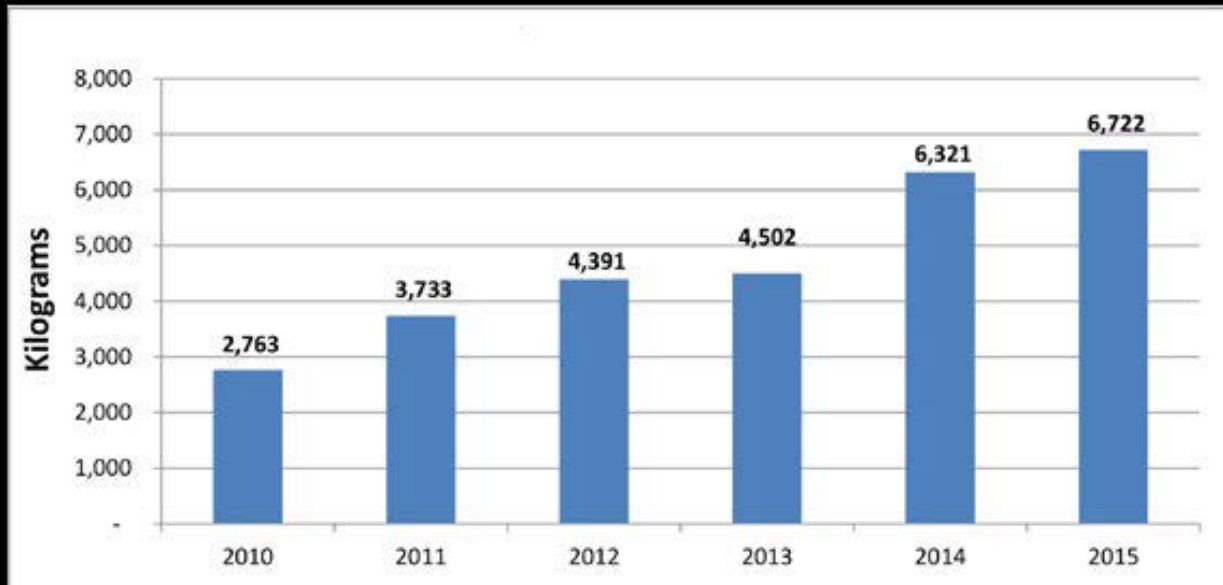
- Rising numbers of heroin users
 - Transitioning from opioid pills
- Heroin becoming more dangerous:
 - New forms
 - Adulteration



Photo: D. Ciccarone

CHANGES IN THE HEROIN SUPPLY

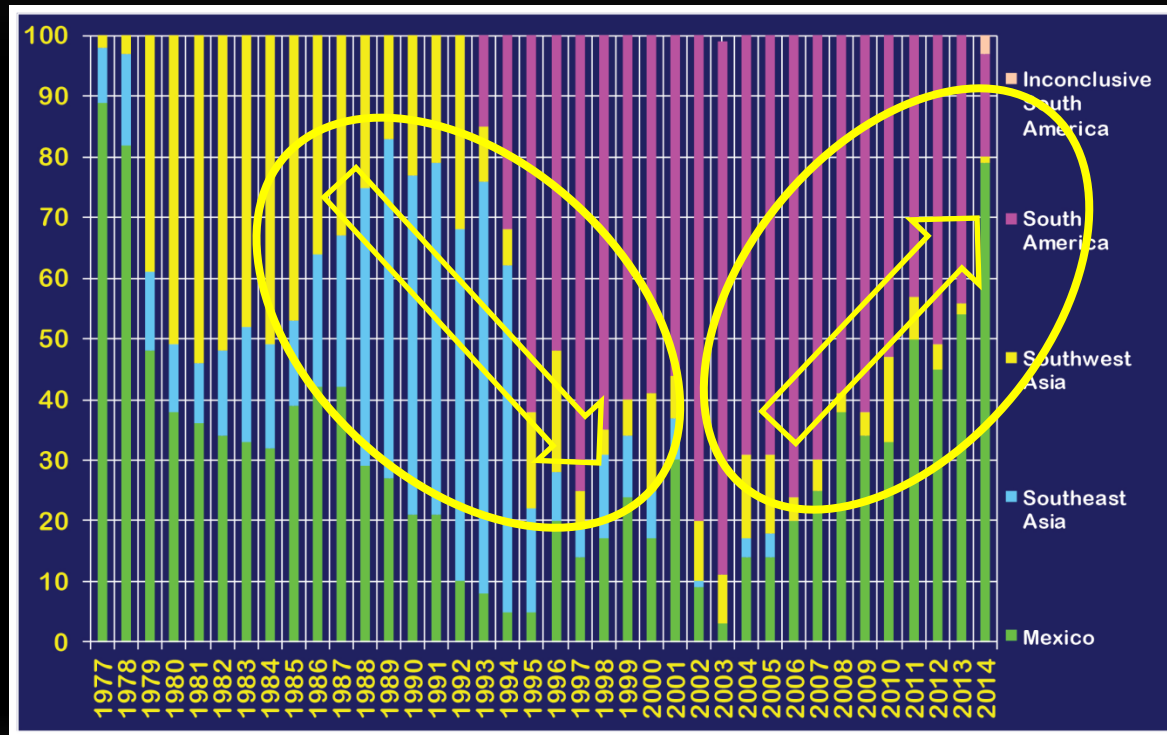
US heroin seizures are up
~ 140%, 2010-15



Source: National Seizure System. Reported in the 2016 National Heroin Threat Assessment Summary; DOJ, DEA, 2016

HEROIN SOURCES OVER TIME

- Four sources down to two
- Colombian dominant to 2010
- Now Mexican dominant: 78% in 2014



Source: Heroin Signature Program. Reported in the 2015 National Drug Threat Assessment Summary; DOJ, DEA, 2015

MEXICAN-SOURCED HEROIN: CHANGES

- Mexican opium/heroin production has grown while Colombian production is down 40%
- Explanations for rising HOD in Midwest (in addition to fentanyl):
 - A more purified product coming from Mexico
 - "Mexican White:" Colombian mimic
 - Traditional Colombian-sourced-heroin retail places
 - Synthetic adulteration > heroin "inconclusive" origin

THIRD WAVE: FENTANYL LACED HEROIN

- Integrated into heroin supply
 - Sold as 'heroin'
- 30-40x stronger than heroin by weight
- Clandestinely-produced fentanyl, not diverted pharmaceutical fentanyl*
- Analogous: Levamisole as adulterant for cocaine

*National Heroin Threat Assessment Summary, DEA, 2015



Cerilliant®

a SIGMA-ALDRICH® company

C-162-0.5ML

Lot: FC12011601

Carfentanil Oxalate
100 µg/mL (as free base)
in 0.5 mL Methanol

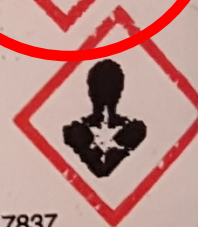
Expires: See COA

Freezer

USDEA Exempt



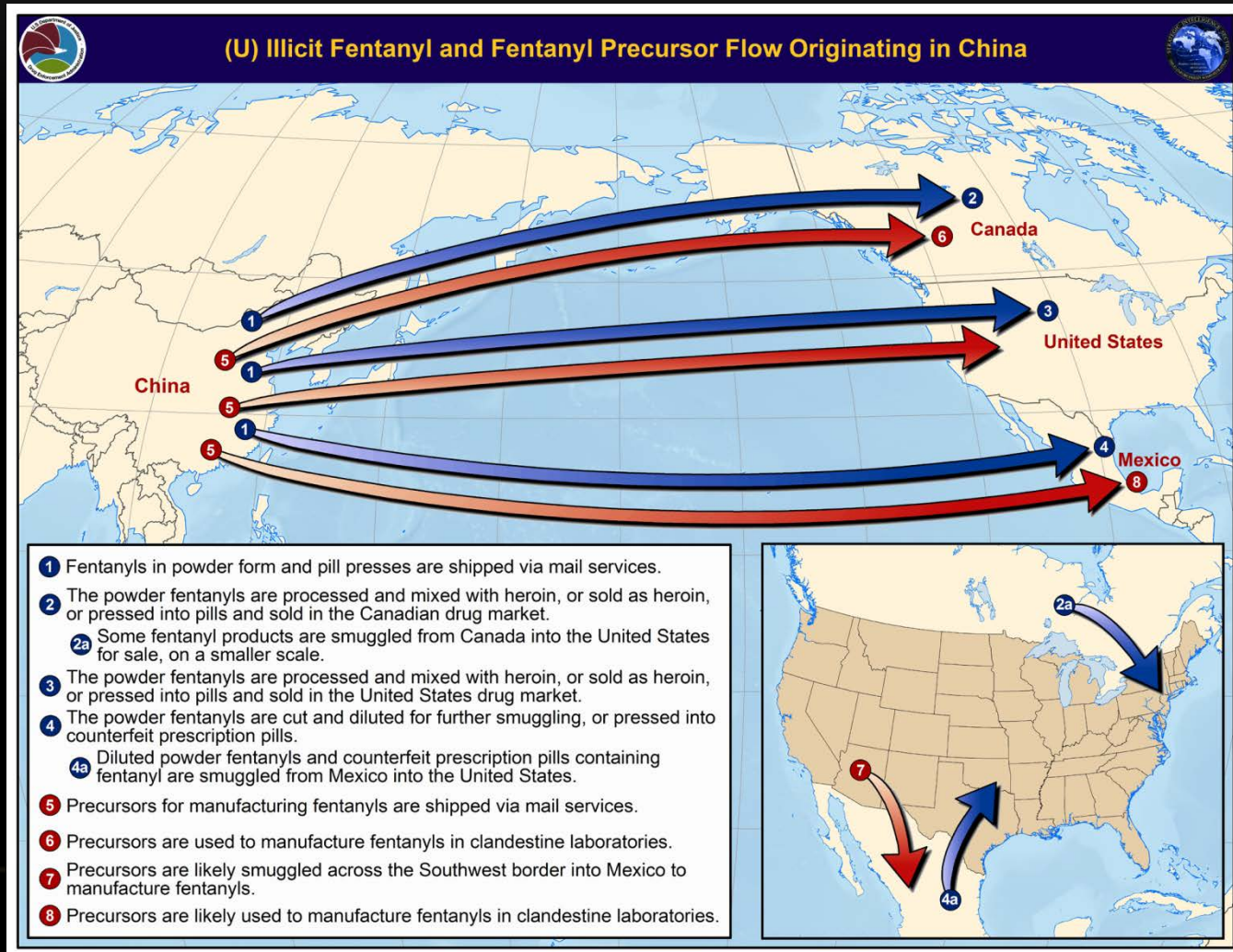
811 Paloma Dr., Suite A, Round Rock, TX, USA, 78665, 800.848.7837



LIFT

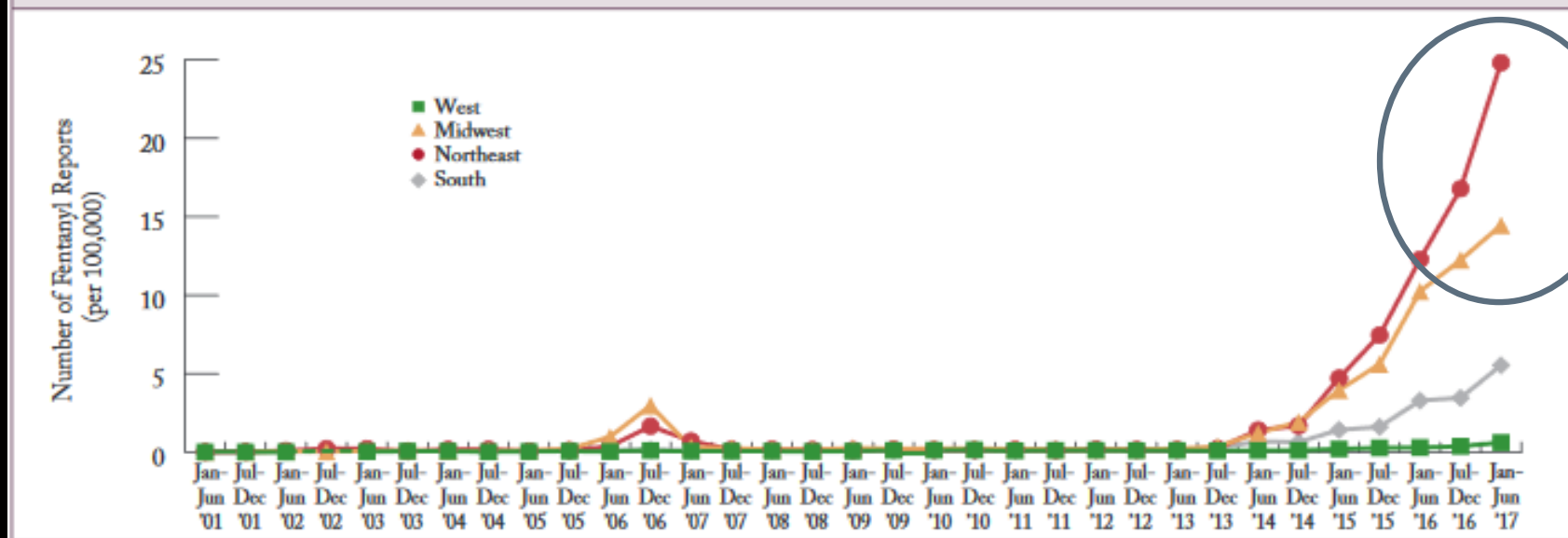
Photo: D. Ciccarone

FLOW OF FENTANYLS



NFLIS: Fentanyl

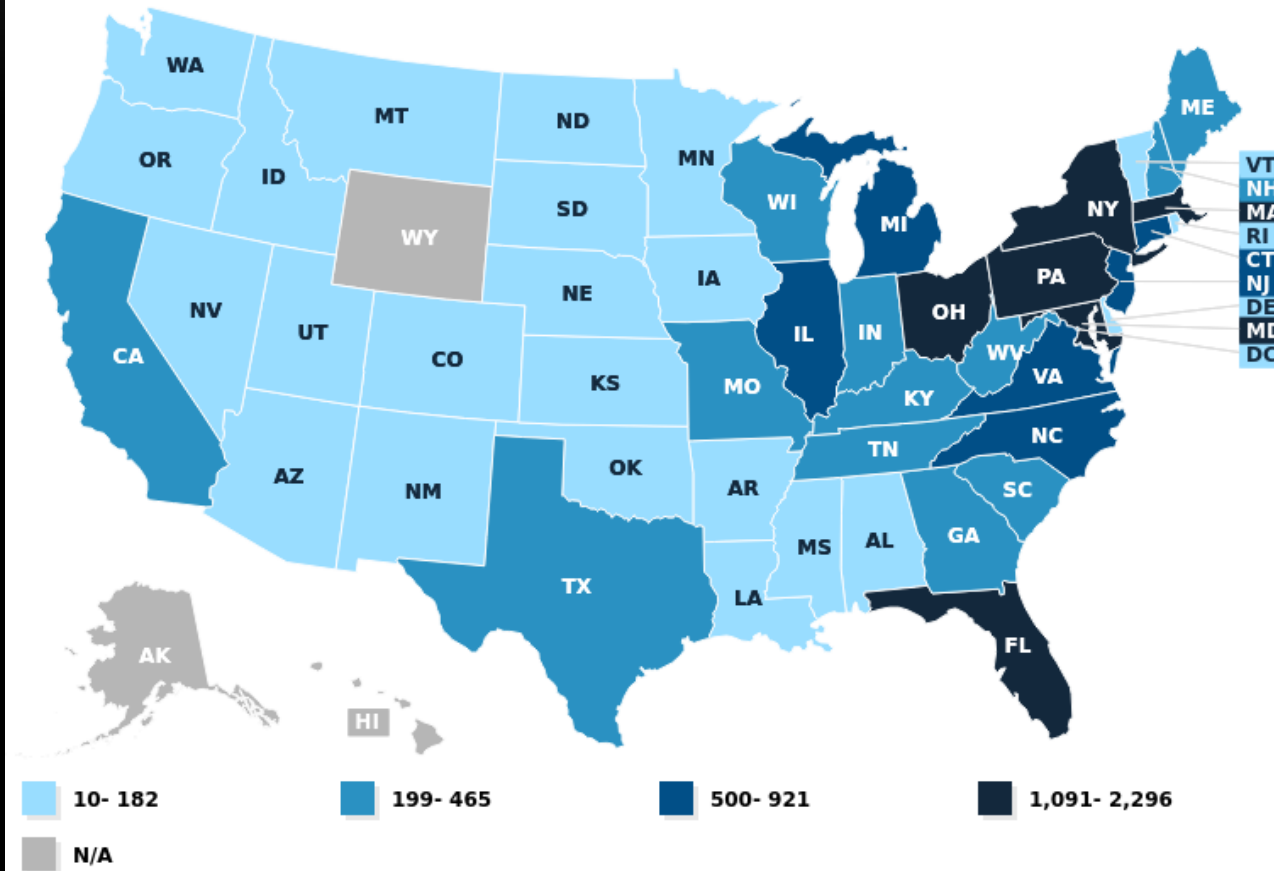
Figure 1.5 Regional trends in fentanyl reported per 100,000 persons aged 15 or older, January 2001–June 2017¹



NATIONAL FORENSIC LABORATORY INFORMATION SYSTEM. NFIS-DRUG 2017 Mid-year Report.
Office of Diversion Control, DOJ, DEA. April 2018

SYNTHETIC OPIOIDS: REGIONAL PROBLEM

Opioid Overdose Deaths by Type of Opioid: Synthetic Opioids, other than Methadone (e.g. fentanyl, tramadol), 2016



SOURCE: Kaiser Family Foundation's State Health Facts.



Photo: D. Ciccarone

OTHER CONSEQUENCES

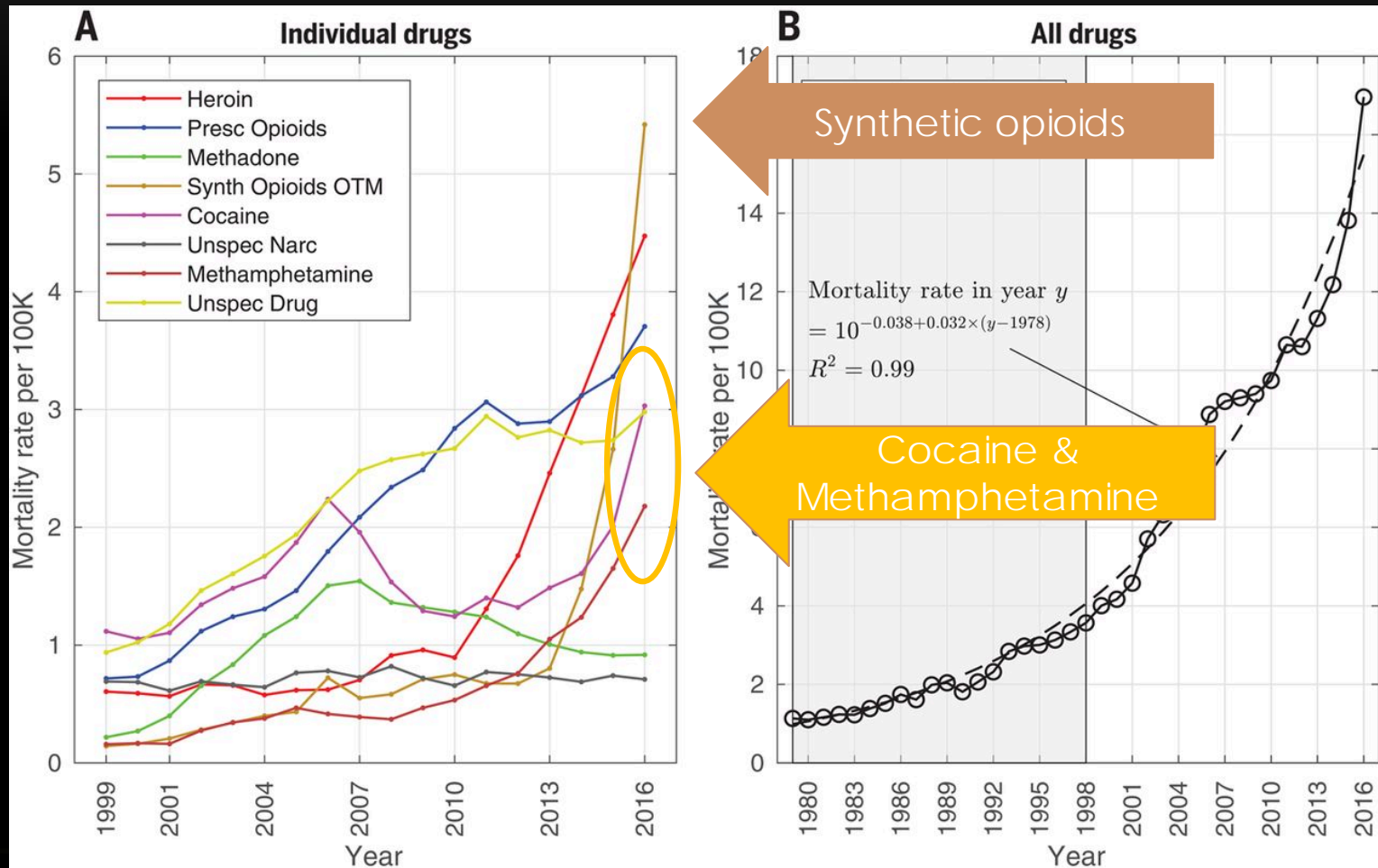
- Infectious disease
 - Blood borne viruses:
 - Hepatitis C virus
 - HIV – Scott County, IN
 - Bacterial:
 - Endocarditis
 - Skin and soft tissue infections



WHAT IF WE DON'T ADDRESS ROOT CAUSES?

- Balloon effects
- Next drug cycle

WAVE FOUR: STIMULANTS AND POLYDRUG USE



Credit: Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. Jalal, Buchanich, Roberts, Balmert, Zhang and Burke. *Science* 21 Sep 2018



Living
2 Pray
4 Wisdom
2 Love myself
2 Know 2 Love
U-Living 2 Learn
The Music 2 express
My Love 4U 2U
UR the 1 right here
that I AM 2 Love
There is no greater
Purpose
I can conceive
Come N2 my Love
May we Create
The Spirit of Peace
give Peace 2 the World
it all goes back
to GOD

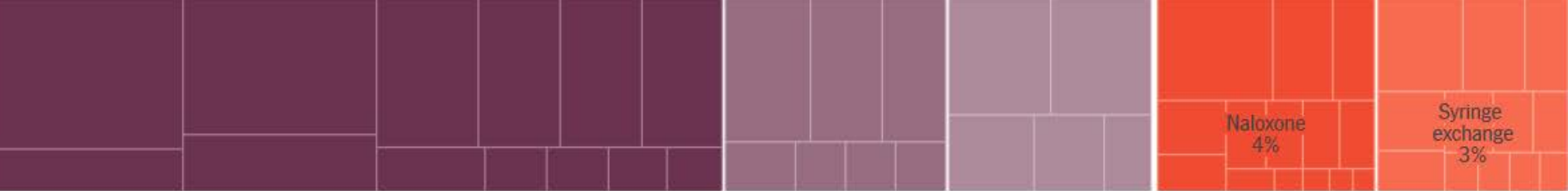
Siddha Sila
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CRISIS RESPONSE

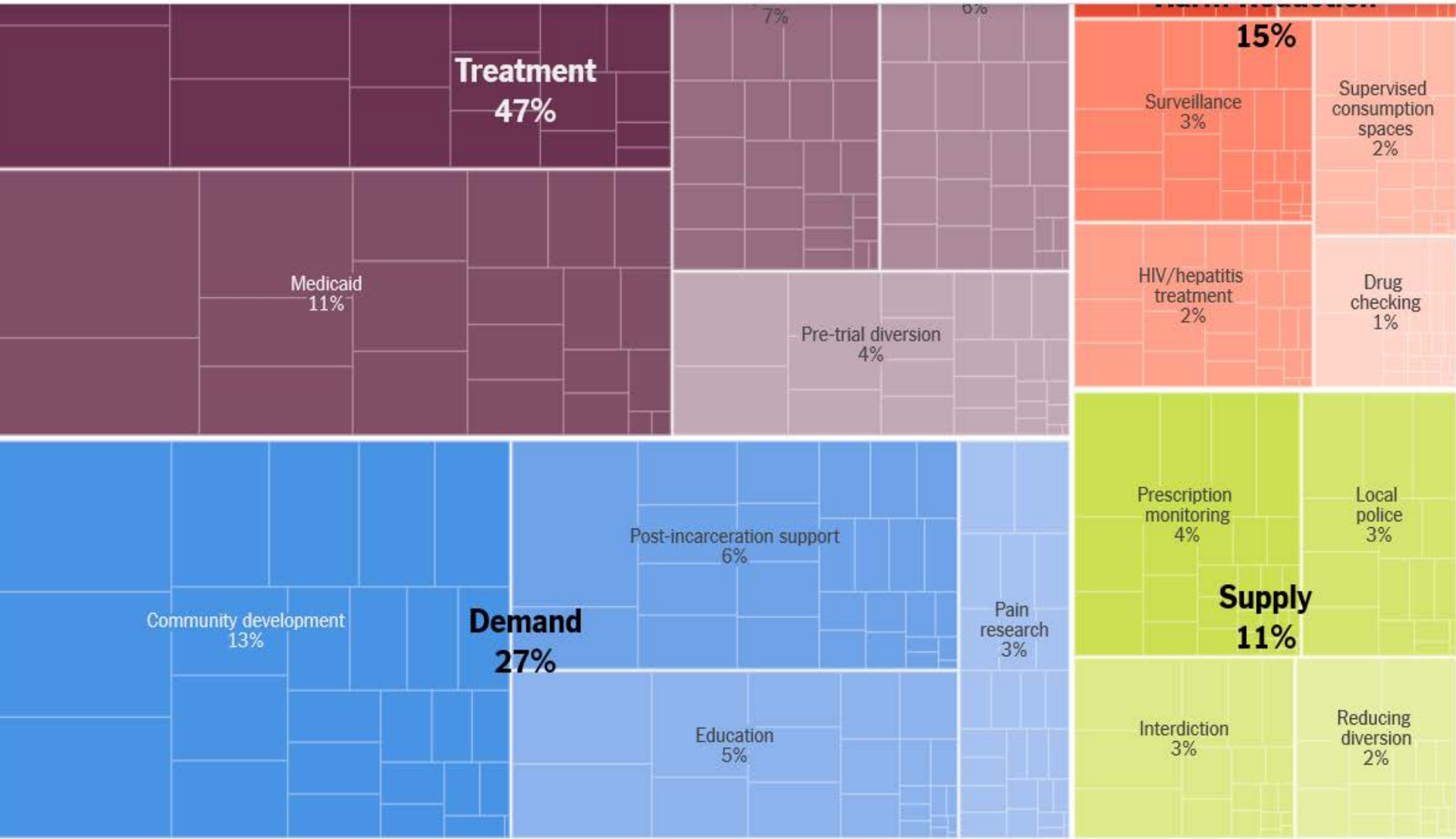
- Triple wave epidemic is unprecedented
 - Worst in decades, perhaps a century
 - Momentum
 - Root causes not addressed
 - Lack of coordinated robust response
 - Stigma, shame

CRISIS RESPONSE

- Comprehensive solution is needed:
 - Supply reduction
 - Demand reduction
 - Harm reduction
 - Community resilience
 - Economic, social, spiritual development
 - ACEs
-



THE UPSHOT | How a Police Chief, a Governor and a Sociologist Would Spend \$100 Billion to Solve the Opioid Crisis



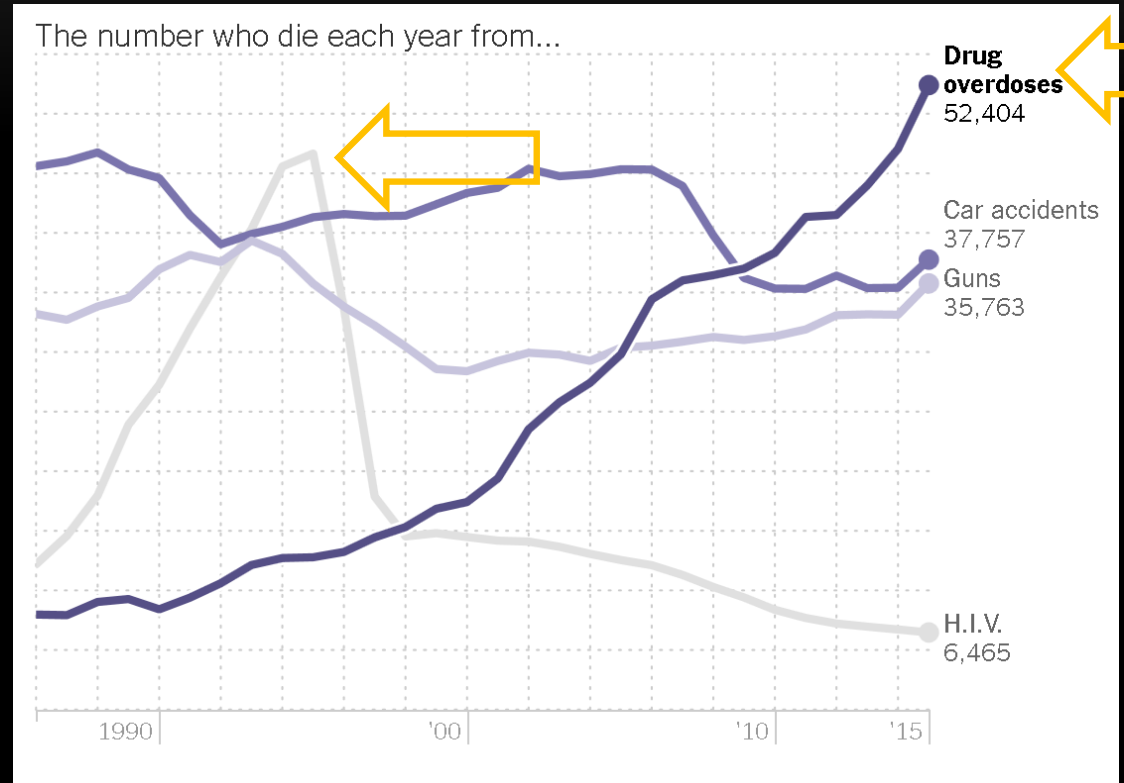


CRISIS RESPONSE

- Stigma remains our biggest enemy
 - Anti-stigma programs helped in the HIV crisis
- Public safety – Public health collaborations
 - Innovations across the country

An Epidemic of Crisis Proportion

- Crisis with Epic Opportunity
- Treatment and Prevention can work!



Source: New York Times, The Upshot; Josh Katz; April 14, 2017

ACKNOWLEDGEMENTS

- 👉 Heroin in Transition study:
 - 👉 HIT team: Sarah Mars, Jay Unick, Jeff Ondocsin, Eliza Wheeler, Mary Howe, Fernando Castillo, Philippe Bourgois, Dan Rosenblum
 - 👉 NIH/NIDA funding: R01DA037820
- 👉 Chicago:
 - 👉 Dan Bigg, Chicago Recovery Alliance
- 👉 Baltimore City Health Dept.
 - 👉 Mishka Terplan, Derrick Hunt, Jeffrey Long and NEP staff
- 👉 Massachusetts:
 - 👉 Gary Langis, Harry Leno, Irving
- 👉 West Virginia:
 - 👉 Mike Brumage, Tina Ramirez;
 - 👉 Staff and volunteers at Kanawha-Charleston Health Dept.
- 👉 Participants!
- 👉 Photo credits: Dan Ciccarone, Fernando Castillo

