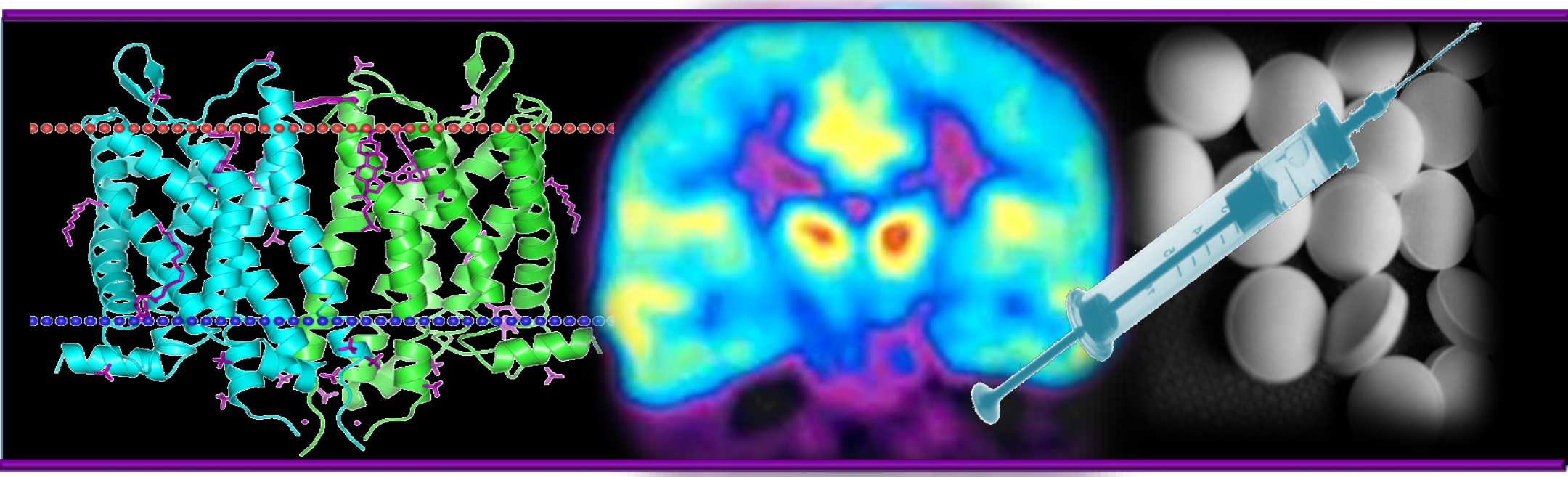
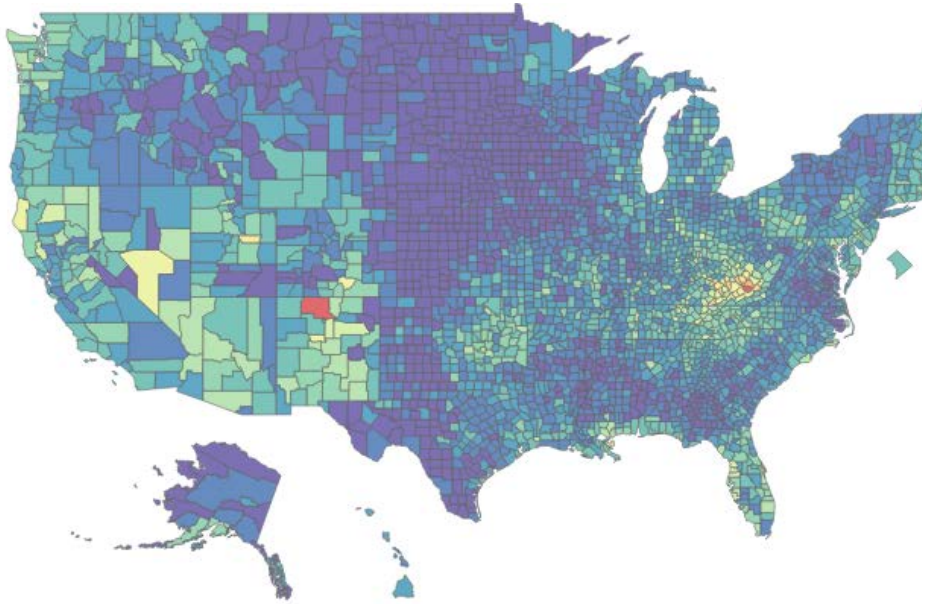
Addressing the Opioid Crisis
(and other Drug Abuse-Related Issues)
Solutions from Science



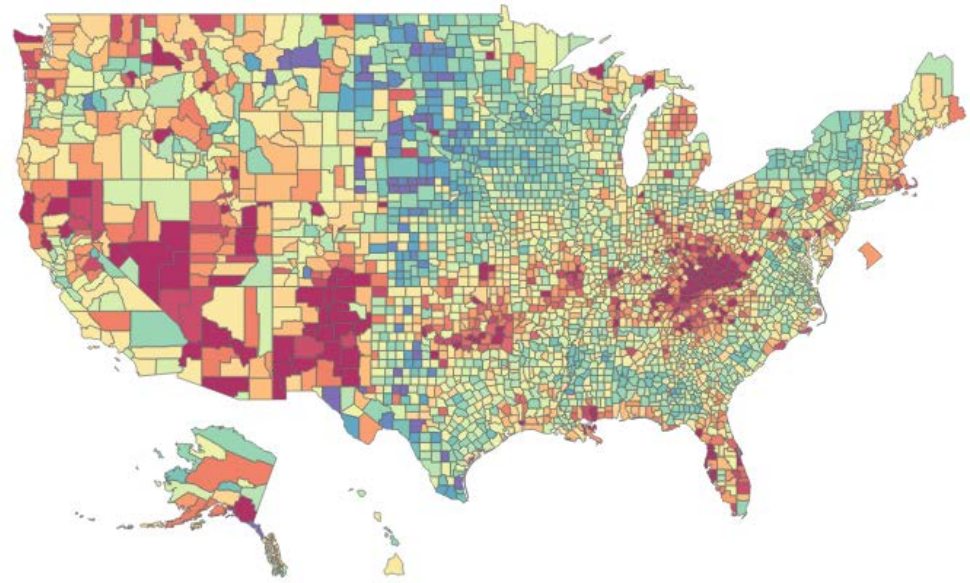
Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse
@NIDAnews

Overdose Death Rates

1999



2016



Legend for estimated age-adjusted death rate (per 100,000 population)

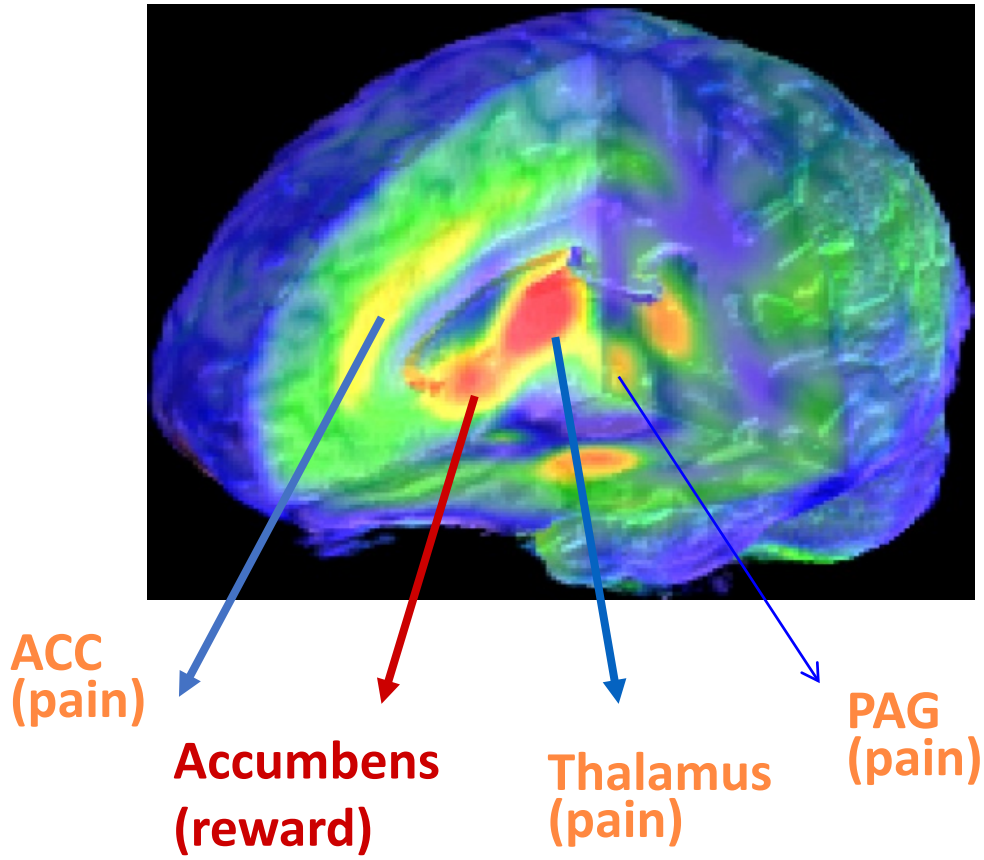
<2	8-9.9	16-17.9	24-25.9
2-3.9	10-11.9	18-19.9	26-27.9
4-5.9	12-13.9	20-21.9	28-29.9
6-7.9	14-15.9	22-23.9	30+

Select Year

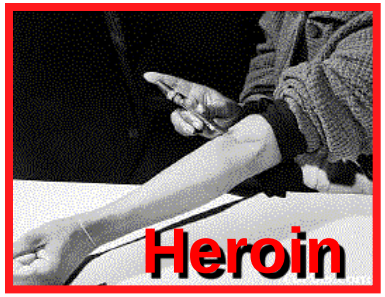
2016

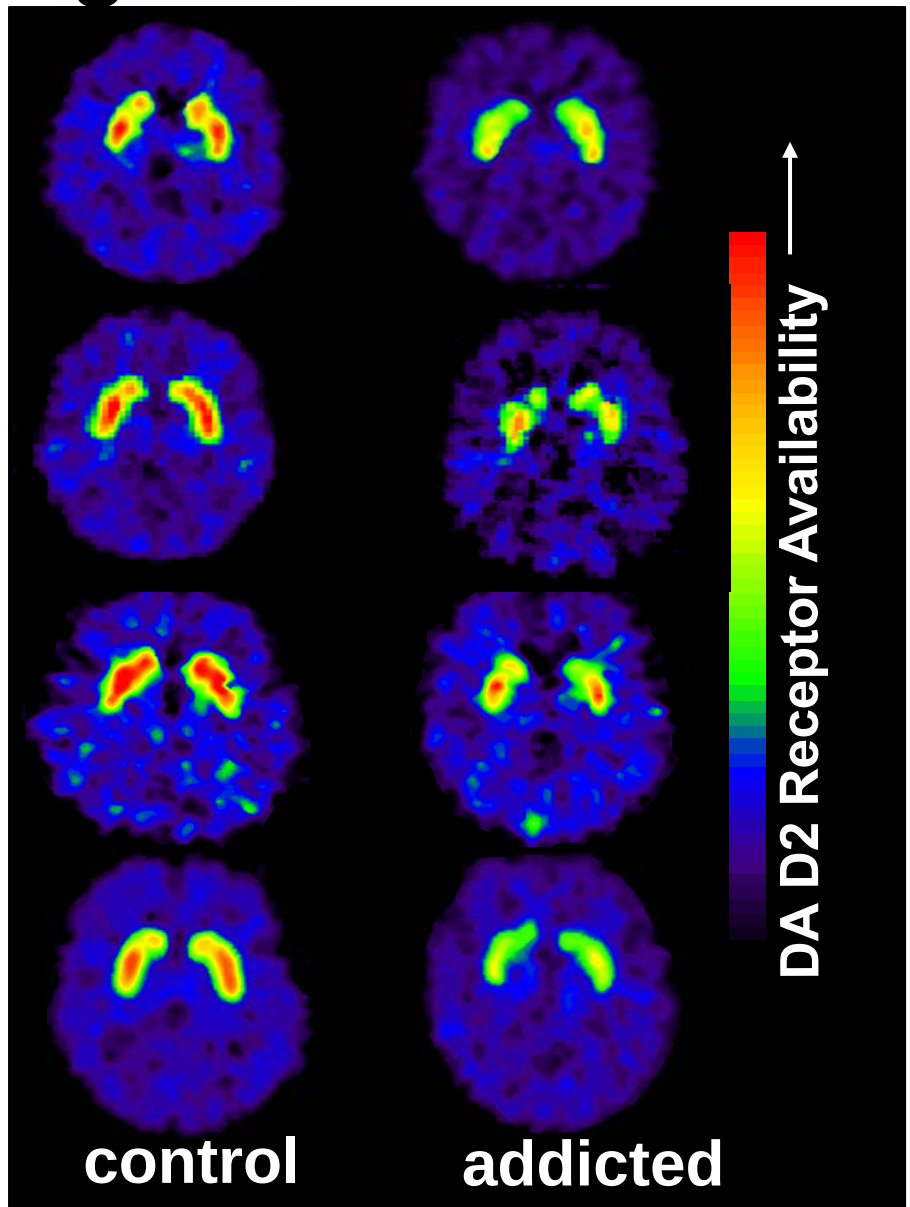
Source: https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/index.htm

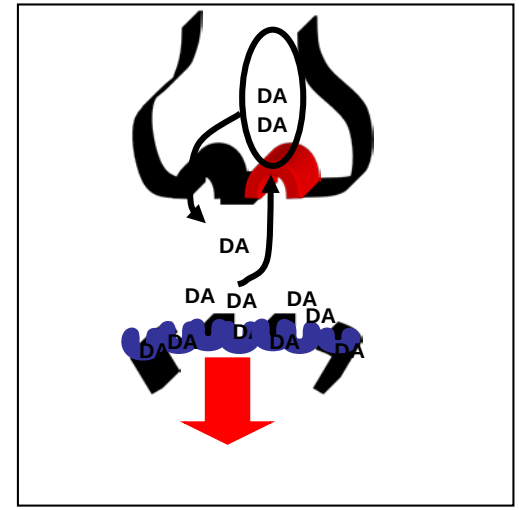
Analgesic & Reward Mechanisms of Mu Opiate Drugs (Heroin, Vicodin, Morphine)



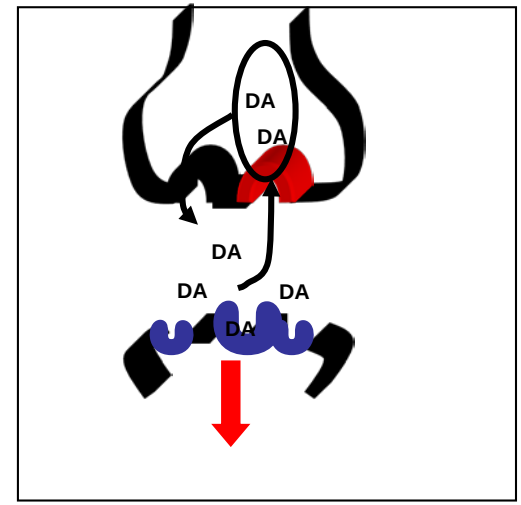
Decreased Levels of DA D2 Receptors in Drug Addicted Individuals







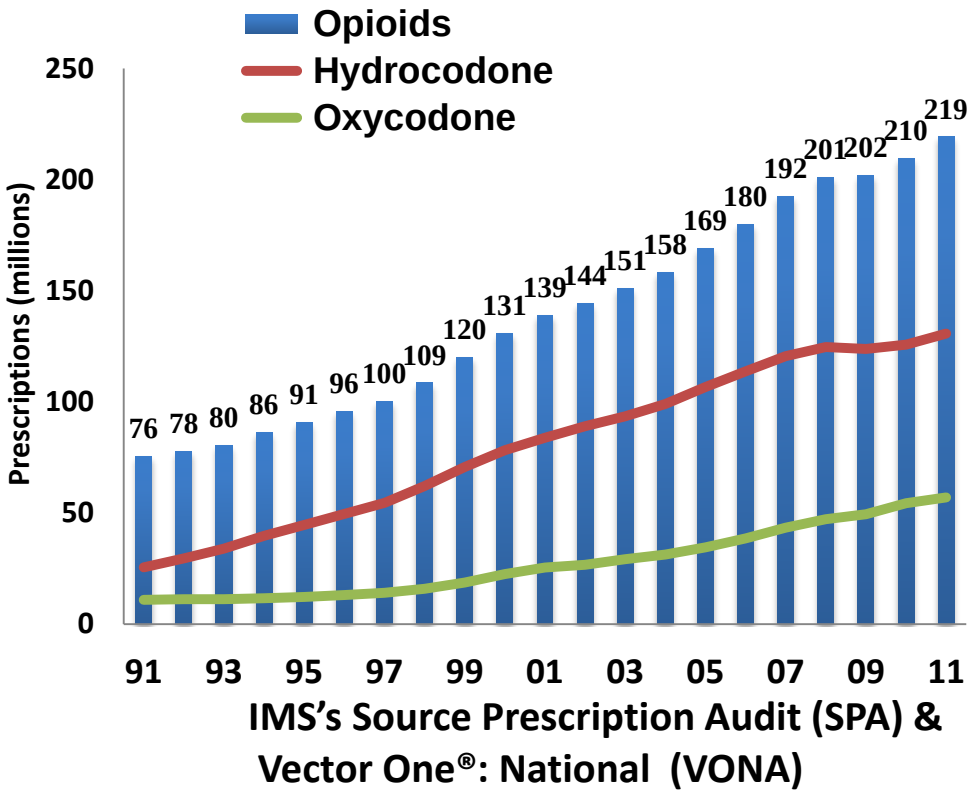
Non-Drug Abuser



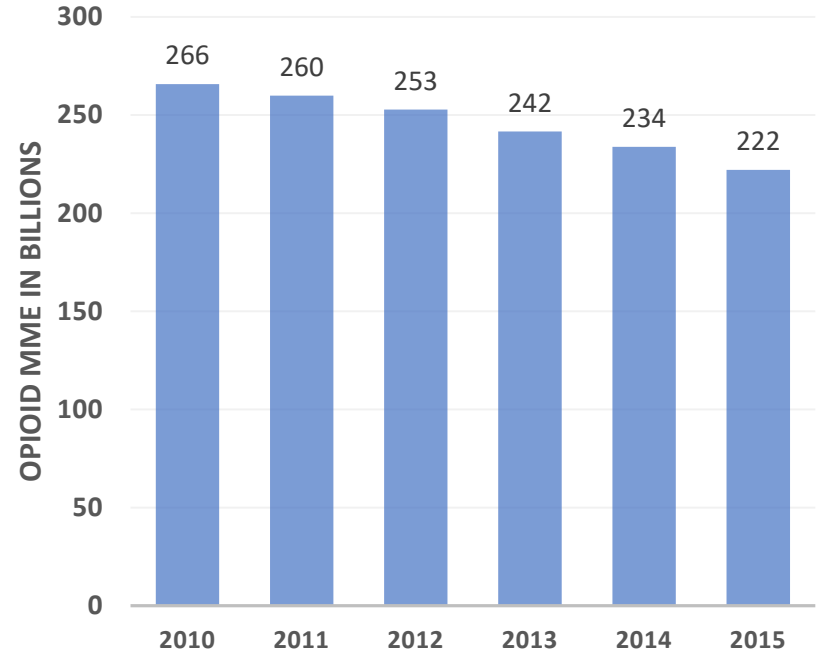
Drug Abuser

Volkow et al., PNAS 2011

Opioid Prescriptions 1991-2011

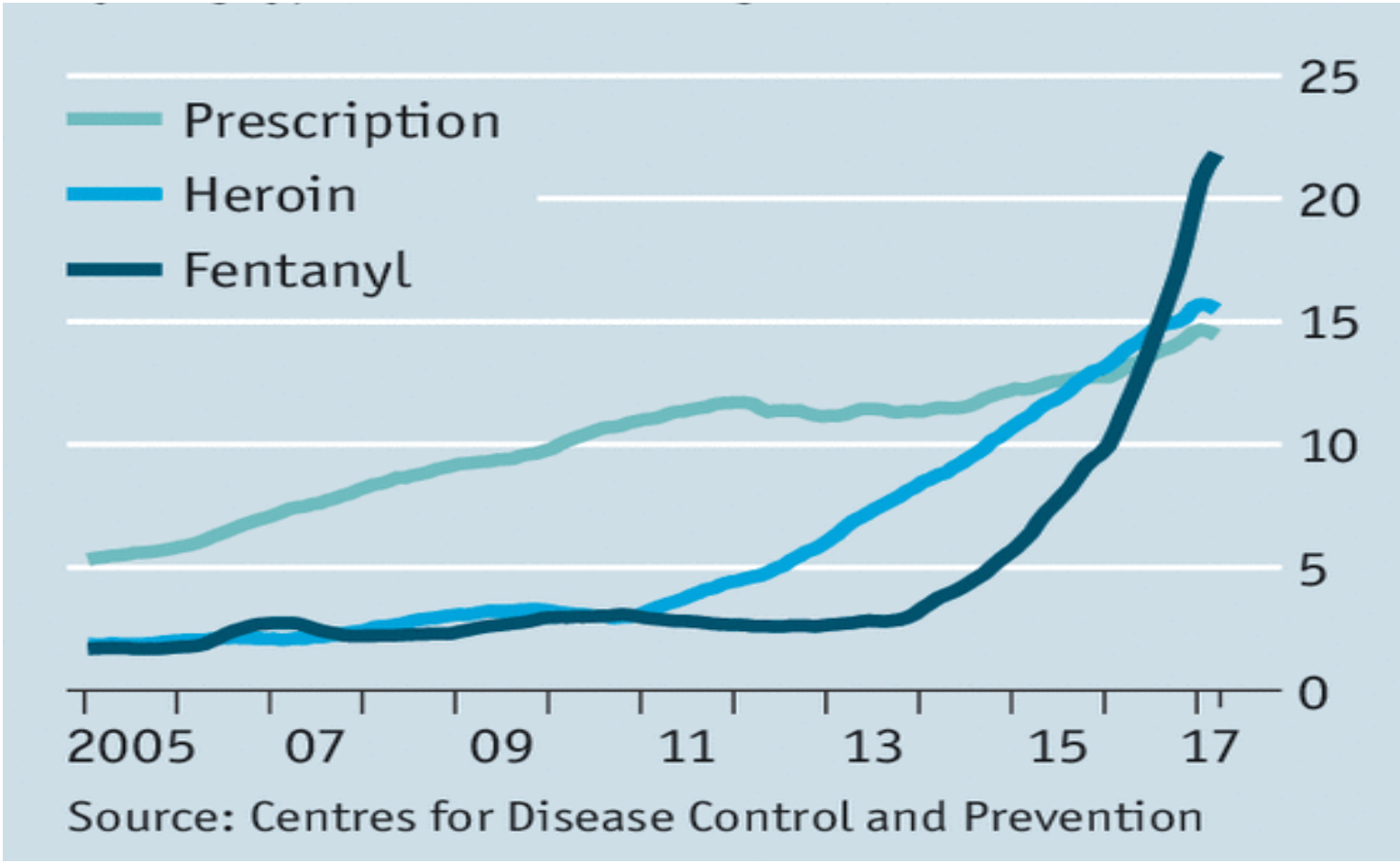


Opioid morphine milligram equivalents (MME) dispensed fell by over 15% from 2010-2015



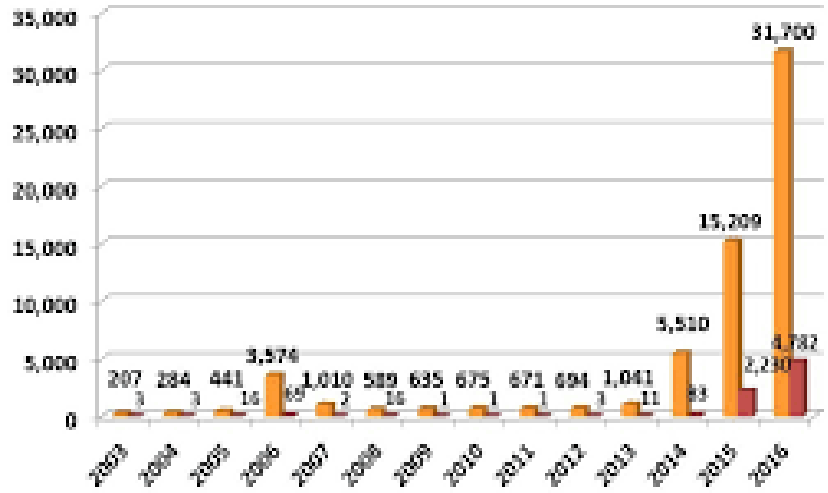
IMS Health, U.S. Outpatient Retail Setting

Evolution of the Opioid Crisis



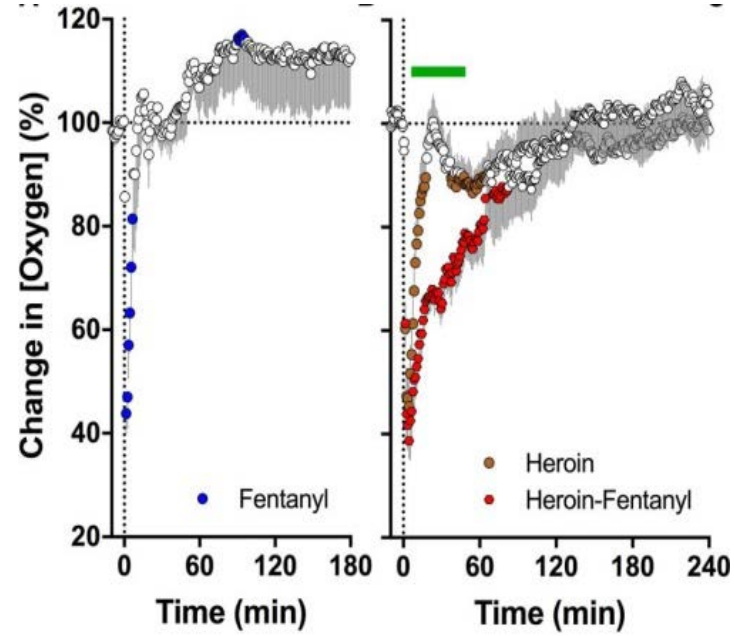
1. Over prescription of opioid medications led to misuse
2. Addiction to prescription opioids led to heroin
3. Emergence of fentanyl(s), with higher potency and greater profitability in the black market than heroin.

More Than Double of the Drugs Seized by DEA Tested Positive for Fentanyl from 2015 to 2016



National Forensic Laboratory Information System (NFLIS).
Fentanyl ORANGE
Fentanyl analogues RED

Heroin Contaminated with Fentanyl Dramatically Enhances Brain Hypoxia



Solis et al., 2017, eNeuro

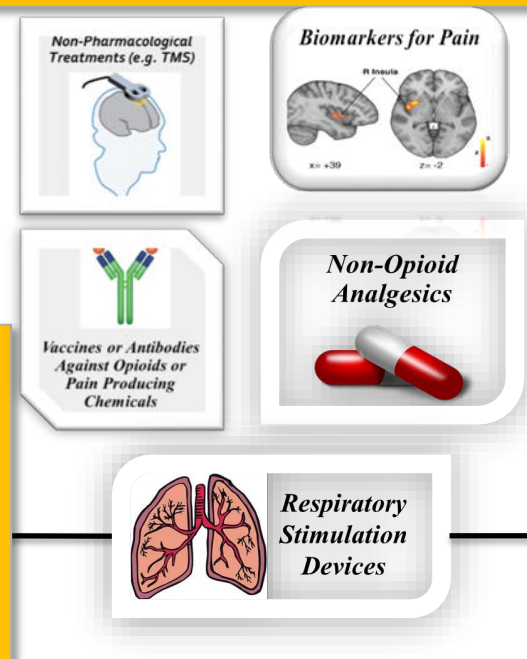
Fentanyl's higher potency contributes to its lethality and when combined with heroin this might enhance their toxicity

NIH OPIOID RESEARCH INITIATIVE

Using Research to End the Opioid Crisis

PAIN MANAGEMENT

Safe, more effective strategies



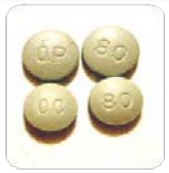
OPIOID ADDICTION TREATMENT

New and innovative medications and technologies

OVERDOSE REVERSAL

Interventions to reduce mortality and link to treatment

Safe, More Effective Strategies for Pain Management

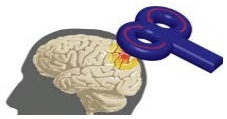


Non-Opioid Analgesics
Cannabinoids;
Inflammatory mediators;
Ion channel blockers

Targeted Opioid Analgesics
with reduced potential for addiction and overdose

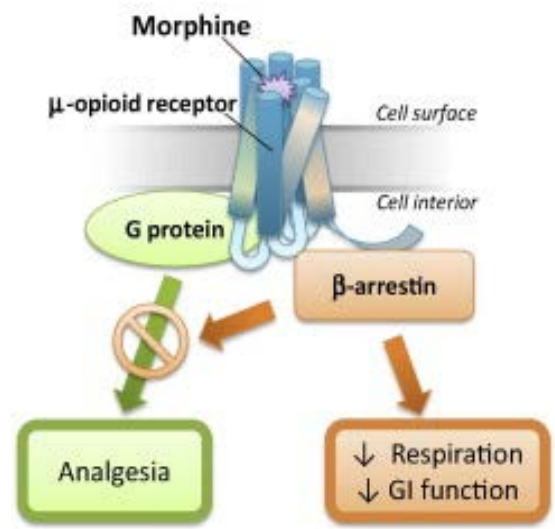
Biologics
e.g. antibodies that bind to pain producing cytokines

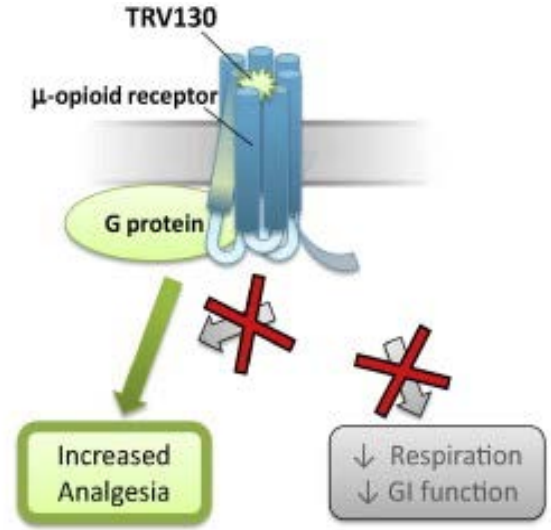
Non-pharmacological treatment



Neural stimulation;
Surgical interventions;
Meditation

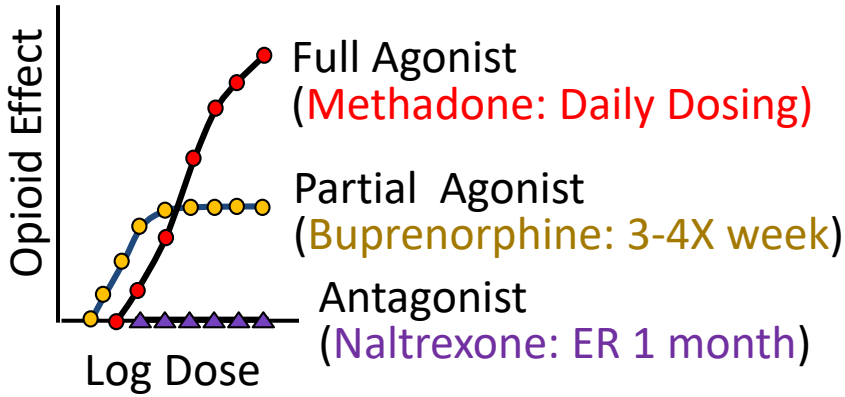
Biased Mu-Opioid Receptor Ligands: New Generation Of Pain Therapeutics





Soergel DG et al., Pain 2014; 155(9):1829–1835.

Medication Assisted Treatment (MAT)



DECREASES:

- **Opioid use**
- **Opioid-related overdose deaths**
- **Criminal activity**
- **Infectious disease transmission**

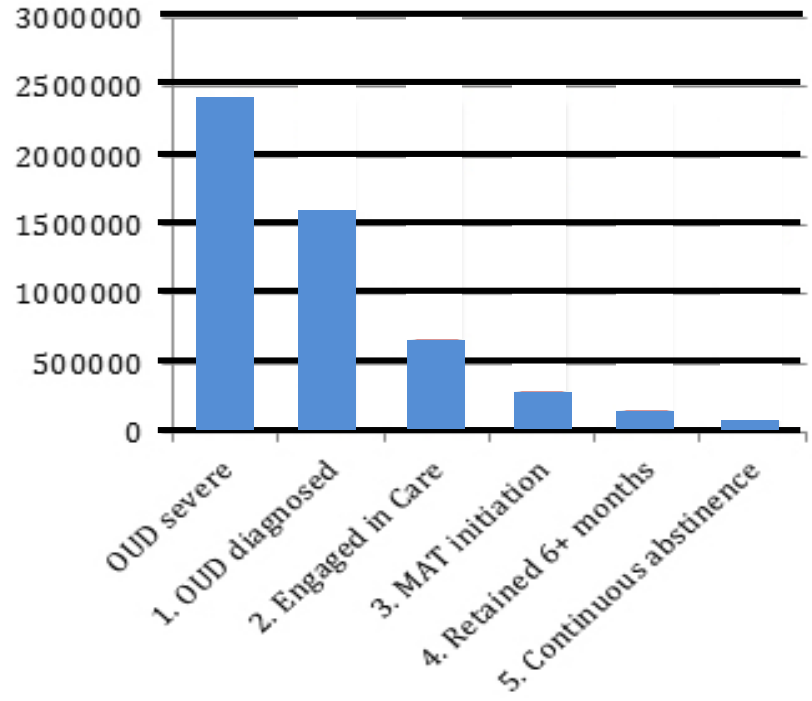
INCREASES

- **Social functioning**
- **Retention in treatment**

MAT is highly underutilized!

Relapse rates are very high (50% in 6 months)

OUD Cascade of Care in USA



Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017

Expand access to MAT

Healthcare system

Criminal Justice system

Medication development

Extended release formulations

Drug combinations

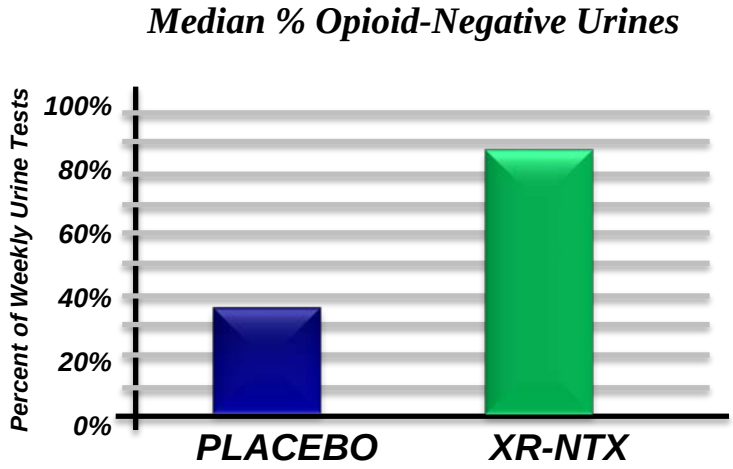
New Targets, Vaccines others

Extended Release Formulations

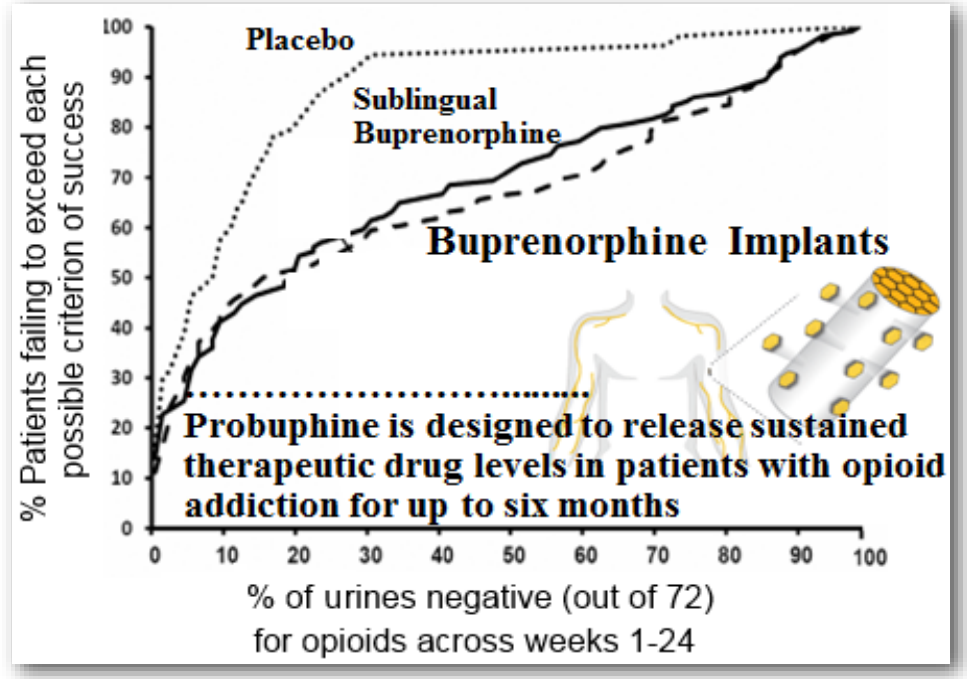
- **Vivitrol®**

- **PROBUPHINE®**

IM Injection q 4 weeks for 24 weeks



Krupitzky et al., Lancet 2011



Rosenthal et al., Addiction 2013;105.

FDA approval – May 26, 2016

Opportunities for Partnership in the Development of Longer Acting Formulations and/or Drug Combinations to Improve Treatment Compliance and Retention

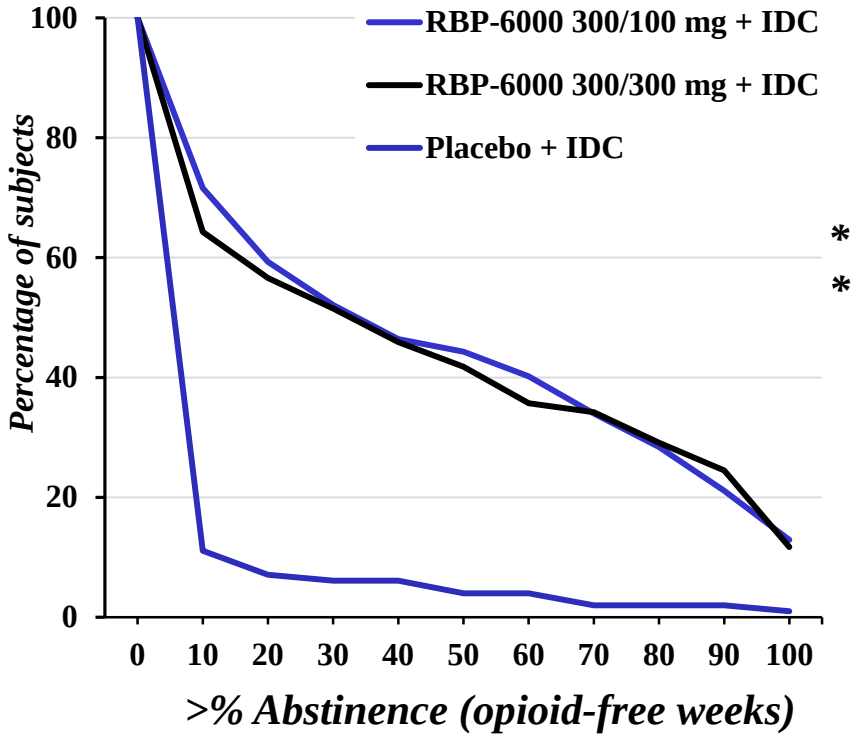
SUBLOCADE™ (Buprenorphine ER), Once-Month Injectable

FDA Approval 11.30.2017

CAM2038: Subcutaneous ER Buprenorphine

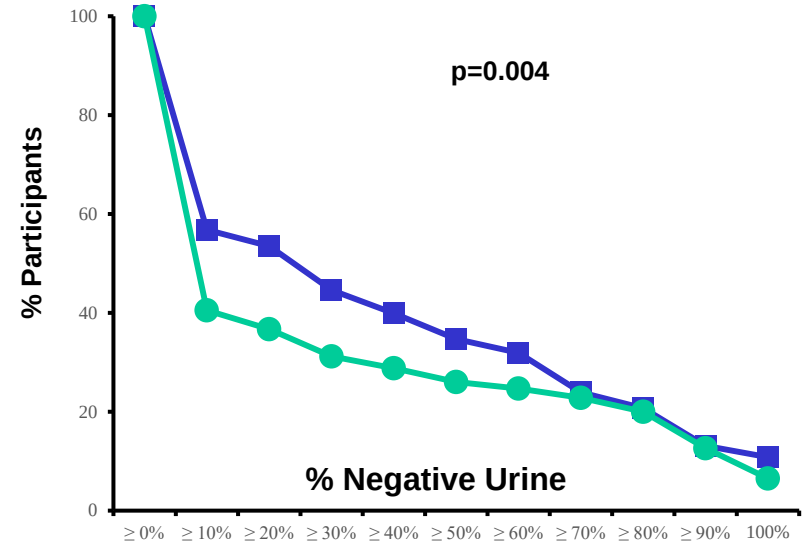
Weekly or monthly injection

% urine samples negative for opioids (Weeks 5 to 24)



Heidbreder et al., CPDD 2017

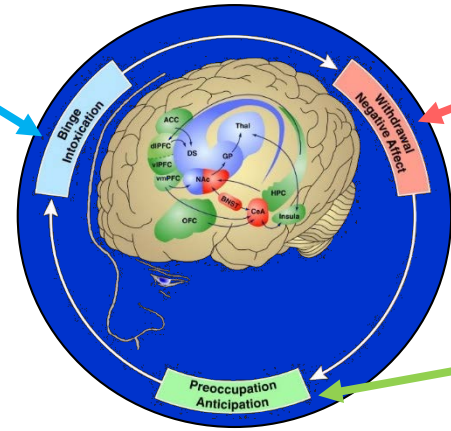
Comparison CAM2038 versus Daily SL BPN



braeburn

Target Selection on the Basis of the Neurocircuitry of Addiction

Targets to interfere with drug reward



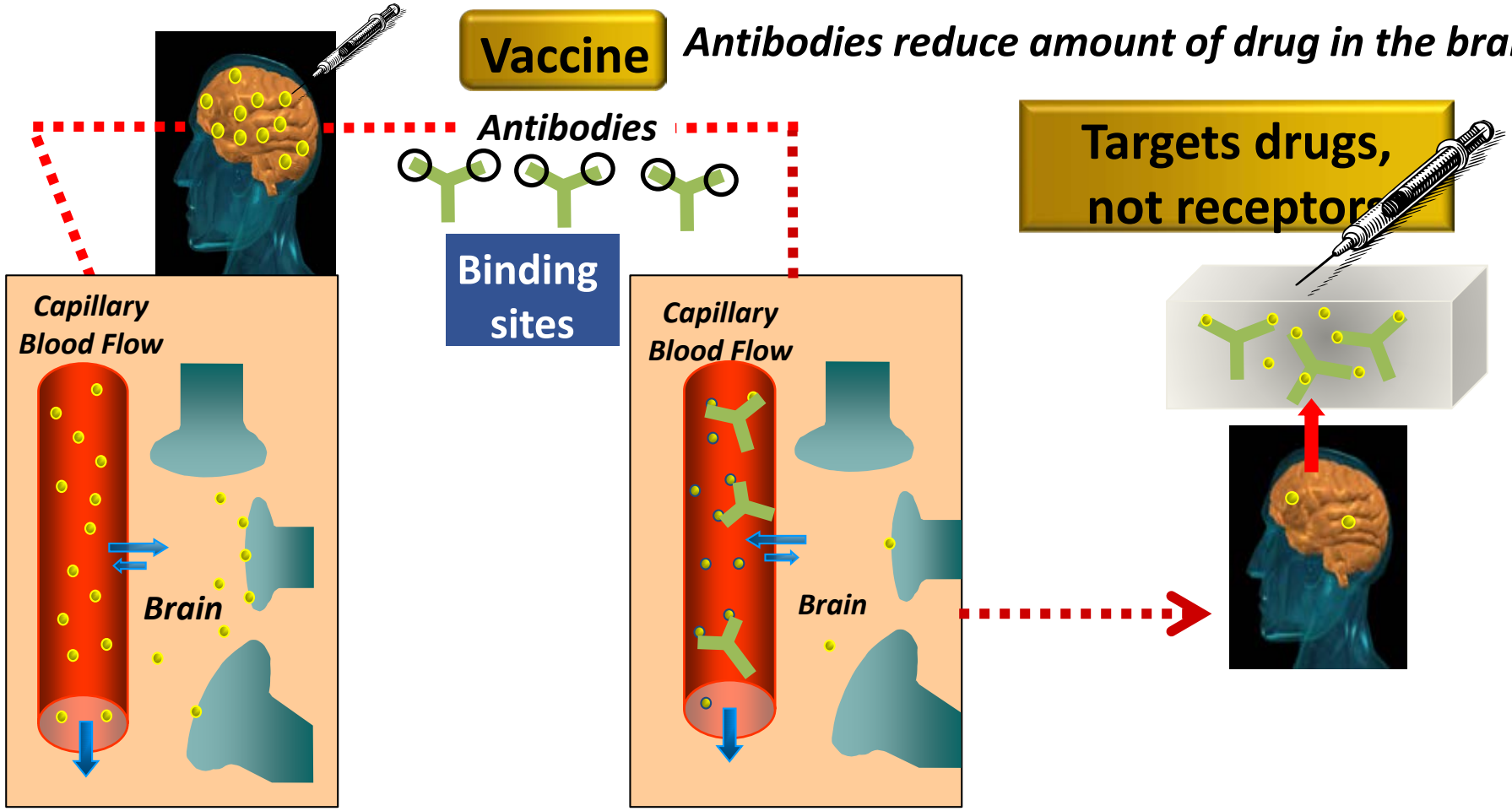
Targets to reduce stress-induced drug seeking and to improve mood

Targets to reduce cue-induced drug seeking and to improve executive function

Diagram: Koob GF, Volkow ND. Neuropsychopharmacol Rev, 2010

Compounds targeted to neurocircuitry could be beneficial not just to addiction but also to diseases for which such circuits are disrupted (i.e., ADHD, depression)

Immunotherapies for Opioid Use Disorder



Hwang et al., Efficacious Vaccine against Heroin Contaminated with Fentanyl. ACS Chem. Neurosci. 2018

Expand access to MAT

Healthcare system

Criminal Justice system

Medication development

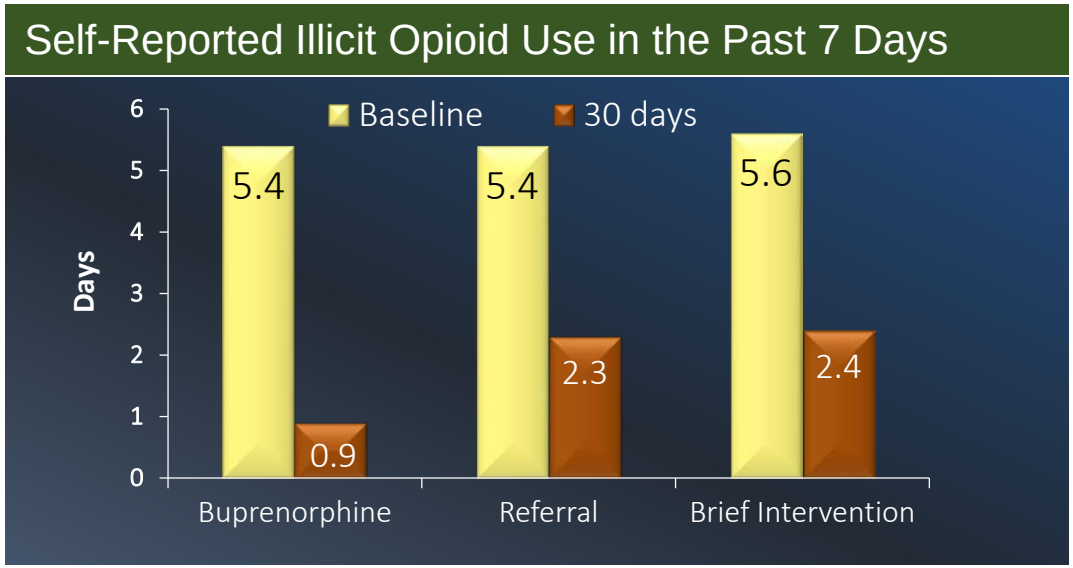
Extended release formulations

Drug combinations

New Targets, Vaccines others

Improving Treatments for Addiction: Implementing Medication-Assisted Treatment

- Emergency department-initiated buprenorphine
  - Reduced self-reported, illicit opioid use
  - Increased engagement in addiction treatment; decreased use of inpatient addiction treatment services



JAMA

Original Investigation

April 28, 2015 Volume 313

Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence

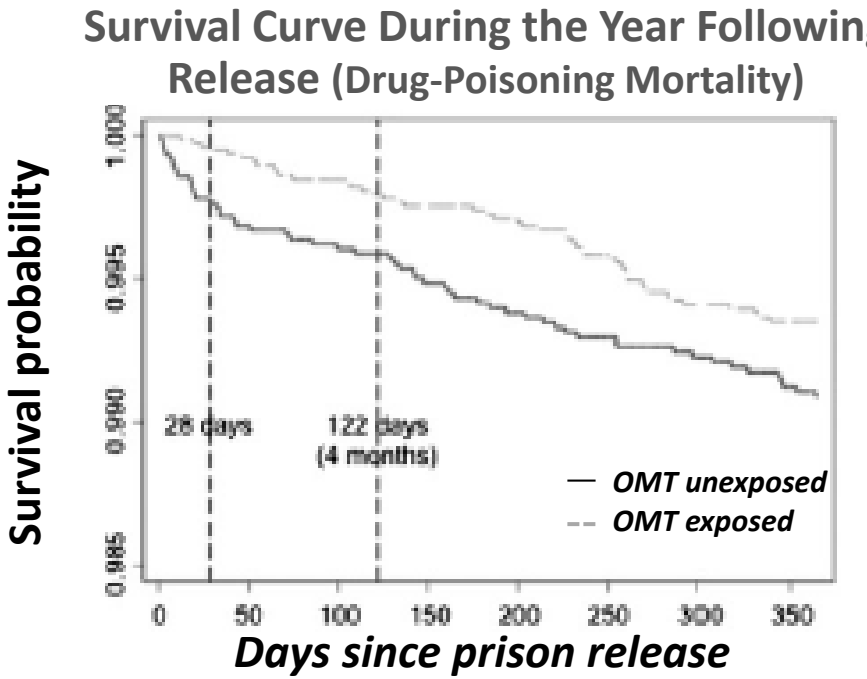
A Randomized Clinical Trial

Gail D'Onofrio, MD, MS; Patrick G. O'Connor, MD, MPH; Michael V. Pantalon, PhD; Marek C. Chawarski, PhD; Susan H. Busch, PhD; Patricia H. Owens, MS; Steven L. Bernstein, MD; David A. Fiellin, MD

D'Onofrio G et al., JAMA April 28, 2015.

Opioid Medication Therapy (OMT) In Prison

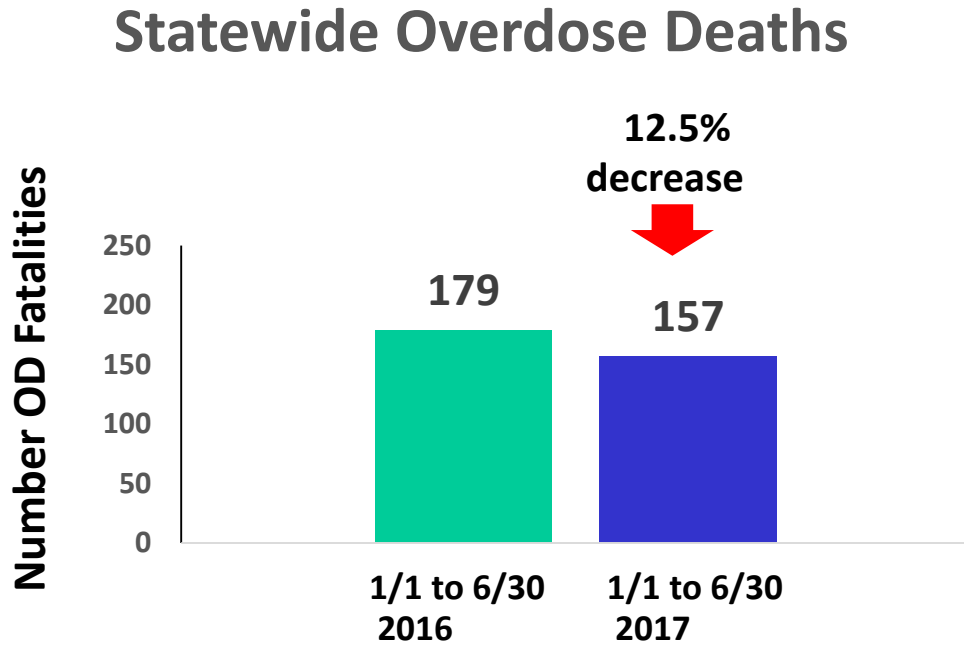
Mortality Post Release



OMT resulted in a 75% reduction in mortality (85% reduction in overdoses) in the first month post release

Marsden J et al., Addiction 2017; 112:1408-1418.

Postincarceration Overdose Deaths After Implementing OMT in a Statewide Correctional System (Rhode Island)



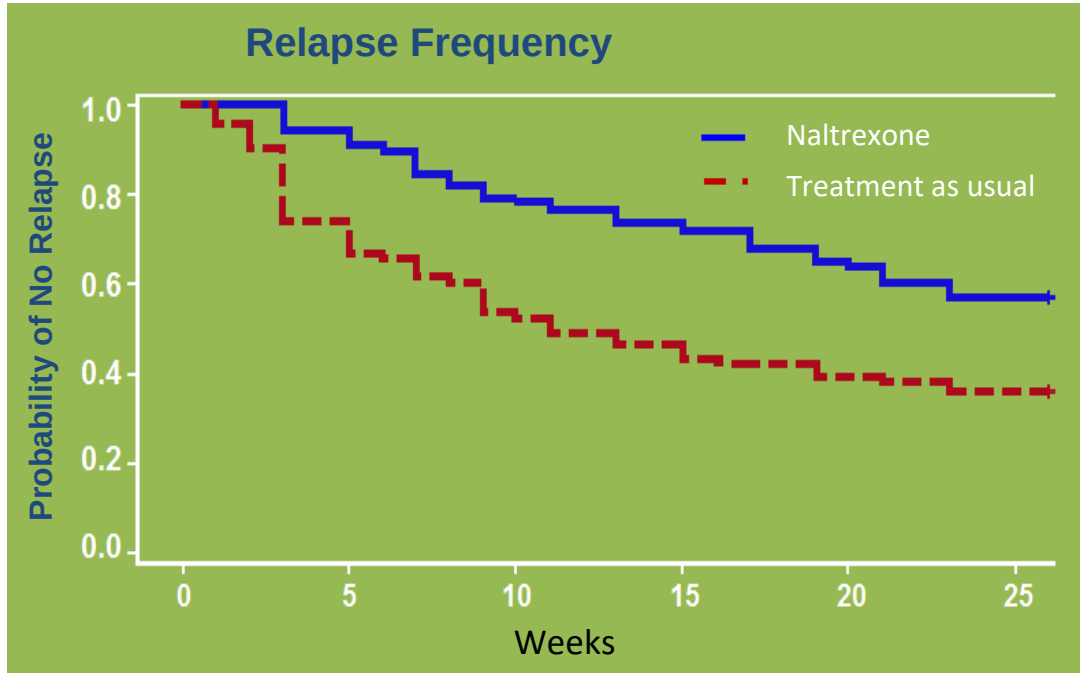
OD fatalities in those who had been incarcerated in 2017 decreased by 60% compared to 2016 (5.7% vs 14.5%)

Green TC and Clarke J. JAMA Psychiatry 2018;75(4).

Improving Treatments for Addiction:

Naltrexone Trial in CJ Populations

- *Participants:* parolees/probationers with opioid addiction – all v*olunteers* – received either
  - –Monthly injections of extended release naltrexone for 6 months
  - –Community treatment, including methadone or Suboxone (encouraged)



Overdoses in 78 weeks:

Control: 7
Naltrexone: 0

Lee et al. NEJM March 31, 2016.

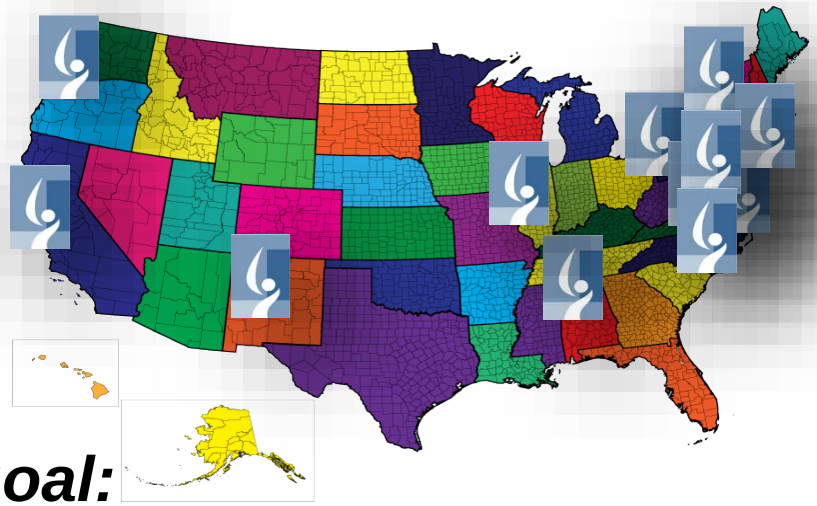
Education

PAIN

NIH Pain Consortium Centers of Excellence in Pain Education

ORWH NIA
OBSSR NINR
NIDA NICHD
NIDCR NIAMS
NINDS NCCIH

CoEPEs
CENTERS OF EXCELLENCE IN PAIN EDUCATION



Goal:
Improve pain treatment through education

SUD

Centers of Excellence for Physician Information

Goal:
Prevent SUD and improve outcomes in addiction through education of health care providers

New NIH Initiative to Address the Crisis:
HEAL: *Helping to End Addiction Long-term*

- Collaborative, cross-cutting research
  - From basic to behavioral – and everything between
  - Innovative partnerships – across agencies, sectors, organizations – will ensure rapid progress
- $500M just added by Congress
  - **Adds to $600M** current funds = $1.1B for FY18
  - Will propel HEAL
- Advances national priorities for pain, addiction research…

NIH Pain Consortium

Federal Pain Research Strategy

National Pain Strategy
A Comprehensive Population Health-Level Strategy for Pain

NIH HEAL Initiative: Some Priorities

Prevention

- Understand Origins of Chronic Pain
- Develop New Non-Addictive Treatments for Pain
- Build Clinical Trial Network for Chronic Pain
- Enhance Precision Pain Management

Treatment

- Improve Therapeutic Approaches to Addiction
- Evaluate Treatments, Consequences of NOWS
- ***Optimize Effective Treatments through Pilot Demonstration Projects***

NIH Public Private Partnership To Address the Opioid Crisis

Focus Area A: Enhance medications for OUD and to prevent/reverse overdoses

- Develop *new formulations* and *combinations of medications* to treat OUD and to prevent overdoses
- Develop *more potent* or *longer lasting opioid antagonists* to reverse overdoses from fentanyl or its derivatives.
- *Develop and validate alternative endpoint* other than abstinence that are acceptable to FDA for approval of OUD medications

Focus Area B: Pain

- Establish *data sharing collaborative* between industry groups
  NIH to serve as a neutral broker
- Determine *objective measures* to understand, predict responses to pain
  Biomarkers for pain – and a "Pain-ometer"
- *Clinical trial network* to accelerate trials on common and rare pain syndromes and to evaluate biomarkers