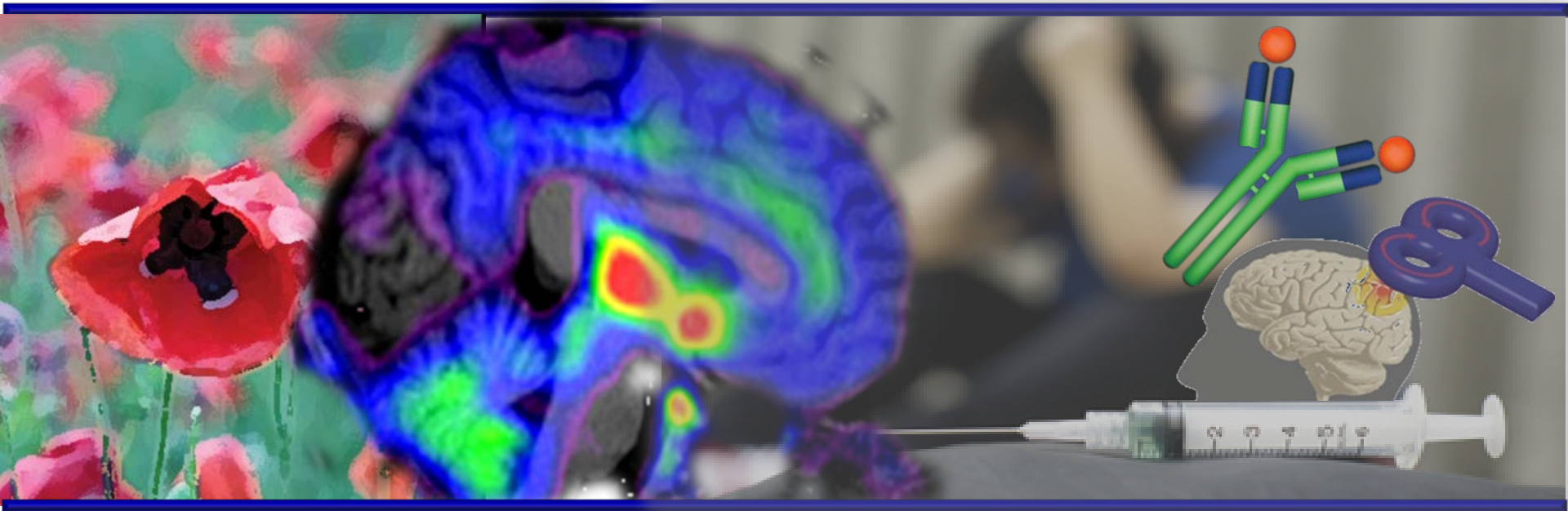


Scientific Solutions for the **OPIOID CRISIS**



Nora D. Volkow, M.D.
Director

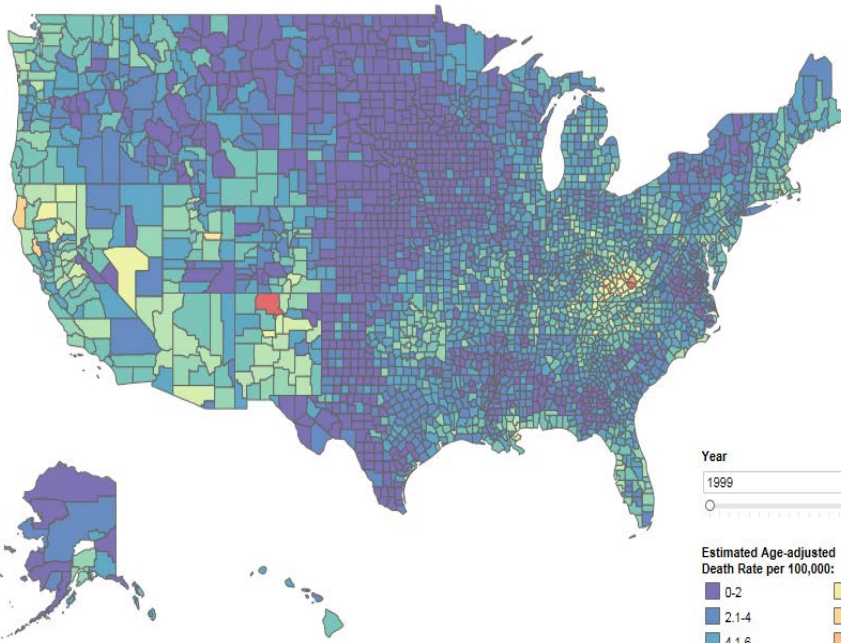


**National Institute
on Drug Abuse**

 [@NIDAnews](https://twitter.com/NIDAnews)

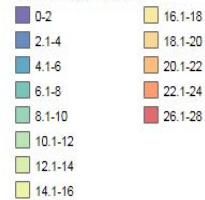
Overdose Death Rates

1999

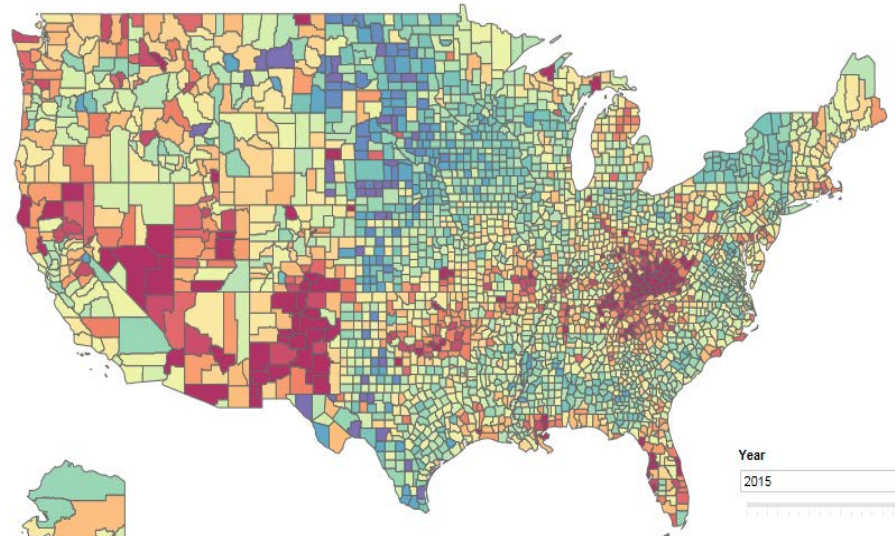


Year
1999

Estimated Age-adjusted
Death Rate per 100,000:

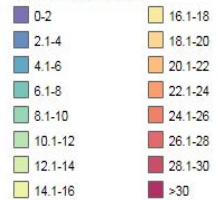


2015

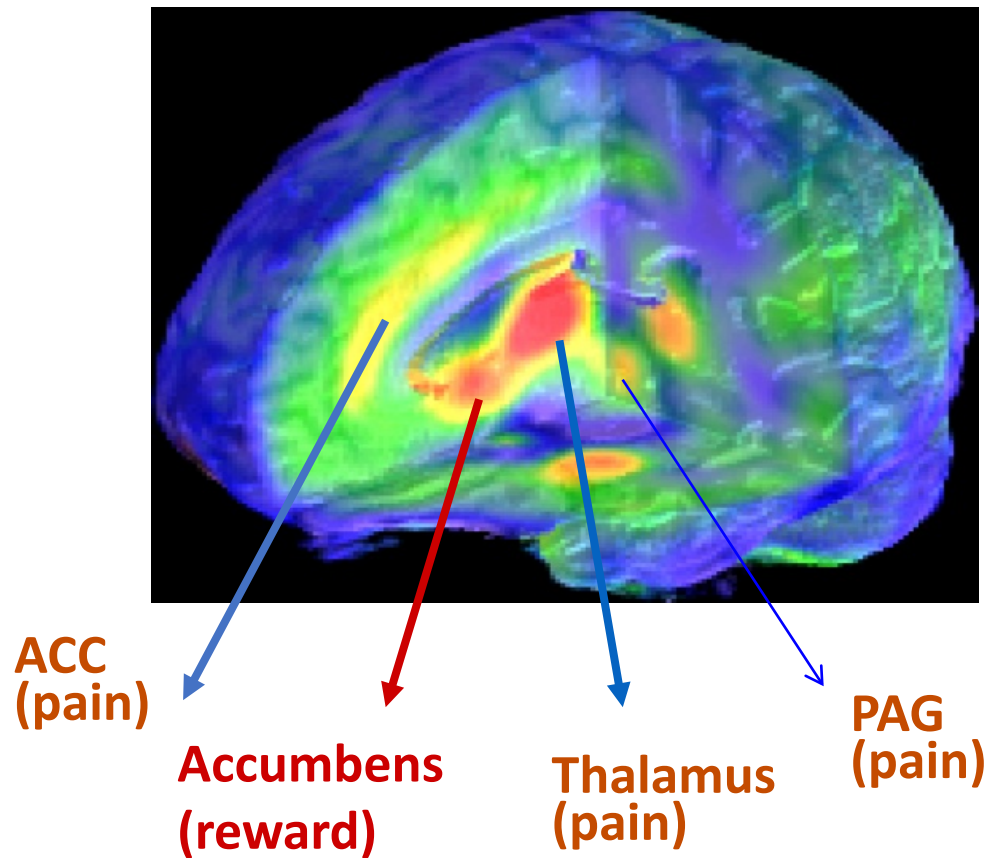


Year
2015

Estimated Age-adjusted
Death Rate per 100,000:

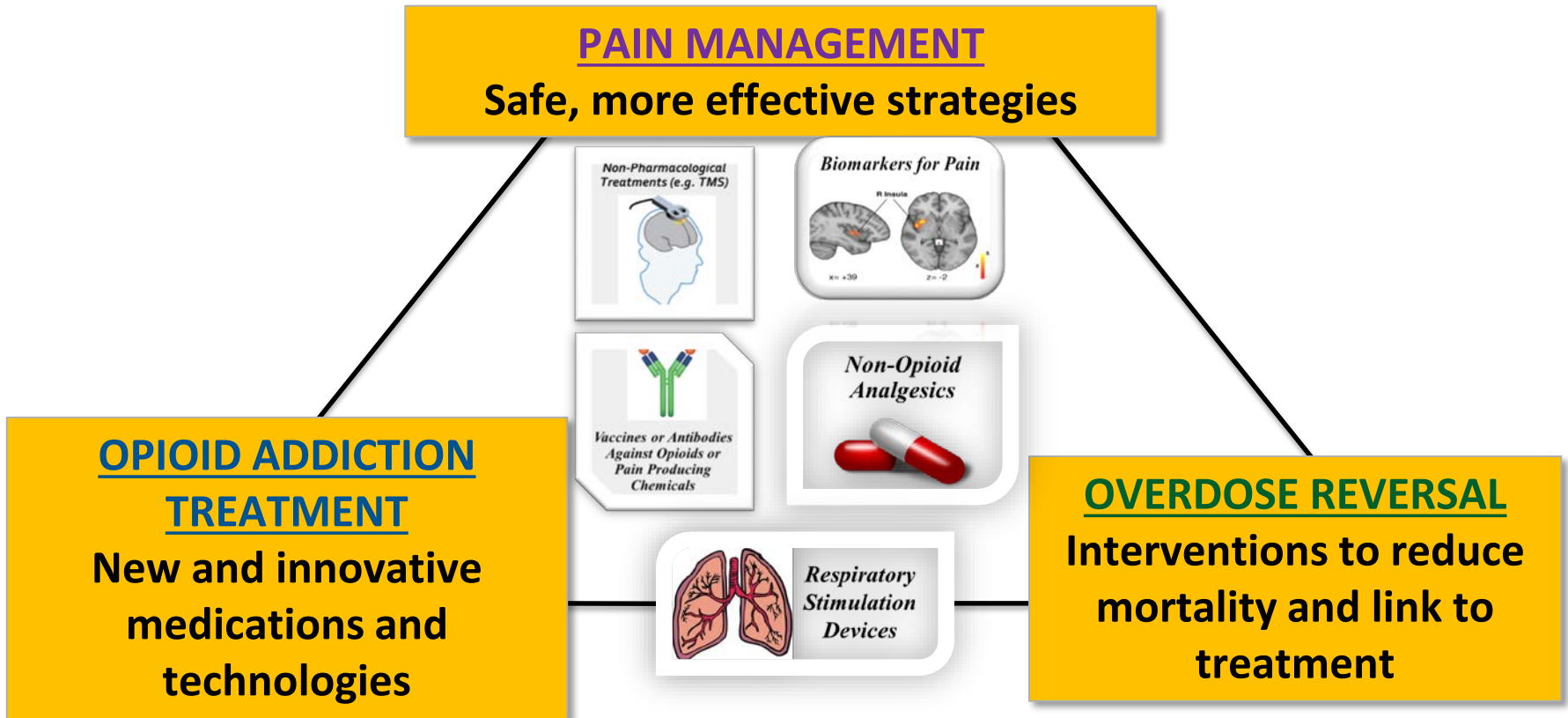


Analgesic & **Reward** Mechanisms of Mu Opiate Drugs (Heroin, Vicodin, Morphine)

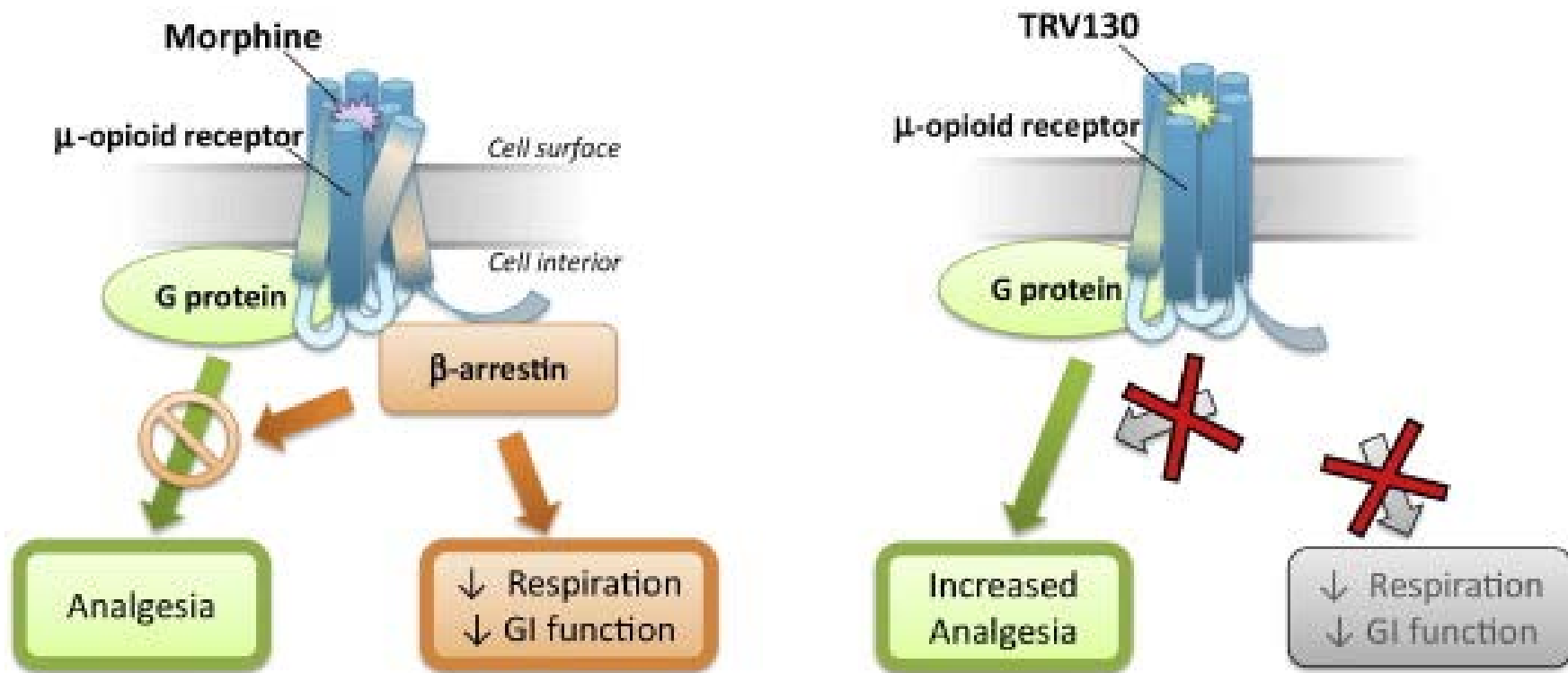


NIH OPIOID RESEARCH INITIATIVE

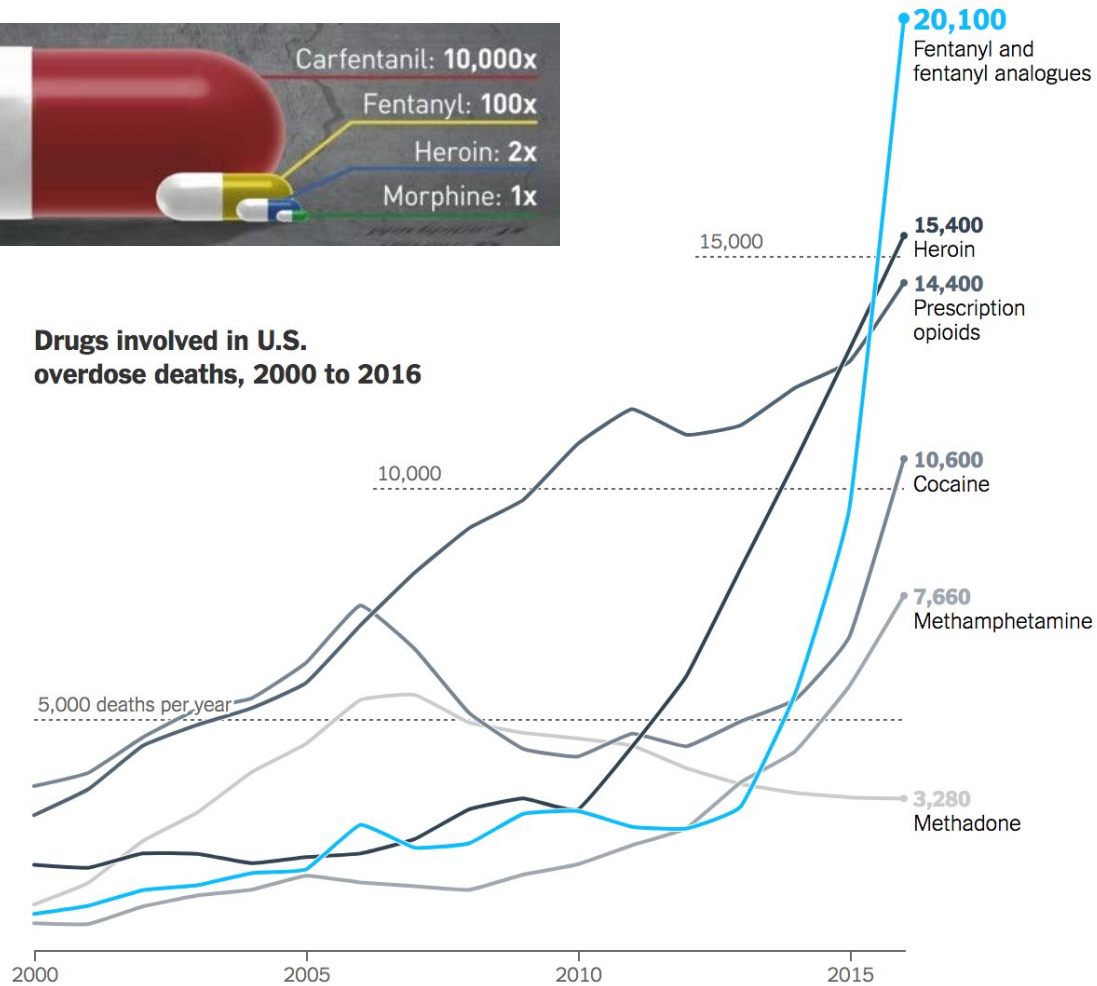
Using Research to End the Opioid Crisis



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



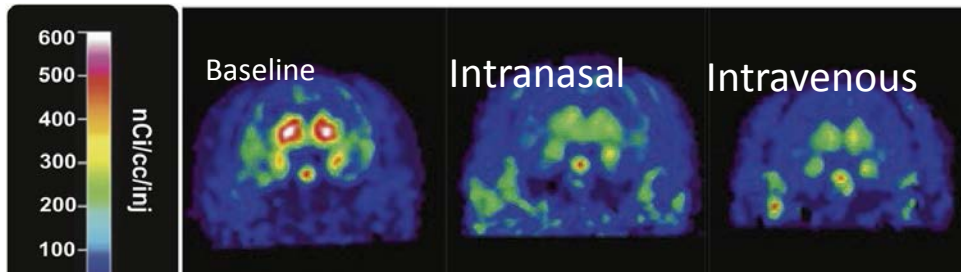
Fentanyl-Related Deaths Surpassed Heroin or Rx Opioids in 2016



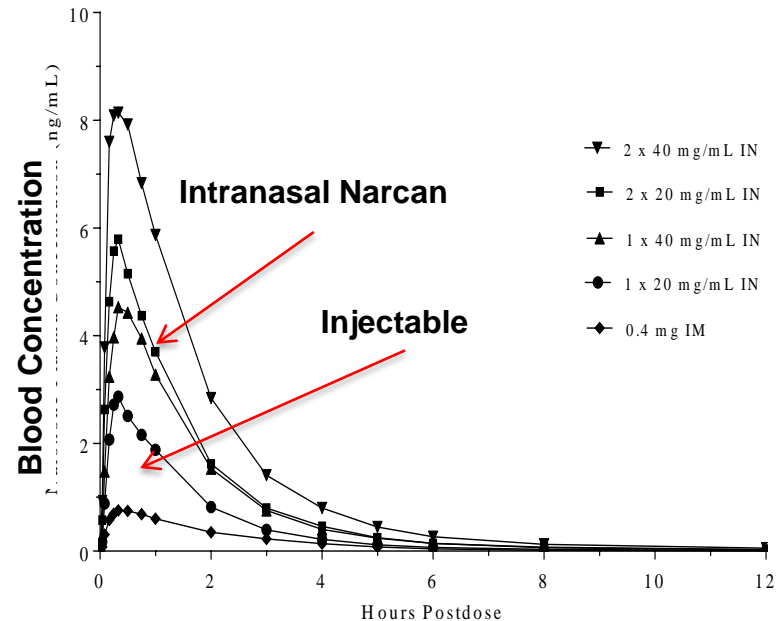
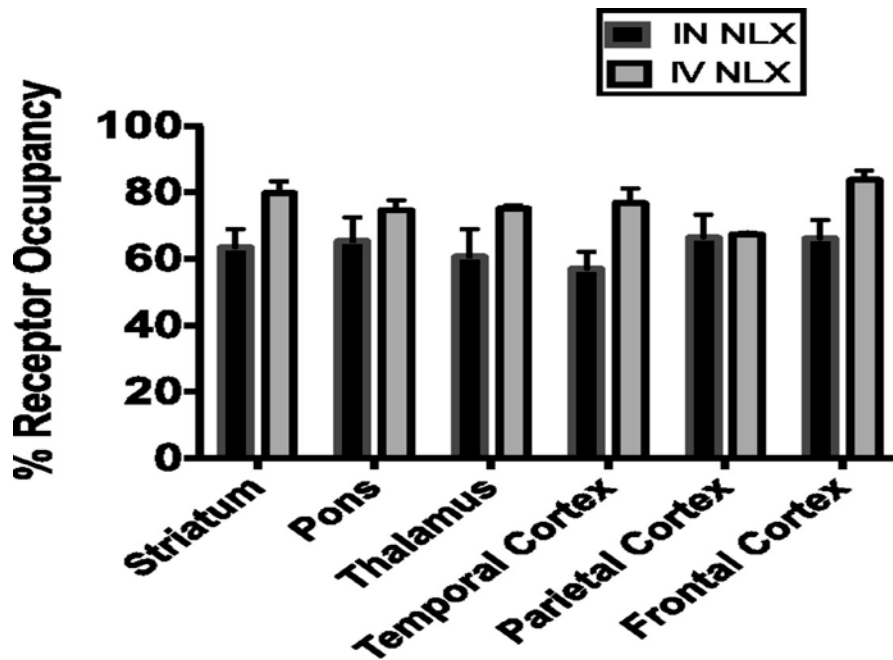
Graphs from [NY Times Article](#) based on [CDC MMWR Report](#) 2017

NALOXONE REQUIRES FAST AND EFFICIENT DELIVERY as achieved with iv injection but few know how to inject

Receptor occupancy by INTRANASAL equivalent to INTRAVENOUS Naloxone

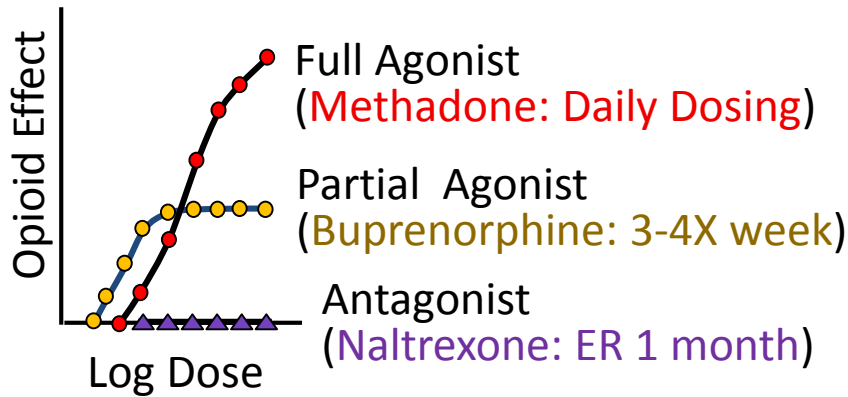


Intranasal naloxone reaches blood as fast as Intramuscular naloxone and achieves higher levels



Saccone PA, J Pharmacol Exp Ther. 2016 Nov;359(2):366-373.

Medication Assisted Treatment (MAT)



DECREASES:

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

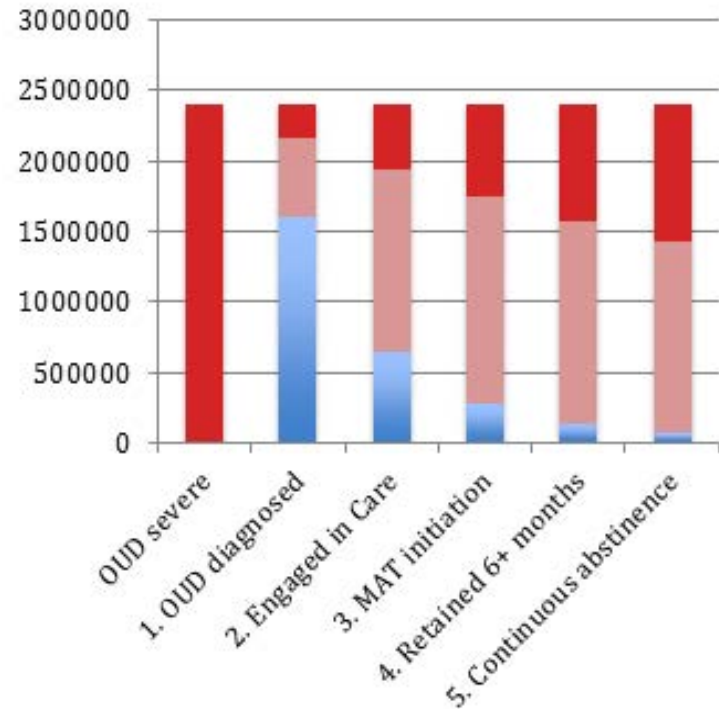
INCREASES

- Social functioning
- Retention in treatment

But MAT is highly underutilized!
Relapse rates are very high!

OUD Cascade of Care in USA

Current estimates
Treatment gap
90% goal



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

Extended Release Formulations

● Vivitrol®

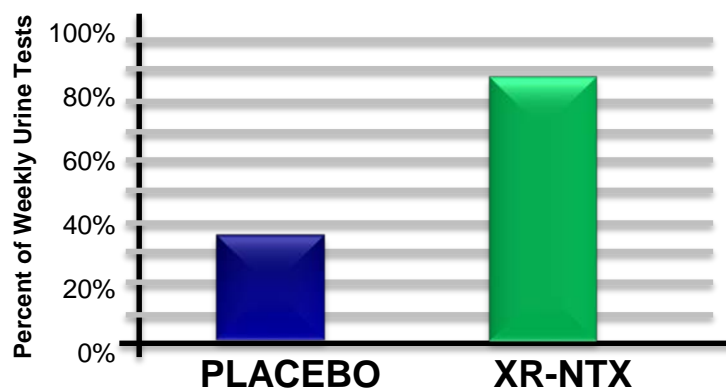


● PROBUPHINE®



IM Injection q 4 weeks for 24 weeks

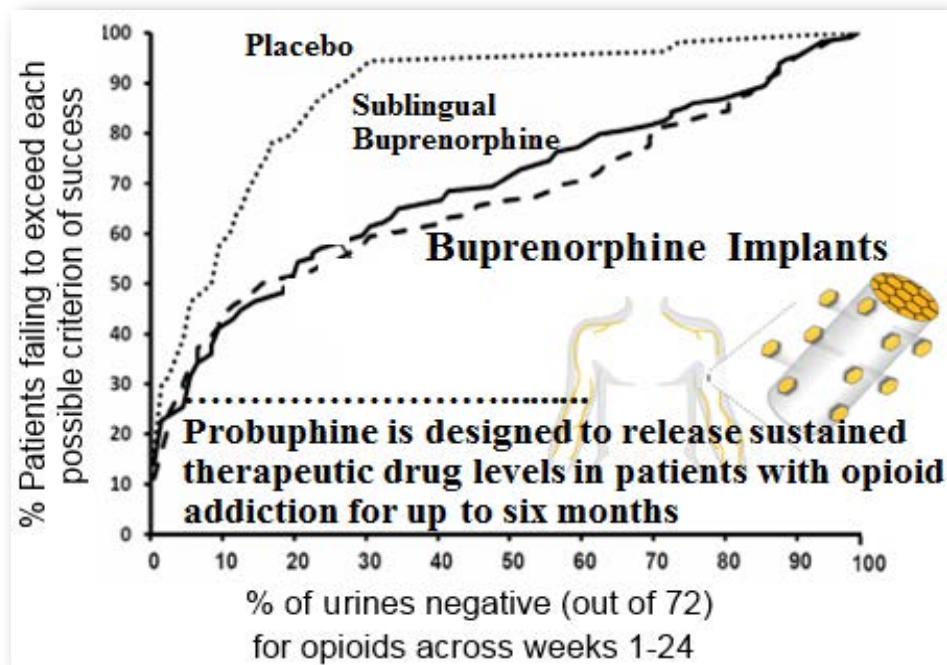
Median % Opioid-Negative Urines



■ Placebo: N=124

■ XR-NTX: N=126

Krupitzky et al., Lancet 2011



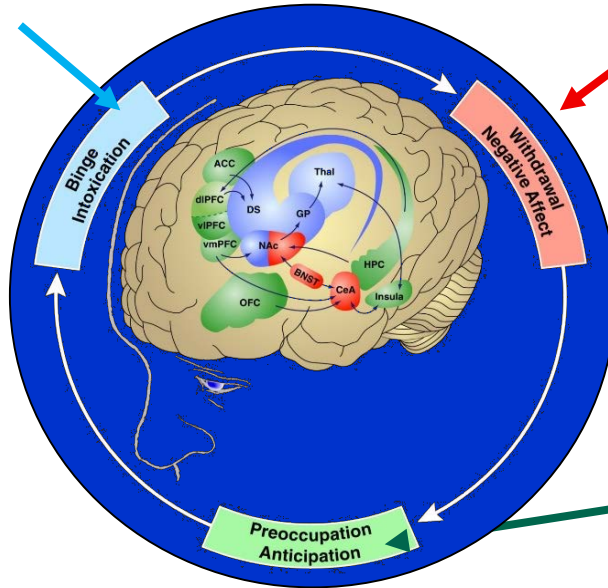
Rosenthal et al., Addiction 2013;105.

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

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

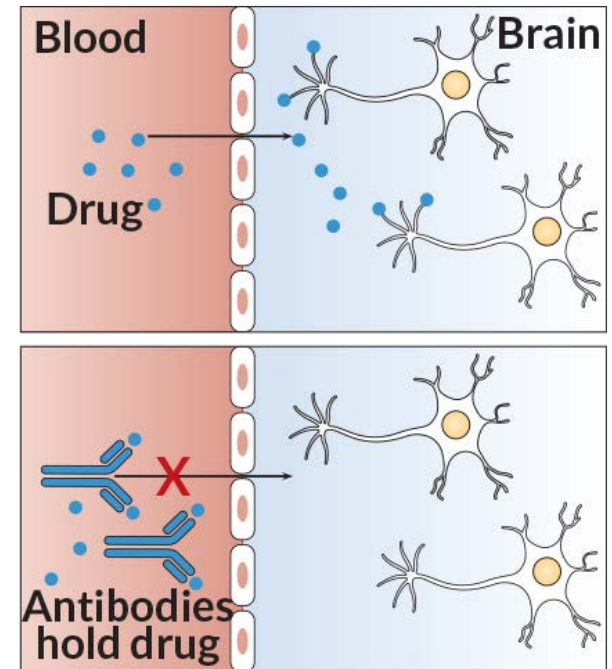
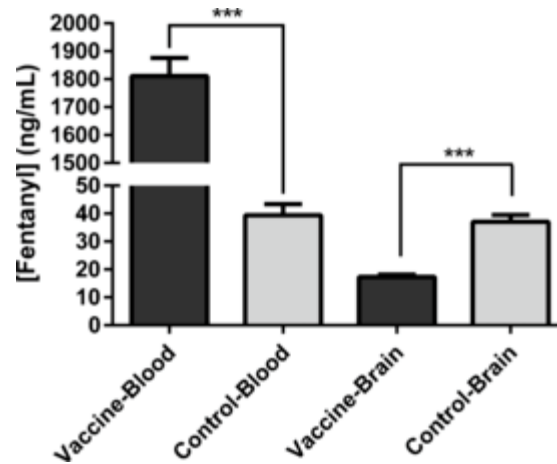
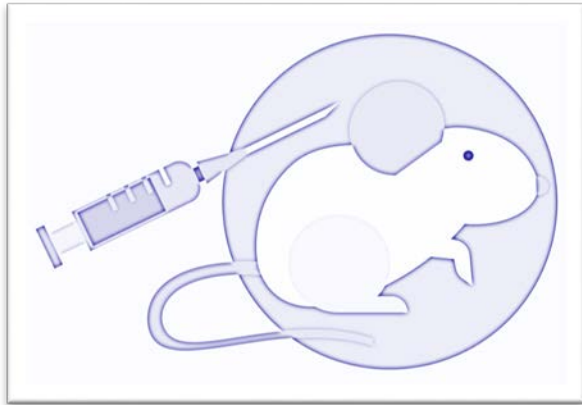
Diagram: Koob GF, Volkow ND. Neuropsychopharmacol Rev, 2010.

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)

Innovative Opioid Addiction Treatments – Fentanyl Vaccine

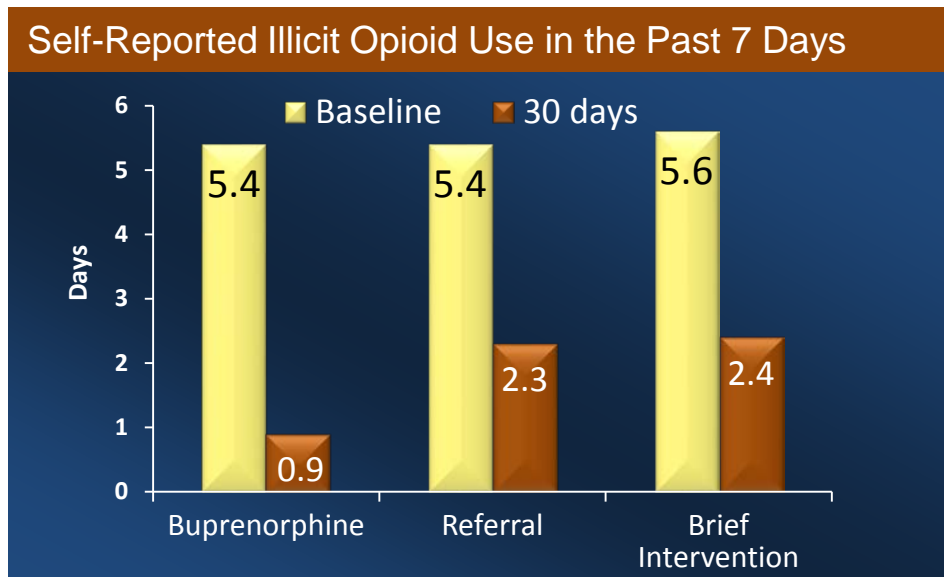
2016: First vaccine for fentanyl and fentanyl analogs reported in a mouse model

- Successfully stimulated antibody production
- Reduced fentanyl reaching the brain
- Reduced analgesia and protected against overdose



Emergency Departments 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

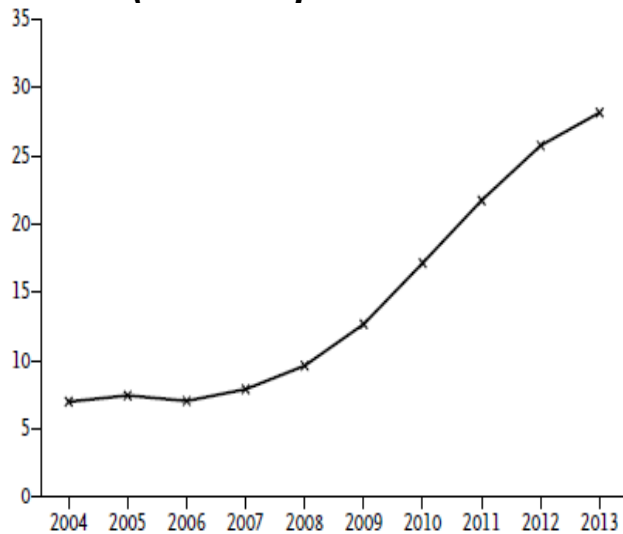
D'Onofrio G et al., JAMA April 28, 2015.

Opioid Use and Misuse During Pregnancy



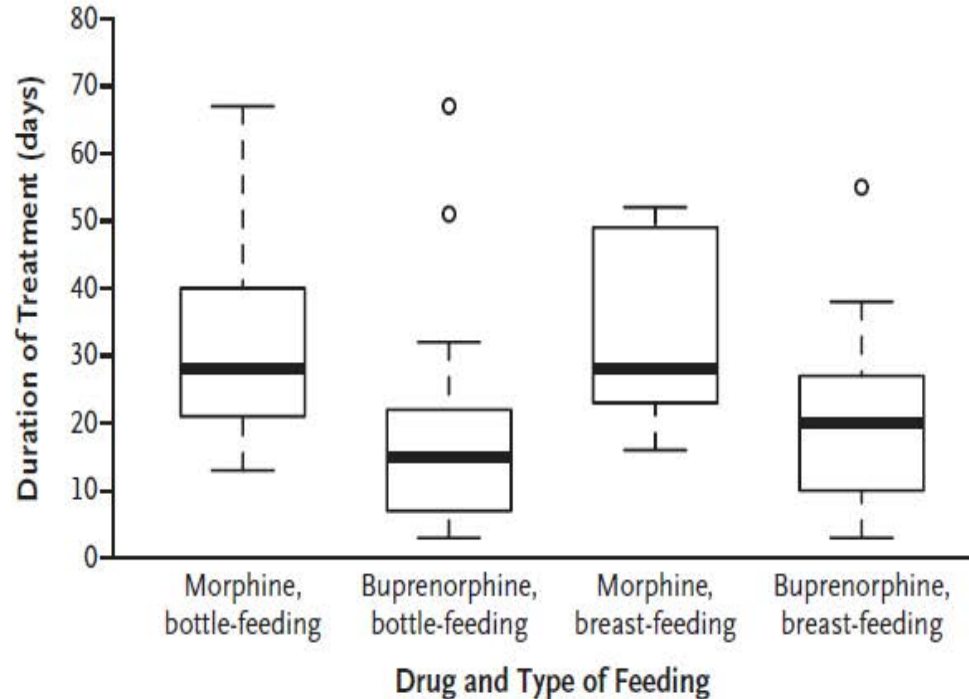
17% of pregnant women are prescribed an opioid during pregnancy

NICU Admissions for Neonatal Abstinence Syndrome NAS (Number per 1000 Admissions)



Source: Tolia VN, Patrick SW, et al. *NEJM* 2015;372:2118-2126.

Buprenorphine for NAS Tx



Buprenorphine resulted in a **shorter duration of NAS treatment** and **length of hospital stay** than treatment with morphine

Kraft WK et al., *N Engl J Med* 2017; 376:2341-2348.

Challenges of the Opioid Epidemic

- 25.5 million adults have pain every day
 - Opioids are overprescribed, not effective for chronic pain
- More than 2 million Americans are addicted to opioids
 - Most started with prescription medicines
- Medication Assisted Treatment (MAT) is available for opioid use disorders and to prevent/reverse overdose
 - But MATs are drastically underutilized
 - Duration of treatment needed is not well understood
- Research has revolutionized our understanding of addiction and pain
 - But alternatives to treat addiction and overdose are limited
 - And new, non-addictive pain medicines are urgently needed

Priorities for Future Research

- ***Strengthen the connection between research and practice***
 - A learning health care system to translate evidence-based practices
 - Need for large-scale implementation pilot
- ***Explore, maximize, and expedite use of all available data sources and study designs***
 - In addition to clinical trials, use observational and secondary data sources as well
 - Consider barriers to using the data, including confidentiality issues
- ***Engage citizen scientists to help develop outcome and quality measures***
 - Need standardized metrics that patients and families can use to report on patient experience and treatment outcomes
- ***Determine criteria to indicate inpatient vs outpatient treatment***
 - Collect longer-term outcomes data to understand the utility of different treatments settings and modalities
- ***Establish which treatment interventions are effective for mild OUD or subclinical opioid misuse***
- ***Research to address cost and sustainability***



Development of Medications to Prevent and Treat Opioid Use Disorders and Overdose (UG3/UH3) (Clinical Trial Optional) RFA-DA-19-002

Issued: December 14, 2017; Open Date: January 25, 2018

- The purpose of this Funding Opportunity Announcement is to support the discovery and development of medications to prevent and treat opioid use disorders (OUD) and overdose.
- The UG3/UH3 Phase Innovation Awards Cooperative Agreement involves 2 phases. The UG3 is to support a project with specific milestones to be accomplished by the end of the 2-year period.
- The UH3 is to provide funding for 3 years to a project that successfully completed the milestones set in the UG3. UG3 projects that have met their milestones will be administratively considered by NIDA and prioritized for transition to the UH3 phase. Investigators responding to this FOA must address both UG3 and UH3 phases.

Using Science to Inform Practice and Policy: A Coordinated Approach to Research Priority Setting

Sponsored by the National Institute on Drug Abuse in Partnership with ECRI Institute





*Using Science to Inform Practice and Policy:
A Coordinated Approach to Research Priority Setting*

PARTICIPANT AGENCIES

- Academy Health
- Addiction Policy Forum
- Agency for Healthcare Research & Quality
- American Association for the Advancement of Science
- America's Health Insurance Plans
- American Hospital Association
- American Medical Association
- Bipartisan Policy Center
- Centers for Disease Control & Prevention
- Centers for Medicare & Medicaid Services
- Defense Health Agency
- ECRI Institute
- Health Resources & Services Administration
- National Academy of Medicine
- National Institute on Drug Abuse
- National Institutes of Health
- Office of the Assistant Secretary of Defense
- Office of National Drug Control Policy
- Research!America
- Patient-Centered Outcomes Research Institute
- Substance Abuse & Mental Health Services Administration
- United States Army Medical Research & Materiel Command
- U.S. Department of Health & Human Services
- U.S. Department of Veterans Affairs
- U.S. Food & Drug Administration

Community Health Centers (Massachusetts)

JAMA Internal Medicine

HEALTH CARE REFORM

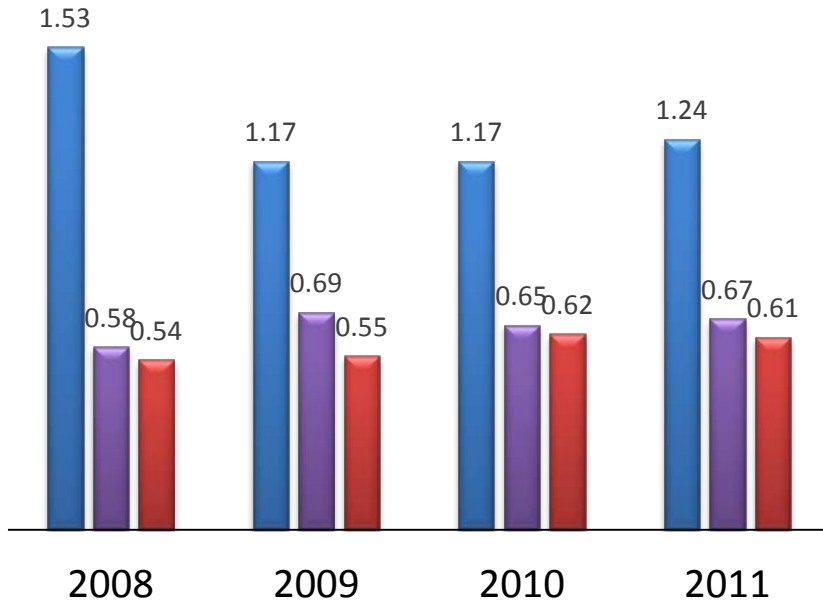
Collaborative Care of Opioid-Addicted Patients in Primary Care Using Buprenorphine

Five-Year Experience

Daniel P. Alford, MD, MPH; Colleen T. LaBelle, RN; Natalie Kretsch, BA; Alexis Bergeron, MPH, LCSW;
Michael Winter, MPH; Michael Botticelli, MEd; Jeffrey H. Samet, MD, MA, MPH

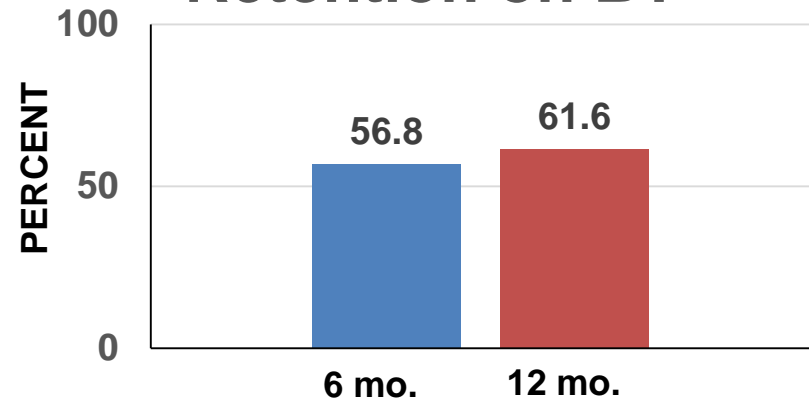
ER Admissions per OBOT Enrollment

■ Prior 6 Months ■ Future 6 Months ■ Future 7-12 Months



Integrating Buprenorphine Treatment Into Federally Qualified Health Centers (FQHC):

Retention on BT



Integrating BT in a large FQHC
network increased **retention rates**
to levels similar to those reported
by clinical trials

Haddad MS et al., DAD 2013 Jul 1;131(1-2):127-135.