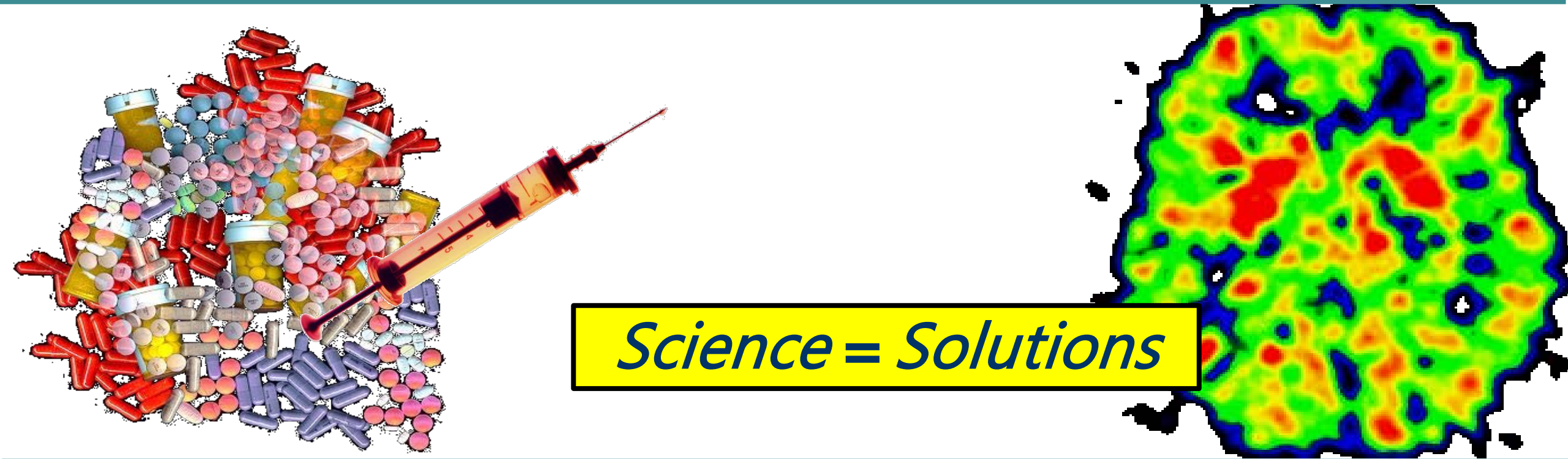


Advancing Addiction Science to Address the Opioid Crisis



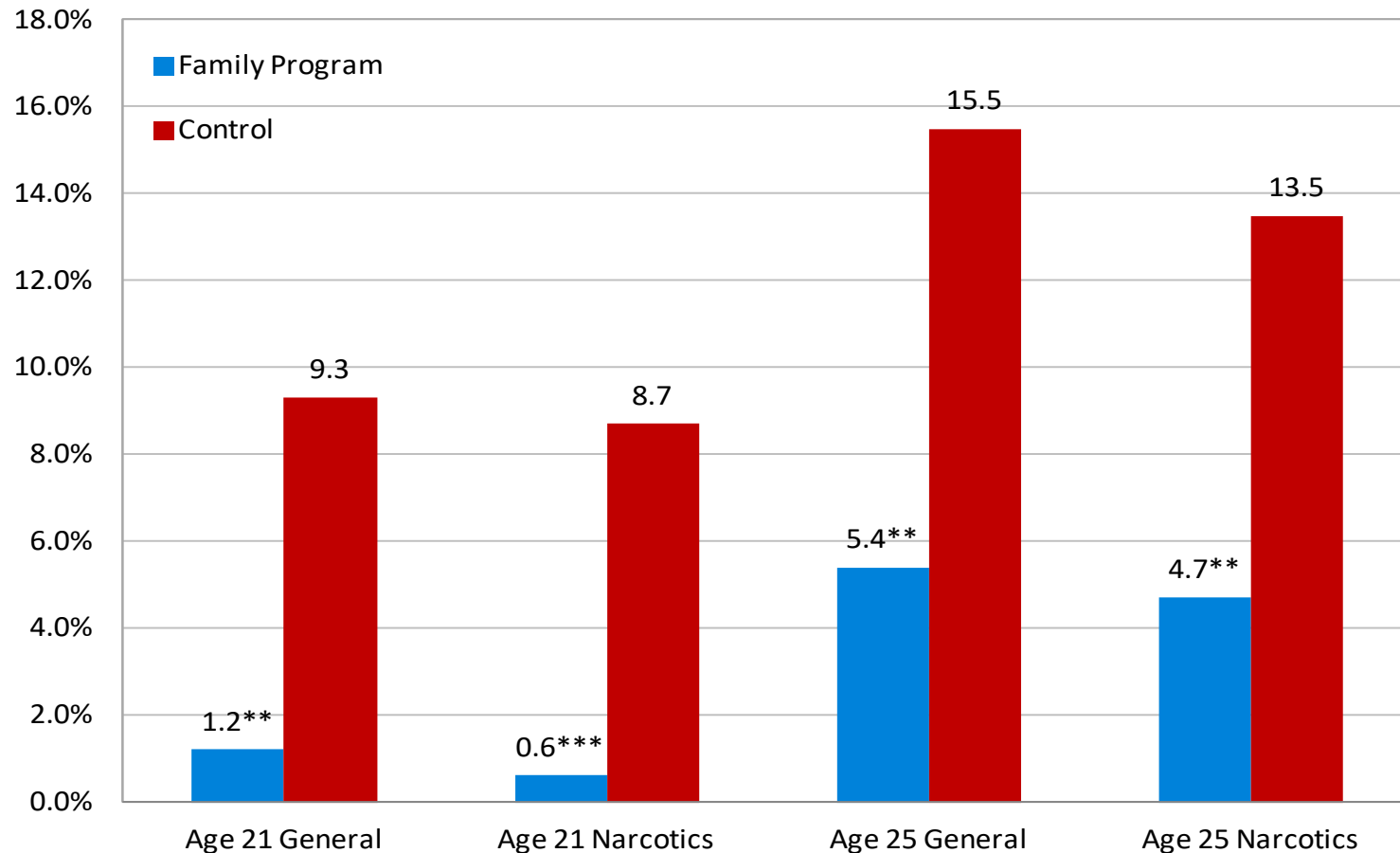
Science = Solutions

U.S. Department of Health and Human Services

OPIOID STRATEGY

- *Better access to prevention, treatment, and recovery services*
- *Better targeting of overdose-reversing drugs*
- *Better timely and specific public health data on the epidemic*
- *Better pain management*
- *Better research on addiction and pain*

Universal Drug Abuse Prevention Reduces Rx Drug Misuse



p<.01; *p<.001; RRRs = 65-93%

Notes: General=Misuse of narcotics or CNS depressants or stimulants.

Source: R Spoth et al. American Journal of Public Health 2013

In this study, for 100 young adults in general population starting Rx abuse, only 35 young adults from an intervention community started.

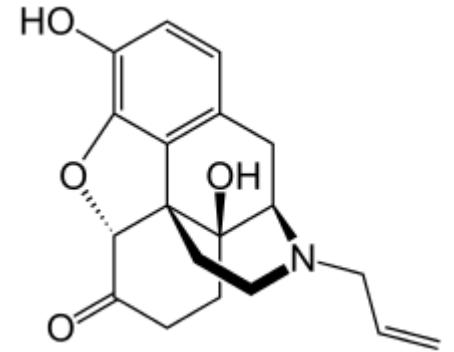
Overall, three studies now suggest the impact of universal prevention on prescription drug abuse.

Science = Solutions

Science = Solutions: Direct Overdose Intervention

Naloxone Distribution for opioid overdose victims.
The ***potential*** for direct intervention to save lives.

- ***Nasal spray*** and ***Auto-injector*** formulations now approved by the FDA



April 5, 2018

Surgeon General's Advisory on Naloxone and Opioid Overdose

*I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, **knowing how to use naloxone and keeping it within reach can save a life.***

BE PREPARED. GET NALOXONE. SAVE A LIFE.

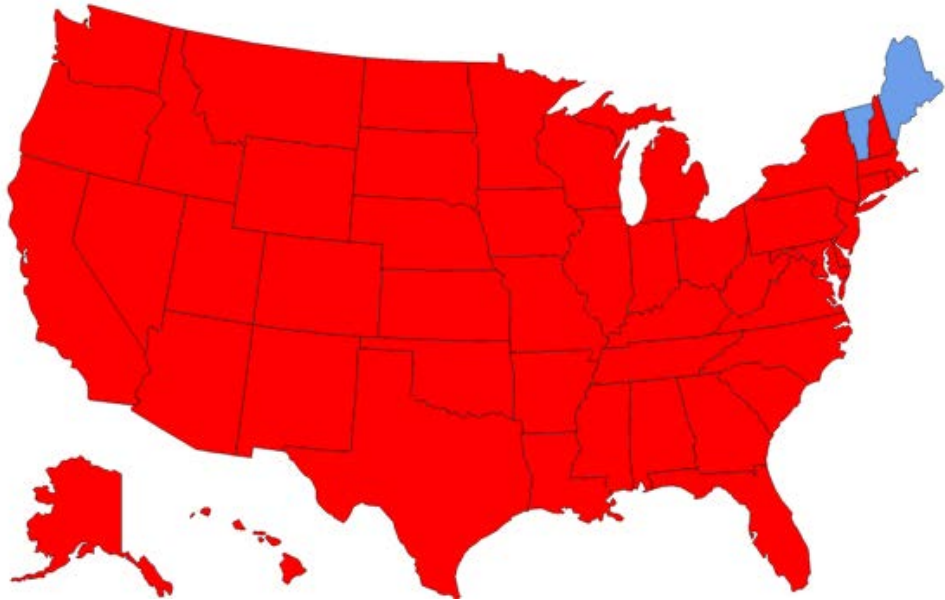


Next steps

- ***Longer acting agents to address fentanyl risks?***
- ***Respiratory stimulation?***
- ***Device development?***

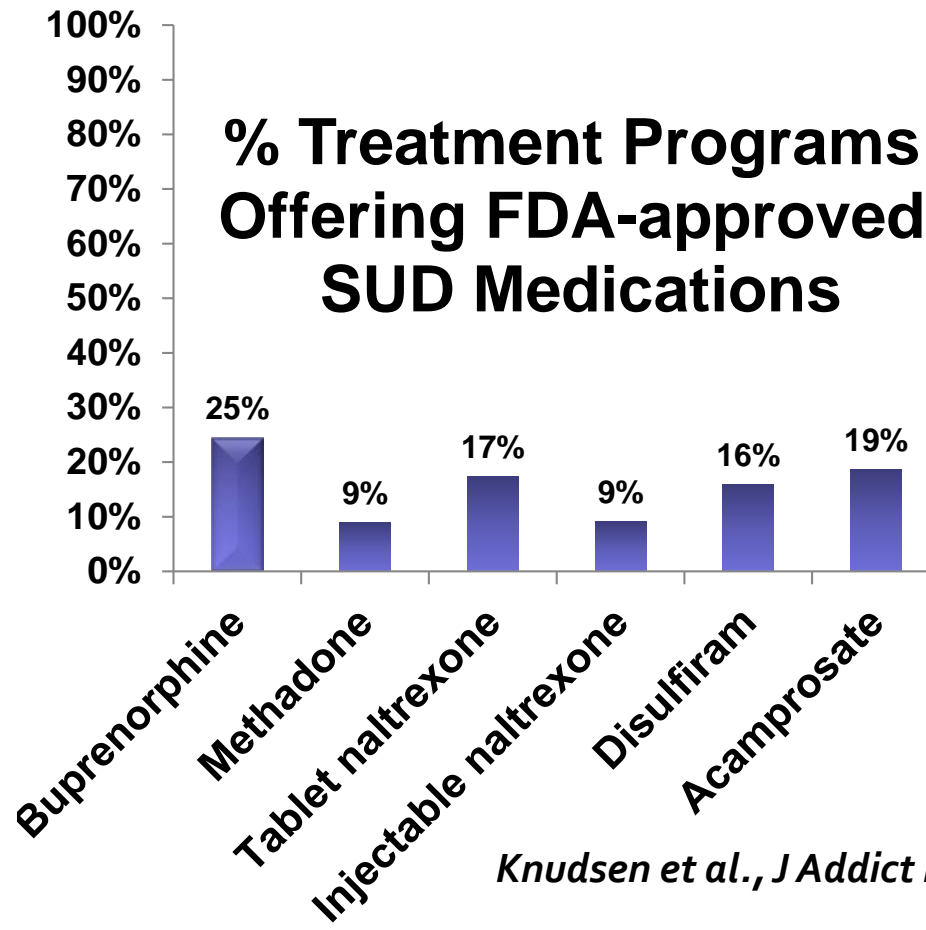
Medications are *Underused*

In 48 states and D.C., Opioid Use Disorder Rates Exceed Buprenorphine Treatment Capacity

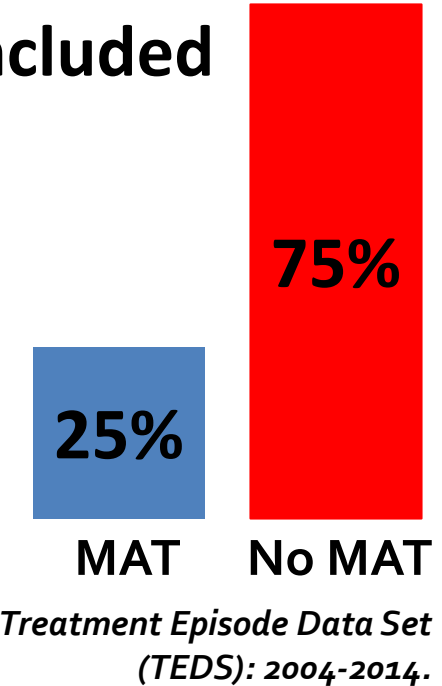


Jones C et al., Am J Public Health 2015.

In 2014, only 25% of opioid admissions had treatment plans that included receiving medications.

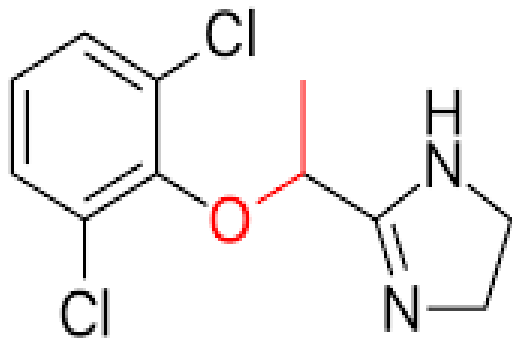


Knudsen et al., J Addict Med 2011



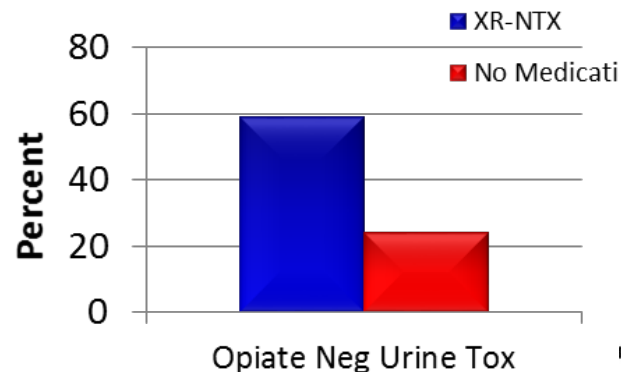
Science = Solutions: Improving Addiction Treatment

- Initiating buprenorphine treatment in the *emergency department* improves treatment engagement and reduces illicit opioid use
- Extended release naltrexone initiated in *criminal justice* settings relapse rates and overdoses
- XR-Naltrexone and BUP-Nx *Equally Safe and Effective* (After Induction)
- Lofexidine* for opioid withdrawal treatment recommended by FDA Advisory Committee March 29, 2018



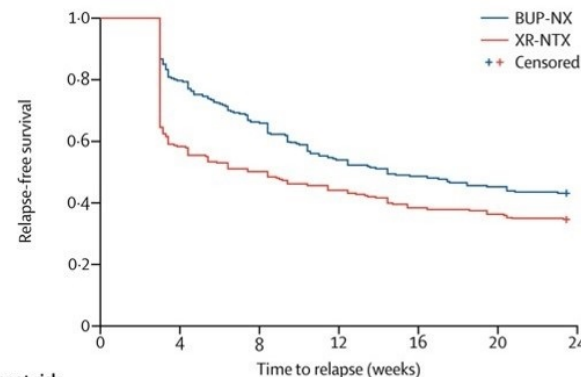
lofexidine

Post Prison-Release Outcomes



Lee JD, et al., *Addiction* 2015;100:1005-10
and *New Eng J Med* 2016;374:1232-1242

Relapse-free survival

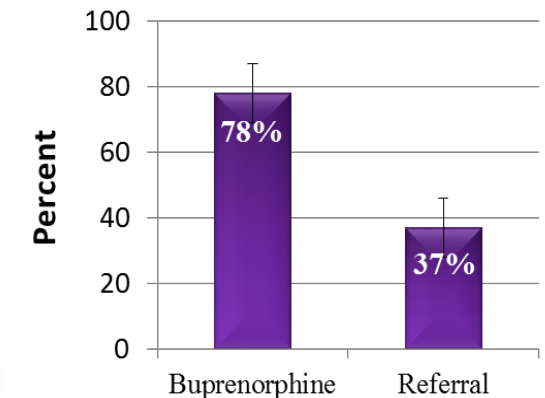


Number at risk (censored)

	0	4	8	12	16	20	24
BUP-NX	287	229	100	155	140	130	0 (124)
XR-NTX	283	165	142	125	109	103	0 (98)

Lee JD et al., *The Lancet* Nov. 14, 2017

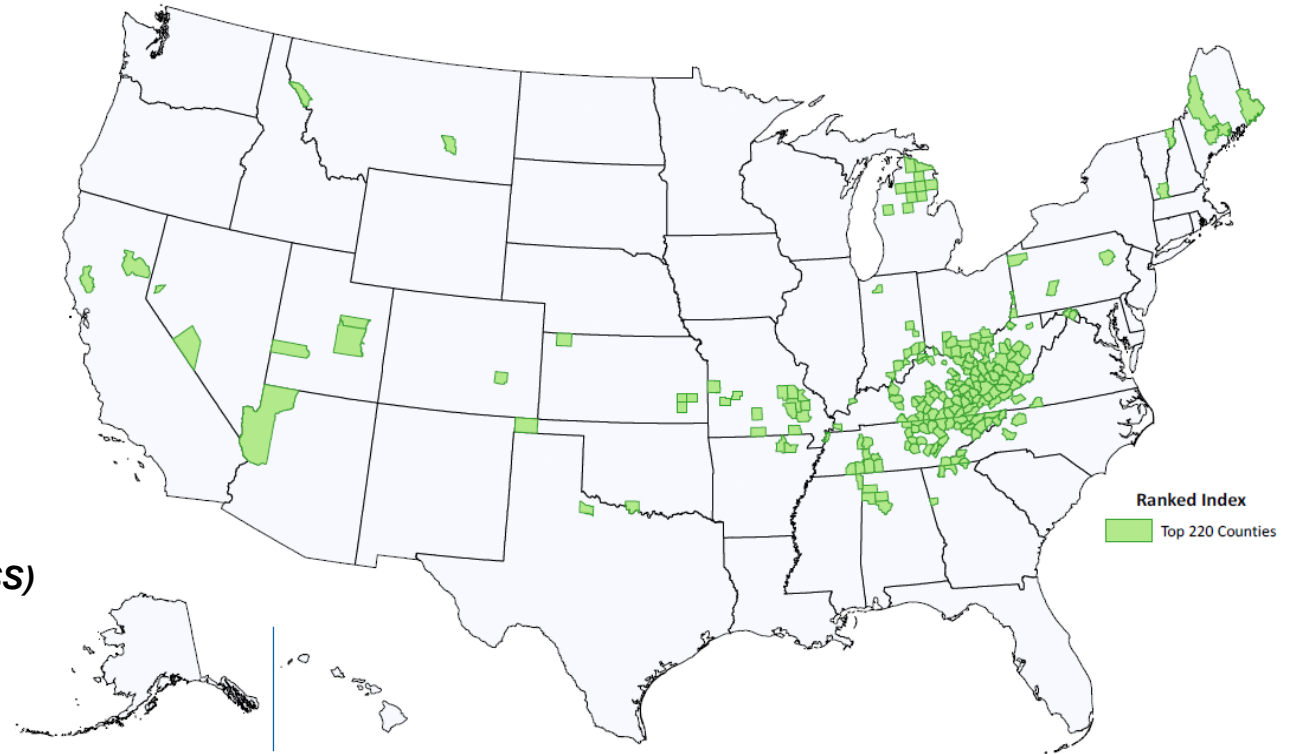
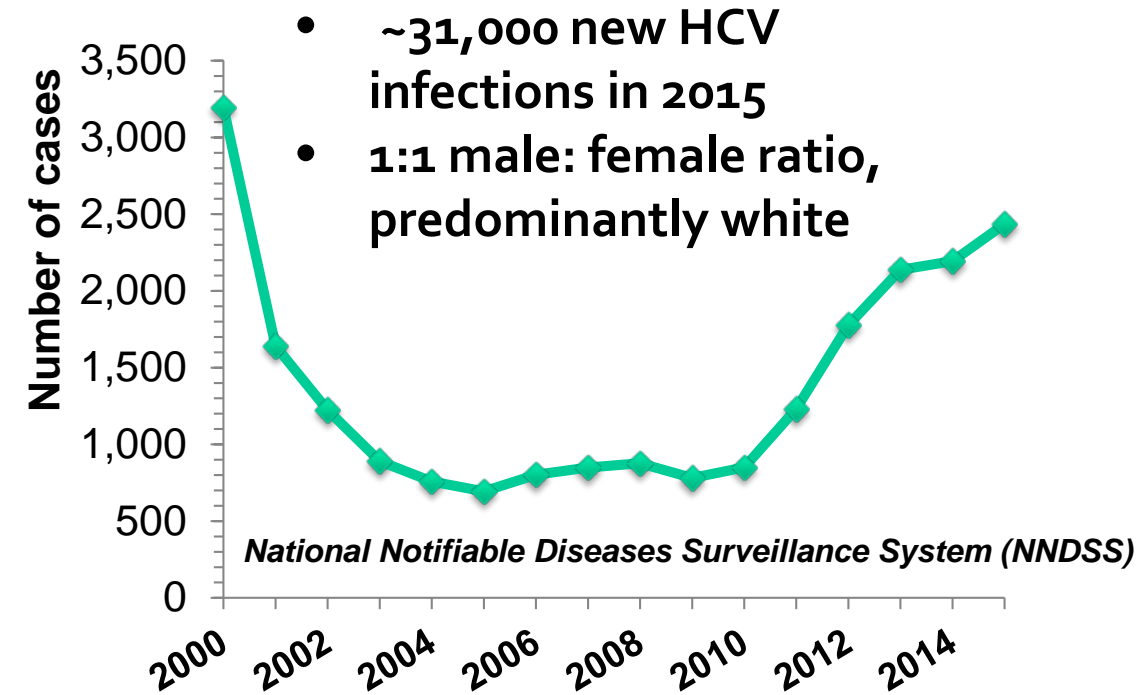
ED-initiated Buprenorphine Increased TX Engagement



D'Onofrio *JAMA*. 2015.

Rising rates of HCV

Counties Deemed Highly **Vulnerable** to Rapid Dissemination of HCV or HIV



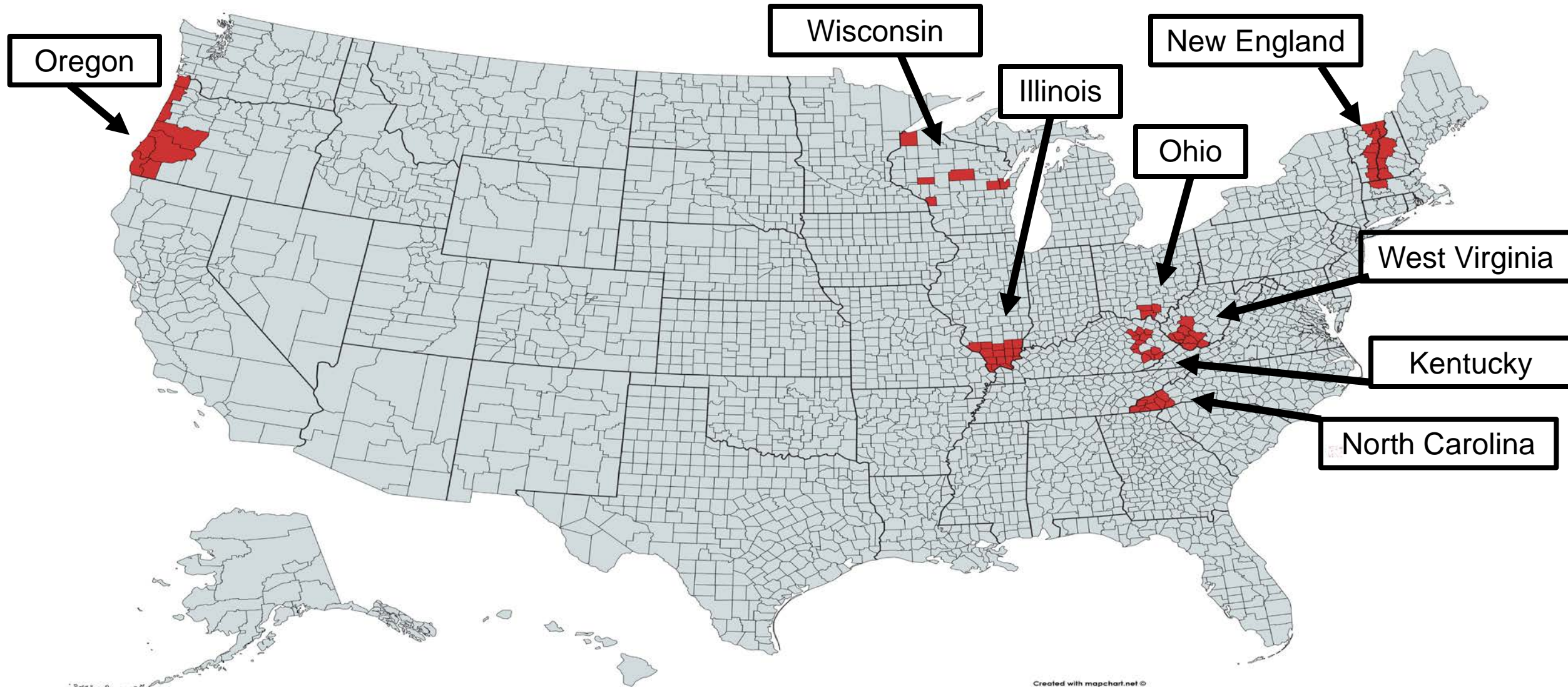
Source: Van Handel et al, JAIDS 2016

HIV (and **Hepatitis C**) Outbreak Linked to Oxycodone Injection Use in Indiana, 2015

Peters et al.

The New England Journal of Medicine
2016;375:229-239

Science = Solutions: NIDA, CDC, SAMHSA, ARC Partnering to Combat HIV and Viral Hepatitis in Rural Areas



Elimination of Hepatitis C

NIDA and NCI are working with CDC to develop a study of the elimination of HCV in a high-risk community in Kentucky.

Work to date includes pilot funding to the University of Kentucky to develop community-based components:

- ***Syringe exchange***
- ***Drug treatment***
- ***Linkages with criminal justice (because of high-risk persons re-entering the community)***
- ***Access to medical care.***
- ***Hepatitis C testing and TREATMENT***

NIDA Joining CDC on the 2018 Update to the *National HIV Behavioral Surveillance among Persons Who Inject Drugs*

22 MSAs:



Plans for 2018

- Improve recruitment of young (<30 years) PWID
- Include HCV testing in NHBS sites
- *Expand recruitment outside of urban core*

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*

Helping to End Addiction Over the Long-term

The Research Plan for the NIH HEAL Initiative

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

Walter J. Koroshetz, MD
National Institutes of Health, Bethesda, Maryland; and National Institute of Neurological Diseases and Stroke, Bethesda, Maryland.

Nora D. Volkow, MD
National Institutes of Health, Bethesda, Maryland; and National Institute on Drug Abuse, North Bethesda, Maryland.

Extraordinary focus by all segments of society is required to respond to the nation's opioid crisis. Now is the time to channel the efforts of the scientific community to deliver effective—and sustainable—solutions to this formidable public health challenge. Recognizing this opportunity, Congress added \$500 million to the base appropriation of the National Institutes of Health (NIH), starting in fiscal year 2018.¹ The NIH will invest these much-needed resources to support science that advances national priorities for addiction and pain research² with a bold new trans-NIH initiative called Helping to End Addiction Long-term (HEAL).³ In this Viewpoint, we outline the initial components of this cross-cutting, interdisciplinary program.

More than 25 million US adults are affected by daily pain.⁴ More than 2 million individuals in the United States have an opioid use disorder (OUD), most starting with opioid analgesics prescribed to them or procured from diverted medications, but once addicted, often shifting to illicit heroin or synthetic opioids.⁵ The scope of these crises is staggering, but scientific advances offer

Table. Research Plan for the NIH HEAL Initiative

Opportunities	Components
Improving Treatments for Opioid Misuse and Addiction	
New treatments for addiction	Identify new targets, develop new medications/immunotherapies; reformulate existing medicines
	Improve overdose reversal medicines
	Develop new therapies for opioid-induced respiratory depression
Optimization of effective treatments for addiction	Enhance NIDA Clinical Trials Network for opioid research
	Establish Justice Community Opioid Intervention Network
	Initiate HEALing Communities Study
NOWS	Expand ACT NOW pilot study; use results to conduct clinical trials to determine best practices for clinical care of NOWS
Enhancing Pain Management	
Better understanding of chronic pain	Establish Acute to Chronic Pain Signatures program
New nonaddictive pain treatments	Identify new targets for pain treatment

NIH HEAL Initiative: Selected 2018 Priorities

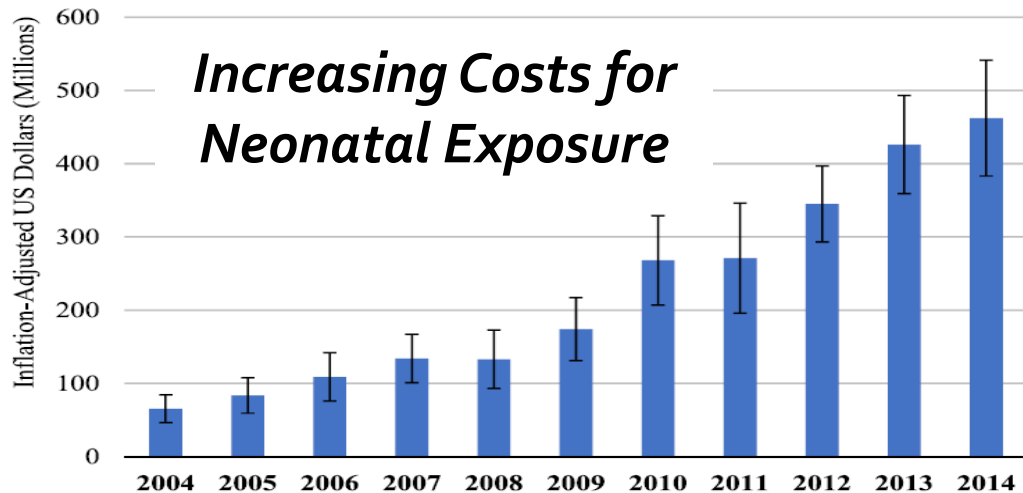
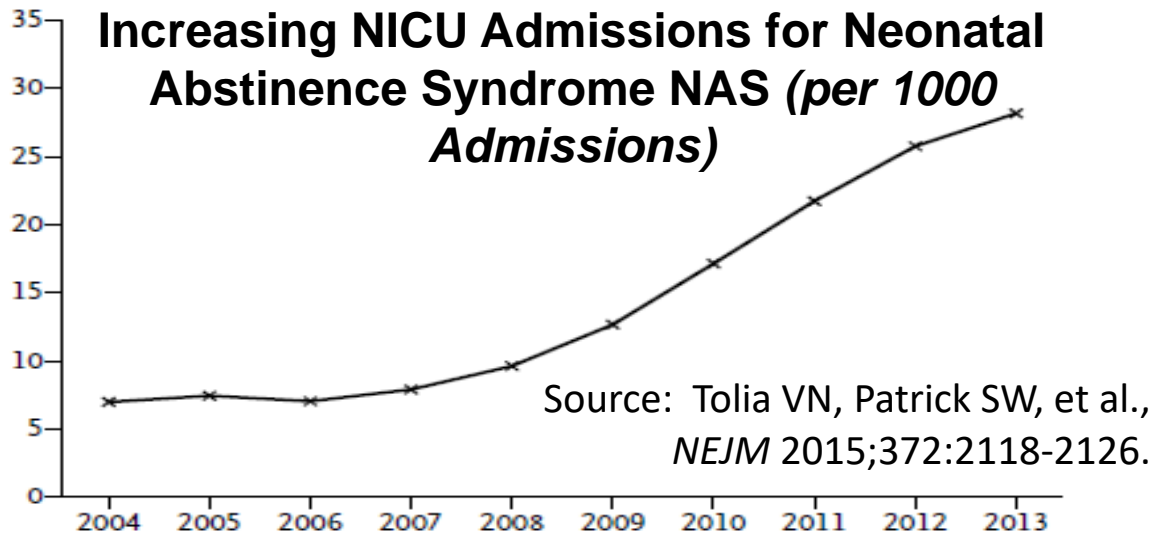
Opioid Use Disorder

- Improve therapeutic approaches to addiction and overdose
- Carry out real world implementation research to optimize interventions
- Evaluate treatments, consequences of Neonatal Opioid Withdrawal Syndrome (NOWS)

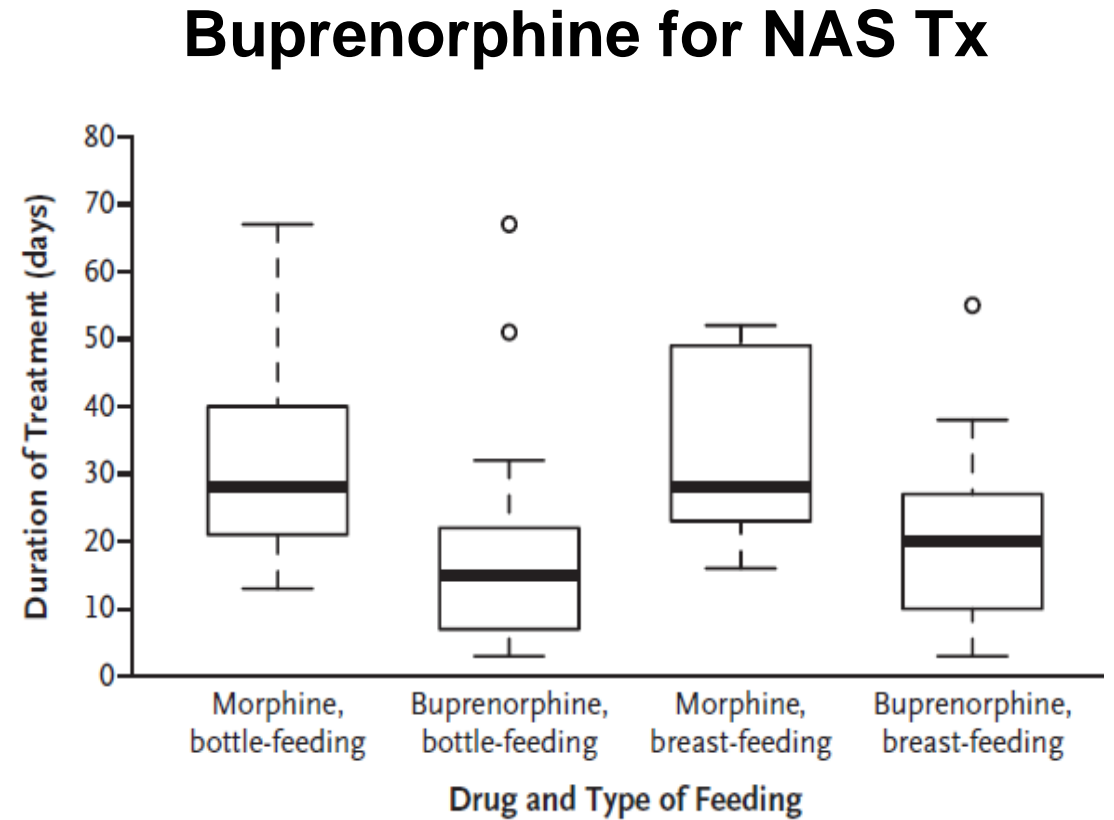
Pain Management

- Understand neurobiology of chronic pain
- Develop new non-addictive treatments for pain
- Build Clinical Trial Network for chronic pain

Science = Solutions : Opioid Use and Misuse During Pregnancy



Source: Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SM.. *Pediatrics*. 2018;141(4):e20173520



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

Source: Kraft WK et al., *NEJM* 2017;376:2341-2348.

HEAL – Neonatal Opioid Withdrawal

Advancing Clinical Trials in NOWs: Pilot Study

- Clinical trials for care of infants with NOWs
 - Determine effectiveness of currently used medications to treat withdrawal
 - Compare pharmacologic approaches to drug-free strategies
 - Eat, sleep, console
 - Assess impact of prenatal exposure to opioids
 - Effects on developing brain structure and function
 - Higher risk for school performance problems
 - Long-term risk for addiction
- Determine best practices to improve short- and long-term outcomes

HEAL – Treatment Enhancements

Advancing NIDA's Clinical Trials Network

- NIDA collaboration with academics and community providers
 - Develop, validate, refine, and translate into practice new treatment options
- Expand the size and scope of the CTN
 - Expand treatment access, options, and education
 - Facilitate implementation science
- Contribute to improved quality of and access to treatment for OUD
 - Introduce sustainable interventions in underserved, highly impacted areas
 - Implement OUD treatment practices in general medical settings
 - Expand of the OUD treatment clinical and research workforce

HEAL – Justice Initiative

Justice Community Opioid Innovation Network (JCOIN)

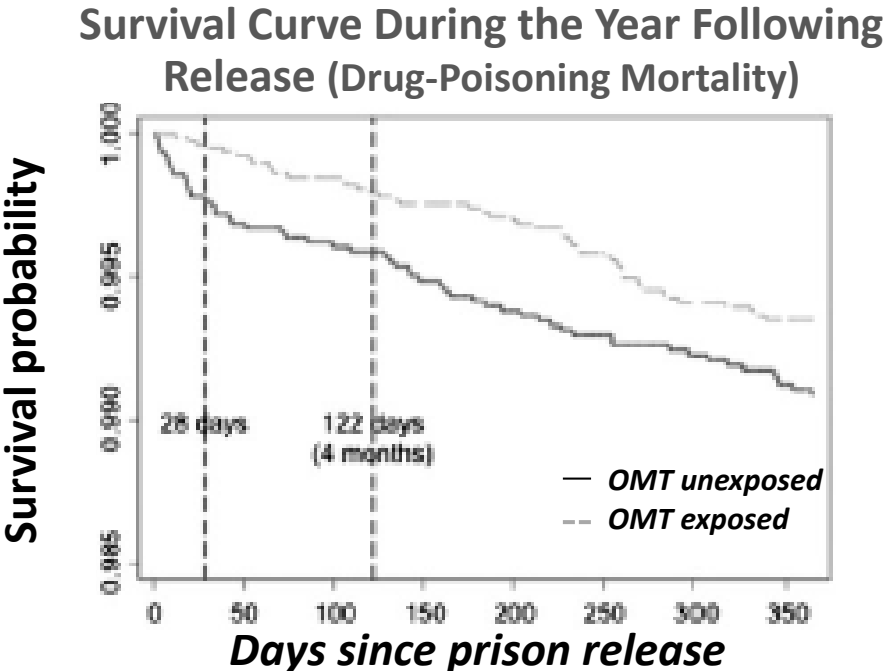
- Increase collaborations between justice systems and community-based treatment providers to improve continuity of care
 - Enhance access and retention in OUD treatment
- Justice community-related research through network of investigators
 - National survey of addiction treatments in jails, prisons and communities
 - Effectiveness and implementation studies of new and existing medications, interventions, and technologies in justice settings
 - Leveraging existing data sources
 - Developing innovative research methods



Opioid Medication Therapy (OMT) In Prison

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

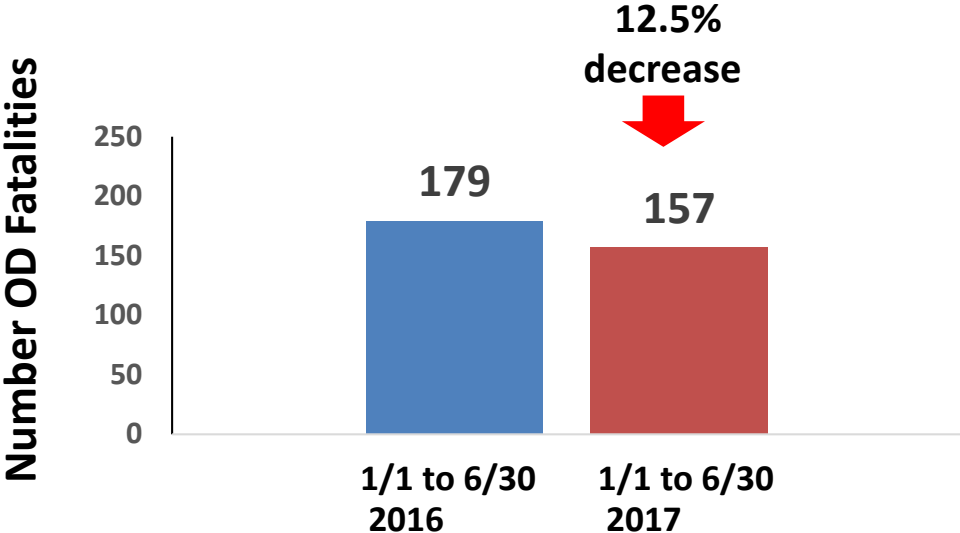
Mortality Post Release



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.

Statewide Overdose Deaths



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).

HEAL – Integrated Treatment

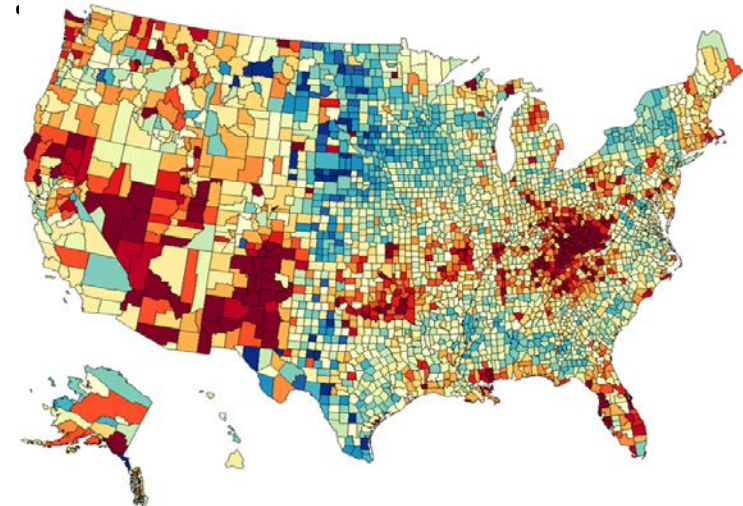
HEALing Communities Research Study

An Immediate Challenge

- OUD crisis is escalating
- Most Americans with an OUD (~80%) don't get effective treatment

Can we draw on all we know *now*... and develop integrated intervention strategies to stem the crisis *quickly*?

- Study ways to integrate evidence-based interventions comprehensively
 - In select areas highly affected by the crisis...



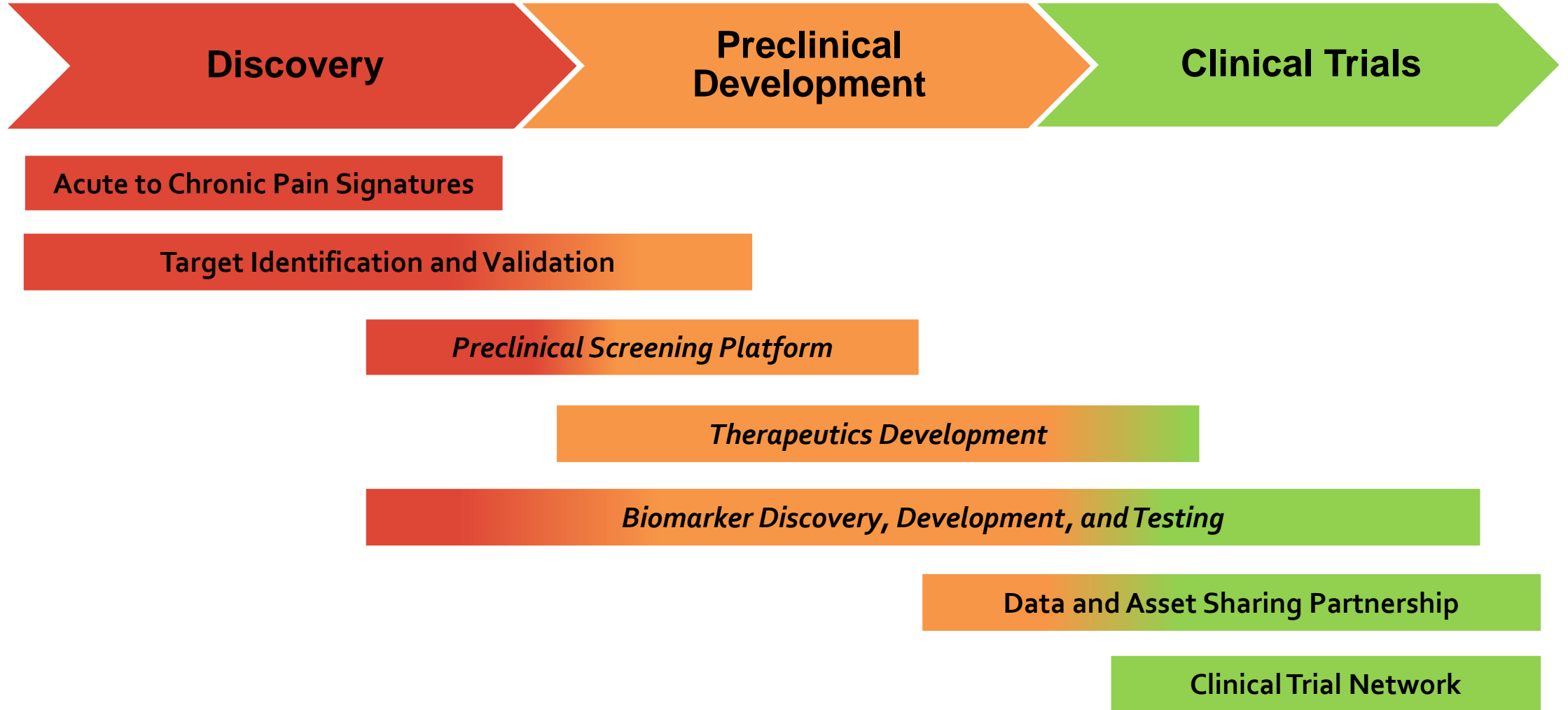
HEAL – Integrated Treatment

HEALing Communities Research Study

- ***Pilot Demonstration Project*** – a competitive process involving wide-ranging federal, state, local partnerships, integrating ALL of the stakeholders
 - Health care, criminal justice, substance treatment, government, emergency departments, first responders
- **Test and evaluate evidence-based prevention and treatment in select communities**
 - Prevent OUD and OD
 - Screen and diagnose
 - Engage and retain in medication-assisted treatment
 - Help sustain long-term recovery
- ***Goal: Decrease OD deaths and OUD***

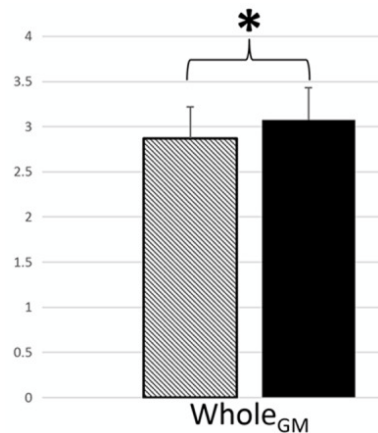
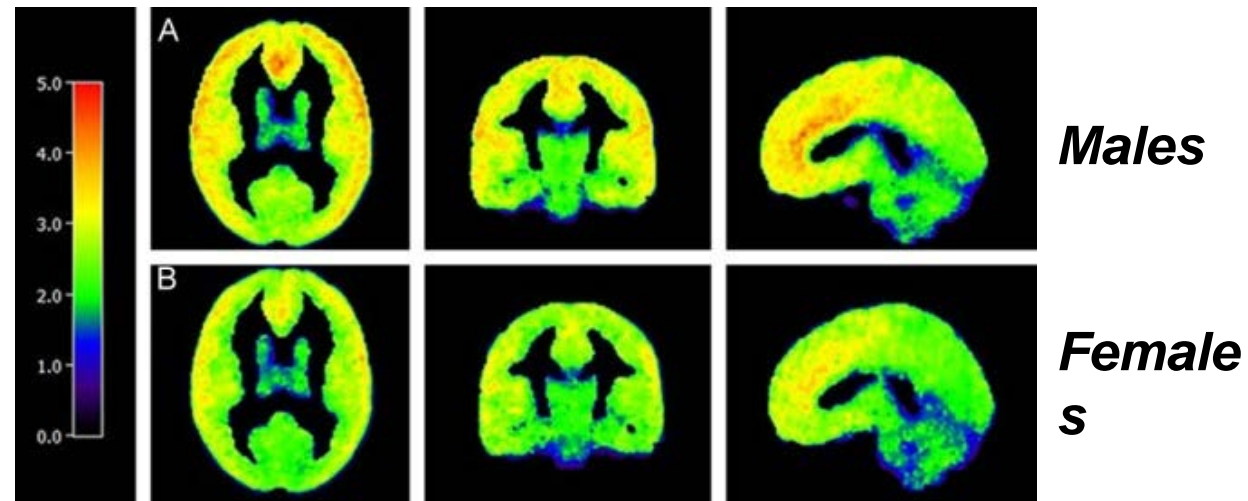


HEAL: *Pain Research Overview* for 2018



Research on the *Neurobiology of Pain*

Gender Differences in Kappa Opioid Receptor Availability



- *Males had higher K opioid receptor availability than females presumably from increased dynorphin.*
- *Could this help explain gender differences in pain catastrophizing??*

New Target for Pain Control

- Congenital analgesia: rare condition, individuals cannot feel pain
 - Mutation identified in gene that encodes for Nav1.7 – sodium channel that regulates pain-sensing neurons
- Targeting Nav1.7 to produce analgesia
 - Several companies now have drugs in pipeline to block channel
- Targeting complications
 - Understanding what happens when Nav1.7 is blocked

nature Vol 444 | 14 December 2006 | doi:10.1038/nature05413

ARTICLES

An SCN9A channelopathy causes congenital inability to experience pain

James J. Cox^{1*}, Frank Reimann^{2*}, Adeline K. Nicholas¹, Gemma Thornton¹, I Gulshan Karbani⁴, Hussain Jafri⁵, Jovaria Mannan⁶, Yasmin Raashid⁷, Lihadi Enza Maria Valente¹⁰, Shaun Gorman¹¹, Richard Williams¹², Duncan P. McHale & C. Geoffrey Woods¹

NEUROBIOLOGY

NATURE | Vol 444 | 14 December 2006

A channel sets the gain on pain

Stephen G. Waxman

Cell

157, June 5, 2014

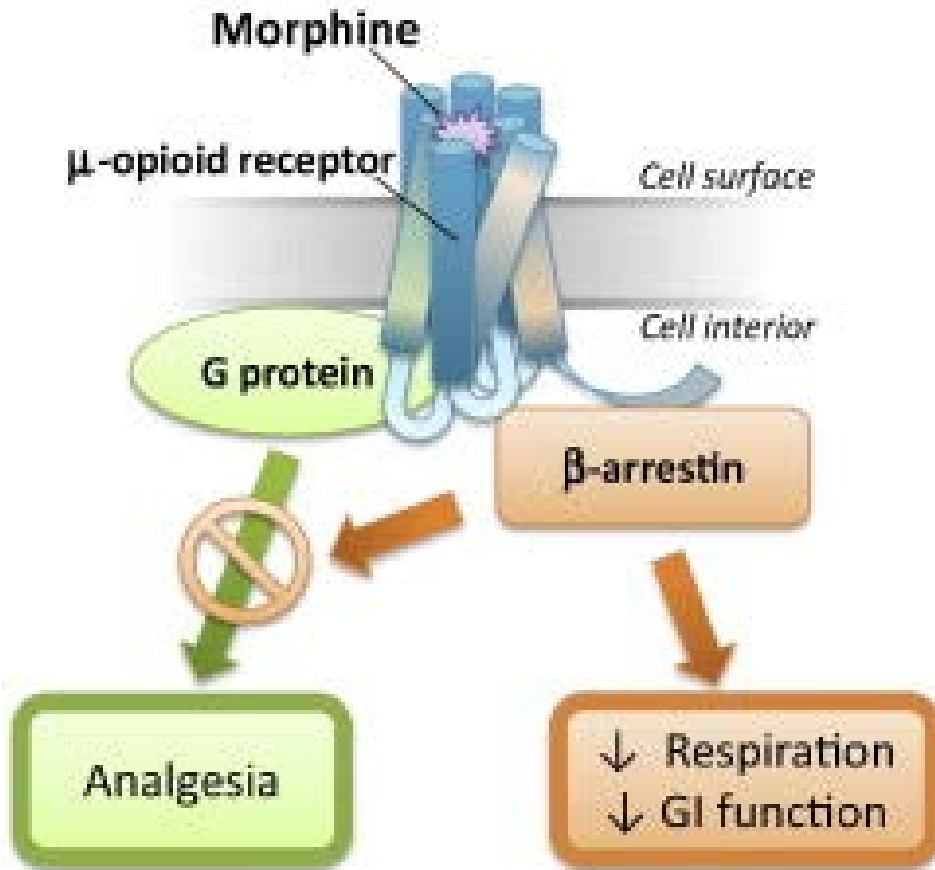
A Monoclonal Antibody that Targets a Nav1.7 Channel Voltage Sensor for Pain and Itch Relief

Jun-Ho Lee,¹ Chul-Kyu Park,² Gang Chen,² Qingjian Han,² Rou-Gang Xie,² Tong Liu,² Ru-Rong Ji,^{2,*} and Seok-Yong Lee^{1,*}

Science = Solutions

A Promising New Generation Of Pain Therapeutics

Biased Mu-Opioid Receptor Ligands



Soergel DG, et al., *Pain* 2014. Manglik A, et al., *Nature* 2016. DeWire SM, et al., *JPET* 2013. Bohn LM, et al., *Science* 1999

Science = Solutions

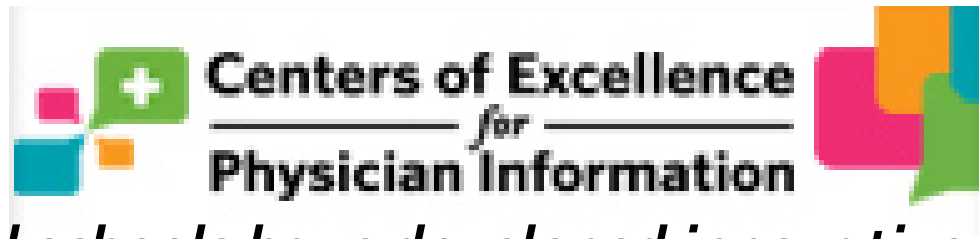
Additional Research Priorities

- Precision treatments for addiction
- Non-pharmacological treatments
- Integrated models of pain management
- Linkages between pain, addiction, mental health
- Education



NIDAMED

Opioid Education



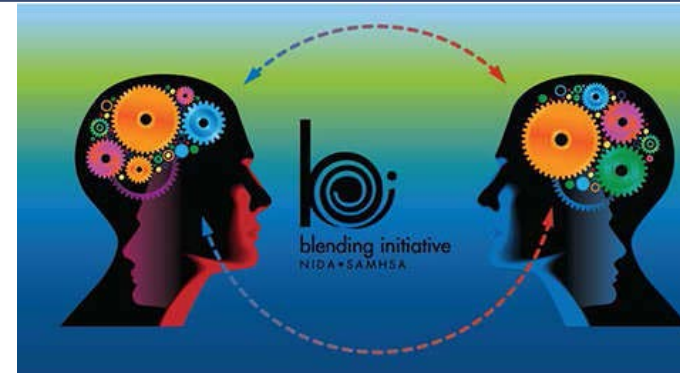
*Resources for Medical Students,
Resident Physicians & Faculty*

www.drugabuse.gov/coe

Medical schools have developed innovative curriculum resources about how to identify and treat patients with substance use disorders



*Web training on pain assessment
and treatment*



*Bringing NIDA
research to
clinical practice*

Archived NIDA CME Courses:

Safe Prescribing for Pain

*Managing Pain Patients
Who Abuse Rx Drugs*

Upcoming NIDA CME Course:

*Adolescent Substance Use
(Prescription Opioid Module)*

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In April 2018, NIH launched the HEAL (Helping to End Addiction Long-term) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. This Initiative will build on extensive, well-established NIH research, including basic science of the complex neurological pathways involved in pain and addiction, implementation science to develop and test treatment models, and research to integrate behavioral interventions with Medication-Assisted Treatment (MAT) for opioid use disorder (OUD). Successes from this research include the development of the nasal form of naloxone, the most commonly used



www.nih.gov/heal-initiative

Summary:

- Complex biological, developmental and social aspects of substance use and addiction suggest *multipronged responses*.
- The severity of the opioid crisis demands *urgent action*.

www.nih.gov/opioid-crisis

Science = Solutions

www.drugabuse.gov