

Director's Report to the National Advisory Council on Drug Abuse

September 6, 2017

Nora D. Volkow, M.D., Director

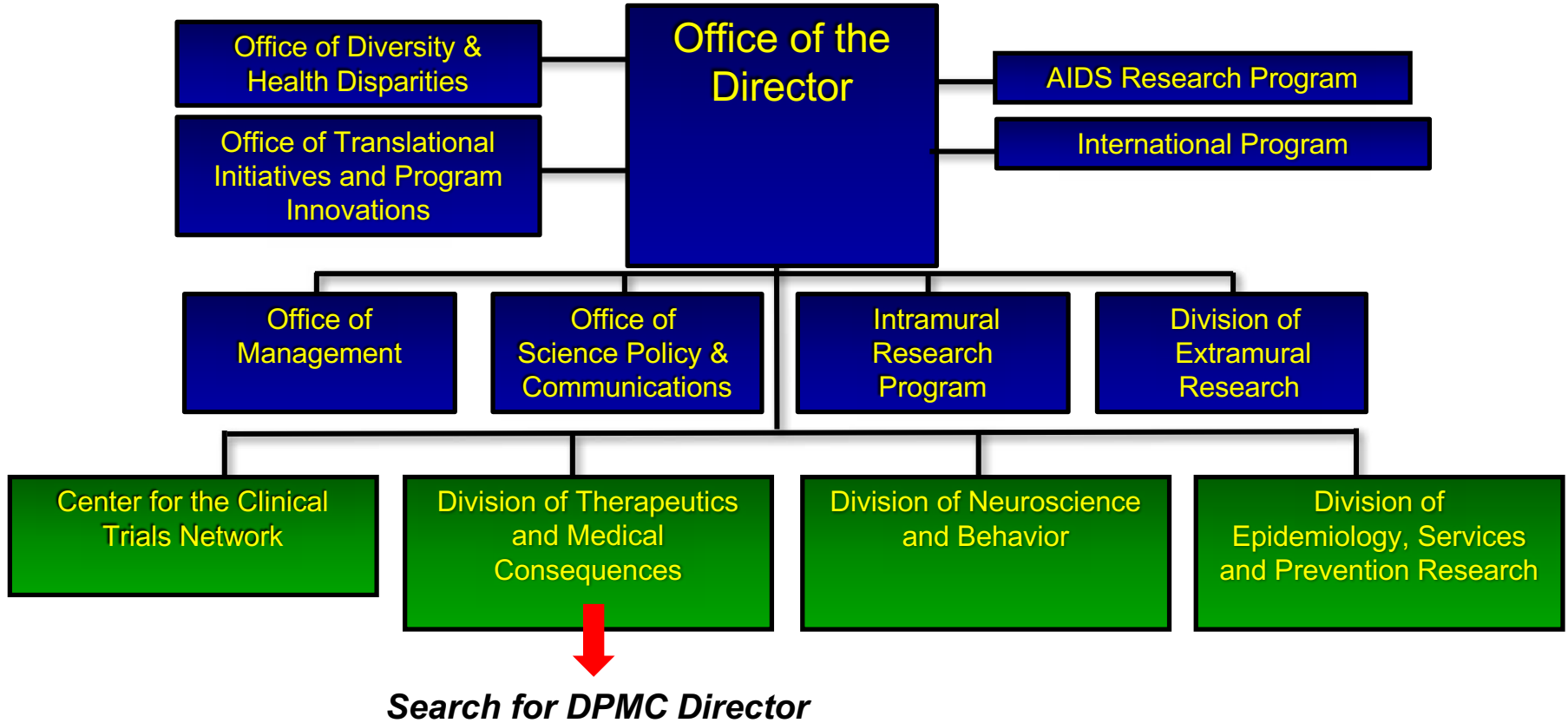


National Institute
on Drug Abuse



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NIDA



Director's Report to the National Advisory Council on Drug Abuse

- **Budget Update**
- **What's New @ HHS/NIH?**
- **Recent NIDA
Activities & Events**

NIDA BUDGET

(Thousands)

	FY 2016 Actuals	FY 2017 Operating Plan	FY 2018 PB
NonAIDS	\$754,727	\$794,135	\$647,674
AIDS	\$294,244	\$276,711	\$217,324
TOTAL	\$1,048,971	\$1,070,846	\$854,998

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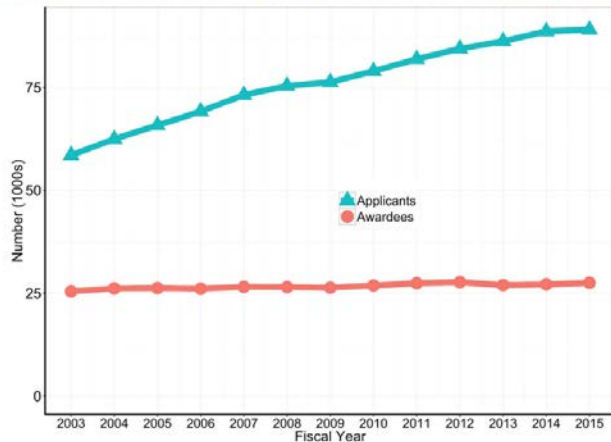
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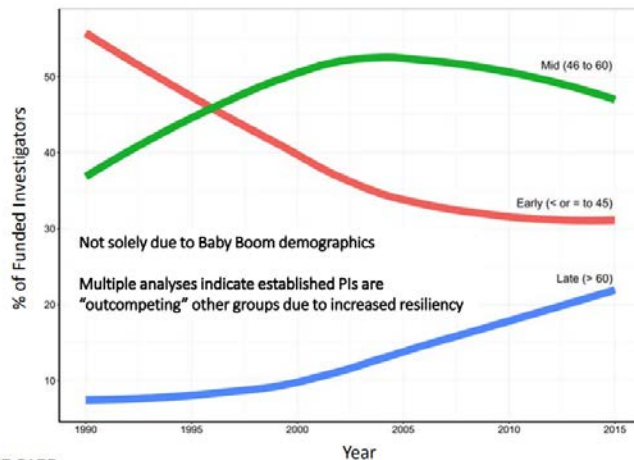
NIH Next Generation Research Initiative

Hypercompetition: Applicants and Awardees for NIH RPGs



OER SARB

Age of Investigators Funded by NIH



OER SARB

Challenge:

- Too many researchers vying for limited resources
- Many highly meritorious applications go unfunded
- Particularly challenging for many early-stage and mid-career investigators

Goal: Focus support for **early-stage** (ESIs – within 10 years of terminal degree) and **early established investigators** (EEl – within 10 years of first major NIH competing award as an ESI)

NIH hopes to support a combined additional ~400 ESIs and EEl in FY 2017, ramping up to ~ \$1.1 billion per year after five years

New NIH Definition of Clinical Trial

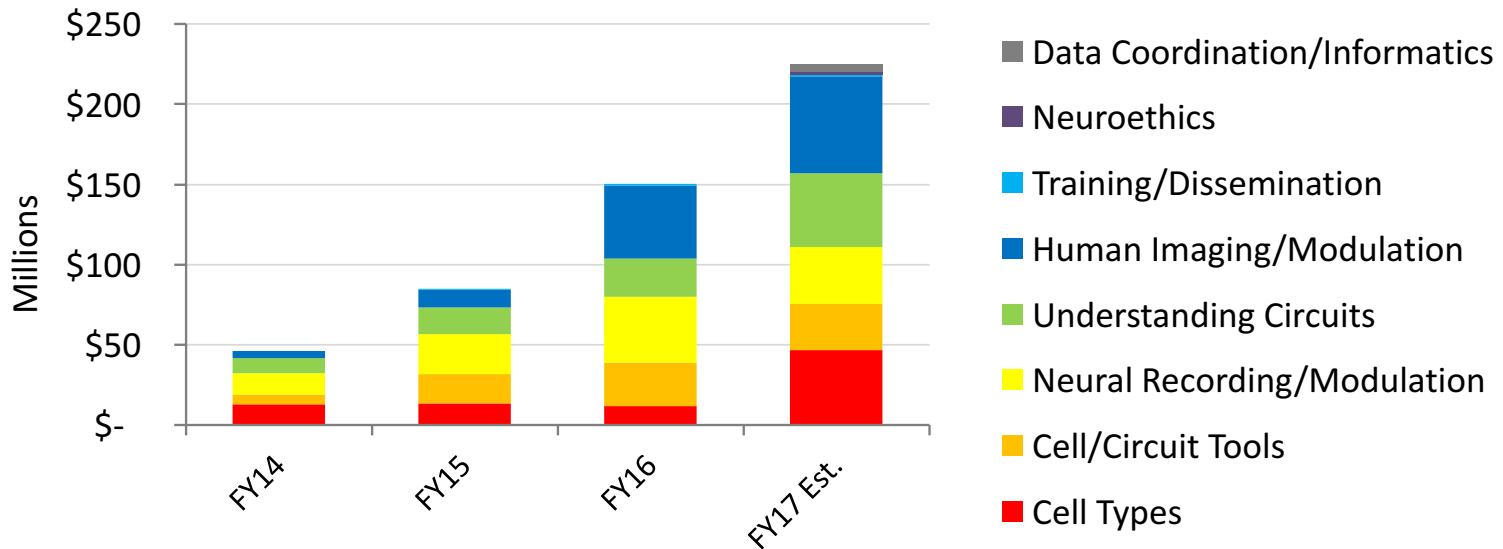
Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Clinical Trials need to:

- ✓ Respond to a **clinical trial-specific FOA**
- ✓ Address additional **review criteria** specific for clinical trials
- ✓ **Register and report** clinical trial in ClinicalTrials.gov

Due Dates on or
after January 25,
2018

All clinical trial applications **MUST** be submitted to an FOA that allows clinical trials



FY17 FOAs receiving FY17 funds

- 1. Census of Brain Cell Types (4 FOAs)
- 2. Tools for Cells and Circuits (1 FOA)
- 3. Technologies for Neural Recording and Modulation (3 FOAs)
- 4. Understanding Neural Circuits (3 FOAs)
- 5. Human Imaging and Neuromodulation (8 FOAs)
- 6. Data Coordination (3 FOAs)
- 7. Technology Dissemination and Training (1 FOA)
- 8. Neuroethics (1 FOA)

** FY17 does not include multi-year funds, and includes some awards that may be made in early 2018.*

A bar graph shows the funding amounts for the different FOAs supporting scientific areas of brain research, for FY 2014, FY 2015, FY 2016, and an estimate for FY 2017 funding. Gradations on the bars represent the scientific areas. The funding amounts in each year for 5 main brain science areas are as follows:

	FY 2014	FY 2015	FY 2016	FY 2017 (estimate)
Census of Brain Cell Types	\$6,428,017	\$17,854,240	\$27,112,667	\$46,884,472
Tools for Cells and Circuits	\$12,888,647	\$25,385,832	\$27,112,667	\$28,877,614
Technologies for Neural Recording and Modulation	\$9,657,719	\$25,385,832	\$40,781,027	\$35,333,994
Understanding Neural Circuits	\$4,330,316	\$19,423,226	\$24,219,895	\$45,607,091
Human Imaging and Neuromodulation	not shown	\$431,998	\$45,110,569	\$60,880,116
Data Coordination /Informaticss				\$ 4,011,774

THE BRAIN INITIATIVE®

BRAIN SFN Events

BRAIN Initiative: New Concepts and Early - Stage Research for Large - Scale Recording and Modulation in the Nervous System (R21) (RFA-EY-17-002)

Posted Date: July 17, 2017; Open Date: September 26, 2017
Application Receipt Date(s): October 26, 2017

BRAIN Initiative: Research on the Ethical Implications Advancements in Neurotechnology and Brain Science (R01) (RFA-MH-18-500)

Posted Date: August 25, 2017; Open Date: November 7, 2017
Application Receipt Date(s): December 7, 2017



*Advancing the Understanding of
the Brain and Nervous System*



Symposia:
Exciting New Tools and Technologies
Emerging From the BRAIN Initiative
Chair: Joshua A. Gordon, MD, PhD

BRAIN Initiative Networking Satellite
When: 6:30pm-9:30pm (EST), November 12, 2017
Sponsor: The BRAIN Initiative Alliance



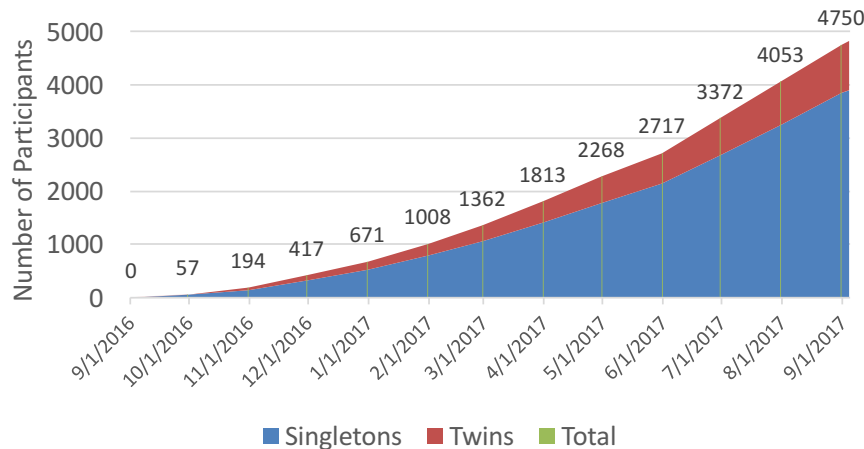
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ABCD Update

4819 as of today

ABCD Enrollment
through of 9/4/17



ABCD Study Fast Track Data

<https://data-archive.nimh.nih.gov/abcd>

Unprocessed neuroimaging data as well as basic participant demographics (age, sex), including:

- High-resolution structural data (3D T1 - and T2-weighted scans)
- Advanced diffusion MRI (multiple b-values and directions)
- Resting State fMRI
- Task fMRI (Monetary Incentive Delay, Stop-Signal, and Emotional N-Back), along with raw E-Prime task files

Annual Curated Data Release

Curated data, including all assessment domains and computational analysis pipelines, will be released annually, starting in **December 2017** with the first 4700 participants.

Adolescent Brain Cognitive Development

Teen Brains. Today's Science. Brighter Future.





Fentanyl Overtakes Heroin as Leading Cause of U.S. Drug Death

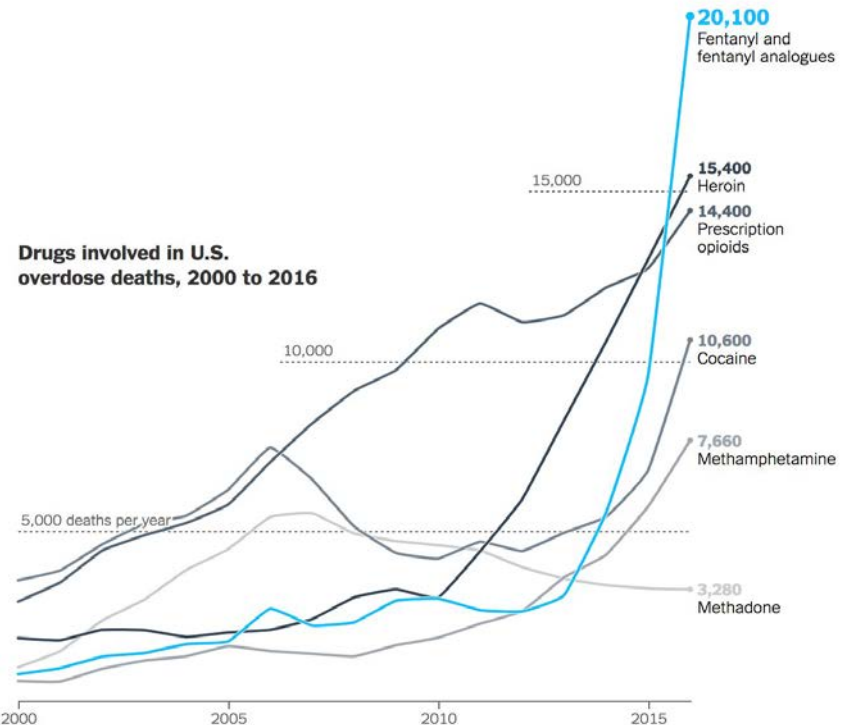
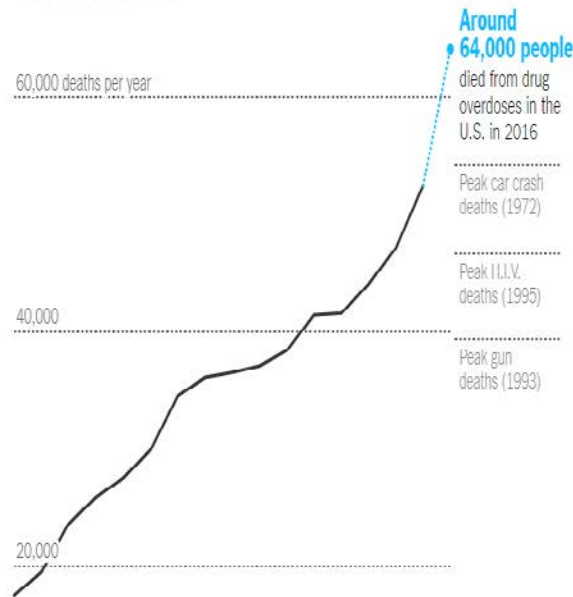
[JOSH KATZ](#) © SEPT. 2, 2017

Drug overdoses killed roughly 64,000 people in USA in 2016; 22% rise over 2015.

Fentanyls are changing equation: Death rate in Maryland last year outpaced that in Kentucky and Maine

Estimate U.S. Drug Deaths in 2016

Total U.S. drug deaths



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

CUTTING EDGE SCIENCE MEETING SERIES TO END THE OPIOID CRISIS

1

Medications Development for Opioid Use Disorders and for Overdose Prevention and Reversal -- June 5, 2017

2

Development of Safe, Effective, Non-Addictive Pain Treatments -- June 16, 2017

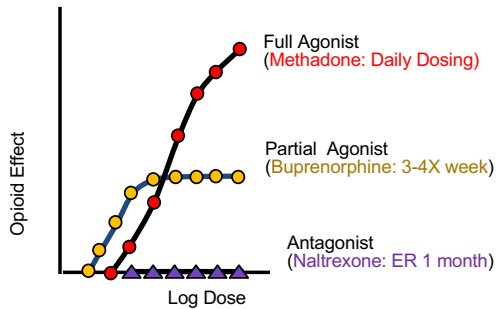
3

Understanding the Neurobiological Mechanisms of Pain -- July 7, 2017



National Institutes of Health

Medication Assisted Treatment (MAT)



DECREASES:

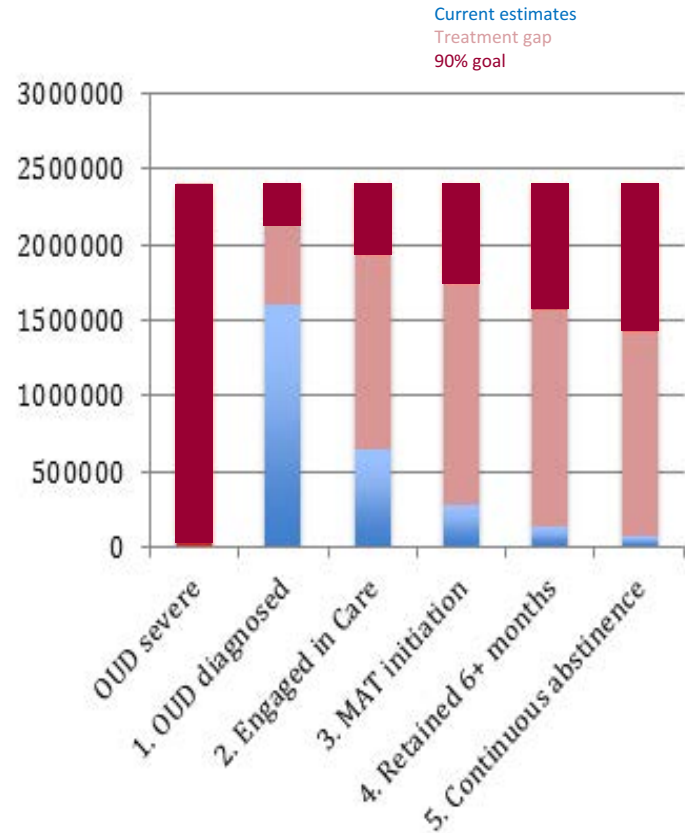
- Opioid use
- Opioid-related overdose deaths
- Criminal activity
- Infectious disease transmission

INCREASES

- Social functioning
- Retention in treatment

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

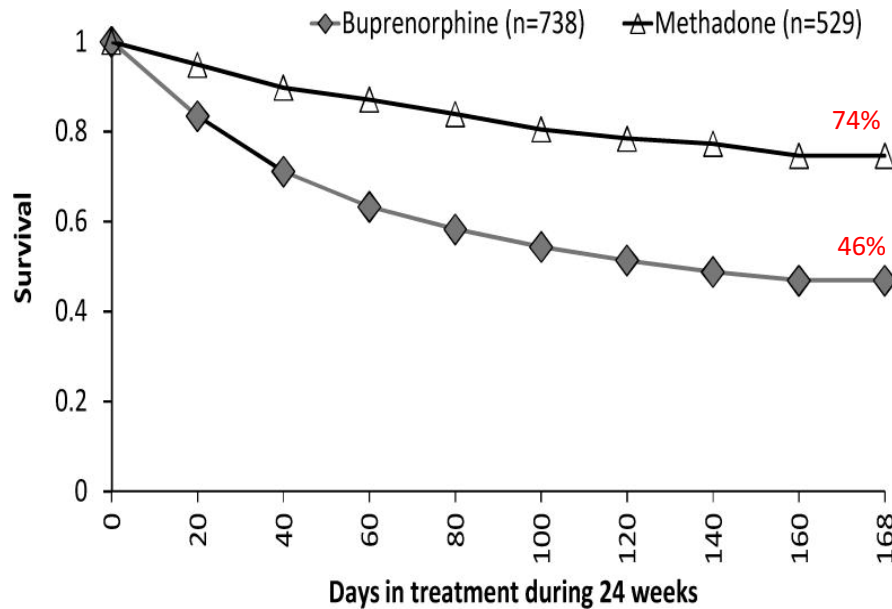
OUD Cascade of Care in USA



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

Medication Dropout in OUD

Treatment completion rate higher for methadone vs. buprenorphine



Hser Y, et al. 2014

- After completing treatment program **50-70% resume substance use in first year** – most within 90 days
- **90%** of patients require additional treatment within 4 years
- **50% patients required 3-4 treatment admissions** to sustain recovery for 1 year or more

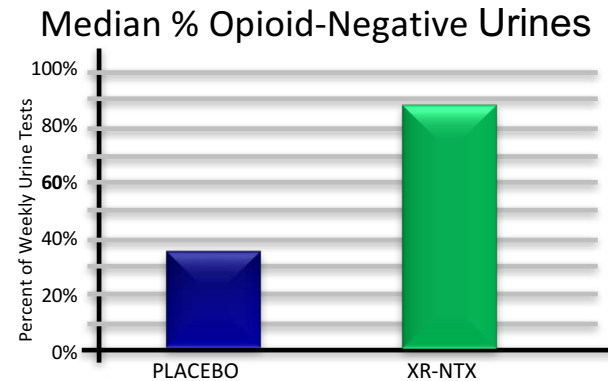
Dennis ML and Scott CK, 2012

Extended Release Formulations

PROBUPHINE®

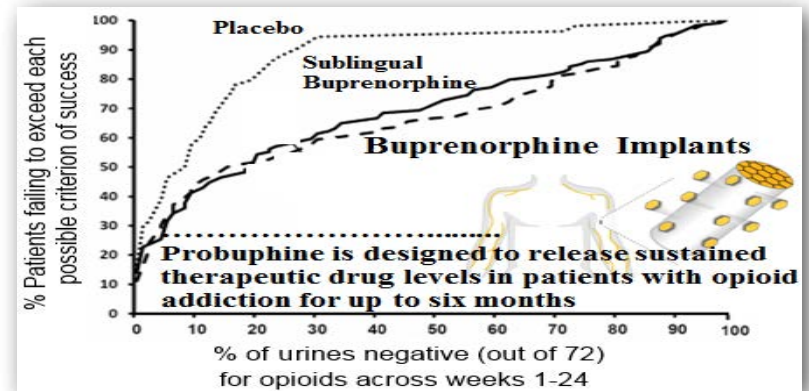
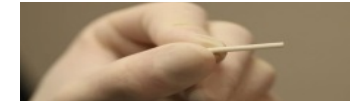


IM Injection q 4 weeks for 24 weeks



■ Placebo: N=124
■ XR-NTX: N=126

Krupitzky et al., Lancet 2011 Apr 30;377(9776):1506-13.



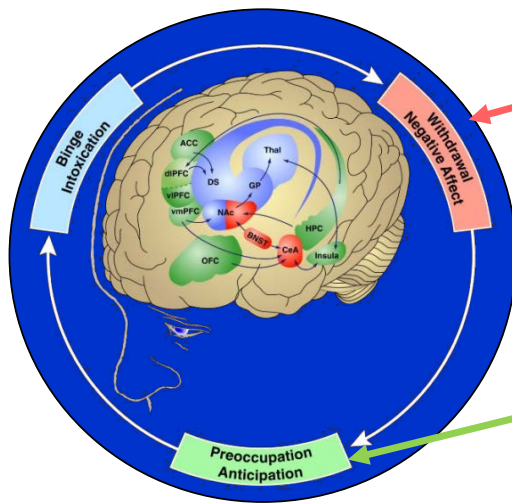
Rosenthal et al., *Addiction* 2013;105.

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

Promising Targets



Mechanisms to reduce stress-induced drug seeking

- *Kappa Opioid Receptor Antagonists*
- *OX-1 Receptor Antagonists*
- *NOP Receptor Agonists*
- *α 2-Adrenergic Receptor Agonists*
- *PDE7 Inhibitors*

Mechanisms to reduce cue-induced drug seeking

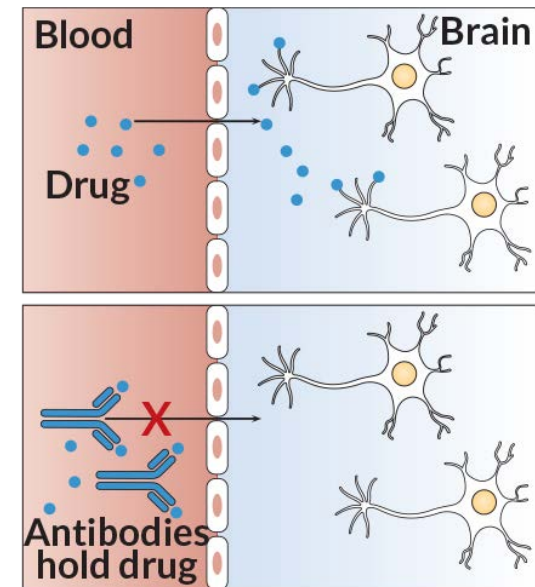
- *D3 Receptor Antagonists*
- *OX-1 Receptor Antagonists*
- *5-HT2C Receptor Agonists*
- *5-HT2A Receptor Inverse Agonists*
- *mGluR2 Positive Allosteric Modulators*
- *5-HT6 Receptor Inhibitors*
- *PDE7 Inhibitors*

*Koob GF, Volkow ND.
Neuropsychopharmacol Rev, 2010*

Opportunities for Partnership in Sharing of Compounds and for de-risking potential new targets for treatment of OUD

Monoclonal Antibodies and Vaccines to Treat OUD and Prevent Overdose

- Heroin vaccine validated in primate model in 2017
- First vaccine for fentanyl and fentanyl analogs reported in a mouse model in 2016
- Reduces drug reaching the brain
- Protect high-risk individuals against overdose



*Bremer et al, 2017;
Bremer et al, 2016;
Janda and Treweek, 2012.*

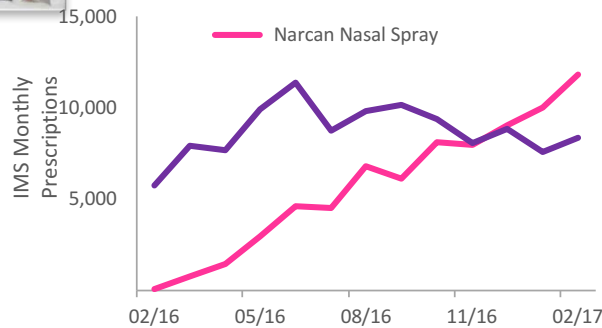
Opportunities for Partnership in Sharing of Reagents and for De-risking Vaccines or Monoclonal Antibodies for Treatment of OUD

Medications for Overdose Reversal and Prevention

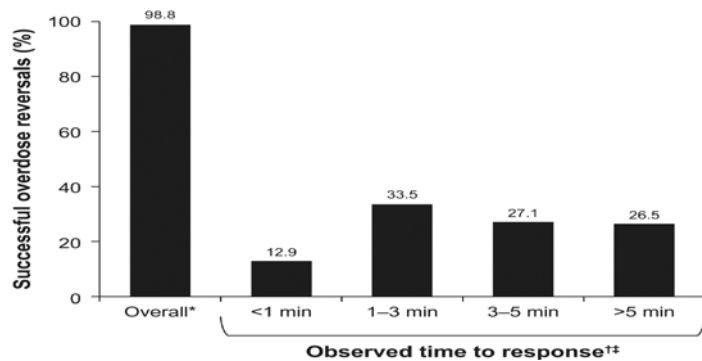


NARCAN® Nasal Spray device
\$37.50 per 4mg

Approved by FDA
November 2015



Opioid Overdose Reversal By Narcan® Nasal Spray



Avetian GE et al., Current Medical Research and Opinion, 23 May 2017.

- Stronger, longer acting formulations for extra potent opioids (e.g. fentanyl)
- Medications and Heroin/Fentanyl Vaccines to prevent Overdoses
- Medications (i.e Ampakines) and Stimulation devices to prevent respiratory depression
- OD detection and autoinjectors
- Post-overdose interventions for treatment engagement

Medications Development for OUD

Key Challenges:

- Minimal Industry Involvement
- Lack of infrastructure for OUD treatment
- Lack of reimbursement for OUD medications is a disincentive for medication development
- Abstinence as main outcome for medication approval by FDA is a major challenge for medication development

Major Needs:

- Incentives to encourage private industry investment.
- Better surveillance and long-term outcomes data on MAT and OD
- Funding

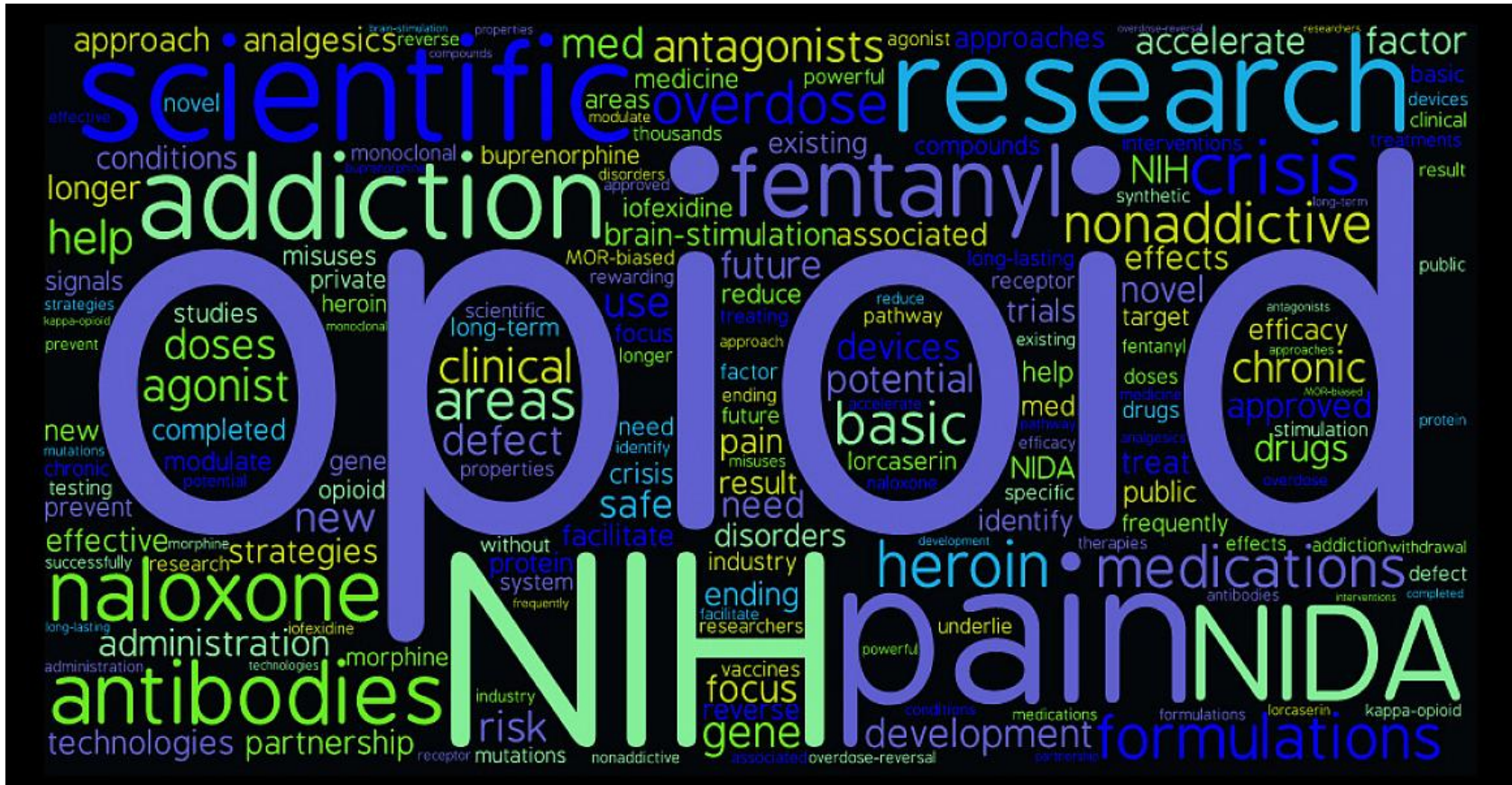
Medications Development for OUD

Next Steps:

- PPP * ***Dr. Collins will describe this***
- Expand Clinical Network to rapidly deploy clinical trials and for epidemiological studies
- Engage CMS to address reimbursement
- Engage FDA for alternative outcomes for medication approval
- Explore mechanisms to expedite NIH review of grant proposals

Later this morning...

NIH Director Dr. Francis Collins will discuss the **public-private partnership** effort that NIH will be launching to address the opioid crisis



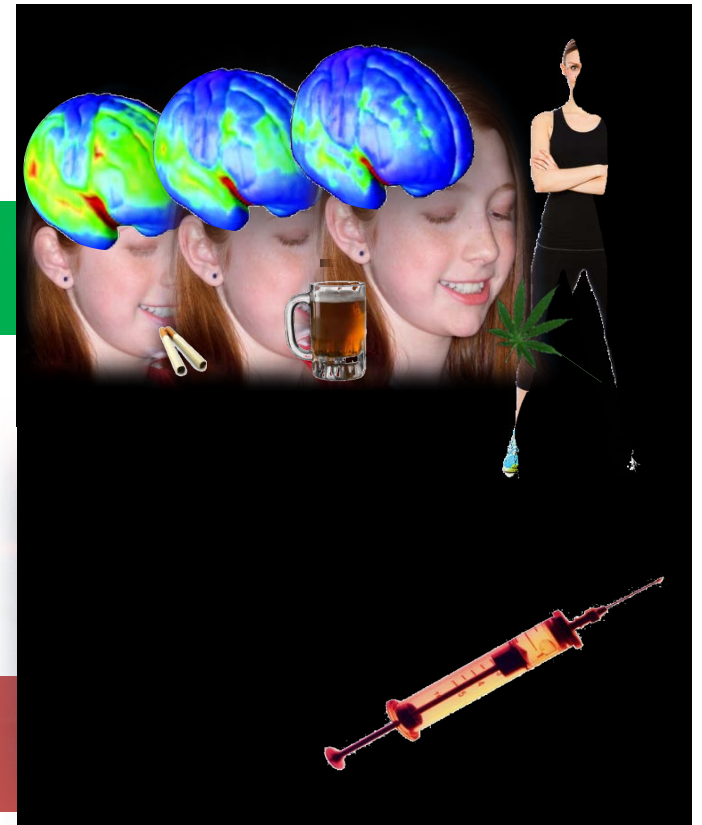
Priority Areas

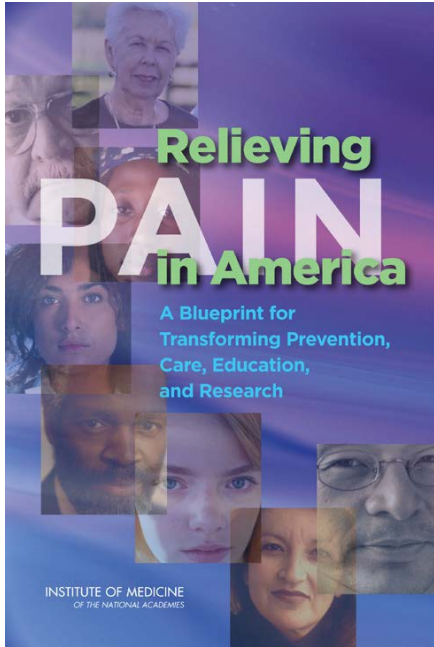
Prevention Research

(Children & Adolescents)
genetics/epigenetics
development
environment
co-morbidity

Treatment Interventions

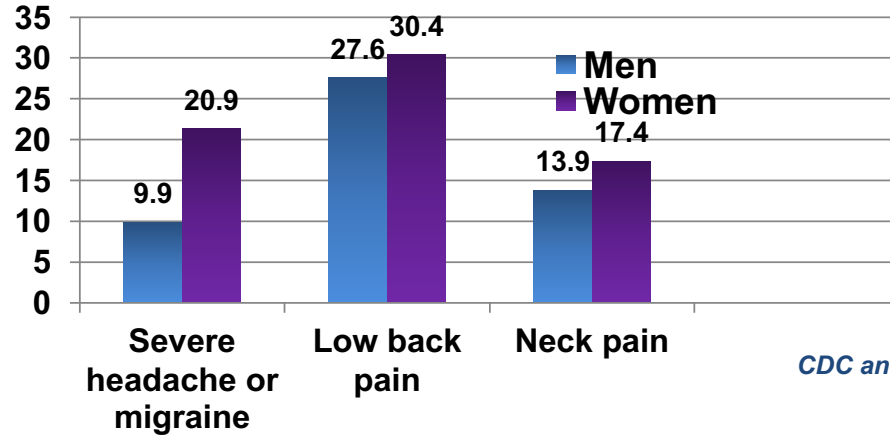
(New Targets & New Strategies)





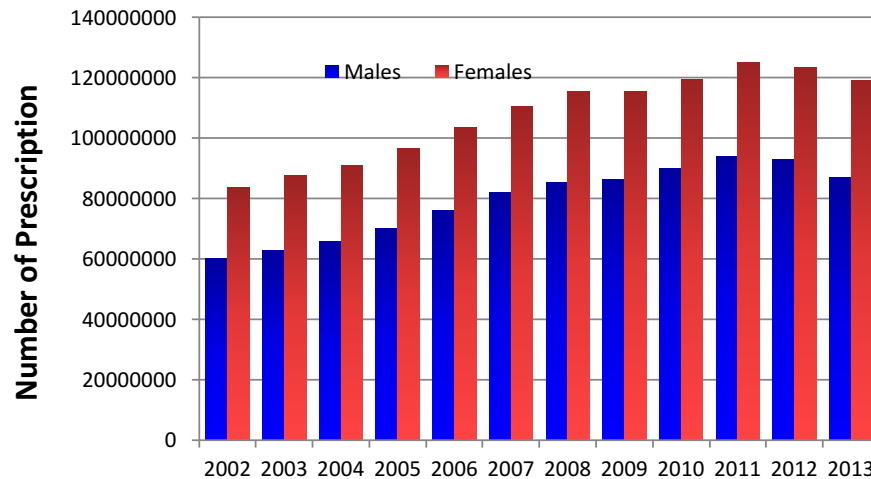
Women suffer more pain in many categories and are Prescribed more Opioids

Rates of U.S. Adults > 18 and Older Reporting Pain, 2015



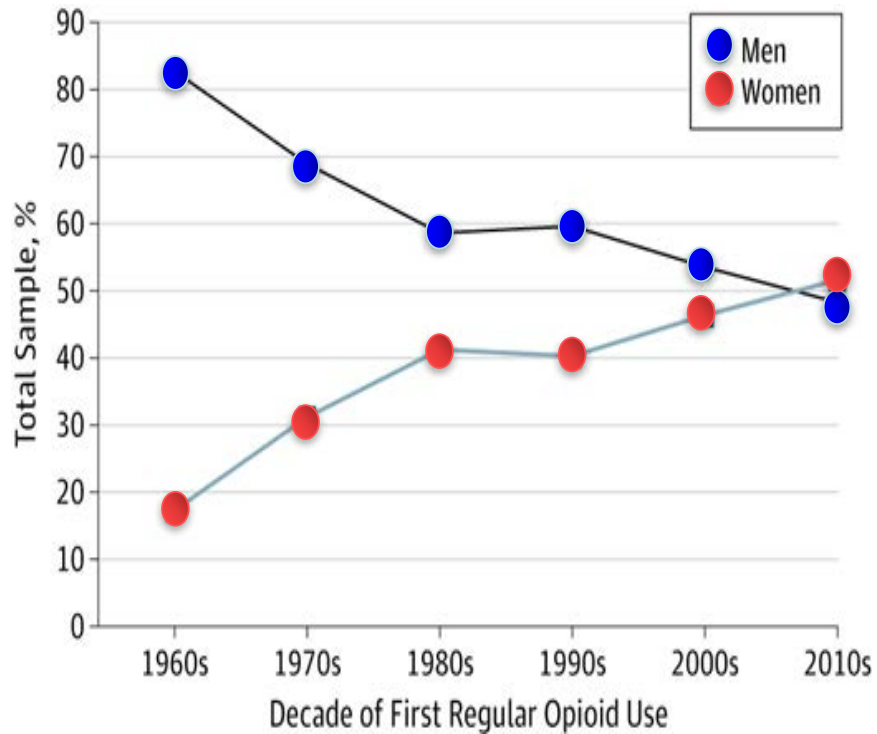
CDC and NCHS, 2015

Opioid Prescriptions U.S. Retail Pharmacies, 2002-2013



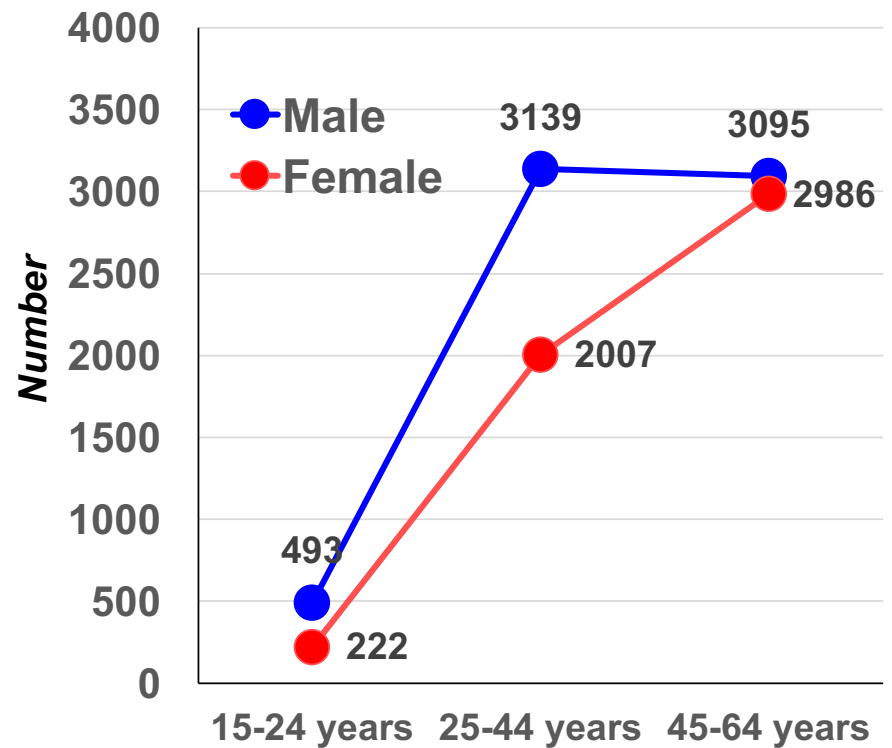
Source: IMS Health, National Prescription Audit

The Changing Face of Heroin Use in the US



Cicero TJ et al., JAMA Psychiatry 2014.

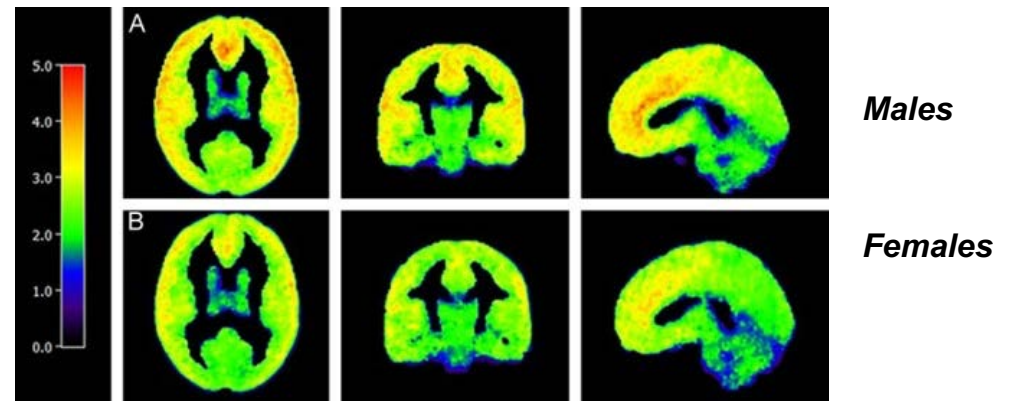
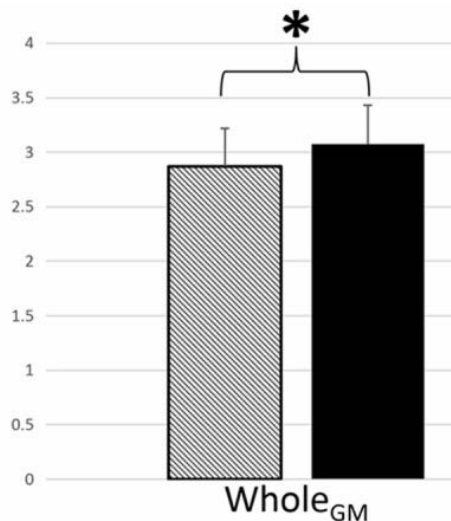
Deaths Involving Natural and Semi-Synthetic Opioids



Rudd RA et al., MMWR Morb Mortal Wkly Rep 2016

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 NIDA FOAs



***Development of a Device to Objectively Measure Pain
(R43/R44) (RFA-DA-18-012); (R41/R42) (RFA-DA-18-013)***

***Posted Date: July 12, 2017; Open Date: November 5, 2017;
Application Due Date(s): December 5, 2017***

The goal of this RFA is to encourage Small Business Concerns (SBCs) to develop a tool to objectively measure pain for research or clinical purposes.

Priority Areas

Prevention Research

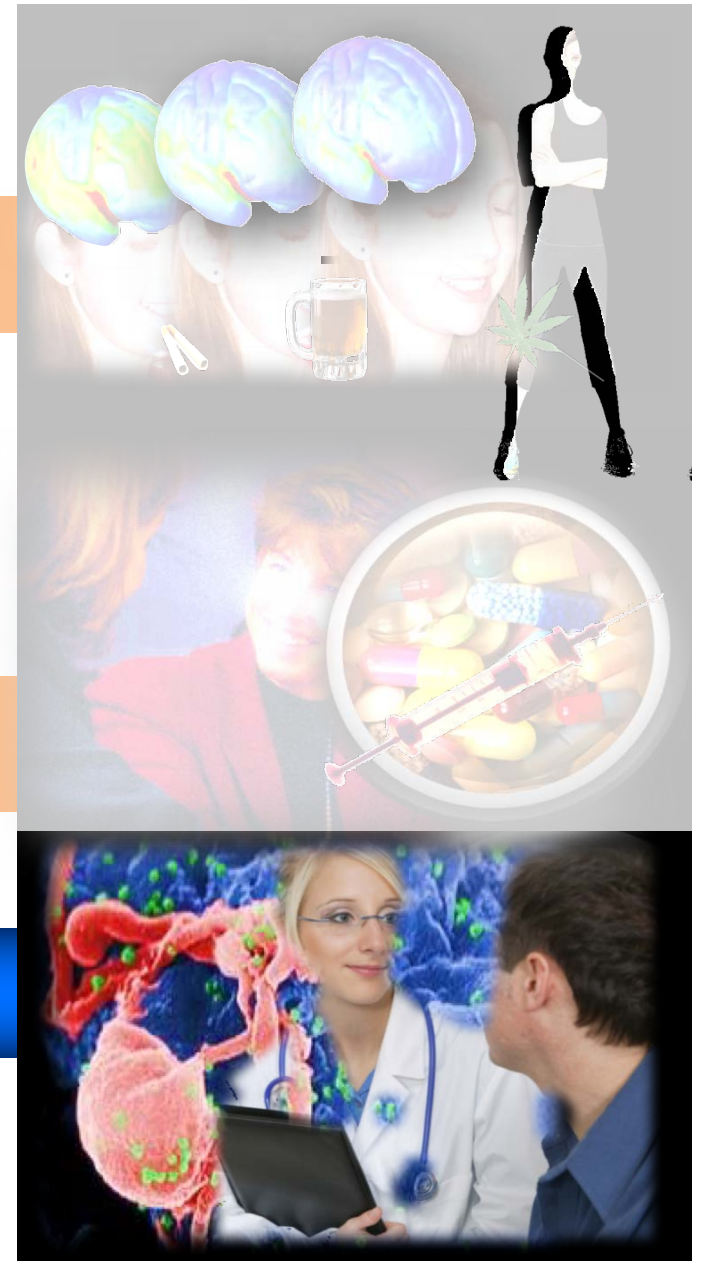
(Children & Adolescents)
genetics/epigenetics
development
environment
co-morbidity

Treatment Interventions

(New Targets & New Strategies)

HIV and Drugs

Prevention
Treatment



New NIDA FOAs

HIV-Associated Neuropathic Pain and Opioid Interaction (R01) (RFA-DA-18-015)

Posted Date: August 3, 2017; Open Date: November 18, 2017;

Application Due Date(s): December 18, 2017

HIV/HCV Co-Infections in Substance Abusers (R01) (PAS-17-311)

Posted Date: June 13, 2017; Open Date: August 7, 2017;

Application Due Date(s): September 7, 2017 & January 7, 2018

- (a) impact of substance abuse on HIV, HIV/HCV co-infection disease progression,***
- (b) interactions between HIV and HCV,***
- (c) hepatic and non-hepatic co-morbidities associated with HIV/HCV co-infections in SUD,***
- (d) effectiveness of interferon-free direct acting antivirals (DAAs) to treat HIV/HCV co-infections in SUDs.***

2017 Intel International Science and Engineering Fair Addiction Science Awards

Anusha Zaman from Baton Rouge Magnet High School, Louisiana
Epigenetic and Biotransformation Effects of Hookah Smoke Extract on Human Oral Keratinocytes

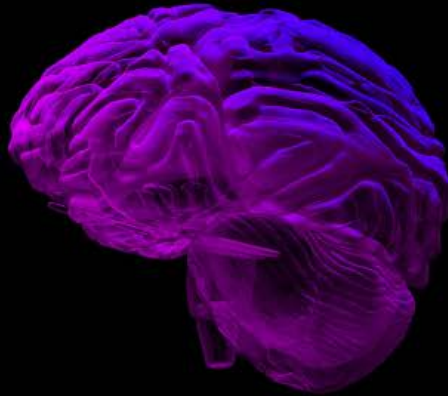
Nkima Stephenson from Rockdale Magnet School for Science and Technology in Conyers, Georgia,
Data Analysis of the Epigenetics of Drug and Alcohol Dependence

Kashfia Rahman from Brookings High School in Brookings, South Dakota
Dynamics of Habituation: A Neural Study of the Effects of Repeated Exposures to Risky Behaviors on Cognitive Control and Emotional Responses in the Adolescent Brain



2017

THE NATIONAL INSTITUTE ON DRUG ABUSE &
THE NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM
PRESENT



FRONTIERS IN ADDICTION RESEARCH



NIDA-NIAAA Mini-Convention
Friday, November 10, 2017 • 8:00 AM – 6:00 PM
Walter E. Washington Convention Center – Room 207A
Washington, DC

[WELCOME](#) [AGENDA](#) [LOGISTICS](#) [NIDA-NIAAA SfN EVENTS](#) [REGISTRATION](#) [CONTACT](#)

- **Session I. Understanding the Role of Astrocytes in Nervous System Function**
- *Jacob P. Waletzky Memorial Award Lecture*
- *Joint NIDA-NIAAA Early Career Investigator Showcase [ECIS]*
- **Session II. Social Stressors, Immune Response and Substance Use Disorders**
- **Session III. Novel Approaches for Translational Research and Drug Discovery**