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

May 15, 2018

Nora D. Volkow, M.D., Director

National Institute on Drug Abuse

@NIDAnews

NIDA

- Office of Diversity & Health Disparities
- Office of Translational Initiatives and Program Innovations
- **Office of the Director**
  - AIDS Research Program
  - International Program
  - Office of Management
  - Office of Science Policy & Communications
  - Intramural Research Program
  - Division of Extramural Research
    - Center for the Clinical Trials Network
    - Division of Therapeutics and Medical Consequences
    - Division of Neuroscience and Behavior
    - Division of Epidemiology, Services and Prevention Research

Kurt Rasmussen, Ph.D., Director, DTMC

Formerly: Senior Research Advisor, Neuroscience Division, Eli Lilly & Co.

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

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

NIDA BUDGET

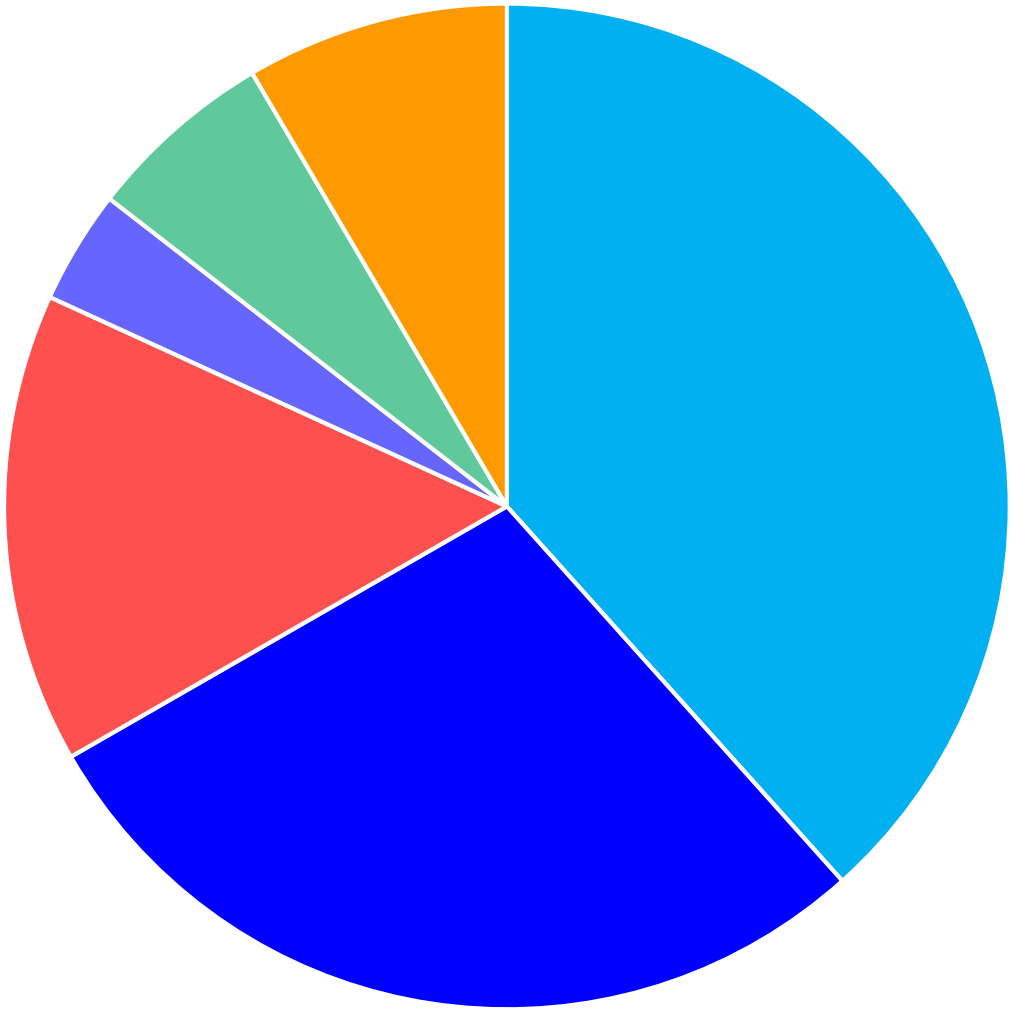
(Thousands)

	FY 2017 Actuals	FY 2018 Operating Plan	FY 2018 Opioid Funding [1]	FY 2019 President's Budget
NonAIDS	$794,102	$858,106	$250,000	
AIDS	$276,711	$268,551		
TOTAL	$1,070,813	$1,126,657	$250,000	$1,137,403

[1] *FY 2018 Opioid Funding expires September 30, 2019*

National Institute on Drug Abuse Portfolio

FY 2017 Actual



- Division of Neuroscience & Behavior -- 38%
- Division of Epidemiology, Services & Prevention Research -- 28%
- Division of Therapeutics and Medical Consequences -- 15%
- Center for the Clinical Trials Network -- 4%
- RMS -- 6%
- Intramural Research -- 8%

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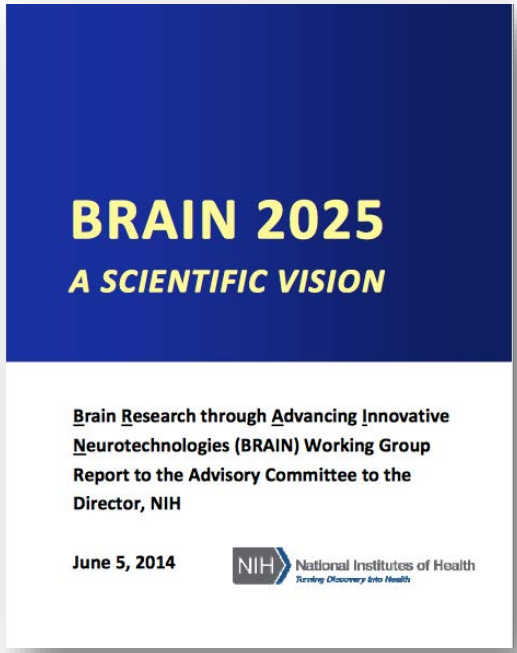
- Recent NIDA Activities & Events



NIH: Focus on Structure and *Function of Brain Circuits*

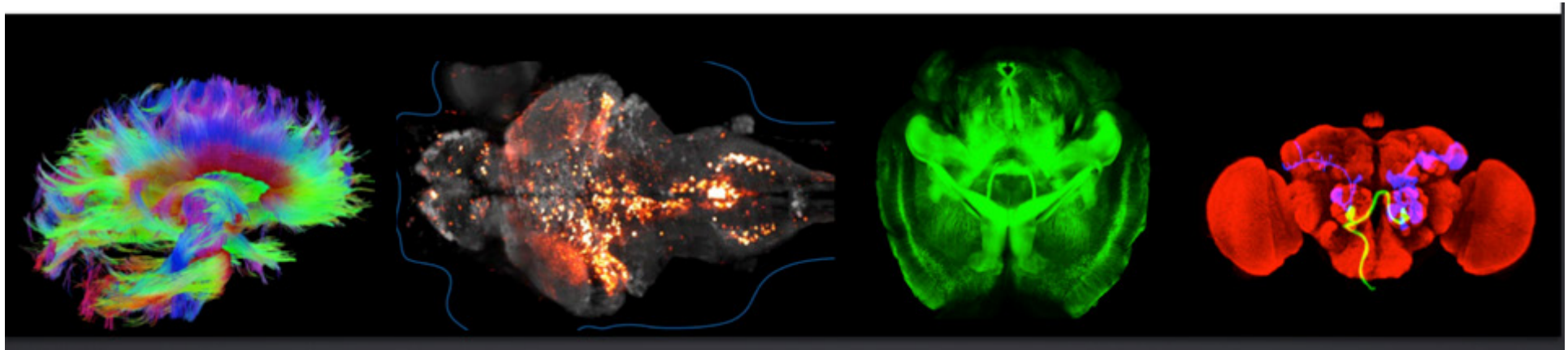
Goal: See the circuits in action to understand:

- How the brain moves, plans, executes
- How to monitor/manipulate circuits for improved function
- How disordered brain circuits cause neuro/mental/substance use disorders

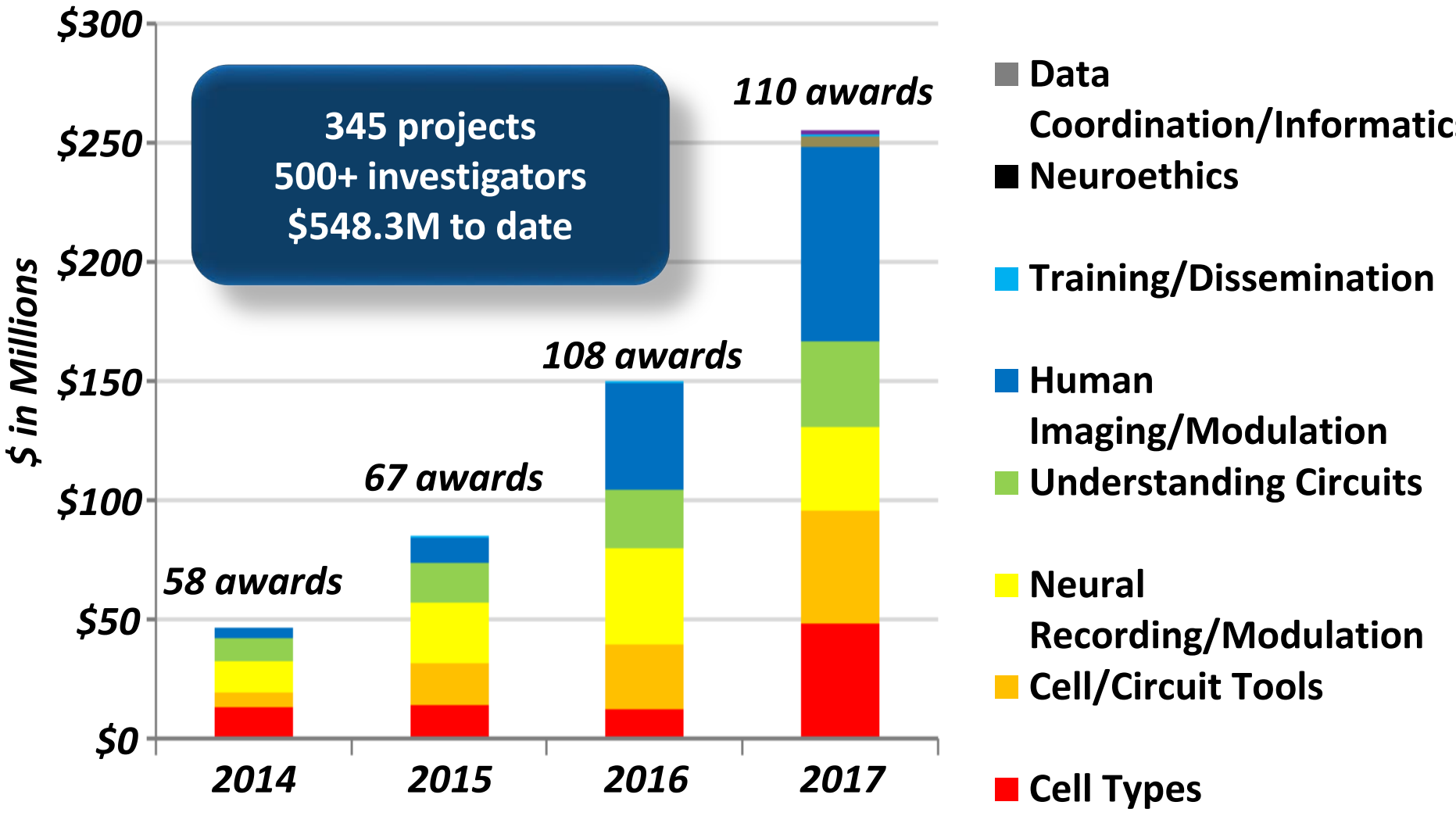
Long-term goal: Make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention

Emphasize technology development

Emphasize discovery driven science



Overall Support for High Priority Research Areas



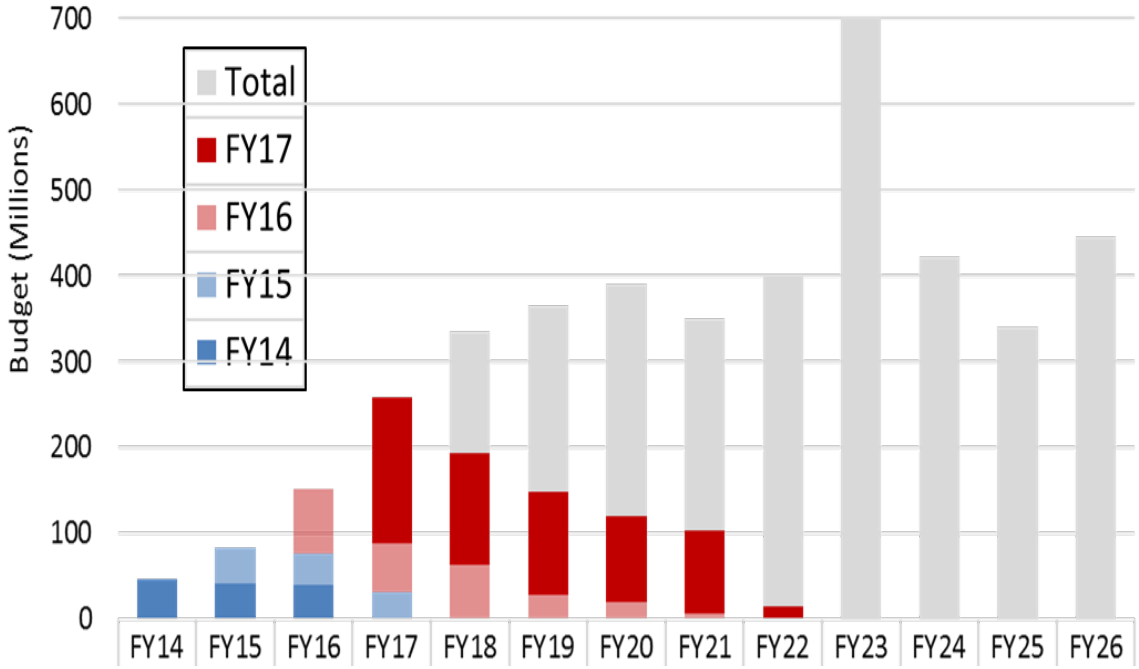


Figure 2. Awarded and committed BRAIN Initiative funds as of FY2017. Each color represents the initial fiscal year of the corresponding competing awards and associated out-year non-competing obligations. Gray represents anticipated funds for the remainder of the initiative, assuming a "base" budget of $150M (now ~$310) plus funds authorized by the 21st Century Cures Act.[2]

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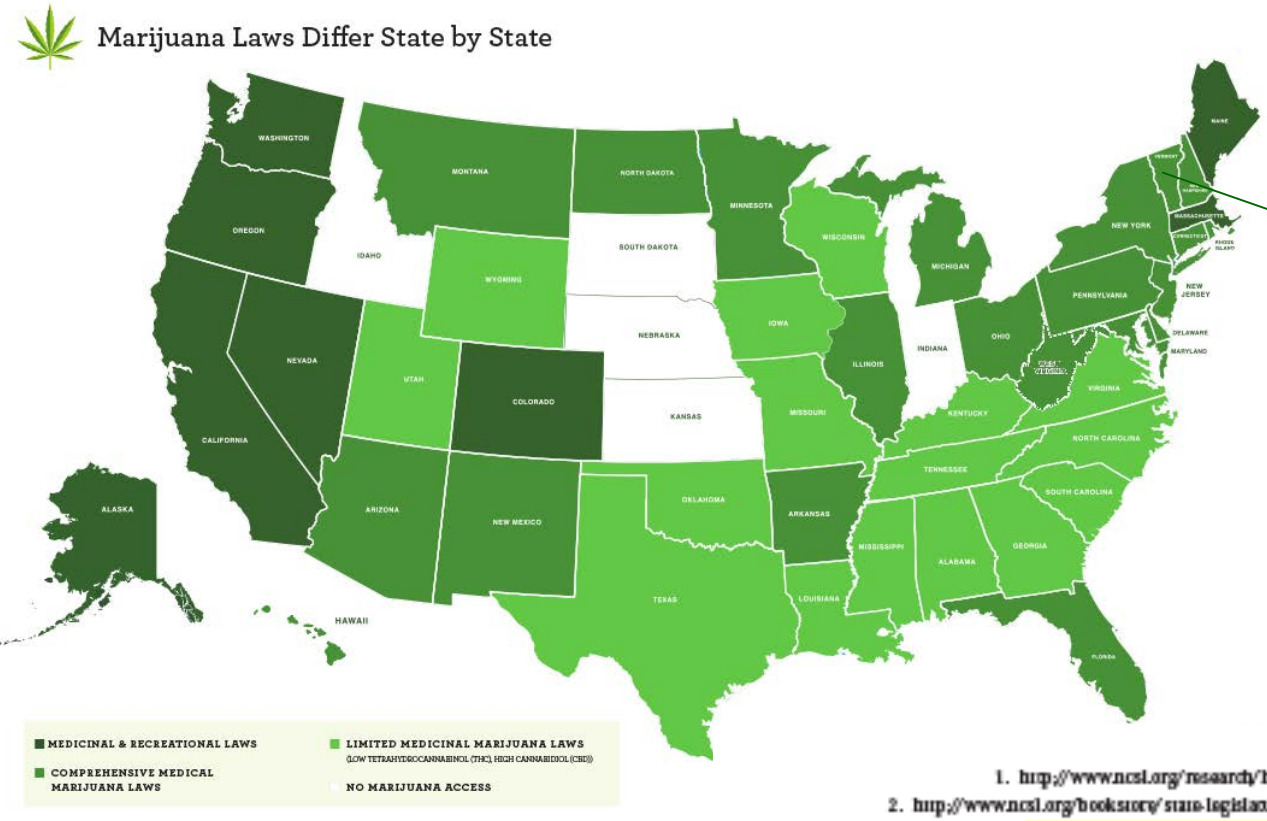
- Budget Update
- What's New @ HHS/NIH?
- **Recent NIDA Activities & Events**

CANNABIS LAWS IN THE U.S.



As of Jan. 22, 2018, the Vermont legislature passed adult-use legalization legislation and the governor signed the bill. The measure does NOT set up a regulatory system for sales or production.

REFERENCES

1. http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx
2. http://www.ncsl.org/bookstore/state-legislatures-magazine/marijuana-deep-dive.aspx

STATES' LAWS STATUS CURRENT AS OF DECEMBER 28.
LOCAL GOVERNMENT WEBSITES HAVE ADDITIONAL INFORMATION ON THE LAWS REGARDING MEDICINAL AND RECREATIONAL MARIJUANA ON A STATE-BY-STATE BASIS.

29 states have legalized medical marijuana along with D.C., Guam and Puerto Rico

States with MML vary on:

- ***Allowable conditions and routes of administration.***
- ***Dispensaries/home growth and registries.***
- ***Testing, regulatory requirements.***

States with Recreational Laws vary on:

- ***Marketing, product labeling, distribution (home growth).***
- ***Taxation.***

National Institute on Drug Abuse

RECOMMENDATIONS FOR NIDA'S CANNABIS POLICY RESEARCH AGENDA

REPORT FROM THE

CANNABIS POLICY RESEARCH WORKGROUP

February 6, 2018

THE EIGHT PRINCIPLES

- The NIDA's research mission is understood to be *inclusive, flexible, and public health oriented*.
- Research must be *neutral about actions, laws, and policies* set by any jurisdiction regarding cannabis.
- Priority should be given to *research that will remain germane under a wide range of policy* frameworks.
- Research should focus on behaviors and *consequences that are associated with the greatest harms or benefits* and the policies that ameliorate or exacerbate those harms.
- Research should consider both *short-and long-term effects*.
- Research should be sensitive to the *realities of cannabis laws and policies*.
- Research should be sensitive to the *realities of cannabis production, marketing, and use*.
- Research should acknowledge that, sometimes, *large gaps can emerge between a law or policy as written and its implementation*.

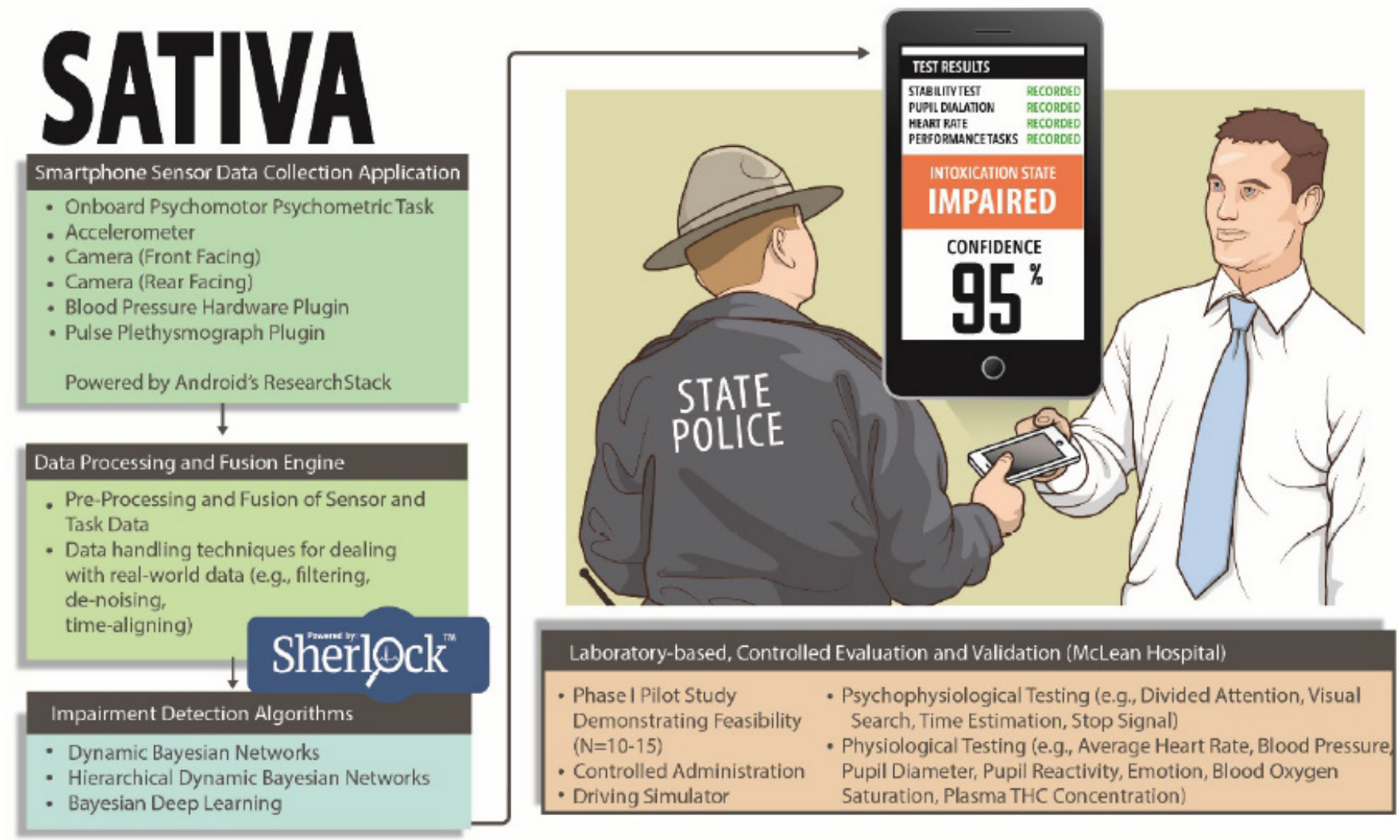
NIDA already doing:

- ***Measures of Intoxication or Impairment:*** **SBIR Request for proposals on Digital Markers for Marijuana Intoxication: 4 funded projects.**
- ***Common measures:*** **working with CDC and other Federal partners on common surveillance measures to evaluate impact of changing laws.**
- ***Policy Databases with up to date information on State laws (Medical and Adult use)***
  - **NIAAA Alcohol Policy Information System (APIS) now contains information on adult use (recreational) cannabis laws for policy researchers**
  - **Law Atlas/now Prescription Drug Abuse Policy System (PDAPS—updated annually)**
- ***Policy research portfolio:*** **DESPR has expanded its research on cannabis policy impact**

Proposed Future plans:

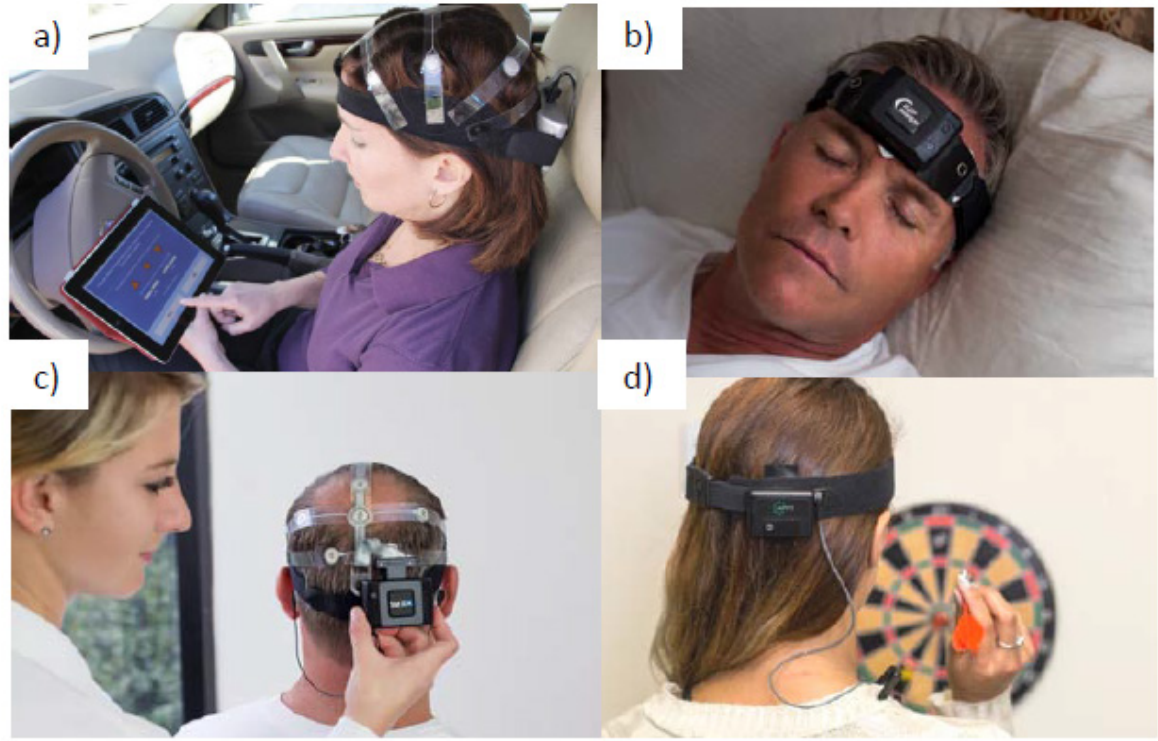
- ***Convene a meeting on measures:*** **Defining a "standardized dose" is challenging —range of products, routes of use, inability to measure what is used (legal issues prevent our accessing state products).**
  - **Partner with Canada for they may have more accurate product measures under their new legalization policies. (Already have this for medical cannabis)**
- ***Expand research on cannabis policy: add as a priority area to Drug Abuse Topics (DAT) of Interest website.*** **Currently have DAT on cannabis and developing brains (prenatal and adolescent)**
- ***Expand interest on intersection with opioids for pain treatment, relation to opioid use/OUD***
- ***Include in NIDA's International priorities—*****to take advantage of changes occurring in Canada, Uruguay and elsewhere**

A system for the Specification of Acute THC Impairment using Validated Algorithms (SATIVA)



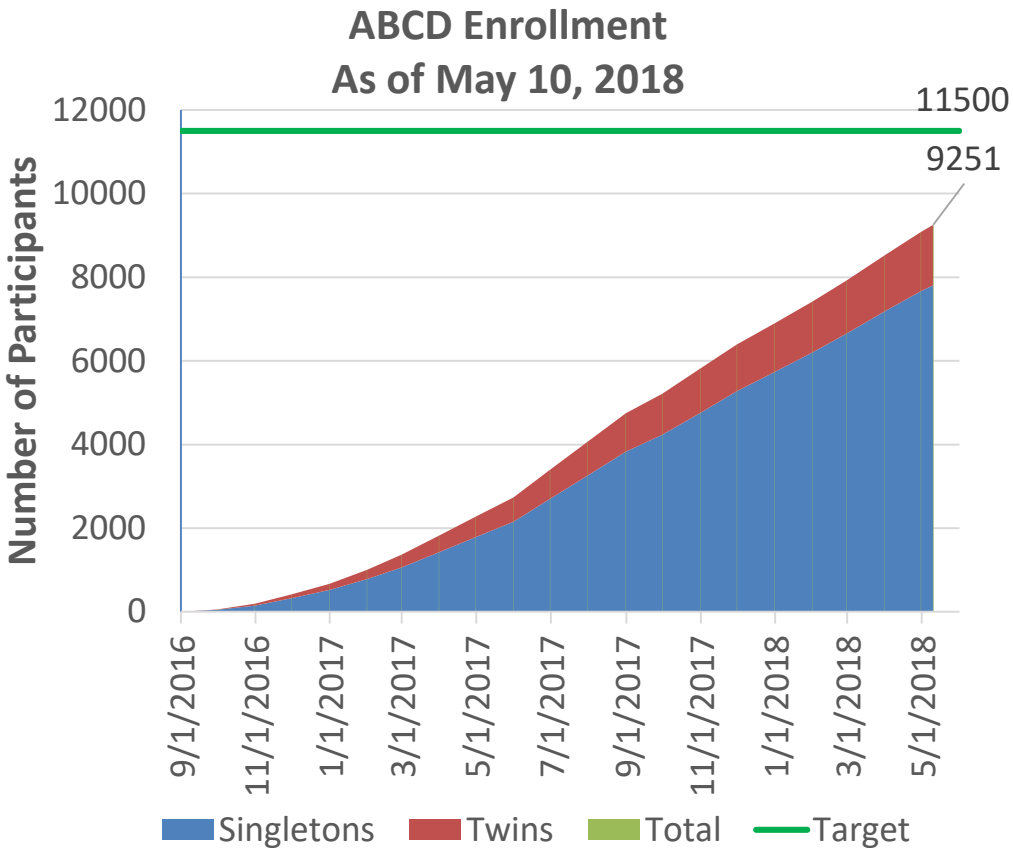
Cannabis Impairment Detection Application (CIDA)

The proposal is based on the family of systems developed by Advance Brain Monitoromg which combines battery-powered hardware with a sensor placement system that provides a lightweight, easy-to-apply method to acquire and analyze up to 20 channels of high-quality EEG, ECG and accelerometry.



a) B-Alert X10 EEG system, b) Sleep Profiler, c) Stat X24 EEG System, d) M4 System

ABCD Update



NIMH Data Archive https://data-archive.nimh.nih.gov/abcd

ABCD Study Fast Track Data

DICOM images from ~6,000 participants currently available.

Interim curated data on first 4,500 participants released Feb 2018!

- Basic demographics
- Assessments of:
  - Physical and mental health,
  - Substance use,
  - Culture and environment, and
  - Neurocognition
- Tabulated structural and functional neuroimaging data
- Minimally processed brain images
- Biological data (e.g., pubertal hormone analyses)
- Residential history derived data related to residential density/walkability, crime, area deprivation, population density, and satellite-based pollution measures

New NIDA FOAs

Workshop on the Use of Adolescent Brain Cognitive Development (ABCD) Data (R25 Clinical Trial Not Allowed)

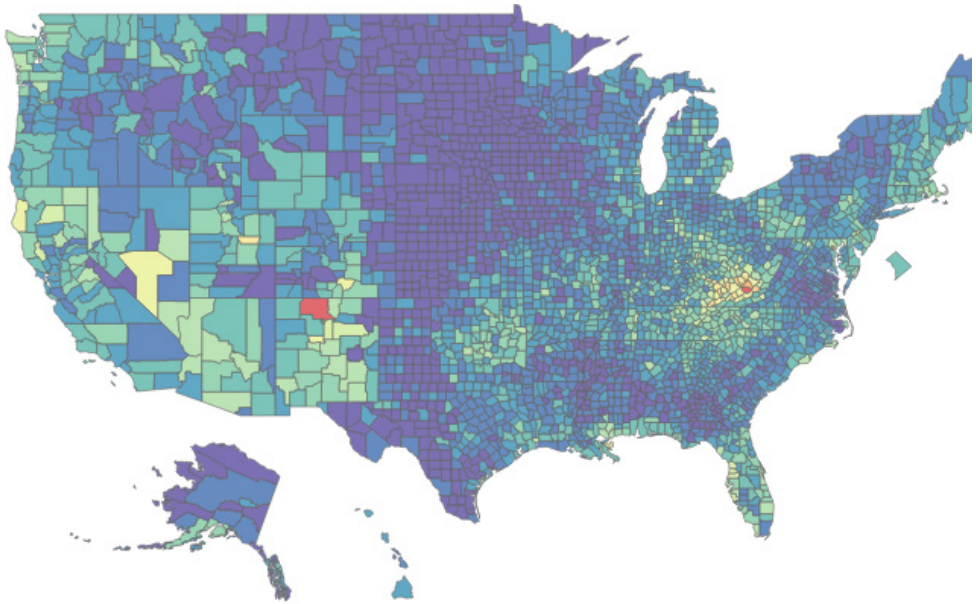
(RFA-DA-19-006)

Issued: March 28, 2018; Application Receipt/Submission Date(s): July 25, 2018.

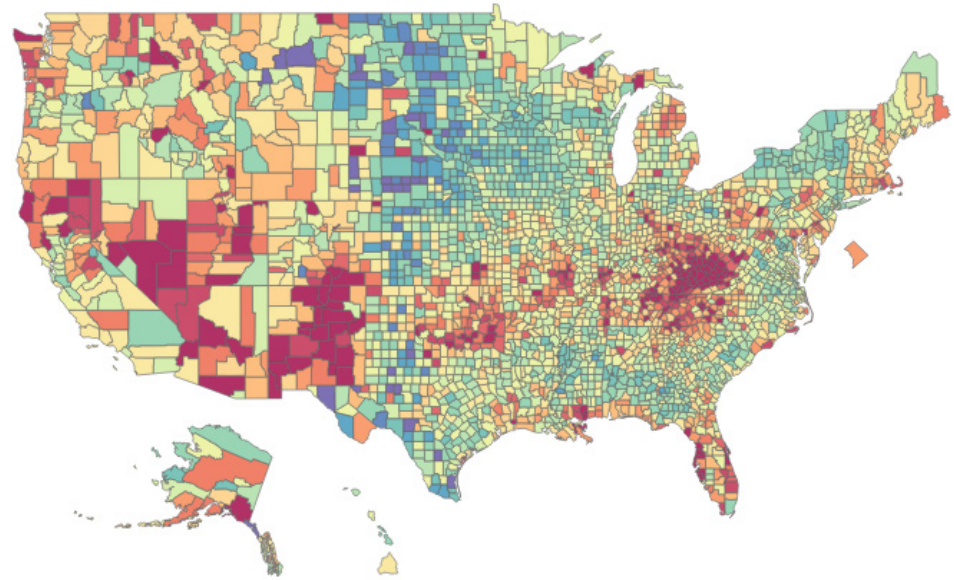
FOA will support creative educational activities with a primary focus on courses for skills developmentthat will allow participants to explore the hands-on use of ABCD data, through cooperative or competitive approaches.

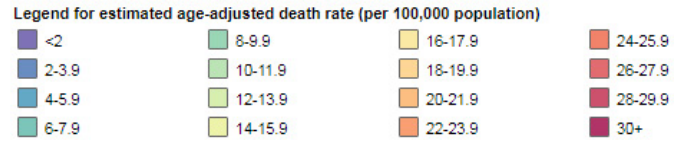
Overdose Death Rates

1999



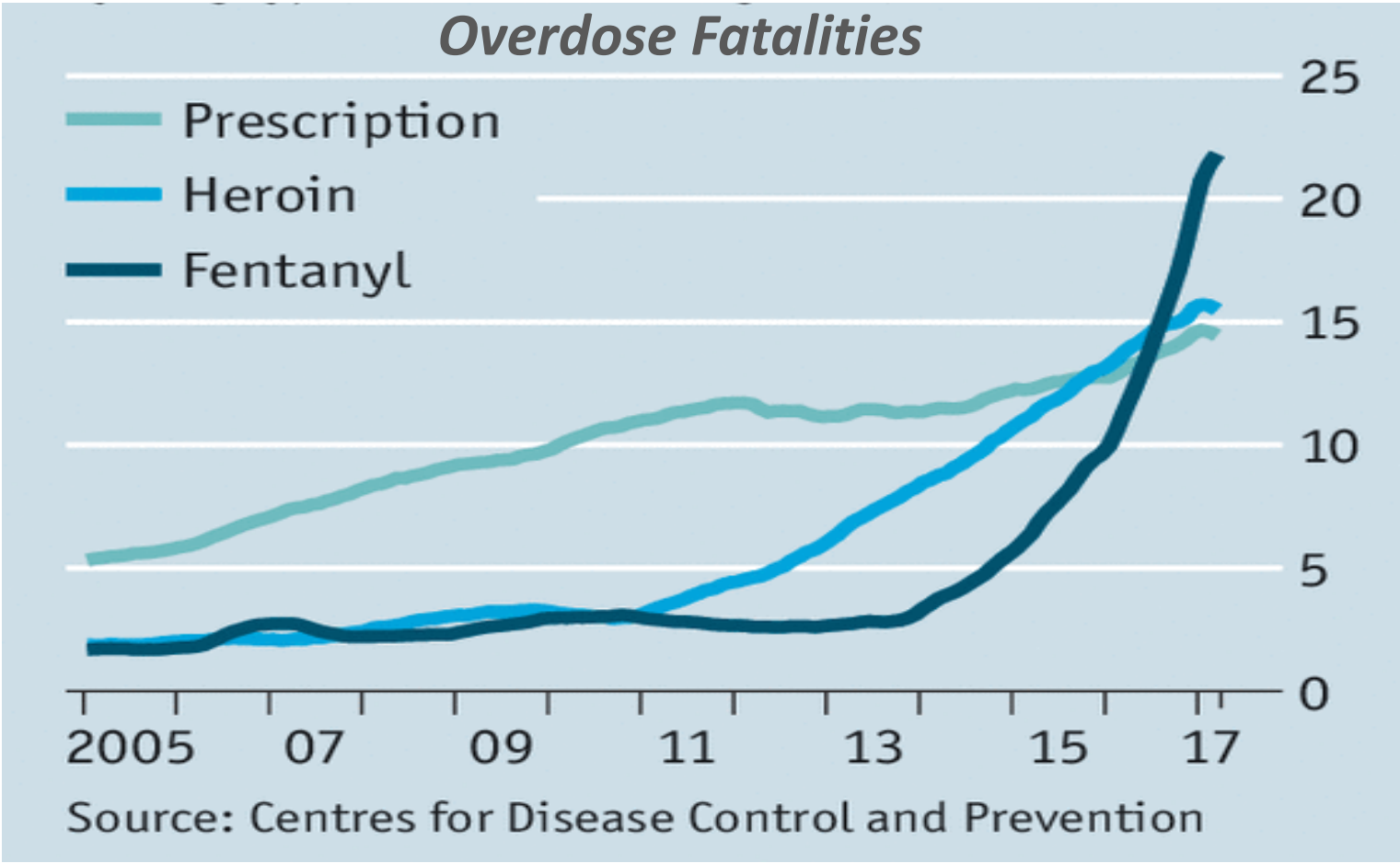
2016





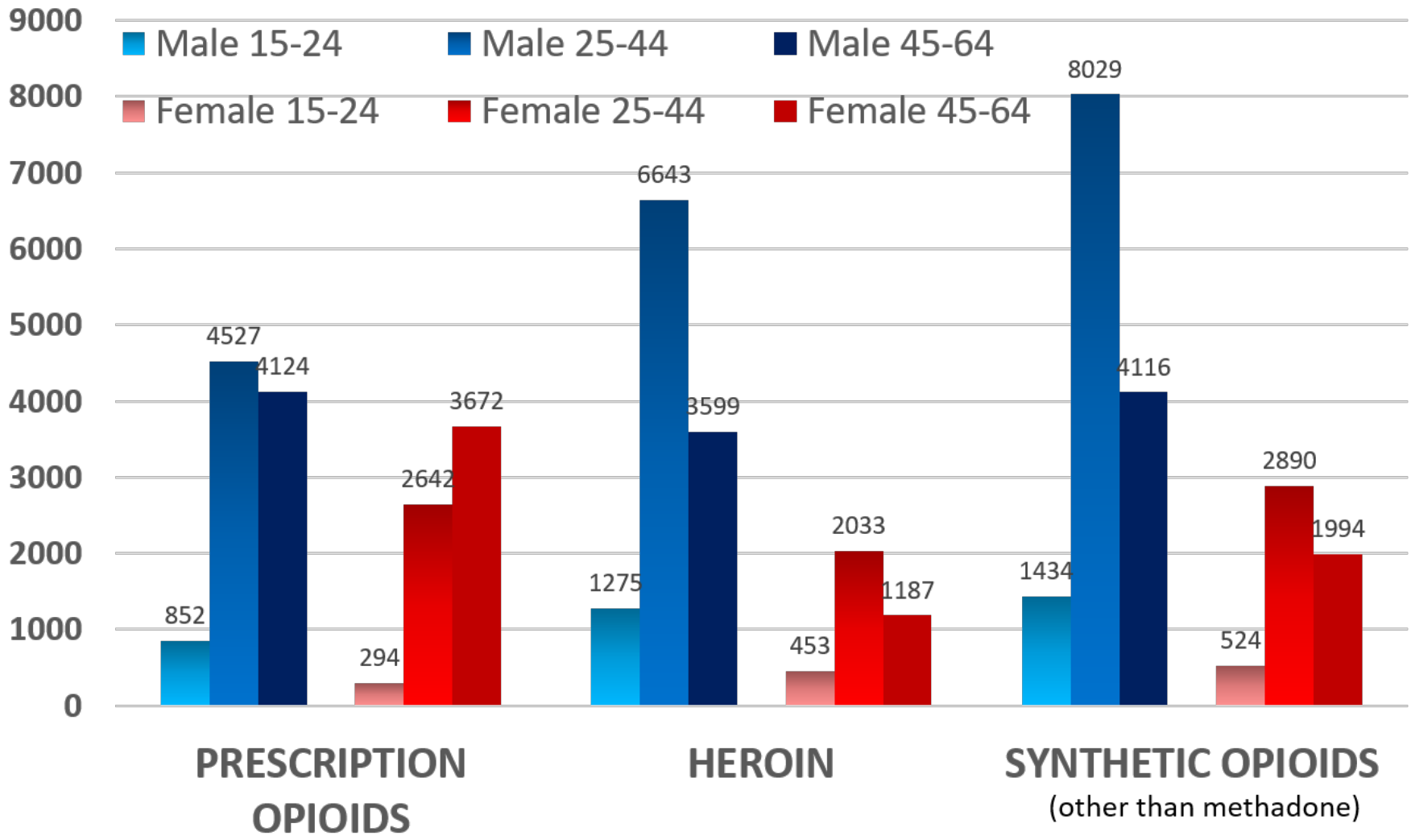
Source: https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/index.htm

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.

Overdose Deaths Involving Opioids, U.S., 2016



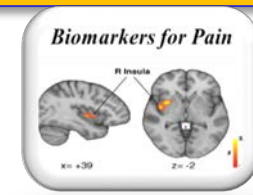
Puja Seth et al., MMWR, Weekly / March 30, 2018 / 67(12);349–358.

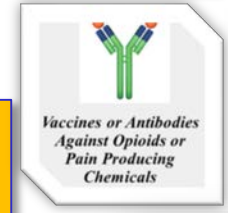
NIH OPIOID RESEARCH INITIATIVE

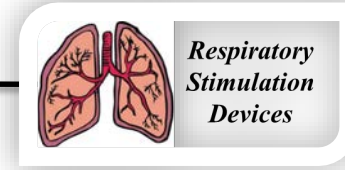
Using Research to End the Opioid Crisis

PAIN MANAGEMENT

Safe, more effective strategies







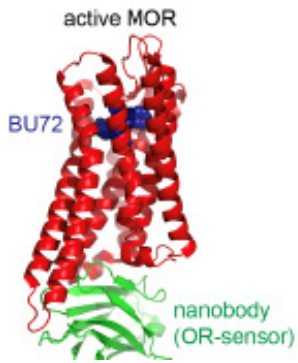
OPIOID ADDICTION TREATMENT

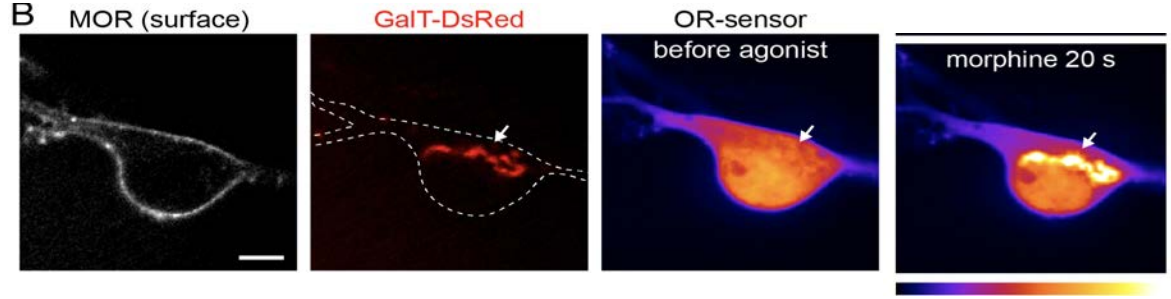
New and innovative medications and technologies

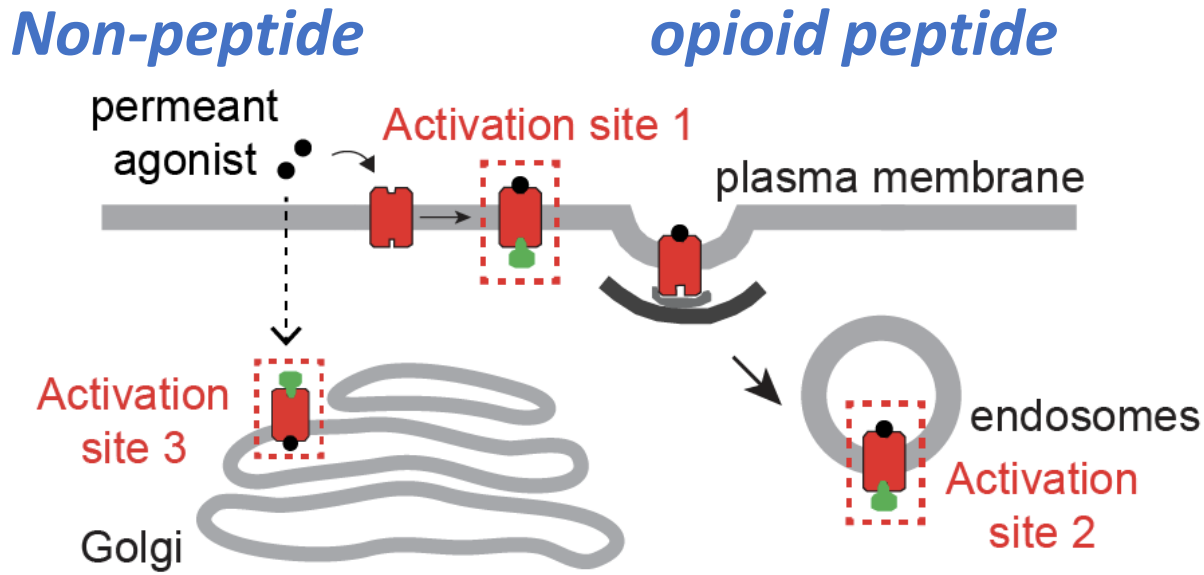
OVERDOSE REVERSAL

Interventions to reduce mortality and link to treatment

How do Endogenous Opioids Differ From Synthetics?

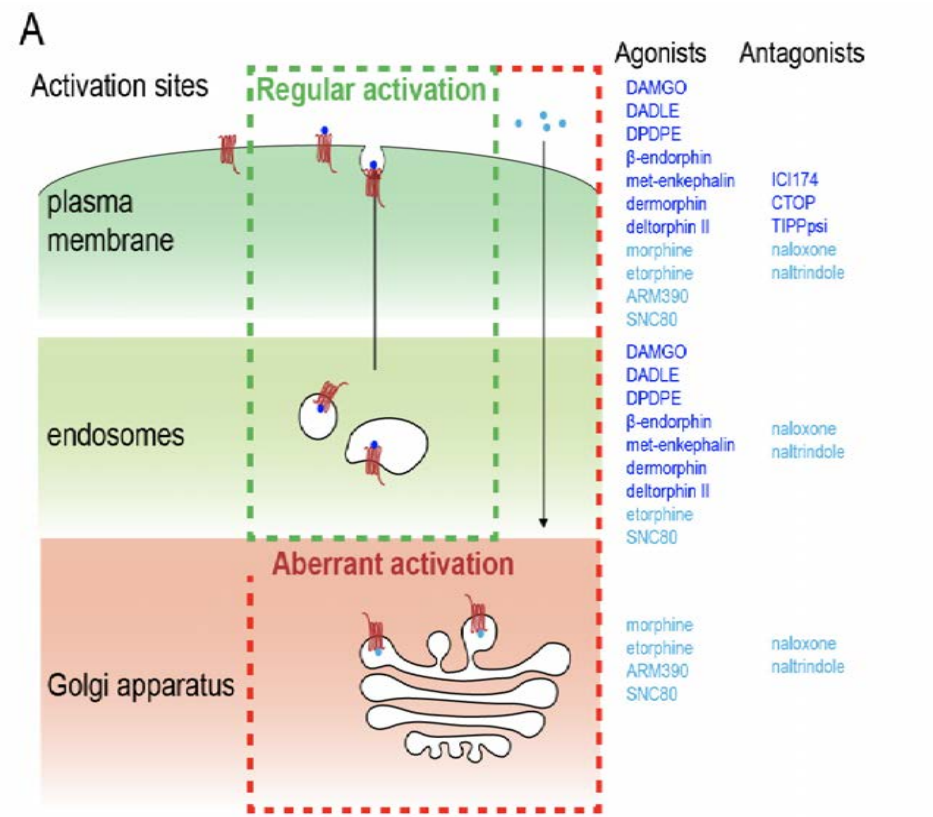


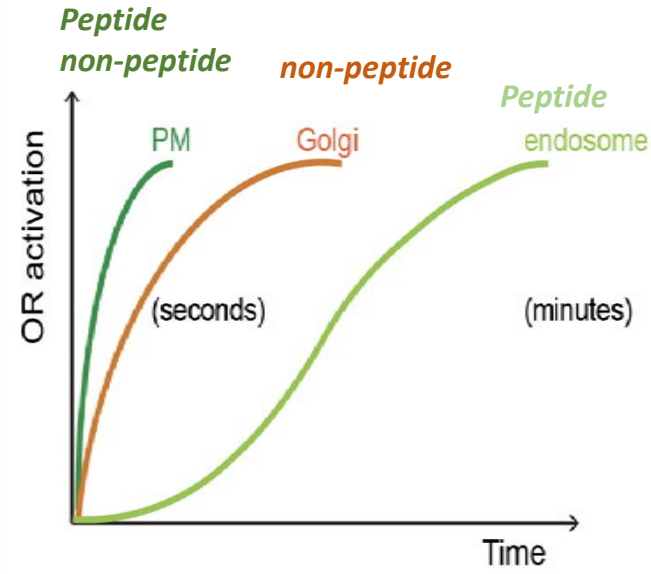




Stoeber M et al., Neuron 2018

Ligand-specific Spatiotemporal Distinctions in Opioid Receptor Signaling





Stoeber M et al., Neuron 2018

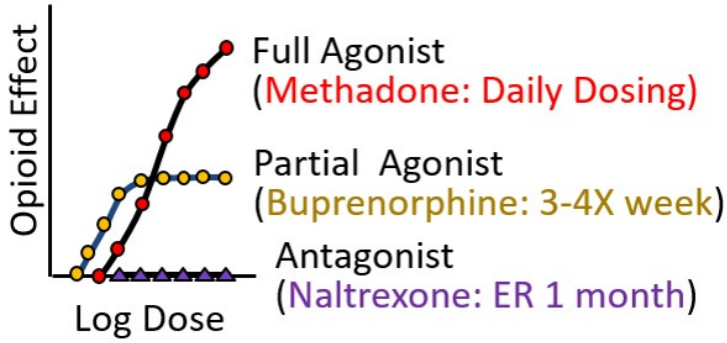
New NIDA FOAs

Exploring Epigenomic or Non-Coding RNA Regulation in the Development, Maintenance, or Treatment of Chronic Pain (R61/R33 Clinical Trial Optional) (PAR-18-742) NIDA & NCCIH

Issued: June 25, 2018; Application Receipt/Submission Date(s): July 17, 2018, November 13, 2018 February 11, 2019, July 17, 2019, November 13, 2019, February 11, 2020, July 17, 2020, November 13, 2020, February 11, 2021.

Research that investigates the role of epigenetic or non-coding RNA regulatory pathways in the development, maintenance, or treatment of chronic pain. Expand knowledge that can be exploited to develop non-addictive pain medications or pain biomarkers.

Medication Assisted Treatment (MAT)



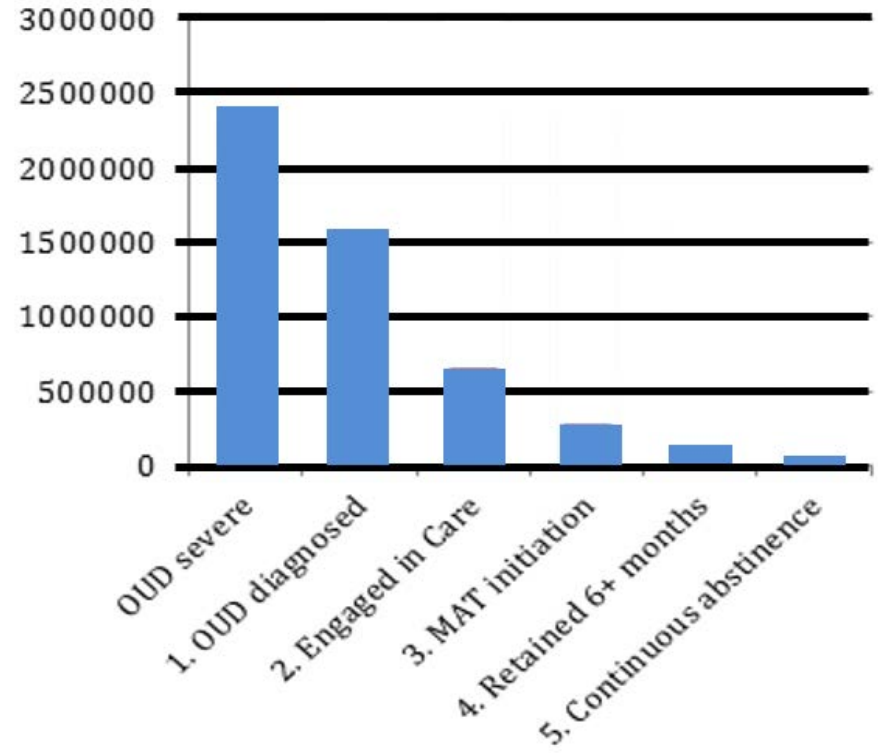
DECREASES:

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

INCREASES

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

OUD Cascade of Care in USA



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

MAT is highly underutilized!

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

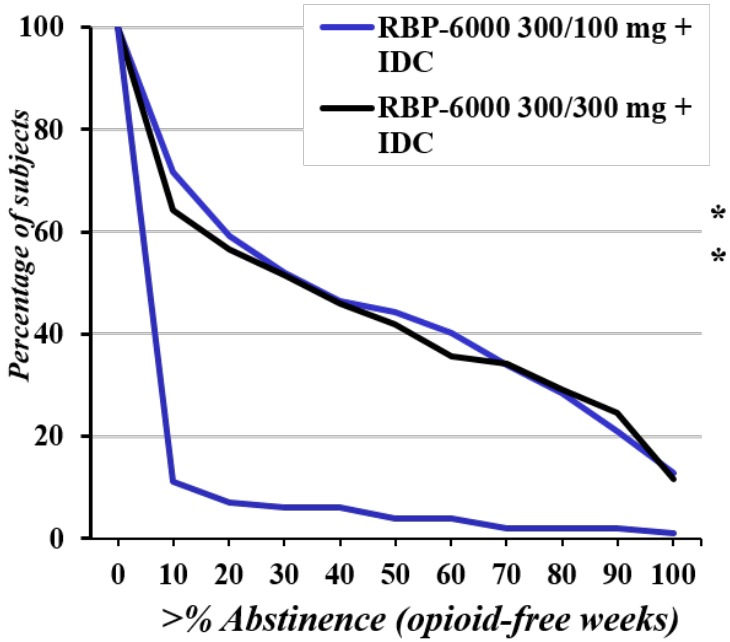
SUBLOCADE™ (Buprenorphine ER), Once-Month Injectable

FDA Approval 11.30.2017

CAM2038: Subcutaneous ER Buprenorphine

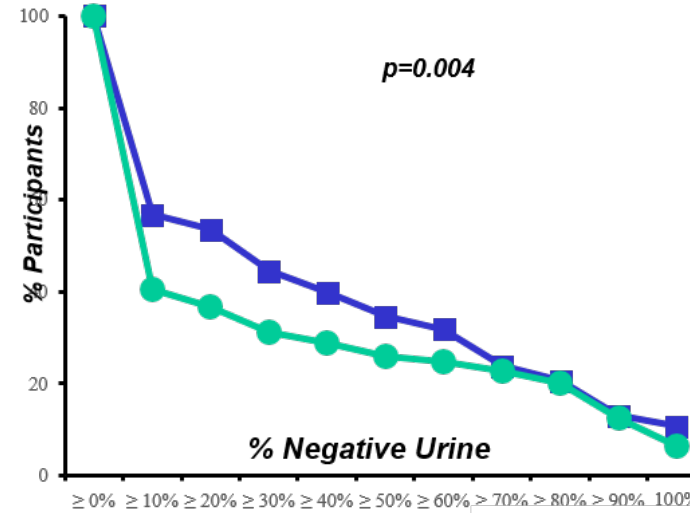
Weekly or monthly injection

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



Heidbreder et al., CPDD 2017

Comparison CAM2038 versus Daily SL BPN



braeburn

New Targets: Medications to Decrease Withdrawal

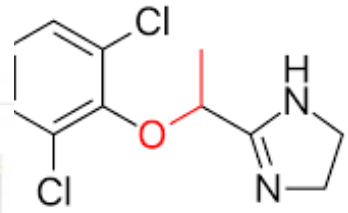
29 MARCH 2018 NEWS

FDA committee votes to approve lofexidine for opioid withdrawal

By **Ellen Daniel**

SHARE

Symptoms of opioid withdrawal include abdominal cramping, diarrhoea, dilated pupils, goose bumps, nausea and vomiting. Credit: Flikr/U.S. Department of Agriculture



lofexidine

The US Food and Drug Administration (FDA) Psychopharmacologic Drugs Advisory Committee has voted to approve lofexidine hydrochloride to treat symptoms of opioid withdrawal.

PATIENT FOCUSED DRUG DEVELOPMENT MEETING FOR OPIOID USE DISORDER (OUD)

U.S. FOOD & DRUG ADMINISTRATION

APRIL 17th, 2018; 10:00 am – 4:00 pm

AGENDA

9:00 – 10:00 am	**Registration**
10:00 – 10:05 am	**Welcome** Sara Eggers, PhD *Office of Strategic Programs (OSP), Center for Drug Evaluatio*
10:05 – 10:10 am	**Opening Remarks** Theresa Mullin, PhD *Associate Director for Strategic Initiatives, CDER, FDA*
10:10 – 10:20 am	**Background on Opioid Use Disorder and Treatment** Maryam Afshar, MD *Division of Anesthesia, Analgesia, and Addiction Products (D* *Office of New Drugs (OND), CDER, FDA*
10:20 – 10:25 am	**The Road from PFDD Meetings to Clinical Trial Endpoints** Eleftheria Papadopoulos, MD, MPH *Associate Director, Clinical Outcome Assessments Staff, OND*
10:25 – 10:35 am	**Overview of Discussion Format** Sara Eggers, PhD OSP, CDER, FDA
10:35 – 11:05 am	**Panel #1 Discussion on Topic 1: Health Effects and Daily Impa** A panel of individuals and families will provide comments to significant health effects and daily impacts on opioid use di
11:05 – 12:00 pm	**Large-Group Facilitated Discussion on Topic 1** Individuals and families in the audience will be invited to add to the dialogue
12:00 – 1:00 pm	**Lunch**
1:00 – 1:05 pm	**Afternoon Welcome** Sara Eggers, PhD OSP, CDER, FDA
1:05 – 1:35 pm	**Panel #2 Discussion on Topic 2: Current Approaches to Treatment of OUD** A panel of individuals and families will provide comments to start the discussion on current approaches to treating opioid use disorder
1:35 – 2:30 pm	**Large-Group Facilitated Discussion: Topic 2** Individuals and families in the audience will be invited to add to the dialogue
2:30 – 2:45 pm	**Break**
2:45 – 3:15 pm	**Large-Group Facilitated Discussion: Topic 2 Continued**
3:15 – 3:45 pm	**Open Public Comment**
3:45 – 4:00 pm	**Closing Remarks** Mitra Ahadpour, MD, DABAM Deputy Director, Office of Translational Sciences (OTS) CDER, FDA

DISCUSSION QUESTIONS

Topic 1: Health effects and daily impacts of Opioid Use Disorder (OUD)

1. Of all the ways that OUD negatively affects your health and well-being, which effects have the most significant impact on your daily life? Examples of negative effects may include:

2. Besides prescription medical treatments, are there other treatments or therapies that you currently use to address your OUD? If so, please describe. How well do these treatments or therapies help address the effects of OUD that are most bothersome to you?

3. Of all treatments, therapies, or other steps that you have taken to address your OUD, what have you found to be most effective in helping you manage your OUD?

4. What are the biggest factors that you take into account when making decisions about seeking out or using treatments for OUD?

5. What specific things would you look for in an ideal treatment for OUD?

6. If you had the opportunity to consider participating in a clinical trial studying experimental treatments for OUD, what factors would you consider when deciding whether or not to participate?

Docket Information: We encourage you to submit your written comments to the docket by June 18, 2018: https://www.regulations.gov/document?D=FDA-2018-N-0987-0001 or go to www.regulations.gov and search for: **opioid use disorder patient-focused drug development.**

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***

1. *Multisite Implementation Research Study*
2. *CTN Expansion*
3. *Justice Community Opioid Intervention Network*
4. *Focused Medications Development*

Priority Areas

Prevention Research

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

Treatment Interventions

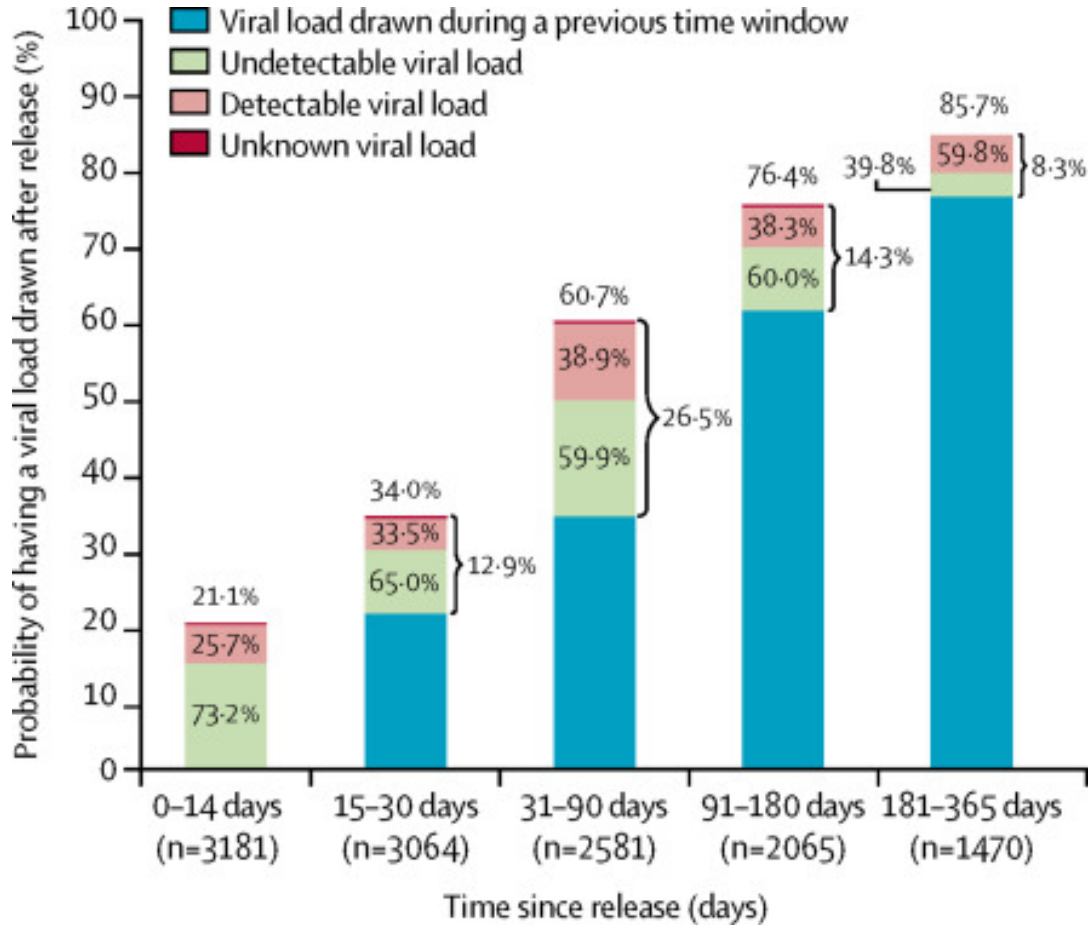
(New Targets & New Strategies)

HIV and Drugs

Prevention
Treatment

Predictors Of Linkage To HIV Care and Viral Suppression After Release From Jails and Prisons

Time to linkage to care as measured by first HIV RNA viral load drawn after release from prison or jail



Loeliger KB et al., Lancet HIV. 2018 Feb;5(2):e96-e106.

New NIDA FOAs

Coordinating Center to Support NIDA Rural Opioid HIV and Comorbidity Initiative (U24 - Clinical Trial Not Allowed) (RFA-DA-19-004)

Issued: March 20, 2018; Application Receipt/Submission Date(s): August 15, 2018.

Fund a single interdisciplinary Coordinating Center to centralize support of the rural opioid initiative administered by NIDA and co-funded by CDC, SAMHSA, and ARC.

NIDA Topics of Special/Continuing Interest (DAT)

Funding

- Funding Opportunities
- Clinical Research
- Post-Award Concerns
- General Information
- Grant & Contract Application Process
- Funding Priorities
  - NIDA Funding Strategy
  - NIDA Topics of Special/Continuing Interest (DAT)
  - Technology Transfer
- Research Training

NIDA Topics of Interest (DAT)

Important: *Please contact the Program Official/Contact(s) before submitting an application.*

NIDA is attempting to limit the number of Program Announcements we issue each year; however, we remain committed to informing applicants about emerging and continuing areas of research interest. The Drug Abuse Topics (DATs) of interest will leverage existing parent funding opportunity announcements to solicit topic-specific applicatio within areas of emerging interest to the Institute. Note that continue to encourage investigator-initiated projects in topi areas not listed here, and that applications submitted in response to the Relevant Funding Opportunities are NOT li to the research and development areas described below.

This website only lists scientific/research topics and cont and instructions for linking applications to specific topic interest to NIDA (DATs). What is not included are additiona application instructions, eligibility restrictions, review criteria, selection criteria, or other items related to the completeness or compliance of an application. These are found in the SF424 application guide.

Instructions for submitting applications:

- Insert "**DAT-**" (four characters) in the beginning of the Project Title of the application. [Note: NIH limits the Project Title to 200 characters (including spaces and punctuation)].
- Insert the DAT Code (e.g., DAT18-01) before the first sentence of the abstract. (This is for internal NIDA tracking purposes only).

Topic	Code	Contacts
Neuroimmune Signaling and Function in Substance Use Disorders **(R01, R21)** (PDF, 84KB)	DAT18-01	Roger G Sorensen, Ph.D., MPA
Drug Abuse Prevention Intervention Research **(R01, R03, R21)** (PDF, 89KB)	DAT18-02	Jacqueline Lloyd, Ph.D., MSW
Epidemiology of Drug Abuse **(R01, R03, R21)** (PDF, 100KB)	DAT18-03	Marsha F. Lopez, Ph.D., MHS
Effects of Cannabis Use and Cannabinoids on the Developing Brain **(R01, R03, R21)** (PDF, 90KB)	DAT18-04	Da-Yu Wu, PhD Karen Sirocco, Ph.D.
Gene-Environment Interplay in Substance Use Disorders **(R01, R21)** (PDF, 108KB)	DAT18-05	Naimah Weinberg, M.D. Amy C. Lossie, Ph.D.