

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

May 2, 2017

Nora D. Volkow, M.D., Director

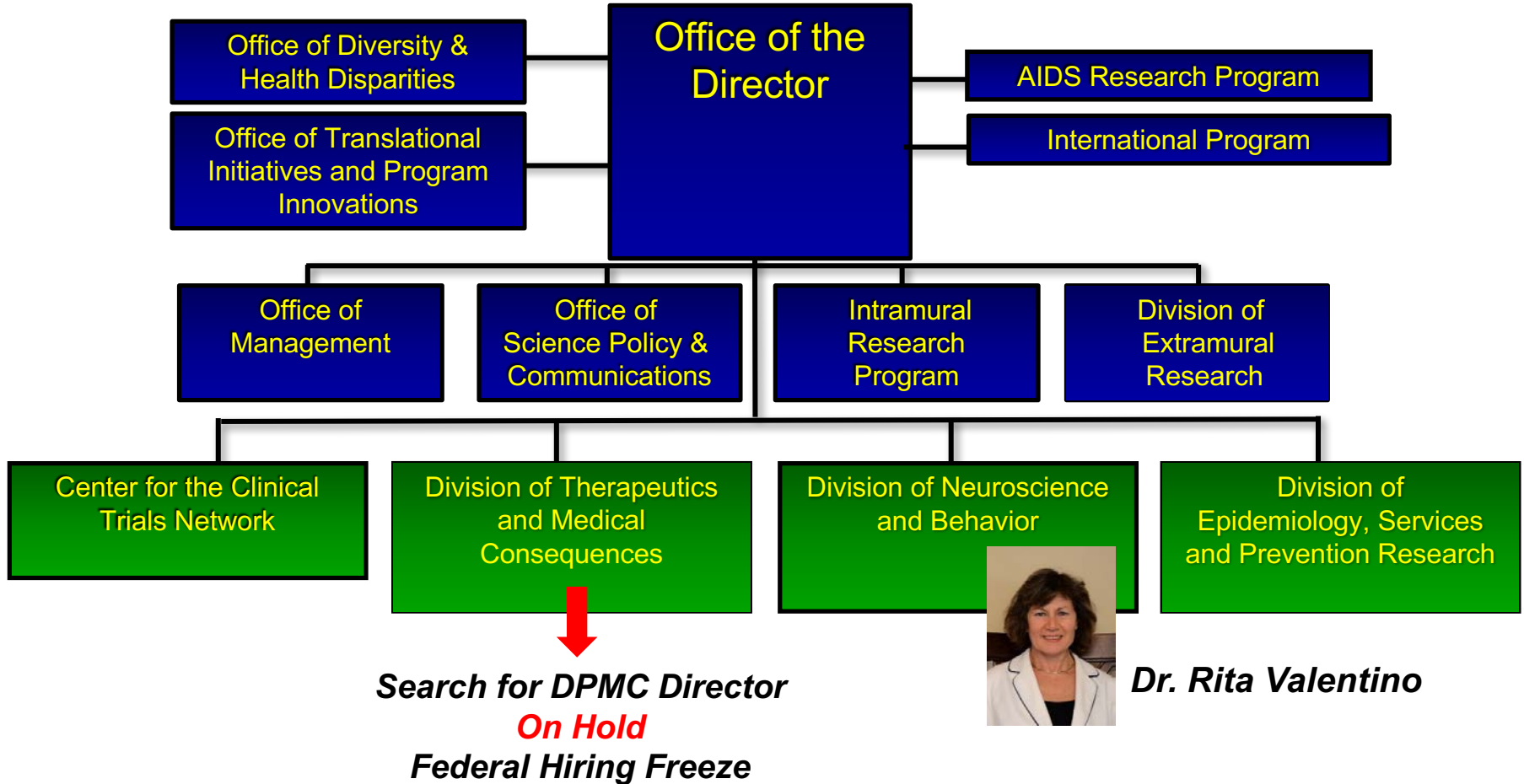


National Institute
on Drug Abuse



@NIDAnews

NIDA





Director, Division of Neuroscience and Behavior
Rita Valentino, Ph.D.

- **Director Stress Neurobiology Division, Dep Anesthesiology, at Children's Hospital of Philadelphia**
- **Professor of Anesthesiology and Critical Care at the University of Pennsylvania School of Medicine**

Her research has focused on the effects of social stress throughout development, the impact of coping style on behavioral and cognitive health and on substance use and on sex differences in responses to stress

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 2015 Actuals | FY 2016 Operating Plan | FY 2017 PB | FY 2017 Senate Markup |
|--------------|----------------------------|-----------------------------------|-----------------------|----------------------------------|
| NonAIDS | \$716,833 | \$756,306 | \$756,306 | |
| AIDS | \$298,862 | \$294,244 | \$294,244 | |
| TOTAL | \$1,015,695 | \$1,050,550 | \$1,050,550 | \$1,103,032 |

Currently under a C.R. until April 28, 2017



President's 2018 NIH Budget Request

House Hearing – May 17, 2017

Senate Hearing – June 22, 2017



House Appropriations Subcommittee on
Labor, Health & Human Services, Education
& Related Agencies



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Goal: Elucidate circuit structure and function to understand:

- How the brain works
- How to manipulate circuits for improved function
- Discover what circuits cause brain disorders

Goal: Make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention

FIRST FIVE YEAR **SECOND FIVE YEAR**

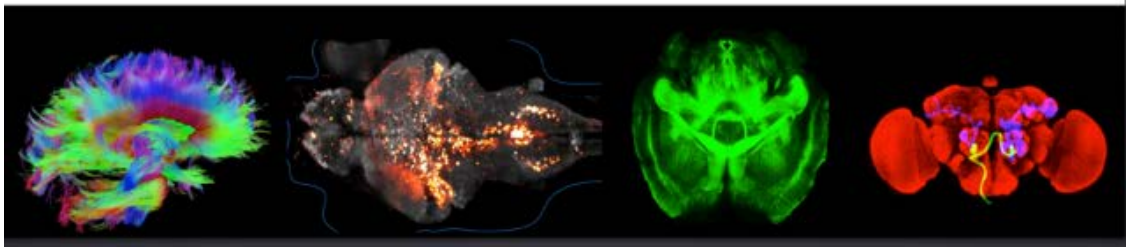
Emphasize technology development

Emphasize discovery driven science

Molecular/Structural Pathology

Circuit Dysfunction

Neuro/Mental/Substance Abuse Functional Disability



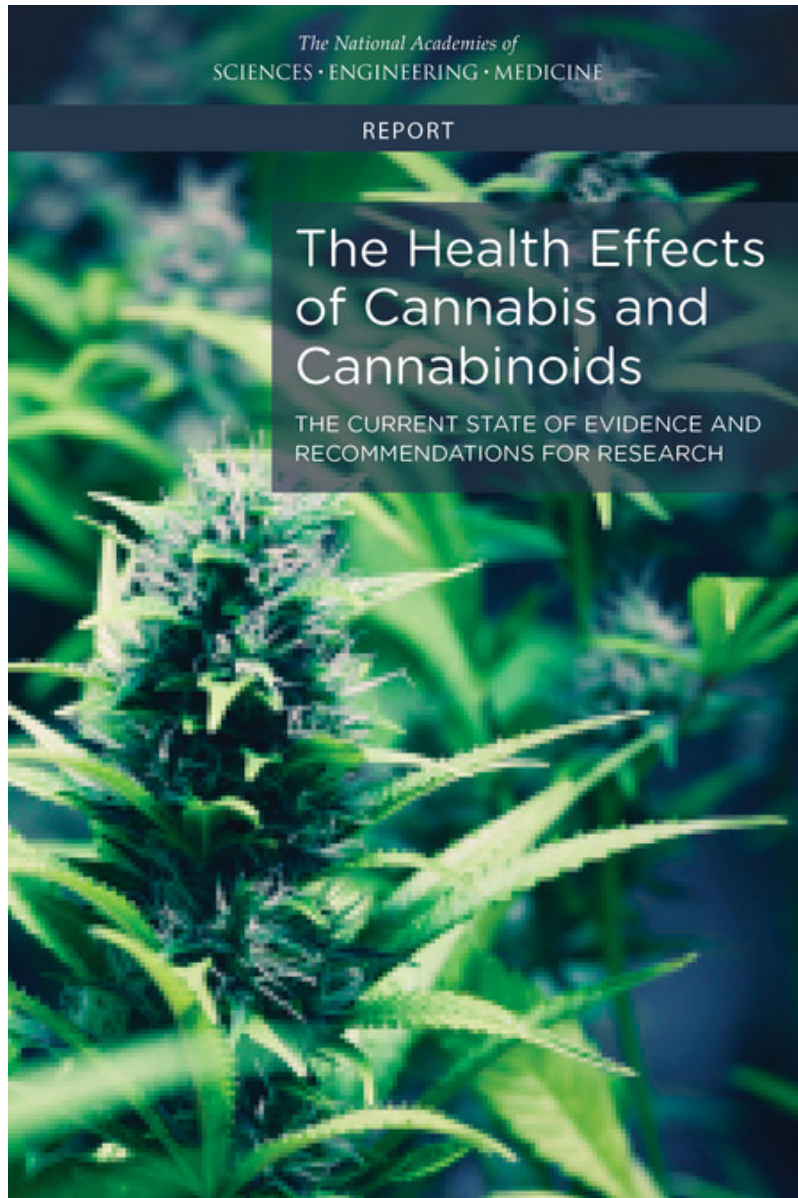
- **Four** on cell phenotyping: Classifying human and non-human brain cells, building a mouse brain atlas, and establishing associated data centers
- **Two** on post-doctoral training and career enhancement
- **Three** on informatics infrastructure
- **Two** support SBIR and STTR
- **One** on ethical issues in human brain research and neurotechnologies
- **Four** on integrated, interdisciplinary research on circuit function
- **Twelve** FOA re-issued from FY 2016
 - Imaging and non-invasive neuro-modulation in humans,
 - Tool and technology development across scales
- **BRAIN Public-Private Partnership Program**, build partnerships between investigators and manufacturers of novel neural stimulation and/or recording devices

Pending passage of the FY17 budget, new awardees will be announced following May and September Councils

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National Academy of Sciences Report

Released: January 12, 2017

PURPOSE:

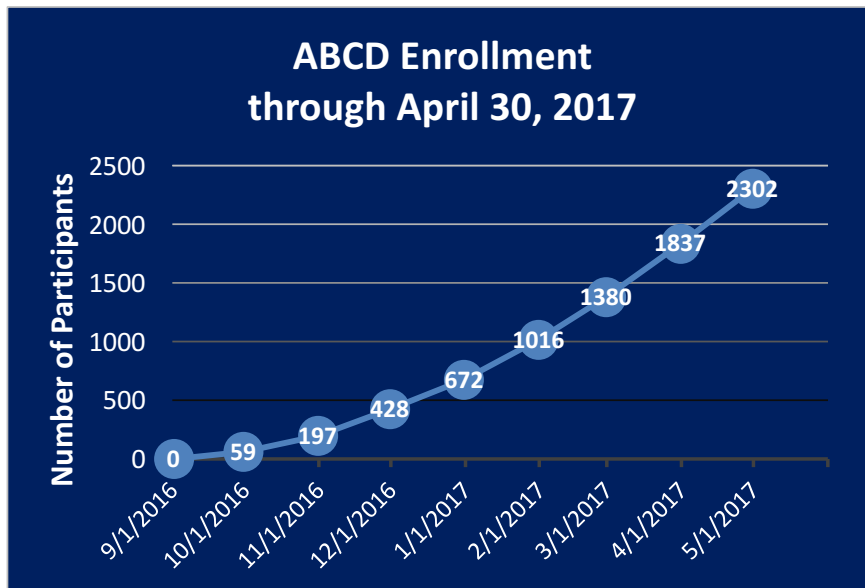
To provide a comprehensive review of the current evidence regarding the health effects of using cannabis and cannabis-derived products

RECOMMENDATIONS:

- 1. Address Research Gaps**
- 2. Improve Research Quality**
- 3. Improve Surveillance Capacity**
- 4. Address Research Barriers**

ABCD Update

ABCD Enrollment
through April 30, 2017



ABCD Study Announces Fast Track Data release - SPRING 2017

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

This inaugural data release contains unprocessed neuroimaging data from 2000 participants, aged 9-10 years old, 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

Adolescent Brain Cognitive Development

Teen Brains. Today's Science. Brighter Future.



National Advisory Council on Drug Abuse (NACDA)
Tobacco Industry Funding Workgroup
Teleconference held on April 10, 2017

Workgroup Members:

Anne C. Andorn, M.D.
Laura Bierut, M.D.
H. Westley Clark, J.D., M.D.
Arthur T. Dean, M.A.
Marie Dyak
Edward Nunes M.D.
(not present)
Robert G. Rancourt, J.D.

NIDA Staff Members:

Susan Weiss, Ph.D.
Carol Alderson
Katia Howlett, Ph.D., M.P.P., M.B.A.
Mary Kautz, Ph.D.
Phylicia Porter, M.P.H.
Mark Swieter, Ph.D.
Kevin Walton, Ph.D.
Ivan Montoya, M.P.H., M.D.

National Cancer Institute Staff:

Mark Parascandola, Ph.D., M.P.H.
Michele Bloch, M.D., Ph.D.
(not present)

NIDA sought guidance:

- ***Tobacco Industry Funding of Investigators:***
--recommend principles and guidelines for funding decisions involving applicants with financial support from tobacco industry
- ***Data Access and Data Repositories:***
--open access databases for studies such as PATH and ABCD

1. Tobacco Industry Funding of Investigators: Selected Recommendations

- ✓ *The applicant's affiliated institution (academic or not) should have a **demonstrated independent infrastructure**.*
- ✓ *Researchers who are funded by tobacco must assure NIDA that they have **complete freedom to publish any results**.*
- ✓ *NIDA should require that any grantee financially supported by tobacco **refrain from mixing those funds with NIDA or NIH funding**.*

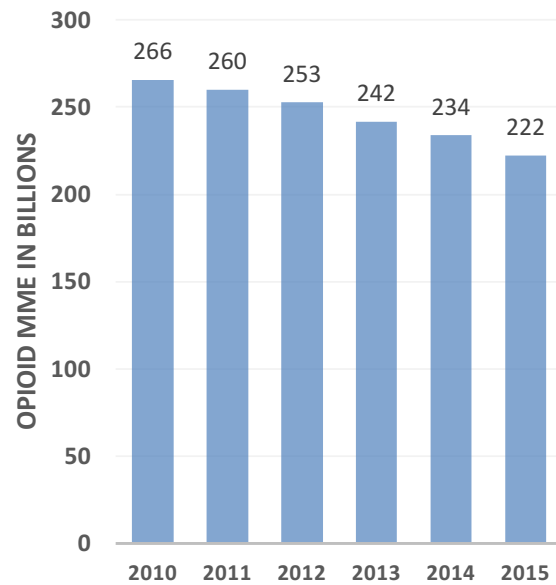
2. Data Access and Data Repositories

Selected Workgroup Recommendations

- ✓ *Open-access data sources may contain **unlimited data** (e.g., from surveys) **and limited data** (e.g., biospecimens); No precautions were recommended for tobacco companies accessing such data; however, NIDA could post a statement conveying **expectations that data will be used to benefit public health**.*
- ✓ *Biospecimens from tobacco industry supported research would be acceptable for our repositories, provided they were **collected in an ethical manner** (with IRB approval etc.) and **appropriate consent**.*

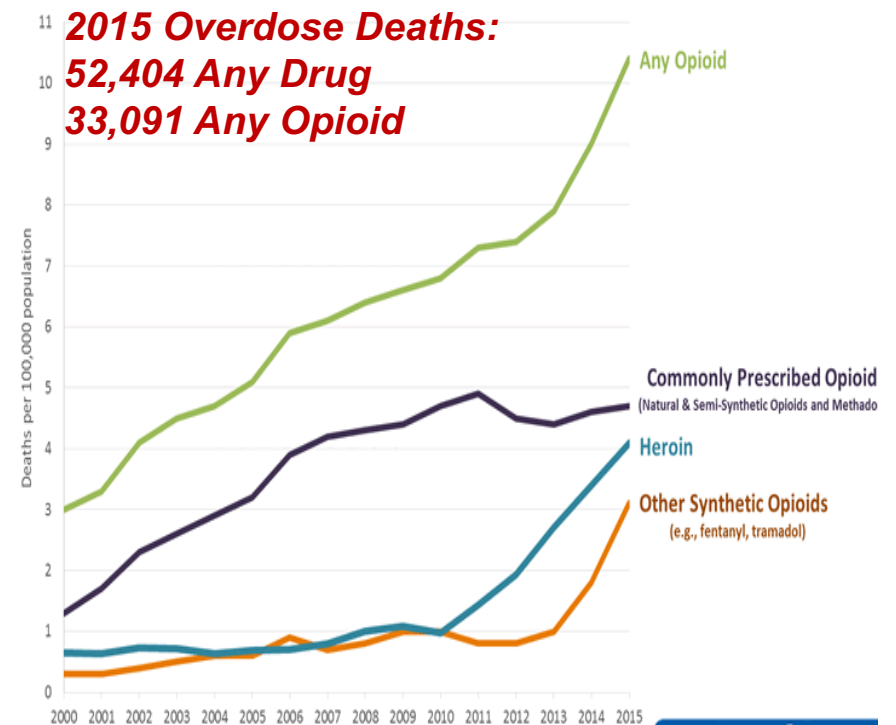
Opioid *Prescriptions* have started to *Decrease* but Opioids *Fatalities* are still *Increasing*

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



Source: IMS Health, U.S. Outpatient Retail Setting

Opioid OD Deaths US, 2000-2015



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA; US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.

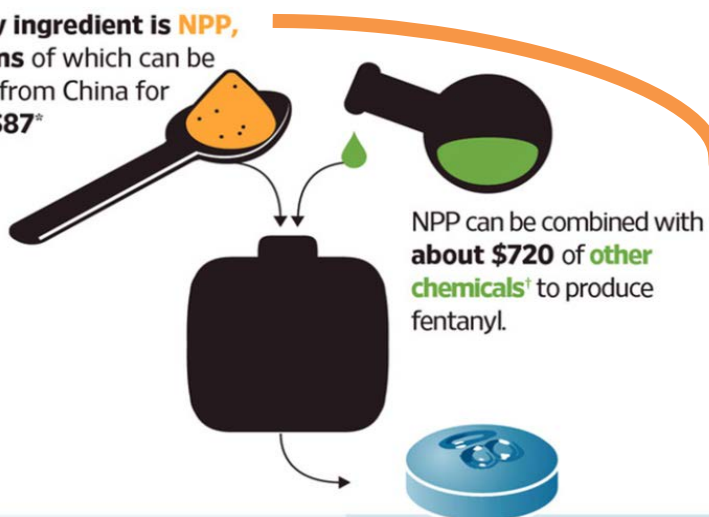


Fentanyl Synthesis from NPP

Criminal Chemistry

Traffickers manufacturing fentanyl often purchase the key ingredient from China, which doesn't regulate its sale. Here's how the chemical building blocks become a highly profitable street drug.

The key ingredient is **NPP**, **25 grams** of which can be bought from China for **about \$87***



The resulting 25 grams of fentanyl cost about \$810 to produce...

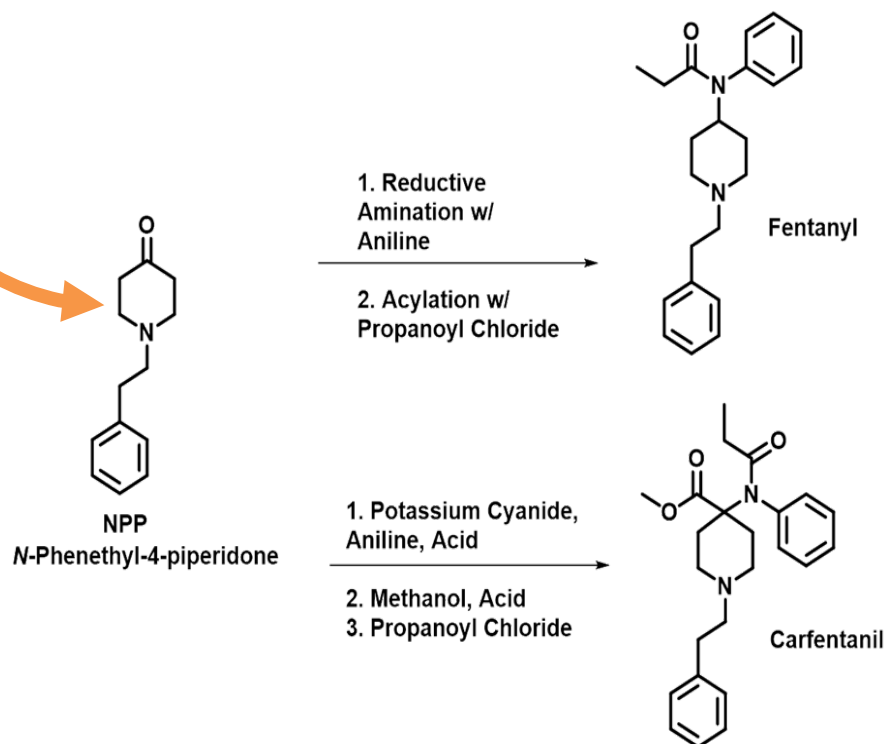
...and are equivalent to up to \$800,000 of pills on the black market.

*Average current price from Chinese suppliers

†Prices from U.S. suppliers

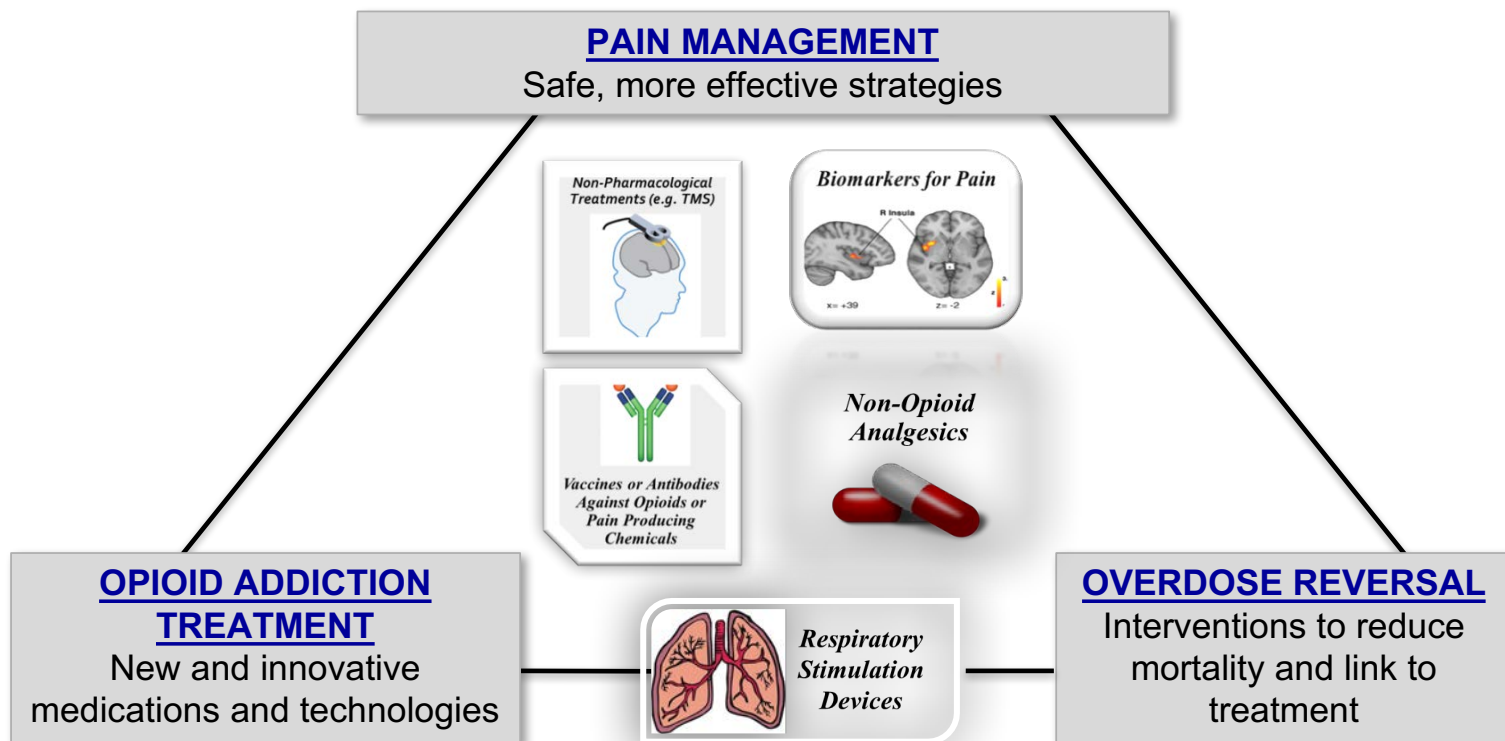
Sources: NES Inc.; Drug Enforcement Administration; Calgary Police

THE WALL STREET JOURNAL.



NIH OPIOID RESEARCH INITIATIVE

Using Research to End the Opioid Crisis



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

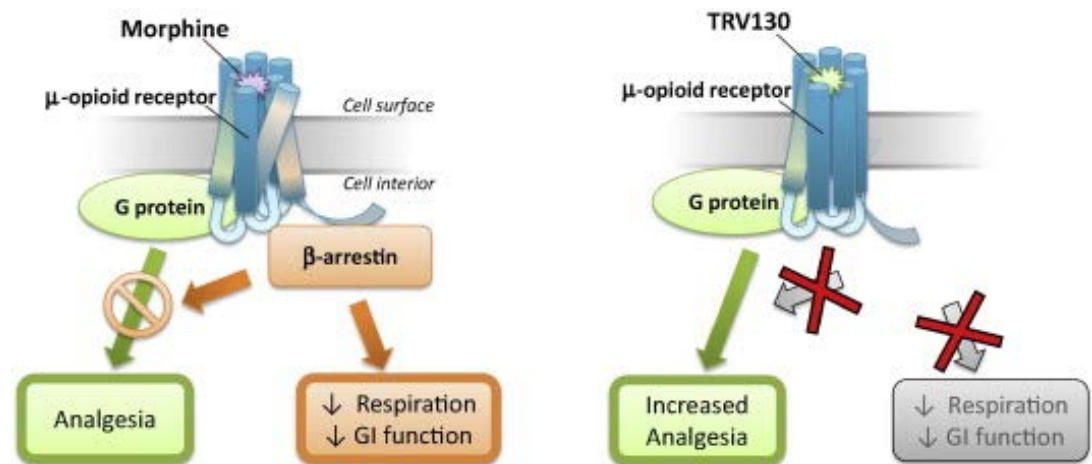
e.g. antibodies that bind to
pain producing cytokines

Non-pharmacological treatment



Neural stimulation;
Surgical interventions;
Meditation

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



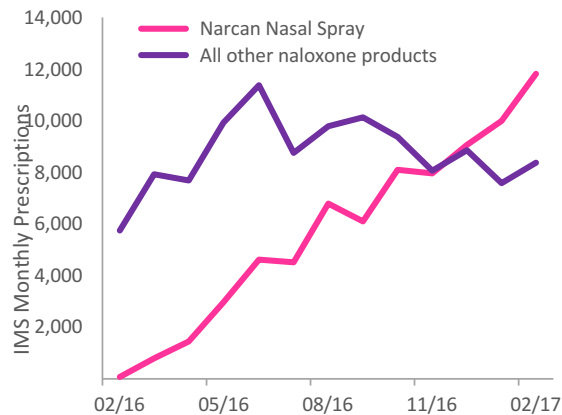
Soergel DG et al., *Pain* 2014; 155(9):1829–1835.

User Friendly Naloxone



NARCAN® Nasal Spray device
\$37.50 per 4mg

Approved by FDA
November 2015



- Naloxone Px increased 3.5X in past year
- NARCAN® Nasal Spray is the most prescribed naloxone
- 900,000 NARCAN® Nasal Spray doses distributed since launch in 2/16

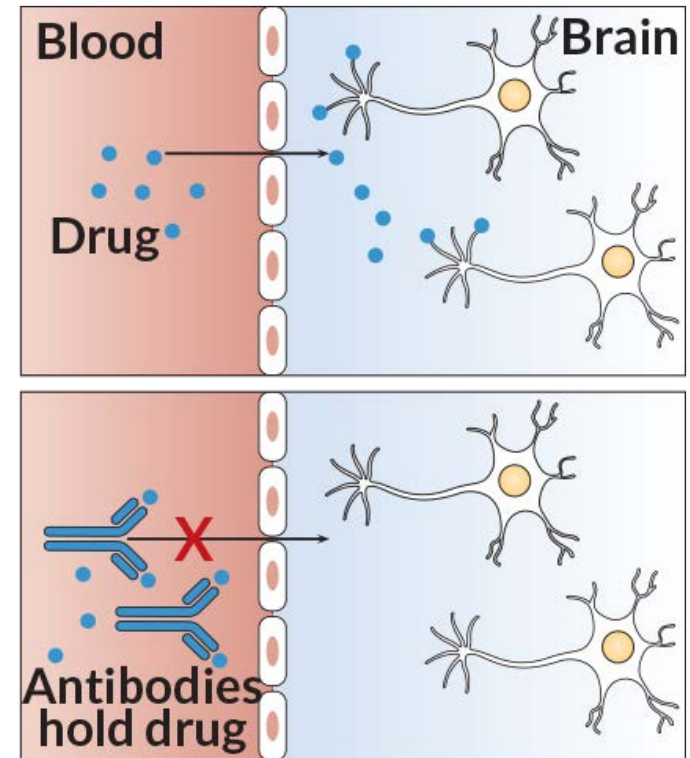
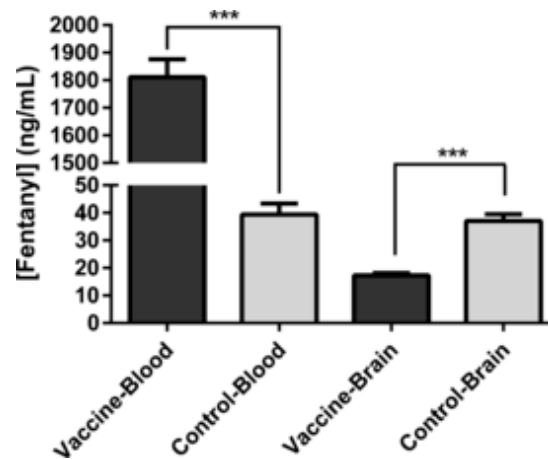
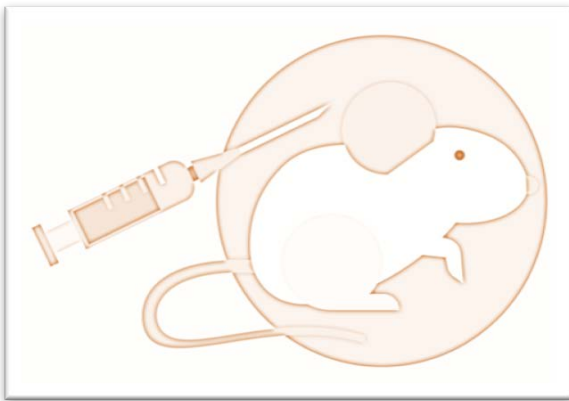
Overdose Treatment: Saving Lives for Future Recovery

- New stronger, longer acting formulations to address more potent opioids (e.g. fentanyl)
- Stimulation devices to prevent respiratory depression
- Overdose detection and alert technologies
- Post-overdose interventions to ensure engagement in treatment

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



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

The Case for a Public-Private Partnership on Development of Non-Addictive Pain Medicines

- Urgent public health crisis
- Absence of highly potent alternatives to opioids – market failure?
- Emergence of numerous potential drug targets
- Possibility of development and validation of biomarkers for pain relief
- Strong support at the highest level of U.S. Government
 - FDA participation will be critical
 - Potential for additional industry incentives



New NIDA FOAs



Expanding Medication Assisted Treatment for Opioid Use Disorders in the Context of the SAMHSA Opioid STR Grants (R21/R33) RFA-DA-18-005

Issued: April 10, 2017; Open Date: May 20, 2017; Application Due Date(s): June 20, 2017.

Solicit applications proposing to test approaches for expanding MAT for OUD in the general health care sector or linking individuals with OUDs who receive naloxone for the reversal of overdose in the context of states' plans for use of funds authorized under the 21st Century Cures Act.

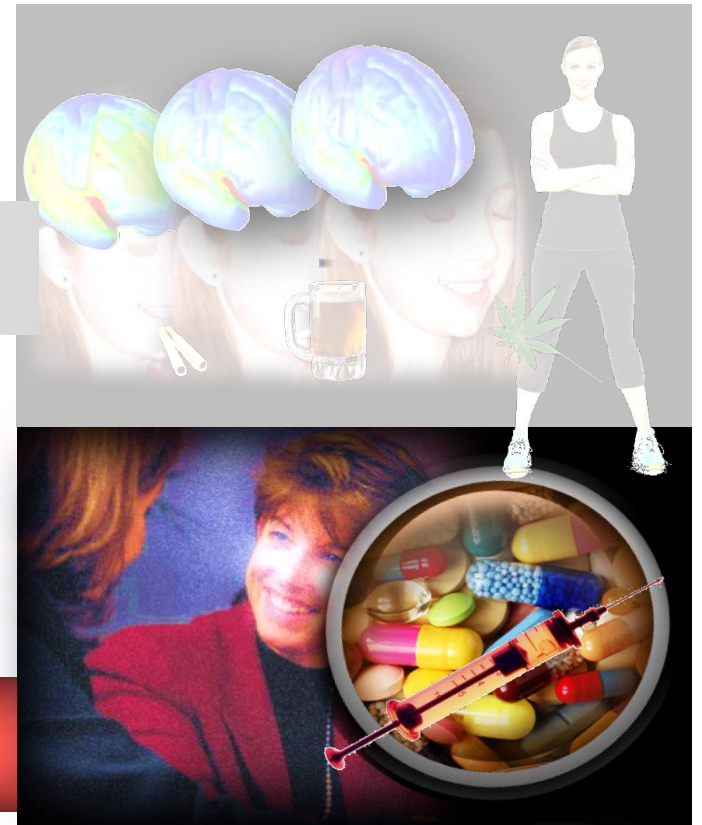
Priority Areas

Prevention Research

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

Treatment Interventions

(New Targets & New Strategies)



Priority Areas

Prevention Research

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

Treatment Interventions

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HIV and Drugs

Prevention
Treatment



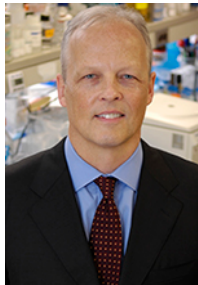
2017 Avant-Garde Awards for HIV/AIDS Research



Michael Farzan, Ph.D., The Scripps Research Institute

A safety switch for an effective HIV-1 vaccine

Preclinical studies on gene therapies for prevention of HIV infection in high-risk populations, such as IDU.



Eric M. Poeschla, Ph.D., University of Colorado Denver

Novel Approaches to Innate Immunity Against HIV-1 and Other Viruses

Will use animal and human cells to explore the use of viral RNA-dependent RNA polymerase (RdRP) to enhance innate immunity against HIV-1 and other viruses.



Peter S. Kim, Ph.D., Stanford University

Making the HIV-1 gp41 pocket amenable to small-molecule drug discovery

Will employ a strategy that increases the structural rigidity in the HIV-1 gp41 region in order to test new therapeutics that target gp41 pocket to prevent HIV infection.

New NIDA FOAs

Advancing Exceptional Research on HIV/AIDS and Substance Abuse (R01) (RFA-DA-18-002)

Posted Date: March 3, 2017; Open Date (Earliest Submission Date) : July 22, 2017; Letter of Intent Due Date(s): July 22, 2017 Application Due Date(s): August 22, 2017; August 22, 2018; August 22, 2019. AIDS Application Due Date(s): August 22, 2017; August 22, 2018; August 22, 2019.

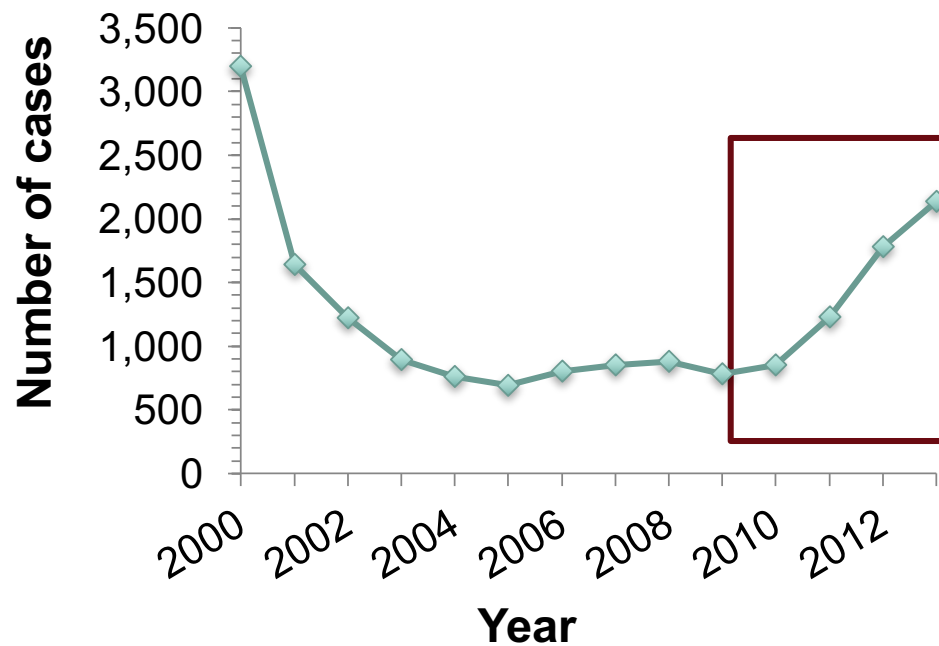
Innovative research projects that have the potential to open new areas of HIV/AIDS research and/or lead to new avenues for prevention and treatment of HIV/AIDS in SUD. Nexus with drug abuse has to be clearly described.

Avant-Garde Award Program for HIV/AIDS and Drug Use Research (DP1) (RFA-DA-18-001)

*Issued: March 7, 2017; Open Date: June 30, 2017;
Application Due Date(s): July 31, 2017, July 31, 2018, July 31, 2019.*

Innovative, basic research that may lead to improved prevention, treatments and outcomes; and creative approaches to eradicating HIV or improving the lives of those living with HIV.

Recent Increases in Reported Number of Acute HCV Infections in USA, 2000–2013



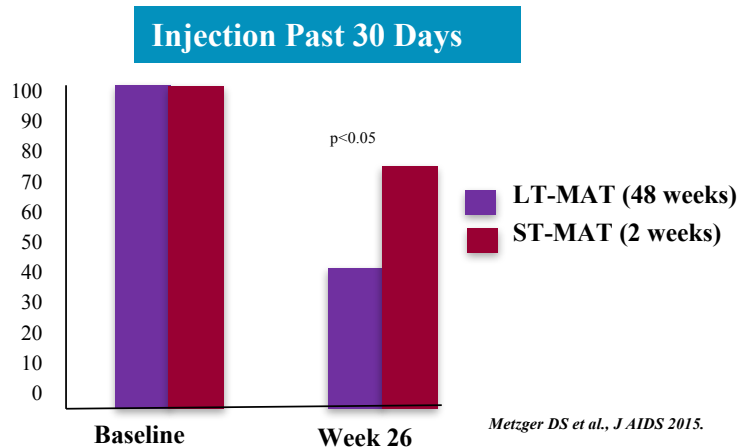
- IDU main source of HCV infection
- Currently 750,000 IDU in USA
- Surge in HCV in young IDUs (18-25 years old)
- 75% of new heroin abusers transitioned from Rx opioids to heroin

National Notifiable Diseases Surveillance System (NNDSS)

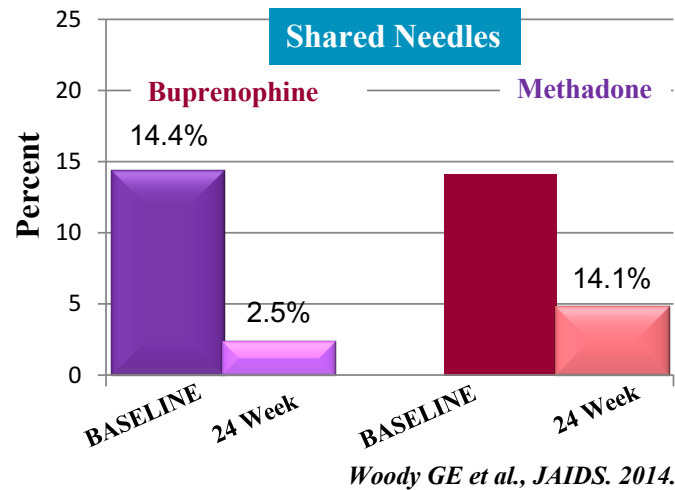
***Better access to effective treatments for OUD to Prevent HCV
Buprenorphine, Methadone and Naltrexone***

MAT Prevents HCV

Long- vs Short-Term Buprenorphine

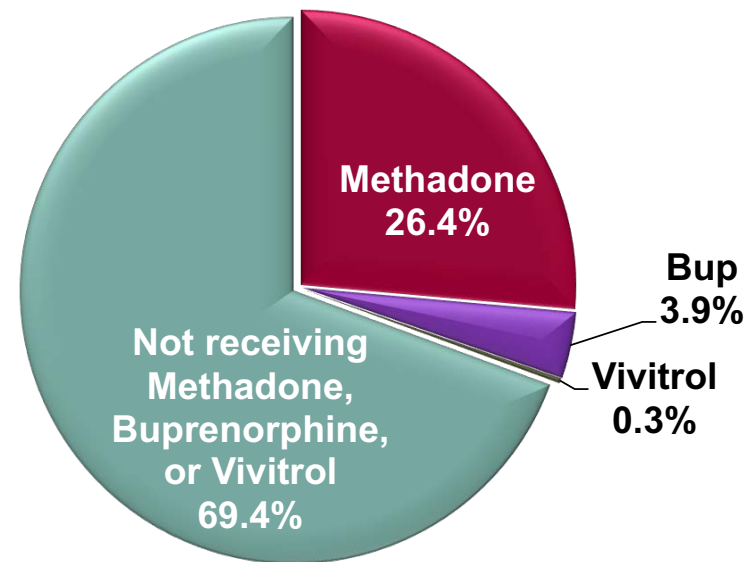


Risky Behavior Reduction



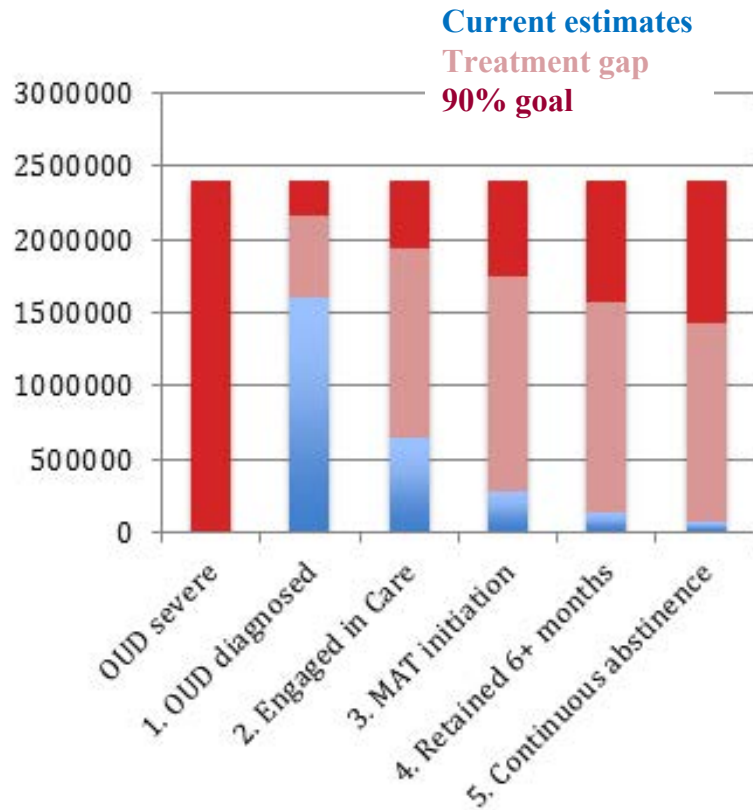
Opioid Treatment Programs in the USA

% OTP patients receiving methadone, buprenorphine, or vivitrol



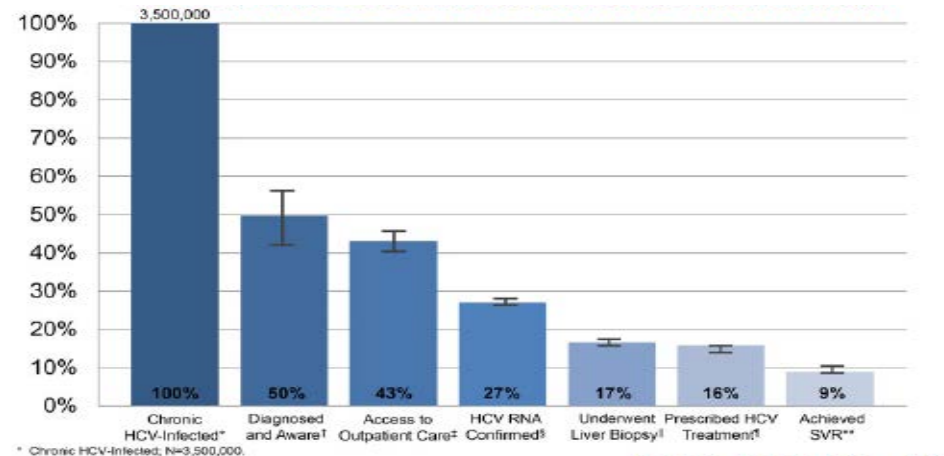
2012 N-SSATS Data, SAMHSA

OUD Cascade of Care in USA



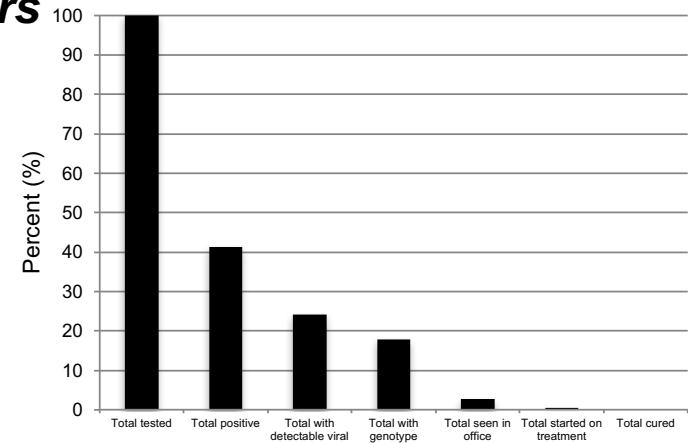
Williams AR, Nunes E, Olfson M. *Health Affairs Blog*, 2017

Cascade of Chronic HCV Care in USA



Yehia BR et al., *Plos One* 2014; 9(7): e101554.

Cascade of HCV Care in NJ Heroin Users



Akyar et al., *Emerg Infect Dis.* 2016;22(5):907-909.

Three bar graphs show the cascade of care, in the USA for OUD, for HCV, and for HCV Care for New Jersey Heroin users.

The first graph, based on national estimates (1,2) and a 90 percent goal of success, shows the estimated OUD treatment gap at each of the five stages of care– diagnosed, engaged in Care, Medication Assisted Treatment initiation, retained 6 or more months, and Continuous Abstinence. The treatment gap estimate is the lowest for OUD diagnosis, but increases consistently for the subsequent stages of the cascade. Only 20-40 percent of those diagnosed are estimated to receive care in any given year. (1.on data extracted from the Substance Abuse and Mental Health Services Administration, Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-48, HHS Publication No. (SMA) 14-4863. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2014),

(2. As reported in <http://healthaffairs.org/blog/2017/03/13/to-battle-the-opioid-overdose-epidemic-deploy-the-cascade-of-care-model/>)

The second bar graph, is of a proposed cascade of care for chronic HCV-infected persons in the U.S.. The estimates are based on data in the literature on HCV care, and the National Health and Nutrition Examination Survey (NHANES) data 1999 through 2002.. The stages in the cascade are: diagnosed and aware, access to outpatient care, HCV RNA confirmed, underwent liver biopsy, prescribed HCV treatment, and achieved sustained virologic response (SVR). Of an estimated 3.5 million people infected with chronic HCV, an estimated 50 percent of them were diagnosed and aware of their infection; 43 percent had access to outpatient care; 27 percent had HCV RNA confirmed; 17 percent underwent liver fibrosis staged by biopsy; 16 percent were prescribed HCV treatment; and 9 percent achieved sustained virologic response (SVR).

The third bar graph, is of HCV care for heroin users in New Jersey. Of 861 unique patients tested (from 10 New Jersey counties), 374 were positive (43.4 %), Of those aged 17-35 years old, 237 were HCV antibody positive (41.4%). The stages of the cascade are those testing positive, the detectable viral load, the genotype identified, those seen in clinician office, those started on treatment, those cured. Those started on treatment and cured was near zero. Sixteen patients had outpatient follow-up appointments, three of them started oral direct-acting antiviral treatment, two failed to adhere to treatment regimen, one cleared infection before drug-treatment began.

HIV, HCV and Related Comorbidities in Rural Communities Affected by Opioid Injection Epidemics in US: Building Systems for Prevention, Treatment & Control (UG3/UH3) RFA-DA-17-014

**NIDA, National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention
NCHHSTP/CDC, & CSAT/SAMHSA**

*Two stage, multi-method research projects that inform community response and **promote comprehensive, integrated approaches to prevent HIV and HCV infection**, along with associated comorbidities, among IDU in **rural US communities**.*

Hepatitis C Virus (HCV) Advanced Molecular Detection in Support of Systems for Prevention, Treatment and Control of HIV, HCV and Related Comorbidities in Rural Communities Affected by Opioid Injection Drug Epidemics in the United States (U24) RFA-DA-17-023

NIDA and NCHHSTP/CDC

*Support a Center for HCV next-generation sequencing using Global Hepatitis Outbreak and Surveillance Technology (“GHOST”) in collaboration with CDC. **The GHOST Center will support HCV next-generation sequencing activities of research projects funded by the companion RFA (RFA-DA-17-014).***



NATIONAL Rx Drug Abuse & Heroin SUMMIT

April 17 - 20, 2017 Atlanta GA



OPERATION
UNITE
Educational Advisor

Featured Speakers:



Thomas E. Price, M.D.,
Secretary,
U.S. Department of Health and Human
Services (HHS)



William R. Brownfield
Assistant Secretary,
Bureau of International Narcotics and
Law Enforcement Affairs,,
U.S. Department of State



**Vice Admiral Vivek H. Murthy, M.D.,
MBA**
United States Surgeon General



Francis Collins, M.D., Ph.D.,
Director,
National Institutes of Health; (NIH)



Nora D. Volkow, M.D.,
Director,
National Institute on Drug Abuse (NIDA)
National Institutes of Health



Anne Schuchat, M.D.,
Acting Director,
Centers for Disease Control and
Prevention, (CDC)



Richard J. Baum
Acting Director,
Office of National Drug Control Policy
(ONDCP);



Kana Enomoto
Acting Deputy Assistant Secretary
Substance Abuse and Mental Health
Services Administration (SAMHSA)



DHHS Secretary Thomas E. Price, M.D.



- Announced **\$485 million in grants** for prevention and treatment of OUD as part of the ***21st Century Cures Act***, passed Dec 2016
- Funds will be followed next year by another half-billion dollar based upon an HHS assessment where funds can be most successful.
- ***HHS's top five priorities*** in addressing the opioid epidemic are:
 - *Expanding access to treatment* and recovery services
 - Supporting use of opioid *overdose reversal drugs*
 - Improving *public health surveillance* of the epidemic
 - *Supporting research on pain and addiction*
 - *Advancing best practices* for pain management



Premiers May 1, 2017 at 10 PM

<http://www.hbo.com/documentaries/warning-this-drug-may-kill-you/video/promo>

- This documentary portrays an emotional description of opioid addiction through the eyes of families who have lost loved ones, or who are struggling to help family members
- NIDA has worked with HBO on this hour long documentary and has helped them build an ***online resource page*** to offer more ***information on MAT and evidenced based treatment***