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

February 6, 2018

Nora D. Volkow, M.D., Director

National Institute on Drug Abuse

@NIDAnews
NIDA

Office of the Director

Office of Diversity & Health Disparities

Office of Translational Initiatives and Program Innovations

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

Search for DTMC Director

Dr. Redonna Chandler

AIDS Research Program

International Program
Director’s Report to the National Advisory Council on Drug Abuse

- Budget Update
- What’s New @ HHS/NIH?
- Recent NIDA Activities & Events
<table>
<thead>
<tr>
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<th>FY 2016 Actuals</th>
<th>FY 2017 Actuals</th>
<th>FY 2018 PB</th>
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<tbody>
<tr>
<td>NonAIDS</td>
<td>$754,727</td>
<td>$794,102</td>
<td>$647,674</td>
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<td>AIDS</td>
<td>$294,244</td>
<td>$276,711</td>
<td>$217,324</td>
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<td>TOTAL</td>
<td>$1,048,971</td>
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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%
Director’s Report to the National Advisory Council on Drug Abuse

• Budget Update

• What’s New @ HHS/NIH?

• Recent NIDA Activities & Events
$4.2B: Projected total for lifetime of BRAIN

$550M: BRAIN Funding through 2017

~12% of the total

21st Century Cures

Base Budget
• NIH will formally revisit **BRAIN 2025’s priorities** to provide an updated scientific vision to guide the second half of the Initiative

• Focus on specific **topics/questions that can now be interrogated** given the emerging set of tools and technologies
BRAIN Initiative: Notice of Support for Research on the Fundamental Neurobiology of Pain Processing

- NIH welcomes BRAIN Initiative applications targeting central nervous system nociceptive and pain circuits, as appropriate to the goals and requirements of specific BRAIN Initiative FOAs.

- It is expected that the unique opportunities of the BRAIN Initiative will enable production of detailed maps of pain circuits, and the adoption of powerful new tools for monitoring and modulating pain circuit activity, leading to significant advances in the understanding of pain and nociception.

DIRECTOR: BRAIN INITIATIVE  
National Institute of Neurological Disorders and Stroke (NINDS)  

APPLICATIONS WILL BE REVIEWED STARTING  
March 5, 2018 (Applications accepted until position is filled.)

DIRECTOR: NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH  

APPLICATION BY March 1, 2018 at 11:59 p.m., ET
Director’s Report to the National Advisory Council on Drug Abuse

• Budget Update

• What’s New @ HHS/NIH?

• Recent NIDA Activities & Events
Past Month **Marijuana Use Remains Steady** while Alcohol and Cigarette Use Declining among High School Seniors

![Chart showing trends in marijuana, alcohol, cigarette, and e-cigarette use among 12th grade students from 1991 to 2017. Marijuana use remains steady, while alcohol and cigarette use decline.]

*SOURCE: University of Michigan, 2017 Monitoring the Future Study*
DAILY MARIJUANA USE MOSTLY STEADY

2007 – 2017

2017

8th graders: 0.8%
10th graders: 2.9%
12th graders: 5.9%

71.0% of high school seniors do not view regular marijuana smoking as being very harmful, but 64.7% say they disapprove of regular marijuana smoking.

PAST-YEAR E-VAPORIZER USE AND WHAT TEENS ARE INHALING

8th graders: 13.3%
10th graders: 23.9%
12th graders: 27.8%

BINGE DRINKING RATES STEADY AFTER DECADES OF DECLINE

Binge drinking appears to have leveled off this year, but is significantly lower than peak years.

TEENS MORE LIKELY TO USE MARIJUANA THAN CIGARETTES

Daily use among 12th graders

1992: 1.9%
1997: 24.6%

Past-year misuse of prescription/over-the-counter vs. illicit drugs

Past-year misuse of Vicodin among 12th graders has disappeared entirely in the past 15 years. In 1992, 12th graders had a higher misuse rate than adults. Today, misuse rates among adults exceed those among students.

Students report lowest rates since start of the survey

Among all grades, past-year use of heroin, methamphetamine, cigarettes, and synthetic cannabinoids are at their lowest by many measures.

NEARLY 1 IN 3 STUDENTS IN 12TH GRADE REPORT
PAST-YEAR USE OF E-VAPORIZERS, RAISING CONCERNS
ABOUT THE IMPACT ON THEIR LONG-TERM HEALTH.
ABCD Study Fast Track Data
https://data-archive.nimh.nih.gov/abcd
The ABCD Study is releasing fast-track neuroimaging data from ABCD Study participants on an ongoing basis - DICOM images from ~4,000 participants currently available.

Annual Curated Data Release
Interim data on the first 4,500 participants will be released in early 2018, including:
- 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, and
- Biological data (e.g., pubertal hormone analyses).
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.

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.

Marijuana Laws Differ State by State

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• Marketing, product labeling, distribution (home growth).
• Taxation.
John Carnevale, Workgroup Chair, will be presenting a summary of the report findings this afternoon...

RECOMMENDATIONS FOR THE NIDA’S CANNABIS POLICY RESEARCH AGENDA

NATIONAL ADVISORY COUNCIL ON DRUG ABUSE CANNABIS POLICY WORKGROUP

FEBRUARY 6, 2018
Overdose Death Rates

1999

2016

Legend for estimated age-adjusted death rate (per 100,000 population):
- <2
- 2.3-2.9
- 3.0-3.9
- 4.0-4.9
- 5.0-5.9
- 6.0-6.9
- 7.0-7.9
- 8.0-8.9
- 9.0-9.9
- 10.0-10.9
- 11.0-11.9
- 12.0-12.9
- 13.0-13.9
- 14.0-14.9
- 15.0-15.9
- 16.0-16.9
- 17.0-17.9
- 18.0-18.9
- 19.0-19.9
- 20.0-20.9
- 21.0-21.9
- 22.0-22.9
- 23.0-23.9
- 24.0-24.9
- 25.0-25.9
- 26.0-26.9
- 27.0-27.9
- 28.0-28.9
- 29.0-29.9
- 30.0+

Medication Assisted Treatment (MAT)

Opioid Effect

- Full Agonist (Methadone: Daily Dosing)
- Partial Agonist (Buprenorphine: 3-4X week)
- Antagonist (Naltrexone: ER 1 month)

Log Dose

**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
Expand access to MAT
Healthcare system
Criminal Justice system

Improve Compliance and Retention
Extended release formulations
Drug combinations
Additional interventions
Public Sector Low Threshold Office-Based Buprenorphine Treatment in Primary Care

- Unobserved induction,
- At most weekly visits,
- No psychosocial treatment.

- Treatment retention of 38 weeks is equivalent to that of office-based opioid treatment.
- Low threshold treatment protocols, as compared to national guidelines, may expand access to buprenorphine.


Collaborative Care for Opioid and Alcohol Use Disorders in Primary Care (FQHC)

Participant Outcomes at 6-Month Follow-up

- In primary care, collaborative care intervention increased _abstinence from alcohol and drugs_ compared to usual care.
- Treatment for OAUDs can be integrated into primary care settings.

_Watkins KE et al., JAMA Intern Med. 2017;177(10):1480-1488._
Opioid Medication Therapy (OMT) In Prison

Mortality Post Release

Survival Curve During the Year Following Release (Drug-Poisoning Mortality)

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.

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

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).
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
Priorities for Future Research

- **Strengthen connection between research and practice**
  - Learning health care system to translate evidence-based practices
  - Large-scale implementation pilot
- **Explore, maximize, and expedite available data sources and study designs**
  - Observational and secondary data sources in addition to clinical trials
  - 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
- **Treatment interventions for mild OUD or subclinical opioid misuse**
- **Research to address cost and sustainability**
Improve Compliance and Retention
Extended release formulations
Drug combinations
Additional interventions
% urine samples negative
for opioids (Weeks 5 to 24)

Comparison CAM2038 versus Daily SL BPN

Heidbreder et al., CPDD 2017
**Focus Area A: Enhance medications for OUD and to prevent/reverse overdoses**

- Develop *new formulations* and *combinations of medications* to treat OUD and to prevent overdoses
- Develop *more potent* or *longer lasting opioid antagonists* to reverse overdoses from fentanyl or its derivatives.
- *Develop and validate alternative endpoint* other than abstinence that are acceptable to FDA for approval of OUD medications

**Focus Area B: Pain**

- Establish *data sharing collaborative* between industry groups
  
  *NIH to serve as a neutral broker*
- Determine *objective measures* to understand, predict responses to pain
  
  *Biomarkers for pain – and a “Pain-ometer”*
- *Clinical trial network* to accelerate trials on common and rare pain syndromes and to evaluate biomarkers
Establishment of the NIDA Advisory Council Workgroup on Opioids

Mission: To provide guidance on the development and implementation of NIDA’s public-private response to help end the opioid crisis.

Chair: Edward V. Nunes, M.D.

Next Steps:

-- Appoint members - February

-- Convene workgroup - March

-- Conduct assessment - March - May

-- Complete and issue final report - June - July

-- Update Council - On-going
• Support 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:
  UG3: will support a project with specific milestones to be accomplished by the end of the 2-year period.
  UH3: will provide funding for 3 years to a project successfully completed in UG3.

• Investigators responding to this FOA must address both UG3 and UH3 phases.
FDA Patient-Focused Drug Development (PFDD) Initiative

In 2012, patient voices joined the science

• 5 patient-centered, community-led Guidances for Industry written:
  
  Artificial Pancreas Device Systems (2012);
  Chronic Fatigue Syndrome, Myalgic Encephalomyelitis (March 2014);
  Duchenne Muscular Dystrophy (June 2015);
  Amyotrophic Lateral Sclerosis, ALS (Draft, 2016),
  Amyloidosis (Draft, December 2016).

• On November 30, 2017, NIDA and Addiction Policy Forum (NGO) submitted LOI to FDA indicating the intent to lead a PFDD meeting for OUD.

• On December 22, 2017, FDA determined that “gathering patient perspectives on OUD will be of great value ..”. FDA accepted NIDA/APF LOI and proposed the transition of the meeting from externally-led into FDA-led. FDA will host the meeting and lead planning, working closely with APF and NIDA.

PFDD Meeting will take place on April 17, 2018
Priority Areas

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

Treatment Interventions
(New Targets & New Strategies)

HIV and Drugs
Prevention
Treatment
HIV infection and risk of overdose: meta-analysis

HIV+ associated with increased risk of overdose mortality (risk ratio 1.74)


Long-term prescription opioids and/or benzodiazepines and mortality among HIV-infected and uninfected patients

Significant interaction between opioid receipt and HIV with mortality: HR was 1.46 in HIV+ and 1.25 in HIV- (p <0.01).
Mortality risk was increased for patients receiving both opioids and benzodiazepines

NIDA Avant-Garde Award Program for HIV/AIDS and Drug Use Research (DP1, Clinical Trial Optional) (RFA-DA-18-019)

Issued: December 6, 2017; Application Receipt/Submission Date(s): April 17, 2018.
March 29, 2017
Presidential Executive Order Establishing the
President’s Commission on Combating
Drug Addiction and the Opioid Crisis

November 1, 2017
56 Recommendations on:
• Federal Funding and Programs
• Opioid Addiction Prevention
  • Prescribing Guidelines, Regulations, Education
  • PDMP Enhancements
  • Supply Reduction and Enforcement Strategies
• Opioid Addiction Treatment, Overdose Reversal, and Recovery
• Research and Development
2320 events Including 180 events in 16 countries outside the U.S., including Pakistan, Afghanistan, Myanmar, Mexico, Northern Marinara Islands, South Africa, the UK, Ireland, Zimbabwe, Ghana, Nigeria, Micronesia, the Ukraine and Zambia.