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

February 13, 2019

Nora D. Volkow, M.D., Director
National Institute on Drug Abuse

@NIDAnews
In Memoriam

Dr. Herbert Kleber
1934-2018

Dr. Conan Kornetsky
1925-2018

Nancy J. Soulen, J.D.
1930-2018
<table>
<thead>
<tr>
<th></th>
<th>FY 2017 Actuals</th>
<th>FY 2018 Budget Authority</th>
<th>FY 2019 Enacted</th>
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</thead>
<tbody>
<tr>
<td>NonAIDS</td>
<td>$794,102</td>
<td>$854,609</td>
<td></td>
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<tr>
<td>AIDS</td>
<td>$276,711</td>
<td>$269,765</td>
<td>$1,169,844</td>
</tr>
<tr>
<td>Total</td>
<td>$1,070,813</td>
<td>$1,124,374</td>
<td></td>
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<tr>
<td>Opioids</td>
<td></td>
<td>$250,000</td>
<td>$250,000</td>
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National Institute on Drug Abuse Portfolio
Annual Appropriation
FY 2018 Actual

- Division of Neuroscience & Behavior -- 41%
- Division of Epidemiology, Services & Prevention Research -- 28%
- Division of Therapeutics and Medical Consequences -- 14%
- Center for the Clinical Trials Network -- 4%
- RMS -- 6%
- Intramural Research -- 8%
NIDA Portfolio HEAL Opioids
(2 Year Average) -- FY 2018 Actual

- Division of Neuroscience & Behavior -- 2%
- Division of Epidemiology, Services & Prevention Research -- 18%
- Division of Therapeutics and Medical Consequences -- 73%
- Center for the Clinical Trials Network -- 7%
Dr. Michelle Freund joined NIDA to Direct the **HEALthy Baby and Child Development (HBCD) Study**.

Dr. Amy Goldstein joined the Division of Epidemiology, Services and Prevention Research as **Prevention Research Branch Chief**.

Dr. Jennifer Hobin joined the **Office of Science Policy and Communications as the Deputy Director** in October 2018.

Dr. Jennifer Villani joined NIDA to serve as the **Associate Director for the HEALing Communities Study**.

Dr. Tisha Wiley was selected as the SRB Branch Chief in DESPR and will be leading NIDA’s **Justice Community Opioid Innovation Network (JCOIN)**.
BINGE DRINKING* RATES CONTINUE DOWNWARD TREND

BINGE DRINKING: SIGNIFICANT DROP IN PAST FIVE YEARS ACROSS ALL GRADES.

PAST-YEAR MISUSE OF PRESCRIPTION/OVER-THE-COUNTER VS. ILLEGIT DRUGS

PRESCRIPTION/OTC

- Sedatives/Tranquilizers: 5.0%
- Adderall®: 4.6%
- Opioids: 3.4%
- Cough/Cold Medicine: 3.4%
- Ritalin®: 0.9%

ILIQUIT DRUGS

- Past-year use among 12th graders

Past-year misuse of Vicodin® and OxyContin® among 12th graders has dropped dramatically in the past 15 years.

STUDENTS REPORT LOWEST RATES SINCE START OF THE SURVEY

Across all grades, past-year use of illicit drugs other than marijuana holding steady at the lowest levels in over 20 years.

*Synthetic cannabinoids are called "synthetic marijuana" in the survey.

*Binge drinking is defined as having 5 or more drinks in a row in the last 2 weeks.
NEARLY 2 IN 5 STUDENTS IN 12TH GRADE REPORT PAST-YEAR VAPING, RAISING CONCERNS ABOUT THE IMPACT ON BRAIN HEALTH AND POTENTIAL FOR ADDICTION.
DAILY MARIJUANA USE MOSTLY STEADY

2008 - 2018

8th graders 0.7%
10th graders 3.4%
12th graders 5.8%

2018

TEENS MORE LIKELY TO USE MARIJUANA THAN CIGARETTES

Past-month use among 12th graders
Past Month Marijuana Use in 2015, 2016 and 2017

- **10% Increase**: 2015 (1.8M) to 2017 (2.2M)
- **23% Increase**: 2015 (1.8M) to 2017 (2.2M)

**Ages**
- 12 to 17: 2015 (7.0M) → 2017 (7.9M)
- 18 to 25: 2015 (6.9M) → 2017 (22.1M)
- 26 or Older: 2015 (13.6M) → 2017 (16.8M)

*National Survey on Drug Use and Health, SAMHSA*
Adolescent Brain Cognitive Development (ABCD) Study

Baseline Assessments Complete – 11,874 Participants!

ABCD Study Fast Track Neuroimaging Data
https://data-archive.nimh.nih.gov/abcd
DICOM images from ~9,000 participants currently available.

Interim Curated Data Release
Data on the first 4,500 participants was released in February 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,
• Biological data (e.g., pubertal hormone analyses),
• Residential history derived data (e.g., crime, area deprivation index, walkability, population density, pollution)

Full Baseline Curated Data Release
Expected Spring 2019

Data Exploration and Analysis Portal (DEAP)
DEAP provides the means to find measures of interest from more than 40,000 shared observations available for each ABCD participant, to test hypotheses using a multi-level regression model suitable for the ABCD study design, and to run novel multi-level statistical analysis directly from the DEAP interface.
ED Visits for Cannabis

Emergency Department Visits with Cannabis Related Diagnosis
San Diego County

Up 830%

The Center for Community Research prepared this analysis for the San Diego County Marijuana Prevention Initiative with data from the California Department of Public Health, March 2016. mpisdcounty.net
Efficacy and safety of fatty acid amide hydrolase inhibitor (PF-04457845) for treatment of cannabis withdrawal and dependence: phase 2a RCT

<table>
<thead>
<tr>
<th></th>
<th>Self-reported cannabis use week 4</th>
<th>Urinary THC-COOH levels week 4</th>
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<tbody>
<tr>
<td></td>
<td>Cannabis use (joints day)</td>
<td>Difference (95% CI)</td>
</tr>
<tr>
<td>Placebo (n=19)</td>
<td>1.27 (0.82 to 1.97)</td>
<td>0.88 (0.29 to 1.46)</td>
</tr>
<tr>
<td>PF-04457845 (n=32)</td>
<td>0.40 (0.25 to 0.62)</td>
<td>..</td>
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This 4-week RCT showed that treatment with the FAAH inhibitor (PF-04457845 4 mg g/d) reduced cannabis withdrawal symptoms, self-reported cannabis use, urinary THC-COOH concentrations, and deficits in stage N3 sleep and was well tolerated.

The Crisis: National Overdose Death Rates

In 2017, there were **70,237** overdose deaths (9.6% higher than 2016)

Medication Assisted Treatment (MAT)

Opioid Effect

Log Dose

Full Agonist (Methadone: Daily Dosing)

Partial Agonist (Buprenorphine: 3-4X week)

Antagonist (Naltrexone: ER 1 month)

DECREASES:

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

INCREASES

• Social functioning
• Retention in treatment

MAT is highly underutilized!

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

Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017.
Implementing Medications for OUD in Healthcare

- ED-initiated buprenorphine
- Reduced illicit opioid use
- Increased treatment retention
- Decreased inpatient treatment

Self-Reported Illicit Opioid Use in the Past 7 Days

<table>
<thead>
<tr>
<th>Days since prison release</th>
<th>Survival probability</th>
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<tbody>
<tr>
<td>MOUD unexposed</td>
<td>MOUD exposed</td>
</tr>
<tr>
<td>28 days</td>
<td>0.97</td>
</tr>
<tr>
<td>122 days (4 months)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

MOUD reduced mortality by 75% in the first month post release

D’Onofrio G et al., JAMA April 28, 2015.

Marsden J et al., Addiction 2017; 112:1408-1418.
Expand Therapeutic Options: Novel Treatments

**Neuromodulation**

*Addiction Cycle and Relevant Brain Regions*

*Koob and Volkow 2017*

- Transcranial Magnetic Stimulation (TMS)
- Transcranial Direct Current Stimulation (tDCS)
- Deep Brain Stimulation (DBS)

**Vaccines and Immunotherapies**

- Vaccines (fentanyl (and analogues), heroin/morphine
- Reduced drug reaching brain
- Protection against overdose

*Bremer et al, 2016; Janda and Treweek, 2012*
# Improving Prevention and Treatment for Opioid Misuse, Addiction and Overdoses

## Priority Research Areas:

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<tr>
<th>Expand Therapeutic Options</th>
<th>Optimize Effective Treatment Strategies</th>
<th>Develop New/Improved Prevention &amp; Treatment Strategies</th>
<th>Enhance Treatments for Infants with NAS/NOWS</th>
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## Research Opportunities:

- New formulations
- Longer duration
- Respiratory depression
- Immunotherapy
- New targets and approaches

- Clinical trials expansion
- Criminal justice innovation
- Collaborative care
- Behavioral interventions
- Multi-site implementation (HEALing Communities Study)

- Treatment of Early/moderate OUD
- Optimal length of MOUD Treatment
- Prevention in Transition to adulthood

- Brain development of opioid-exposed infants
- ACT NOW
Expand Therapeutic Options: OUD and Overdose Reversal

• New Targets for OUD
• Drug combinations to improve retention (lofexidine + Bup)
• Stronger, longer acting formulations and new targets for OD from synthetic opioids (e.g. fentanyl) and drug combinations (bdz + opioids)
• Stimulation devices to prevent respiratory depression
• OD, alert technologies and naloxone autoinjectors
• *Post-overdose interventions to ensure engagement in treatment*

New Medication Outcomes

• Craving,
• Insomnia,
• Depression
Medications Development Research Project

- **RFA DA-19-002: Development of Medications to Prevent and Treat Opioid Use Disorders and Overdose** (Contact PO: Ivan Montoya)
  - 4 cycles of reviews (since May, 2018)
  - 103 applications reviewed
  - 22 applications approved for funding
  - Rolling acceptance of applications
  - Length of time between application receipt to approval for funding has been shortened from 9 months to < 2 months
CTN OUD Expansion Project

Expand CTN to 1) increase scientific and clinical research capabilities, and 2) better cover geographic regions most impacted by epidemic

- Optimizing Retention, Duration and Discontinuation Strategies for OUD medications (MOUD) in healthcare
- Strategies for *inducting* MOUD in hospitalized patients and *enhancing* post-discharge care
  - More effective linkage models (Bridge clinics)
- *Implement ED-initiated BUP* in multiple EDs and compare BUP-SL and BUP-XR
- *Rural expansion* of MOUD treatment using *telemedicine* and *mHealth* approaches.
- *Opioid registry* in diverse health care delivery systems
- Efficacy of *“Subthreshold OUD Prevention (STOP)” intervention* in primary care
- Compare BUP-XR, BUP-SL on *OUD expecting Mothers* on infant outcomes.
- *Surmounting naltrexone (NTX) induction hurdle*
NIDA will launch a new **Council Workgroup**

**Charge:**
- To provide external scientific input and recommendations for current and future research projects of NIDA’s National Drug Abuse Treatment Clinical Trials Network (CTN)
- To provide annual updates to Council on CTN initiatives

**Chair:** Carlos del Rio, M.D.
Emory University

**Co-Chair:** Hillary Kunins, M.D. Ph.D. *(invited)*
NYC Department of Health and Mental Hygiene
Albert Einstein College of Medicine
Justice Community Opioid Innovation Network (JCOIN) Update

Progress to Date:

• 11 supplement awards made in September 2018
• Solicitations released December 10, 2018 for Research Centers, Coordination and Translation Center, and Methodology and Analytics Center
• Expected awards total $30M
• Technical Assistance webinar held January 9, 2019
• Applications Due: February 27, 2019
• Review: Summer 2019
• Awards expected: Late Summer/Early Fall 2019
The HEALing Communities Study: **Goals**

- Develop and test strategies to help communities respond rapidly and effectively to opioid crisis with a focus on achieving 40% reduction in 3 years for OD fatalities and improving other outcomes.


- Determine factors (structural, organizational, policy, etc.) that contribute to successful implementation and sustainability of the integrated interventions.

- Determine cost-effectiveness of integrated intervention compared to standard of care.
The HEALing Communities Study: *Actions to Date*

- Application receipt date: December 4, 2018
- Research Site application in-person review: January 30-31, 2019
- Data Coordinating Center in-person review: February 20, 2019
- Research Site application site visits: February 25-March 15, 2019
- Earliest estimated award date: April 19, 2019
HEALthy Brain and Child Development (HBCD) Study

Large multi-site longitudinal study to examine brain, cognitive, behavioral, social, and emotional development beginning *prenatally* and extending through *childhood*.

- Oversample for prenatal opioid exposure

**Progress to Date:**

  - Expert Panel Meeting on Research Methodologies – September 24, 2018
  - Expert Panel Meeting to Discuss Study Design – October 22, 2018
  - R34 Planning Grant Funding Opportunity Announcements - RFA-DA-19-029; RFA-DA-19-036
    - Published – December 21, 2018
    - Pre-application webinar – February 6, 2019
    - Application deadline – March 25, 2019
    - Review – June/July 2019
    - Earliest start date – September 2019
HEAL Prevention Initiative: Preventing OUD in Older Adolescents and Young Adults (ages 16 –30)

Goal: Develop the evidence base for interventions and strategies to prevent initiation of opioid misuse and development of OUD in at-risk older adolescents and young adults

Focus on:
Healthcare, justice and other systems and settings opportune for accessing and engaging at risk adolescents and young adults

Components:

HEAL Prevention Cooperative – up to 10 research projects and 1 coordinating center.

Two FOAs published:
- UG3/UH3 Research Projects (RFA-DA-19-035)
- U24 Coordinating Center (RFA-DA-19-034)

Administrative Supplements
- Application due – 3/13, 2019;
- Review – Summer 2019
- Earliest start date – 10/2019

Next steps: Internal review
Priority Areas

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

Treatment Interventions
(New Targets & New Strategies)

HIV and Drugs
Prevention
Treatment
Scalable, Integrated Intervention To Engage IDU In HIV Care and MOUD (HPTN 074)

Systems navigators facilitate engagement, retention, adherence in HIV care and MAT Psychosocial counseling, at least 2 sessions ART at any CD4 count

All incident HIV infections among partners occurred in the SOC arm:

\[
\begin{align*}
\text{Intervention: (0 cases/215.6 p-y)} \\
\text{(7 cases/683.6 p-y)}
\end{align*}
\]

IR: 0.0/100 p-y (CI 0.00, 1.7) SOC:
IR: 1.0/100 p-y (CI 0.41, 2.1)

January 22 – 27th 2019

There were **1918 events** held in the U.S. and 23 other countries, including Pakistan, Nigeria, Afghanistan, Myanmar, South Africa, India, Mexico and Ukraine.

Gibson County High School in Dyer (Tennessee)

Boys & Girls Club Starkville (Mississippi)