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

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse
September 12, 2023
## NIDA Budget

(all dollars are in $k)

<table>
<thead>
<tr>
<th></th>
<th>FY 2022 Final</th>
<th>FY 2023 Enacted</th>
<th>FY 2024 President’s Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base</strong></td>
<td>$1,250,828</td>
<td>$1,308,070</td>
<td>$1,308,070</td>
</tr>
<tr>
<td><strong>HEAL</strong></td>
<td>$345,295</td>
<td>$355,295</td>
<td>$355,295</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$1,596,123</td>
<td>$1,663,365</td>
<td>$1,663,365</td>
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</tbody>
</table>

*NIDA’s FY 23 budget includes a 3.8% general increase as well as a $10m increase for the HEAL program and a $10m increase for research on pain and pain management.*
Helping to End Addiction Long-term (HEAL) Initiative – Administrative Transition

• HEAL, which was launched in 2018 has released $2.5 billion to fund > 1,000 research projects and > 40 research programs across the US.

• Beginning October 1, 2023, operations supporting HEAL will move from the Office of the NIH Director to NIDA and NINDS.

• This change does **not** reflect a reduced commitment by NIH leadership. The HEAL Initiative and addressing the overdose and opioid crisis and advancing the understanding and treatment of pain remains a top NIH priority.

• Goal of the administrative shift is to ensure its long-term sustainability, streamline scientific decision-making, and leverage scientific expertise and infrastructure of NIDA and NINDS.

• HEAL will remain a trans-NIH effort, engaging expertise of nearly all NIH Institutes and Centers.

• HEAL will remain intact and continue to publish funding opportunities and maintain broad engagement with external partners to ensure it continues to respond to the evolving opioid crisis.
HEAL Coordination

- Cross-cutting research involving Pain & OUD
- Increasing Participant Diversity, Inclusion, and Engagement
- Data
- Research-Dissemination and Engagement Center: HEAL Connections
- Tribal Health Research (N-CREW)

*Scientific leads correspond to subject matter experts across the HEAL Initiative/trans-NIH including NIDA and NINDS Divisions and relevant Teams, Work Groups
Native Collective Research Effort to Enhance Wellness: Addressing Overdose, Substance Use, Mental Health and Pain or *N-CREW*

Background: Tribal Consultations in 2018 and 2022-Research Needed to Address the Opioid Crisis

**Themes**

- High priority to address overdose crisis including opioid/methamphetamine use and pain
- Support Native organizations to lead research, requiring building capacity and infrastructure—“For us, by us”
- More accurate and real-time data
- Specifically design and test interventions for/with Native populations
- Research and intervention to rely on Indigenous Knowledge, including traditional healing practices, spirituality, holistic conceptions of health, and strength based solutions
- Pain
- Drugs as self-medication for pain (physical and psychological) and impact of SDOH

Phase I Development and Planning
FY24-25  $~25 million
- ROA OTA 23-007: T/NASOs will plan, develop, pilot, and/or implement research and/or data improvement projects.
- ROA OTA 23-008: T/NASOs and Ally Organizations will form a Native Research Resource Network (NRRN) to provide comprehensive training, resources, and program coordination.

Phase II will build on Phase I
FY26-30  $~240 million

Contact: NCREW@NIH.GOV

T/NASOs: Tribes and Native American Serving Organizations
Adolescent Brain Cognitive Development Study

96.7 Percent Retained

As of August 31, 2023

ABCD 5.0 Data Released through NIMH Data Archive
- New Data Dictionary Explorer (https://data-dict.abcdstudy.org/)

Publications using ABCD Data
N=635

As of August 31, 2023
• Year 4 data only contained n=4754 of the cohort. It is expected that the rates of use in the latter half of the cohort may be higher. Therefore, these data should not be considered “finalized rates of use.”

Preliminary results from Krista Lisdahl and Ryan Sullivan
Data from Annual Release 5.0 DOI: 10.15154/8873-zj65
The purpose of this meeting is to:
• Share innovative findings and emerging insights about adolescent development through data presentations, roundtable discussions, and interactive poster sessions.
• Foster collaboration among scientists from multiple disciplines and career stages and provide opportunities for researchers to connect with members of the ABCD consortium and NIH program staff.

Registration and abstract submission will open soon.
The deadline for abstract submissions will be Friday, December 1, 2023.
HEALthy Brain and Child Development Study

- 21/27 sites cleared to enroll participants
- 82 participants enrolled
- Piloting for visits 4-6 will begin mid-October
- HBCD PI meeting in San Diego Sept 19-21
<table>
<thead>
<tr>
<th></th>
<th>ALL DRUGS</th>
<th>HEROIN</th>
<th>NAT &amp; SEMI SYNTHETIC</th>
<th>METHADONE</th>
<th>SYNTHETIC OPIOIDS (mainly illicit fentanyl)</th>
<th>COCAINE</th>
<th>OTHER PSYCHO-STIMULANTS (mainly meth)</th>
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<tbody>
<tr>
<td>3/2022*</td>
<td>110,392</td>
<td>8,482</td>
<td>13,521</td>
<td>3,592</td>
<td>74,217</td>
<td>26,256</td>
<td>34,598</td>
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<tr>
<td>8/2022*</td>
<td>109,303</td>
<td>6,920</td>
<td>12,506</td>
<td>3,446</td>
<td>74,211</td>
<td>27,164</td>
<td>34,584</td>
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<tr>
<td>3/2023*</td>
<td>110,469</td>
<td>5,305</td>
<td>11,644</td>
<td>3,381</td>
<td>76,472</td>
<td>28,770</td>
<td>35,756</td>
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<tr>
<td>Percent Change 3/22-3/23</td>
<td>0.001%</td>
<td>-37.5%</td>
<td>-13.9%</td>
<td>-5.9%</td>
<td>3.0%</td>
<td>9.6%</td>
<td>3.3%</td>
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*NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months. The numbers for 2022 differ from final data in slide 1 because provisional data includes all deaths that occurred in the US including foreign residents. Final data through 2021 on slide 1 is limited to deaths in US residents.

Intranasal Nalmefene Formulation for the Treatment of Opioid Overdose

FDA Approves Prescription Nasal Spray to Reverse Opioid Overdose

Nalmefene Hydrochloride Product in Nasal Spray Form May 2023

- Nalmefene + absorption enhancer dodecyl maltoside
- Inverse agonist MOR (Ki = 0.24 nM)
- Very fast action
- Tmax 0.25 hours
- High affinity, fast onset, and long half-life (T1/2 11 hours) advantageous for overdoses from longer-lived synthetic opioids

FDA Approves New Buprenorphine Treatment Option for Opioid Use Disorder

FDA Approves First Over-the-Counter Naloxone Nasal Spray

Agency Continues to Take Critical Steps to Reduce Drug Overdose Deaths Being Driven Primarily by Illicit Opioids
# Opioid Use Disorder

**KEY:** Black: New Molecular Entity  Red: Repurposed  Blue: New Formulation

<table>
<thead>
<tr>
<th>Drug Discovery / Early Preclinical</th>
<th>Late Preclinical</th>
<th>Clinical Trials</th>
<th>New Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPR151 antagonist</td>
<td>Brexpiprazole</td>
<td>Cannabidiol</td>
<td>Naltrexone 2-month injection</td>
</tr>
<tr>
<td>AT-121</td>
<td>Bezafibrate</td>
<td>Ketamine</td>
<td>BICX104 Naltrexone 3-month implant</td>
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<tr>
<td>PTPRD inhibitor</td>
<td>Tezamanpanel</td>
<td>Lemborexant</td>
<td>Naltrexone 6-month implant</td>
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<tr>
<td>SBI-553</td>
<td>BTRX-246040</td>
<td>Liraglutide/Semaglutide</td>
<td>Naltrexone 6-month implant</td>
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<tr>
<td>SHT2R agonist</td>
<td>DCUKA/Kindolor</td>
<td>Lofexidine</td>
<td>Naltrexone 1-year implant</td>
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<tr>
<td>HBS087/HBS093</td>
<td>EC5026</td>
<td>Dexmedetomidine</td>
<td>Novel naltrexone transdermal patch (NNTP)</td>
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<tr>
<td>CS-1103</td>
<td>PFS190457</td>
<td>Olanzapine</td>
<td>LAAM Oral</td>
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<tr>
<td>PN6041/PN6047</td>
<td>SBS-1000</td>
<td>ASP8062</td>
<td>LYN-014-Long-acting methadone</td>
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<tr>
<td>D-CYSee</td>
<td>Biased MOR Agonist</td>
<td>CVL-354</td>
<td>OPNT003 - Nasal Nalmefene</td>
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<tr>
<td>SBI-0801315/SBI-0799220</td>
<td>Methoximox</td>
<td>CVL-936</td>
<td>Nalmefene implant</td>
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<tr>
<td>D24M</td>
<td>Mitragynine analogs</td>
<td>INDV-2000</td>
<td>AP007 Extended-release Nalmefene</td>
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<tr>
<td>NAY (NAN/NAQ)</td>
<td>NRS-033 methadone prodrug</td>
<td>ST-2427</td>
<td>LYN-013 - BUP/NX Oral, long acting</td>
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<tr>
<td>Opioid biased agonist</td>
<td>RM2520 (PZM21)</td>
<td>AZD4041</td>
<td>Nanoparticle-based ADF</td>
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<tr>
<td>MOR Selective Agonist</td>
<td>R-methadone prodrug</td>
<td>KNX100</td>
<td>Nafamostat/PF614 – Oxycodone</td>
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<tr>
<td>Carfentanyl mAb</td>
<td>Heroine vaccine</td>
<td>NYX-783</td>
<td>Naloxone</td>
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<tr>
<td>Oxy/Fentanyl nano-vaccine</td>
<td>Heroin vaccine</td>
<td>ITI-333</td>
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<tr>
<td>Fentanyl/heroin vaccine</td>
<td>P1A4 Fentanyl mAb</td>
<td>Oxycodone vaccine</td>
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<tr>
<td>GDNF gene therapy</td>
<td>Fentanyl vaccine</td>
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<tr>
<td></td>
<td>mAb Fentanyl</td>
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**Division of Therapeutics and Medical Consequences**
Cessation Therapeutics Announces FDA Authorization for First-in-Human Clinical Trial of Antibody for Prevention of Fentanyl Overdose

CSX-1004 is a monoclonal antibody that binds to fentanyl and its analogues with picomolar affinity but has very low affinity for other opioids developed for prevention of fentanyl overdose.

Trial to start August of 2023

www.cessationtherapeutics.com/media 27 July 2023
NOSI encourages research on:

- Pharmacology: including PK in humans
- Prevalence and consequences of xylazine co-use with opioids or opioid/stimulants
- Impact of treatment of OUD and overdose
  - Characterization of xylazine withdrawal and protocols for withdrawal management alongside opioid withdrawal
  - Xylazine wound mechanisms and care best practices in different settings
- Best practices and infrastructure for xylazine testing for people who use drugs and in clinical settings

Kacinko, S et al., J Analytical Toxicology, 46(8), 911-917.
Unintentional drug overdose death rates among US youth aged 15-19

Warren et al., JAMA Netw Open. 2023

Opioid misuse has been decreasing in adolescents

Opioid Misuse Among 12 to 21 Year Olds in the US

Prevalence Past-Year (PY) Opioid Misuse
NASEM will convene an ad hoc committee to develop a blueprint with specific, actionable steps for building and sustaining an infrastructure for delivering prevention interventions targeting risk factors for behavioral health disorders.

- Identify **best practices** for creating a sustainable behavioral health prevention infrastructure
- Identify **funding needs and strategies** for supporting the prevention infrastructure
- Identify **research gaps** germane to the widespread adoption of evidence-based behavioral health prevention interventions
- Make **actionable recommendations** on how federal and state policies could be expanded or implemented to develop and sustain the behavioral health prevention infrastructure
IRP Publication Metrics Comparison by NIH Institute/Center, 2018-2022
Per Million Dollars Invested (limited to ICs with budget >200 Million over the same period)
HHS Provides Marijuana Scheduling Recommendation to DEA

Statement from President Biden on Marijuana Reform

“I am asking the Secretary of Health and Human Services and the Attorney General to initiate the administrative process to review expeditiously how marijuana is scheduled under federal law.”

--Statement from President Bident on Marijuana Reform
Prevention of Acquisition of HIV: Preexposure Prophylaxis

Persons at increased risk of HIV acquisition:
1. Sexually active adults and adolescents weighing at least 35 kg who have engaged in anal or vaginal sex in past 6 months and have any of the following:
   1. A sexual partner who has HIV
   2. Sexually transmitted infection in past 6 months
   3. Inconsistent or no condom use particularly with high risk partners
2. Persons who inject drugs and have a drug-injecting partner who has HIV or shares injection equipment.

USPSTF recommends that clinicians prescribe preexposure prophylaxis using effective antiretroviral therapy to persons at increased risk of HIV acquisition to decrease the risk of acquiring HIV. (A recommendation)
THANK YOU!