

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)

	FY 2022 Final	FY 2023 Enacted	FY 2024 President's Budget
Base	\$1,250,828	\$1,308,070	\$1,308,070
HEAL	\$345,295	\$355,295	\$355,295
Total	\$1,596,123	\$1,663,365	\$1,663,365

*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.



Nathaniel "Natty" Davis
Executive Officer and
Deputy Director for
Management

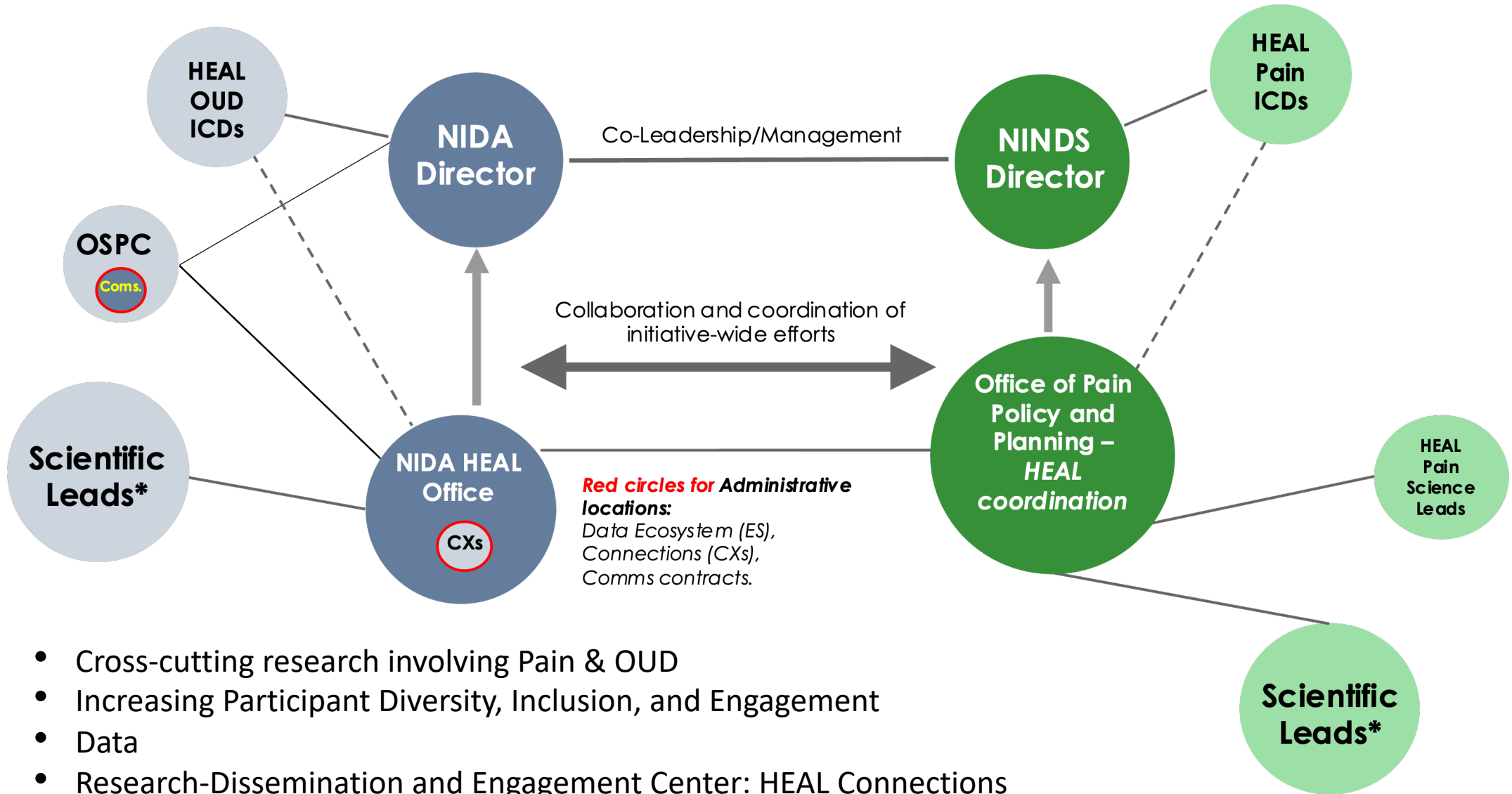


**Search for
Director, DTMC**

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

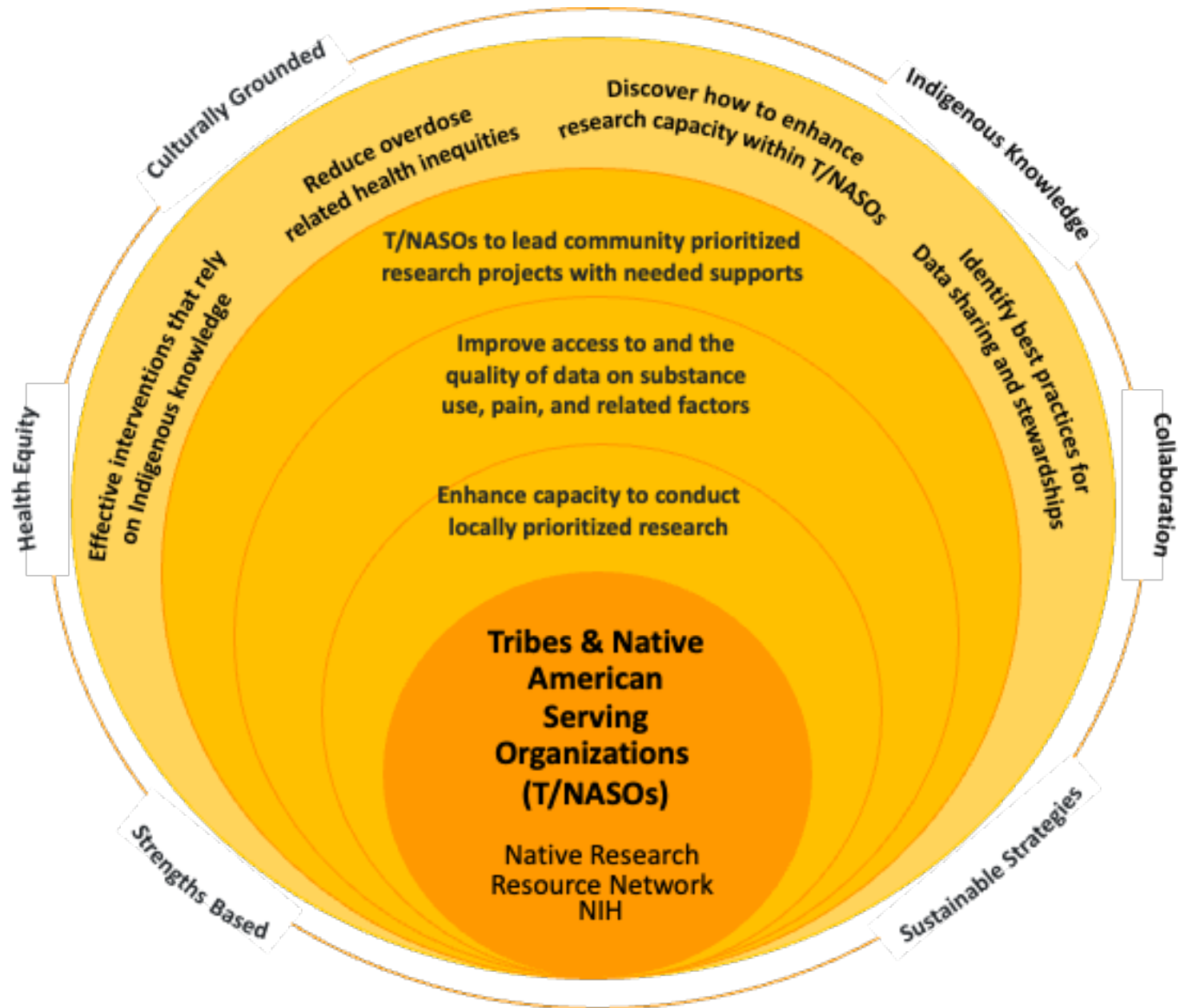
N-CREW

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.

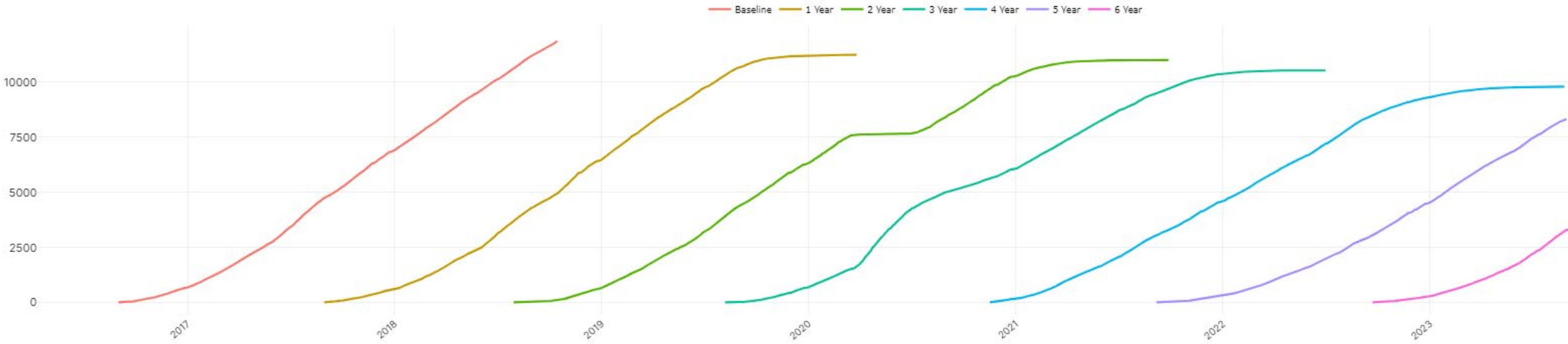
Phase II will build on Phase I FY26-30 \$~240 million

Contact: NCREW@NIH.GOV

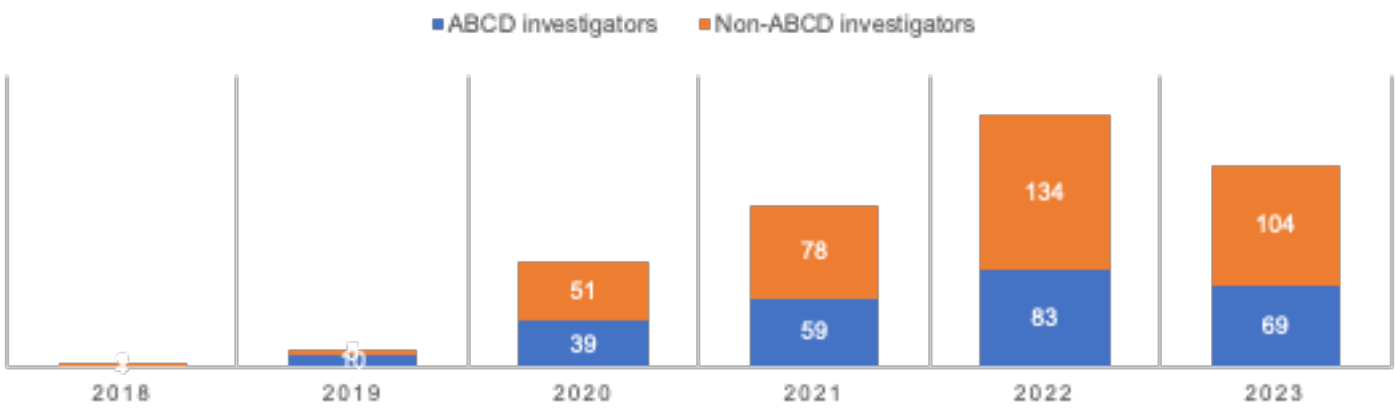


Adolescent Brain Cognitive Development Study

96.7 Percent Retained



PUBLICATIONS USING ABCD DATA N=635

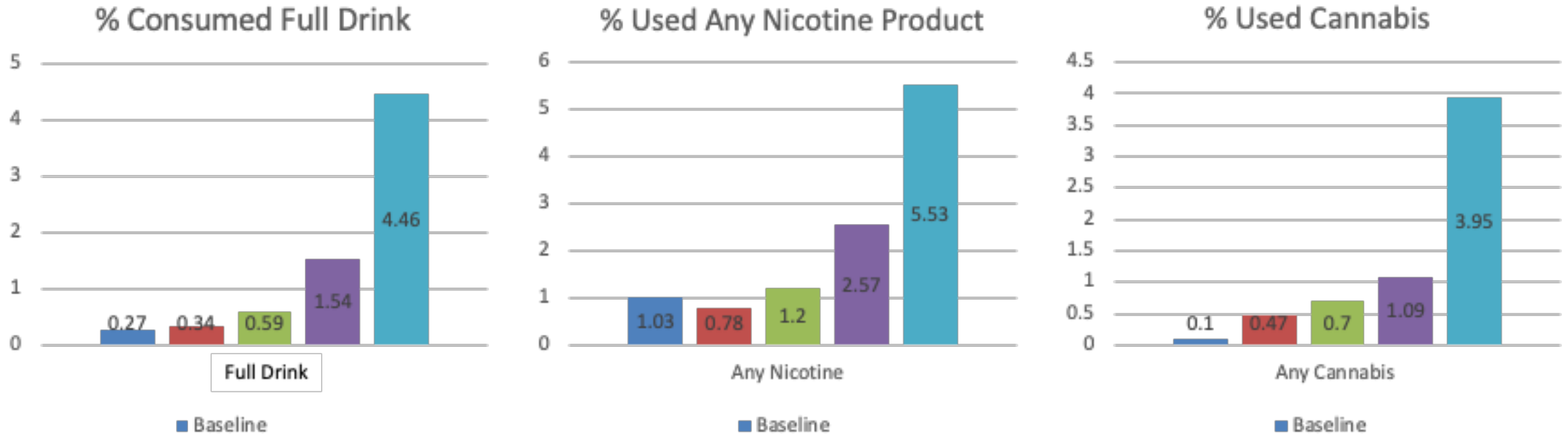


ABCD 5.0 Data Released through NIMH Data Archive

- New Data Dictionary Explorer (<https://data-dict.abcdstudy.org/>)
- New ABCD Wiki Release Notes (<https://wiki.abcdstudy.org/>)



ABCD Substance Use: Data release 5.0



- 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

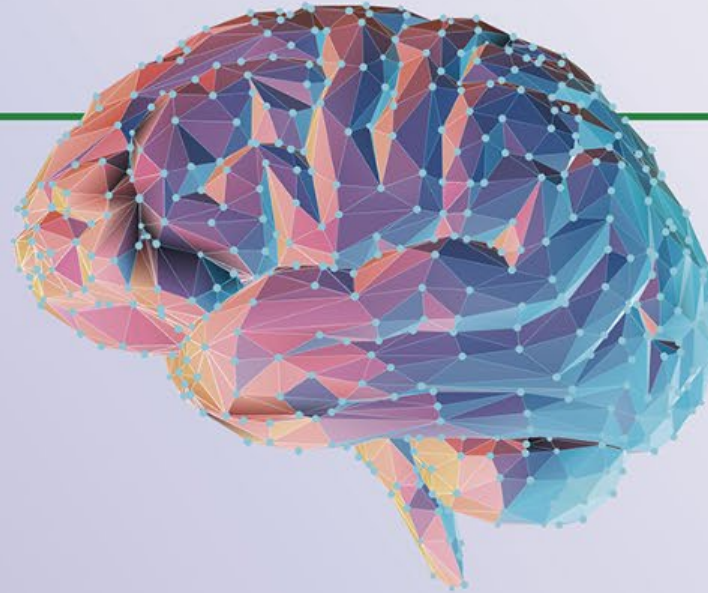
ABCD Insights & Innovations Meeting (AIM)

March 4-5, 2024

Day 1 • 11:00 am – 5:30 pm ET

Day 2 • 11:00 am – 3:15 pm ET

**Natcher Auditorium, NIH Campus
Bethesda, Maryland**



<https://apps1.seiservices.com/aiim/Default.aspx>



Adolescent Brain Cognitive Development®
Teen Brains. Today's Science. Brighter Future.

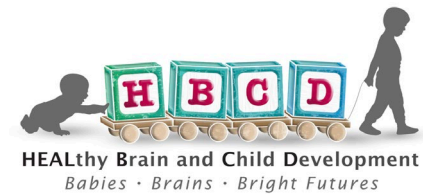
The purpose of this meeting is to:

- 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.

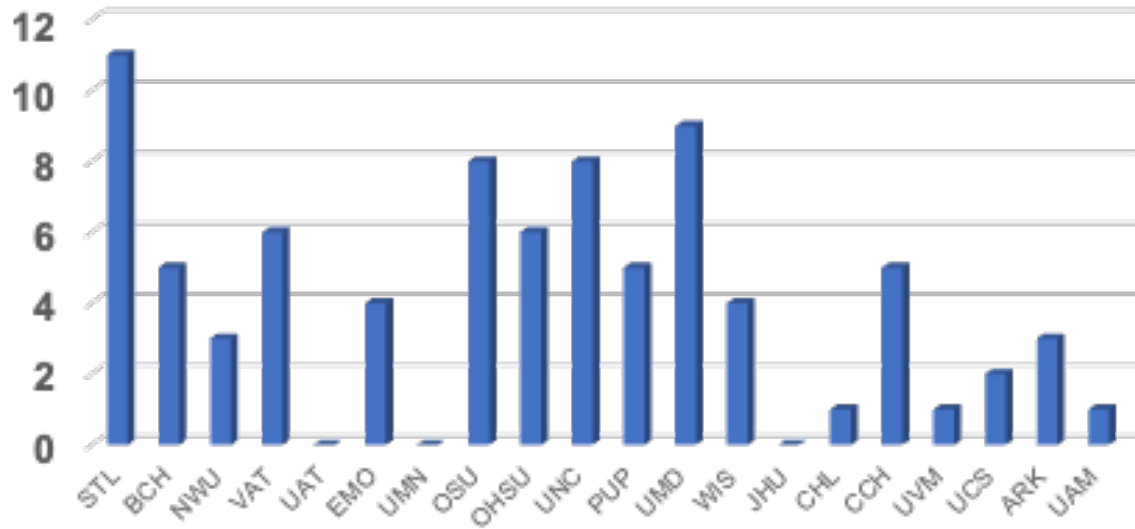
Registration and abstract submission will open soon.

The deadline for abstract submissions will be Friday, December 1, 2023.

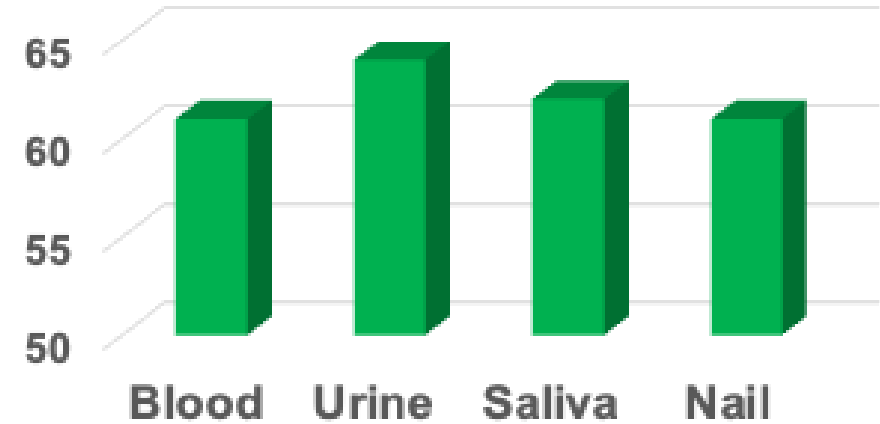
HEALTHy Brain and Child Development Study



enrolled



Biospecimen Type



- 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



2022-2023: Provisional* Drug Overdose Deaths 12-months ending in select months

	ALL DRUGS	HEROIN	NAT & SEMI SYNTHETIC	METHADONE	SYNTHETIC OPIOIDS (mainly illicit fentanyl)	COCAINE	OTHER PSYCHO-STIMULANTS (mainly meth)
3/2022*	110,392	8,482	13,521	3,592	74,217	26,256	34,598
8/2022*	109,303	6,920	12,506	3,446	74,211	27,164	34,584
3/2023*	110,469	5,305	11,644	3,381	76,472	28,770	35,756
Percent Change 3/22-3/23	0.001%	-37.5%	-13.9%	-5.9%	3.0%	9.6%	3.3%

*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.

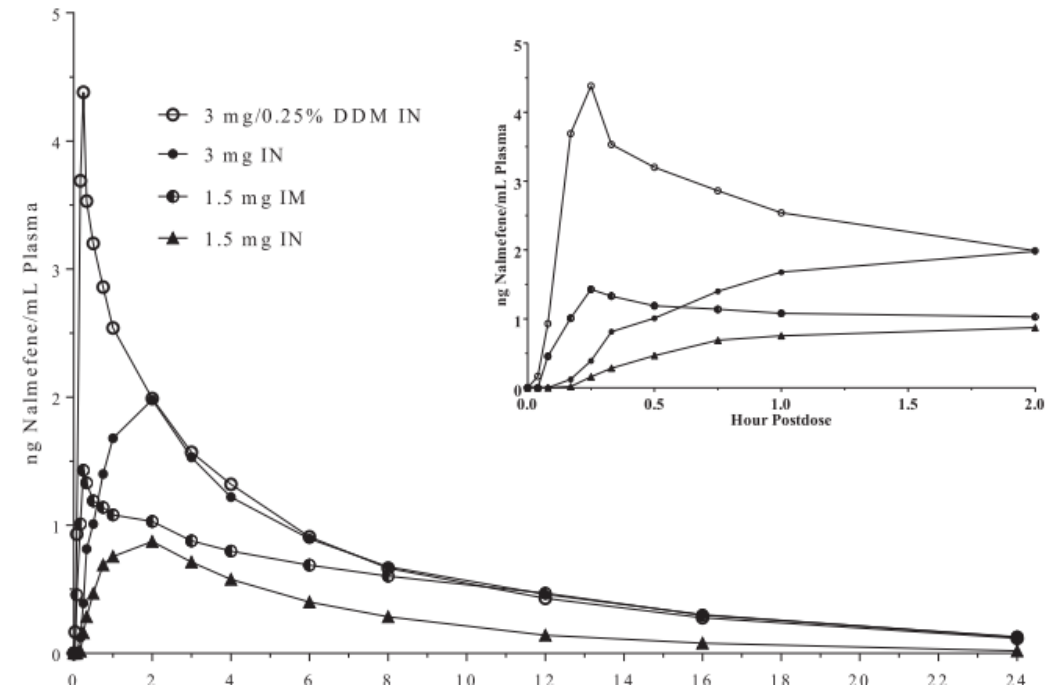
<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>



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 ($K_i = 0.24$ nM)
- Very fast action
- T_{max} 0.25 hours
- High affinity, fast onset, and long half-life ($T_{1/2}$ 11 hours) advantageous for overdoses from longer-lived synthetic opioids



FDA NEWS RELEASE

FDA Approves New Buprenorphine Treatment Option for Opioid Use Disorder

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Brixadi (Braeburn)

FDA NEWS RELEASE

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

Narcan (Emergent BioSolutions)
RiVive (Harm Reduction Therapeutics)

Opioid Use Disorder

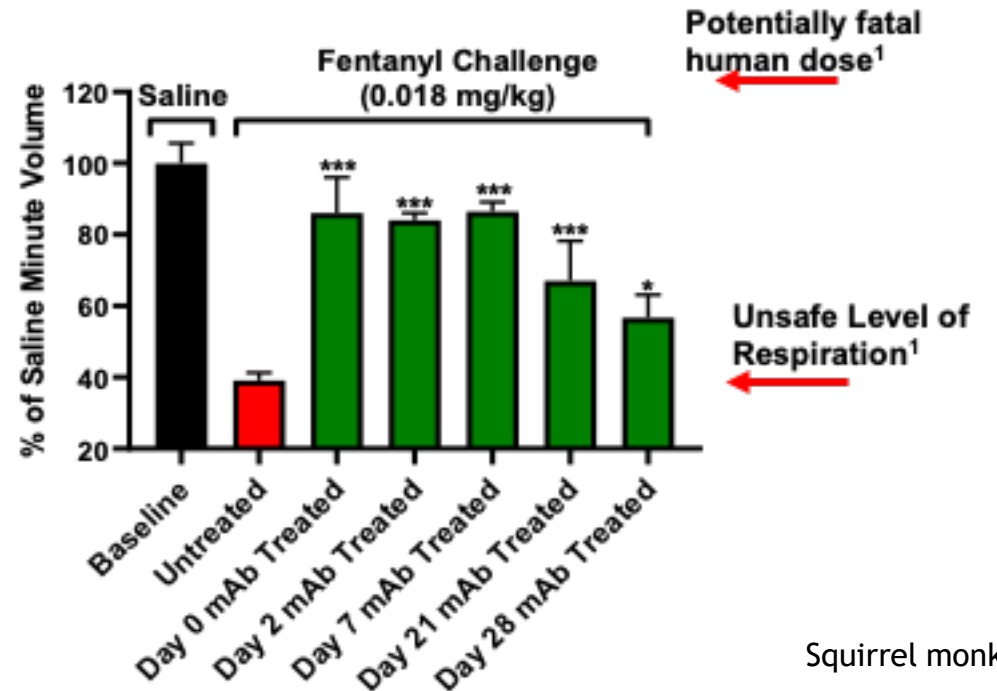
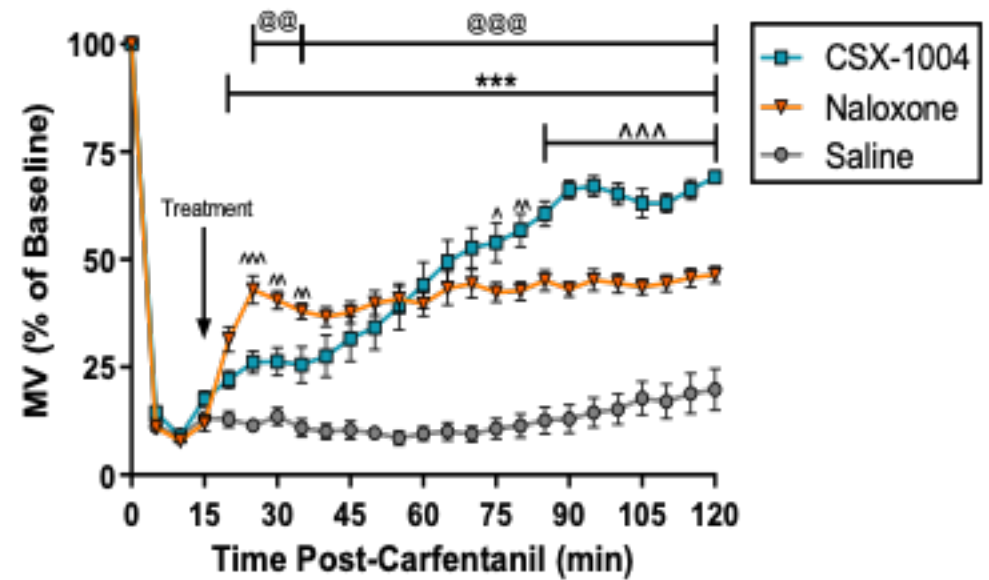
KEY: **Black:** New Molecular Entity **Red:** Repurposed **Blue:** New Formulation

Drug Discovery / Early Preclinical	Late Preclinical	Clinical Trials		New Formulation
		Phase I	Phase II	
<u>GPR151 antagonist</u>	<u>Brexiprazole</u>	<u>Cannabidiol</u>	<u>Cannabidiol</u>	<u>Naltrexone 2-month injection</u>
<u>AT-121</u>	<u>Tezampanel</u>	<u>Ketamine</u>	<u>Guanfacine</u>	<u>BICX104 Naltrexone 3-month implant</u>
<u>PTPRD inhibitor</u>	<u>BTRX-246040</u>	<u>Lemborexant</u>	<u>Pregabalin + Lofexidine</u>	<u>Naltrexone 6-month implant</u>
<u>SBI-553</u>	<u>DCUKA/Kindolor</u>	<u>Liraglutide/Semaglutide</u>	<u>Suvorexant</u>	<u>Naltrexone 6-month implant</u>
<u>5HT2R agonist</u>	<u>EC5026</u>	<u>Lofexidine</u>	<u>Pramipexole</u>	<u>Naltrexone 1-year implant</u>
<u>HBS087/HBS093</u>	<u>PF5190457</u>	<u>Dexmedetomidine</u>	<u>Olanzapine</u>	<u>Novel naltrexone transdermal patch (NNTP)</u>
<u>CS-1103</u>	<u>SBS-1000</u>	<u>Olanzapine</u>	<u>Buprenorphine + Naltrexone</u>	<u>LAAM Oral</u>
<u>PN6041/PN6047</u>	<u>Biased MOR Agonist</u>	<u>ASP8062</u>		<u>LYN-014-Long-acting methadone</u>
<u>D-CYSee</u>	<u>Methocinnamox</u>	<u>CVL-354</u>		<u>OPNT003 - Nasal Nalmefene</u>
<u>SBI-0801315/SBI-0799220</u>	<u>Mitragynine analogs</u>	<u>CVL-936</u>		<u>Nalmefene implant</u>
<u>D24M</u>	<u>NRS-033 methadone prodrug</u>	<u>INDV-2000</u>		<u>AP007 Extended-release Nalmefene</u>
<u>NAY (NAN/NAQ)</u>	<u>RM2520 (PZM21)</u>	<u>ST-2427</u>		<u>LYN-013 - BUP/NX Oral, long acting</u>
<u>Opioid biased agonist</u>	<u>R-methadone prodrug</u>	<u>AZD4041</u>		<u>Nanoparticle-based ADF</u>
<u>MOR Selective Agonist</u>	<u>Heroin vaccine</u>	<u>KNX100</u>		<u>Nafamostat/PF614 –Oxycodone</u>
<u>Carfentanyl mAb</u>	<u>Heroin vaccine</u>	<u>NYX-783</u>		<u>Naloxone</u>
<u>Oxy/Fentanyl nano-vaccine</u>	<u>P1A4 Fentanyl mAb</u>	<u>ITI-333</u>		
<u>Fentanyl/heroin vaccine</u>	<u>Fentanyl vaccine</u>	<u>Oxycodone vaccine</u>		
<u>GDNF gene therapy</u>	<u>mAb Fentanyl</u>			

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



Xylazine

Detection, 2019-2021

Notice of Special Interest (NOSI): Xylazine: Understanding Its Use and Consequences

Notice Number: NOT-DA-24-012

Release Date: August 28, 2023

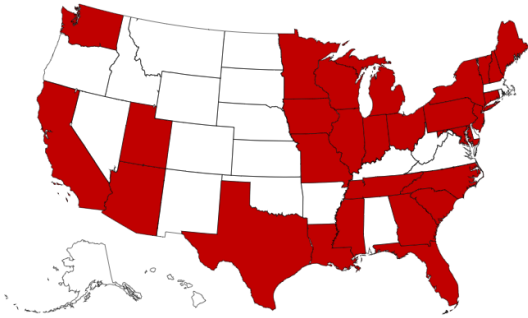
First Available Due Date: October 16, 2023

Expiration Date: January 08, 2025

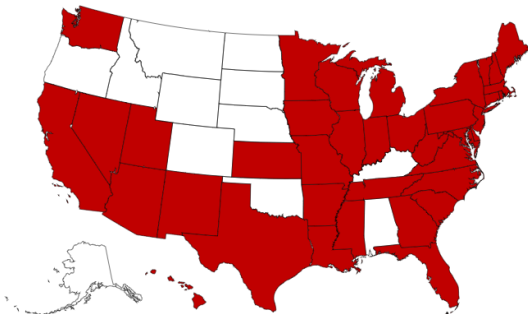
Jan 2019



Jan 2020



Jun 2021

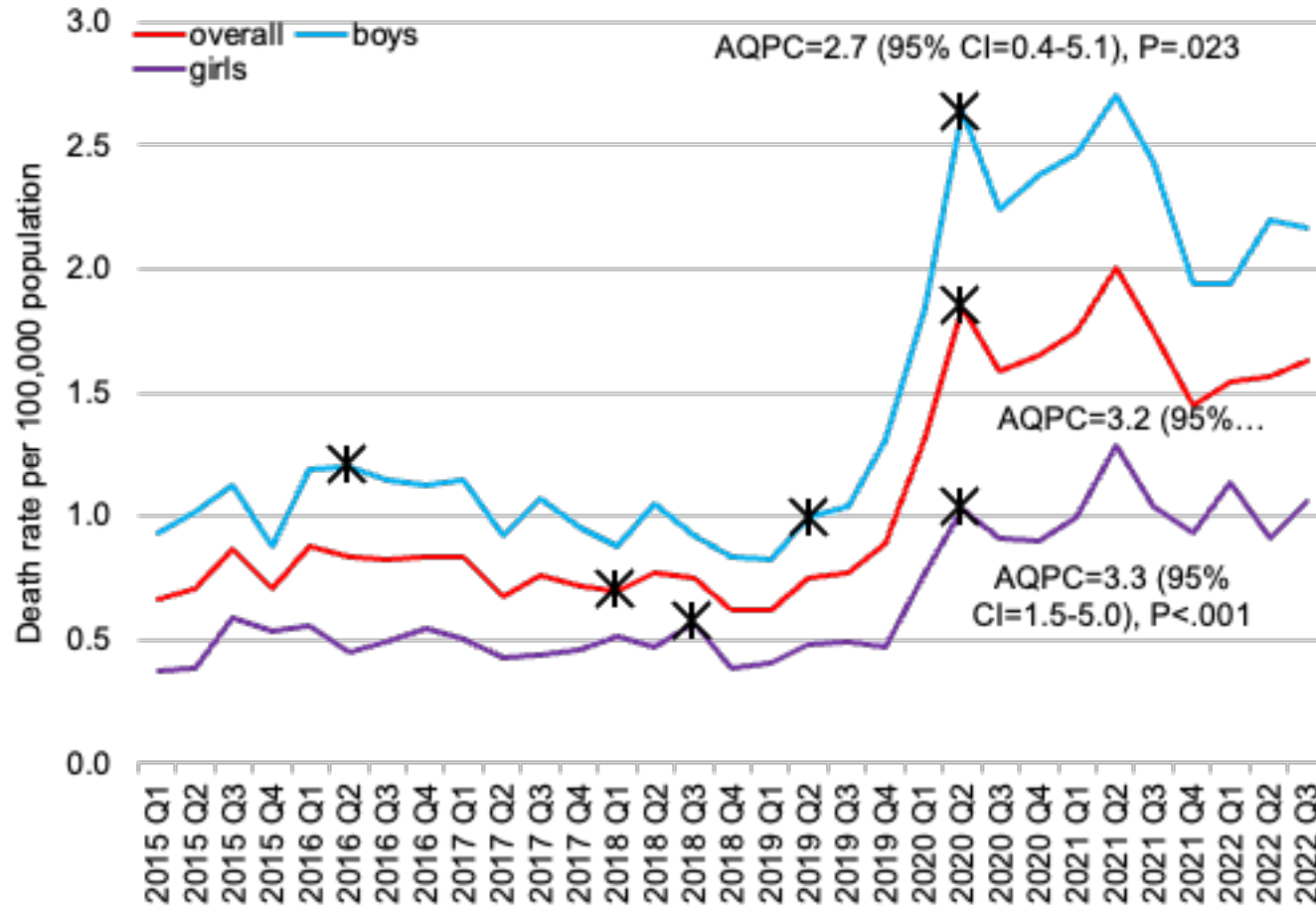


NOSI encourages research on:

- 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

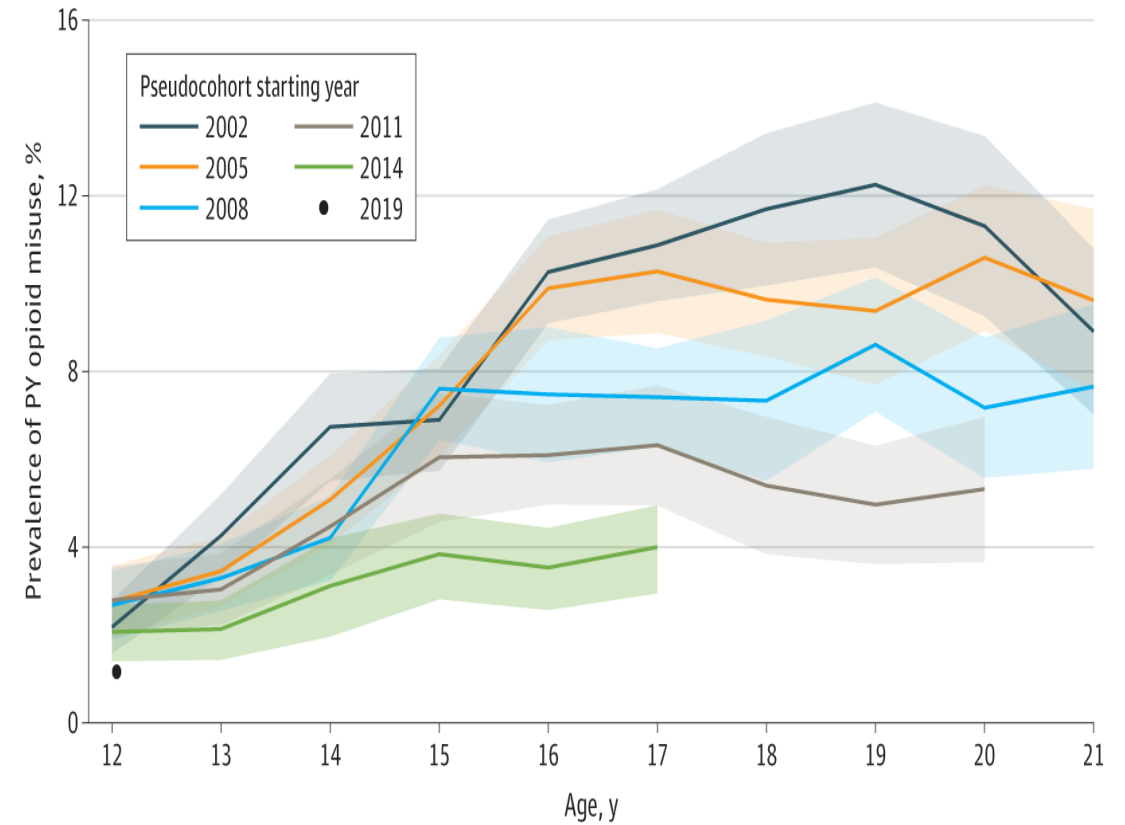


Unintentional drug overdose death rates among US youth aged 15-19



Opioid Misuse Among 12 to 21 Year Olds in the US

Prevalence Past-Year (PY) Opioid Misuse



Opioid misuse has been decreasing in adolescents

Blueprint for a National Prevention Infrastructure for Behavioral Health Disorders

- 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

By September 19
Committee member
nominations due

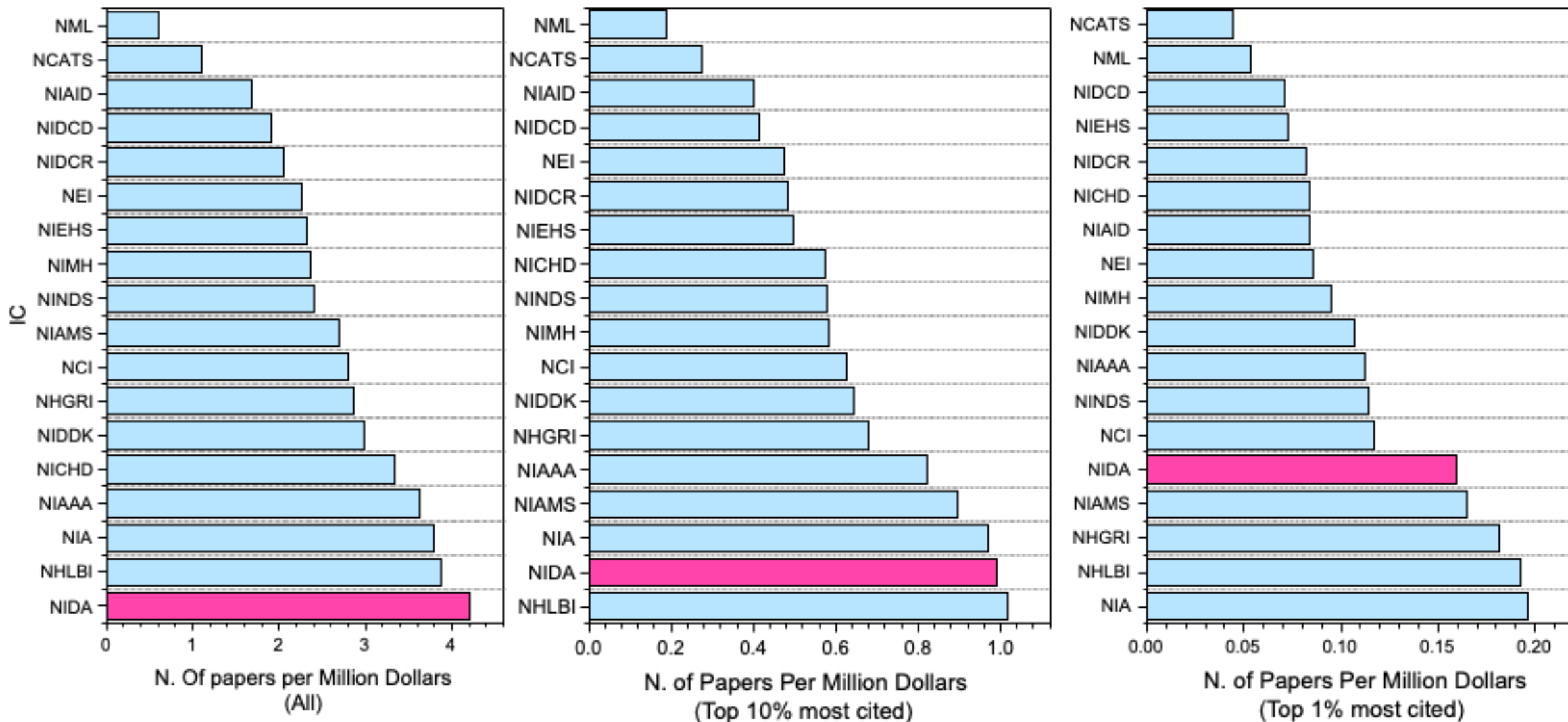
Dec 2023/Jan. 2024:
First committee meeting

TBD:
Open stakeholder meeting

June/July 2025:
Final Report

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



[Administration](#) [Priorities](#) [The Record](#)

OCTOBER 06, 2022

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 Biden on Marijuana Reform



Secretary Xavier Becerra

@SecBecerra · Follow



I can now share that, following the data and science, @HHSGov has responded to @POTUS' directive to me for the Department to provide a scheduling recommendation for marijuana to the DEA.

We've worked to ensure that a scientific evaluation be completed and shared expeditiously.



Prevention of Acquisition of HIV: Preexposure Prophylaxis



Clinical Review & Education

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Preexposure Prophylaxis to Prevent Acquisition of HIV
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

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)

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.

THANK YOU!