

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

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Director

National Institute on Drug Abuse

February 8, 2023

NIDA BUDGET

(all dollars are in \$k)

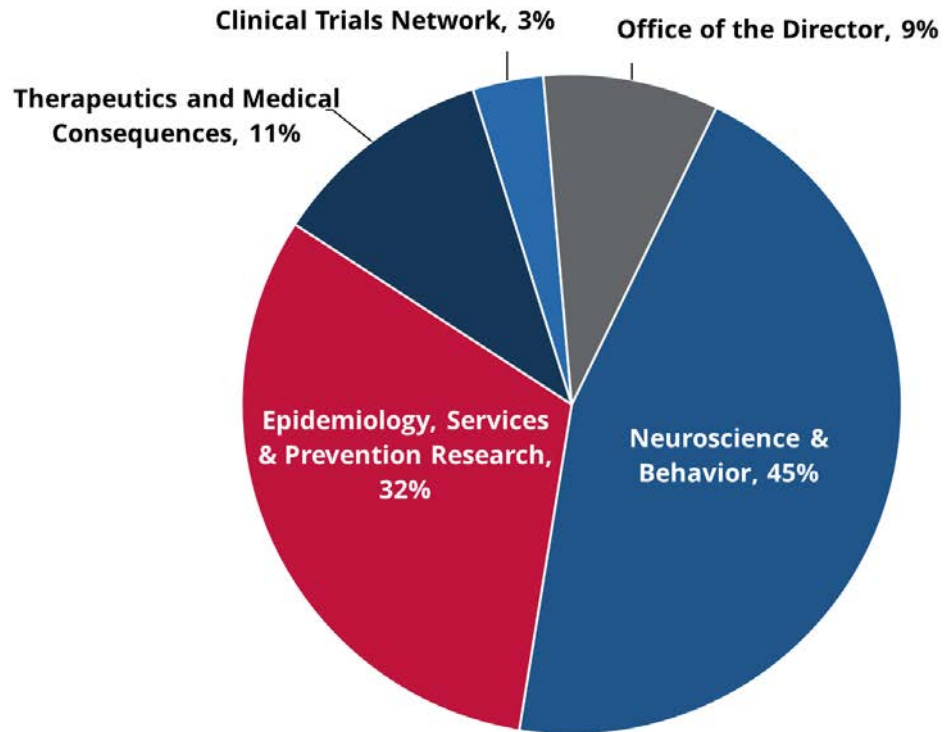
	FY 2022 Enacted	FY 2023 President's Budget	FY 2023 Appropriated**
Base	\$1,250,828	\$1,437,883 *	\$1,307,400
HEAL	\$345,295	\$405,443	\$355,295
Total	\$1,596,123	\$1,843,326	\$1,662,695

* The FY 23 President's Budget included a request for \$196.3m in support of non-HEAL opioid and pain research.

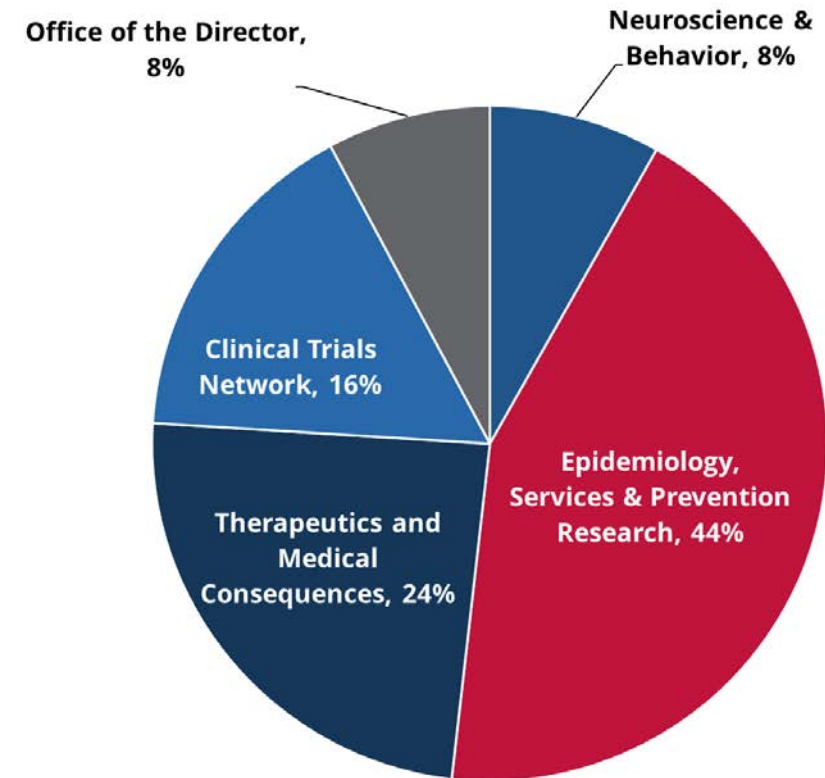
** NIDA's FY 23 appropriated budget included a 3.8% general increase as well as a \$10m increase for the HEAL program and a \$10m increase for research on pain and pain management.

FY 22 Funding Overview

Non-HEAL Research



HEAL Research*



*Includes all NIDA HEAL projects regardless of funding source



Aria D. Crump, ScD
Director, ODHD and
Deputy Director, ORTDD

Office of Research
Training, Diversity &
Disparities

Office of Translational
Initiatives and Program
Innovations

Office of the
Director
NIDA

HIV Research Program

Search for
Clinical Director

Search for
Executive Officer

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
Director, DTMC

Proposed Changes to RPG Peer Review Criteria

Goal: To facilitate the identification of the strongest, potentially highest-impact research

- Refocus peer review on assessment of scientific/technical merit of grant applications
 - reduce burden of administrative items
- Mitigate reputational bias in the peer review process
 - evaluation of *Investigator* and *Environment* in the context of the proposed research

Summary of New Framework

- Reorganize the current five criteria (**Significance, Investigators, Innovation, Approach, and Environment**) into three factors:
 - **Factor 1: Importance of Research** (*Significance and Innovation*) – scored 1-9
 - **Factor 2: Feasibility & Rigor** (*Approach*) – scored 1-9
 - **Factor 3: Expertise & Resources** (*Investigator, Environment*) each to be rated “appropriate” or “additional resources needed”
- **Overall Impact Score** (1-9) to be based on Factors 1-3 and “Additional Review Criteria”, e.g. Human Subjects
- Most “Additional Review Considerations”, which have no bearing on overall impact score, removed

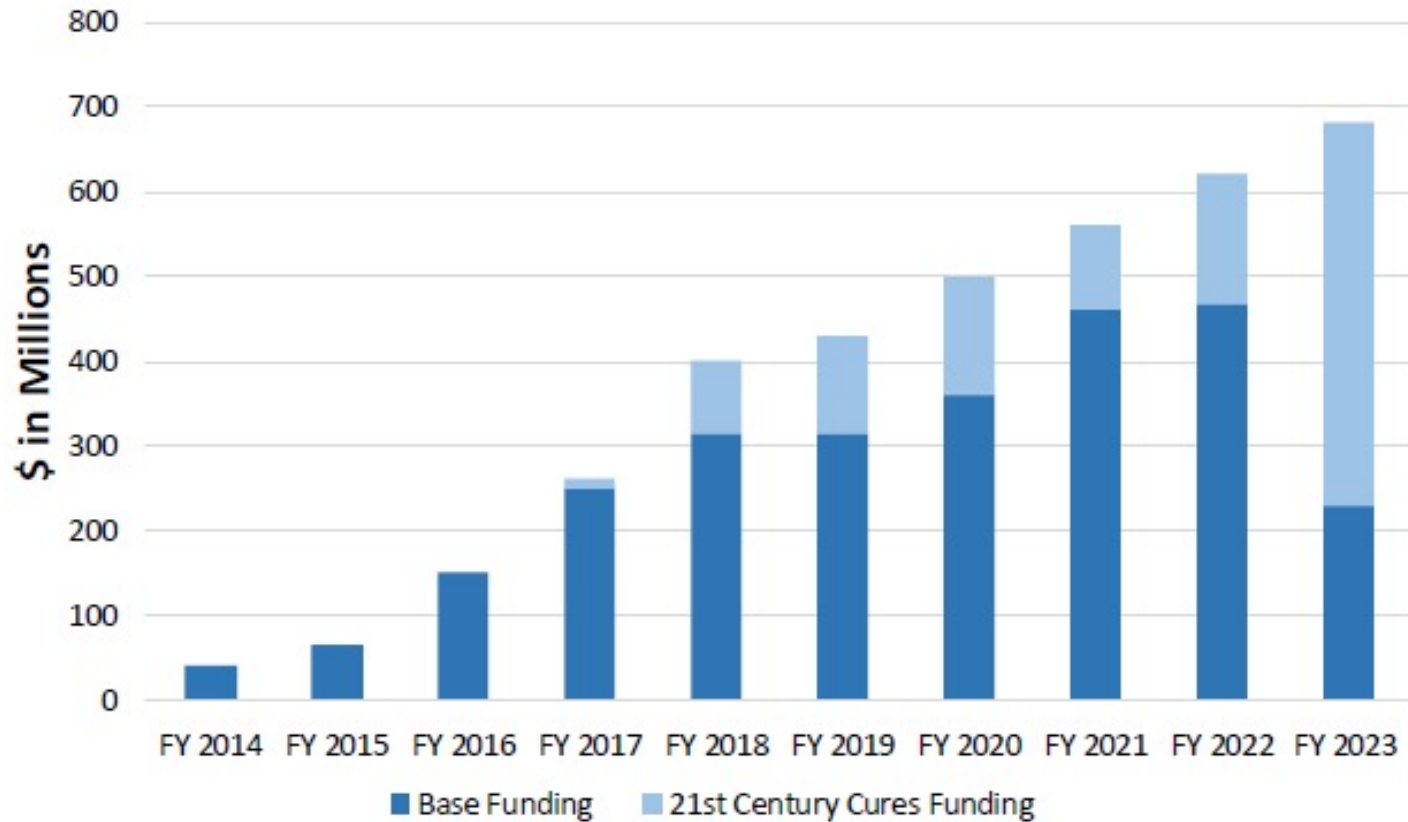
NIH seeks additional input via an **RFI through March 10, 2023**

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-23-034.html>

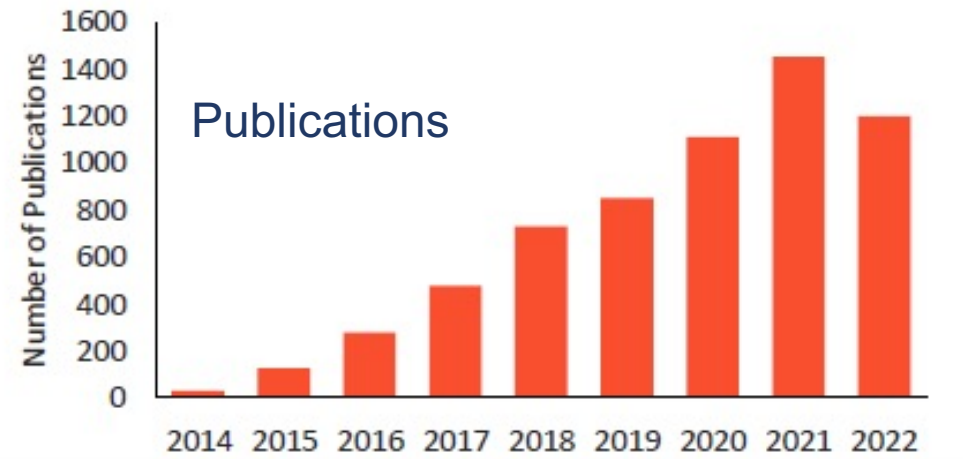
More information: <https://grants.nih.gov/policy/peer/Proposed-Framework>



NIH has invested over \$3B in ~1300 BRAIN projects since 2014



1166 PIs across
234 Institutions
 supported by
952 BRAIN Awards





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Meeting

Open Science, New Tools

Join us **June 12-13, 2023** for the
9th Annual BRAIN Initiative Meeting!

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2022 Monitoring the Future Study

Key Findings and Concerns to Watch

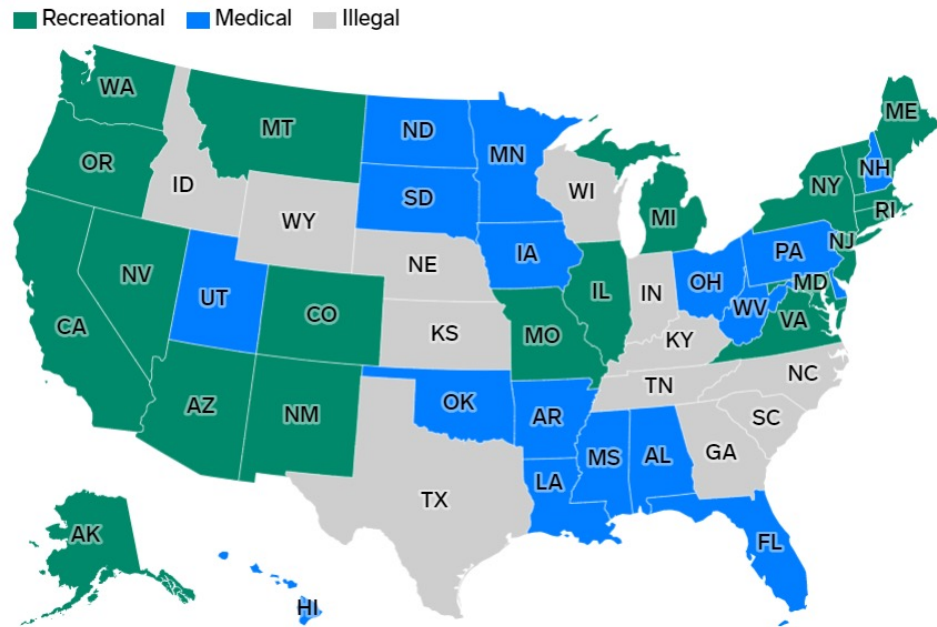


- **Most prevalences remained at or below pre-pandemic levels of use**



- **Few rebounds (notable one **alcohol 12th graders**) from last year's unprecedented number of decreases in drug use among youth**
- **How will the decreases impact outcomes longer term?**

States With Legal Cannabis

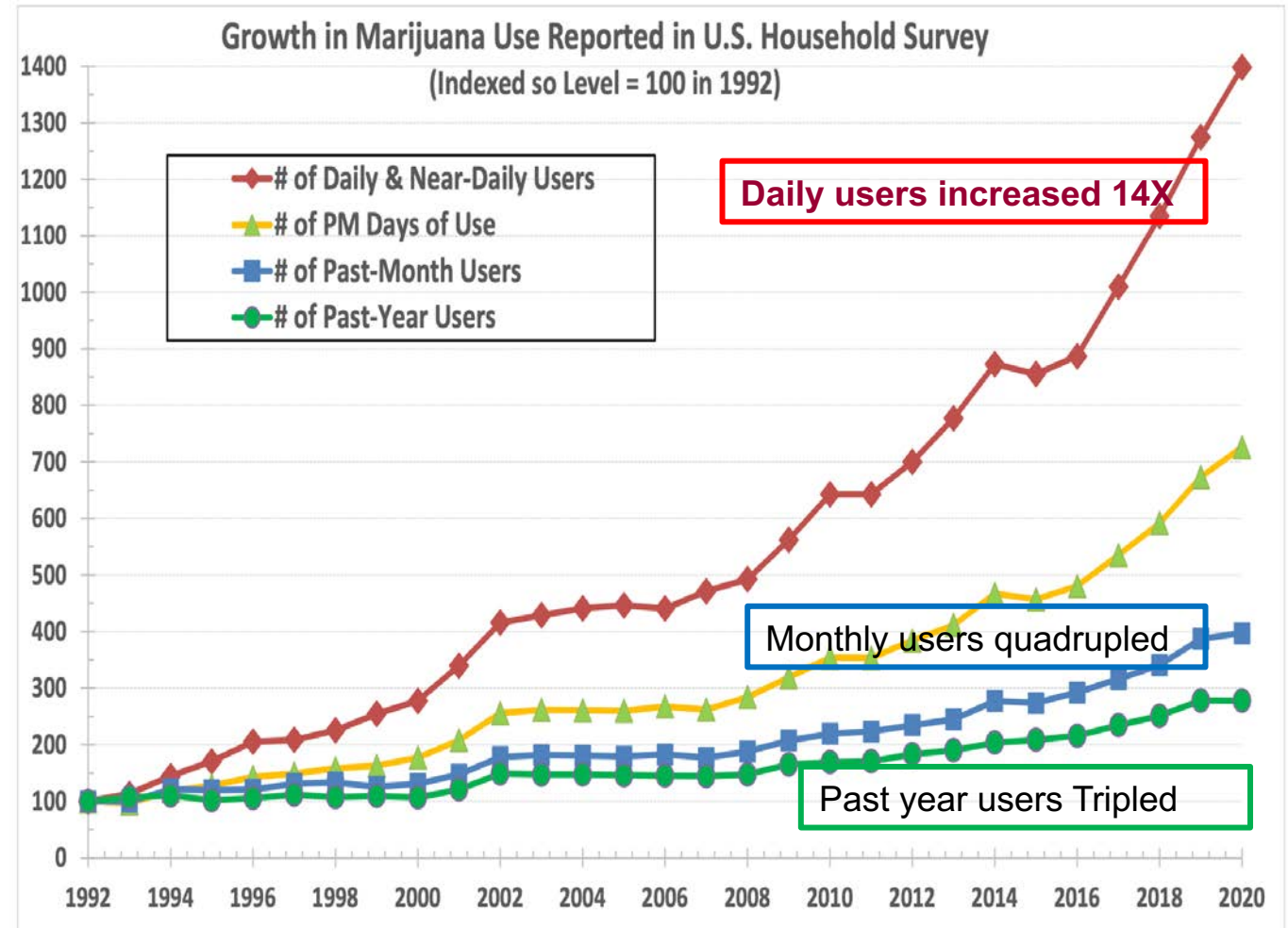


Note: Updated as of Nov 9, 2022.

INSIDER

- Recreational Marijuana legal in 21 states & DC.
- Medical marijuana: legal in 38 states & DC

Changes in Patterns of Cannabis Consumption 1992 to 2020



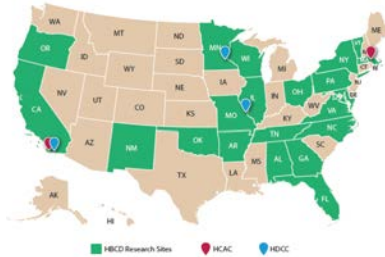
Source: Slide from Caulkins J

Brain Development: Effects of Drugs, ACE and Genetics

HEALTHY Brain and Child Development (HBCD) Study



Longitudinal study (n=7,500 infants) to assess normative neurodevelopment from birth to 9-10 years and investigate impact of drug exposures and of genes and environment



Adolescent Brain Cognitive Development (ABCD) Study

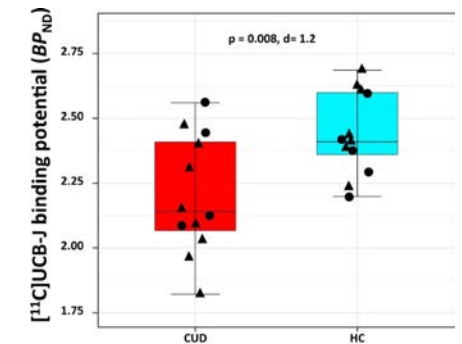


Longitudinal study (11,880 children) from ages 9-10 through early adulthood to assess factors that influence individual brain development trajectories and functional outcomes

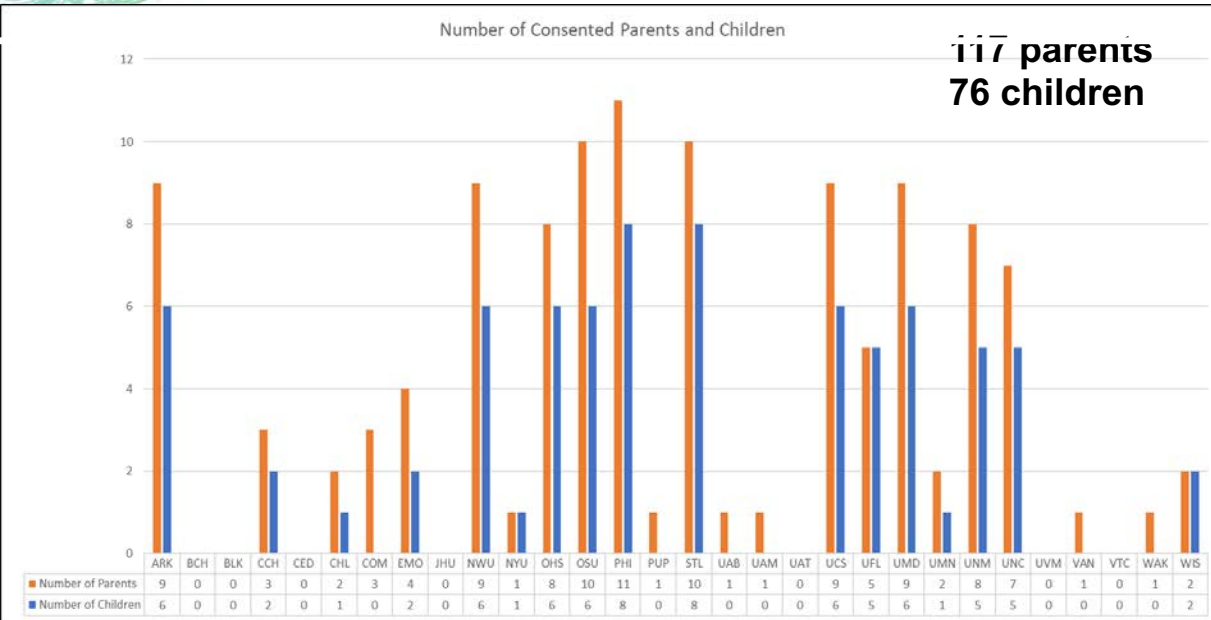
RESEARCH PRIORITIES

- Cannabis (THC, CBD, others) actions at molecular, epigenetic, cellular (neurons, glia, endothelium), circuits, energetics, behavioral levels.
- Risk for cannabis use and CUD (genetic, developmental, SDH).
- Consequences of cannabis use in brain health and behaviors across the lifespan including effects in neurodevelopment (fetal and childhood) and in neurodegeneration
- Prevention and therapeutic Interventions for CUD
- Impact of different policies on patterns of cannabis consumption and its consequences
- Medical cannabis potential in management of SUD, HIV or pain.

Hippocampal synaptic density (PET [^{11}C]UCB-J BP_{ND})



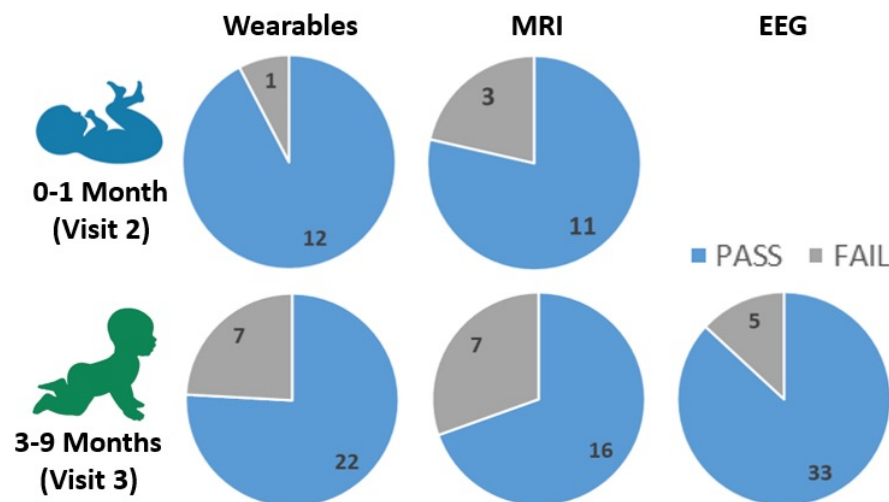
HEALthy Brain and Child Development Study



- 22/27 sites cleared for piloting
- Protocol finalized for visits 1-3
- Train the Trainer (visits 4-6) scheduled for April

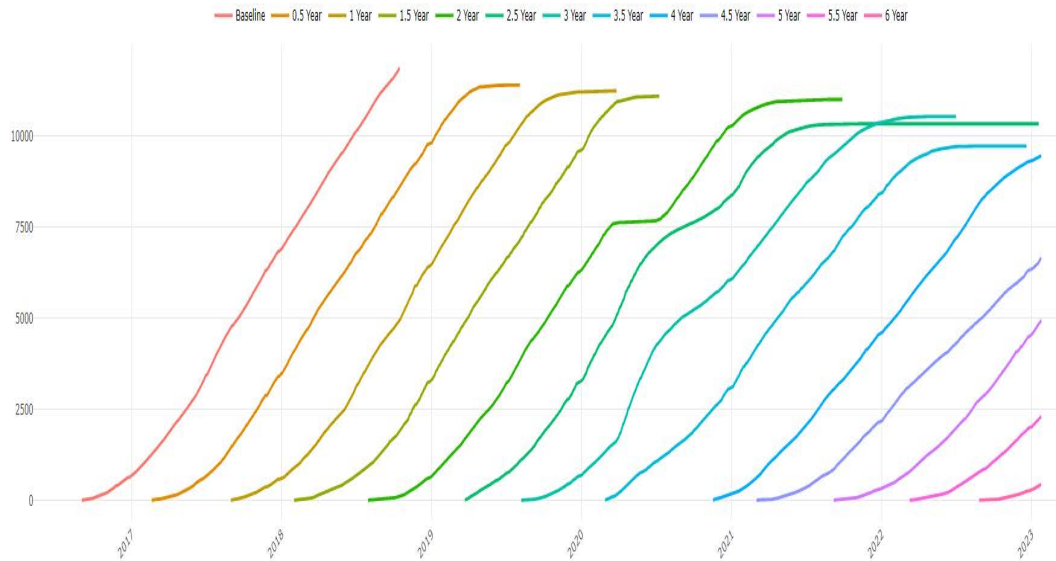
○ **Enrollment of study cohort expected in May**

○ Child Welfare & Research workshop in development

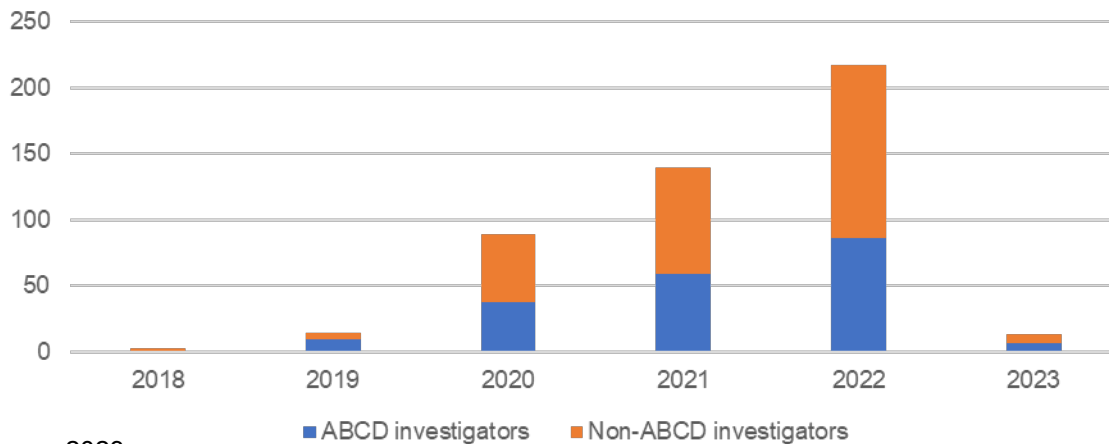


Adolescent Brain Cognitive Development Study

97.6 Percent Retained



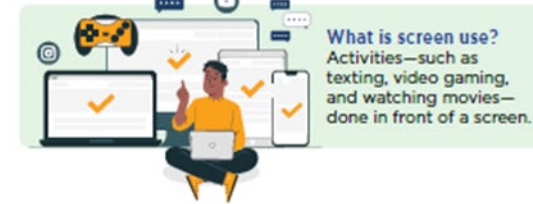
Publications Using ABCD Data
N=478



Screen use by Teenagers



Research using data from the ABCD Study*, the largest long-term study of brain development and child health in the United States, has shown both positive and negative associations of screen use for preteens.



Youth use screens more as they get older



Every additional hour spent watching videos meant less sleep

Together, more video watching and less sleep were related to small increases in:



More than 2 hours of screen use* per day was associated with a slight increased risk for having a depressive disorder, suicidal thoughts/attempts, and self-harm in boys and girls. It was also associated with an increased likelihood of anxiety in boys, but not girls.

*Defined as video chat, social media, texting, gaming, online videos, TV, and movies.

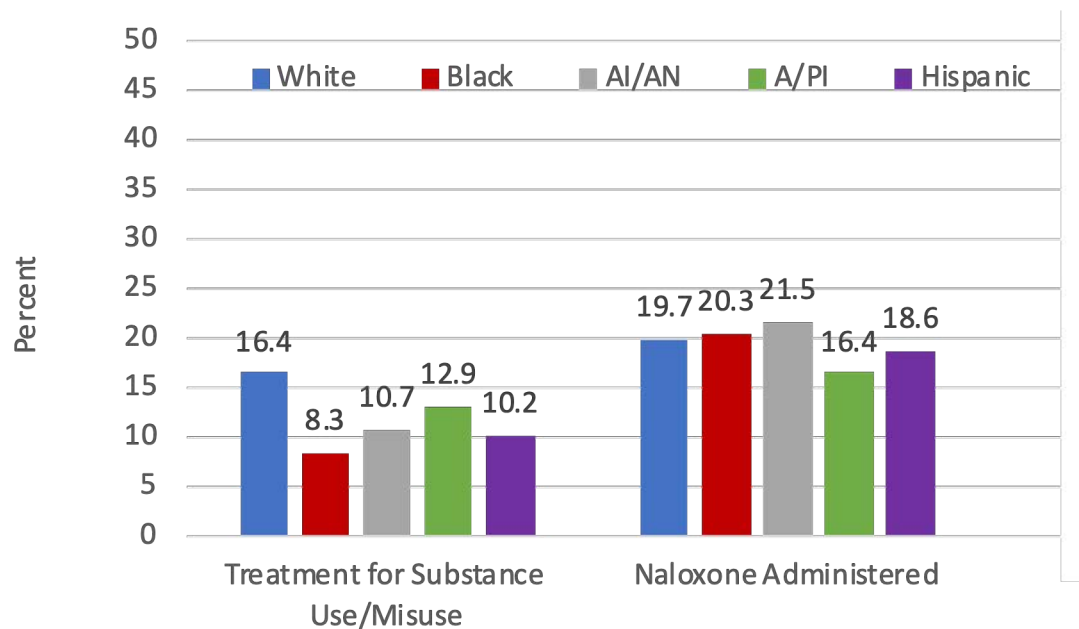
Studies have shown both negative (depression and anxiety with excessive use) and positive (faster reaction times and improved working memory) outcomes from screen use

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)
8/2021 *	104,038	10,488	13,970	3,708	67,624	22,571	30,876
12/2021 *	109,179	9,411	13,906	3,765	72,484	25,174	33,637
8/2022 *	107,477	6,863	12,272	3,357	73,102	26,786	33,534
Percent Change 8/21-8/22	3.3%	-34.5%	-12.2%	-9.5%	8.1%	18.7%	8.6%

* NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months.
<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

Drug Overdose Deaths: 2019–2020



[Kariisa M et al., MMWR Morb Mortal Wkly Rep. 2022](#)

NIDA Clinical Trials Network



Conducts rigorous, multisite clinical trials to determine effectiveness of treatment strategies in diverse clinical settings and populations

- Optimizing Retention MOUD
- Subthreshold OUD Trial
- ED-INNOVATION
- ER Buprenorphine for OUD
- Polysubstance Use Disorder
- Rural Initiative
- Telehealth for SUD

HEAL
INITIATIVE

JCOIN
JUSTICE COMMUNITY OPIOID INNOVATION NETWORK

Build Evidence for OUD treatment in justice populations

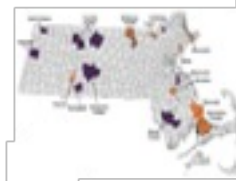


NIH
HEAL
INITIATIVE

HEALing
Communities
Study

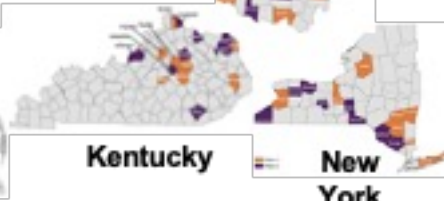
Massachusetts

Ohio



Kentucky

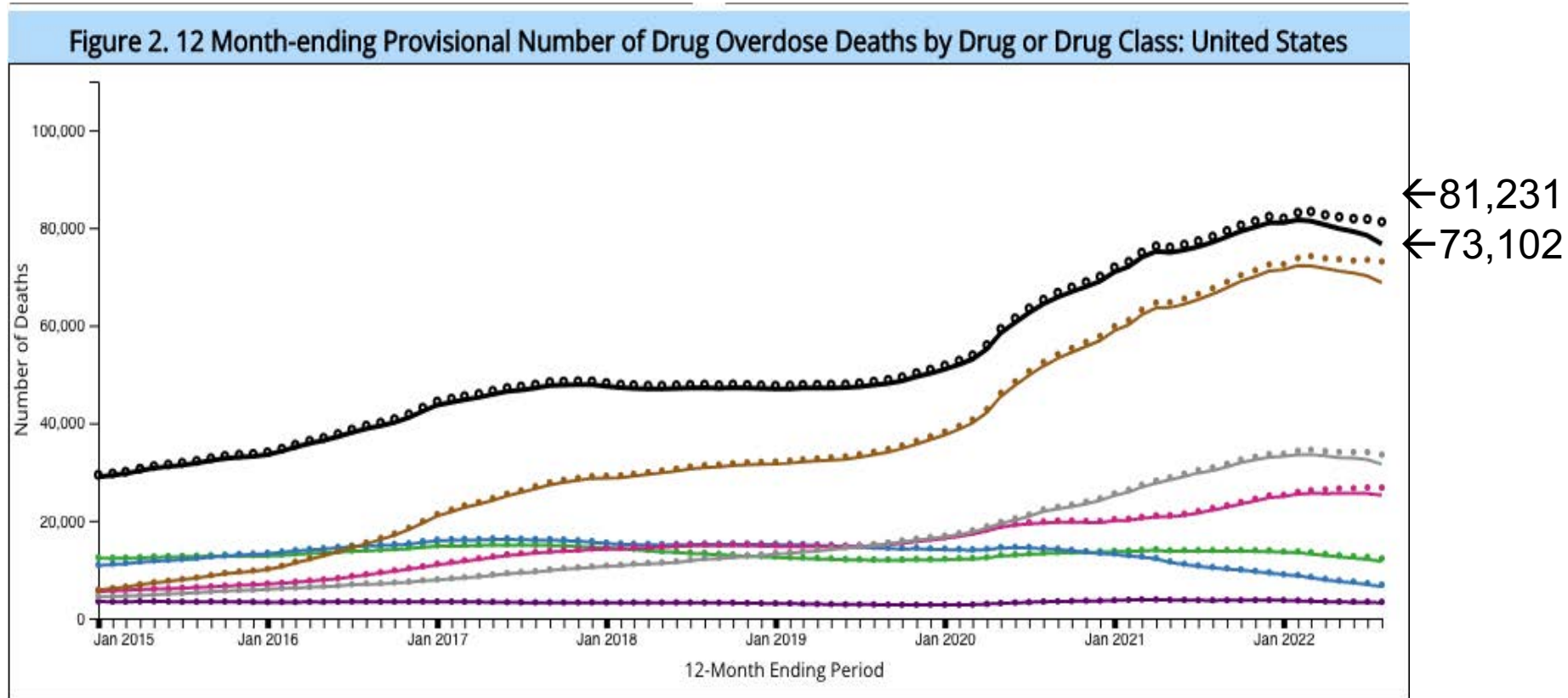
New York



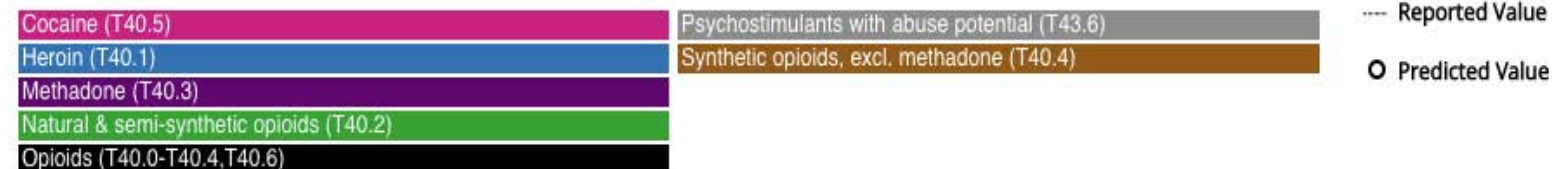
Testing integration of EB prevention and treatment interventions in 67 communities in 4 states

- 66 approved research protocols
- 12 multisite clinical trials: including MOUD trials
- National surveys: stigma, SUD services, state/local policies
- Simulation, predictive & geospatial modeling
- Pilot studies on emerging service delivery
- Diversity supplements
- Goal: Reduce opioid-related OD deaths 40%
- OD education and naloxone distribution
- Increase access/utilization MOUD
- Decrease high-risk prescribing

Synthetics Are Now Linked to Almost 90% of Opioid Overdose Deaths



Legend for Drug or Drug Class



counts.

Why are FENTANYL and analogues so dangerous?

- Potency: fentanyl is ~50x more potent (mg/kg basis) than heroin; 2mg can be lethal
- Lack of pharmaceutical standards; fentanyl doses used to lace other drugs vary (ie for counterfeit pills DEA reports that doses can range from .02 to 5.1 mg)
- Fentanyls are more lipophilic than heroin; rapid brain penetration → faster onset [reduced time for naloxone rescue]
- **Overdose reversals from fentanyl require higher and multiple naloxone doses**
- **Physical dependence from fentanyl is stronger than for heroin making treatment initiation with medications for OUD more challenging.**

Highly Lipophilic Synthetic Opioids Access MOR Via Two Routes

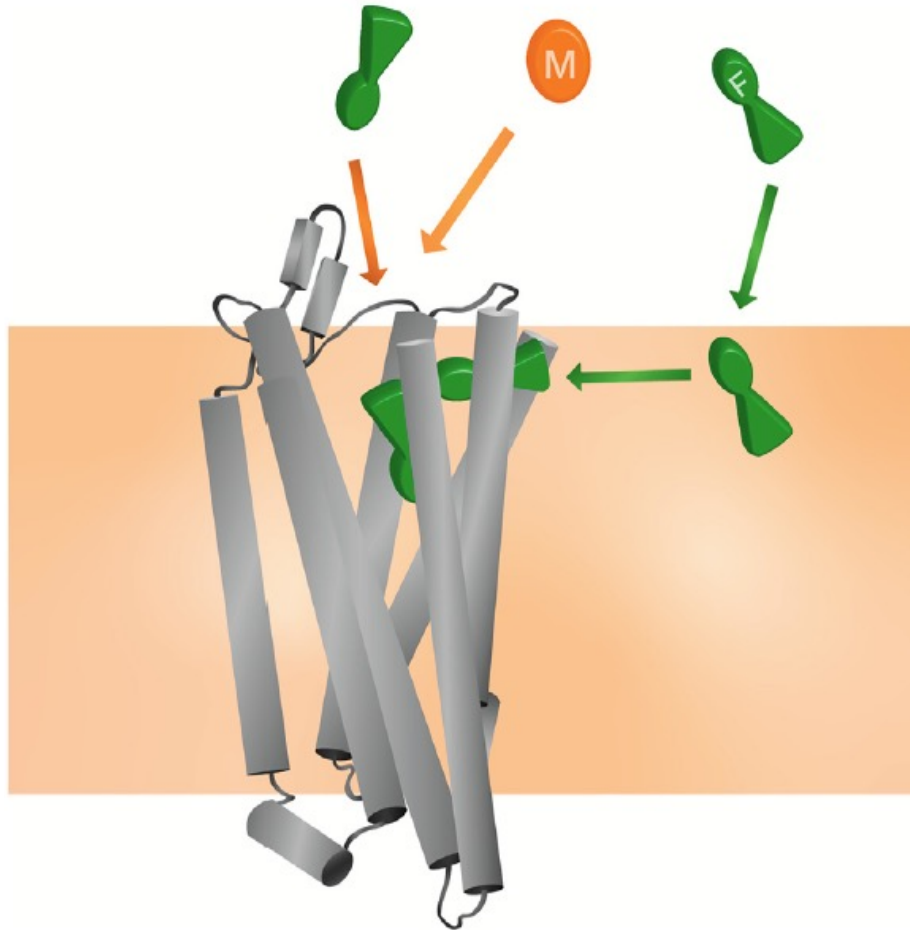
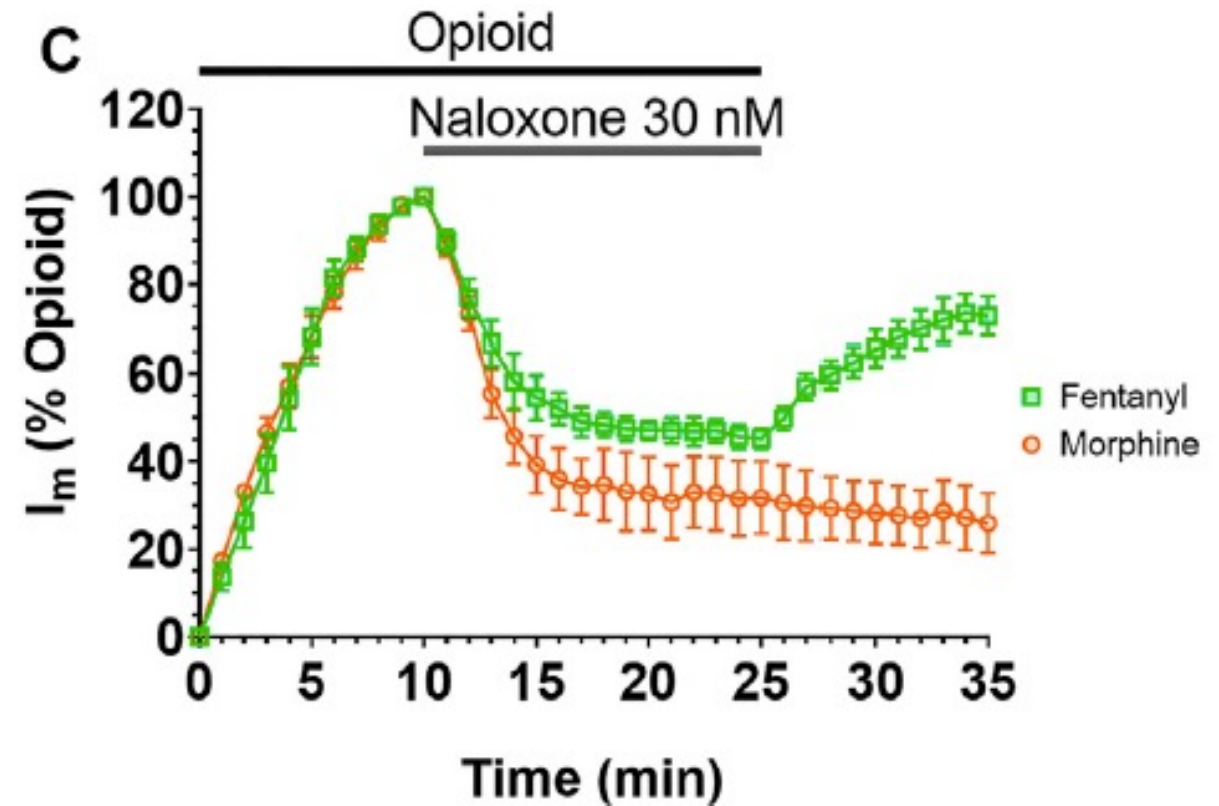


FIGURE 8 | Model for the unique pharmacology of fentanyls at the MOR. In competition with a morphinan ligand (such as morphine or naloxone), fentanyl (green) can access the orthosteric pocket *via* two binding routes; the canonical aqueous pathway and by the novel lipid pathway. In contrast, the morphinan ligand (orange) only has access to one binding route.

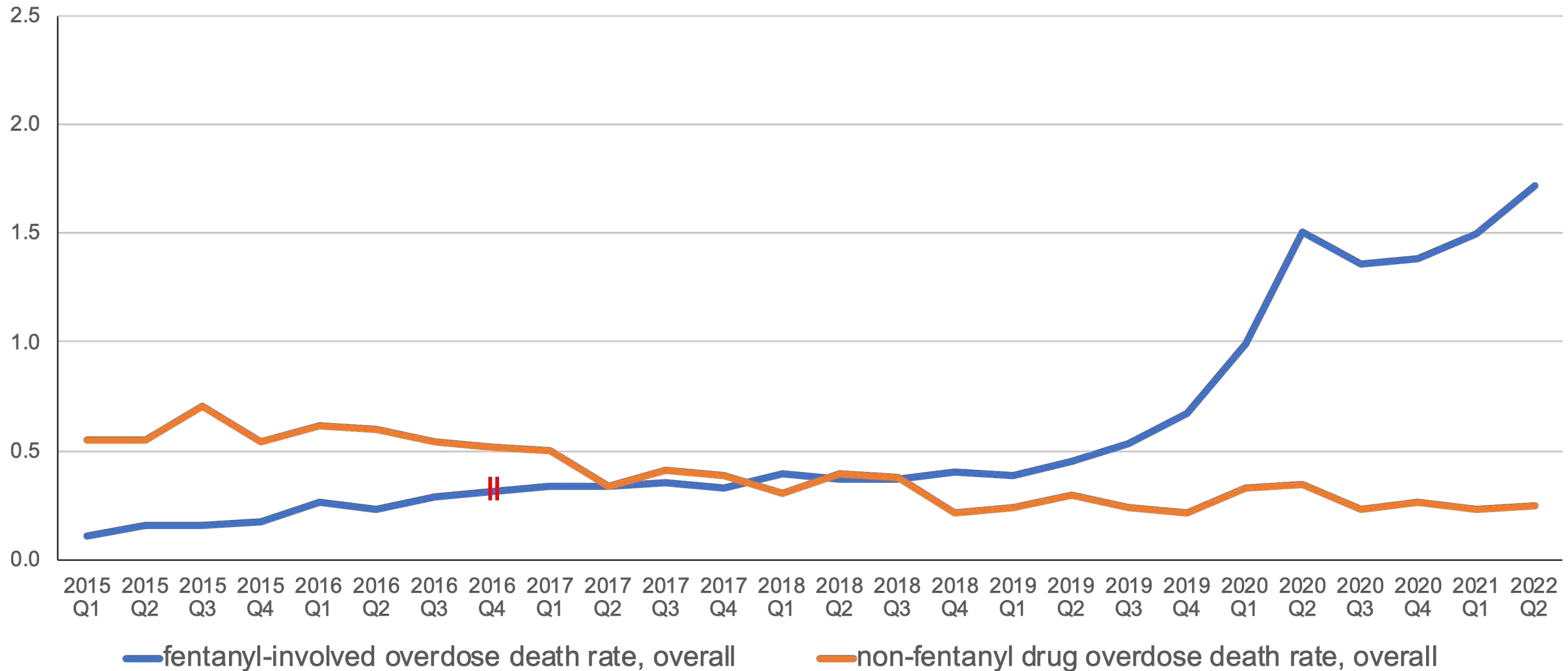
Fentanyl, But Not Morphine, Can Reassert Its Action (GIRK Currents) After Washout



Why have synthetic opioids supplanted other opioids and used to contaminate other illicit drugs?

- Easier to produce than heroin (no opium poppy cultivation) – supply chain issues largely absent
- Synthesis is not complex (3-4 steps)
- More easily transported: a 40 g Altoids tin of illicit fentanyl powder is equivalent to ~ 1 kg of heroin
- Fentanyl high potency makes it easy for drug dealers to mix with other illicit drugs (heroin, cocaine and methamphetamine), which are then diluted to increase profits
- Profits much larger than for other illicit drugs including illicitly manufactured prescription pills (Oxycontin, Vicodin, Aderall, benzodiazepines) such that **fentanyl pills are now being disguised and sold as prescription drugs**

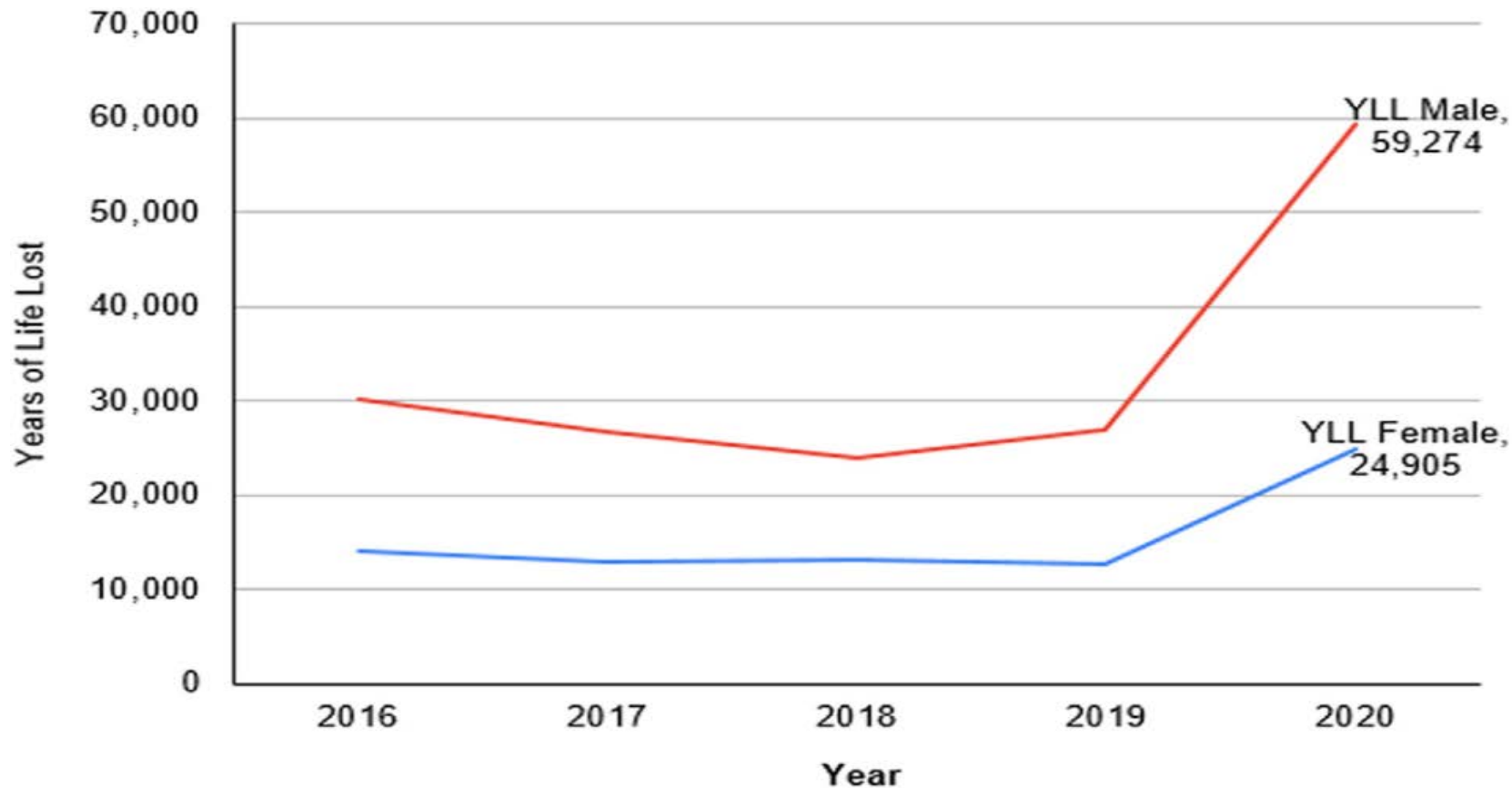
Fentanyl-involved and non-fentanyl overdose death rates in US youth aged 15-19 prior to and during the COVID pandemic



National Vital Statistics System multiple-cause-of-death 2015-2020 final and 2021 provisional data U.S. census monthly data. ||: Joinpoints indicate significant changes in nonlinear trends using Bayesian Information Criterion. AQPC=average quarter percentage change during 2015 Q1-2022 Q2. ICD-10 cause of death code: synthetic opioids other than methadone (T40.4, primarily fentanyl and analogs).

Years of Life Lost (YLL) to Unintentional Drug Overdose Rapidly Rising in the Adolescent Population, 2016-2020

YLL to unintentional overdose in adolescents by gender from 2016 to 2020.



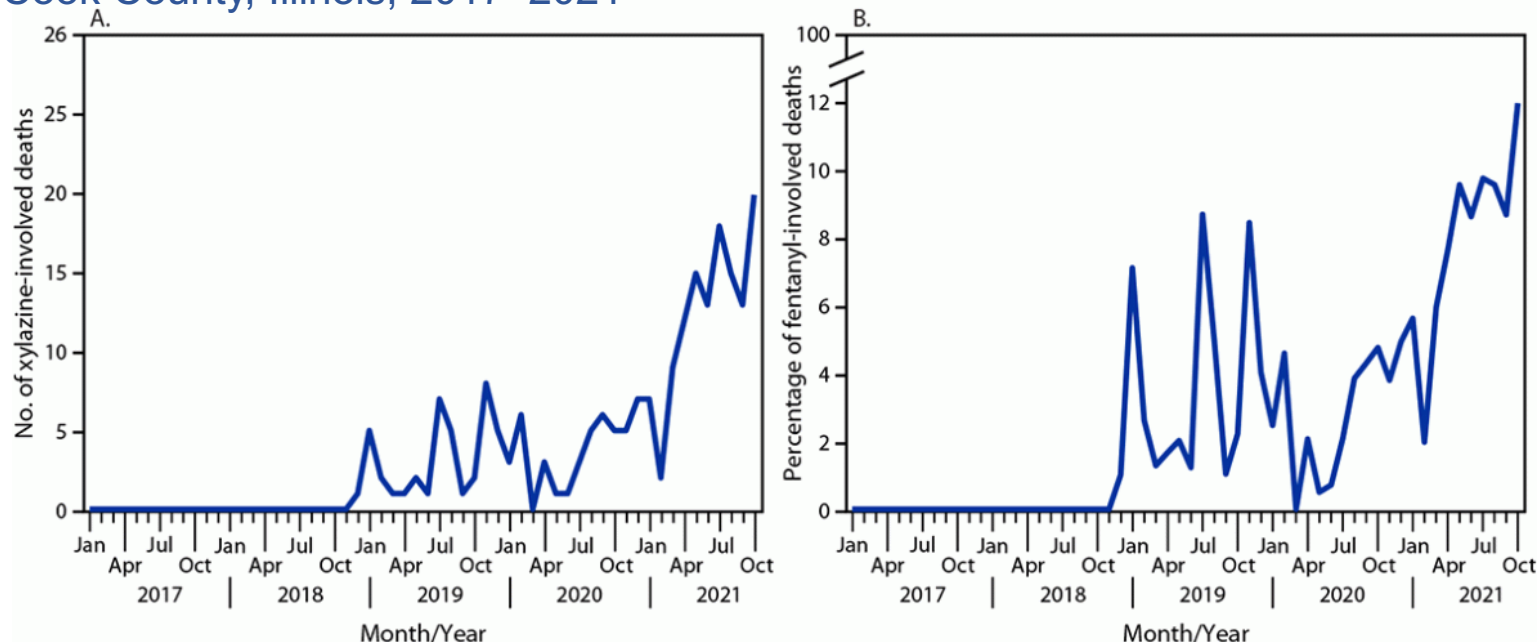
The number of adolescent YLL to unintentional drug overdose in the US more than doubled from 2019 to 2020 after remaining relatively stable between 2016 and 2019

Xylazine

- Alpha-2 agonist used as a veterinary sedative, muscle relaxant, and analgesic
- Not reversed by naloxone
- Associated with severe tissue injury

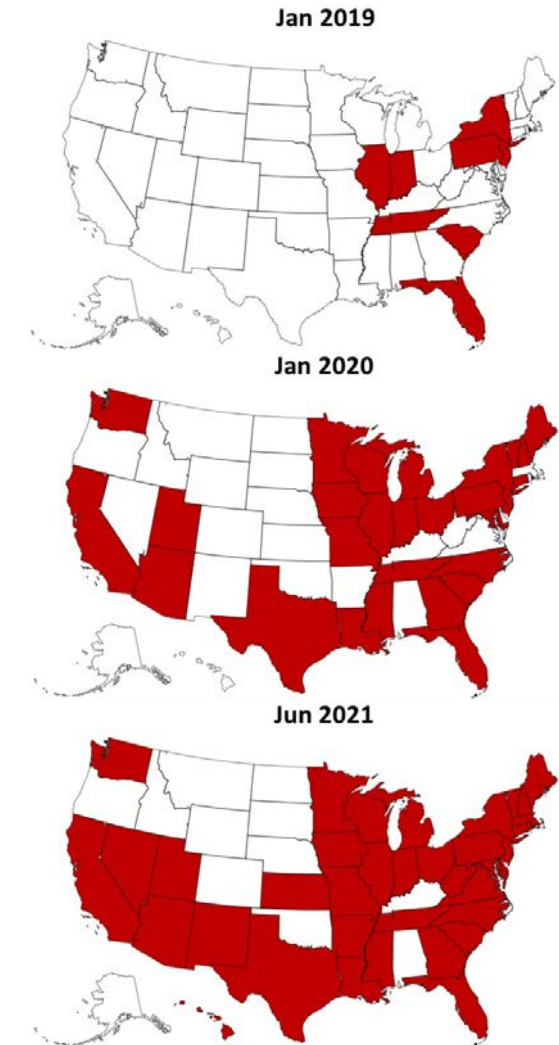
Xylazine-involved Deaths (A) And Percentage Of Fentanyl-involved Deaths With Detectable Xylazine (B)

Cook County, Illinois, 2017–2021



MMWR / April 1, 2022 / Vol. 71 / No. 13, CDC. *Erratum*: Vol. 71, No. 13. MMWR Morb Mortal Wkly Rep 2022;71:641. DOI: http://dx.doi.org/10.15585/mmwr.mm7118a5external_icon

States with at least one positive xylazine detection, 2019-2021



Kacinko, S. L., Mohr, A. L., Logan, B. K., & Barbieri, E. J. (2022). Xylazine: Pharmacology Review and Prevalence and Drug Combinations in Forensic Toxicology Casework. *Journal of Analytical Toxicology*, 46(8), 911-917.

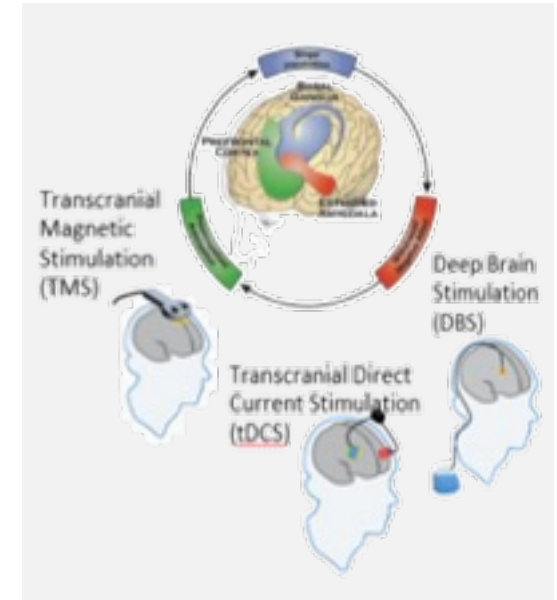
Removal of the DATA-2000 Waiver

- December 29, 2022: President signed into law H.R. 2617, the “Consolidated Appropriations Act, 2023” which included:
 - **Mainstreaming Addiction Treatment (MAT) Act** – eliminated the X-Waiver and removed the associated patient cap for buprenorphine prescribing
 - **Medication Access and Training Expansion (MATE) Act** – Established a requirement for training on substance use for practitioners renewing or applying for DEA registration.
- Practitioners prescribing buprenorphine for OUD will still be held to state laws, insurance rules, and other applicable state or local requirements – could lead to **heterogeneity in access** to buprenorphine across states.

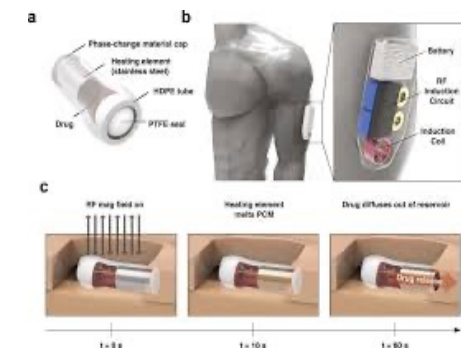
Research to Address Overdose Deaths in 2022

- **Pain** treatments
- Treatment of **opioid use disorder**
 - Implementation and services research to expand MOUD
 - Therapeutic development: medications and immunotherapies
 - New formulations
 - Novel targets
 - Alternative outcomes: craving, sleep, SUD severity
 - Neuromodulation
 - Combined Treatments
- Treatment of other **substance use disorders, polysubstance UD, co-morbidities**
- **Overdose treatments:** automatic reversals opioid OD, OD from drug combinations, OD from **stimulants**
- **Prevention** of drug use including but not limited to opioids
 - Screening and treatment intervention for SUD (mild-severe)
- **DATA:** Timely data of fatal and non-fatal overdoses, patterns of consumption on emerging new drugs and drug mixtures (xylazine)
- **Social Determinants of Health**

Neuromodulation Techniques



Automatic naloxone autoinjector



THANK YOU!