

# The National Institute on Drugs and Addiction

CONGRESSIONAL JUSTIFICATION FY 2025

Department of Health and Human Services National Institutes of Health

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### DEPARTMENT OF HEALTH AND HUMAN SERVICES

### NATIONAL INSTITUTES OF HEALTH

### National Institute on Drugs and Addiction<sup>1</sup>

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### **General Notes**

- 1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
- 2. Detail in this document may not sum to the subtotals and totals due to rounding.

<sup>&</sup>lt;sup>1</sup> The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.

### **Cover Page**

NIDA investigators have found that GABA-producing neuronal cells in the mouse brainstem (red, with long string-like projections) are involved in increased pain sensitivity during opioid withdrawal. Credit: Alvarez-Bagnarol, et al. *Neuropsychopharmacology*, 2023.

### **Director's Overview**

The National Institute on Drugs and Addiction (NIDA) supports research to understand the shifting landscape of drug use; develop more effective interventions for preventing and treating addiction, overdose, and other drug-related harms; and make these advances available to all Americans. According to provisional data through March 2023, over 110,000 Americans are dying from drug overdoses each year, driven in large part by synthetic opioids (such as fentanyl) and stimulants (such as methamphetamine and cocaine), with increasing levels of combined (polysubstance) use. Often unknown to the consumer, fentanyl is increasingly adulterated with novel substances such as xylazine—a veterinary tranquilizer that has been designated as an emerging drug threat by the White House. While these are sobering developments, NIDA



Nora Volkow, M.D. Director, NIDA

has moved swiftly to counteract them and save lives; in the last year alone, NIDA-funded research helped improve the availability of new and existing overdose reversal agents, with many more therapeutics for overdose and substance use disorder (SUD) in the pipeline. Research also shows that entrenched ways of communicating about substance use, including the phrase "substance abuse," can perpetuate stigma, which is why NIDA is proposing to change its name from the "National Institute on Drug Abuse" to the "National Institute on Drugs and Addiction."

Through the NIH Helping to End Addiction Long-term (HEAL) Initiative<sup>®</sup> in FY 2023, NIDA has launched a number of new programs to prevent and treat SUD and overdose. These include research to improve prevention and treatment services for polysubstance use, and to develop new interventions for polysubstance use disorders. (See "Multi-pronged strategies to address multiple substance use.") As part of the White House xylazine response plan, NIDA is funding new research to understand, prevent, and treat xylazine-related harms, including severe flesh wounds that can lead to amputation. NIDA also is expanding its research on approaches such as wastewater-based epidemiology to gather real-time, comprehensive data on community levels of xylazine and other emerging substances. (See "Pioneering research on wastewater testing to detect drugs and infectious diseases.")

NIDA also tracks changing attitudes about substance use and their impact on public health. For example, e-cigarettes, cannabis, and certain psychedelic drugs are increasingly perceived as low risk despite their addiction liability and potential long-term harms, especially among youth. NIDA continues to fund the Monitoring the Future (MTF) survey, which measures substance use and related attitudes among adolescents, and the Population Assessment of Tobacco and Health (PATH) Study, which focuses on tobacco use, attitudes, and health outcomes of people aged 12 and older. In addition, NIDA recently funded a cannabis registry that will capture data on cannabis product use and health outcomes, and conduct testing on products associated with adverse outcomes. NIDA is also funding research to better understand the effects of psychedelic drugs, their potential for treating SUD, and the impact of shifting policies in this area.

### Driving discovery through fundamental research

NIDA continues to support fundamental, investigator-initiated research into how licit and illicit drugs affect the brain and body. These investments lay a foundation for understanding mechanisms of SUD, its prevention and treatment, and approaches to harm reduction and recovery. For example, basic research on opioids is yielding insights into their effects on pain and their potential to lead to SUD and overdose—which may ultimately lead to more effective, less risky opioid analgesics. In a structure-function study of opioids and the mu opioid receptor (the primary binding site for fentanyl and other opioids), researchers found that compared to morphine, fentanyl occupies unique sub-pockets of the receptor, activating unique cell signaling pathways. This may help explain why fentanyl and its analogs are 100-10,000 times more potent than morphine. In another study, these researchers used structure-function analyses to design synthetic opioid analgesics with lower risks of addiction and overdose. Continued basic research also lays a foundation that enables addiction science to shift rapidly to new challenges when necessary. For example, as xylazine spread across the United States in 2022, NIDA scientists who study the body's responses to opioids were able to pivot their work to study how adding xylazine to opioids affects brain function and opioid-induced respiratory suppression.

### Untangling complex SUD risk factors to develop more effective prevention

In alignment with the Federal Overdose Prevention Strategy, NIDA has increased its focus on primary prevention of substance use and SUD, especially during early life. Childhood and adolescence are critical periods for learning and brain development when life experiences can become etched into malleable brain circuits. In fact, it is known that early-life exposures to trauma and substance use are independently associated with SUD and other behavioral health disorders in adulthood. Largely unknown, however, is why such exposures translate to negative long-term outcomes for some young people and not others—and how best to intervene for at-risk youth.

With support from other NIH Institutes and Centers, NIDA leads two large studies exploring early-life factors and their influence on brain health throughout the lifespan. Since 2016, the Adolescent Brain Cognitive Development (ABCD) study has been collecting brain imaging, genetic, and other data from nearly 12,000 young people, starting at ages 9-10. Funded in part by the HEAL Initiative, the HEALthy Brain and Child Development (HBCD) study will collect similar data from thousands of children starting in the prenatal period through adolescence. These studies promise unprecedented insight into brain development and vulnerability to mental illness, including SUD. In fact, one recent analysis using ABCD data suggests that diverse mental health disorders share a common feature—a failure to prune excess brain connections in early life. This hyper-connectivity could one day serve as a biomarker to support early interventions for mental illness.<sup>3</sup> Other recent findings show that social determinants of health (SDOH), such as family income, can have powerful effects on brain development and mental health and that policy interventions can mitigate these effects.

<sup>&</sup>lt;sup>1</sup> pubmed.ncbi.nlm.nih.gov/36411392

<sup>&</sup>lt;sup>2</sup> pubmed.ncbi.nlm.nih.gov/36450356

<sup>&</sup>lt;sup>3</sup> pubmed.ncbi.nlm.nih.gov/37095248

NIDA also supports research to translate knowledge about SUD risk factors into primary prevention. For example, a series of projects focuses on targeting SDOH to prevent opioid use disorder (OUD) and co-occurring mental health conditions. This includes a study on blight remediation efforts—such as cleaning up vacant lots, abandoned buildings, and dilapidated homes—and whether this can reduce rates of opioid misuse and overdose in Philadelphia. Other projects are evaluating SUD prevention interventions for high-risk youth, including those living with psychiatric disorders, transitioning out of carceral settings, or experiencing homelessness. In partnership with other NIH components and Federal health agencies, NIDA is also supporting a consensus study by the National Academies of Sciences, Engineering, and Medicine to develop actionable recommendations to address the prevention research-to-practice gap and establish the infrastructure needed to implement SUD and other behavioral health prevention interventions.

### Advancing SUD treatment, harm reduction, and recovery

The increasing diversity and potency of illicit drugs requires diverse, powerful treatments for SUD and overdose. NIDA has answered this need by greatly expanding its SUD therapeutics development portfolio; since September 2019, NIDA-supported research has led to more than 50 Investigational New Drug applications and 2 Investigational Device Exemptions submitted to the Food and Drug Administration (FDA) for evaluation in clinical trials.

NIDA-funded research led to the first naloxone nasal spray, approved by the FDA in 2015 as an effective medication to reverse opioid overdose. Years of follow-up research established that wider distribution of naloxone, especially to people who use drugs, could reduce community overdose rates, helping lead to FDA approval of the first non-prescription versions of naloxone in 2023. More recent NIDA investments helped lead to a nasal spray formulation of nalmefene, another opioid-blocking agent, which also received FDA approval in 2023. Nalmefene lasts hours longer than naloxone—which is not always sufficient, even after more than one dose, to fully reverse overdoses that involve increasingly powerful opioids.

NIDA is increasing support for therapies using psychedelic drugs, such as psilocybin (from "magic mushrooms") and dissociative drugs, such as ketamine. While these substances carry risk, there is evidence that when used in clinical settings in combination with psychotherapy, they can help people recover from SUD. In FY 2023, NIDA announced it would commit up to \$1.5 million to advance research on psychedelic-based therapies. This work is part of NIDA's broader therapeutics development portfolio, which encompasses diverse strategies such as immunotherapies, sequestrants, repurposed medications, neuromodulation therapies, and others. (See "Accelerating therapeutics development for drug addiction and overdose.")

Harm reduction and recovery are pillars of the Federal Overdose Prevention Strategy and significant focus areas of NIDA-funded research. Harm reduction approaches include, but are not limited to, naloxone distribution, syringe services programs (SSP), and tools such as fentanyl test strips (FTS) for checking whether drugs contain fentanyl. Among ongoing harm reduction projects, the HEALing Communities Study is testing strategies to increase FTS and naloxone uptake in diverse, high-risk communities, and to measure the impact on overdose rates. Another study aims to better understand people's experiences with xylazine to inform harm reduction strategies.

With HEAL Initiative funding in FY 2022, NIDA launched a new research network focused on harm reduction. Network priorities include testing new harm reduction strategies, evaluating new ways to deliver existing strategies, and reaching underserved populations. In addition to data on opioids, stimulants, and other commonly misused drugs, the network is also collecting data on xylazine exposures. HEAL funding also enabled NIDA to expand an existing recovery research network that aims to build evidence for effective addiction recovery support services.

### Expanding access to SUD interventions and addressing racial-ethnic disparities

NIDA supports implementation research on how to effectively deploy proven prevention and treatment approaches in diverse healthcare settings and beyond—including community, education, social service, and justice settings—in order to reach people at highest risk of SUD and poor outcomes. For example, the HEALing Communities Study aims to reduce rates of OUD and overdose in nearly 70 communities through an integrated model of evidence-based care that includes increasing access to medications for OUD (MOUD), such as methadone, buprenorphine (BUP), and naltrexone. Researchers have worked closely with participating communities to select and deploy those practices most likely to have an impact in each one. The Justice Community Opioid Innovation Network (JCOIN) supports research and capacity building to strengthen connections between the justice system and SUD treatment systems. JCOIN has found that ensuring access to MOUD in prisons and jails could reduce overdose deaths among recently incarcerated people by one-third. NIDA plans to extend JCOIN in FY 2025 to test large-scale implementation of OUD interventions across justice settings.

In recent years, risk of overdose mortality has increased steeply among Black Americans and American Indian/Alaska Natives (AI/AN), although absolute overdose numbers remain highest among whites. In FY 2022, as part of its Racial Equity Initiative (REI), NIDA released a suite of funding opportunities to enhance research on racial inequities in substance use, addiction, and related outcomes. One funded project is testing a culturally informed, peer-led intervention to connect Black individuals to BUP treatment at community health centers. In partnership with the Shawnee Tribe, another project is using neuroimaging to examine how the brain responds to tribal traditions and culture that are associated with substance use prevention. With HEAL funding and in close partnership with other NIH Institutes, Centers, and Offices, NIDA and the National Institute of Neurological Disorders and Stroke (NINDS) are supporting a new program focused on AI/AN and Native Hawaiian health called the Native Collective Research Effort to Enhance Wellness (N-CREW). N-CREW researchers will work in partnership with AI/AN Tribes and Native American-serving organizations to identify community-based priorities related to overdose, substance use, mental health, and pain in Native communities; collaborate in research toward culturally grounded interventions; and build local capacity as needed for this research.

### Supporting a talented diverse cadre of addiction scientists

Since ending the overdose epidemic will require multi-faceted solutions, NIDA funds a variety of training and career development programs to empower emerging scientists from diverse

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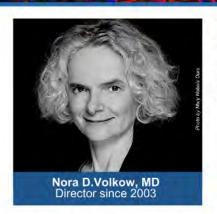
<sup>&</sup>lt;sup>4</sup> pubmed.ncbi.nlm.nih.gov/36123106

<sup>&</sup>lt;sup>5</sup> pubmed.ncbi.nlm.nih.gov/32712165

backgrounds to bring their talents to bear on substance use and addiction. NIDA continues to prioritize early-career support, including special consideration for research applications from Early-Stage Investigators. In addition, NIDA participates in a HEAL-funded NIH Pathway to Independence Award program in pain and SUD research intended to help postdoctoral scientists transition to independence. NIDA also has increased its NIH Loan Repayment Program funding to relieve student debt for early-career scientists of limited means.

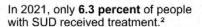
NIDA sees a critical need for an addiction science workforce that reflects the Nation's diversity. At the same time, this workforce should represent diverse and growing disciplines, such as data science. Thus, in FY 2023, NIDA announced new programs designed to help diverse students and postdoctoral researchers cross-train in addiction science, Big Data, and artificial intelligence (AI). One program will support research education activities, and another will support student research projects at institutions that do not receive substantial funding from NIH. Program applicants are required to submit plans to increase trainee diversity. Other NIDA programs helping to foster a diverse addiction workforce include the Diversity Scholars Network and the NIDA Summer Research Internship Program.

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### The Addiction Public Health Crisis

**46.3 million** people in the United States had an SUD in 2021.<sup>2</sup>



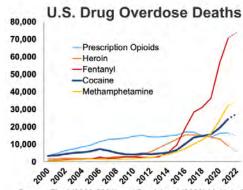
In 2022, about **110,000** people died of drug overdoses.<sup>3</sup>

Black and American Indian/Alaska Native people are estimated to have the highest rates of fatal overdose.<sup>4</sup>

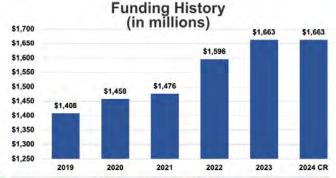
### NIDA's FY 2023 Research Investment

- . 419 Full-time equivalents
- 399 New research project grants
- 566 Unique investigators
- 106 Early-stage investigators
- . \$753M for opioids research
- \$279M for HIV/AIDS research

The National Institute on Drugs and Addiction¹ (NIDA) advances science on substance use and addiction to improve individual and public health. After decades of research, substance use disorder (SUD) is now understood to be a chronic, treatable brain condition. NIDA-funded research has led to effective prevention and treatment approaches, helping millions of Americans lead healthier lives, reduce their overdose risk, and recover from SUD.



Source: Final (2000-2021) and Provisional (2022) Multiple Cause of Death Data, CDC WONDER. Accessed 11/28/23.



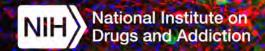
FY25 Budget Request \$1,668 million.

### Fostering the Next Generation of Addiction Scientists

- NIDA is helping grow an addiction science workforce that represents the Nation's diverse populace while
  also capturing diverse disciplines. As part of its Racial Equity Initiative, NIDA recently announced new
  programs designed to help diverse students and postdoctoral researchers cross-train in addiction science,
  Big Data, and artificial intelligence.
- NIDA's training programs support addiction scientists at all career stages, from undergraduates to
  postdoctoral trainees and clinicians working to become independent investigators.
- NIDA continues to prioritize early-career support, including special consideration for research applications from Early-Stage Investigators.

- <sup>2</sup> 2021 National Survey on Drug Use and Health
   <sup>3</sup> 2022 CDC/National Center for Health Statistics
- \* CDC WONDER Provisional Mortality data

¹ The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.



### Recent Accomplishments and New Programs

### Investing in Basic Neuroscience

- Through structure-function analyses of the mu-type opioid receptor, NIDA-funded researchers designed synthetic opioid analgesics that have lower risks of addiction and overdose.
- Recent research shows that people with opioid use disorder (OUD) have unique daily rhythmic patterns of
  gene activity in brain regions that influence addiction. The interplay of sleep, circadian rhythms, and SUD is
  the focus of a new NIDA research program.

### Understanding Risk, Strengthening Prevention

- The Adolescent Brain Cognitive Development (ABCD) Study has found that childhood adversity can have significant effects on brain development and mental health, including the risk of SUD. Ongoing research is exploring ways to intervene in early-life risks for SUD.
- The NIDA Clinical Trials Network has developed and validated simple tools for early screening of substance use and SUD and is investigating ways to integrate SUD screening into primary care.
- Working with other NIH Institutes and federal partners, NIDA is supporting a National Academies
  consensus study to advise on a prevention infrastructure for SUD and other mental health disorders.

### Therapeutics Development and Testing

- NIDA support has led to more than 50 Investigational New Drug applications for SUD since 2019.
- A NIDA-pharma collaboration led to the Food and Drug Administration's 2023 approval of intranasal nalmefene—an opioid reversal agent with longer-lasting effects than naloxone.
- Potential therapies under development include vaccines, monoclonal antibodies, and sequestrants
  designed to trap drugs, as well as psychedelic-based therapies to reset brain circuits underlying addiction.

### Innovation and Entrepreneurship

- NIDA provided early funding to startups to tackle the overdose crisis in unique ways, such as by monitoring wastewater for patterns of drug use and providing SUD care by telehealth.
- A new NIDA program calls for research on deployable, low-cost, point-of-need approaches and technologies to lower barriers to SUD care.

### **Bringing Proven Interventions into Broader Practice**

- The Justice Community Opioid Innovation Network (JCOIN) found that expanding access to medications
  for OUD in prisons and jails could reduce overdose deaths among recently incarcerated people. JCOIN's
  new online tool even helps prison and jail administrators budget for these medications.
- A new harm reduction research network supports research on interventions to reduce overdose and other harms from SUD, with a focus on reaching underserved populations.

### **Addressing Disparities**

- The NIDA Racial Equity Initiative has called for transformative research to address racial/ethnic disparities in SUD treatment and outcomes. Ongoing studies are examining culturally informed approaches to improve evidence-based prevention and treatment among minoritized groups.
- The HEAL-funded program Native Collective Research Effort to Enhance Wellness (N-CREW) will partner researchers with Tribes and Native American-serving organizations to support community-based research and solutions for overdose, substance use, mental health, and pain.

### **Major Changes in the Budget Request**

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanism and activity detail and these highlights will not sum to the total change for the FY 2025 President's Budget. The FY 2025 The President's Budget request for the National Institute on Drugs and Addiction (NIDA) is \$1,668.3 million, which is a \$5.0 million increase over FY 2023 Final level.

Research Project Grants (RPGs) (+\$3.2 million; total \$1,035.7 million): The total amount of support to RPG awards will increase by \$3.2 million over the FY 2023 Final level. The number of competing RPG awards will decrease by 93 in comparison to FY 2023. These reductions in competing and noncompeting awards will be distributed across programmatic areas and basic, epidemiology and/or clinical research.

<u>Research Centers (-\$13.1 million; total \$54.6 million):</u> NIDA will continue supporting existing specialized/comprehensive centers projects. Potential savings in this area will be applied to support other mechanisms.

Other Research (+\$3.3 million; total \$206.3 million): NIDA will continue supporting research career development awards, research training awards, and cooperative clinical research projects.

<u>Ruth L Kirchstein Training (+\$0.4 million; total \$29.1 million):</u> NIDA will increase its numbers of full-time training positions to 539, an increase of 7 positions in comparison to the FY 2023 Final level.

### **BUDGET MECHANISM TABLE**

### NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

# Budget Mechanism\* (Dollars in Thousands)

EV	2023 Final	EV	7 2024 CD	FY 2025 President's		FY 2025 +/- FY 2023	
F 1	2023 Final	Budget		Budget		25 1/- F1 2025	
Number	Amount	Number	Amount	Number	Amount	Number	Amount
952	\$670,130	990	\$731,846	909	\$732,968	-43	\$62,838
(107)	\$16,305	(92)	\$14,000	(92)	\$14,000	-(15)	-\$2,305
27	\$14,861	27	\$15,000	29	\$16,000	2	\$1,139
371	\$279,071	264	\$215,337	277	\$221,721	-94	-\$57,350
1	\$108	0	\$0	0	**	-1	-\$108
399	\$294,039	291	\$230,337	306	\$237,721	-93	-\$56,318
1,351	\$980,473	1,281	\$976,183	1,215	\$984,688	-136	\$4,215
78	\$52,012	79	\$52,581	77	\$51,045	-1	-\$967
1,429	\$1,032,485	1,360	\$1,028,764	1,292	\$1,035,733	-137	\$3,248
30	\$67,767	26	\$58,539	24	\$54,633	-6	-\$13,134
0	\$0	0	\$0	0	\$0	0	\$0
0	\$0	0	\$0	0	\$0	0	\$0
0	\$0	0	\$0	0	\$0	0	\$0
0	\$0	0	\$0	0	\$0	0	\$0
30	\$67,767	26	\$58,539	24	\$54,633	-6	-\$13,134
262	\$49,623	266	\$50,346	268	\$50,688	6	\$1,065
0	\$0	0	\$0	0	\$0	0	\$0
28	\$83,766	28	\$83,606	28	\$83,171	0	-\$596
0	\$0	0	\$0	0	\$0	0	\$0
0	\$2,039	0	\$1,984	0	\$1,371	0	-\$668
84	\$67,565	87	\$70,249	87	\$71,044	. 3	\$3,480
374	\$202,993	381	\$206,185	383	\$206,274		\$3,281
1,833	\$1,303,245	1,767	\$1,293,488	1,699	\$1,296,640		-\$6,606
FTTPs		<u>FTTPs</u>				<u>FTTPs</u>	
178	\$8,172	179	\$8,360	182	\$8,544	4	\$373
354	\$20,545	354	\$20,766	357	\$20,601	3	\$56
532	\$28,717	533	\$29,126	539	\$29,146	7	\$429
							-\$512
1 ' 1		' '	, ,	' '		1 ' '	(\$434)
							\$4,349
294	\$85,597	320		345	\$92,915	51	\$7,318
	(\$92)		(\$209)		(\$220)		(\$128)
	0.9		0.9		90		\$0
						1	\$0
410		415		470			\$4,978
	Number   952 (107)   27   371   1   399   1,351   78   1,429   30   0   0   0   0   0   0   0   0	952 \$670,130 (107) \$16,305 27 \$14,861 371 \$279,071 1 \$108 399 \$294,039 1,351 \$980,473 78 \$52,012 1,429 \$1,032,485 30 \$67,767 0 \$0 0 \$0 0 \$0 0 \$0 0 \$0 0 \$0 28 \$83,766 0 \$0 29 \$2,039 84 \$67,565 374 \$202,993 1,833 \$1,303,245 FTTPs 178 \$8,172 354 \$20,545 532 \$28,717 109 \$129,265 (1) (\$1,753) 125 \$116,541 294 \$85,597 (\$92)	Number         Amount         Number           952         \$670,130         990           (107)         \$16,305         (92)           27         \$14,861         27           371         \$279,071         264           1         \$108         0           399         \$294,039         291           1,351         \$980,473         1,281           78         \$52,012         79           1,429         \$1,032,485         1,360           30         \$67,767         26           0         \$0         0           0         \$0         0           0         \$0         0           0         \$0         0           0         \$0         0           262         \$49,623         266           0         \$0         0           28         \$83,766         28           0         \$0         0           28         \$83,766         28           0         \$0         \$0           0         \$2,039         0           84         \$67,565         87           374         \$202,993 </td <td>Number         Amount         Number         Amount           952         \$670,130         990         \$731,846           (107)         \$16,305         (92)         \$14,000           27         \$14,861         27         \$15,000           371         \$279,071         264         \$215,337           1         \$108         0         \$0           399         \$294,039         291         \$230,337           1,351         \$980,473         1,281         \$976,183           78         \$52,012         79         \$52,581           1,429         \$1,032,485         1,360         \$1,028,764           30         \$67,767         26         \$58,539           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           262         \$49,623         266         \$50,346           0         \$0         \$0         \$0</td> <td>  Number</td> <td>  Number   Amount   Number   Amount   Number   Amount    </td> <td>  Number</td>	Number         Amount         Number         Amount           952         \$670,130         990         \$731,846           (107)         \$16,305         (92)         \$14,000           27         \$14,861         27         \$15,000           371         \$279,071         264         \$215,337           1         \$108         0         \$0           399         \$294,039         291         \$230,337           1,351         \$980,473         1,281         \$976,183           78         \$52,012         79         \$52,581           1,429         \$1,032,485         1,360         \$1,028,764           30         \$67,767         26         \$58,539           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           0         \$0         \$0         \$0           262         \$49,623         266         \$50,346           0         \$0         \$0         \$0	Number	Number   Amount   Number   Amount   Number   Amount	Number

<sup>\*</sup> All items in italics and brackets are non-add entries.

# NATIONAL INSTITUTES OF HEALTH

### NATIONAL INSTITUTE ON DRUGS AND ADDICTION

For carrying out section 301 and title IV of the PHS Act with respect to drugs and addiction, \$1,668,343,000.

## NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

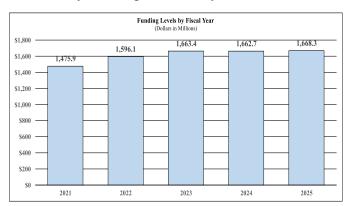
### **Summary of Changes**

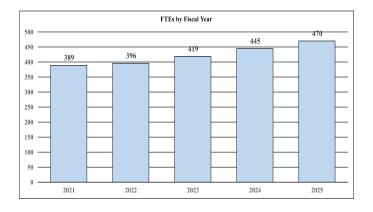
(Dollars in Thousands)

	FY 2023 Final			5 President's Budget		Change from 023 Final
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority	FTEs	Budge Authority
1. Intramural Research:		,				
A. Built-in cost changes:						
a. FY 2024 effect of FY 2023 pay & benefits increase		\$33,010		\$35,840		\$389
b. FY 2024 effect of FY 2024 pay & benefits increase		\$33,010		\$35,840		\$1,285
c. FY 2024 paid days adjustment		\$33,010		\$35,840		\$127
d. Differences attributable to FY 2024 change in FTE		\$33,010		\$35,840	İ	\$0
e. FY 2025 effect of FY 2024 pay & benefits increase		\$33,010		\$35,840		\$430
f. FY 2025 effect of FY 2025 pay & benefits increase		\$33,010		\$35,840		\$58
g. FY 2025 paid days adjustment		\$33,010		\$35,840		\$
h. Differences attributable to FY 2025 change in FTE		\$33,010		\$35,840		\$0
i. Payment for centrally furnished services		\$12,601		\$13,512		\$91
j. Cost of laboratory supplies, materials, other expenses, and non-		\$70,927		\$71,538		\$4,30
recurring costs		\$70,927		\$71,556		54,50
Subtotal, IR built-in cost changes						\$8,04
2. Research Management and Support:						
A. Built-in cost changes:						
a. FY 2024 effect of FY 2023 pay & benefits increase		\$49,199		\$54,926		\$58.
b. FY 2024 effect of FY 2024 pay & benefits increase		\$49,199		\$54,926		\$1,91
c. FY 2024 paid days adjustment		\$49,199		\$54,926	ļ	\$18
d. Differences attributable to FY 2024 change in FTE		\$49,199		\$54,926	1	\$5,37
e. FY 2025 effect of FY 2024 pay & benefits increase		\$49,199		\$54,926	1	\$64
f. FY 2025 effect of FY 2025 pay & benefits increase		\$49,199		\$54,926		\$88
g. FY 2025 paid days adjustment		\$49,199		\$54,926		\$6
h. Differences attributable to FY 2025 change in FTE		\$49,199		\$54,926		\$4,91
i. Payment for centrally furnished services		\$5,159		\$5,531	İ	\$373
j. Cost of laboratory supplies, materials, other expenses, and non-		621 106		622.459		¢1.93
recurring costs		\$31,196		\$32,458		\$1,823
Subtotal, RMS built-in cost changes						\$16,70
	FY 2	023 Final		5 President's Budget	_	Change from 023 Final
CHANGES	No.	Amount	No.	Amount	No.	Amoun
B. Program:	ĺ		Ĭ			
1. Research Project Grants:						
a. Noncompeting	952	\$686,434	909	\$746,968	-43	\$60,53
b. Competing	399	\$294,039	306	\$237,721	-93	-\$56,31
c. SBIR/STTR	78	\$52,012	77	\$51,045	-1	-\$96
Subtotal, RPGs	1,429	\$1,032,485	1,292	\$1,035,733	-137	\$3,24
2. Research Centers	30	\$67,767	24	\$54,633	-6	-\$13,13
3. Other Research	374	\$202,993	383	\$206,274	9	\$3,28
4. Research Training	532	\$28,717	539	\$29,146	7	\$429
5. Research and development contracts	109	\$129,265	110	\$128,753	1	-\$51
Subtotal, Extramural	103	\$1,461,227	110	\$1,454,538	•	-\$6,689
6. Intramural Research	125	\$116,541	125	\$120,890	О	-\$3,69
7. Research Management and Support	294	\$85,597	345	\$92,915	51	-\$9,38
8. Construction		\$0		\$0		\$
9. Buildings and Facilities		\$0		\$0		\$
Subtotal, program changes		30		\$0		-\$19,760
,, ,						
Total built-in and program changes	419	\$1,663,365	470	\$1,668,343	51	\$4,97

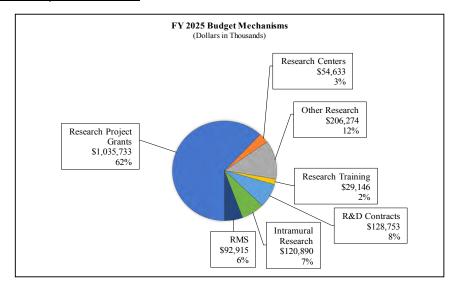
### **BUDGET GRAPHS**

### History of Budget Authority and FTEs:

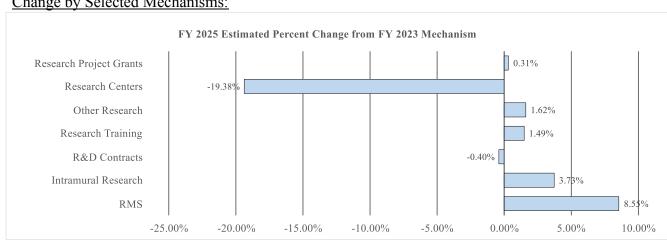




### **Distribution by Mechanism:**

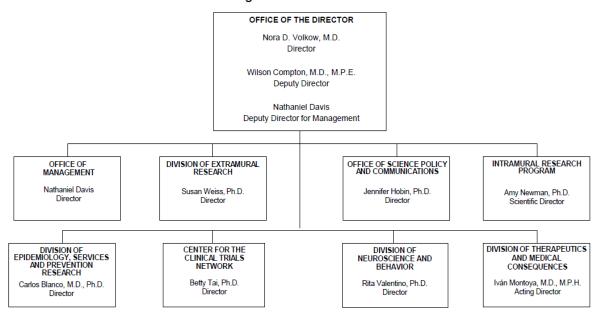


### Change by Selected Mechanisms:



### **National Institutes of Health**

National Institute on Drugs and Addiction Organizational Structure



# NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

### Budget Authority by Activity $^*$

(Dollars in Thousands)

	FY 2023 Final FY 20		024 CR	FY 2025 President's Budget		FY 2025 +/- FY 2023 Final		
Extramural Research	FTE	Amount	FTE	Amount	FTE	Amount	<u>FTE</u>	Amount
<u>Detail</u>								
Division of Therapeutics and Medical Consequences		\$110,301		\$109,851		\$109,842		-\$459
Division of Neuroscience and Behavior		\$534,398		\$532,218		\$532,174		-\$2,224
Division of Epidemiology, Services and Prevention Research		\$392,721		\$391,119		\$391,087		-\$1,634
Center for the Clinical Trials Network		\$35,842		\$35,695		\$35,693		-\$149
Office of Translational Initiatives and Program Innovations		\$43,419		\$43,242		\$43,238		-\$181
HEAL Initiative <sup>1</sup>		\$344,547		\$342,995		\$342,505		-\$2,042
Subtotal, Extramural		\$1,461,227		\$1,455,120		\$1,454,538		-\$6,689
Intramural Research	125	\$116,541	125	\$118,519	125	\$120,890	0	\$4,349
Research Management & Support	294	\$85,597	320	\$89,055	345	\$92,915	51	\$7,318
TOTAL	419	\$1,663,365	445	\$1,662,695	470	\$1,668,343	51	\$4,978

Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

<sup>&</sup>lt;sup>1</sup> Total for HEAL Initiative including RMS is (in thousands) \$355,295 in FY 2023, \$355,295 in FY 2024, and \$355,295 in FY 2025.

### **National Institute on Drugs and Addiction**

Authorizing Legislation: Section 301 and Title IV of the Public Health Service Act, as amended.

Budget Authority (BA):

			FY 2025	
			President's	FY 2025 +/-
	FY 2023 Final	FY 2024 CR	Budget	FY 2023
BA	\$1,663,365,000	\$1,662,695,000	\$1,668,343,000	+ \$4,978,000
FTE	419	445	470	+51

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Overall Budget Policy: The FY 2025 President's Budget request for the National Institute on Drugs and Addiction (NIDA) is \$1,668.3 million, which is \$5.0 million above the FY 2023 Final level. Within this amount, funding for the Helping to End Addiction Long-term (HEAL) Initiative® will remain at \$355.3 million, the FY 2023 Final level. NIDA will continue to support basic and applied research on substance use and addiction—including building the addiction science workforce—toward improving prevention, treatment, recovery, and harm reduction related to substance use, so that all Americans can live healthier lives.

### **Program Descriptions**

The Division of Neuroscience and Behavior (DNB) supports research to understand the biological mechanisms that underlie drug use and addiction, and to inform the development of novel prevention and treatment strategies for substance use disorders (SUD). This includes identifying the effects of illicit drugs on brain structure and function throughout the lifespan, and how genes, the environment, and other factors such as sex and gender influence the risk of SUD and its outcomes. DNB also supports research on the pharmacology of drugs with addiction potential; data science; foundations of neuromodulation technology; and research tools to enable the study of the living brain from cells to circuits to networks.

A recent study exemplifies DNB support for research on the genetics of addiction. In that study, researchers combed through genomic data from over 1 million people, including children participating in the Adolescent Brain Cognitive Development (ABCD) study, and found nearly 20 gene variants associated with SUD, regardless of the substance involved. The researchers then developed a genetic risk score that was able to discern between healthy individuals and

people with an SUD diagnosis, with the highest accuracy for those who had polysubstance use disorder. Although genetic approaches like this cannot fully predict who will develop SUD, they could someday aid in SUD risk assessment, lead to more personalized interventions, and inform potential targets for new SUD therapeutics.

Since people who use drugs are at higher risk for HIV infection, DNB also supports fundamental research on HIV. With funding through a data science program, one recent study investigated how HIV manages to persist in some people despite antiretroviral therapy, and found that HIV-infected cells sometimes multiply and continue producing the virus, acting as a viral reservoir. With funding through the NIDA Avante-Garde program, another study identified genes that are down-regulated during HIV-related brain inflammation, suggesting a potential early step in HIV-associated neurocognitive disorder, which affects up to half of people with HIV. Both of these programs were renewed in FY 2023.

DNB also supports research focused on the intersection of SUD and sleep disorders, which have a strong bidirectional association. Substance use can lead to sleep disturbances, and sleep disturbances can increase the risk of drug withdrawal, craving, and relapse. In fact, a recent DNB-funded study found that SUD and sleep disturbances are linked at a molecular level; compared to healthy individuals, people with opioid use disorder (OUD) had unique daily rhythmic patterns of gene activity in the brain, specifically in brain regions involved in addiction. In FY 2023, DNB announced new funding to explore the mechanisms that link sleep, circadian rhythms, and SUDs.

**Budget Policy:** The FY 2025 President's Budget request is \$532.2 million, a decrease of \$2.2 million compared with the FY 2023 Final level.

# <u>Multi-pronged strategies to address multiple</u> substance use

Polysubstance use is a growing factor in fatal overdose and other adverse outcomes. In 2021, about one in three overdose deaths involved both fentanyl and stimulants. Moreover, people with opioid addiction and a co-occurring substance use disorder (SUD) have lower odds of staying in treatment with medications for opioid use disorder (MOUD).

NIDA leads several research efforts to better understand polysubstance use and to develop more effective multi-pronged interventions for it. A program initiated in FY 2023 supports research to understand the neurobiology of polysubstance use and its effects on drug craving, addiction, and other outcomes. For example, one project is examining how interactions between fentanyl and xylazine affect the risk of overdose and responses to treatment.

One program funded with HEAL Initiative dollars supports research to define polysubstance use patterns and outcomes, and to improve prevention and treatment. One project is examining how changes in housing status and other factors affect patterns of combined fentanyl and stimulant use among people experiencing homelessness. Clinical trials funded through the program will investigate interventions for co-use of opioids and stimulants, including contingency management (CM) delivered by a smartphone app. CM involves providing small financial incentives for abstinence and other recoveryoriented behaviors and is currently the only intervention effective for reducing stimulant use. Two trials will examine the potential for integrating smartphone-based CM into MOUD treatment programs, reducing substance use, and improving MOUD adherence.

Another study also supported with HEAL funds is the Co-Care Study, in which NIDA's Clinical Trials Network is investigating whether team-based collaborative care in primary healthcare settings—a common approach used to manage chronic conditions—can help reduce polysubstance use and overdose risk. Finally, a new program co-led by NIDA and other Institutes using HEAL funds will support research to inform safe and effective medication-based, psychosocial, and complementary interventions for people with co-occurring opioid use disorder and alcohol use disorder.

<sup>&</sup>lt;sup>7</sup> pubmed.ncbi.nlm.nih.gov/37250466

<sup>&</sup>lt;sup>8</sup> pubmed.ncbi.nlm.nih.gov/35320704

<sup>9</sup> pubmed.ncbi.nlm.nih.gov/36525955

<sup>&</sup>lt;sup>10</sup> pubmed.ncbi.nlm.nih.gov/35347109

The Division of Epidemiology, Services, and Prevention Research (DESPR) supports studies to understand and address the interactions between individuals and environments that contribute to drug use, addiction, and related health problems. DESPR also supports epidemiologic research that informs the development of evidence-based prevention, harm reduction, treatment, and recovery interventions, including the Monitoring the Future (MTF) survey and the Population Assessment of Tobacco and Health (PATH) Study.

DESPR's research is shedding light on e-cigarette use among youth and its relation to smoking and other substance use. For example, many studies suggest that e-cigarette use, or vaping, in adolescence is a gateway to smoking later. New PATH data suggest that vaping also entrenches smoking among teens who have already tried it. Meanwhile, MTF has found that compared to teens who do not use nicotine, odds of cannabis use are higher among those who vape nicotine—about 40 times higher among those who both vape and smoke nicotine. Even accounting for smoking and cannabis use, youth who use e-cigarettes are more likely to experience wheezing, bronchitis, and shortness of breath. These findings highlight the need for interventions to address the health risks of vaping during youth.

DESPR also supports the ABCD study, which is advancing knowledge about the impacts of social determinants of health (SDOH) on brain development. In one analysis, researchers found that Black children ages 9-10 faced greater adversity than white children—including lower parental education and income, living in disadvantaged neighborhoods, and more exposure to trauma such as vehicle accidents and assault—and that this adversity was associated with differences in brain structure. When the differences in adversity were controlled statistically, the brain differences largely evaporated. Another analysis found that compared to children from high-income families, those from low-income families were likely to have structural brain differences as well as symptoms of anxiety and depression. More importantly, those disparities narrowed significantly among children living in states with robust antipoverty programs. These studies provide real-world evidence that intervening on SDOH can help ensure healthy brain development.

DESPR also supports implementation science to identify and address gaps in translating evidence-based interventions into practice. For instance, a study of national Medicare data found that adults who received buprenorphine (BUP) following an overdose had a 62 percent lower risk of fatal overdose over the next year. However, fewer than 1 in 20 patients received it, and most recipients waited more than 30 days. DESPR is funding research on innovative solutions to this challenge, such as collaborative care models that bring together BUP providers and pharmacists. A pilot trial in which the pharmacist handled BUP management including adjustments for withdrawal, in consultation with the provider, found that this model significantly boosts retention in treatment compared to usual provider-based care. 17

<sup>11</sup> pubmed.ncbi.nlm.nih.gov/37072167

<sup>&</sup>lt;sup>12</sup> pubmed.ncbi.nlm.nih.gov/37198725

<sup>&</sup>lt;sup>13</sup> pubmed.ncbi.nlm.nih.gov/37582630

<sup>&</sup>lt;sup>14</sup> pubmed.ncbi.nlm.nih.gov/36722118

<sup>15</sup> pubmed.ncbi.nlm.nih.gov/37130880

<sup>&</sup>lt;sup>16</sup> pubmed.ncbi.nlm.nih.gov/36906496

<sup>&</sup>lt;sup>17</sup> pubmed.ncbi.nlm.nih.gov/36630629

**Budget Policy:** The FY 2025 President's Budget request is \$391.1 million, a decrease of \$1.6 million compared with the FY 2023 Final level.

The Division of Therapeutics and Medical Consequences (DTMC) supports research to evaluate the safety and efficacy of pharmacotherapies, behavioral interventions, and medical devices to prevent and treat SUD and drug overdose. This work spans all phases of medical product development including synthesis and preclinical evaluation of potential therapeutics, clinical trial design and execution, and preparing regulatory submissions.

DTMC supports research on a diverse array of pharmacotherapies, including repurposing of drugs used for other conditions and developing new compounds with novel molecular targets. For example, diabetes drugs like semaglutide, which are based on the hormone glucagon-like peptide-1 (GLP-1), may hold potential for treating SUD. GLP-1 analogs help control food cravings, and anecdotal reports from people taking these drugs for diabetes or weight loss suggest they might help reduce drug cravings, too. NIDA is supporting preclinical studies of GLP-1 analogs for alcohol and opioid addiction and a small clinical trial for smoking cessation. While stimulants generally work by increasing dopamine signals in the brain, methamphetamine and cocaine use disorder (MtUD and CcUD) also involve changes in glutamate signaling. A phase I clinical trial is underway to investigate treating CcUD with a small-molecule inhibitor of the glutamate receptor mGluR5.

DTMC also supports research on therapies involving psychedelic and dissociative drugs. For example, a large randomized controlled trial is investigating whether psilocybin in combination with psychotherapy can improve smoking cessation. Other trials are investigating ketamine-assisted

therapy for CcUD and MtUD, and as a bridge to start MOUD. (For more, see "Accelerating therapeutics development for drug addiction and overdose.")

# Accelerating therapeutics development for drug addiction and overdose

Additional treatments for substance use disorders (SUD) are urgently needed. Although there are effective medications for opioid, tobacco, and alcohol use disorders, they do not work for everyone. Moreover, no proven-effective medications exist for other SUDs. To address these gaps, NIDA has made significant investments in the following areas of drug development:

New formulations of medications for opioid use disorder (MOUD) are under study, including oral methadone formulations designed to last longer by resisting stomach acids, and devices that provide longer-lasting drug delivery, like transdermal naltrexone patches and subdermal nalmefene implants.

Vaccines for SUD contain small molecules that structurally mimic a drug. If the drug is taken, the vaccine generates antibodies that stick to it and prevent it from entering the brain. Anti-cocaine and anti-opioid vaccines are currently in human testing. Monoclonal antibody therapies, which bypass the vaccination step but work on the same principle, are also under study.

Sequestrants—small molecules designed to trap drugs and clear them from the body—are under development to reverse opioid overdose and methamphetamine intoxication.

Repurposing drugs, like the diabetes drug semaglutide, is another active area. NIDA intramural researchers recently found that semaglutide reduces binge-link drinking and alcohol dependence in rodent models.

Respiratory stimulants are intended to reverse overdose by activating critical brain pathways to restore breathing, instead of blocking the drug. Some respiratory stimulants activate the carotid bodies, sensory organs in the carotid arteries, alerting the brain to low oxygen levels in the blood.

New compounds with novel targets include small molecules that target nociceptin receptors. Nociceptin is a small protein named for its role in perceiving pain (nociception), and its receptor is closely related to the mu opioid receptor. The nociceptin system was discovered less than three decades ago through NIDA-funded research, and there is still much to learn about its potential roles in treating pain and addiction.

Another focus of DTMC's portfolio is neuromodulation, which involves stimulating the brain to reset the circuitry underlying brain disorders. Deep brain stimulation— which involves inserting electrodes into the brain and is approved by the Food and Drug Administration (FDA) for treating Parkinson's disease and epilepsy—is in clinical trials for refractory OUD. DTMC also supports research on non-invasive neuromodulation therapies, including low-intensity focused ultrasound and transcranial magnetic stimulation (TMS). TMS is FDA-approved as an adjunct therapy for smoking cessation, in part due to NIDA-funded research, and is now being investigated for other SUDs.

DTMC has a growing portfolio of research to address OUD and other co-occurring mental health disorders. For example, 40-60 percent of people with OUD suffer from chronic pain and depression, which can increase their risk of opioid misuse. To improve health outcomes for these patients, researchers are evaluating an approach in which primary providers and behavioral health specialists provide collaborative care. In FY 2023, DTMC announced new funding to develop pharmacotherapies, behavioral therapies, and devices for co-occurring OUD and mental illness.

**Budget Policy:** The FY 2025 President's Budget request is \$109.8 million, a decrease of \$0.5 million compared with the FY 2023 Final level.

The Center for Clinical Trials Network (CCTN) manages NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN), which provides a collaborative framework for healthcare providers, researchers, and patients to conduct clinical trials on the safety and efficacy of SUD interventions. The CTN includes 16 research nodes and more than 240 community-anchored treatment programs across the country. This unique structure enables clinical research on behavioral, pharmacological, and integrated therapies across diverse settings and populations, and implementation studies that help bring research results into practice. Active CTN studies are exploring primary prevention of SUD; increasing patient access and adherence to MOUD, especially in rural and underserved populations; evaluating potential medications for stimulant use disorder; and addressing stigma and other barriers to SUD treatment.

Since adolescence is a critical time for susceptibility to SUD and responsiveness to interventions, the CTN prioritizes development and testing of screening tools tailored to this age range. A recent study tested three brief SUD screening tools in a large, diverse adolescent population and found that they performed well compared to an in-depth diagnostic interview. <sup>18</sup> Through the ongoing Subthreshold OUD Prevention (STOP) trial, the CTN seeks to determine if screening and intervention for low-severity OUD in primary care can reduce OUD progression and overdose risk.

The CTN is also testing strategies to identify OUD patients and start MOUD treatment in emergency departments (EDs)—at the frontline of the overdose epidemic. In one approach, the CTN designated champions to educate ED and community clinicians on BUP treatment and how to overcome stigma and other barriers to its use. Implementing this approach for six months led to higher rates of standard oral BUP initiation in the ED and referral to ongoing OUD treatment

<sup>&</sup>lt;sup>18</sup> pubmed.ncbi.nlm.nih.gov/37213103

in the community, and was feasible even in rural and low-resource EDs. <sup>19</sup> The CTN is now conducting a similar implementation trial, called ED-INNOVATION, to compare initiation with oral BUP vs. a longer-lasting injectable form, which could help keep patients stable while providers address any barriers to referral.

The CTN also recently leveraged the ED-INNOVATION trial to address concerns about precipitated withdrawal—debilitating withdrawal symptoms that can occur within hours of receiving BUP. For patients who use potent opioids such as fentanyl, some clinicians prescribe BUP at lower doses to avoid precipitated withdrawal, but that practice may not adequately curb opioid craving and subsequent relapse. An interim analysis of trial data found that while most patients had used fentanyl, only one percent experienced precipitated withdrawal after BUP initiation, similar to rates seen for patients using less potent opioids.<sup>20</sup>

The CTN is developing and evaluating potential treatments for MtUD and CcUD, for which there are no FDA-approved therapies. A recent CTN trial found that a combination of injectable naltrexone and oral bupropion, a commonly prescribed medication for depression and nicotine cessation, was effective in helping people with MtUD reduce their use. A secondary analysis focused on men who have sex with men—who are at higher risk for MtUD and harmful outcomes, including HIV infection—and found they had higher response rates to this treatment than heterosexual men.<sup>21</sup> Two other CTN trials will examine whether patients with MtUD or CcUD and

# Pioneering research on wastewater testing to detect drugs and infectious diseases

Turning the tide of the overdose epidemic requires faster, more comprehensive measures of community drug use patterns. Traditional measures such as ED visits and SUD treatment admissions have a significant lag time and typically only capture people who seek healthcare for their drug use. Wastewater-based epidemiology (WBE), an approach for measuring drugs and other substances in sewage wastewater, can provide data in near real-time from the community at large. NIDA has provided seminal and ongoing support for WBE to monitor drug threats and even helped pioneer its use to monitor SARS-CoV-2, the virus that causes COVID-19.

NIDA supported one of the earliest studies of WBE-based drug monitoring in the United States, published in 2009, which found that it can complement more traditional methods. Within a decade, NIDA began supporting several projects to improve the utility of WBE for drug monitoring, including the development of an automated robotic system called Biobot to test wastewater at manholes.

This research helped provide a foundation for applying WBE to monitor the spread of SARS-CoV-2. NIH-funded studies showed that wastewater detection of the virus precedes clinical case reports by several days, and the Centers for Disease Control and Prevention continues to operate a national WBE system to provide early warnings of COVID-19 surges.

NIDA is now supporting research to implement WBE-based drug monitoring on a larger scale. For example, NIDA's National Drug Early Warning System (NDEWS) uses and evaluates methods to provide real-time surveillance of potential drug threats. In FY 2021 and FY 2023, NIDA provided additional funding for NDEWS to invest in WBE and integrate its data with other drug data streams. NIDA is also funding Biobot to conduct a yearlong analysis of community fluctuations in drug use across the United States.

opioid co-use will benefit from injectable naltrexone and monthly injectable BUP.

**Budget Policy:** The FY 2025 President's Budget request is \$35.7 million, a decrease of \$0.1 million compared with the FY 2023 Final level.

The Office of Translational Initiatives and Program Innovations (OTIPI) translates discoveries in addiction research into candidate health applications. OTIPI supports translational research through NIDA's Small Business Innovation Research/Technology Transfer

<sup>&</sup>lt;sup>19</sup> pubmed.ncbi.nlm.nih.gov/37017967; pubmed.ncbi.nlm.nih.gov/37140493

<sup>&</sup>lt;sup>20</sup> pubmed.ncbi.nlm.nih.gov/36995717

<sup>&</sup>lt;sup>21</sup> pubmed.ncbi.nlm.nih.gov/33497547; pubmed.ncbi.nlm.nih.gov/37478502

(SBIR/STTR) programs, as well as Challenge competitions. OTIPI also develops training programs that help scientists move their discoveries from the lab to the real world.

In FY 2023, OTIPI issued a Primary Care Challenge competition to propose models for how primary care providers can more effectively identify people at risk for substance use and deliver interventions to reduce this risk. Three winning projects were selected. One project will focus on recently incarcerated adults, who are at high risk for drug use and overdose, with community health workers leading patient outreach, substance use screening, and linkages to preventive care. Another project will screen teens with a mental health diagnosis for substance use risk, and the third will use artificial intelligence (AI) to identify high-risk pre-teens based on their electronic health records.

OTIPI supports medical device development, including devices to treat neonatal opioid withdrawal syndrome (NOWS), which can affect infants exposed to opioids in the womb. For example, an SBIR project has developed a vibrating crib mattress to soothe infants with NOWS. In a large trial, infants who slept on this mattress needed less medication to manage withdrawal symptoms and left the hospital three days earlier on average than infants who received only usual care. Another SBIR project focuses on treating NOWS by retooling an FDA-approved technology for opioid withdrawal in adults, called transcutaneous auricular neurostimulation. This technology uses an earpiece to painlessly stimulate nerves near the ears, transmitting signals that are believed to cause release of the brain's own endogenous opioids and help control withdrawal. A safety trial found that this technology was well-tolerated by infants with NOWS, and efficacy trials are planned. As a planned.

OTIPI also supports development of SUD treatment modalities that are powered by AI. One example is Woebot, a conversational smartphone app originally designed to help people struggling with depression. SBIR-funded researchers have modified Woebot to help people with SUD track their mood and drug cravings, and to provide coaching in behavior change. In a pilot study, after using Woebot-SUD for eight weeks, participants reported increased ability to resist craving and had improved scores on SUD screening tests.<sup>24</sup> Results from a larger trial are expected soon. Other researchers are working on a wrist-worn device for MOUD patients that would record biometric data, including mobility and skin temperature; use AI to read those data for signs of opioid withdrawal or relapse; and alert providers so that they can adjust treatment.

OTIPI is also supporting the development of tools to remove barriers to methadone treatment for OUD, which is available only from federally regulated opioid treatment programs (OTPs). Continuing flexibilities implemented during the COVID-19 pandemic allow OTPs to dispense up to 28 days of take-home methadone for stable patients, but clinicians have significant discretion—and difficult decisions—regarding take-home doses for less stable patients. In a pilot study, an OTP in Washington enabled patients to submit video confirmation that they were using their take-home methadone as prescribed. Compared to regular OTP clients, pilot participants had more days of observed dosing and were more often approved for increased take-

<sup>&</sup>lt;sup>22</sup> pubmed.ncbi.nlm.nih.gov/37184872

<sup>&</sup>lt;sup>23</sup> pubmed.ncbi.nlm.nih.gov/33762918

<sup>&</sup>lt;sup>24</sup> pubmed.ncbi.nlm.nih.gov/33755028

home doses.<sup>25</sup> Other researchers are developing a wearable biosensor to remotely monitor patients' adherence to their take-home methadone, and a new OTIPI-led program calls for further research on low-cost point-of-need approaches to lower barriers to SUD care.

**Budget Policy:** The FY 2025 President's Budget request is \$43.2 million, a decrease of \$0.2 million compared with the FY 2023 Final level.

The NIH HEAL Initiative, which is co-led by NIDA and the National Institute of Neurological Disorders and Stroke (NINDS), aims to accelerate scientific solutions to the opioid crisis. One of its major focus areas has been research on how to implement effective prevention and treatment interventions for OUD and overdose across healthcare and non-healthcare settings. The HEALing Communities Study (HCS), led by NIDA in collaboration with the Substance Abuse and Mental Health Services Administration (SAMHSA), is testing the impact of integrating evidence-based interventions for OUD and overdose in 67 communities spanning 4 states. HCS communities have deployed over 1,000 evidence-based strategies to expand access to MOUD, implement overdose education and naloxone distribution, and reduce high risk prescribing. Lessons learned from the HCS have been captured in two practice guides to help providers, public health agencies, and others assemble community coalitions and implement effective approaches to reduce overdose deaths.

The Justice Community Opioid Innovation Network (JCOIN) is studying approaches to improve evidence-based treatment for people with OUD in criminal-legal settings. JCOIN has found that MOUD access during incarceration not only saves lives but is also associated with 32 percent lower recidivism after release.<sup>26</sup> JCOIN recently disseminated a first-of-its-kind MOUD Budget Impact tool to helps jail and prison administrators estimate the cost of providing MOUD services.<sup>27</sup> NIDA plans to extend JCOIN through at least FY 2030, with a focus on research to scale up MOUD and other evidence-based interventions across justice settings and where they intersect with community-based treatment.

The HEAL Harm Reduction Research Network is developing and testing strategies to prevent overdose, transmission of HIV and hepatitis C virus, and other harms associated with drug use. Current projects are studying delivery of harm reduction services during emergency care, and via mobile vans and smartphones for hard-to-reach patients. The network is also examining the impact of state and local harm reduction policies. In New York and Rhode Island, researchers are conducting an observational study to examine outcomes associated with overdose prevention centers, which allow people to consume pre-obtained drugs under the supervision of staff who are trained in addiction and overdose treatment.

With HEAL funding, NIDA's Recovery Research Networks are working to build an evidence base for effective recovery support services. While such services have strong foundations in the lived experiences of people with SUD, most have not been formally evaluated. These networks are engaging recovery service providers and people with lived experience in research to examine

<sup>&</sup>lt;sup>25</sup> pubmed.ncbi.nlm.nih.gov/36215911

pubmed.ncbi.nlm.nih.gov/35063323
 pubmed.ncbi.nlm.nih.gov/36880906; www.jcoinctc.org/resources/budget-impact-tool

what types of recovery services work best for different people and to help link recovery services with established standards of care including MOUD.

A new HEAL program funded in FY 2023—Research to Foster an OUD Treatment System Patients Can Count On—is supporting four projects in which researchers are working with providers, patients, payors, and public health agencies to develop quality measures to improve patient outcomes in OTPs and other settings.

**Budget Policy:** The FY 2025 President's Budget request is \$355.3 million, which is equal to the FY 2023 Final level. This includes \$12.8 million for Research Management and Support related to this area of research.

**The NIDA Intramural Research Program** (IRP) conducts research to inform strategies for prevention and treatment of SUD and related health outcomes. The IRP portfolio includes research to elucidate the mechanisms underlying SUDs, evaluate potential new therapies, and identify and characterize emerging drugs such as synthetic opioids, stimulants, and cannabinoids.

IRP researchers who study how opioids affect brain and respiratory functions were able to pivot quickly to study the additive effects of xylazine. In preclinical studies, they found that fentanyl exposure causes respiratory suppression, which produces a rapid, robust decrease in oxygen flow to the brain, followed by a gradual rebound. Adding xylazine to fentanyl eliminated this rebound, prolonging the brain's oxygen deficit—which could contribute to the increasing involvement of xylazine in opioid overdose deaths.<sup>28</sup>

The IRP Designer Drug Research Unit focuses on emerging synthetic drugs with addiction potential, including stimulants called synthetic cathinones. Like other stimulants, cathinones increase dopamine levels at synapses, sometimes by blocking the activity of transporters that clean up excess dopamine. Illicit synthetic cathinones, also called "bath salts," can be extremely potent, with longer lasting effects than cocaine. IRP researchers found that this is due to unusually long-lasting inhibition of dopamine transporters. These researchers are also investigating cathinone derivatives that act preferentially on serotonin transporters as an alternative to selective serotonin reuptake inhibitors (like Prozac) for depression and anxiety. The serotonin reuptake inhibitors (like Prozac) for depression and anxiety.

IRP researchers also are examining the neurobiological basis for opioid withdrawal symptoms, which contribute to relapse risk. One recent study investigated brain pathways responsible for increased pain sensitivity (or hyperalgesia) during opioid withdrawal. Through a combination of brain imaging and chemogenetics—the use of designer drugs and receptors to control neuronal activity—researchers identified a cell type in the mouse brainstem that contributes to hyperalgesia (see cover image).<sup>31</sup> Future neuromodulation therapies or other approaches could target those cells to reduce hyperalgesia and relapse risk.

<sup>29</sup> pubmed.ncbi.nlm.nih.gov/36730201

<sup>&</sup>lt;sup>28</sup> pubmed.ncbi.nlm.nih.gov/37340247

<sup>&</sup>lt;sup>30</sup> pubmed.ncbi.nlm.nih.gov/36352123

<sup>&</sup>lt;sup>31</sup> pubmed.ncbi.nlm.nih.gov/35728954

Other IRP researchers are studying the addiction potential of S-ketamine. While S-ketamine is FDA-approved for treating severe depression, it has addiction potential that is thought to occur through opioid signaling. IRP researchers with expertise in functional brain imaging partnered with other NIH researchers to investigate this idea. They found that in rats, S-ketamine acts on opioid receptors to stimulate activity in the nucleus accumbens—a brain region associated with addiction—and that self-administration of S-ketamine leads to opioid tolerance.<sup>32</sup> Those findings have implications for monitoring the safety of S-ketamine therapy—both its current use for depression and emergent uses for opioid and stimulant addiction.

**Budget Policy:** The FY 2025 President's Budget request is \$120.9 million, an increase of \$4.3 million or 3.7 percent compared with the FY 2023 Final level.

Research Management and Support (RMS) activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. Staff supported by NIDA's RMS budget also coordinate training and career development programs to sustain a talented, diverse workforce of addiction scientists. Other RMS functions include strategic planning, coordination, dissemination of research findings and funding opportunities, program evaluation, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. NIDA RMS funding also supports evidence-based education and outreach about substance use and addiction to inform health policy and practice and provide the public with timely, accessible, trustworthy information about drug research in English and Spanish.

**Budget Policy:** The FY 2025 President's Budget request is \$92.9 million, an increase of \$7.3 million or 8.6 percent compared with the FY 2023 Final level.

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<sup>32</sup> pubmed.ncbi.nlm.nih.gov/36841701

# NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

### **Appropriations History**

Fiscal Year	<b>Budget Estimate</b>	House	Senate	Appropriation
riscai itai	to Congress	Allowance	Allowance	Appropriation
2016	\$1,047,397,000	\$1,050,875,000	\$1,069,086,000	\$1,077,488,000
Rescission				\$0
2017 1	\$1,050,550,000	\$1,107,700,000	\$1,103,032,000	\$1,090,853,000
Rescission				\$0
2018	\$864,998,000	\$1,107,497,000	\$1,113,442,000	\$1,383,603,000
Rescission				\$0
2019	\$1,137,403,000	\$1,400,126,000	\$1,420,591,000	\$1,419,844,000
Rescission				\$0
2020	\$1,296,379,000	\$1,489,237,000	\$1,490,498,000	\$1,462,016,000
Rescission				\$0
2021	\$1,431,770,000	\$1,476,590,000	\$1,505,192,000	\$1,479,660,000
Rescission				\$0
2022	\$1,852,503,000	\$1,860,329,000	\$1,832,906,000	\$1,595,474,000
Rescission				\$0
2023	\$1,843,326,000	\$1,712,832,000	\$1,684,230,000	\$1,662,695,000
Rescission				\$0
2024	\$1,663,365,000	\$1,662,695,000	\$1,672,695,000	\$1,662,695,000
Rescission				\$0
2025	\$1,668,343,000			

<sup>&</sup>lt;sup>1</sup> Budget Estimate to Congress includes mandatory financing.

### **AUTHORIZING LEGISLATION**

# NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

### Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2024 Amount Authorized	FY 2024 CR	2025 Amount Authorized	FY 2025 President's Budget
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
			>	\$1,662,695,000	>	\$1,668,343,000
National Institute on Drugs	Section 401(a)	42§281	Indefinite		Indefinite	
and Addiction	Section 401(a)	42g201	Indefinite )		indefinite )	
Total, Budget Authority				\$1,662,695,000		\$1,668,343,000

### NATIONAL INSTITUTES OF HEALTH

### National Institute on Drugs and Addiction

# Amounts Available for Obligation <sup>1</sup>

(Dollars in Thousands)

			FY 2025
Source of Funding	FY 2023 Final	FY 2024 CR	President's
			Budget
Appropriation	\$1,662,695	\$1,662,695	\$1,668,343
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	(\$0)	(\$0)	(\$0)
Other Mandatory financing	(\$0)	(\$0)	(\$0)
Subtotal, adjusted appropriation	\$1,662,695	\$1,662,695	\$1,668,343
OAR HIV/AIDS Transfers	\$670	\$0	\$0
Subtotal, adjusted budget authority	\$1,663,365	\$1,662,695	\$1,668,343
Unobligated balance, start of year	\$0	\$0	\$0
Unobligated balance, end of year (carryover)	\$0	\$0	\$0
Subtotal, adjusted budget authority	\$1,663,365	\$1,662,695	\$1,668,343
Unobligated balance lapsing	-\$46	\$0	\$0
Total obligations	\$1,663,319	\$1,662,695	\$1,668,343

Excludes the following amounts (in thousands) for reimbursable activities carried out by this account: FY 2023 - \$15,468 FY 2024 - \$15,000 FY 2025 - \$15,000

### NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

# Budget Authority by Object Class <sup>1</sup> (Dollars in Thousands)

		FY 2024 CR	FY 2025 President's Budget
Total co	mpensable workyears:		
	Full-time equivalent	445	470
	Full-time equivalent of overtime and holiday hours	1	1
	Average ES salary	\$191	\$195
	Average GM/GS grade	13.0	13.0
	Average GM/GS salary	\$144	\$148
	Average salary, Commissioned Corps (42 U.S.C. 207)	\$163	\$170
	Average salary of ungraded positions	\$144	\$148
	OBJECT CLASSES	FY 2024 CR	FY 2025 President's Budget
	Personnel Compensation		
11.1	Full-Time Permanent	\$39,741	\$42,351
11.3	Other Than Full-Time Permanent	\$15,018	\$15,438
11.5	Other Personnel Compensation	\$2,114	\$2,173
11.7	Military Personnel	\$547	\$573
11.8	Special Personnel Services Payments	\$7,633	\$7,847
11.9	Subtotal Personnel Compensation	\$65,053	\$68,382
12.1	Civilian Personnel Benefits	\$21,618	\$22,341
12.2	Military Personnel Benefits	\$40	\$42
13.0	Benefits to Former Personnel	\$0	\$0
	Subtotal Pay Costs	\$86,711	\$90,766
21.0	Travel & Transportation of Persons	\$1,221	\$1,248
22.0	Transportation of Things	\$48	\$49
23.1	Rental Payments to GSA	\$0	\$0
23.2	Rental Payments to Others	\$3	\$3
23.3	Communications, Utilities & Misc. Charges	\$72	\$73
24.0	Printing & Reproduction	\$0	\$0
25.1	Consulting Services	\$85,946	\$84,538
25.2	Other Services	\$26,260	\$25,238
25.3	Purchase of Goods and Services from Government Accounts	\$110,812	
25.4	Operation & Maintenance of Facilities	\$1,812	\$1,812
25.5	R&D Contracts	\$7,980	\$8,155
25.6	Medical Care	\$564	\$586
25.7	Operation & Maintenance of Equipment	\$3,907	\$3,993
25.8	Subsistence & Support of Persons	\$0	\$0
25.0	Subtotal Other Contractual Services	\$237,281	\$235,559
26.0	Supplies & Materials	\$6,108	\$6,135
31.0	Equipment	\$8,551	\$8,640
32.0	Land and Structures	\$0	
33.0	Investments & Loans	\$0	
41.0	Grants, Subsidies & Contributions	\$1,322,700	\$1,325,870
42.0	Insurance Claims & Indemnities	\$0	
43.0	Interest & Dividends	\$0	\$0
44.0	Refunds	\$0	\$0
	Subtotal Non-Pay Costs	\$1,575,984	· ·
	Total Budget Authority by Object Class	\$1,662,695	

Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

### NATIONAL INSTITUTES OF HEALTH

### National Institute on Drugs and Addiction

### **Salaries and Expenses**

(Dollars in Thousands)

		FY 2025
Object Classes	FY 2024 CR	President's
,		Budget
Personnel Compensation		
Full-Time Permanent (11.1)	\$39,741	\$42,351
Other Than Full-Time Permanent (11.3)	\$15,018	\$15,438
Other Personnel Compensation (11.5)	\$2,114	\$2,173
Military Personnel (11.7)	\$547	\$573
Special Personnel Services Payments (11.8)	\$7,633	\$7,847
Subtotal, Personnel Compensation (11.9)	\$65,053	\$68,382
Civilian Personnel Benefits (12.1)	\$21,618	\$22,341
Military Personnel Benefits (12.2)	\$40	\$42
Benefits to Former Personnel (13.0)	\$0	\$0
Subtotal Pay Costs	\$86,711	\$90,766
Travel & Transportation of Persons (21.0)	\$1,221	\$1,248
Transportation of Things (22.0)	\$48	\$49
Rental Payments to Others (23.2)	\$3	\$3
Communications, Utilities & Misc. Charges	\$72	\$73
(23.3)	·	Φ13
Printing & Reproduction (24.0)	\$0	\$0
Other Contractual Services		
Consultant Services (25.1)	\$70,401	\$72,152
Other Services (25.2)	\$26,260	\$25,238
Purchase of Goods and Services from	\$99,591	\$100,015
Government Accounts (25.3)		·
Operation & Maintenance of Facilities (25.4)	\$1,812	\$1,812
Operation & Maintenance of Equipment (25.7)	\$3,907	\$3,993
Subsistence & Support of Persons (25.8)	\$0	\$0
Subtotal Other Contractual Services	\$201,971	\$203,211
Supplies & Materials (26.0)	\$6,108	\$6,135
Subtotal Non-Pay Costs	\$209,423	\$210,719
Total Administrative Costs	\$296,134	\$301,485

# NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

### **Detail of Full-Time Equivalent Employment (FTE)**

O.CC	F	FY 2023 Final FY 2024 CR			FY 2025 President's Budget				
Office	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Office of the Director Direct:	2.5		25	27		27	20		20
Total:	25 25	-	25	27	-	27	29 29	-	29 29
Total:	23	-	25	21	-	21	29	_	29
Division of Extramural Research									
Direct:	55	1	56	60	1	61	62	1	63
Total:	55	1	56	60	1	61	62	1	63
Office of Management									
Direct:	82	-	82	86	-	86	92	-	92
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	82	-	82	86	-	86	92	-	92
Office of Science Policy and Communication									
Direct:	29	_	29	29	-	29	31	-	31
Total:	29	-	29	29	-	29	31	-	31
Division of Epidemiology, Services and Prevention									
Research									
Direct:	32	2	34	36	2	38	38	2	40
Reimbursable:	_	_	_	_	[ <u> </u>	_	_	_	_
Total:	32	2	34	36	2	38	38	2	40
Division of Neuroscience and Behavior									
Direct:	28	-	28	29	-	29	31	-	31
Total:	28	-	28	29	-	29	31	-	31
Division of Therapeutics and Medical Consequences									
Direct:	27	_	27	28	_	28	30	_	30
Total:	27	_	27	28	-	28	30	-	30
Center for the Clinical Trials Network									
Direct:	13	_	13	14	<u>-</u>	14	14	_	14
Total:	13	-	13	14	-	14	14	-	14
Intramural Research Program									
Direct:	123	1	124	131	1	132	138	1	139
Reimbursable:	1	<u> </u>	1	1	<u>^</u>	132	1 1		1
Total:	124	1	125	132	1	133	139	1	140
Total	415	4	419	441	4	445	466	4	470
Includes FTEs whose payroll obligations are supporte						113	100	· ·	1,0
FTEs supported by funds from Cooperative Research	0			0	0	0	0	0	0
and Development Agreements.	0	L 0	U				U	U	
FISCAL YEAR	Average GS Grade								
2021	13.0								
2022 2023					13.0 13.2				
2023					13.2				
2024					13.2				

# NATIONAL INSTITUTES OF HEALTH National Institute on Drugs and Addiction

### **Detail of Positions** <sup>1</sup>

GRADE	FY 2023 Final	FY 2024 CR	FY 2025		
	F 1 2025 Final	F1 2024 CK	President's Budget		
Total, ES Positions	1	1	1		
Total, ES Salary	\$181,544	\$190,984	\$194,804		
General Schedule					
GM/GS-15	63	68	72		
GM/GS-14	90	97	103		
GM/GS-13	115	124	133		
GS-12	42	46	48		
GS-11	14	15	16		
GS-10	0	0	0		
GS-9	5	5	6		
GS-8	6	6	7		
GS-7	2	2	2		
GS-6	1	1	1		
GS-5	4	4	5		
GS-4	1	1	1		
GS-3	0	0	0		
GS-2	0	0	0		
GS-1	0	0	0		
Subtotal	343	369	394		
Commissioned Corps (42 U.S.C.					
207)					
Assistant Surgeon General	0	0	0		
Director Grade	0	0	0		
Senior Grade	3	3	3		
Full Grade	1	1	1		
Senior Assistant Grade	0	0	0		
Assistant Grade	0	0	0		
Junior Assistant	0	0	0		
Subtotal	4	4	4		
Ungraded	92	92	92		
Total permanent positions	347	373	398		
Total positions, end of year	440	466	491		
Total full-time equivalent (FTE)	419	445	470		
employment, end of year					
Average ES salary	\$181,544	\$190,984	\$194,804		
Average GM/GS grade	13.2	13.2	13.2		
Average GM/GS salary	\$137,104	\$144,233	\$147,118		

<sup>&</sup>lt;sup>1</sup> Includes FTEs whose payroll obligations are supported by the NIH Common Fund.