National Institutes of Health
Turning Discovery Into Health

HELPING TO END ADDICTION LONG-TERM® INITIATIVE: ACCOMPLISHMENTS 2018 – 2025

About the NIH HEAL Initiative

The National Institutes of Health (NIH) Helping to End Addiction Long-term® Initiative, or NIH HEAL Initiative®, launched in 2018, is an NIH-wide effort that seeks to speed scientific solutions to the overdose epidemic, including opioid and stimulant use disorders, and the crisis of chronic pain. The initiative is jointly led by the National Institute on Drug Abuse (NIDA) and the National Institute of Neurological Disorders and Stroke (NINDS).

Now in its eighth year of funding, HEAL is making progress toward improving the lives of individuals and communities affected by substance use, overdose, and pain. To date, HEAL has supported research leading to more than 40 investigational new drug and device designations from the U.S. Food and Drug Administration (FDA) to begin human trials for novel treatments for pain, opioid and other substance use disorders, and overdose; driven change in clinical practice for opioid and other substance use disorders within different health care settings and justice systems; and changed the way babies with neonatal opioid withdrawal syndrome (NOWS) are treated. Building on this success, HEAL is extending programs such as the Justice Community Overdose Innovation Network (JCOIN) and launching new efforts such as the HEAL PAIN Cohort program, which will advance the field in the long term by rigorously training early career clinical pain researchers across scientific disciplines.

Key HEAL Achievements

- **Accelerating overdose-reversal and SUD therapeutic development**: Launched phase II clinical trials of monoclonal antibodies and antidote drugs which prevent fentanyl or methamphetamine from entering the brain. Supported development of Naloxometer, an advanced pacemaker-like device technology to automatically detect and treat overdose by delivering naloxone. Launched clinical trials to test the efficacy of GLP-1 receptor agonist medications for reducing drug cravings and fostering remission in opioid and stimulant use disorders patients.
- **Developing and Optimizing non-addictive therapies to treat pain:** Contributed to fundamental research leading to the recent FDA approval of suzetrigine for moderate to severe acute pain. Launched phase II clinical trial for ATX101, an implantable medication designed to provide extended pain relief after total knee replacement surgery, which may reduce the need for opioids and improve patient recovery. Initiated clinical testing for a new non-opioid drug for neuropathic pain, AFA-281, and wearable pain assessment system called KnowPain.
- **Expanding evidence-based practice research in different healthcare settings**: Developed models for initiating buprenorphine in emergency room, primary care, infectious disease clinics, and in pharmacies and deploying innovative models for nurses and clinicians to bring treatment to rural areas through local clinics and telehealth.
- **Leveraging screening platforms for non-addictive pain therapeutics:** Established models to rigorously profile, screen, and validate viable non-opioid treatment interventions using a high-throughput screening platform for pain. Identified and validated novel targets for inflammatory pain, osteoarthritis pain, chronic pain, and post-surgical pain.
- **Increasing and optimizing treatments in justice settings:** Demonstrated that implementing the use of medications for opioid use disorder (MOUD) in jails and prisons prior to the release of incarcerated individuals with OUD increased their retention in treatment post release, reduced by 52% their risk of a fatal opioid overdose, by 24% their risk of a non-fatal opioid overdose, by 56% their risk of death from any cause, and by 12% their risk of reincarceration.
- **Reducing pain and opioid use:** Tested an adapted behavioral (pain coping skills) intervention for people with end-stage kidney disease undergoing long-term dialysis that reduced the extent to which pain affected daily activities, mood, and relationships. Showed that enabling women to personalize their pain relief strategy following C-section surgery resulted in fewer opioid prescriptions but with the same effectiveness as the current standard of care in a study conducted through the Pain Management Effectiveness Research Network.
- **Advancing the science of recovery**: Launched network to build the infrastructure for conducting rigorous research on evaluating recovery support services, including youth programs, recovery housing, and recovery community centers, to better understand what works.
- **Developing novel chemistry, biomarkers and testing methodologies for HEAL:** Created a comprehensive, annotated HEAL library of compounds, including drugs, probes, and tools for addiction and pain-relevant targets. Nearly 3,000 small molecules associated with approximately 60 known and hypothesized HEAL-relevant

targets have been assembled, curated, and annotated for developing novel treatments for both addiction and pain.

- **Understanding chronic pain signatures in the brain:** For the first time, researchers measured pain-related brain activity in real time in the brains of people with chronic pain disorders caused by stroke or amputation. This study is an important step toward developing personalized therapies for treating pain by altering brain activity.
- **Advancing care for neonatal opioid withdrawal:** Showed that newborns with NOWS who were cared for with the Eat, Sleep, Console (ESC) approach were ready for release from hospital almost 1 week earlier compared to infants with NOWS receiving usual care. The infants cared for with ESC were also less likely to require opioids to manage withdrawal symptoms. Funded the development of an alternative approach for treating NOWS that utilizes a hospital bassinet pad that delivers gentle, random vibration called Stochastic Vibrotactile Stimulation (SVS) that reduces hyperirritability in opioid-exposed newborns.

HEAL Program Highlights

- **HEALthy Brain and Child Development (HBCD) Study** – First release of study data to the public completed in 2025, allowing researchers to examine a wide-range of questions, including how environments and substances impact infant and child development.
- **Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR) Program** – Starting phase 2 in 2025 and continuing support for real-world, patient-centered research targeting both chronic pain and harmful opioid use at the same time.
- **Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM)** – Completed enrollment for five clinical trials and scheduled to publish first primary outcome paper in mid-September 2025.
- **Back Pain Consortium (BACPAC) Research Program** – Investigators designed and launched the Biomarkers for Evaluating Spine Treatments (BEST) clinical trial and scheduled to publish the primary outcome paper at the end of 2025.
- **Native Collective Research Effort to Enhance Wellness (N CREW) Program** – Launched in 2024 to advance research led by Native American communities on substance use and pain.
- **Pain Management Effectiveness Research Network (ERN)** – Completed enrollment for seven multisite randomized comparative effectiveness trials addressing a variety of pain conditions in real-world settings. Primary results for two trials have been published with results for the other five trials expected soon.
- **Justice Community Overdose Innovation Network (JCOIN)** – Launched phase 2 in 2024, focused on the prevention and treatment of OUD among the high-risk justice-involved population.
- **HEAL Data Ecosystem (HDE)** – Invested in an innovative cloud-based environment that supports open science by allowing scientific partners to easily find and analyze HEAL supported data and research results.

HEAL by the Numbers

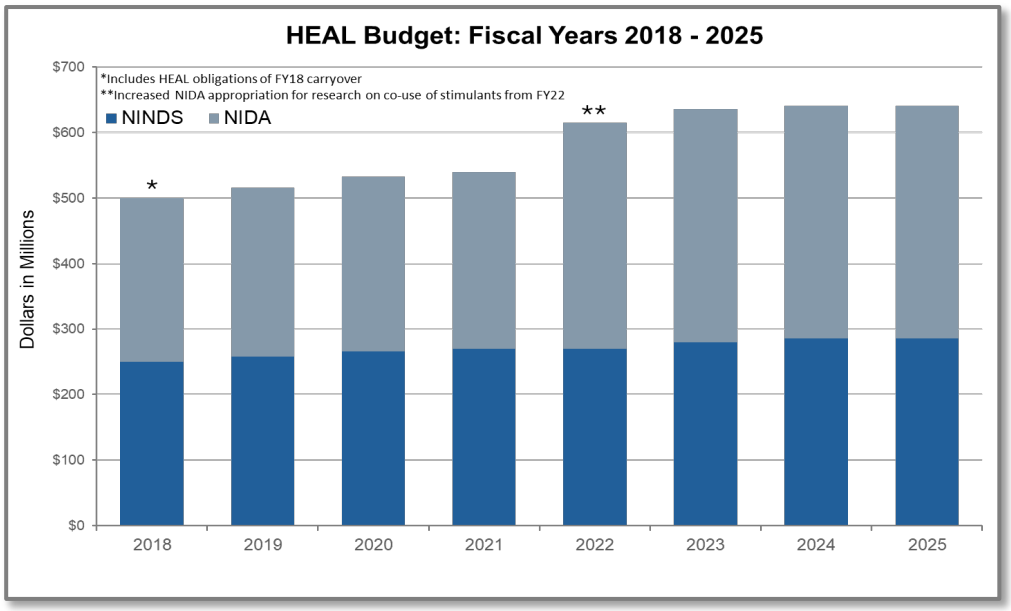
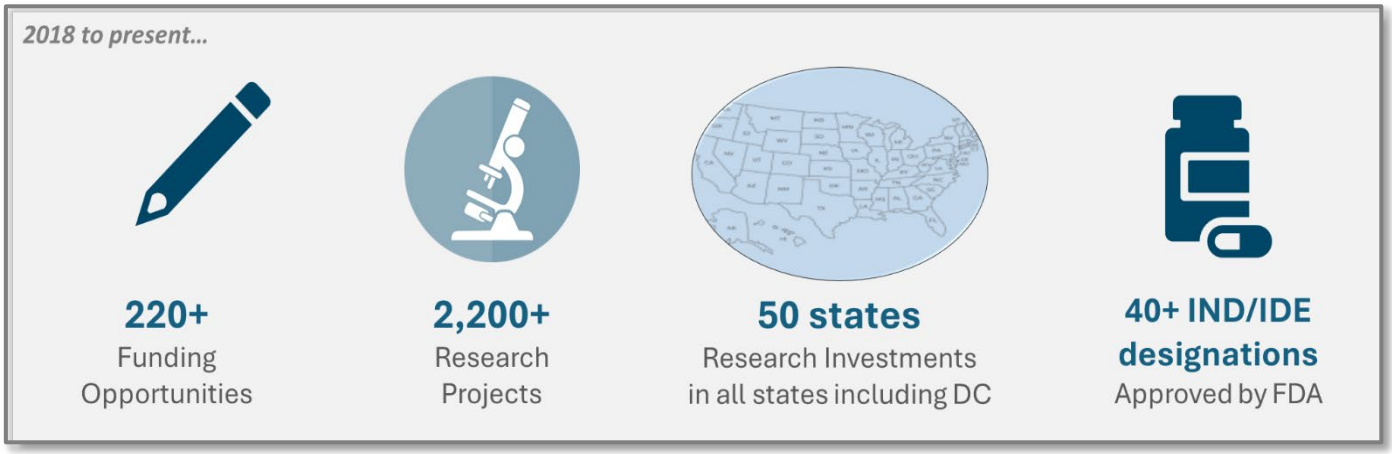


Figure 1. NIH HEAL Initiative Funding by IC (NIDA and NINDS)

Supported more than 8,000 publications between FY18 to FY24



Future Outlook

The U.S. overdose epidemic, after reaching a peak of 108,000 annual fatalities in 2022, has finally begun to subside, with CDC provisional data of drug overdose deaths showing a 25% annual decline in March 2025. Despite this encouraging decline, far too many people suffer from and still die of drug overdose, and it remains the leading cause of death for Americans ages 18-24. Chronic pain continues to burden more than 50 million Americans and is on the rise, affecting nearly 1 in 4 adults in the U.S. in 2023 – up from 1 in 5 adults in 2019. Continued investment in the NIH HEAL Initiative is critical to build upon the significant progress already made possible by HEAL-funded investigators to improve the lives of all individuals affected by overdose, substance use, and pain. HEAL looks forward to working with other federal agencies, researchers, people with lived and living experience of substance use and pain, and key community partners, toward this goal.