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NIH National Institutes of Health
HEAL Initiative

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REPORT**

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Research in Action



NIH • Helping to End Addiction Long-term

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DIRECTOR'S MESSAGE

The NIH Helping to End Addiction Long-term® Initiative, or HEAL, enters its third year facing an evolving public health crisis of chronic pain and opioid misuse, addiction, and overdose. The crisis has shifted from overdoses involving prescription opioids in the 1990s to heroin overdoses the next decade to today's overdose crisis¹ driven by powerful synthetic opioids such as fentanyl along with overdoses from psychostimulants. Science too changes, and HEAL's research efforts combine the urgency of the task at hand with creative ideas and hard work partnering with communities to save lives. HEAL's research efforts align with the U.S. Department of Health and Human Services Overdose Prevention Strategy,² and strive to address the wide-ranging needs of people who live with pain and those who use drugs.

HEAL-funded research acknowledges the vital role an individual's personal environment plays in drug use, development of chronic pain, and related health outcomes. For this reason, HEAL is funding science to advance health equity³ that combines interventions at individual and community levels. We are deliberately testing integrated approaches that reflect real-world scenarios and their associated challenges. Social and environmental factors such as poverty and lack of access to care have created stark inequities in the ability of some people to get adequate treatment for pain and substance use disorders. HEAL research will probe these systems of influence, toward designing and testing multilevel interventions in disproportionately affected populations.

Guided by formative work by the HEAL Community Partner Committee,⁴ HEAL will continue to actively seek input from people with lived experience of pain, drug use, addiction, and recovery to shape study design, research, recruitment – and the way we think about the dual crises of poorly treated pain and addiction. The HEAL research landscape is broad and deep, and the initiative is committed to accelerating translation and implementation of findings to improve health and save lives. One strategy is through research conducted in places where people seek care, toward building an evidence base for insurers and opening the door to wider availability of scientifically sound treatments for both pain and addiction.

This vital research builds on progress in fundamental science in the areas of medication development for both pain and substance use disorders, nonpharmacological approaches to pain management, integrating mental health into primary care, and testing multimodal and multidisciplinary systems of care for both pain and addiction. Several HEAL-funded studies involve partners in healthcare including primary care providers, nurse care managers, pharmacists, and others to identify patients at risk for progressing from moderate to a more

severe opioid use disorder, as well as to tailor pain management strategies to patient needs and preferences.

HEAL-funded research is also working to identify (and overcome) roadblocks that prevent effective treatments from being used by providers and patients, including building the evidence base for large insurers to cover safe and effective treatments for pain and addiction. Ongoing HEAL research is teaming with communities to ensure research is relevant and applicable – a necessity since there is no time to waste. HEAL also continues to monitor, and increase, when necessary, the workforce of people equipped to address topics central to the HEAL mission as efforts continue, and HEAL’s impact is ever more apparent, as demonstrated across our 31 programs and described in this report.

SELECTED ACCOMPLISHMENTS FROM THE NIH HEAL INITIATIVE

This past year, HEAL-funded scientists have worked hard, partnering with communities to find scientific solutions for public health challenges that continue to evolve. The HEAL community encountered another year of pandemic-related impediments but pressed ahead, launching clinical trials, and recruiting research participants, advancing promising targets and devices along the drug development pipeline – keeping a clear focus on the gravity of these crises and the need to obtain perspectives and guidance from people with lived experience.

Putting Science Into Action for People and Communities

While it is important to identify novel approaches for treating opioid use disorder (OUD), overdose, and pain, HEAL funds research to determine the best ways to improve integration of existing evidence-based treatments into practice, as well as to address disparities in access to these treatments. These ongoing studies have made considerable progress over the past year.

As the largest community-based implementation study in the field of addiction research, the HEALing Communities Study aims to reduce fatal overdoses in 67 communities across New York, Massachusetts, Kentucky, and Ohio. Despite delays due to COVID-19, researchers have conducted tailored communications campaigns and worked alongside communities to select and implement hundreds of evidence-based practices to increase overdose education, naloxone distribution, access to medications for OUD, and safe opioid prescribing in the initial group of participating communities. This past year, the HEALing Communities Study research team gathered data stratified by race and ethnicity, sex, and age, to observe impacts of the opioid crisis and effects of interventions on specific populations. This analysis demonstrated a

disturbing increase in overdose death rates for Black/African American individuals from 2018 to 2019, especially since rates for other race and ethnicity groups held steady or decreased.⁵

Although effective medications used to treat OUD hold great potential to improve outcomes for incarcerated and recently released individuals, most U.S. jails and prisons do not offer these treatments. The Justice Community Opioid Innovation Network (JCOIN)⁶ is designed to advance scientific knowledge on effective policies, practices, and interventions for treating OUD, and to expand their use in daily practice. JCOIN research is carried out in partnership with local and state justice systems and community-based treatment providers to ensure that interventions being tested are feasible in real-world settings. Many studies have already generated important findings. For example, one study⁷ showed that offering buprenorphine to people in jail with OUD reduced rearrest and reconviction, a finding that could encourage jails and prisons to offer treatment and linkage to support systems for people with OUD.

The Pain Management Effectiveness Research Network (ERN)⁸ aims to improve pain care by evaluating the effectiveness of a broad range of therapies to guide clinical practice. The Network has taken on trials of treatments for pain associated with chronic overlapping pain conditions, cancer pain, musculoskeletal pain, perioperative pain, post-Cesarean delivery pain, and knee osteoarthritis pain, and plans to welcome new research teams who will conduct effectiveness clinical trials aiming to improve pain management for people with sickle cell disease. Despite COVID-19 delays, all ERN clinical trials continue to recruit participants and implemented study design changes such as remote data collection, when possible.

The Pragmatic and Implementation Studies to Improve the Management of Pain (PRISM)⁹ program supports research conducted within healthcare systems that are evaluating whether interventions can improve pain management in routine healthcare settings. For example, one trial is testing two complementary and integrative treatment approaches – guided relaxation and acupuncture – in people who have sickle cell disease to determine the effectiveness of both approaches for relieving pain and for reducing opioid use. Lessons learned from PRISM research were recently added to the NIH Pragmatic Trials Collaboratory's online *Living Textbook of Pragmatic Clinical Trials*¹⁰ to inform the conduct of future research.

This past year, the Hemodialysis Opioid Prescription Effort (HOPE)¹¹ research program launched its pain coping skills training intervention and began enrolling research participants. The HOPE study is testing the use of pain coping skills and buprenorphine in people with end-stage renal disease receiving hemodialysis. The HOPE study is emblematic of a whole-person, multidisciplinary approach for treating pain, and it continues to be a leader in including patients

as partners in various stages of the research process. Currently, 18% of HOPE research participants are Hispanic/Latino, and 53% of participants are Black/African American.

A new HEAL research program designed to be holistic in its approach to meeting people's real-world needs is the Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR)¹² program involving research participants with both chronic pain and risky opioid use or OUD. HEAL developed this program recognizing that these individuals often fall through the cracks of the healthcare system because of fragmented care, stigma from healthcare providers, and a lack of evidence-based treatments for both OUD and chronic pain. The program is expected to begin recruiting research participants in summer 2022 and will test a range of interventions including behavioral therapies (such as acceptance commitment therapy with mindfulness-based relapse prevention), novel healthcare delivery approaches, and flexible or non-standard buprenorphine dosing that could ease the transition off opioids for people with chronic pain.

Advancing Promising Therapeutics to Clinical Application

For the second year in a row, HEAL made progress advancing experimental treatments and medical devices for pain and OUD toward approval by the U.S. Food and Drug Administration (FDA). The first step in this process is applying for Investigational New Drug (IND) status, which, if granted, permits scientists who have demonstrated in animal studies that a therapy is safe to begin testing that therapy in humans. The evidence generated from these early phases of testing meant to establish safety profiles sets the stage for larger studies, which will begin testing how well the drugs work while continuing to monitor for adverse events.

This past year, HEAL researchers completed a phase 1 clinical trial of a brand-new type of non-opioid, oral treatment for inflammatory and neuropathic pain, showing that the drug is safe to use in humans. Other HEAL clinical studies have shown clinically meaningful pain reduction through use of virtual reality psychological therapy.

As of March 2022, HEAL investigators had filed 21 INDs for medications development, exceeding its 5-year goal of producing 15 INDs in its first 5 years.¹³ Maintaining this momentum, this past year, the FDA cleared four additional IND applications from HEAL-funded researchers. One of the new HEAL INDs is for a once-weekly form of methadone, an effective treatment for opioid use disorder but one that people must take every day, creating challenges. HEAL-funded phase I clinical trials will begin soon to test an enriched, "strong," form of methadone that releases drug into the body over time, making it more convenient for people to take this medication. This past year, HEAL scientists also showed that a 6-month implant of the

medication naltrexone was safe to use in humans and more stable in the bloodstream than currently used monthly Vivitrol®.

Other HEAL projects already granted an IND reported exciting progress in 2021. The first group of research participants who received an experimental opioid vaccine meant to block the rewarding effects of oxycodone did not experience any health problems from the vaccine, meaning this important research can progress to testing in more people with opioid use disorder. HEAL researchers are also pursuing vaccines against fentanyl and heroin. In addition, the HEAL-funded HOPE study received an IND to use buprenorphine for pain relief in people with end-stage kidney disease receiving dialysis.

Some FDA-approved medications for other conditions are also potential treatments for OUD and pain. For example, the insomnia treatment suvorexant is being tested for its ability to improve sleep and address other withdrawal symptoms in people with OUD. HEAL scientists showed that suvorexant effectively treats sleep problems related to withdrawal, mitigates opioid craving, and has little potential for harmful use. Based upon earlier research in animals and a small study in humans, another HEAL study is testing whether cannabidiol, or CBD, can prevent heroin craving.

Advancing Health Equity

Black Americans are less likely than Whites to receive pain treatment (including opioids) when they are needed, and non-Whites are less likely to receive advanced diagnostic imaging to guide pain treatment and less likely to be treated with non-pharmacological rehabilitative approaches such as physical therapy or surgery.¹⁴ For many people, pain and the consequences of inadequate treatment, including harmful opioid use and addiction, are made worse by social and environmental factors such as poverty and lack of access to care.¹⁵ These factors are themselves influenced by systemic racism, stigma, and bias from some providers – as well as discrimination against some patients. Facing these serious gaps in pain and addiction care, HEAL is funding new research on evidence-based interventions that target health disparities in pain management¹⁶ and social factors affecting behavioral health.¹⁷

HEAL maintains a clear and consistent focus on patient engagement such that its research and results are relevant for patients, and to help engender trust between researchers and communities. Minority communities may be mistrustful of scientific research, don't see the relevance of participation, or have other reasons to question the value and purpose of research. The HEAL Community Partner Committee was established in 2021 to provide input on key issues faced by individuals affected by pain conditions or opioid use disorder to ensure the relevance and generalizability of HEAL-supported research. Input from the committee is helping

to identify, refine, and prioritize patient and community engagement activities and scientific research activities and protocols across the initiative. The committee is made up of people with lived experience, advocates, and/or family members of someone with pain or addiction. In 2021, this group tasked HEAL with developing a survey to determine the extent of patient engagement that currently exists across HEAL studies to serve as a baseline for monitoring progress and gaps. The HEAL research community is currently completing the survey.

As many HEAL studies began enrolling participants in 2021, HEAL provided investigators with funds to enhance patient engagement activities and recruitment, retention, and meaningful inclusion of patients from backgrounds typically underrepresented in research. Examples of HEAL program approaches include a cohort study to investigate barriers to enrollment for ethnic and racial minority patients in large-scale postoperative pain clinical trials (ERN); including peer navigators within study teams (HEALthy Brain and Child Development Study and Advancing Clinical Trials for Neonatal Opioid Withdrawal); meetings with community advisory boards (IMPOWR); and the HOPE study's translation of recruitment materials, pain coping skills materials, and consent forms into Spanish and hiring of Spanish-speaking coaches and research coordinators to make the trial accessible to Spanish-speaking patients.

Harnessing the Power of Novel Technologies

As HEAL invests in research to develop new behavioral interventions, drugs, and devices for both pain and OUD, the initiative is also investing in novel technologies to leverage development of non-addictive therapies and interventions. HEAL's targeted support in this area is an important component of its research portfolio and will help expand pre-existing scientific knowledge to help individuals as quickly as possible, and progress is evident.

Numerous HEAL research studies are trying to expand the number of user-friendly options for treatment. For example, one HEAL-supported Small Business Innovation Research (SBIR) awardee has developed a text-based peer support app in which individuals can support each other at any time from any place. The key innovation behind this technology is use of natural language processing algorithms that identify messages within peer groups that need specialized moderator attention (for example, screening for abusive content or an alert that a person is at risk to themselves or others or may relapse). This research team is now partnering with a state healthcare plan to offer the app to more than 10,000 people with OUD to help them get peer support.

HEAL is leveraging other technologies to address risky opioid use and overdose. For example, HEAL-funded investigators are developing an implanted medical device that can sense the presence of an opioid overdose (via dangerously low blood oxygen levels), automatically inject

naloxone, and alert first responders if no one is around to give this lifesaving treatment. To date, this experimental device has worked well in rodents and will be tested next in larger animals, such as pigs, whose body functions more closely resemble those of the human body.

Many questions need to be answered before new technologies and devices can be used to treat conditions like addiction and pain in humans. For this reason, the HEAL Initiative also funds translational research, including studies to determine the effectiveness of new approaches to pain management. The HEAL Back Pain Consortium Research Program (BACPAC)¹⁸ is funding work that aims to develop and perfect a robotic exosuit to help individuals with low back pain. In preliminary tests, the technology has been shown to comfortably offload the back, minimize a user's pain, and increase users' confidence to perform various physical tasks. The HEAL researchers next plan to test this wearable technology in two clinical trials to determine if the technology can prevent the occurrence or recurrence of lower back pain and improve function and/or reduce pain in individuals undergoing physical therapy for low back pain.

HEAL is also supporting two clinical trials to test research technologies that have received an FDA Investigational Device Exemption. The first is a clinical study to test deep brain stimulation in people with opioid use disorder that have not responded to treatment. Excitingly, the study's preliminary results show that two of three research participants stopped using drugs, with one participant still drug-free after more than 24 months. The scientists will next determine how well this approach works in keeping people drug-free for even longer periods of time. Another HEAL device study received FDA approval to test a high-resolution spinal cord device that precisely delivers stimulation therapy to treat neuropathic pain. This HEAL research team has successfully implanted a 64-lead stimulator into 11 individuals to date and plans to recruit more research participants in the coming year.

Identifying Promising Therapeutics and Interventions

Only a small fraction of potential treatments tested are suitable for testing in humans. Researchers must screen many potential medications to identify even one promising molecule. HEAL aims to improve this crucial research infrastructure with novel screening platforms for both pain and harmful opioid use and addiction.

Bioengineering approaches that mimic body systems can be used to sort quickly through many possible treatments. This past year, HEAL scientists developed a 3D engineered cellular model of brain circuits responsible for addiction, intended to assess the addictive potential of emerging pain treatments. In this research, the scientists created a lab-grown circuit that screens molecules in minutes. Another HEAL-funded group created and tested an innervated knee joint bioreactor to study osteoarthritis pain toward informing a more personalized

medicine-based approach for this pain condition that affects millions of people. In addition, five translational device projects are currently in early-stage clinical trials to demonstrate safety of their interventions and test outcome measures of pain relief.

Screening platforms of pain and addiction

The HEAL Preclinical Screening Platform for Pain (PSPP)¹⁹ identifies and profiles non-opioid treatments (small molecules, biologics, devices, or natural products) for their potential in treating acute or chronic pain. Currently, this program is profiling 30 potential treatments in models that mimic human pain-related conditions including chemotherapy-induced neuropathic pain, joint damage-associated pain, post-surgical pain, and other conditions, while also ruling out liability for harmful use. Some of these are treatments being studied for other indications and others are new.

Additionally, through the SBIR program, four HEAL-funded small businesses have identified and validated novel targets for inflammatory pain, osteoarthritis pain, chronic pain, and post-surgical pain.

Expanding clinical trial networks

HEAL continues to work with the National Drug Abuse Treatment Clinical Trials Network (CTN)²⁰ to build on existing research networks that are already well-connected within communities across the nation. In 2021, the CTN launched a clinical trial to test use of long-acting buprenorphine for people with methamphetamine use disorder with risky opioid use. Through the CTN, another HEAL-funded study showed that delivery of high-dose buprenorphine in the emergency department is safe and well tolerated in people with OUD experiencing withdrawal.²¹ While these findings need to be replicated, this study suggests that emergency medicine providers can safely and effectively begin high-dose buprenorphine therapy. These findings are an important step forward to improve existing treatment strategies for people with OUD. The dosing strategy provides better protection against overdose while also blunting the euphoric and reinforcing effects of any opioids taken after a person leaves the emergency department and before obtaining follow-up care. This is a particularly high-risk time given the increasing prevalence of fentanyl.

The NIH-funded Early Phase Pain Investigation Clinical Network (EPPIC-Net)²² is a nationwide web of 12 pain research programs focused on quickly and efficiently conducting simultaneous, multisite research studies to evaluate a variety of pain treatments, including repurposed drugs that were originally tested to treat conditions other than pain. EPPIC-Net is testing not only medications but also surgical interventions, devices, and novel approaches like cell-based

therapies. In 2021, EPPIC-Net began recruiting research participants for its first clinical trial testing a novel treatment for pain due to moderate to severe knee osteoarthritis, a common and debilitating condition. An innovative aspect of this pain trial network is the use of objective pain measures in response to tested treatments, including quantitative sensory testing (which detects subtle changes in sensory function, including hot, cold, touch, and vibration) and ecological momentary assessment that monitors an individual's behaviors and experiences in real time using digital platforms. EPPIC-Net has also begun developing a master platform protocol for painful diabetic peripheral neuropathy, an extremely painful condition with few effective treatments. Modeled after the success of platform protocols in oncology clinical trials, this study approach enables multiple experimental treatments to be tested in a single trial framework.

Developing Tools to Facilitate Data Sharing: The HEAL Data Ecosystem

Through the HEAL Data Ecosystem,²³ the initiative promotes maximum transparency with respect to data sharing among the broad community of researchers, healthcare providers, community leaders, policy makers, and other HEAL stakeholders who can benefit from the results of initiative research. One way HEAL is approaching this important goal is by offering additional financial resources and outside expertise to help HEAL scientists to make their data FAIR (findable, accessible, interoperable, and reusable). This past year, HEAL funded an expert group of data scientists, the HEAL Stewards, which works routinely with HEAL research teams to provide guidance in making their data FAIR and best practices for sharing the diverse datasets generated by HEAL-funded projects. HEAL is currently continuing to build the HEAL Platform, a cloud-based environment for sharing and analyzing data. In the coming year, HEAL plans to fund a large community engagement contract to ensure HEAL data, through the platform, is accessible to communities, providers, and policy makers.

Across the initiative, HEAL research programs are working hard to standardize data collection and terminology to make it sharable and open for discovery by other researchers. For example, the HEAL Prevention Cooperative program agreed upon a standard strategy to measure prevention intervention start-up and delivery costs, toward enabling broader use of research findings to inform policy. The JCOIN program created a free, open-source data warehouse focused on the multi-dimensional risk environment affecting opioid use and health outcomes, particularly for justice communities across the country. JCOIN has also developed nationally representative public opinion surveys to provide a pulse check on Americans' views toward opioids, individuals with criminal justice involvement, and other topical issues (e.g., COVID-19).

Conclusion

Research provides hope for saving lives and creating healthy futures, and the NIH HEAL Initiative continues to invest in a range of research strategies to end addiction long-term. There are still many questions about biological and sociocultural determinants of the intertwined public health challenges of poorly treated pain and risky opioid use and addiction. HEAL has issued dozens of new funding announcements to solicit new ideas across the investigational spectrum from basic science to implementation research, and the initiative will persevere to help individuals and communities in the throes of the opioid crisis.

Many people living with chronic pain and opioid use disorder do not seek help because their illnesses are highly stigmatized, making it difficult for them to receive compassionate, evidence-based care. HEAL research continues to look holistically at the intersection of pain and addiction in the context of research and care – including identifying and developing an able and creative workforce to carry out this important work in partnership with individuals and communities affected by the opioid crisis.

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Table of HEAL Programs and Accomplishments: FY 2022

Focus Area	Program	Accomplishments
Novel Therapeutic Options for Opioid Addiction and Overdose	Focused Therapeutic Development for Opioid Use Disorder and Overdose	<ul style="list-style-type: none"> • 71 awards, \$330 million to date • 5 new INDs filed with FDA in 2021, bringing total cleared INDs for OUD within HEAL’s first 3 years to 20 (exceeding HEAL’s goal) • Drug to treat sleep disturbance symptoms of OUD withdrawal shown effective in first phase of testing
	Novel Immunotherapies to Opioids	<ul style="list-style-type: none"> • 10 awards, \$30 million to date
Enhanced Outcomes for Infants and Children	Advancing Clinical Trials in Neonatal Opioid Withdrawal (ACT NOW)	<ul style="list-style-type: none"> • \$47 million to date • Launched two clinical trials (“Trial to Shorten Pharmacologic Treatment of Newborns with NOWS”, and the “Eat, Sleep, Console” trial for soothing without medication) and one longitudinal study (“Outcomes of Babies with Opioid Exposure”) • All trials enrolling at more than 50 sites nationwide
	HEALTHy Brain and Child Development Study (HBCD)	<ul style="list-style-type: none"> • \$24 million to date • Launched in October 2021 at 25 sites; peer navigators supported in study

Focus Area	Program	Accomplishments
New Prevention & Treatment Strategies for Opioid Use Disorder	Preventing Opioid Use Disorder in At-Risk Populations	<ul style="list-style-type: none"> • 9 awards, \$57 million to date • Research addressing substance use among vulnerable adolescents and young adults, including research developing and testing 10 interventions to prevent opioid misuse and OUD among homeless youth; those involved in justice, welfare, or healthcare systems; and American Indian/Alaska Native (AI/AN) youth
	Optimizing Care for People with Opioid Use Disorder and Mental Health Conditions	<ul style="list-style-type: none"> • 13 awards, \$60 million to date • Testing collaborative care model for OUD treatment; improving treatment, management, and services for people with co-occurring conditions and suicide risk
	Sleep Dysfunction	<ul style="list-style-type: none"> • 10 awards, \$25.6 million to date • Basic mechanistic studies, clinical trials, and supplements for objective assessments of sleep during OUD treatment and recovery
Translation of Research Into Practice for Effective Treatments for OUD	Behavioral Research to Address Medications for the Treatment of OUD (BRIM)	<ul style="list-style-type: none"> • 8 awards, \$33 million to date • Testing if behavioral/social interventions, mhealth, peer delivery help improve long-term outcomes for medication-based OUD treatment
	HEALing Communities Study	<ul style="list-style-type: none"> • 5 awards, \$305 million to date • Communications campaign for community uptake of naloxone and medications for OUD
	Expanding the NIDA Clinical Trials Network to Address Opioids	<ul style="list-style-type: none"> • 28 awards, \$186 million to date
	Justice Community Opioid Innovation Network (JCOIN)	<ul style="list-style-type: none"> • 15 awards, \$105 million to date • Collaborative with justice systems in 27 states studying the quality of care for opioid misuse and OUD in justice populations • Completion and release of Opioid Environment Policy Scan (OEPS) Data Warehouse: a free, open-source data warehouse focused on the multi-dimensional risk environment impacting opioid use and health outcomes, particularly for justice communities, across the United States.

Focus Area	Program	Accomplishments
Preclinical and Translational Research in Pain Management	Discovery and Validation of Novel Targets for Safe and Effective Pain Treatment	<ul style="list-style-type: none"> • 34 awards, \$69 million to date • Multiple diverse target types and pain conditions (e.g., neuropathic, post-surgical, osteoarthritis, and chemotherapy-induced pain)
	Optimizing Non-Addictive Therapies to Treat Pain	<ul style="list-style-type: none"> • 6 awards focused on four small molecules and two biologics, \$7.5 million to date
	Translating Discoveries into Effective Devices for Pain Treatment	<ul style="list-style-type: none"> • 11 awards, \$35 million to date • Received an FDA Investigational Device Exemption (IDE) to initiate a clinical trial on high-resolution spinal cord stimulation to treat neuropathic pain.
	Human-Based Models and Candidate Testing for Nociception, Addiction, and Overdose	<ul style="list-style-type: none"> • \$98 million to date • Intramural-extramural collaborative • Generated an innervated knee joint bioreactor for a personalized medicine-based approach to osteoarthritis pain management.
	Biomarkers, Signatures, and Endpoints for Pain	<ul style="list-style-type: none"> • 9 awards, \$31.7 million to date • Pain associated with sickle cell disease, eye pain, musculoskeletal disease, nerve pain and spinal cord injury, persistent headache after concussion
	Small Business Innovation Research (SBIR/STTR)	<ul style="list-style-type: none"> • 7 patents have been filed by small businesses as a result of HEAL funding to date
	Analgesic Development for Pain Management	<ul style="list-style-type: none"> • Funded 1 early-stage translational award and 3 planning awards for groups to build multidisciplinary research teams that would accelerate projects through the early translational space, feeding into the preclinical development pipeline.
	Preclinical Screening Platform for Pain	<ul style="list-style-type: none"> • \$31 million to date • Optimized several preclinical models including chemotherapy-induced neuropathy, joint damage, and incisional pain. • Evaluating 30 potential treatments and launched a website for disseminating validated and optimized protocols as well as data with clinical standards.

Focus Area	Program	Accomplishments
Clinical Research in Pain Management	Early Phase Preclinical Investigation Network (EPPIC-Net)	<ul style="list-style-type: none"> • 14 awards for infrastructure, \$50 million to date • Enrollment began for trial of CCR2 antagonist for knee osteoarthritis pain
	Back Pain Consortium (BACPAC)	<ul style="list-style-type: none"> • 14 awards, \$130 million to date • 3 mechanistic research centers, 7 technology sites, 2 phase II trials, data center, and 1 supplement to study back pain in the context of OUD • Launched BEST trial of biomechanical technologies developed through BACPAC to provide a low-cost means of assessing and predicting treatment responsiveness for chronic low back pain patients.
	Hemodialysis Opioid Prescription Effort (HOPE)	<ul style="list-style-type: none"> • 8 clinical sites and data center, \$28 million to date • Developed the Pain Coping Skills Training Intervention for end stage renal disease patients receiving dialysis
	Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR)	<ul style="list-style-type: none"> • 5 awards, \$19 million to date • Focused on integrative treatments for comorbid chronic pain and OUD
	Pain Effectiveness Research Network (Pain ERN)	<ul style="list-style-type: none"> • 13 awards, \$80 million to date • Pain conditions studied: knee osteoarthritis, postsurgical pain in adolescents, post-mastectomy pain, acute pain post cesarean, chronic pain in cancer survivors, chronic pain in veterans with OUD
	Pragmatic and Implementation Studies for Management of Pain to Reduce Opioid Prescribing (PRISM)	<ul style="list-style-type: none"> • 7 awards, \$23 million to date • Nonpharmacological management of pain (fibromyalgia, post-surgical, sickle cell, chronic low back)