



# **2024 ANNUAL REPORT**

# Research in Action

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NIH · Helping to End Addiction Long-term®

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### FROM THE HEAL SCIENTIFIC DIRECTORS

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As scientific directors of the <u>Helping to End Addiction Long-term</u> Initiative, or NIH HEAL Initiative, we are inspired by the progress and potential of this critical research effort as it enters its sixth year. The expansive HEAL research portfolio represents an unprecedented commitment to advancing science through more than 1,800 projects in all 50 states. We are living up to our promise to create innovative solutions with the potential to transform lives and communities affected by opioid use disorder and pain.

As demonstrated in the following pages of this year's HEAL Annual Report, the initiative is an innovative approach to science that is comprehensive, whole-person-focused, and integrated. As a research community, HEAL embraces the complexity of addiction, pain, and the intersection of both – recognizing their multifaceted biological, psychological, social, and environmental dimensions. Overcoming health disparities, improving clinical care, and developing new treatment options demand that we work closely with patients and communities to put new findings into practice. Meanwhile, we continue to address foundational issues including data collection and sharing, as well as building and sustaining a workforce of researchers dedicated to finding scientific solutions for pain, substance use disorders, and overdose.

A core HEAL value is reaching underserved populations, acknowledging many existing inequities that have exacerbated these intertwined health crises. Nearly 110,000 lives are lost annually to overdose, and 20 percent of Americans live with chronic pain. As devastating as these statistics are, they do not adequately capture the impact of this crisis, particularly on people historically underserved by the medical system. These include people who are Black, Hispanic, or American Indian/Alaska Native, those living in rural areas, people with co-occurring conditions, and people who experience social and economic disadvantages and often face barriers to accessing effective treatment and comprehensive care.

HEAL efforts are driven by the imperative to ensure inclusive and culturally competent research that can bridge gaps in care. For example, the <a href="Native Collective Research Effort to Enhance Wellness">N CREW</a>) program will build collaborations with Tribes and Native American Serving Organizations to reduce health disparities and increase wellness. Recognizing that Native Americans have been disproportionately affected by overdose and chronic pain, and that understanding and leveraging community strengths are critical, N CREW fosters community-prioritized and -led research to address opioid use, pain, and related factors such as mental health



and wellness in Native communities. The program also recognizes the value and legitimacy of Indigenous Knowledge and local expertise to advance science and strengths-based and sustainable solutions that are relevant and effective for Native American communities.

We also see the urgent need to address disparities in pain diagnosis and care through HEAL research. A new HEAL program is aiming to find pain management interventions that work for rural populations, leveraging infrastructure from existing HEAL clinical research. HEAL pain research studies dedicated to populations that experience health disparities are underway and meeting their milestones, developing strategies for enrolling participants who are typically underrepresented in research and ensuring that planned interventions are culturally appropriate, scalable, and sustainable, and which are centered around meaningful patient and community engagement practices. The Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR) research program supports a network of multidisciplinary teams bringing a whole-patient focus to care for patients. This research network is developing and testing combined therapies including medications for opioid use disorder, behavioral treatments, and pain self-management – and they are examining implementation barriers. We also know that many individuals with chronic pain without an opioid use disorder experience additional opioidrelated harms. The newly launched Multilevel Interventions to Reduce Harm and Improve Quality of Life for Patients on Long Term Opioid Therapy (MIRHIQL) program aims to develop and put into place actionable solutions for these individuals, including reducing opioid-related harms, improving pain, and enhancing quality of life.

Some individuals with substance use disorders are not ready or able to enter treatment. Keeping these people safe is a HEAL focus and a priority of the Biden-Harris Administration. We are funding research on overdose prevention including naloxone distribution and fentanyl test strips as part of the newly launched <a href="Harm Reduction Research Network">Harm Reduction Research Network</a>, which will also study innovative ways of expanding the reach of these life-saving measures through mobile vans, tools delivered via smartphones, and other means. Several HEAL programs are working hard to implement evidence-based care within a variety of health care and community settings (such as primary care, emergency departments, jails, and child welfare).

Given very little industry investment in medications for either substance use disorders or pain, the National Institutes of Health (NIH) must fill this gap by supporting the development of new treatments for these conditions. And, indeed, the NIH HEAL Initiative has enabled tremendous strides in treatment development. Progress to expand the pipeline of medications for opioid use disorder and overdose continues to be exceptional – far exceeding HEAL's initial goal of filing 15 investigational new drug (IND) applications to the U.S. Food and Drug Administration (FDA) in the first 5 years of initiative. In the past year alone, five new IND applications were submitted, and



another five were cleared by the FDA. Currently, the program has 25 active INDs, including first-inclass monoclonal antibodies against fentanyl and methamphetamine, and one active investigational device exemption (IDE) that allows an experimental technology to be tested in people. Progress has been made in pain as well. This past year, HEAL scientists developed a chronic pain "brain signature" by measuring real-time, pain-related brain recordings in people with chronic pain disorders caused by stroke or amputation. Knowing more about how to use these pain signatures paves the way for developing non-invasive, targeted treatments.

After 5 years of research, we will soon have results from many HEAL clinical trials currently underway. We expect the results of these critical studies to yield new medications and interventions for opioid use disorder and overdose, including invasive and non-invasive neuromodulation tools — as well as a range of new, non-addictive pain management strategies, including medications, behavioral therapies, physical therapy and exercise-based interventions, and technologies. As you will see in this year's HEAL Annual Report, our research is rooted in collaboration, partnership, and a shared commitment to advancing science for the greater good. Among the accomplishments that follow are solutions that offer patients and communities hope and provide the groundwork for future research successes.

### SELECTED RESEARCH ACCOMPLISHMENTS

### SCIENTIFIC SOLUTIONS FOR EQUITABLE CARE

Health care for people with pain, opioid use disorder, and co-occurring conditions continues to be inequitable. HEAL research will continue to look for contributors to treatment disparities and develop solutions for communities in need. These include racial and ethnic minority groups, people with limited income and resources, sexual and gender minorities, and people with disabilities, as well as those with unique needs such as <u>youth involved with the justice system</u> or pregnant women with opioid use disorder.

This past year, HEAL researchers identified geographically based disparities in addiction treatment and care. They found that compared to people in urban settings, people in rural and suburban areas face shortages of opioid use disorder treatment providers who can prescribe buprenorphine. Communities with lower buprenorphine access experienced higher rates of opioid-related incidents such as fatal overdoses. Research from other HEAL scientists studying substance use and overdose in the criminal justice system echoed this lack of access, showing that many rural areas have only one provider of medication for opioid use disorder within 50 miles. Another HEAL research team examined federal funding allocated to local authorities to fund



opioid-related services. They found that <u>only two-thirds of the money</u> was distributed in a way that matched the severity of state overdose rates and drug-related arrests.

HEAL research also aims to close geographic treatment gaps for people with pain. A trial of more than 2,000 participants is testing the effectiveness of cognitive behavioral therapy-based pain management using an online program and live virtual sessions. The study finished recruiting participants and is anticipating results this year. Research is being conducted in places serving people in both urban and rural settings who may benefit from being able to access these kinds of treatments from home. The BeatPain Utah clinical trial is testing telehealth-delivered physical therapy to reach patients who receive care from federally qualified health centers, including those in remote and rural locations. Expanding this research focus, in 2023, HEAL launched a program to adapt currently available pain management interventions for rural populations. These strategies include virtual physical therapy and mindfulness-based pain coping skills offered via telehealth.

It would be impossible to address health disparities and inequitable access to health care without efforts to ensure that diverse communities across the country trust and are willing to participate in research that is relevant to their needs. Throughout HEAL's research portfolio, projects prioritize partnering with community members, patients, and others with lived and living experience with substance use disorders and pain, so that prevention and treatment options being studied are relevant for the people who need them. American Indian/Alaska Native communities in the United States have been disproportionately affected by the opioid crisis, and more must be done to leverage local knowledge and strengths to support community-driven solutions. As noted earlier in this report, HEAL is launching the N CREW program to support Native community-led research to address pain, substance use, and drug overdose and related factors such as mental health and wellness. This program will provide funding specifically to Tribes and Native American Serving Organizations for developing and leading research projects driven by community priorities and integrating Indigenous Knowledge and culture. A Native Research Resource Network will provide comprehensive training and support to Tribes as well as coordination of resources, reporting, and cross-site activities.

Despite the effectiveness of prevention interventions to reduce risk of addiction, implementation and sustainability remain challenging. To overcome this challenge, HEAL scientists work with a range of community partners to develop and adapt prevention interventions, guided by the notion that research results are more likely to be adopted by individuals and providers when their peers had a role in designing and conducting the studies. HEAL prevention researchers are developing and adapting interventions to prevent opioid misuse in ways that align with Centers for Disease Control and Prevention (CDC)-adapted Public Participation Framework levels of community engagement. Resources developed to date include culturally responsive prevention strategies co-



developed with American Indian/Alaska Native communities. This work recognizes the value of developing long-standing relationships with community partners and ensuring Tribal and elder oversight.

HEAL-funded clinical trials testing various pain management strategies are also conducting extensive patient and community engagement to drive interest and tailor interventions to community needs. For example, the Hemodialysis Opioid Prescription Effort (HOPE) research program, which aims to improve pain management for people with kidney failure treated with hemodialysis, involves patient advisors throughout the stages of its research. These individuals experience several types of chronic pain; opioid use rates among kidney disease patients are also high, carrying a risk of addiction and health harms. HOPE research is meeting patients where they are – testing a telehealth training that uses psychologically based pain coping skills with participants while they are in dialysis centers where these patients spend a considerable amount of time each week. The trial met its enrollment target 2 months ahead of schedule, and participants completed 83 percent of expected weekly sessions with a health coach. These numbers are notable for this patient population, given frequent hospitalizations from dialysis- and kidney-related complications.

As noted earlier in this report, this past year, HEAL researchers <u>aiming to increase equity in pain management</u> worked with patient and community partners to adapt interventions for specific groups, for example, <u>Latinos</u> or <u>Asian Americans</u> who experience cancer pain. While there are multi-level and collaborative approaches for cancer pain that are safer and more effective than medication alone, structural and cultural barriers limit reach to these groups. HEAL researchers developed more culturally appropriate versions of these tools in the hopes of better reaching these populations, and clinical trials have launched to test these interventions. HEAL also continues to encourage and strengthen addiction recovery support services through <u>equity-based</u> <u>community-academic partnerships</u> that include building trusting relationships and compensating community partners financially for their time.

### RESEARCH TO ADDRESS WHOLE PERSON NEEDS

People with pain and opioid use disorder often have co-occurring conditions such as mental illness, infections, or other disorders that can complicate or worsen their health. HEAL research aims to provide a foundation of evidence to help guide health care decisions tailored to an individual's unique needs and circumstances.

In the past year, HEAL researchers learned that some conditions are more likely to result in chronic pain. For example, pregnant women with mood disorders are nearly <u>twice as likely as non-pregnant women to experience chronic pain</u> – providing an important opportunity for screening



and treatment during this life period. Elsewhere, HEAL scientists in the Back Pain Consortium (BACPAC) research program designed, validated, and pilot-tested "<u>CAPER TREATMENT</u>," an online questionnaire that gauges patient preferences for evidence-based non-surgical treatments for back pain. The researchers learned that people were willing to trade risk of adverse effects and care inconveniences for better pain control and increased physical activity, depending on their unique perception of pain intensity. For example, those with higher pain intensity prioritized pain relief and its duration, while those with less pain sought increased physical function (such as being able to walk a mile).

HEAL researchers are also finding that the health care system can miss opportunities to facilitate appropriate treatments for those with substance use disorder. <u>HEAL investigators observed</u> that when persons with substance use disorder were admitted for complications of intravenous drug use, these patients were often not offered medically assisted therapy such as suboxone or methadone, and upon discharge were not effectively linked to outpatient substance use disorder programs.

As other HEAL researchers reported this past year, the emergency department can provide an opportunity to initiate care for people with untreated substance use disorder. The researchers determined that beginning treatment with a long-lasting version of buprenorphine or sublingual buprenorphine in the emergency department appears to be both safe and effective for individuals who use fentanyl. This past year, HEAL research also demonstrated the value of peer recovery specialists and other approaches as an adjunct to medications such as methadone. A HEAL-supported randomized clinical trial showed that telehealth-delivered training in mindfulness, reappraisal, and savoring skills as part of group therapy added value to methadone treatment – addressing drug use, pain, depression, and the ability to stay in treatment. Each of these strategies addresses personal, situation-specific circumstances that influence treatment preferences, availability, and effectiveness.

Beyond treatment for substance use disorders and addiction, many people who use drugs need help staying safe in the context of an increasingly deadly drug supply that is driving record high overdose rates. Harm reduction services include provision of naloxone to reverse overdoses, sterile syringes and injection equipment, vaccines, drug testing, and connections to medications to reduce the spread of infectious diseases. As noted earlier in this report, the recently launched <a href="https://december/HEAL Harm Reduction Research Network">HEAL Harm Reduction Research Network</a> is testing various harm reduction approaches in diverse environments across the country. Notably, the U.S. Department of Health and Human Services listed the new network as <a href="https://december/one-network-net



HEAL research has also led to the <u>validation</u> of diagnostic assessments for opioid use disorder and stimulant use disorder for use by non-clinicians. These findings may improve access to lifesaving treatments by reducing barriers to diagnosis, particularly in non-clinical environments such as jails, soup kitchens, or parks. Being diagnosed with an opioid or stimulant use disorder in non-clinical settings can offer the chance to connect an individual to treatment, education, and critical harm reduction services. Many people at risk for overdose are also at risk for suicide. <u>New findings</u> highlight the nuanced relationship between prescription opioids, pain, and other health conditions, including suicide risk. This research underscores the necessity of suicidality screening and intervention for people with severe mental illness who take high-dose opioids.

### FIGHTING STIGMA

People living with chronic pain or opioid use disorder often face stigma that stands in the way of effective diagnosis and treatment. Pervasive stigma contributes to having symptoms undertreated or ignored and feeling generally unwelcome in health care settings. As part of a wider research network to improve care for people with co-occurring pain and opioid use disorder, this past year, HEAL scientists with the IMPOWR research program confirmed the existence of stigma against both people with opioid use disorder and the clinicians treating them.

In addition to testing telehealth-delivered pain coping skills for people with kidney failure treated with hemodialysis, the HOPE study is also studying buprenorphine for pain management in this population. The researchers sought to better understand stigma faced by these individuals, given buprenorphine's primary use as a treatment for opioid use disorder. In the coming year, HEAL scientists will work to better understand stigma among research participants, their family members, and those working in the health care system – toward developing ways to address and prevent stigma in health care settings. Some HEAL research has already led to a new tool to measure stigma experienced by pregnant women who have used opioids. The Prenatal Opioid Use Perceived Stigma (POPS) stigma scale can be used to help improve relationships between providers and patients, as well as to help train providers to be aware of stigma and its effects on health outcomes.

This past year, a HEAL research team also showed that among people hospitalized with complications from injection opioid use, most had health care providers who logged their condition as "abuse" rather than a "use disorder." The scientists learned that individuals described as having a "use disorder" were more likely to receive a treatment plan for opioid use disorder. These findings highlight the importance of changing the culture around treating opioid use disorder to improve health outcomes for individuals. Another HEAL research project is seeking to understand how implicit bias can affect children from Hispanic and Black backgrounds who seek pain care in the emergency department.

### PUTTING RESEARCH INTO PRACTICE

Despite the availability of multiple effective evidence-based treatments and programs for opioid use disorder, most Americans at risk for or who have this condition do not receive treatment. To fill this urgent gap, HEAL supports implementation research to improve the integration of evidence-based treatments into practice. These ongoing studies have made considerable progress over the past year.



The HEALing Communities Study (HCS) partners with a diverse set of communities hit hard by the opioid crisis. This research program is testing the integration of evidence-based strategies to increase education about overdose and distribution of lifesaving naloxone, expand access to medications for opioid use disorder, and improve safety of opioid prescribing practices. This past year, new HCS research reported that among people with opioid use disorder who have Medicaid coverage, telehealth-delivered buprenorphine helped people stay in treatment. These findings add to an emerging body of evidence showing that innovative telehealth approaches that grew in prevalence during the COVID-19 pandemic offer promise for enhanced care and better outcomes for individuals living with pain and addiction. Lessons learned from the HCS were also instrumental in informing the development of a guide developed by the Substance Abuse and Mental Health Services Administration to provide tools and real-world examples for community coalitions to use to reduce opioid overdose deaths.

Through the Justice Community Opioid Innovation Network (JCOIN), HEAL is accumulating scientific knowledge that will inform effective policies, practices, and interventions for treating opioid use disorder in criminal justice-involved populations. This past year, JCOIN scientists and community partners generated important findings about the effect of <a href="implementing a program">implementing a program</a> for treatment with medications for opioid use disorder in a statewide correctional system. The research <a href="showed positive impacts">showed positive impacts</a> for incarcerated individuals, including increased treatment engagement and a decrease in opioid-related overdose, even after release. Researchers also developed a <a href="budget tool">budget tool</a> to help decision makers at specific facilities choose the best program for implementing lifesaving medications to treat opioid use disorder.

HEAL research continues to address the medical and social needs of individuals across the lifespan, including infants, children, and pregnant women. This past year, the Advancing Clinical Trials in Neonatal Opioid Withdrawal (ACT NOW) program's Eat, Sleep, Console (ESC) study showed that using the ESC care approach can cut hospital stays for newborns experiencing withdrawal symptoms as well as reduce their need to receive medication as part of their treatment. The ESC approach determines a baby's level of withdrawal severity based on the ability to eat, sleep, and be consoled, and provides appropriate treatment minimizing the use of medication when possible. The findings are already influencing clinical practice guidelines: The Washington State Department of Health now recommends ESC as the new best practice for birthing hospitals.

The Pain Management Effectiveness Research Network (ERN) and Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM) research programs aim to reduce reliance on opioids and expand real-world use of alternative pain management interventions. For example, this past year, ERN scientists tested an individualized approach to opioid prescribing for women who undergo a C-section, the most common surgical procedure



among American adults. The results showed that enabling women to personalize their postsurgery pain relief resulted in fewer opioid prescriptions with the same effectiveness as the current standard of care, a fixed prescription of 20 opioid tablets.

Other ERN and PRISM clinical trials have completed enrollment this past year and will soon be reporting results. Examples include testing a virtually delivered mindfulness-based stress reduction program for managing chronic low back pain in primary care settings and acupuncture for chronic back pain in older adults. Other projects aim to improve pain management for people with sickle cell disease. This past year, HEAL researchers published the results of qualitative interviews with individuals with the condition and their providers. The findings reveal that despite interest in the use of approaches other than medication, misconceptions about these treatments remain. To address this imbalance, HEAL research conducted in three large health systems is currently testing the use of acupuncture and guided relaxation to treat sickle cell disease pain. Another HEAL clinical trial will be the first study to test the effectiveness of cognitive behavioral therapy with and without peer support for adolescents and young adults living with sickle cell disease.

### TARGETED DISCOVERY

Supporting research to better understand the biology of pain and addiction will pave the way for the identification of molecules and mechanisms that can lead to new potential treatments.

This year, for example, HEAL researchers developed human models of pain and overdose. A novel pain model incorporates both neurons and non-neuronal glial cells, acknowledging the newly recognized relevance of multiple cell types in pain processing. Other HEAL researchers developed the first human cell model of the brain region responsible for opioid-induced respiratory depression. The initiative also supports the development of novel non-opioid pain medications that target the body's capacity to feel pain associated with different cellular processes, including endocytosis and signaling by NaV1.7 channels in sensory neurons. This past year, HEAL research also made progress toward first-in-human clinical testing by submitting to the FDA INDs for (i) a blocker of the common metabolic enzyme epoxide hydrolase for neuropathic pain; (ii) a novel pain medication (AFA-281) for inflammatory and neuropathic pain; and (iii) a novel, non-opioid treatment for moderate-to-severe acute and chronic pain (SRP-001).

As noted earlier in this report, in a technology breakthrough this past year, HEAL scientists measured pain-related brain activity in real time from inside the brains of people with chronic pain disorders caused by stroke or amputation. The researchers measured pain signals in regions of the brain associated with pain perception as well as the emotional response to pain. <a href="Chronic pain">Chronic pain</a> "signatures" that measure pain episodes in real time may lead to personalized approaches to



effective, non-addictive pain management. This past year, HEAL researchers also developed a refined version of electroencephalography technology for use with spinal cord stimulation, and could enhance understanding of pain mechanisms and prevention. HEAL scientists also observed significant reduction of pain-associated behaviors using <a href="low-intensity transcranial focused ultrasound">low-intensity transcranial focused ultrasound</a> in a mouse model of sickle cell disease.

HEAL research continues to expand the pipeline of new and reformulated experimental medications and technologies for opioid use disorder and overdose. HEAL has made major strides in advancing several potential medications to clinical testing – far exceeding targets set at the outset of HEAL research. This past year, <u>HEAL researchers</u> showed that a modified version of the molecule ibogaine reduced motivation to seek both heroin and alcohol in animals with a history of self-administering both substances. HEAL research also submitted INDs to the FDA to advance clinical testing of several medications. These include: (i) a once-weekly oral version of the opioid use disorder treatment containing buprenorphine and naloxone; (ii) a short-acting opioid blocker intended to prevent unwanted physical opioid withdrawal symptoms; (iii) a non-opioid molecule that targets the body's system for controlling sleep and appetite as a treatment for opioid use disorder; and (iv) a human monoclonal antibody to prevent fentanyl overdose. HEAL studies of other vaccines and monoclonal antibodies that prevent opioids from reaching the brain are ongoing. For example, a morphine/heroin vaccine will be evaluated in a clinical trial this coming year. HEAL research is also exploring use of kratom, an herbal substance that can produce opioidand stimulant-like effects. While there are no FDA-approved uses for kratom, people report using kratom to manage drug withdrawal symptoms and cravings (especially related to opioid use), pain, fatigue, and mental health problems. HEAL researchers are conducting research to evaluate specific medicinal uses and potential addiction liability of kratom and related chemical compounds.

Alongside research being directly funded by HEAL, private enterprises are crucial partners in developing and commercializing new medications or technologies that could improve upon existing treatments for opioid use disorder, overdose, and pain. However, early stage biotech companies are often formed by technical experts who may lack business experience. To address this gap, the HEAL Embedded Entrepreneur Program was launched this past year to bolster entrepreneurial expertise within HEAL small business leadership teams. As part of this first-of-its-kind program at NIH, four HEAL-funded small businesses received awards to support their business development expertise toward commercializing new pain treatments.



## SUSTAINING HEAL'S FUTURE

While the accomplishments described in this report represent progress on the path toward finding new treatments for pain and addiction and ensuring their widespread use, the need for additional research is still urgent as the opioid crisis continues to evolve, unabated. Achieving the HEAL mission will require the creative and diligent efforts of many people: study participants, scientists, caregivers, community members, clinicians, and policymakers across the United States. Collaboration and interdisciplinary exchange of information can uncover new insights and approaches to entrenched challenges.

HEAL is committed to open science, made possible by support of the <u>HEAL Data Ecosystem</u>, which this year launched "<u>HEAL Semantic Search</u>." This tool allows users of the <u>HEAL Data Platform</u> to easily connect data and concepts that are seemingly unrelated – with the potential to expand discovery beyond existing research questions. As HEAL research proceeds and new programs are launched, the Data Ecosystem continues to pursue innovative tools and strategies to facilitate sharing and reuse of HEAL data. These efforts ensure that data generated by HEAL research is FAIR – findable, accessible, interoperable, and reusable – extracting maximum value from HEAL's investments.

The long-term success of HEAL research relies on a highly trained and qualified workforce. HEAL has built several new and innovative programs to expand the numbers and enhance the training of pain and substance use disorder researchers. For example, to begin to meet the deep need for implementation scientists in addiction medicine, newly launched HEAL research will address staffing shortages, emotional stressors in this workforce, workforce diversity, and disparities in care by promoting recruitment, training, and retention of behavioral health professionals. Newly funded research aims to retrain scientists from other fields to conduct implementation science. These projects will (i) adapt chronic disease management often used by social workers in primary care to serve individuals who have addiction and mental illness; (ii) leverage mHealth expertise for equitable treatment of co-occurring opioid use disorder and mental illness; and (iii) improve implementation of evidence-based substance use prevention programs in community settings such as schools.

The initiative also launched a national program to mentor and train promising <u>pain clinical</u> <u>research scholars</u>. At this early stage, the program already has helped to advance the scholars' careers and research opportunities. Another <u>recently launched HEAL program</u> aims to increase the independent investigator workforce in research areas supported by the initiative. Mirroring the <u>NIH-wide Pathway to Independence program</u>, this research support facilitates a timely



transition of mentored, postdoctoral scientists in pain and substance use disorder research to independent faculty members.

In addition to research support, high-quality mentorship also is critical for success. HEAL built a comprehensive network to provide opportunities for researchers to interact, collaborate, and build their research knowledge. The goal of this HEAL-funded network, called <a href="PURPOSE">PURPOSE</a> (Positively Uniting Researchers of Pain to Opine, Synthesize, & Engage) is to connect researchers across the continuum of pain research, from all disciplines and at all career stages, and to expand the pain research workforce. It also fosters connection to people with living or lived pain experience to ensure that research meets their needs. As evidence of the network's value, more than 1,500 pain researchers actively engaged with the PURPOSE platform in the first 6 months after launch.

Just as HEAL could not function without a robust and well-trained research community, HEAL research would not be possible without input from patients, people with lived and living experience, communities, and health care providers. The initiative's emphasis on working intentionally and inclusively with these groups is meant to help elevate engagement as an essential component of the research process, and ensure that these creative, dedicated individuals and communities are true partners in research. HEAL's commitment to inclusive research makes it more likely that the initiative's findings will be put into place in the real world – to benefit the people and communities who most need help for pain, recovery from opioid use disorder, and prevention of overdose.

