





Rebecca G. Baker, Ph.D. Director, NIH HEAL Initiative

Many Institutes— One Mission







A Trans-NIH Approach to Address the Opioid Crisis

Lawrence A. Tabak, D.D.S., Ph.D., Performing the Duties of the NIH Director

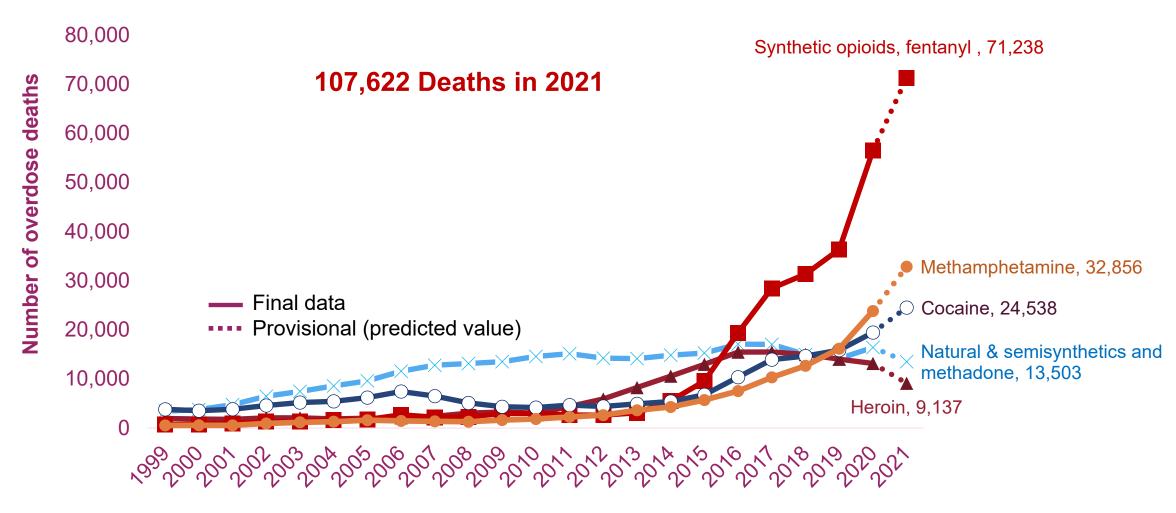


The Evolving Opioid and Overdose Crisis

Nora D. Volkow, M.D., Director, National Institute on Drug Abuse

Evolution of Drivers of Overdose Deaths, All Ages

Analgesics → Heroin → Fentanyl → Stimulants



Source: The Multiple Cause of Death data are produced by the Division of Vital Statistics, National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), United States Department of Health and Human Services (US DHHS).

What Makes Fentanyl So Dangerous?

- Fentanyl is a synthetic opioid drug that is 50 to 100 times more potent than morphine and highly addictive.
- The high potency of fentanyl and its fast entry into the brain greatly increases risk of overdose
- Illicitly manufactured fentanyl and analogues are the most common drugs involved in overdose deaths.

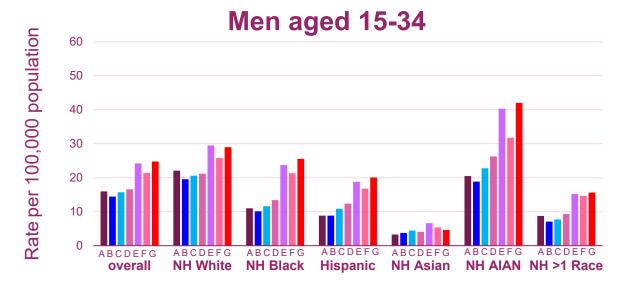


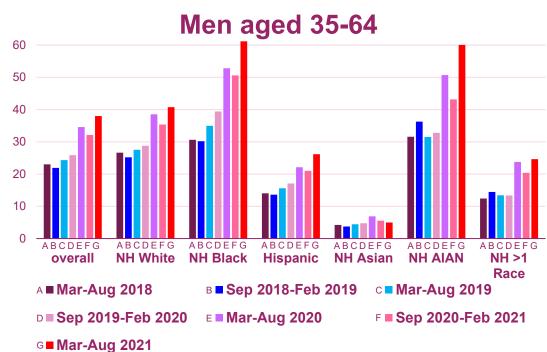
What Makes Fentanyl So Dangerous?

- Fentanyl is cheap to manufacture offering big profits to drug dealers. Thus, its **being mixed with other drugs** (cocaine, heroin, methamphetamine) to maximize profits. This is especially dangerous because **people are often unaware** of this and have no tolerance to opioids.
- Naloxone is effective in reversing fentanyl overdose. Multiple naloxone doses might be necessary.

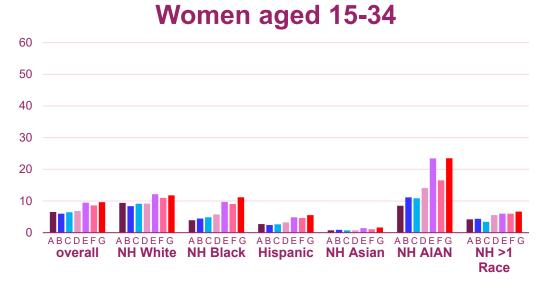


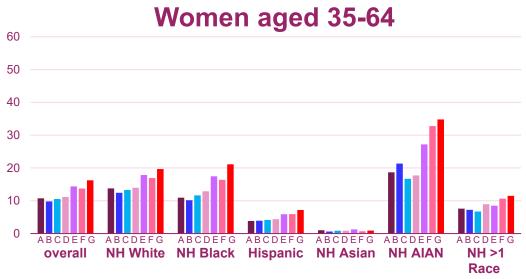
Overdoses Before and During the COVID-19 Pandemic





Rate per 100,000 population





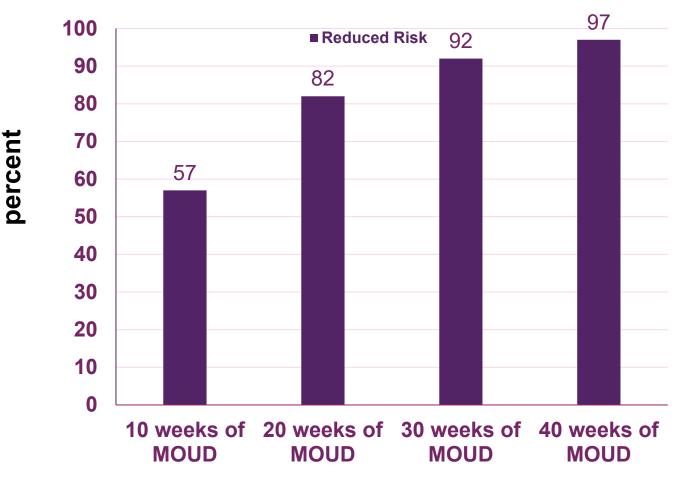
NH: non-Hispanic. AIAN: American Indian/Alaska Native. March-August 2020: COVID-19 pandemic.

Han et al., unpublished



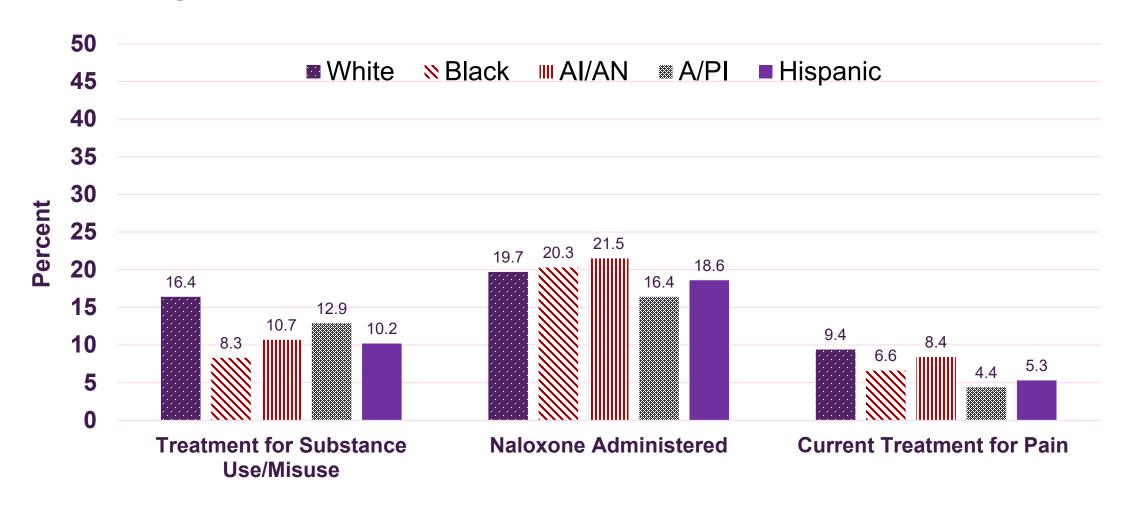


Reduced Risk Overdose in Pregnant Women Given Medications for OUD



Jarlenski M et al., JAMA Network Open. 2022;5(4):e227964.

Characteristics Of Drug Overdose Deaths, Overall and By Race and Hispanic Origin*, — 25 States and The District Of Columbia, 2019–2020



Implementation Science: CTN, JCOIN, HCS, Prevention



Enhancing the National Drug Abuse Treatment Clinical Trials Network to Address Opioids

Expand research conducted by NIDA CTN to address emergent needs presented by the opioid crisis.

NIH HEAL JCOIN INITIATIVE JUSTICE COMMUNITY OPIOID INNOVATION NETWORK

Justice Community Opioid
Innovation Network Study
quality care for OUD in justice
populations. Help create
partnerships between local and
state justice systems and
community-based treatment
providers.

NIH HEAL INITIATIVE

HEALing Communities Study

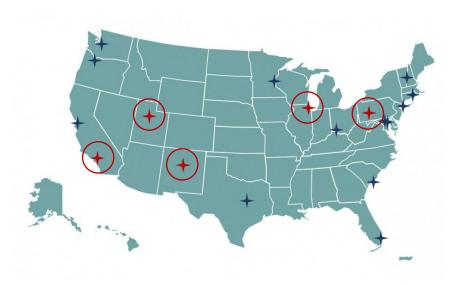
HEALing Communities Study

is investigating coordinated approaches for deploying evidence-based strategies to prevent and treat OUD in 67 communities in 4 states.

NIDA's Clinical Trials Network

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





HEAL funds have enabled:

- 5 new research nodes (circled)
- _o 26 new protocols

Select NIDA CTN studies being funded through HEAL:

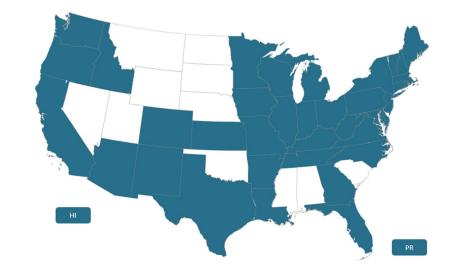
- Optimizing Retention, Duration and Discontinuation for OUD
 Medication (RDD): pharmacologic and behavioral strategies to
 optimize OUD treatment retention and outcomes, including
 stable patients who want to discontinue medication
- Subthreshold OUD Trial (STOP): testing interventions in primary care settings to prevent OUD
- ED-INNOVATION: testing effectiveness of buprenorphine initiation in the ED on the engagement in addiction treatment
- Monthly Injectable Buprenorphine for Methamphetamine Use
 Disorder (MURB): testing long-acting buprenorphine for
 treatment of methamphetamine use disorder



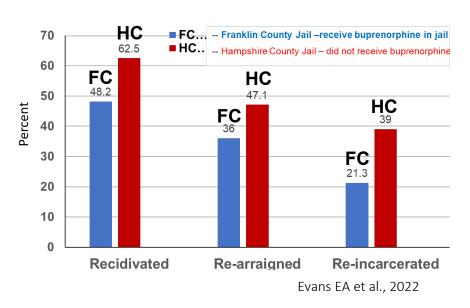


Building evidence for OUD treatment in justice populations

- Stakeholder/community-engaged research
- 66 approved research protocols
 - 12 multisite clinical trials
 - MOUD trials; peer navigation; state policy rollouts
 - National surveys: opioids/stigma, SUD services, state/local policies
 - Simulation, predictive & geospatial modeling
 - Pilot studies on emerging service delivery
 - Diversity supplements



Research activity in 141 counties and 39 states



XR-Bup prior to release from jail **increased adherence and reduced recidivism**, without increasing diversion or SAEs

Integrative Management of Chronic Pain and OUD for Whole Recovery

Goal: Generate evidence-based, patient-centered solutions for integrated management of cooccurring chronic pain and OUD and rapidly disseminate knowledge to impact population health

- Four research centers and a coordinating center, launched in 2021
- 9 effectiveness/implementation studies Pharmacological, Models of Care, MOUD & integrated behavioral treatments
- Diverse health care settings and populations Primary Care, Hospital, OTPs
- Partner engagement on every study

Understanding Polysubstance Use and Improving Service Delivery

Goal: Understand dynamics of polysubstance use and improve personalized prevention and treatment

Projects will examine opioid, stimulant, or tobacco co-use in a range of settings and populations, such as homeless
populations and peer-delivered interventions in rural populations



Recovery Research Networks

Goal: Expand research capacity to build evidence on recovery service approaches

- Multi-stakeholder networks (researchers, payors, providers, people in recovery) to train researchers and build infrastructure, tools, methods, and relationships to support research
- Projects involve peer recovery support interventions, recovery community centers, active recovery communities, and continuing care, in a range of populations across the country



Novel Therapeutic Options for Opioid/Stimulant Use Disorder and Overdose

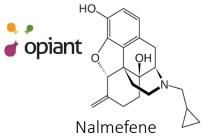
- New formulations of existing medications to treat OUD to facilitate retention
- Longer-duration opioid antagonist formulations to counteract overdoses from fentanyl
- Interventions for respiratory depression
- Novel medications to treat withdrawal, craving, insomnia to prevent relapse
- Immunotherapeutics for opioid addiction

Progress:

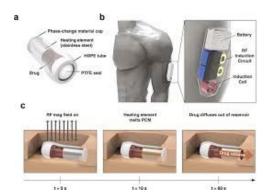
- 70 compounds and 9 new targets being evaluated
- 31 Investigational New Drug applications filed with FDA
- 44 New Molecular Entities (NME) being evaluated

Monoclonal antibodies and vaccines

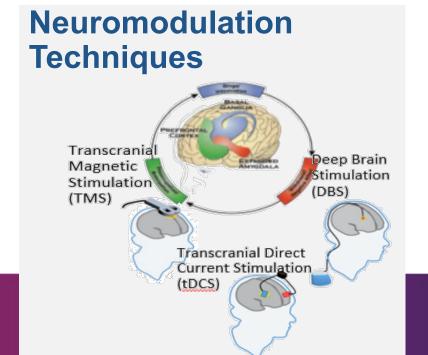




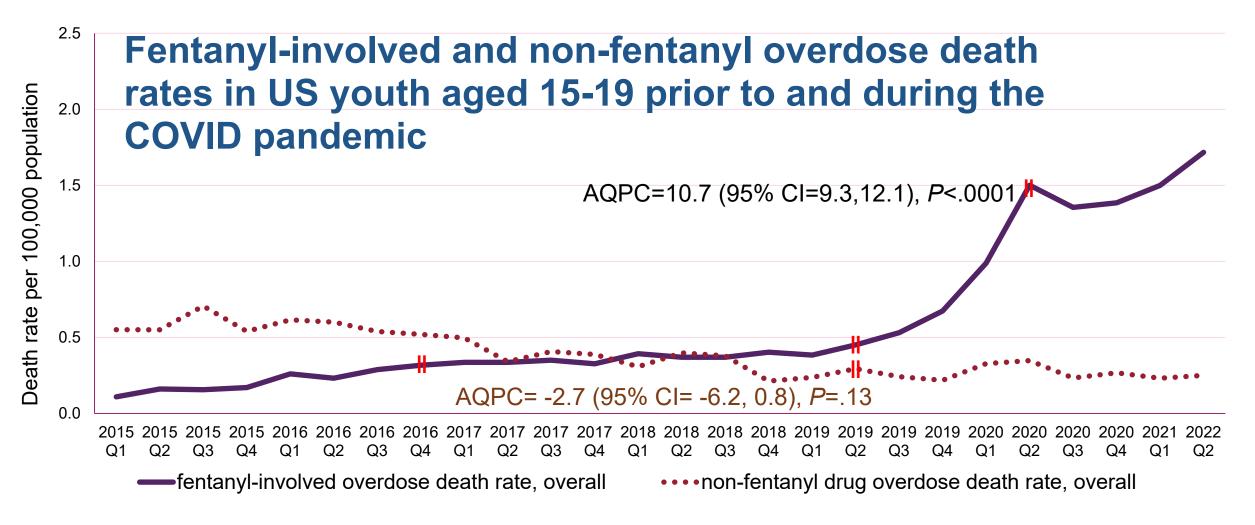
Longer acting MOR antagonists



Automatic naloxone autoinjector







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



Addressing Overdose Deaths in 2022

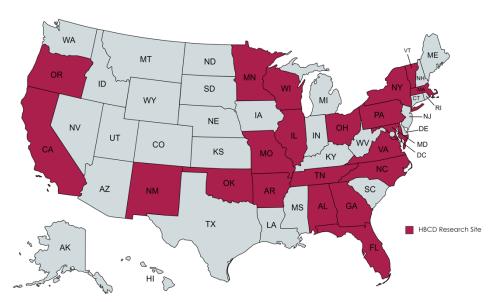
- Providing effecting treatment to pain patients including the appropriate use of opioids when needed is necessary but not sufficient
- Treatment of Opioid Use Disorders is CRUCIAL but not sufficient
- Treatment of Substance Use Disorders in addition to OUD is now necessary to prevent overdose deaths
- Prevention of drug use including illicit prescription drug use is necessary to prevent overdoses



HEALthy Brain and Child Development Study



- Funded through a partnership of Institutes, Centers, and Offices across NIH, including the HEAL Initiative
- Longitudinal study to understand normative neurodevelopment from birth to 9-10 years and assess impact of in utero exposures to drugs and harmful environments
- Will enroll approximately 7,500 families from 25 research sites across the country
- Currently enrolling pilot participants





What is the HBCD Study?

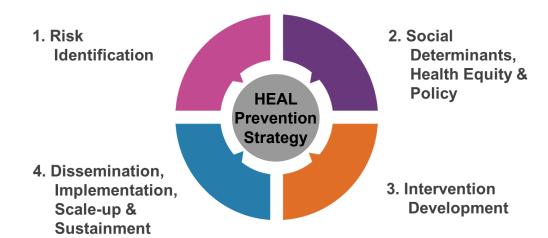
The HBCD Study will enroll a large cohort of participating families from across the U.S. and follow them and their children through early

http://hbcdstudy.org

HEAL Preventing OUD Research Program

Goal: Establish evidence-based interventions to <u>prevent</u> initiation of opioid misuse and OUD in at-risk older adolescents and young adults

 Impacts of existing interventions and development and implementation of novel interventions in diverse settings (justice, homeless shelters, child welfare, ED, community health centers, etc.) with focus on community/systems-engaged research



HEAL Prevention Cooperative (HPC)

Evidence-based interventions for immediate implementation

10 research projects

1 coordinating center



Administrative supplements, development research, and pilot studies supporting the Preventing OUD vision (21 awards)

Thank you



Forging a New Path in Pain Management

Walter J. Koroshetz, M.D., Director, National Institute of Neurological Disorders and Stroke

Pain - Public Health Crisis and Individual Burden

Nationwide prevalence of pain is high

50 million adults with chronic pain
25 million report severe pain daily

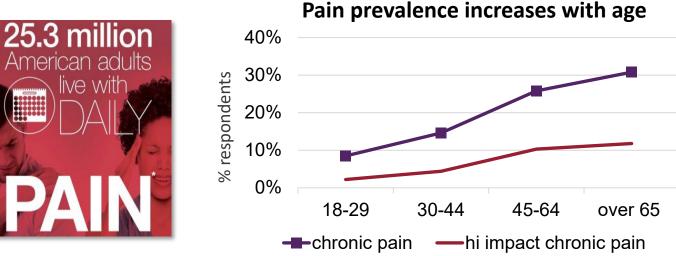
20 million with high impact chronic pain*

More adult women than men have pain

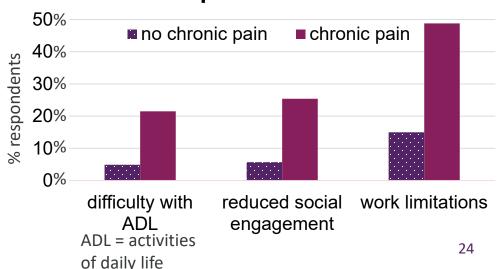
22% of women & 19% of men with chronic pain 8.5% of women & 6.3% of men with high impact chronic pain

More rural than urban dwellers report pain

28% of rural & 16% of urban residents with chronic pain 11% of rural & 6% of urban residents with hi impact chronic pain

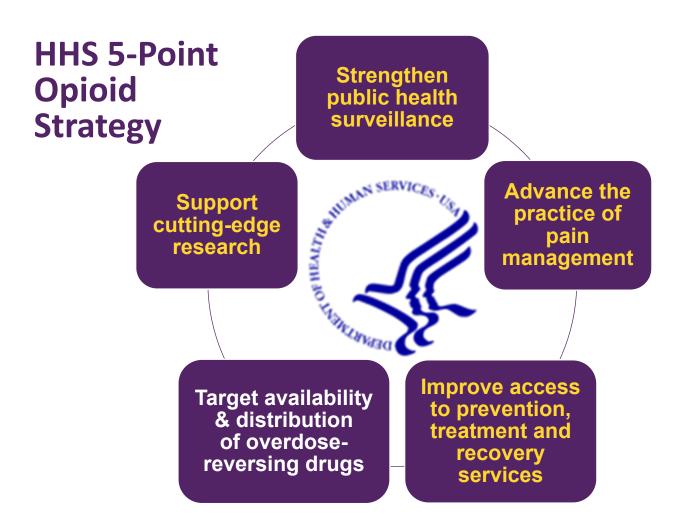


Chronic pain interferes with life



^{*}high impact chronic pain = pain lasting more than 3 months that interferes with life (school, work, social life, etc.)

The Opioid Crisis Highlights Need for Safe, Effective Pain Care



HHS Overdose Prevention Strategy Primary Prevention Recovery Harm Support Reduction **Evidence-Based**

NIH: develop and promote evidence-based treatments to effectively manage pain

Treatment



HHS.gov

Why is Pain Management so Challenging?



- Not insured
- Not covered



- Geographic
- Demographic



- **Disparities**
- Bias
- Stigma
- Population differences



Training

- Limited education
- Poor cross discipline integration disciplines



Work Force

- No protected time to mentor
- Mentors retiring



Complexity

- Overlapping pain conditions
- Other chronic conditions
- Different pain mechanisms



Lifespan

- Age related risks
- Age related changes

Research is aimed to develop treatments and inform evidence-based pain care



HEAL Pain Research Priorities

Enhance Pain Management

- Understand the biological underpinnings of chronic pain
- Accelerate the discovery and pre-clinical development of non-addictive pain treatments
- Advance new non-addictive pain treatments through the clinical pipeline
- Inform best practices for effective pain management while minimizing risk of addiction



Clinical Trials to Embed Evidence-based Pain Treatments

Into the Clinic

Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM)

"Pragmatic" study design emphasizes efficacy in real-world clinical settings

- Non-pharmacological treatments
- Set in large health care systems
- Variety of populations

Conditions studied

- Fibromyalgia
- Sickle Cell Disease
- Low back pain
- Post operative pain

Approaches

- Electrical stimulation
- Physical therapy
- Acupuncture
- Relaxation
- Mindfulness
- Shared clinical decision making













Clinical Trials to Test Efficacy of Interventions for Acute and Chronic Pain

Comparative Effectiveness Research Network for Pain Management (ERN)

- Pharmacological & Non-pharmacological treatments
- Many settings: primary care, hospital, telehealth, etc.
- Variety of populations



Pain conditions studied

- Knee Osteoarthritis
- Post caesarian acute pain
- Post mastectomy chronic pain
- Chronic musculoskeletal pain

- Chronic pain
- Chronic pain and OUD
- Cancer pain
- Perioperative pain

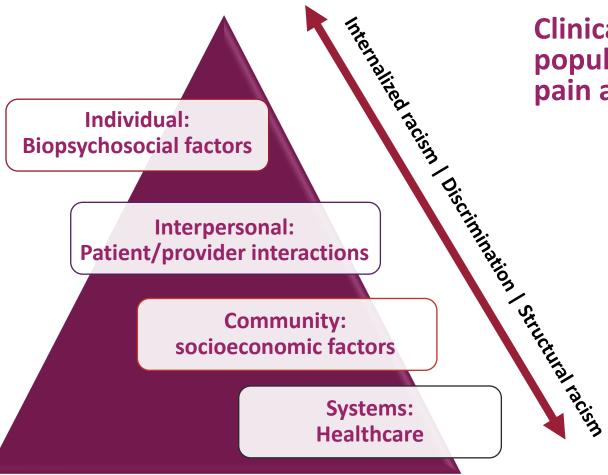
Interventions studied

- Shared clinical decision making
- Opioid reduction
- Non-opioid Medications
- Behavioral therapies
- Self-management programs





Health Equities in Pain Care



Clinical trials to improve health equity populations with health disparities who have pain and other chronic conditions

Populations

- African-Americans
- Hispanic Americans
- Asian Americans
- Low socioeconomic status
- Children to older adults

Interventions

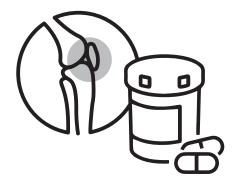
- Behavioral therapies
- Mindfulness
- Self-management
- Electric brain stimulation
- Provider training





Clinical Trials for Care of Those with OUD and Chronic Pain

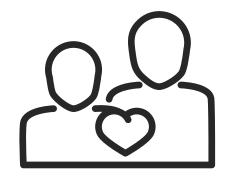
Integrative Management of Chronic Pain and OUD (opioid use disorder) for Whole Recovery (IMPOWR)



- Chronic pain (CP) 50 million
- Opioid misuse 10 million
- OUD 2 million
- 40-60% adults with OUD also have chronic pain



- Health care for CP & OUD is fragmented
- Need evidence-based integrated treatments
- Limited resources, expertise, & communication



- Develop integrated interventions
- Facilitate integrated care beyond referrals
- Focus on the whole person
 - Co-occurring conditions
 - Stigma
 - Health Disparities





Treating Pain in Hemodialysis Patients

Hemodialysis Opioid Prescription Effort (HOPE): Multicenter, randomized, controlled trial to evaluate cognitive behavioral therapy to enhance pain coping skills and buprenorphine vs full agonist opioids, for patients with kidney failure on hemodialysis



Risk: Opioid use in people on dialysis are 3 times higher than the general population.

Need: Safer and more effective personalized treatments.

Objective: Evaluation and implementation of non-pharmacological approaches with conversion to buprenorphine in dialysis patients.





Personalizing Back Pain Treatment

Back Pain Research Consortium (BACPAC): Studies to probe mechanisms of back pain to develop and test integrated precision care

Link structural, dynamic, cellular, molecular abnormalities to patient-reported symptoms and function

Research Program Technology Research Sites

Clinical trials for non-addictive drugs, biologics, devices, complementary approaches

Phase 2 Clinical Trials

Develop patient-centered algorithms to predict optimal treatment

Research Program Data Integration, Algorithm Development and Operations Management Center Research Program: Mechanistic Research Centers







HEAL Accomplishments: Back Pain Consortium Research Program

Development, Evaluation and Translation of Robotic Apparel for Alleviating Low Back Pain

The Spine Phenome Project: Enabling Technology for Personalized Medicine

Wearable nanocomposite sensor system for diagnosing mechanical sources of low back pain and guiding rehabilitation



Imaging Epigenetic

Dysregulation in Patients

with Low Back Pain

Novel imaging of endplate biomarkers in chronic low back pain





Preclinical and Translational Research in Pain Management

Non-addictive therapeutic development programs

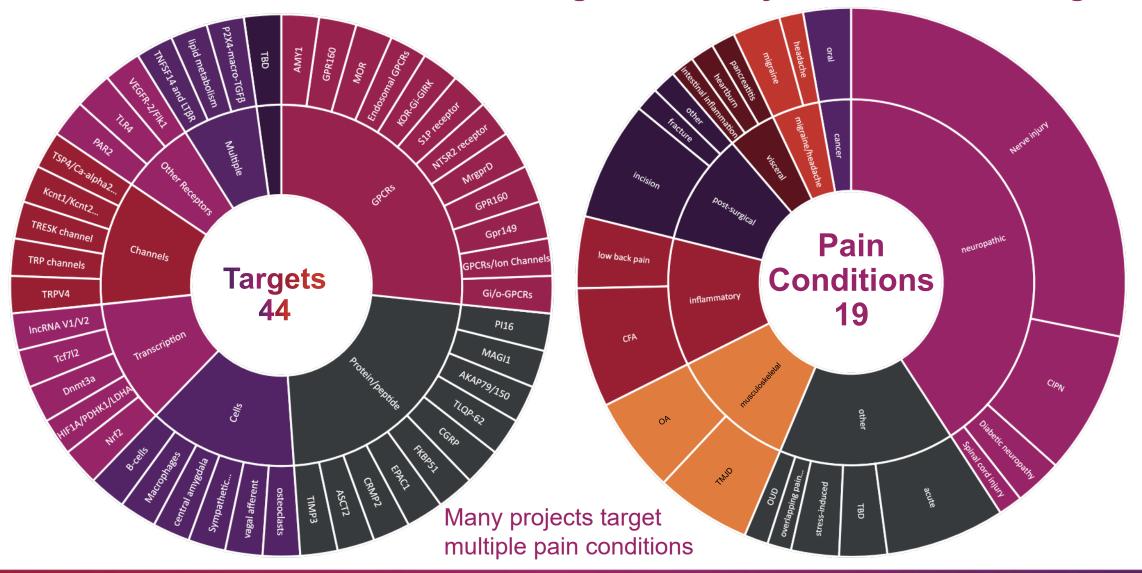
- Expanded analgesic therapeutics development programplanning studies and phased awards
- Novel targets and devices for pain relief, including small business grants
- Team-based research frameworks
- Screening and testing platforms, tissue chips and optimization research
- Studying pain in human genes & cells
- Expands workforce with expertise in overlap of pain and opioid use disorder







Overview of the HEAL Preclinical Target Discovery and Validation Program

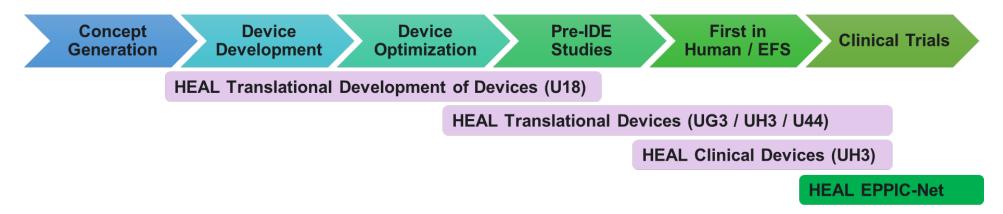




Translating Discoveries into Effective Devices to Treat Pain

Goal

To foster the development of next-generation medical devices to diagnose and treat pain by supporting preclinical development and demonstration of safe, effective, and non-addictive device-based technologies and approaches. It will also support the translation of promising devices into clinical trials that will inform function, final design, safety, and/or efficacy.



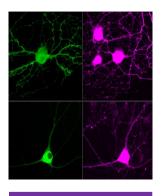
Translational device programs can tee up therapeutic candidates for larger EPPIC-Net trials.

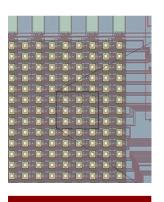


Human Cell-based Research Resources

The National Center for Advancing Translational Sciences (NCATS) is lead in bioengineered devices for predictability of efficacy and safety of drugs







- Screening library
- Tissue chips
- Induced pluripotent stem cells

PRECISION Human Pain Network

Datasets of molecular signatures, cell types, and cellular function phenotypes that underlie human pain signal transduction, transmission, and processing

Tissue sources

- Transplant centers
- National repositories

Tissue demographics

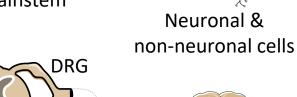
- Lifespan
- Sex

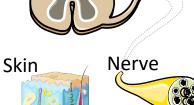
Associated Disorder

- Specific pain conditions
- Substance use/disorder

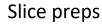
















Research to Identify Biomarker Signatures of Pain Conditions

Biomarker Program

- Facilitate Phase 2 clinical trials
- Targeted pain conditions
- Type of biomarker: response prediction/monitoring signature
- Phased
 - Biological signature with strong detection method credibility
 - Biological signature with scientific and regulatory consensus credibility
- Clinical validation to follow



Developing Quantitative Imaging & Other Biomarkers of Myofascial Tissues

Myofascial Pain

- Muscles, fascia, other soft tissues
- Interaction with neural & immune systems
- Low back, TMD, neck, shoulder pain, headache

Biomarkers

- Predictive and prognostic
- Quantitative, non-invasive: Imaging, electrophysiology
- Integration: immune, genomic, physiological factors
- Multiscale modeling or machine learning analysis

Outcome

• Evidence base for clinical decisions & coverage





Clinical Trials to Test Safety of Promising New Drugs and Devices

Early Phase Preclinical Investigation Network: EPPIC Net

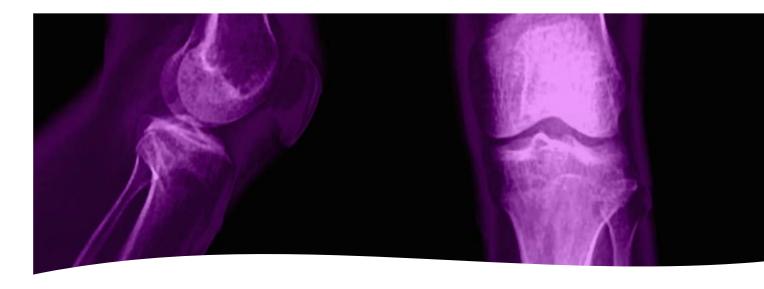
- Non-opioid treatments
- Multiple study sites nationwide
- Specific pain conditions

Conditions studied

- Knee Osteoarthritis
- Diabetic nerve pain

Approaches

- Test for safety
- Collect patient characteristics



22% of adults over age 40 have knee Osteoarthritis (OA)





Enhancing the Pain Research Workforce

The Opioid Crisis: All Hands On Deck

A formidable and rapidly evolving crisis demands a uniquely powerful response.

We must ensure an expanded, enduring, and diverse pool of highly trained scientists to perform high quality pain research in the face of a diminishing community and expanding research opportunities.









Thank You!

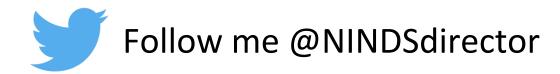
Walter J. Koroshetz, M.D.

Director

National Institute of Neurological Disorders and Stroke

Email: koroshetzw@ninds.nih.gov

Website: http://www.ninds.nih.gov/







HEAL Research: Making Scientific Advances to Stem the Opioid Crisis

Rebecca G. Baker, Ph.D., Director, NIH HEAL Initiative

NIH HEAL Initiative

NIH HEAL INITIATIVE RESEARCH OVERVIEW

- Over \$2.5 billion in research
- More than 1,000 research projects
- 42 research programs
- Projects underway in all 50 states
- Crisis-focused research across the investigational spectrum



In partnership with federal agencies, industry, academia, and communities



HEAL Funding Allocation

- Congressionally appropriated funds currently for this year: \$616 million
- President's budget request ~ 30% increase (\$811 million)
- Additional funding pending Congress passing a budget



HEAL Research Guiding Principles



Focus on the whole person



Address systemic challenges and inequities



Work with communities to bring research to life



Understand biology of pain and addiction



Share findings rapidly and usefully



HEAL Pain Research: Selected Examples

Tissue chips screen pain medications





Phase 2 clinical trials

Personcentric treatments for back pain





Pragmatic clinical trials in health settings



HEAL Opioid Research: Selected Examples

Targeting social determinants of health for prevention





Starting buprenorphine in the emergency department

Implantable naloxone to reverse overdose





Standardizing care for infants with NOWS

HEAL Cross-Cutting Research: Selected Examples

Stigma interventions





Patients and communities as research partners

Co-occurring mental illness and addiction





Whole-person care for pain and opioid use disorder



HEAL Small Business Programs: >100 Companies in 20 States

- Mobile apps: recovery, medications, behavioral health
- Novel pain medications: absorbable film, nasal spray, gene therapy, bone glue, virtual reality
- Human-on-a-chip for screening potential medications
- Low-cost urine drug test for clinicians
- Many more ...





HEAL Research Guiding Principles



Use a whole-person research focus



Address system problems and inequities



Work with communities to bring research to life



Understand biology of pain and addiction



Share findings rapidly and usefully

Open science is a guiding principle for HEAL research

This urgent public health challenge requires that HEAL results be shared widely and rapidly



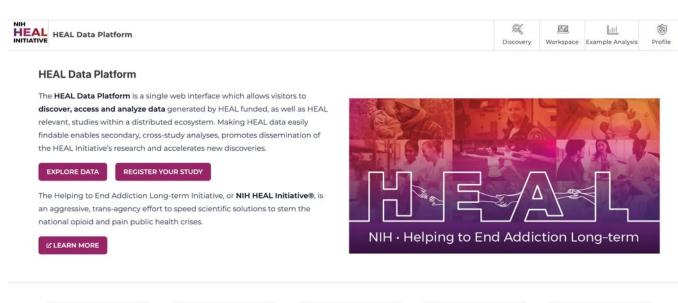
HEAL Data Ecosystem

Make HEAL data accessible

- HEAL-generated data indexed and searchable, with clear routes to access
- Data management and sharing support
- User-friendly search and interface

Build the research community

- HEAL researcher engagement and consensusbuilding, foster cross-awareness of research projects and drive collaborations
- Broad researcher, community, stakeholder, and user engagement



healdata.org



Search HEAL studies and

related datasets for

download or analysis in

Explore Tutorials and

Explore helpful resource

for Prevention, Treatment

and Support related to

Watch tutorial videos to

learn how to interact with

Progress: HEAL-Generated Data

- Opioid use disorder treatment improved health, reduced re-arrest
- Four diverse urban, academic medical centers successfully implemented unique buprenorphine in emergency departments
- Standardizing safe and effective treatment for infants with NOWS
- Insomnia drug relieves craving and withdrawal symptoms









Progress: HEAL-Generated Data

Publications are necessary but not sufficient to address the opioid crisis

HEAL data analysis, re-use, and dissemination is key for durable scientific solutions

We need stakeholders to help guide implementation of research findings

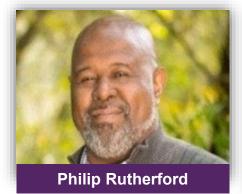


Making Research Results Useful for Communities

- Help HEAL researchers work with communities
 - Understand community needs
 - Make findings user-friendly
- Build partnerships with communities that can benefit from HEAL research findings
 - HEAL Community Partner Committee



Voices of Lived Experience HEAL Community Partner Committee

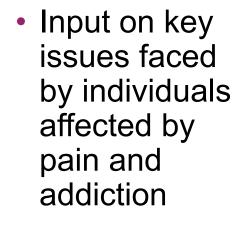












refine, and

engagement

activities and

links to HEAL

prioritize

science

Identify,



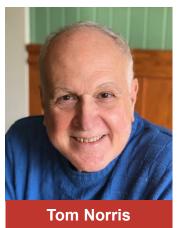












Adapting to the Crisis: New Directions for HEAL Research

- Patterns of drug use are shifting
- Difficult to target treatment and services
- Pain management remains uncoordinated and fragmented
- Health inequities in pain and addiction persist

COVID-19 **Stimulants** Mental Illness Polysubstance Inequity Burnout Stigma



New Research: Adapting to Emerging Opioid Threats and Shifting Drug Use

- Addressing polysubstance use in primary care
- Healthcare service delivery for polysubstance use
- Buprenorphine for reducing methamphetamine use
- Opioid use disorder and infectious complications of drug use



New Research: Harness Real-Time and Existing Data to Tailor Services and Care

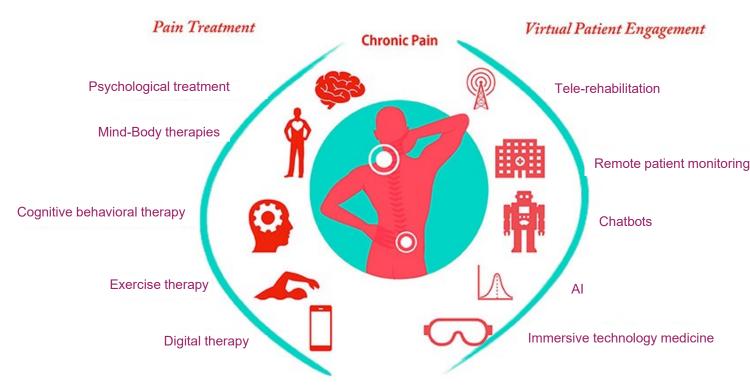
- Data dashboards (overdose, services)
- Data mining to identify patients at risk for harmful opioid use
 - Clinical trials, social media, CMS, electronic health records
- Compare long-term outcomes of pain management





Future Research: Coordinate Pain Management

- Coordinated care in healthcare systems
- Chronic pain treatment in rural populations
- Improve quality of life for patients on long-term opioid therapy
- New sickle cell treatments





Future Research: Optimizing Pain and Addiction Care and Prevention

- Improve addiction care and quality
- Target social determinants (e.g., housing, employment, exposure to violence and trauma)
- Opioid exposure in post-surgical adolescents
- Enhance pain and addiction workforce
- Oral complications of buprenorphine



Connect With HEAL



October 12, 2022

Research Spotlight



Lessons From the Field: Patient and Community
Engagement

HEAL values patient engagement as an essential research component. Learn how HEAL scientists are soliciting and incorporating input from patients and communities.

Funding Opportunities



July 27, 2022

Making HEAL Data Speak: Finding Scientific Solutions for People and Communities



Dear HEAL Community,

HEAL research is addressing the urgent public health crisis of opioid misuse, addiction, and overdose that demands teamwork, maximum transparency, and speed. We have a responsibility to deliver as quickly as possible the results of HEAL research so people can

make evidence-based decisions about treatment, and so we can continue to find more scientific solutions for people and communities in need.

HEAL has worked hard over the past 2 years to build a comprehensive data ecosystem that will help people and communities affected by the opioid crisis through maximal data sharing and re-use. Achieving this goal means making sure all HEAL data are

What answers do you want from HEAL results? Join this interactive exercise to tell us.

Monthly information about progress, funding opportunities

Subscribe at <u>heal.nih.gov</u>

HEALquestion@od.nih.gov



Imagine a Future ...

- Clinical decision-making tools allow safe, personalized pain treatment and addiction screening
- Communities adopt evidence-based treatments for people in jails and prisons
- Babies exposed to opioids live healthy lives
- Immunotherapies treat addiction and reverse overdose
- Telehealth opens access to pain and addiction treatment
- People in long-term recovery are community leaders





Discussion

Moderator: Diana Morales, Communications Director, NIH HEAL Initiative



Rebecca G. Baker, Ph.D. Director, NIH HEAL Initiative

Thank You