

HEAL Pain Research Overview Congressional Staff Briefing

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February 9, 2024

Mission: HEAL pain research aims to reduce pain and the risk of opioid use disorder by developing safe and effective pain treatment and prevention strategies to improve quality of life for all people.

Pain – A Public Health Crisis

Nationwide prevalence

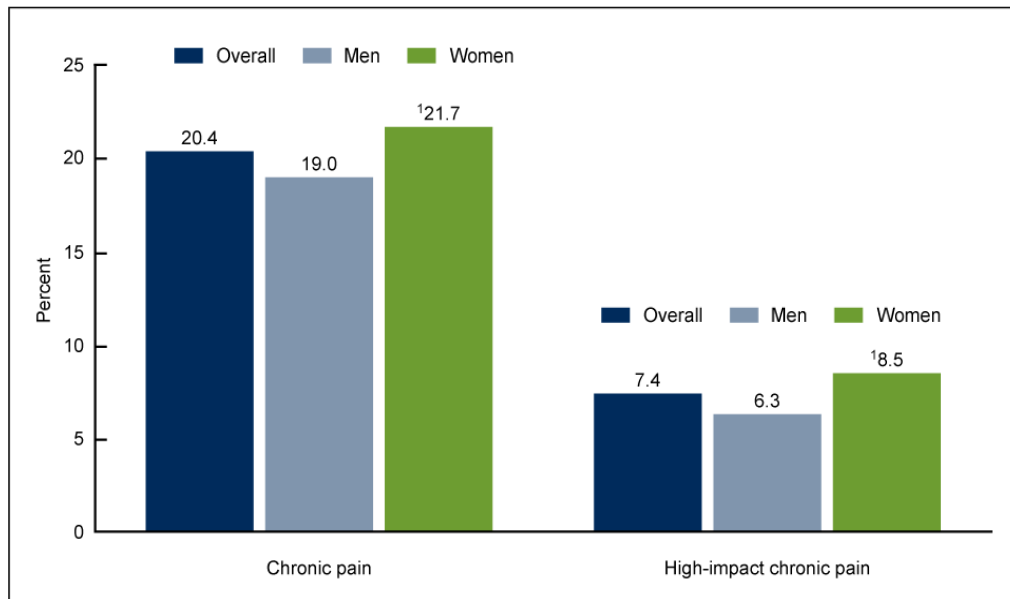
50 million adults with chronic pain
 25 million report severe pain daily
 20 million with high impact chronic pain*

More rural than urban dwellers report pain

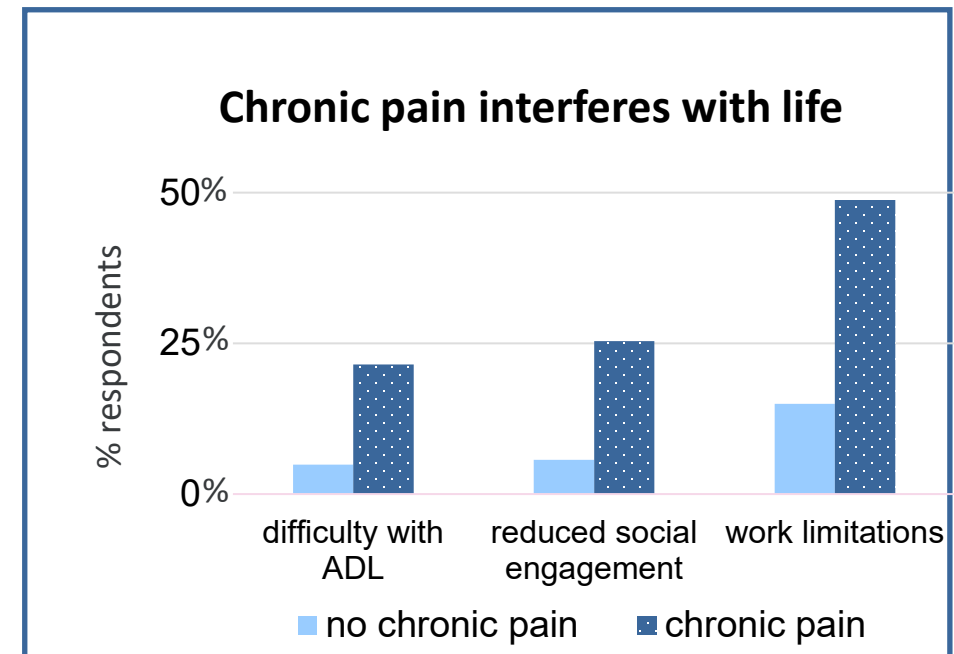
28% of rural & 16% of urban residents with chronic pain
 11% of rural & 6% of urban residents with hi impact chronic pain



More women than men report pain



National Center for Health Statistics: NHIS 2019
Pain and Therapy volume 10, pages287–314 (2021)



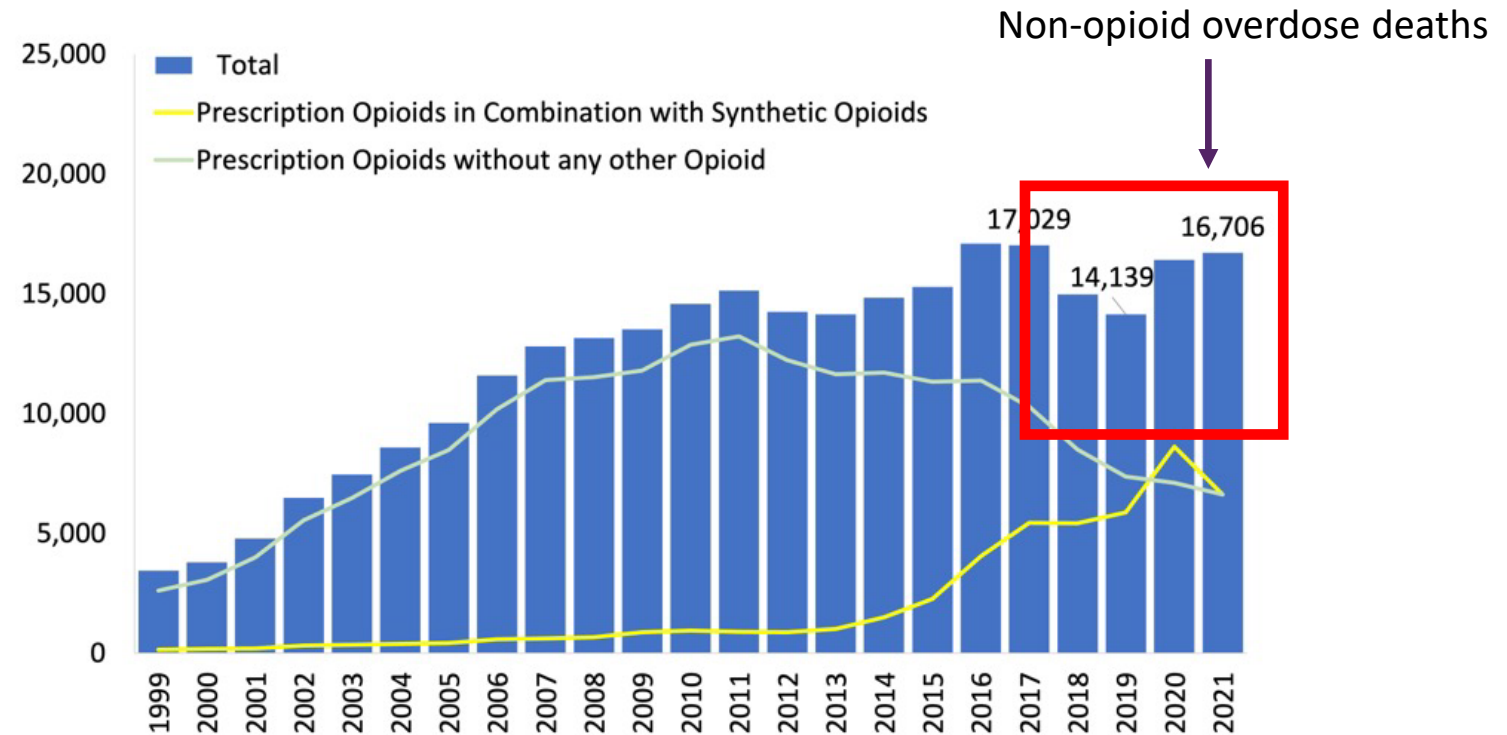
*high impact chronic pain = pain lasting more than 3 months that interferes with life (school, work, social life, etc.) <https://www.cdc.gov/nchs/products/databriefs/db390.htm>

Human and Societal Costs of Pain in the U.S.

- Pain is the most common reason people seek medical care
- There are now more new cases of chronic pain compared to diabetes, depression, and high blood pressure
- ~ \$600 billion/year in health care and lost productivity*

*2012 study - likely much more now

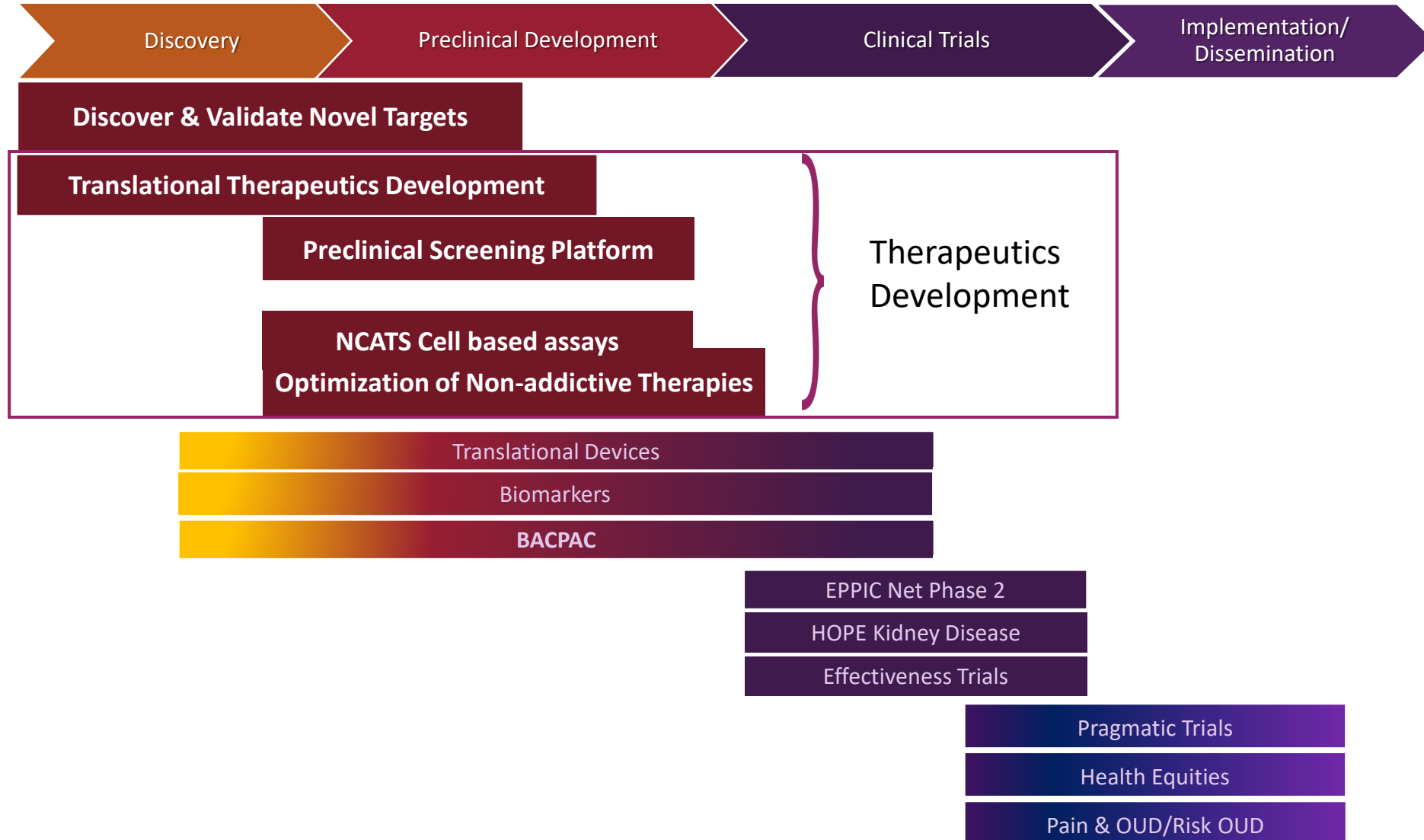
**National Overdose Deaths Involving Prescription Opioids
(All ages, 1999-2021)**



Drug Overdose Death Rates

<https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>

HEAL Therapeutics Development Program

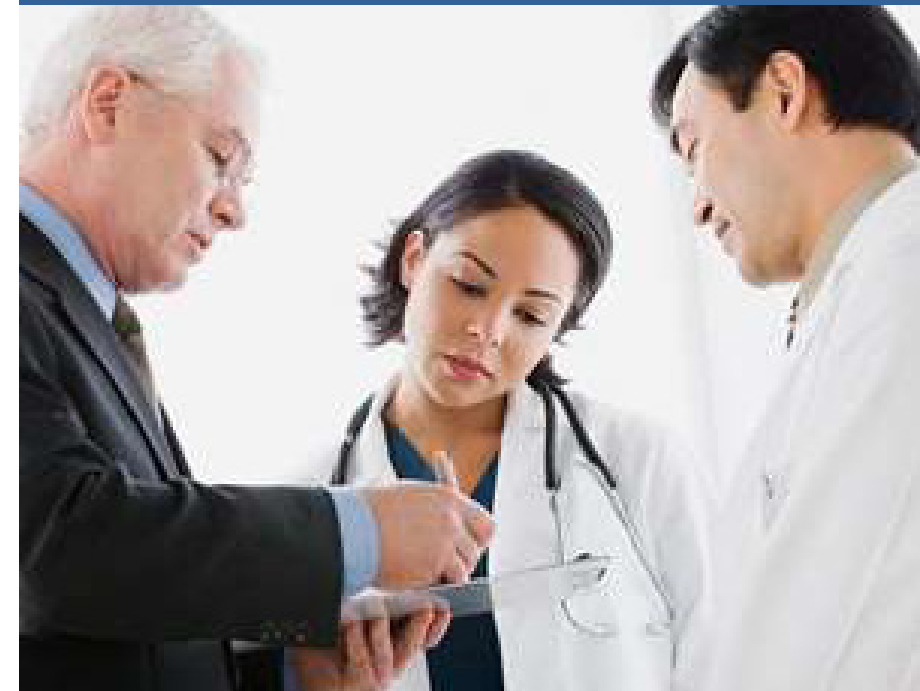


Challenge: Lack of industry interest in pain therapeutics

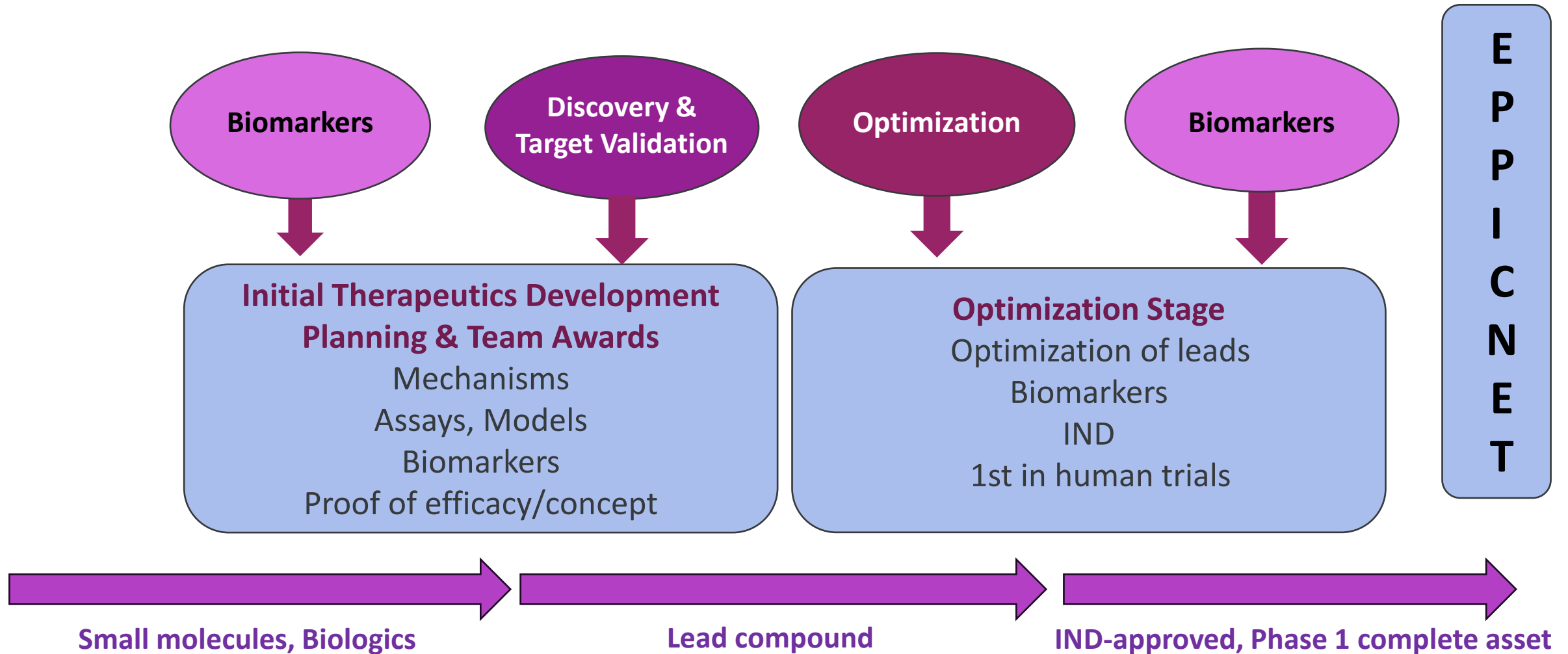
The Pain Therapeutics Industry Landscape

- Industry-wide, the industry pipeline for analgesics **declined 44%** in the past five years.
- Venture capital for novel pain drug programs were **\$860 million** over the last 10 years compared to **\$35.7 billion** for cancer.
- Need to partner with small and large businesses to de-risk projects and move into phase II and commercialization.

No drugs with novel targets approved in the last five years for pain other than for migraine

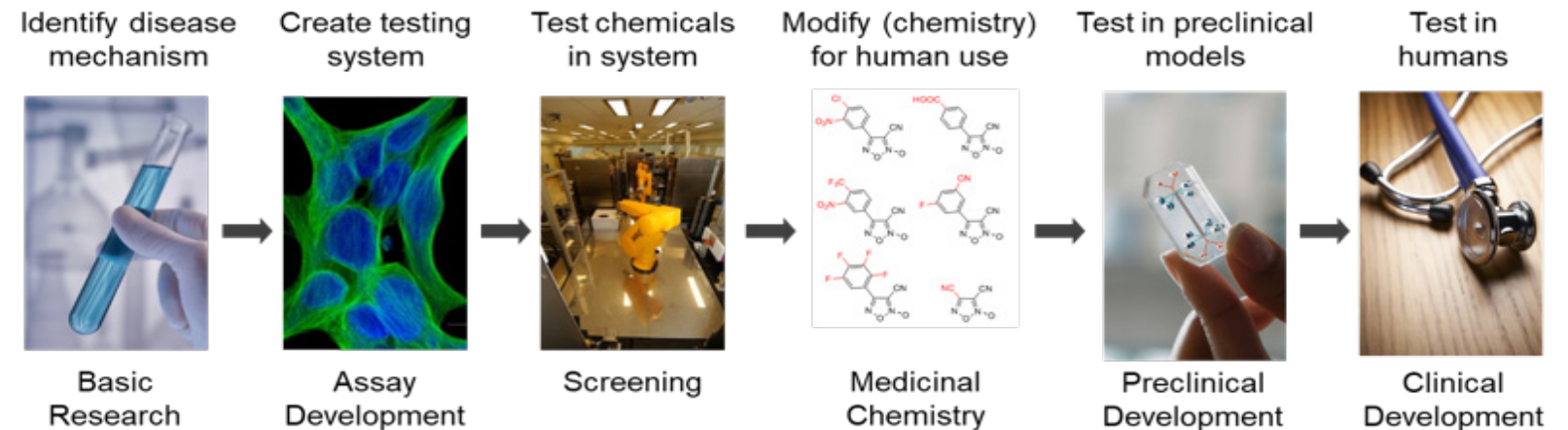


HEAL Analgesic Development Program



NIH HEAL Therapeutics Progress

- Pain therapeutics development program
 - 16 awards, 8 INDS, 2-3 INDs ex
- PSPP therapeutics characterization for acute & chronic pain
 - >40 assets – *In vitro*, PK, behavioral models, side effects, specific disease models
- NCATS collaborative partnerships
 - Drug discovery - 14 projects
 - Assay development – tissue chip and iPSC
 - Compound library



BIOTECH

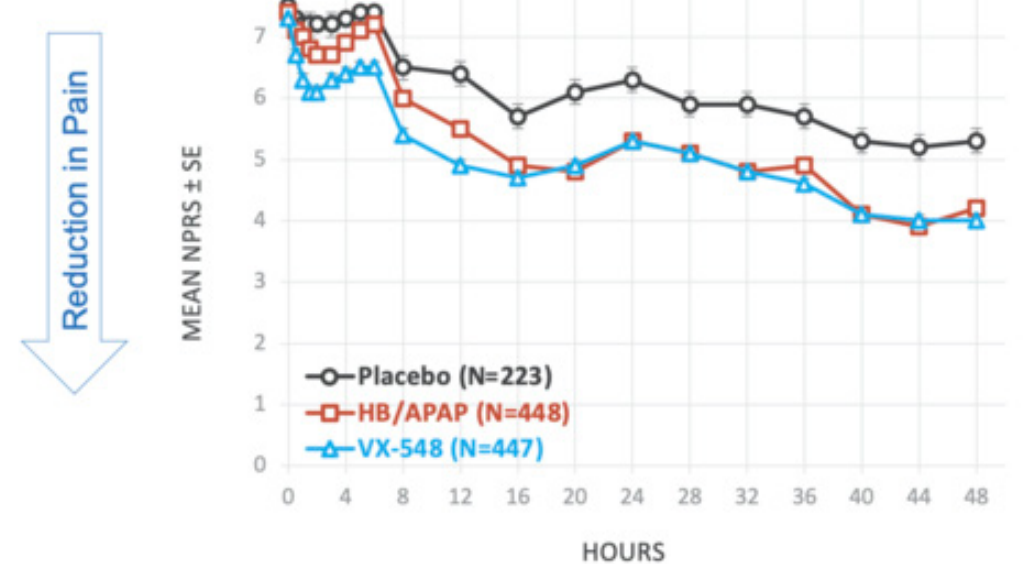
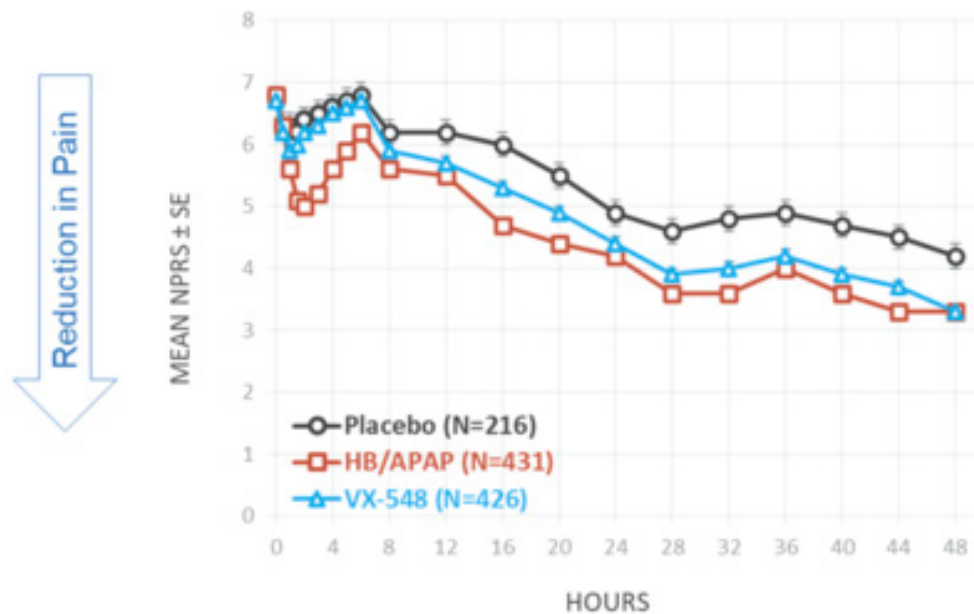
Vertex's pain prospect hits main goal in phase 3 trials but fails to beat Vicodin

Na⁺V 1.8 inhibition

By Nick Paul Taylor
Jan 30, 2024 8:00am

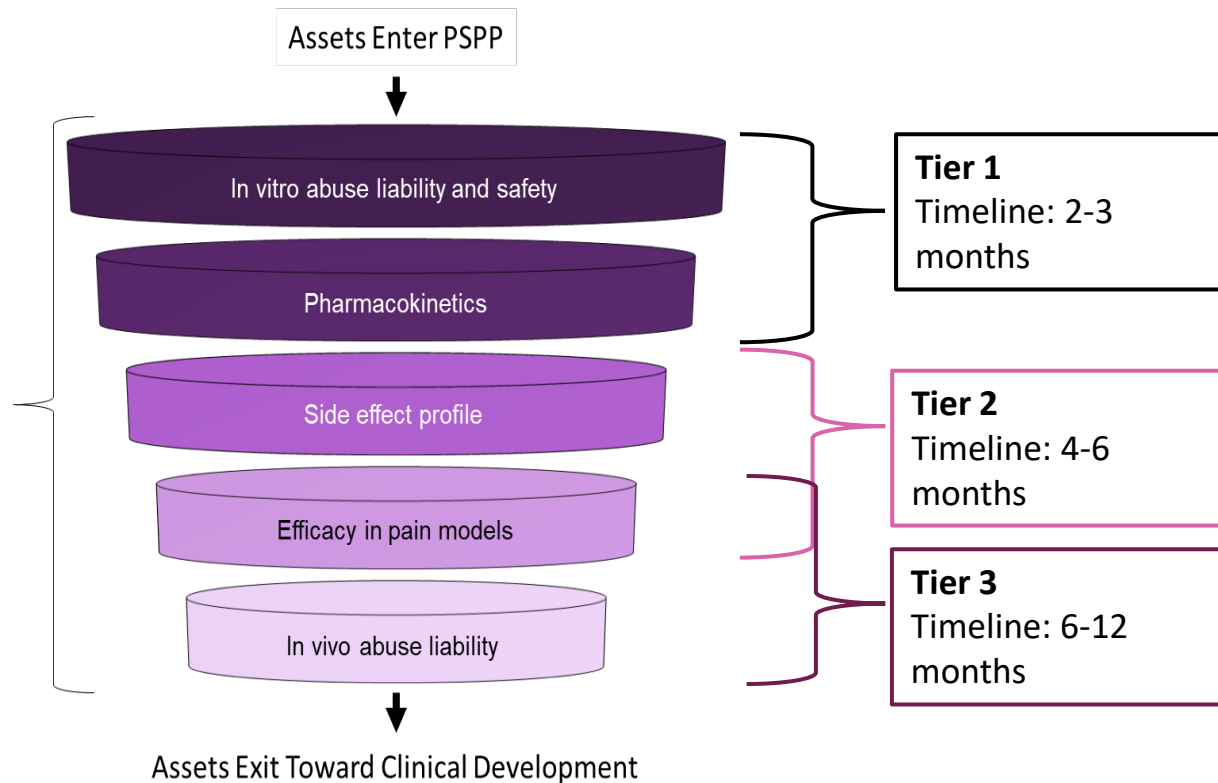
Mean NPRS Over Time in Phase 3 Study of Acute Pain Following Bunionectomy

Mean NPRS Over Time in Phase 3 Study of Acute Pain Following Abdominoplasty

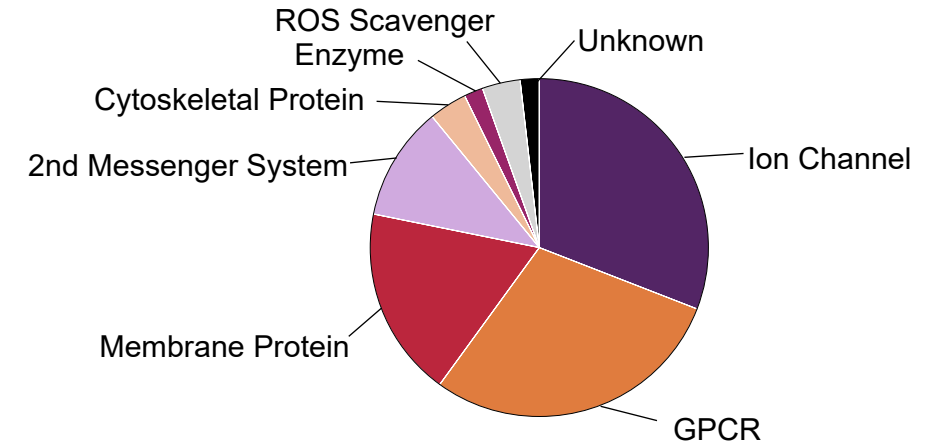


Preclinical Screening Platform for Pain (PSPP)

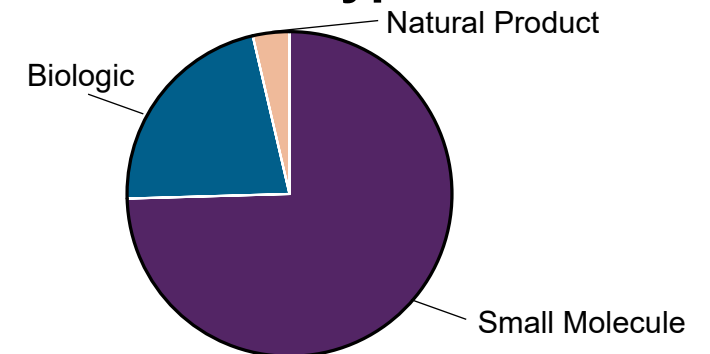
Accelerate the discovery and preclinical development of non-opioid, non-addictive treatments for pain



Target Class



Asset Type



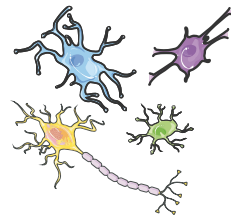
PRECISION Human Pain Network

Human tissues and cells to generate datasets of molecular signatures, cell types/phenotypes/signatures underlying human pain

Tissue Resources

- Transplant centers
- National Disease Research Interchange
- NIH NeuroBioBank Brain Bank Network

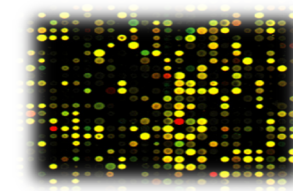
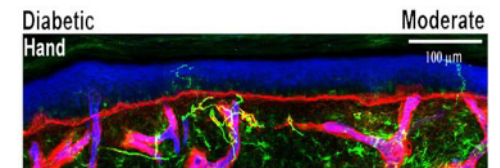
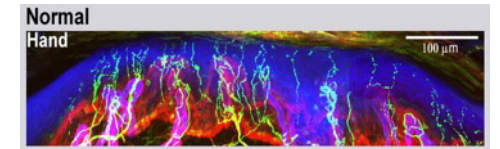
Diverse samples, specific pain & substance use conditions



Across the nervous system

- Brain, brainstem
- Spinal cord, dorsal root ganglia
- Peripheral nerve bundles
- Skin

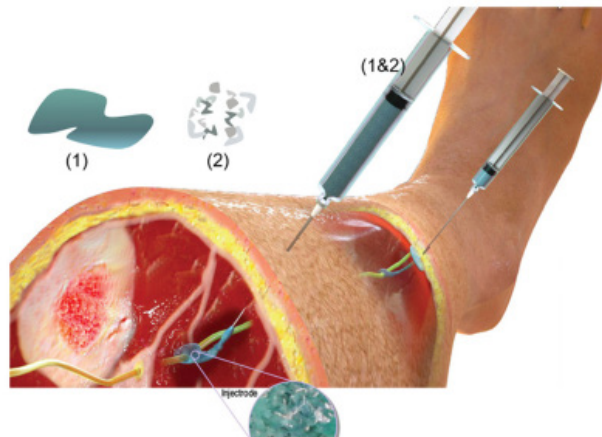
- Neuronal, non-neuronal cells
- Slice preps



- Omics
- Functional phenotyping
- Tissue histology

HEAL Program on Device Development for Pain Management

- Advance device-based treatments
- Support target identification, late-stage translational therapeutic and diagnostic device development, validation, early clinical studies.



Injectable liquid [polymer](#) next to or around the target nerve, provides a localized stimulus that avoids side effects of other types of neuromodulation.

HEAL RESEARCH SPOTLIGHTs

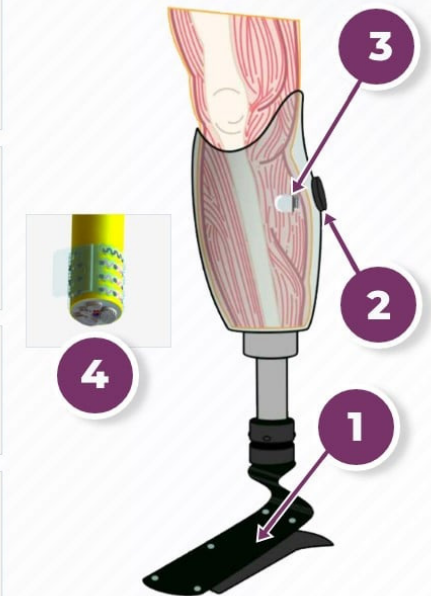
PERIPHERAL NERVE STIMULATOR SYSTEM: HOW IT WORKS

1 Sensors on the **prosthesis** convey information about contact, force, and angle to the sensor processor.

2 The **sensor processor** interprets the signals from the prosthesis and conveys a command to the implantable stimulator.

3 The **implantable stimulator** relays the command to the nerve cuff.

4 The **nerve cuff** wraps around the nerve endings and relays the command to the correct neurons.

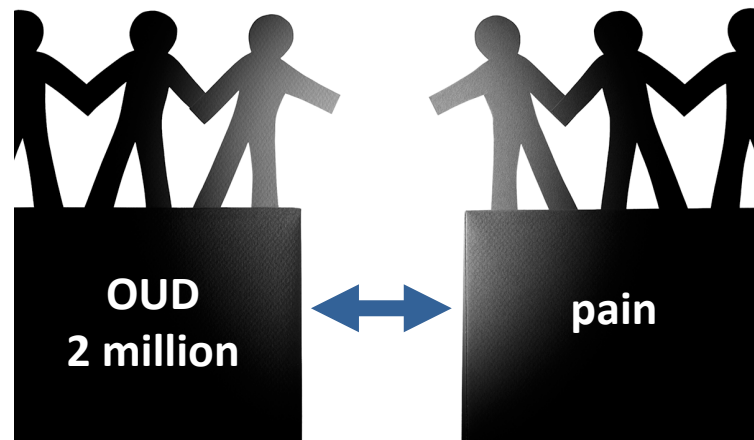


Credit: Ripple, LLC

<https://heal.nih.gov/news/stories/nerve-stimulation>
<https://heal.nih.gov/news/stories/phantom-limb-pain>

HEAL Trials for Integrative Management of Chronic Pain & OUD

IMPOWR & MIRQYL



40-60% with OUD + chronic pain

Integrated care beyond referrals

Whole person recovery

- Co-occurring conditions
- Stigma
- Health Disparities

HEAL: Advancing Health Equity in Pain and Comorbidities

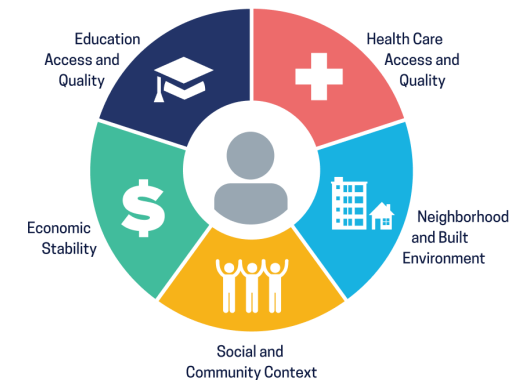
Purpose:

- Adapt and evaluate effectiveness of pain interventions in populations that experience health disparities

Essential Elements:

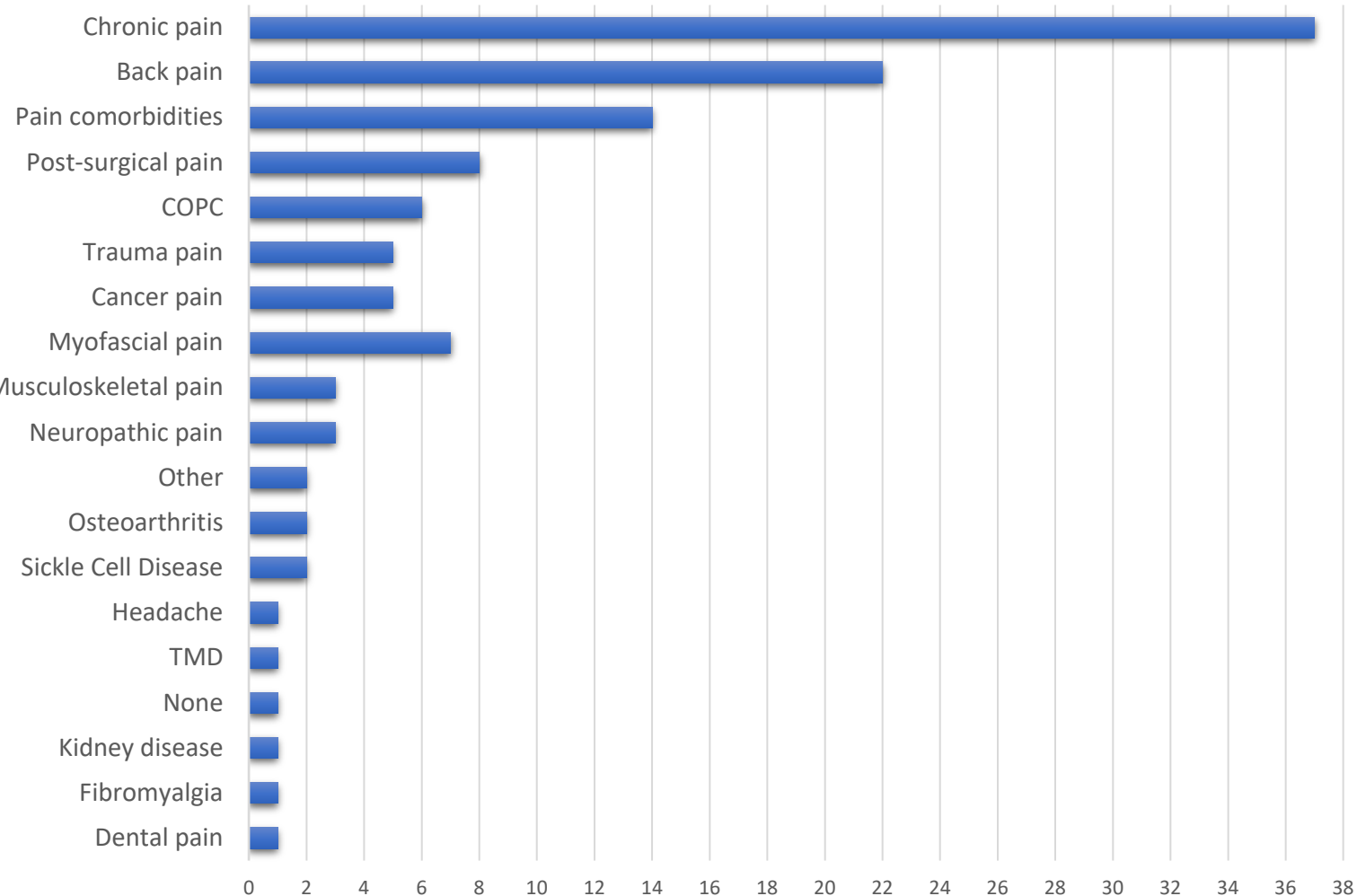
- Focus on targeted populations
- Extensive stakeholder & community engagement
- SDOH barriers
- **Pain and comorbid conditions:** mental Health; OUD; Chronic conditions

Social Determinants of Health



HEAL Clinical Research Networks in Pain Management to Accelerate Research into Practice

Pain Conditions in the HEAL Clinical Research Program



Number of awards

- ## HEAL Pain Research Networks and Consortia
- Biomarkers
 - Back Pain Consortium
 - EPPIC NET: Early phase 2 trials for therapeutics
 - ERN: comparative effectiveness research network
 - PRISM: pragmatic trials in health care systems
 - Pain and OUD
 - HOPE: trial for pain in late-stage renal disease
 - Health Equities
 - Rural Health
 - KIDS Pain: acute and chronic pain

HEAL Workforce Enhancement for pain research

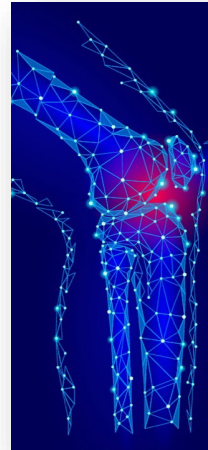
- **Diversity in Pain Research:** supplements to awarded grants to support researchers in underrepresented populations
- **K-12 National Clinical Pain Career Development Program:** mentored career development program to focus on training with experienced mentors
- **PURPOSE Network:** to connect pain researchers across the continuum of pain research, from all disciplines and at all career stages
- **Support Career Enhancement Related to Clinical Research on Pain**
Administrative Supplements
- **K99/R00 Independent Basic Experimental Studies with Humans:**
Advanced Postdoctoral-to-Independent Career Transition Award in PAIN and SUD Research to Promote Diversity



HEAL Biomarker Programs

Restoring Joint Health and Function to Reduce Pain

- characterize normal and altered joint innervation
- Explore modulation of neural activity to reduce pain
- prevent progression of joint deterioration

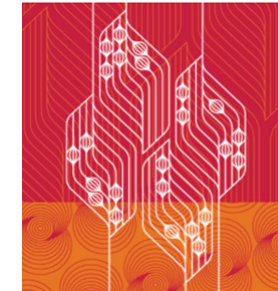


Condition Specific* and Clinical Trial Biomarkers

- discover and validate diagnostic, prognostic biomarkers to assess pain conditions and progression
- discover and validate biomarkers to predict and monitor treatment response in clinical trials

Biomarkers of Latent and Painful Myofascial Tissues

- technology to measure properties, identify pathology
- data analysis to develop markers, assessment tools, treatments



Biomarkers for Evaluating Spine Treatments

- Deep phenotyping to optimize personalized care
- collaborative multi-site BACPAC effort to understand what treatments are most effective for whom based on individual characteristics
- sequential randomization, such that the interventions can be maintained, added to or dropped according to the outcome from the initial randomization, reflecting real-world practice
- Enrollment complete
- Data harmonization, integration, analysis



Maximizing the Value of HEAL Data

The **HEAL Data Ecosystem** promotes **open science** through data sharing and long-term unlimited access and transparency. HEAL data must be **Findable, Accessible, Interoperable, and Reusable** (FAIR).

