The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Advancing Therapeutic Development
for Pain and Opioid Use Disorder
through Public-Private Partnerships

Federal Pain Research Strategy

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Designated Federal Official, IPRCC

The NIH Pain Consortium

National Institutes of Health

Mission

To enhance pain research and promote collaboration among researchers across the NIH Institutes and Centers that have programs and activities addressing pain

Leadership

Dr. Walter Koroshetz, Director NINDS, Chair NIH Pain Consortium

Dr. Josephine Briggs, Director NCCIH

Dr. Patricia A. Grady, Director NINR

Dr. Martha Somerman, Director NIDCR

Dr. Nora Volkow, Director NIDA

Support: Office of Pain Policy

Dr. Linda Porter, Director Office of Pain Policy

Dr. Cheryse Sankar, Dr. Leah Pogorzala, Dr. Khara Ramos, Pain Policy Analysts

The Interagency Pain Research Coordinating Committee

https://iprcc.nih.gov/

Federal Advisory Committee

Affordable Care and Patient Protection Act

Advisory to Secretary, Department of Health and Human Services

Mission

Enhance pain research efforts, promote collaboration across the government, with the goals of advancing fundamental understanding of pain and improving pain-related treatment strategies.

Members

Public, scientific, NIH, FDA, CDC, AHRQ, VHA, DoD

Key Activities

Federal pain research portfolio analysis and data base

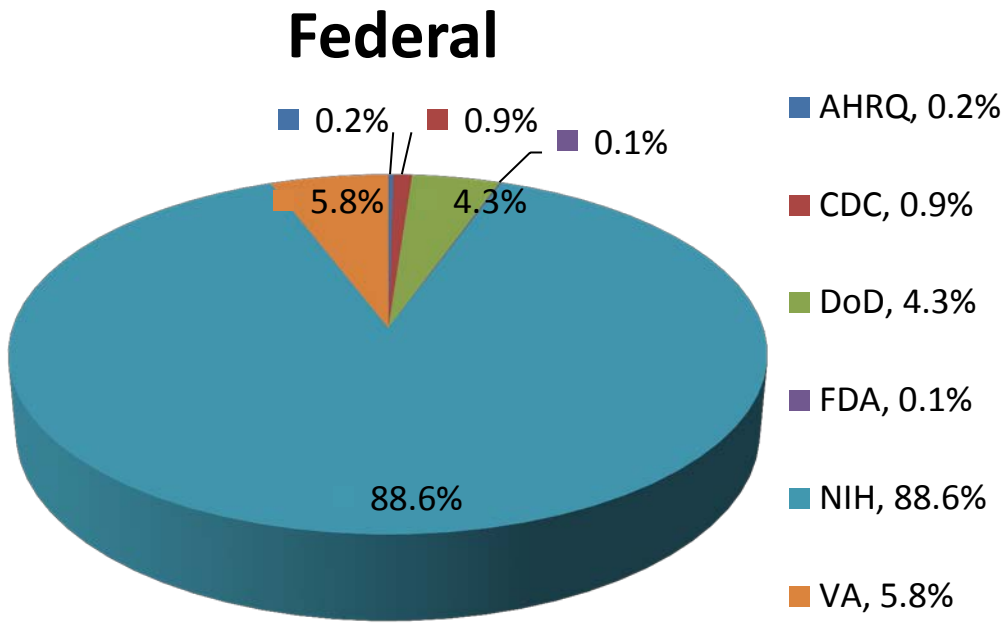
Science advances

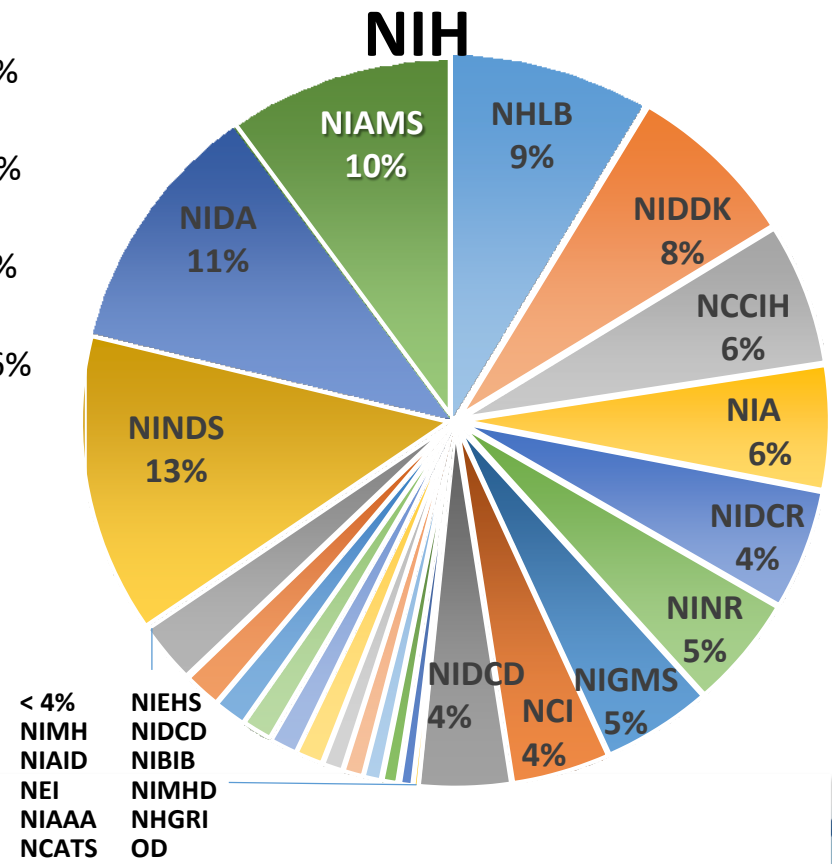
National Pain Strategy

Federal Pain Research Strategy

Federally Funded Pain Research

- Pain Mechanisms
- Basic to Clinical
- Disparities
- Risk Factors & Causes
- Tools & Instruments
- Surveillance & Human Trials
- Overlapping Conditions
- Use of Services, Treatments, & Interventions





https://iprcc.nih.gov/

NIH The Interagency Pain Research Coordinating Committee

Federal Pain Research Strategy

Fulfill the IPRCC mandate

"Identify critical gaps in basic and clinical research on the symptoms and causes of pain.

Make recommendations to ensure that the activities of the National Institutes of Health and other Federal agencies are free of unnecessary duplication of effort."

Complete the National Pain Strategy

"Include an agenda for developing physiological, clinical, behavioral, psychological, outcomes, and health services research and appropriate links across these domains that align with the NPS."

NIH National Institutes of Health

CDC

FDA

AHRQ

U.S. Department of Veterans Affairs

Federal Pain Research Strategy

Interagency Pain Research Coordinating Committee and the National Institutes of Health effort to **oversee development of a long-term strategic plan** for federal agencies and departments that support pain research.

Scientific experts, patient advocates, and federal representatives to **identify and prioritize research recommendations** to coordinate and advance the federal pain research agenda.

Federal Pain Research Strategy

CONTINUUM of PAIN

- PREVENTION OF ACUTE & CHRONIC PAIN
- ACUTE PAIN & ACUTE PAIN MANAGEMENT
- TRANSITION FROM ACUTE TO CHRONIC PAIN
- CHRONIC PAIN & CHRONIC PAIN MANAGEMENT
- DISPARITIES

WHAT HAPPENS AND TO WHOM?

WHY AND HOW DOES IT HAPPEN?

HOW TO MANAGE?

BASIC SCIENCE

CLINICAL SCIENCE

UNDERSTAND MECHANISMS

TRANSLATE/ TREAT

Federal Pain Research Strategy

Comprehensive set of prioritized pain research recommendations

- current state of the science
- ongoing research
- technological advances
- needs of people with pain
- continuum of pain
- top, most impactful, greatest near term value

Guidance for federal agencies and departments that support pain research

- agency representation and mission relevance
- collaborative research efforts to optimize resources
- incorporate FPRS priorities into mission-specific research strategic planning
- note “top”, “most impactful” and “greatest near term value” in funding decisions

Ten year timeframe

Federal Pain Research Strategy

Top Priorities

- **Develop a pain research network**
- **Develop safer opioids, new non-opioid analgesics, first generation of disease modifying drugs**
- Develop, evaluate, improve models of pain care
- **Develop approaches of precision medicine to prevent & effectively treat chronic pain**
- **Prospective studies for susceptibility & resilience factors underlying the transition from acute to chronic pain**
- **Understand & address plasticity mechanisms that promote persistent pain & resolution mechanisms**
- **Mechanistic trials of risk & resilience to chronic pain with meaningful outcome measures**
- **Determine mechanisms that sustain or resolve chronic pain & which can be intrinsically, extrinsically modulated**
- **Determine optimal safe and effective chronic pain management**
- Determine optimal approaches for use of self-management strategies for pain
- Determine the bidirectional relationship between common comorbidities and chronic pain
- Understand mechanisms of childhood chronic pain

Session II: Identifying Opportunities for Therapeutic Development in Non-Addictive Pain Medicines

Novel methods to identify pain targets: genetics, circuitry, cell based models

Develop safer opioid/non-opioid analgesics & 1st generation disease modifying agents

Heterogeneity of circuitry involved in acute pain sensation and modulation

Improve target validation for analgesics: successes & failures, preclinical efforts

What are the most sensitive and specific preclinical models of acute pain that are representative of naturally occurring pain conditions?

Whole brain imaging in animal models compared to human models

Session III: Addressing Clinical Challenges and Immediate Needs for Developing Pain Therapeutics: Biomarkers & therapies to prevent pain transition

Biomarkers for target engagement/proof of principle: imaging, circulating

Develop approaches incorporating the principles of precision medicine to prevent and effectively treat chronic pain.

Developing therapies to prevent the transition from acute to chronic pain: preclinical and clinical gaps, homogeneous populations

Develop a research network.

Understand and address plasticity mechanisms that promote persistent pain and resolution mechanisms that may reverse persistent pain.

Determine similarities &difference across chronic pain states

The FPRS at Work

Common Fund Concept: Acute-to-Chronic Pain Transition Signatures

Research Gap: No objective signatures of the transition from acute to chronic pain. This study will enable identification of patients at risk for chronic pain. prevention plans.

Why Common Fund?: Chronic pain is a symptom of many diseases and can be a disease in of itself. The project will involve scientists from diverse areas of research and employ advanced technologies. We foresee omics, imaging, sensory testing, PRO assessments that encompass a transition risk signature.

External Input

Understanding the Neurobiological Mechanisms of Pain, July 7, 2017

- Objective biomarkers that will predict the response to treatment
- Extensive phenotyping to develop objective biomarkers for precision medicine approaches
- Mechanisms of the transition from acute to chronic pain.

External Input

Federal Pain Research Strategy

Understand and Address Plasticity Mechanisms that Promote Persistent Pain and Resolution Mechanisms that May Reverse Persistent Pain.

Prospective Studies for Susceptibility and Resilience Factors Underlying the Transition from Acute to Chronic Pain

Trials to Determine Acute Pain Management Strategies that Promote or Prevent Development of Chronic Pain

Proposed CF Program

Discovery-focused clinical trial to identify objective signatures (genetic, imaging, molecular, PRO) of the transition from acute to chronic pain

- Recruit patients with **T=0 acute pain event** with known incidence of transition to chronic pain
  - T =0 surgery, trauma, injury
  - Follow for ~6 months to identify risk or resiliency factors Clinical records
    - Psychosocial and psychophysical assessment
    - Neuroimaging
    - Multi'omic phenotyping: Genomics, Metabolomics, Proteomics, Transcriptomics

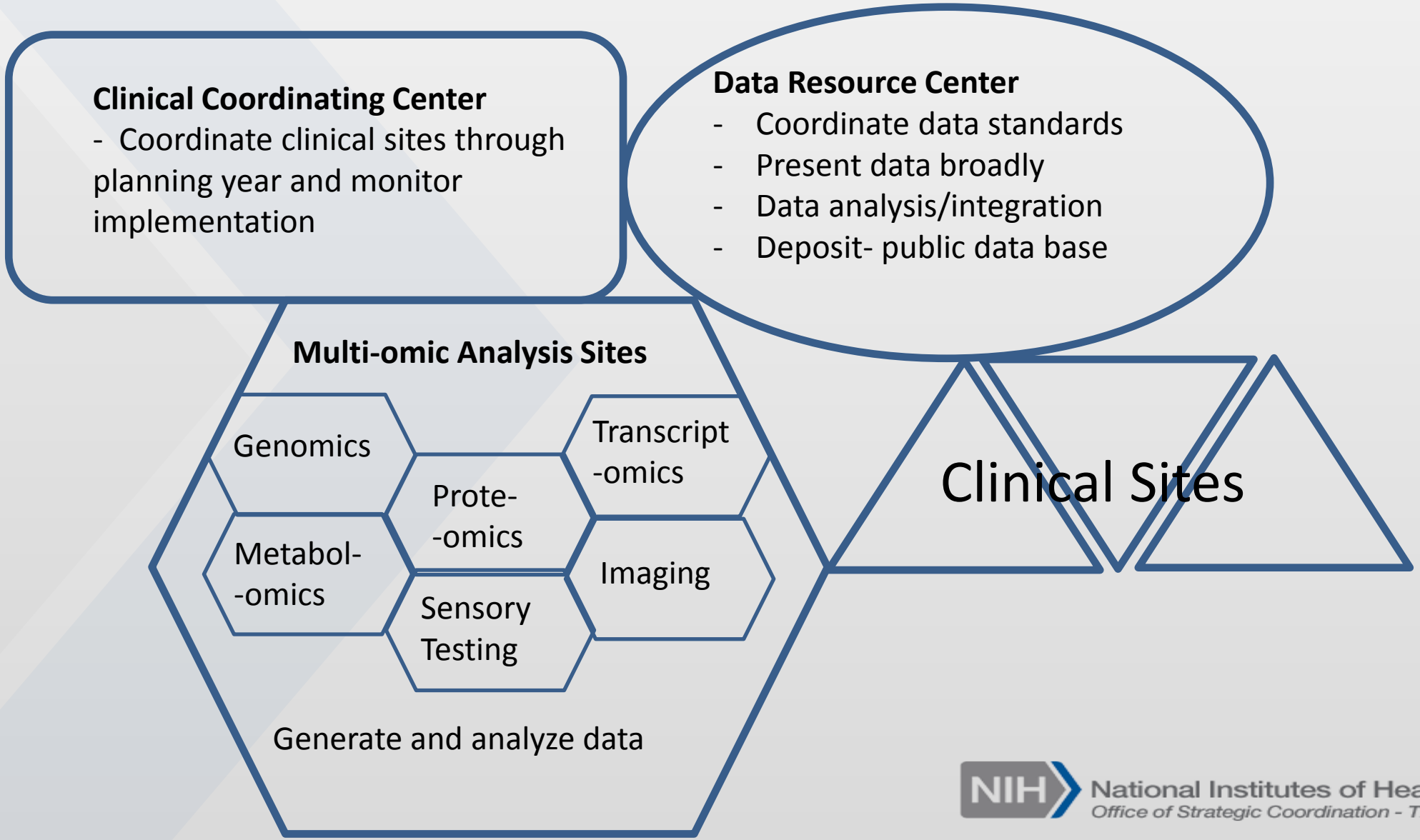
Parallel discovery-focused clinical study to identify objective signatures (genetic, imaging, molecular, biochemical) that associate with established chronic pain

- Recruit patients with selected acute pain event
  - Assess factors as in the transition cohort

Data Coordination and Analysis

- Signatures that predict transition to chronic pain
- Signatures that define established chronic pain
- Signatures that predict efficacy of pain management strategies?

Proposed CF Pain Program



Federal Pain Research Strategy
Next steps

Roll out plan

Agency engagement, inform investigators, public awareness

Public Private Partnership Support

Common Fund support

Funding Opportunity Solicitation Support

Agency Collaboration

Future Benchmarks