

Helping to End Addiction Long-term (HEAL) Update

117th Meeting of the Advisory Committee to the Director (ACD)

December 13, 2018

- Francis Collins, MD, PhD, Director, National Institutes of Health
- Nora Volkow, MD, Director, National Institute on Drug Abuse
- Walter Koroshetz, MD, Director, National Institute of Neurological Disorders and Stroke
- Rebecca Baker, PhD, Office of the NIH Director



Helping to End Addiction Long-term (HEAL) Update

Francis Collins, MD, PhD

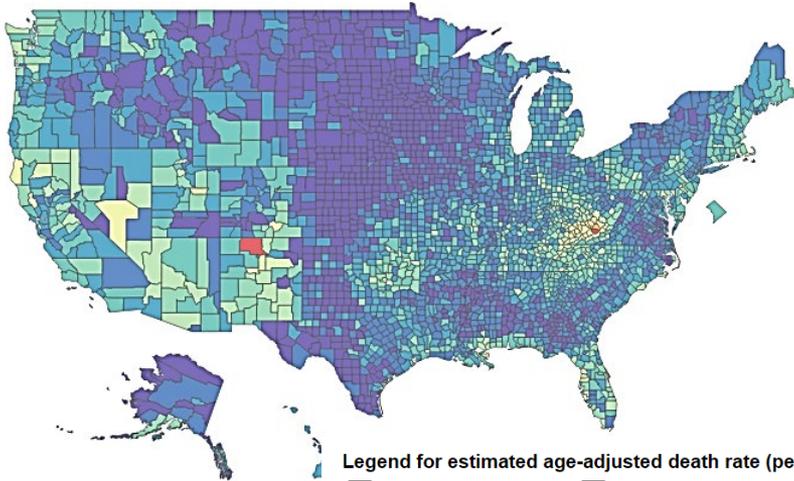
Director, National Institutes of Health



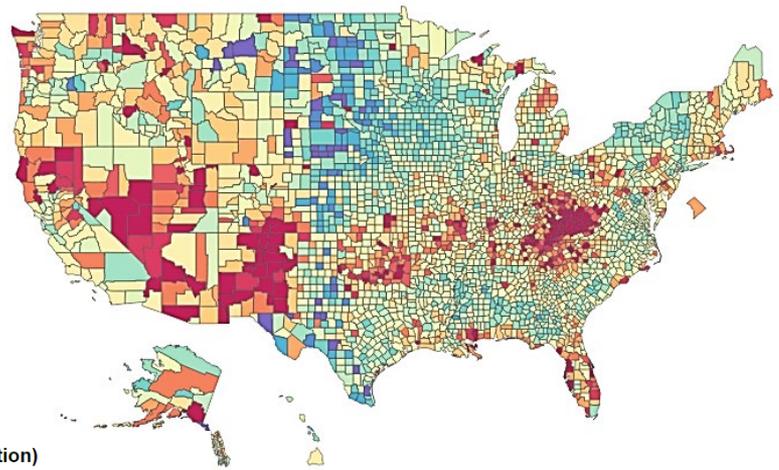
The Crisis: National Overdose Death Rates

In **2017**, there were **70,237** overdose deaths (9.6% higher than 2016)

1999



2016



Legend for estimated age-adjusted death rate (per 100,000 population)



The Response: Helping to End Addiction Long-term (HEAL) Initiative

- Trans-NIH research initiative to:
 - Improve prevention and treatment strategies for opioid misuse and addiction
 - Enhance pain management
- Goals are scientific solutions to the opioid crisis
- Coordinating with the HHS Secretary, Surgeon General, federal partners, local government officials and communities



Helping to End Addiction Long-term (HEAL) Initiative: At a glance

- \$500M/year Trans - NIH effort
 - Over \$850M to be obligated in FY2019
- 12 NIH Institute and Centers leading 26 HEAL research projects
 - Over 20 collaborating Institutes, Centers and Offices
 - From prevention research, basic and translational research, clinical trials, to implementation science
 - Multiple projects integrating research into new settings
 - e.g. health care, criminal justice, Medicare populations etc.
- Released 36 funding announcements for FY2019

Helping to End Addiction Long-term (HEAL) Update

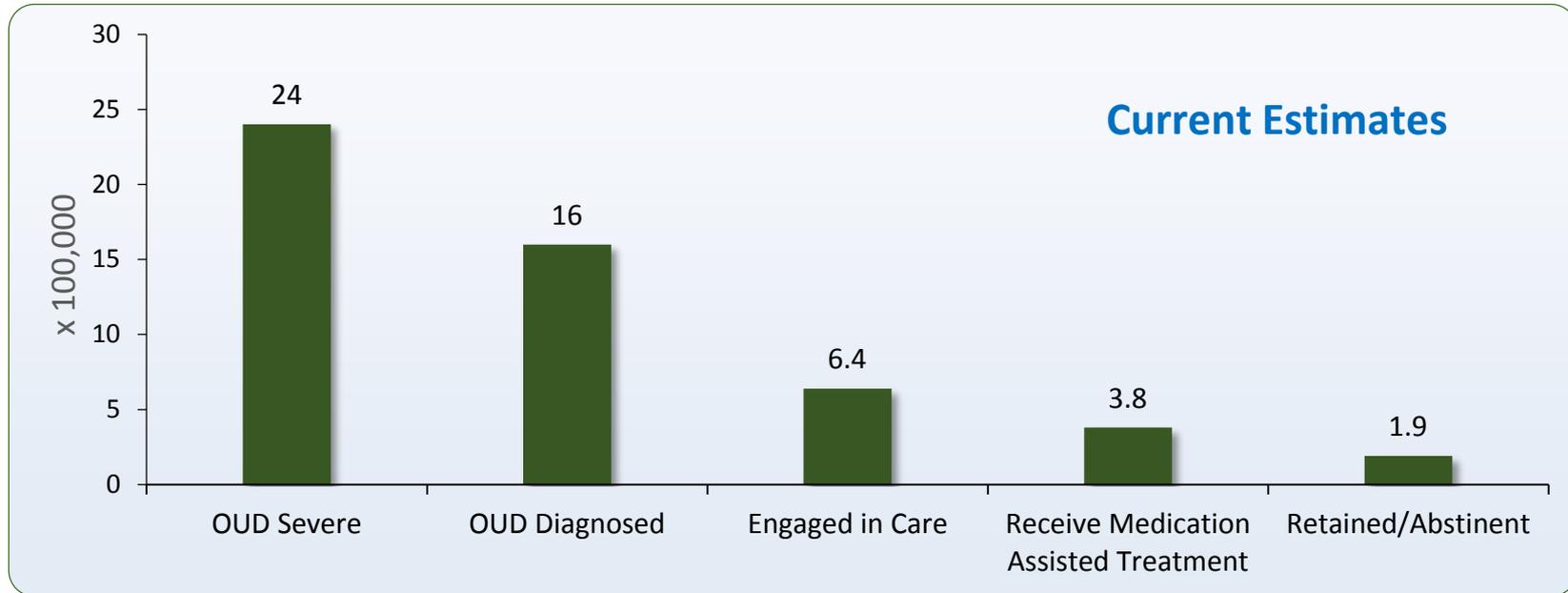
Nora Volkow, MD

Director, National Institute on Drug Abuse



OUD Cascade of Care in the United States

> 2 million Americans have an opioid use disorder



Improve prevention and treatment strategies for opioid misuse and addiction

- Risk of overdose death is 2-3 times higher when not on medication
- **Not sufficient SUD programs** that can provide with OUD medications
- Thousands of infants born annually with NAS/NOWS
- **Poor involvement of healthcare and criminal justice settings** in the treatment of OUD
- **Need of OUD prevention interventions** in the transition from adolescence to young adulthood when opioid misuse increases

Improving Prevention and Treatment for Opioid Misuse and Addiction

Priority Research Areas:

Expand Therapeutic Options

Optimize Effective Treatment Strategies

Develop New/Improved Prevention & Treatment Strategies

Enhance Treatments for Infants with NAS/NOWS

Research Opportunities:

- New formulations
- Longer duration
- Respiratory depression
- Immunotherapy
- New targets and approaches

- Clinical trials expansion
- Criminal justice innovation
- Behavioral interventions
- Multi-site implementation (HEALing Communities Study)

- Transition to adulthood
- Sleep dysfunction
- Early/moderate OUD
- Optimal length of Tx
- Collaborative care

- Advancing ACT NOW
- Cognitive development of opioid-exposed infants

Recent Advances in Medications Development

- Narcan Nasal Spray
 - First FDA-approved nasal spray version of naloxone, November 2015
- Sublocade™ (Buprenorphine ER)
 - Once-a-month injectable
 - FDA Approval, November 2017
- XR-Naltrexone and Buprenorphine-Naloxone
 - Shown to be equally safe, effective in preventing relapse, January 2018
- Lofexidine
 - Treat opioid withdrawal symptoms
 - FDA approved, May 2018



THE LANCET Vol 391 January 27, 2018

Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial

Joshua D Lee, Edward V Nunes Jr, Patricia Nova, Ken Bachrach, Genie L Bailly, Snehal Bhatt, Sarah Farkas, Marc Fishman, Phoebe Gauthier, Candace C Hodgkins, Jacquie King, Robert Lindblad, David Liu, Abigail G Matthews, Jasmine May, K Michelle Peavy, Stephen Ross, Dagmar Salazar, Paul Schlotnick, Dilka Shmueli-Blumberg, Den Stablin, Gretha Subramaniam, John Robinson

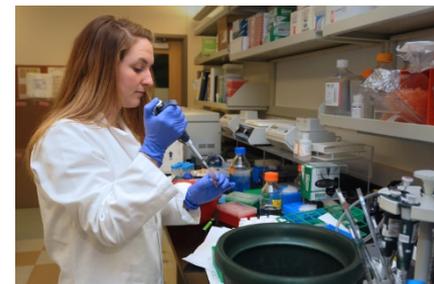
Medscape

FDA Panel Backs Approval of Lofexidine for Opioid Withdrawal

March 28, 2018

Research Priority: Expand Therapeutic Options

- New Formulations of Existing Medications
 - promote adherence to treatment and prevent medication misuse
- Longer Duration Formulations
 - Opioid antagonists to reverse overdose
- Interventions Against Respiratory Depression
 - New classes of compounds and devices
- Novel Medications, Immunotherapies and Devices
 - Treatment of withdrawal, craving, and relapse
- New Medication Targets
 - New addiction treatments via focused medications development



Research Priority: Optimize Effective Treatment Strategies

- NIDA Clinical Trials Network (CTN) Expansion
 - New research sites and studies (e.g., duration of treatment) in general medical/other settings
- Opioid Innovation in the Criminal Justice System
 - Justice Community Opioid Innovation Network (JCOIN)
 - Generate real-world evidence to address needs of individuals with OUD in justice-settings
- Behavioral Interventions
 - Behavioral Research to Improve Medication Assisted Treatment (BRIM)
 - Collaboration with SAMHSA to enhance behavioral or social interventions to improve adherence to medication assisted treatment for OUD
- HEALing Communities Study
 - Test integrated strategies in communities highly-affected by opioid crisis



Research Priority: Develop New/Improved Prevention and Treatment Strategies

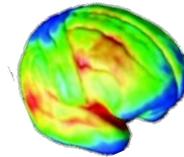
- Transition to Adulthood
 - Studies to prevent OUD in older adolescents and young adults
- Sleep Dysfunction
 - Sleep and circadian factors relevant to addiction
- Management of Subsyndromal and Low-severity OUD
 - Identify and treat patients in general medical settings with co-occurring pain/mental health disorders
- Optimal Length of Medication Treatment
 - Randomized clinical trial of buprenorphine and methadone
- Collaborative Care Model
 - Adapted to patients with OUD and mental health conditions



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Research Priority: Enhance Treatments for Infants with NAS/NOWS

- Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW)
 - Innovative ways to identify and treat newborns exposed to opioids
- Cognitive Development of Opioid-exposed Infants
 - Understand changes in brain and behavior resulting from early exposure to opioids
- HEALthy Brain and Child Development Study
 - HEALthy (BCD) Study



Courtesy pixabay.com, CC0

Helping to End Addiction Long-term (HEAL) Update

Walter Koroshetz, MD

Director, National Institute of Neurological Disorders and Stroke



NIH HEAL Initiative: Enhance Pain Management

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
- Establish the best pain management strategies for acute and chronic pain conditions



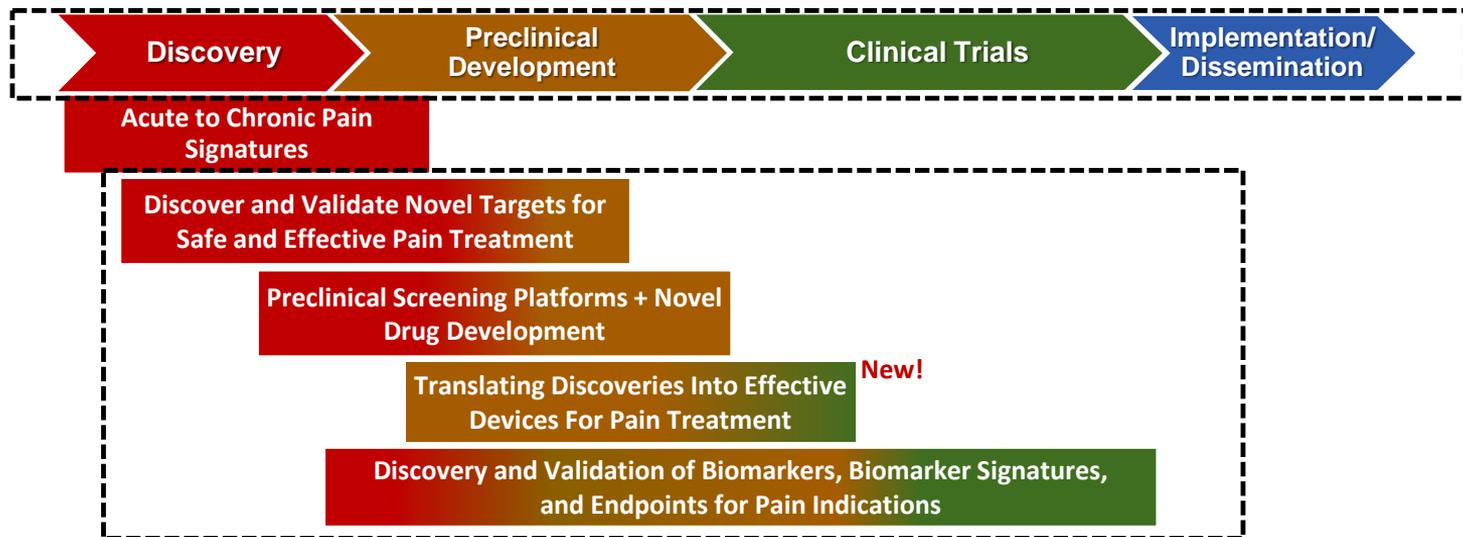
Read about the 2019 research plan:

www.nih.gov/heal-initiative

Understand the Biological Underpinnings of Chronic Pain



Accelerate the Discovery and Pre-Clinical Development of Non-Addictive Pain Treatments



Translating Discoveries into Effective Devices for Pain Treatment

Reduce reliance on opioids through the enhanced targeting and reduced invasiveness of diagnostic and therapeutic pain management devices

Brain
Research through
Advancing
Innovative
Neurotechnologies

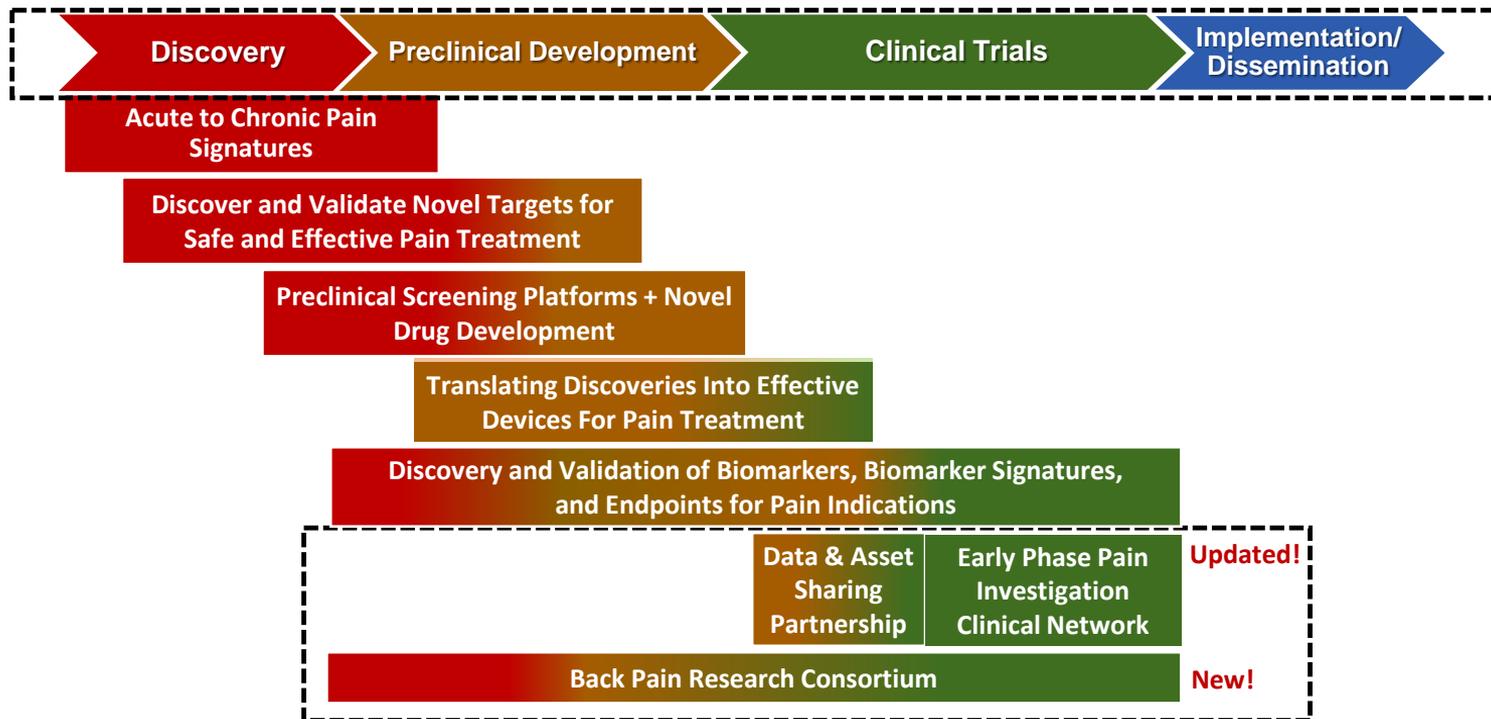


Stimulating
Peripheral
Activity to
Relieve
Conditions



- Leverage ongoing mapping / target discovery activities
- Late stage device development
- Verification and validation to accelerate regulatory approval
- Early clinical studies to de-risk new treatments

Advance new non-addictive pain treatments through the clinical pipeline



Early Phase Pain Investigation Clinical Network + Data and Asset Sharing Partnership

Improve quality, consistency, efficiency of early phase pain clinical trials

- EPPIC-net will test peer-reviewed compounds and devices from industry and academia
- Clinical Coordination Center, Data Coordination Center, 10 specialized clinical sites (hub and spoke design)
- Incentivize, accelerate Phase II trials
- Focus on well-defined pain conditions with high-unmet need
- Reduce the time to start, enroll, run, and complete trials
- Incorporate biomarker studies
- Accommodate platform trial designs

Data and Asset Sharing Partnership

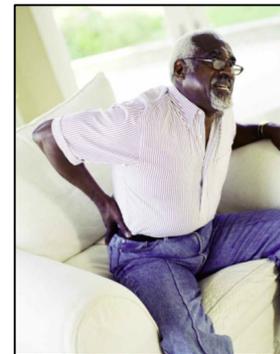
- EPPIC-net Data Coordination Center will host data and biosample repositories from HEAL programs and industry partners



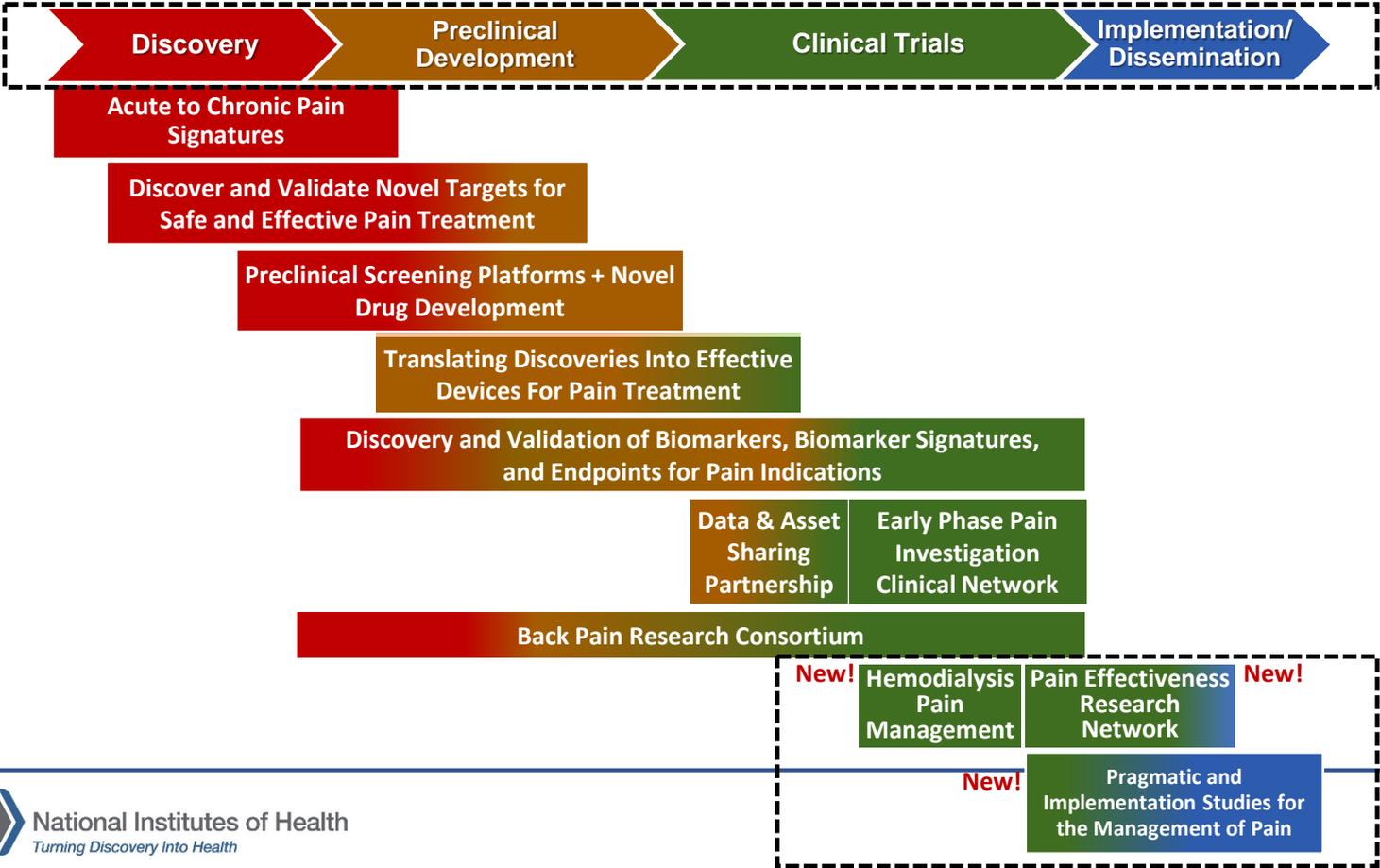
Back Pain Research Consortium: BACPAC

Probe biopsychosocial mechanisms of back pain, test new precision treatments, and develop predictive algorithms for integrated, multimodal back pain care

- Explore linkages between structural, dynamic, cellular, or molecular abnormalities to specific patient-reported symptoms and function
 - Characterize mechanisms and improve phenotyping in clinical cohorts
 - Develop and deploy technology for discovery, diagnostics, and treatment
 - Data integration and modeling
- Conduct clinical trials for new non-addictive drugs, biologics, devices and complementary approaches to relieve pain and improve physical function
 - safety and efficacy trials
 - integrated care trials
 - mechanistic trials
- Develop patient-centered algorithms to predict optimal treatment
 - Collect and analyze data from across the consortium's studies



Establish the Best Pain Management Strategies for Acute Pain and Numerous Chronic Pain Conditions



Pain Management Effectiveness Research Network and Trials

Evaluate effectiveness of pharmacologic and nonpharmacologic therapies for a broad array of pain conditions

- Comparative Effectiveness Research leveraging NCATS' Trial Innovation Network
- Pain expertise in coordinating centers
- NIH will solicit proposals for Phase 3 clinical trials to inform best practices in pain management and minimize risk of addiction
- Coordinate data elements and storage with EPPIC-net and PRISM

Integrated Approach to Pain and Opioid Use in Hemodialysis Patients

Develop tailored interventions for pain control for hemodialysis patients

- Evaluate non-addictive analgesics to reduce pain
- Evaluate behavioral approaches for pain management
- Identify risk factors for opioid dependence
- Assess and treatment co-morbid conditions
- Enhance electronic health records to capture study outcome data

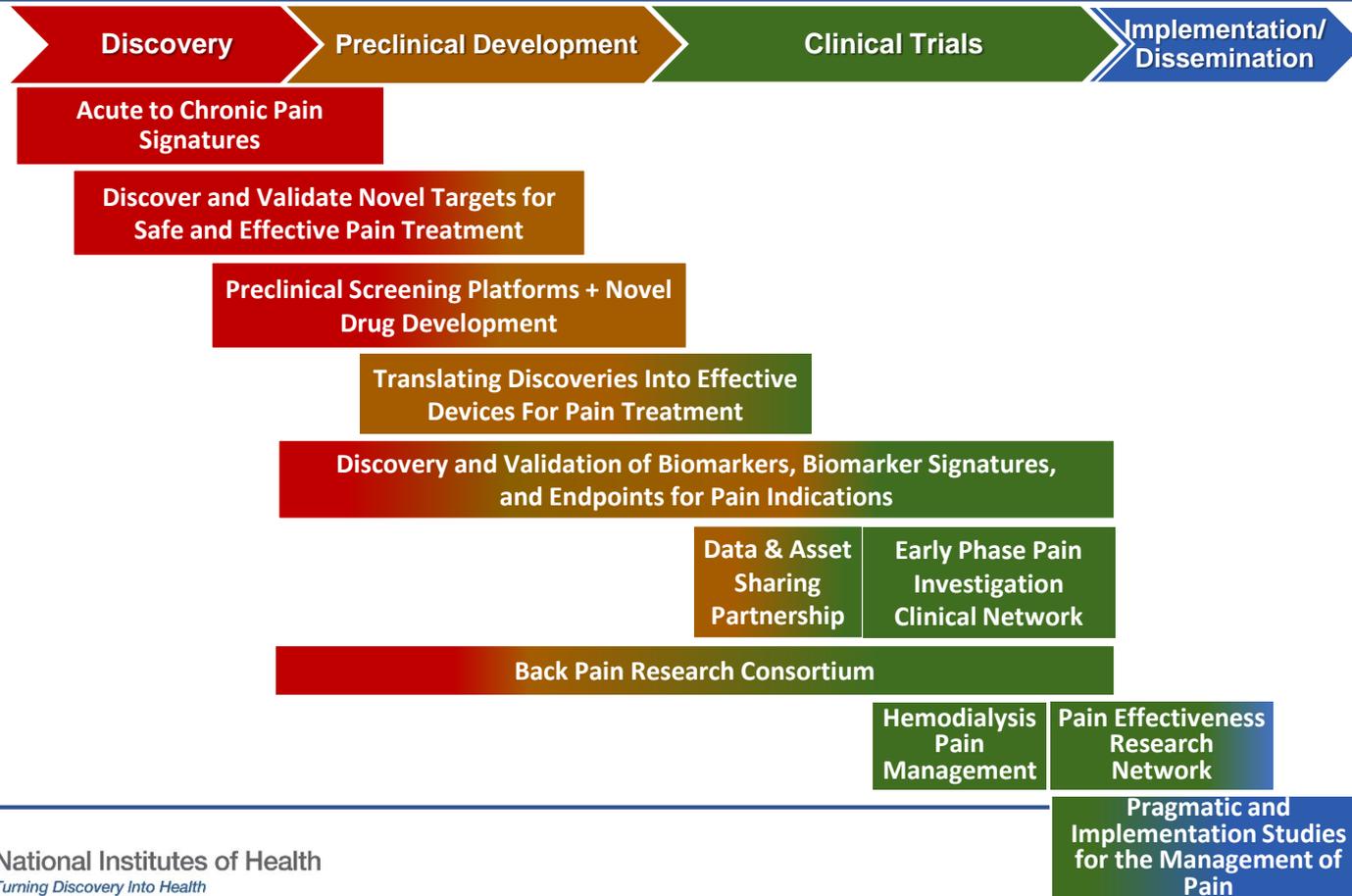
Pragmatic and Implementation Studies for Management of Pain to Reduce Opioid Prescribing: PRISM

Integrate evidence-based pain management interventions with demonstrated efficacy into health care systems

- Embed the intervention under study into real world settings
- Collect data through the electronic records
- Leverage the NIH Health Care Systems Collaboratory
- Focus on non-pharmacological approaches
- Collaborate with CMS for Medicare coverage consideration



Heal Programs for Pain Cover the Research Spectrum



Helping to End Addiction Long-term (HEAL) Update

Rebecca Baker, PhD

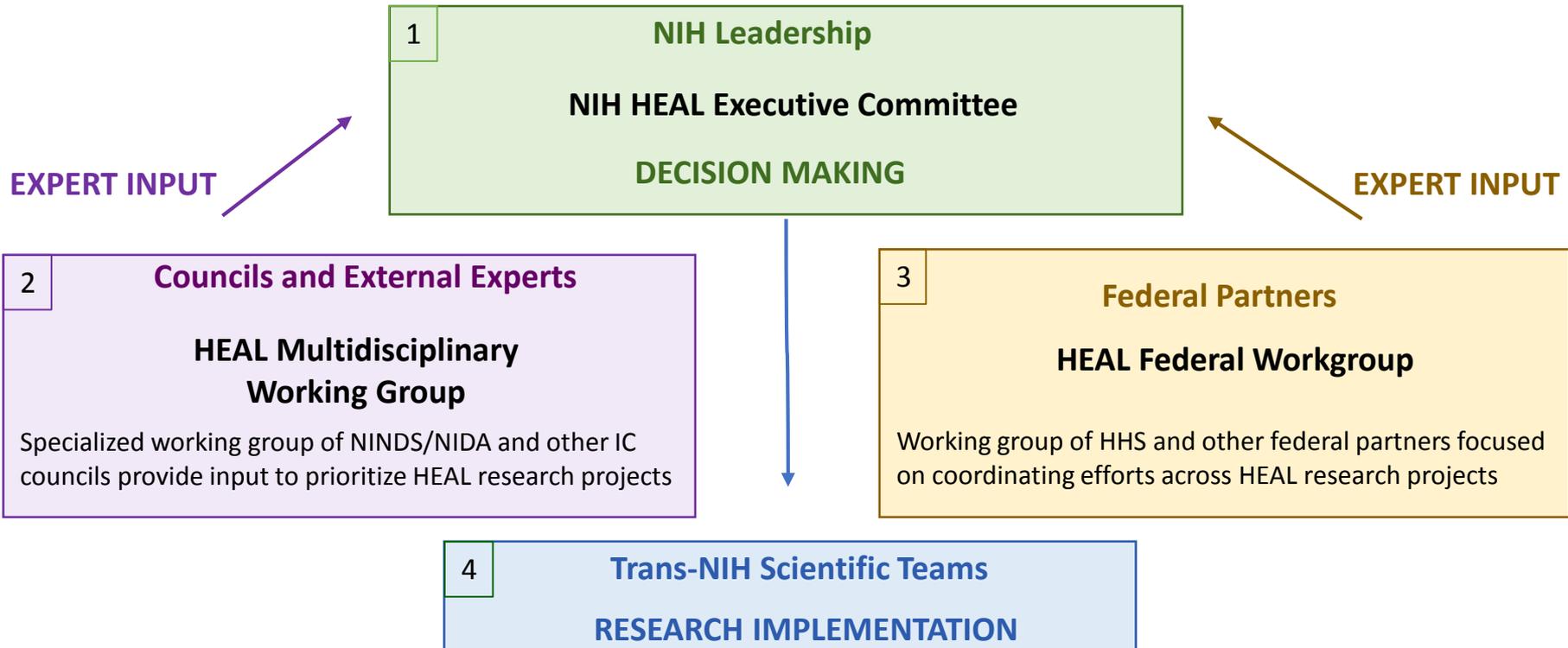
Office of the NIH Director



Helping to End Addiction Long-term (HEAL) Initiative: Governance

- Promise of the HEAL Initiative: Scientific solutions to the opioid crisis
 - **Ambitious:** Matching the urgency of the crisis
 - **Broad in scope:** Leveraging resources across disciplines and disease areas at NIH
 - **Timely:** Delivering real solutions to patients with pain and addiction
- Need for trans-NIH structure to guide research and ensure HEAL meets this promise

NIH Helping to End Addiction Long-term (HEAL) Initiative: Governance Overview



HEAL Initiative Governance: Executive Committee

1

Francis Collins

Nora Volkow

Walter Koroshetz

NIH HEAL Executive Committee

- Composed of 8-10 NIH Institute and Center Directors
 - Institutes with equities in HEAL
- Example decision:
 - Which trials to run through Pain Management Effectiveness Research Network

EXPERT INPUT

Councils and External Experts

EXPERT INPUT

Federal Partners

Trans-NIH Scientific Teams

HEAL Initiative Governance: Multidisciplinary Working Group

EXPERT INPUT

NIH HEAL Executive Committee
DECISION MAKING

2

Councils and External Experts

RESEARCH PRIORITIZATION

NINDS Council

HEAL multidisciplinary
Working Group

NIDA Council

Addiction focused
subgroup

- Specialized working group of NINDS, NIDA, other IC councils provide expert input on HEAL research
- No more than 16 members – some council some ad hoc members
- Will not review every FOA
 - Some FOAs to go directly to relevant IC council – determined by Executive Committee
- Provides input on state of the science in HEAL research areas and different pain conditions
 - Health services research, multi-disciplinary research and emerging opportunities

HEAL Initiative Governance: Multidisciplinary Working Group

EXPERT INPUT

NIH HEAL Executive Committee

DECISION MAKING

2

Councils and External Experts

RESEARCH PRIORITIZATION

HEAL Partnership
Forum

HEAL Partnership
Committee

HEAL multidisciplinary
Working Group

NIDA Council

NINDS Council

- Oversee activities of public-private partnership through the “HEAL Partnership Committee”
 - Composed of experts from pharmaceutical, biotech, device industries, along with patients, ethicist, and academic researchers
 - Help develop products such as template for industry submissions to new clinical trials network

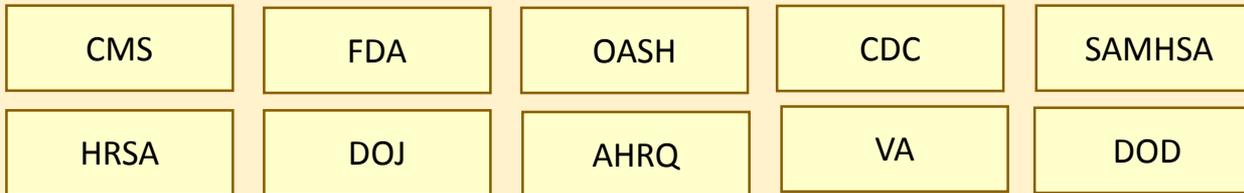
HEAL Initiative Governance: Federal Partners Working Group

NIH HEAL Executive Committee
DECISION MAKING

**EXPERT
INPUT**

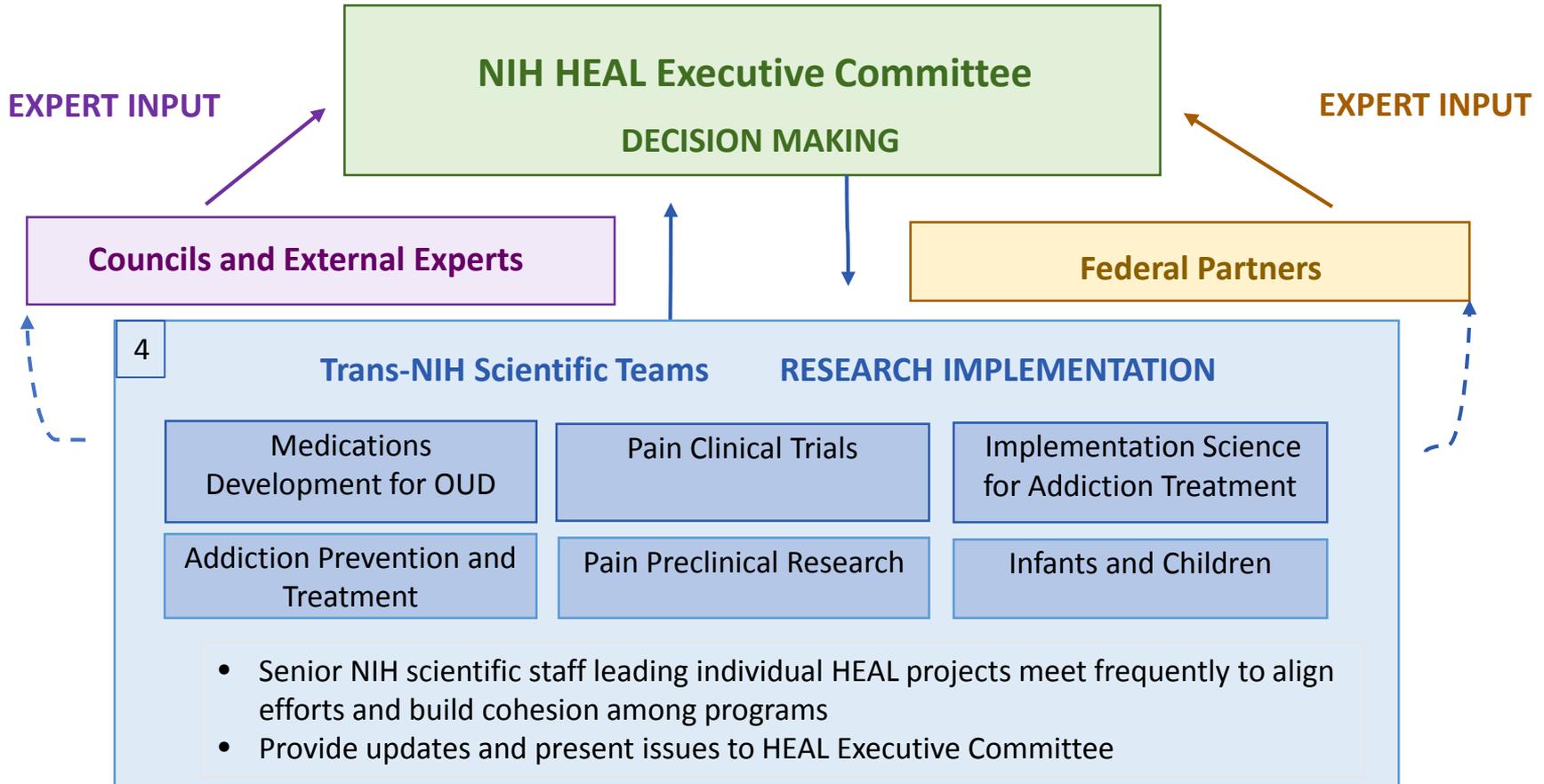
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Federal Partners



- Working group of federal partners focused on coordinating efforts across HEAL
- Example area of input: integrate data from SAMHSA State Targeted/Opioid Response awards in Behavioral Research and the HEALing Communities Studies

HEAL Initiative Governance: Trans-NIH Scientific Teams



Timeline for HEAL Multidisciplinary Working Group

- December 2018
Finalize governance plan
Seek nominations and develop roster of members
Present governance plan to HHS and ACD
- February 2019
First meeting, receive charge and overview of HEAL
- May 2019
Second meeting, provide input on NCATS/NINDS preclinical research programs
- August 2019
Third meeting, assess/prioritize studies for Pain Management ERN and other trials networks, receive general updates and prioritize research for other HEAL programs
- Ongoing
Meets tri-annually, usually before council meetings

Thank you!

Questions?



www.nih.gov/heal-initiative