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)

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

www.nih.gov/heal-initiative
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
> 2 million Americans have an opioid use disorder

Current Estimates

- OUD Severe: 24
- OUD Diagnosed: 16
- Engaged in Care: 6.4
- Receive Medication Assisted Treatment: 3.8
- Retained/Abstinent: 1.9

Williams AR, Nunes E, Olfson M. Health Affairs Blog, 2017
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
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
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
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

Discovery

Preclinical Development

Clinical Trials

Implementation/Dissemination

Acute to Chronic Pain Signatures
Accelerate the Discovery and Pre-Clinical Development of Non-Addictive Pain Treatments

Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints for Pain Indications

Discover and Validate Novel Targets for Safe and Effective Pain Treatment

Preclinical Screening Platforms + Novel Drug Development

Translating Discoveries Into Effective Devices For Pain Treatment

New!
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

- 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

Discovery → Preclinical Development → Clinical Trials → Implementation/Dissemination

- Acute to Chronic Pain Signatures
- Discover and Validate Novel Targets for Safe and Effective Pain Treatment
- Preclinical Screening Platforms + Novel Drug Development
- Translating Discoveries Into Effective Devices For Pain Treatment
- Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints for Pain Indications
- Data & Asset Sharing Partnership
- Early Phase Pain Investigation Clinical Network
- Back Pain Research Consortium

Updated!

New!
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

[Logo of FNIH: Foundation for the National Institutes of Health]
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

- **Discovery**
  - Acute to Chronic Pain Signatures
  - Discover and Validate Novel Targets for Safe and Effective Pain Treatment
  - Preclinical Screening Platforms + Novel Drug Development
  - Translating Discoveries Into Effective Devices For Pain Treatment
  - Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints for Pain Indications

- **Preclinical Development**
  - Data & Asset Sharing Partnership

- **Clinical Trials**
  - Early Phase Pain Investigation Clinical Network

- **Implementation/Dissemination**
  - Back Pain Research Consortium
  - New! Hemodialysis Pain Management
  - Pain Effectiveness Research Network
  - New! Pragmatic and Implementation Studies for the Management of Pain

**New!**

**NIH**
National Institutes of Health
Turning Discovery Into Health
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

Discovery

Preclinical Development

Clinical Trials

Implementation/Dissemination

Acute to Chronic Pain Signatures

Discover and Validate Novel Targets for Safe and Effective Pain Treatment

Preclinical Screening Platforms + Novel Drug Development

Translating Discoveries Into Effective Devices For Pain Treatment

Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints for Pain Indications

Data & Asset Sharing Partnership

Early Phase Pain Investigation Clinical Network

Back Pain Research Consortium

Hemodialysis Pain Management

Pain Effectiveness Research Network

Pragmatic and Implementation Studies for the Management of Pain

NIH National Institutes of Health

Turning Discovery Into Health
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

1. NIH Leadership
   - NIH HEAL Executive Committee
   - Decision Making

2. Councils and External Experts
   - HEAL Multidisciplinary Working Group
     Specialized working group of NINDS/NIDA and other IC councils provide input to prioritize HEAL research projects

3. Federal Partners
   - HEAL Federal Workgroup
     Working group of HHS and other federal partners focused on coordinating efforts across HEAL research projects

4. Trans-NIH Scientific Teams
   - Research Implementation
HEAL Initiative Governance: Executive Committee

**NIH HEAL Executive Committee**

- Francis Collins
- Nora Volkow
- Walter Koroshetz

- 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

NIH HEAL Executive Committee
DECISION MAKING

EXPERT INPUT

COUNCILS AND EXTERNAL EXPERTS

- 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

NIH HEAL Executive Committee

DECISION MAKING

EXPERT INPUT

2

Councils and External Experts

HEAL Partnership Forum

HEAL Partnership Committee

HEAL multidisciplinary Working Group

NIDA Council

NINDS Council

RESEARCH PRIORITIZATION

• 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

Federal Partners

CMS  FDA  OASH  CDC  SAMHSA
HRSA  DOJ  AHRQ  VA  DOD

- 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
Senior NIH scientific staff leading individual HEAL projects meet frequently to align efforts and build cohesion among programs.

Provide updates and present issues to HEAL Executive Committee.
## Timeline for HEAL Multidisciplinary Working Group

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| 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?