Advancing Addiction Science to Address the Opioid Crisis



NAtional Institute on Drug Abuse Advancing Addiction Science Wilson M. Compton, M.D., M.P.E.

Deputy Director National Institute on Drug Abuse



Drug Overdose Rates are Increasing: Estimated Age-adjusted Death Rates per 100,000 for Drug Poisoning by County.



63,362 Deaths in 2016 (42,249 from Prescription and Illicit Opioids)



Source: https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/index.htm

Evolution of Drivers of Opioid Overdose Deaths: Analgesics Heroin Fentanyl



Source: NCHS WONDER, NCHS Data Brief 294

NIH <u>Helping to End Addiction Long-term (HEAL)</u> Initiative

\$500M/year funding provides opportunity to:

- Improve prevention and treatment strategies, both in clinic and real world settings, for opioid misuse and addiction
- Enhance pain management by furthering understanding of neurobiology of pain, developing non-addictive treatments, and building a Clinical Trial Network for pain
- Develop shared platforms through public and private partners
- Coordinating with Surgeon General, other HHS agencies, local government officials



All Hands on Deck!

HEAL Research Projects on Opioid Use Disorder (OUD)

- Develop new treatments for opioid addiction, including more flexible medications options and novel immunotherapies to opioids
- Advance clinical trials for Neonatal Opioid Withdrawal syndrome to improve short- and long-term outcomes for infants and children
- Enhance the NIDA Clinical Trials Network to build linkages with primary care, emergency departments, and the justice system
- Establish a Justice Community Opioid Innovation Network
- Optimize effective treatments for OUD in the field through the HEALing Communities Study



Helping to End Addiction Over the Long-term Francis S. Collins, Walter J. Koroshetz, Nora D. Volkow. The Research Plan for the NIH HEAL Initiative JAMA July 10, 2018

Science = Solutions: Direct Overdose Intervention

Naloxone Distribution for opioid overdose victims. The potential for direct intervention to save lives.

Nasal spray and Auto-injector formulations now approved by the FDA

April 5, 2018 Surgeon General's Advisory on Naloxone and Opioid Overdose

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdosereversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, **knowing how to use naloxone and keeping it within reach can save a life.**

BE PREPARED. GET NALOXONE. SAVE A LIFE

Next steps

- Longer acting agents to address fentanyl risks?
- Respiratory stimulation?
- Device development?



Science = Solutions: Improving Addiction Treatment

- Initiating buprenorphine treatment in the *emergency department* improves treatment engagement and reduces illicit opioid use
- Extended release naltrexone initiated in *criminal justice* settings relapse rates and overdoses
- XR-Naltrexone and BUP-Nx *Equally Safe and Effective* (After Induction)
- Lofexidine for opioid withdrawal treatment recommended by FDA Advisory Committee March 29, 2018



HEAL – Treatment Enhancements Focused Medications Development

Despite availability of safe and effective OUD pharmacotherapies utility is limited due to:

- Low treatment rates
- Adherence challenges
- Lack of medications that act on non-opioid targets
- Increased potency of illicit opioids

Goal is to advance rapidly the development of compounds to prevent and reverse overdose and treat the different stages of OUD including:

- New formulations of existing medications to improve treatment compliance, prevent relapse and reduce diversion
- Stronger, longer-acting formulations to counteract overdose
- Interventions against respiratory depression induced by opioids
- Novel medications and immunotherapies to treat withdrawal, craving, progression, and relapse
- New medication targets

Projected impact is to accelerate NIDA's medication development, resulting in FDA submissions of approximately:

- 15 Investigational New Drug (IND) applications
- 5 New Drug Applications (NDAs)



HEAL – Opioid Misuse and Addiction Novel Immunotherapies for OUD

- Decrease challenges associated with relapse in OUD treatment:
 - Provide a needed safety net for patients at "high risk" of OD, Complement existing therapies for OUD, Reduce long-term opioid use and overdose, with minimal risk of side effects
- Opioid vaccines will not interfere with use of:
 - Non-opioid pain relievers, Structurally distinct opioids for emergency situations
- Opioid Vaccine Consortium
 - Vaccine development, Immunogen design and optimization, Adjuvants to improve antibody affinity, titers, and duration, Formulation, dosing, and delivery, cGMP manufacturing
- Vaccine pre-clinical testing in animal models
 - Vaccine efficacy, Pharmacology and toxicology
- Phase I-II clinical trials

HEAL – Treatment Enhancements Advancing NIDA's Clinical Trials Network

- NIDA collaboration with academics and community providers
 - Develop, validate, refine, and translate into practice new treatment options
- Expand the size and scope of the CTN
 - Expand treatment access, options, and education
 - Facilitate implementation science
- Contribute to improved quality of and access to treatment for OUD
 - Introduce sustainable interventions in underserved, highly impacted areas
 - Implement OUD treatment practices in general medical settings
 - Expand of the OUD treatment clinical and research workforce

<u>RFA-DA-19-008:</u>

GRANT APPLICATIONS DUE December 14, 2018

HEAL – Justice Initiative

Justice Community Opioid Innovation Network (JCOIN)

- Increase collaborations between justice systems and communitybased treatment providers to improve continuity of care
 - Enhance access and retention in OUD treatment
- Justice community-related research through network of investigators
 - National survey of addiction treatments in jails, prisons and communities
 - Effectiveness and implementation studies of new and existing medications, interventions, and technologies in justice settings
 - Leveraging existing data sources
 - Developing innovative research methods

Opioids During Pregnancy: Neonatal Abstinence Syndrome



Increasing Costs for Neonatal Exposure



Source: Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SM.. *Pediatrics.* 2018;141(4):e20173520

HEAL – Neonatal Opioid Withdrawal Advancing Clinical Trials in NOWs: Pilot Study

- Clinical trials for care of infants with NOWs
 - Determine effectiveness of currently used medications to treat withdrawal
 - Compare pharmacologic approaches to drug-free strategies
 - Eat, sleep, console
 - Assess impact of prenatal exposure to opioids
 - Effects on developing brain structure and function
 - Higher risk for school performance problems
 - Long-term risk for addiction
- Determine best practices to improve short- and long-term outcomes





HEAL – Integrated Treatment HEALing Communities Research Study

An Immediate Challenge

 OUD crisis is escalating; most Americans with an OUD (~80%) don't get effective treatment

Can we draw on all we know *now*... and develop integrated intervention strategies to stem the crisis *quickly*?

- Study ways to integrate evidence-based interventions comprehensively
 - In select areas highly affected by the crisis...

<u>RFA-DA-19-016 and -017:</u> GRANT APPLICATIONS DUE December 11, 2018

HEAL Research Projects on Pain Management

- Pinpoint acute to chronic pain signatures to identify those at risk for transition to chronic pain
- Discover and validate novel treatments for pain
 - Work across entire NIH to include all therapeutic development programs
 - Identify potential small molecules, biologics, devices, and natural products
 - Develop preclinical screening platforms for testing
 - Move successful compounds/devices to clinical trials





Helping to End Addiction Over the Long-termFrancis S. Collins, Walter J. Koroshetz, Nora D. Volkow.The Research Plan for the NIH HEAL InitiativeJAMA July 10, 2018

HEAL: Pain Research Overview for 2018



Additional Research Priorities

- Precision treatments for addiction
- Non-pharmacological treatments
- Integrated models of pain management
- Linkages between pain, addiction, mental health
- Education







- Complex biological, developmental and social aspects of substance use and addiction suggest *multipronged responses*.
- The severity of the opioid crisis demands *urgent action*.

www.nih.gov/opioid-crisis



www.drugabuse.gov