

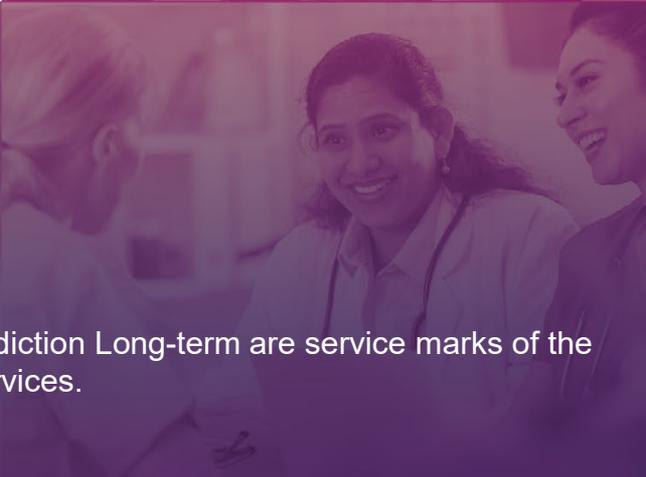


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# NIH HEAL Multi-Disciplinary Working Group



September 1, 2020



**NIH** National Institutes of Health  
*HEAL Initiative*

NIH HEAL Initiative and Helping to End Addiction Long-term are service marks of the U.S. Department of Health and Human Services.

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**Welcome**

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# Health Disparities and Research Diversity in HEAL

Lawrence A. Tabak, DDS, PhD  
Principal Deputy Director, NIH  
Department of Health and Human Services

# CALL TO ACTION - NIH IS COMMITTED TO ADDRESSING RACIAL AND HEALTH DISPARITIES.

BLACKS, DISCRIMINATION, TRAUMA, UNCONSCIOUS BIAS

## NIH Director Message: Grieving For Loss and Confronting Social Injustice



June 5, 2020

By: Francis S. Collins, M.D. Ph.D.

**The long history of discrimination against racial minorities in America bears directly on NIDA's mission to address addiction as a disease ...**

*Nora Volkow 2020, August 5. A Message from the Director on Racially Motivated Violence.*



**I am charged with striving to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.**

*Joshua Gordon, 2020, June 19. Racism and Mental Health Research: Steps Toward Equity.*



**The mission of NINDS is to generate knowledge to reduce the burden of neurological disorders, *for all people.***

*Walter Koroshetz 2020, June 19. A time for change: NINDS' commitment to diversity and eliminating racial bias.*



# NIH GOALS

**Reduce Health  
Disparities**

**Enhance Inclusive &  
Diverse Clinical Trials  
and Studies**

**Increase Scientific  
Workforce Diversity**

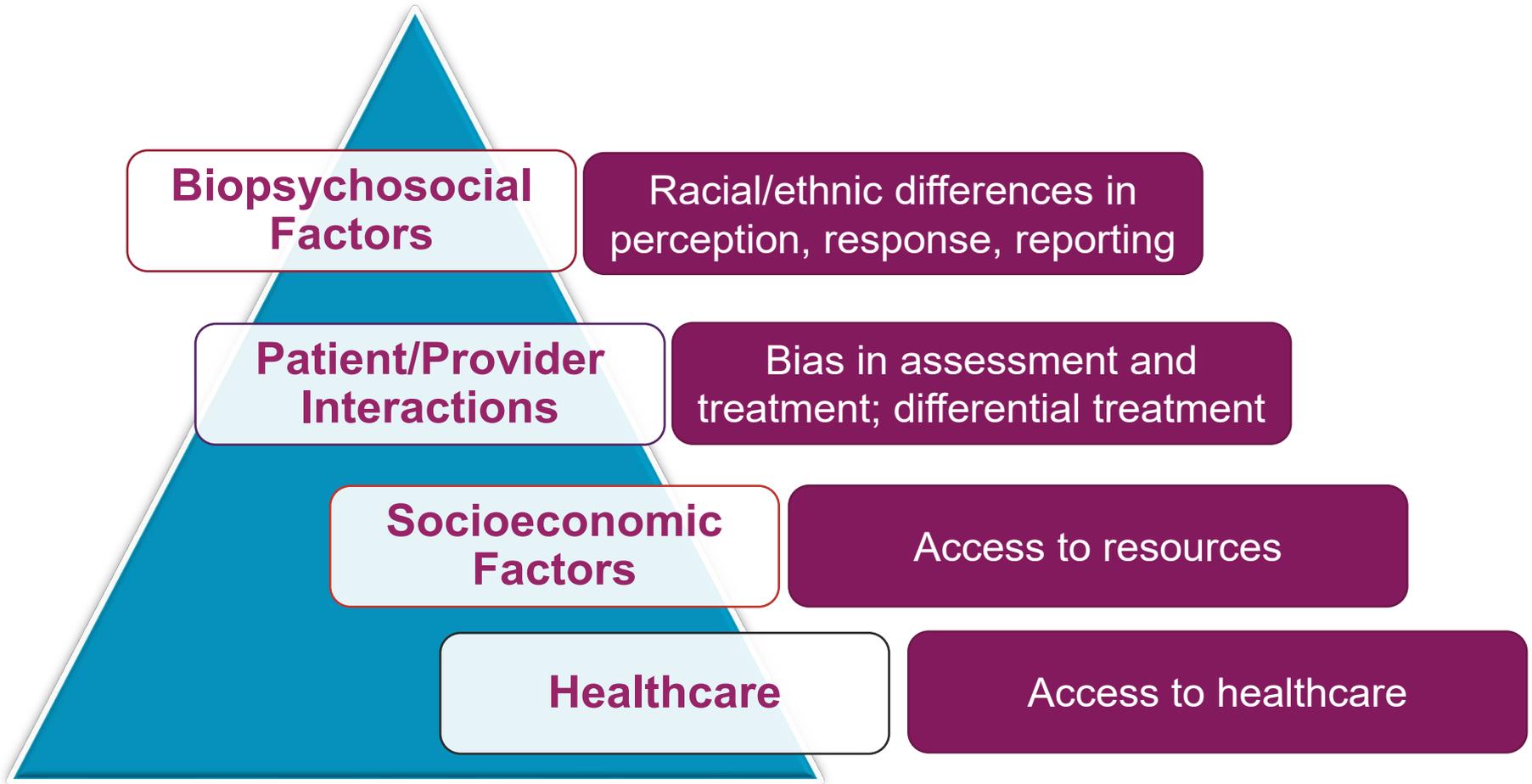
## Overarching Goals

- Reduce burden of chronic pain and OUD in vulnerable populations
- Diversity recruitment in clinical trials to better represent patient populations
- Accelerate diversity inclusion policies, processes, and programs

# Health Disparities: Inequalities among Different Populations

- Despite advances made in healthcare over the past century, we still deal with a disproportional burden of disease, worse clinical outcomes, and premature mortality for some groups.
- These health disparities affect a wide range of populations:
  - racial/ethnic minorities
  - less privileged socio-economic status
  - underserved rural residents, and/or
  - sexual and gender minorities

# Health Disparities: Barriers to quality care

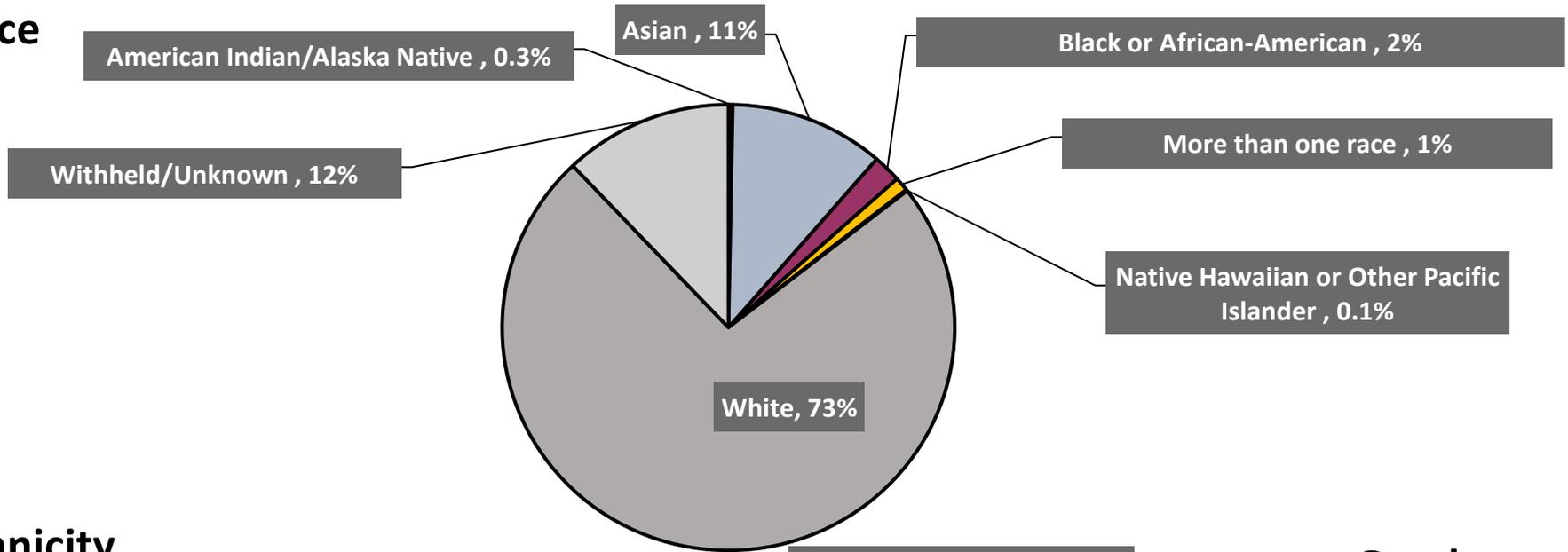


Developed by Cheryse Sankar, Ph.D, NINDS

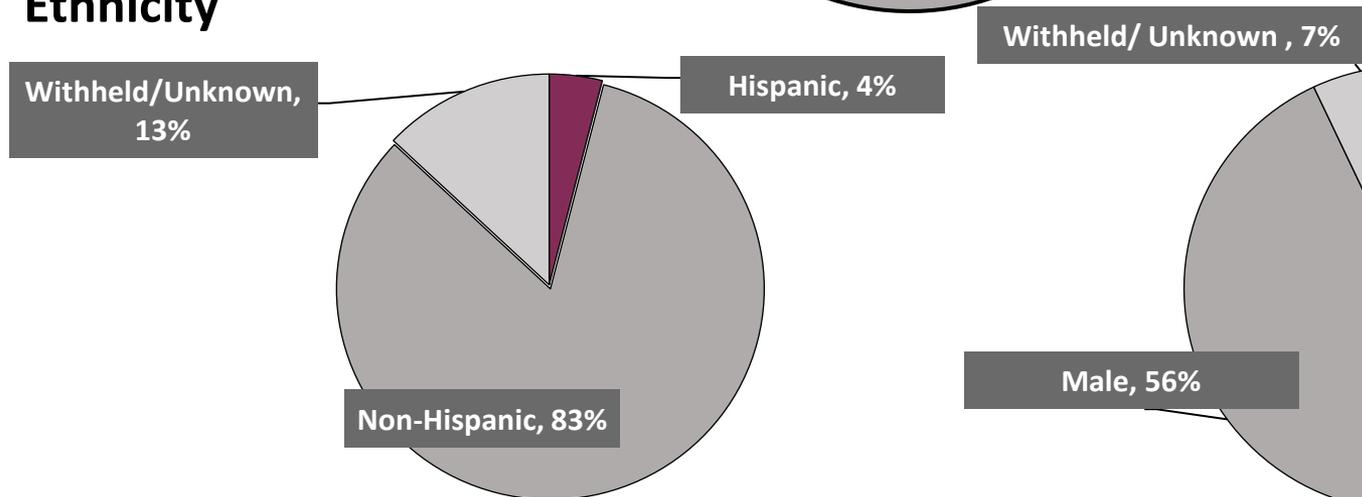
# Promote Scientific Workforce Diversity

## HEAL FY2019 Investigators

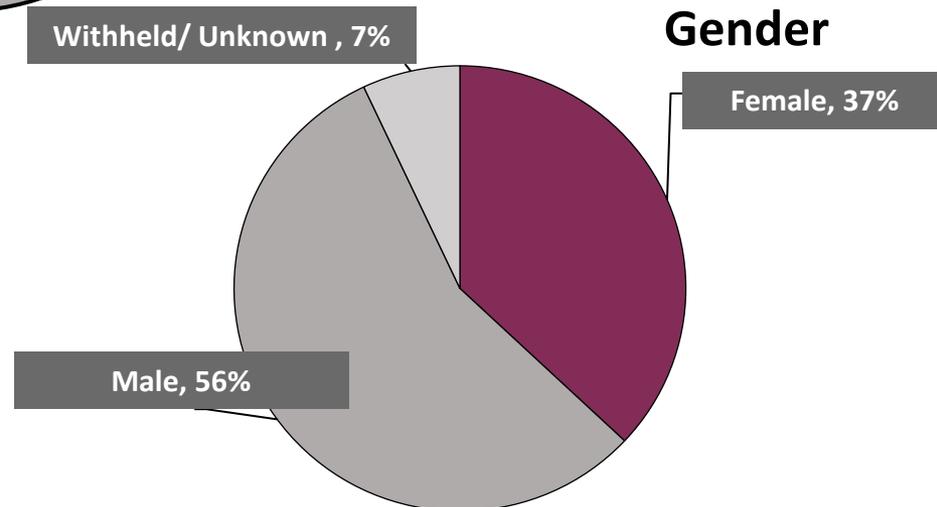
### Race



### Ethnicity

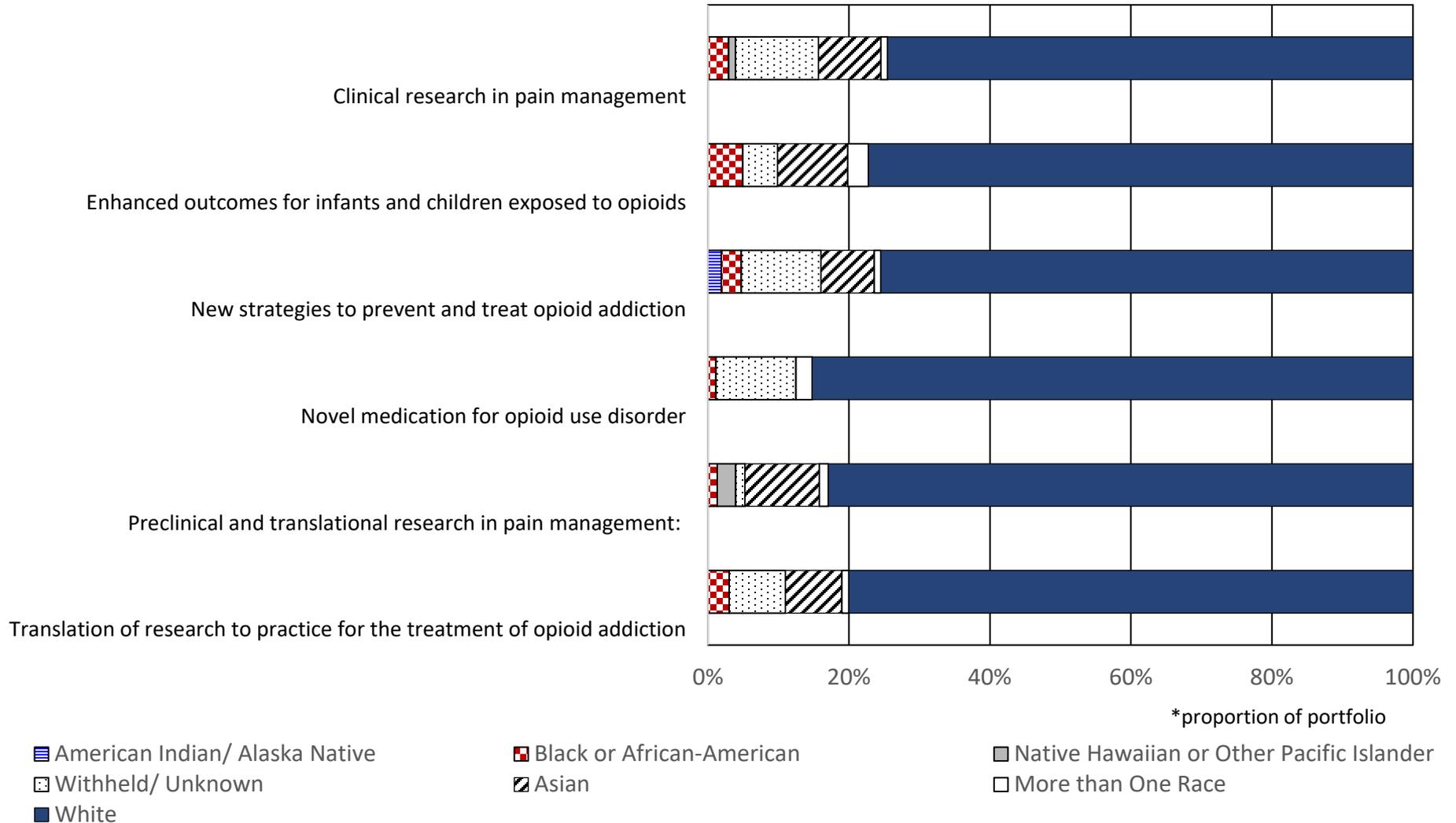


### Gender



# Promote Scientific Workforce Diversity

## Race & Research Focus Area for HEAL Investigators



# NIH Efforts to Increase Workforce Diversity

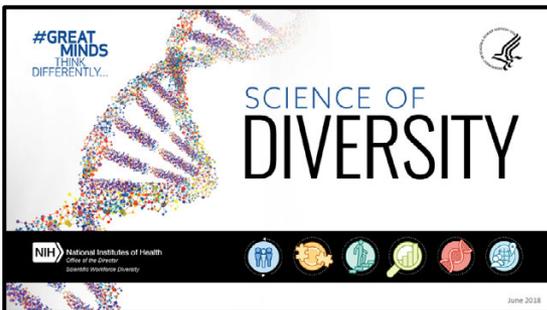
## A Diverse Biomedical Workforce Is Critical to NIH's Mission

### NIH-Wide Strategic Plan

Fiscal Years 2016-2020

#### Enhance Stewardship

- Recruit/retain outstanding research workforce
- Enhance workforce diversity
- Encourage innovation
- Optimize approaches to inform funding decisions
- Enhance rigor and reproducibility
- Reduce administrative burden



### Underway across NIH

- Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC)
  - Aims to enhance postdoctoral career transitions to faculty through supports of postdoctoral scientists from diverse backgrounds
- Faculty Institutional Recruitment for Sustainable Transformation Program Structure (FIRST)
  - Aims to enhance and maintain cultures of inclusive excellence in the biomedical research community.
- All Diversity Related FOA: <https://extramural-diversity.nih.gov/guidedata/data>

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NIH's Interest in Diversity: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-031.html>

MOSAIC: <https://www.nigms.nih.gov/training/careerdev/Pages/MOSAIC.aspx>

FIRST: <https://commonfund.nih.gov/first>

# HEAL Efforts to Increase Workforce Diversity

- **HEAL Notice of Special Interest: Research Supplements to Promote Diversity in Health-Related Research**
  - **Goal:** Enhance diversity of the pain research workforce by recruiting and supporting eligible junior investigators from groups that have been shown to be nationally underrepresented in the biomedical, behavioral, clinical and social sciences.

<https://grants.nih.gov/grants/guide/notice-files/NOT-NS-20-023.html>

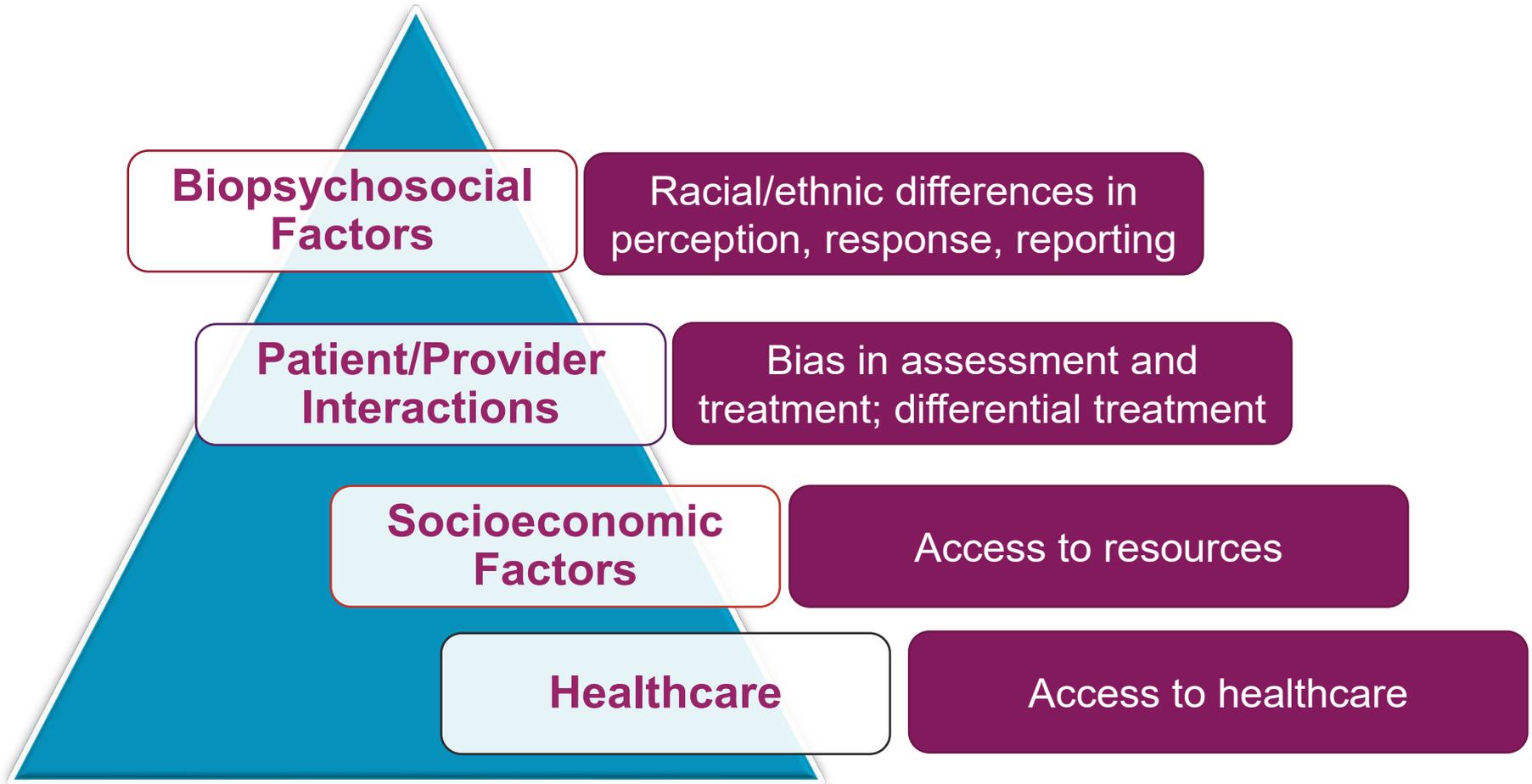


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# Health Disparities and Research Diversity in HEAL

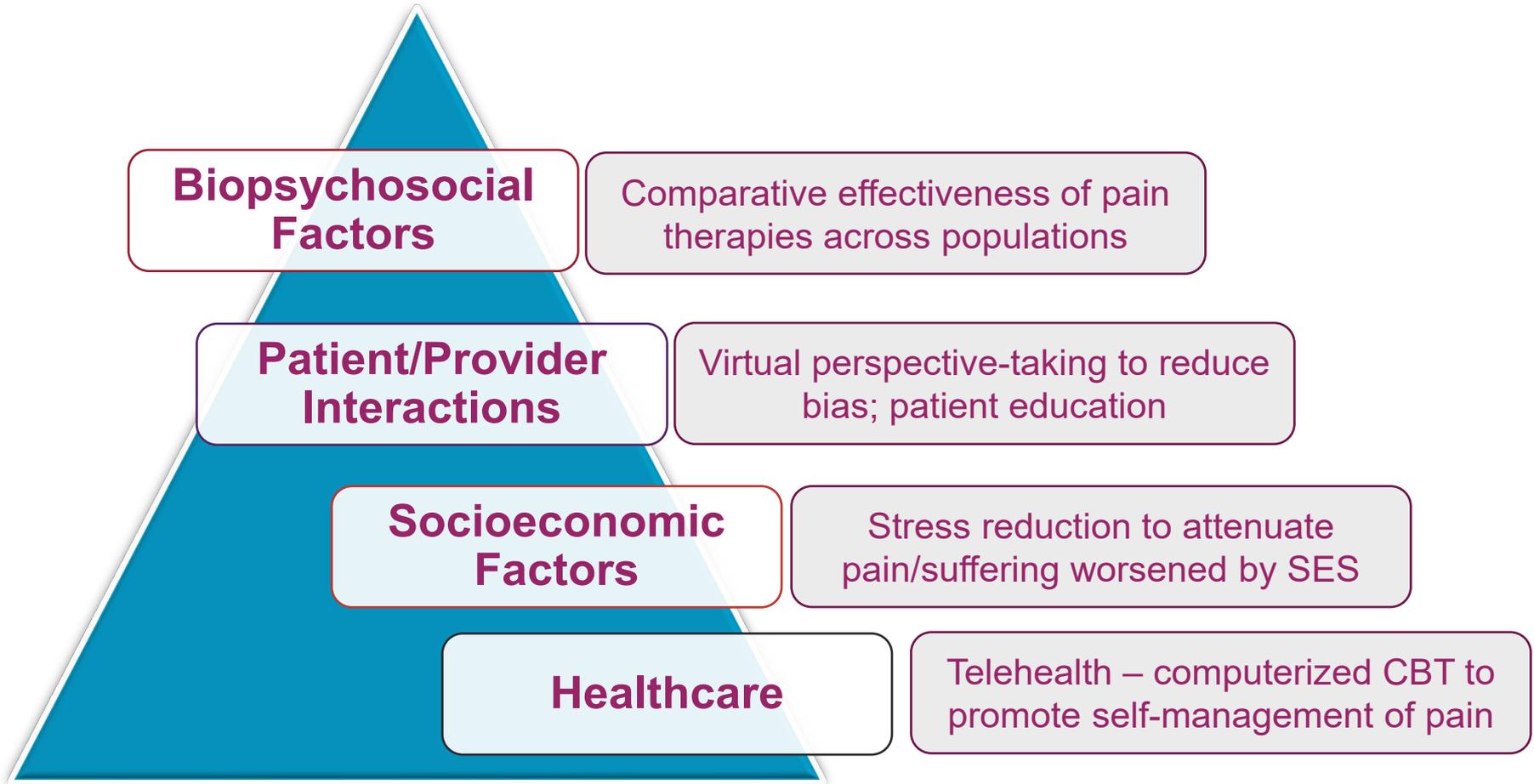
Walter Koroshetz, Cheryse Sankar, NINDS  
Nora Volkow, NIDA  
Joshua Gordon, NIMH

# Health Disparities in Pain: Barriers to quality pain care



Developed by Cheryse Sankar, Ph.D, NINDS

# Health Disparities in Pain: Opportunities for Intervention



## Increase Research on Health Disparities

- **Opportunities for Research in Pain Management**
  - Stimulate new collaborative research on pain disparities among investigators who do not normally conduct this type of research
  - Encourage partnerships between experienced pain researchers and disparities focused researchers.
- **Opportunities for Research in Prevention, Health Services, and Addiction Treatment**
  - Diversify clinical trial participation
  - Expand addiction treatment in justice settings
  - Address the unique needs of vulnerable and under-served populations
- **Exploratory/Developmental Grant Programs**
  - Health disparity FOAs using the NIMHD framework
  - HEAL virtual meeting to advance health equity

## Discussion Questions

1. How can we strengthen diverse enrollment in clinical trials? What do successful research sites have in common?
2. Diversity of scientists helps bring forward advancements in science. What can we do to expand recruitment and retention?
3. How can we reduce health disparities and promote health equity in the HEAL initiative?



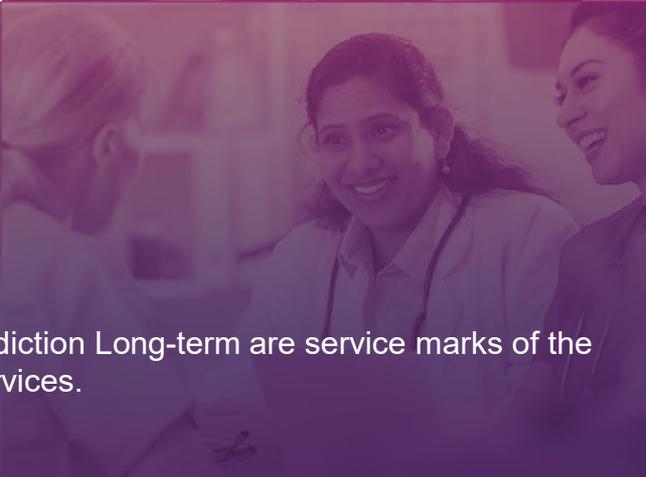
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## Addressing the Medical and Social Needs of Children Affected by Opioids:

### The ACT NOW Program



September 1, 2020 Andrew A Bremer, MD, PhD



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*HEAL Initiative*

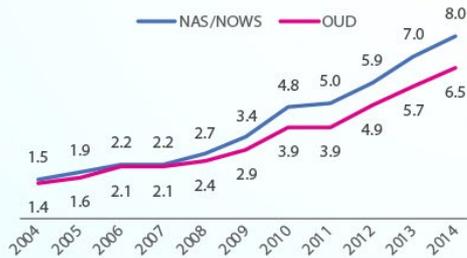
NIH HEAL Initiative and Helping to End Addiction Long-term are service marks of the U.S. Department of Health and Human Services.

# Neonatal opioid withdrawal syndrome is increasing with the rise in maternal opioid use



**EVERY ~ 15 MINUTES,  
A BABY IS BORN SUFFERING  
FROM OPIOID WITHDRAWAL.**

**NAS/NOWS and Maternal  
Opioid Use Disorder on the Rise**  
Rates per 1,000 Hospital Births



**Growing Hospital Costs for  
Treatment of NAS/NOWS**  
Inflation-Adjusted U.S. Dollars (millions)



Honein et al. Pediatrics 2019, Winkelman et al. Pediatrics 2018, Haight et al. MMWR 2018.



Athenahealth.com 2019 08 16



Kidspot.com.au 2019 08 16

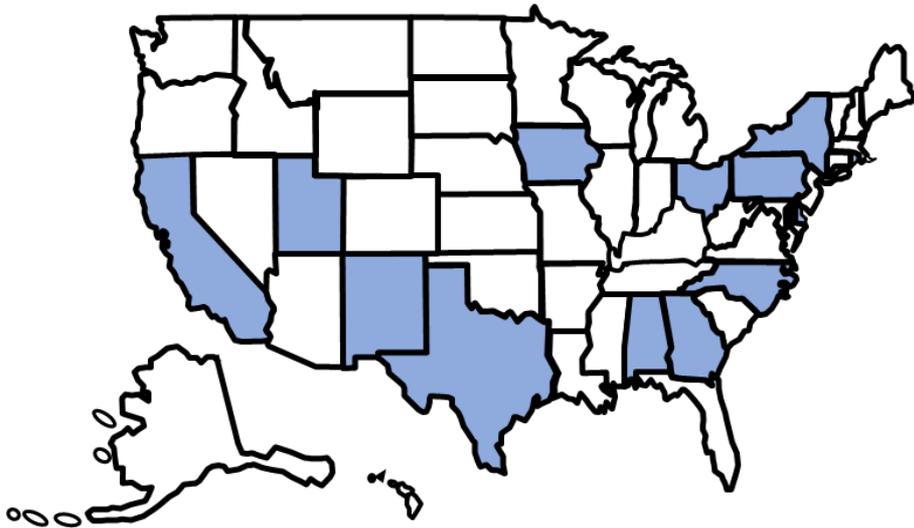
**Jittery, Fussy, Tremors, Poor sleep, Hard to console, Poor feeding**

# Summary of the ACT NOW Program (to date)

- How are clinicians treating babies now? How much variability exists?
  - ACT NOW Current Experience Study
    - COMPLETED – manuscripts under review
- What happens to these babies in the longer term? To what extent is NOWS associated with atypical neurodevelopmental outcomes?
  - ACT NOW Longitudinal Cohort Study
    - LAUNCHED (08/05/2020)
- Do all babies need opioids for withdrawal symptoms? Can some babies be treated non-pharmacologically? Is it safe to do so? What are the long-term consequences?
  - ACT NOW Eat, Sleep, Console (ESC) Cluster Randomized Clinical Trial
    - WILL LAUNCH NEXT WEEK (target launch date: 09/08/2020)
- For those babies who do need opioids, can clinicians get them off the medications earlier? Is it safe to do so? What are the long-term consequences?
  - ACT NOW Weaning Randomized Clinical Trial
    - WILL LAUNCH NEXT WEEK (target launch date: 09/08/2020)

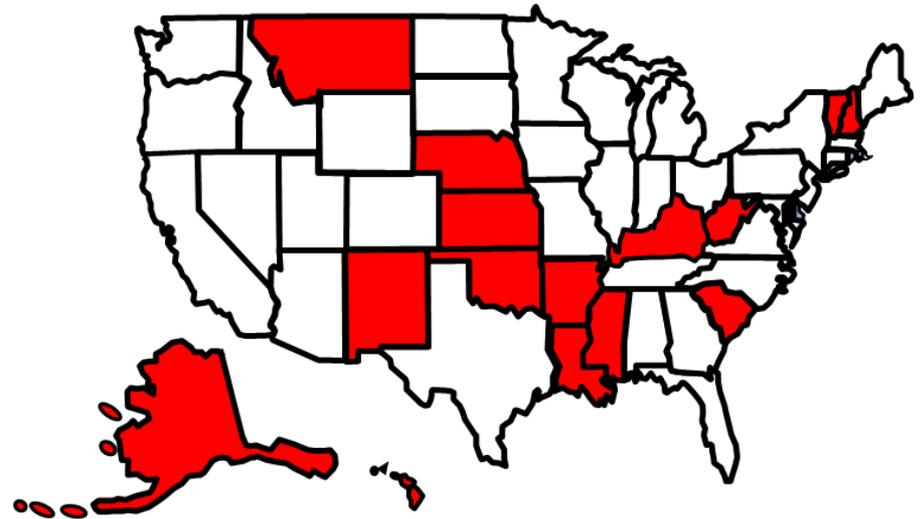
# ACT NOW Clinical Trial Networks

## NICHD Neonatal Research Network (NRN) Centers



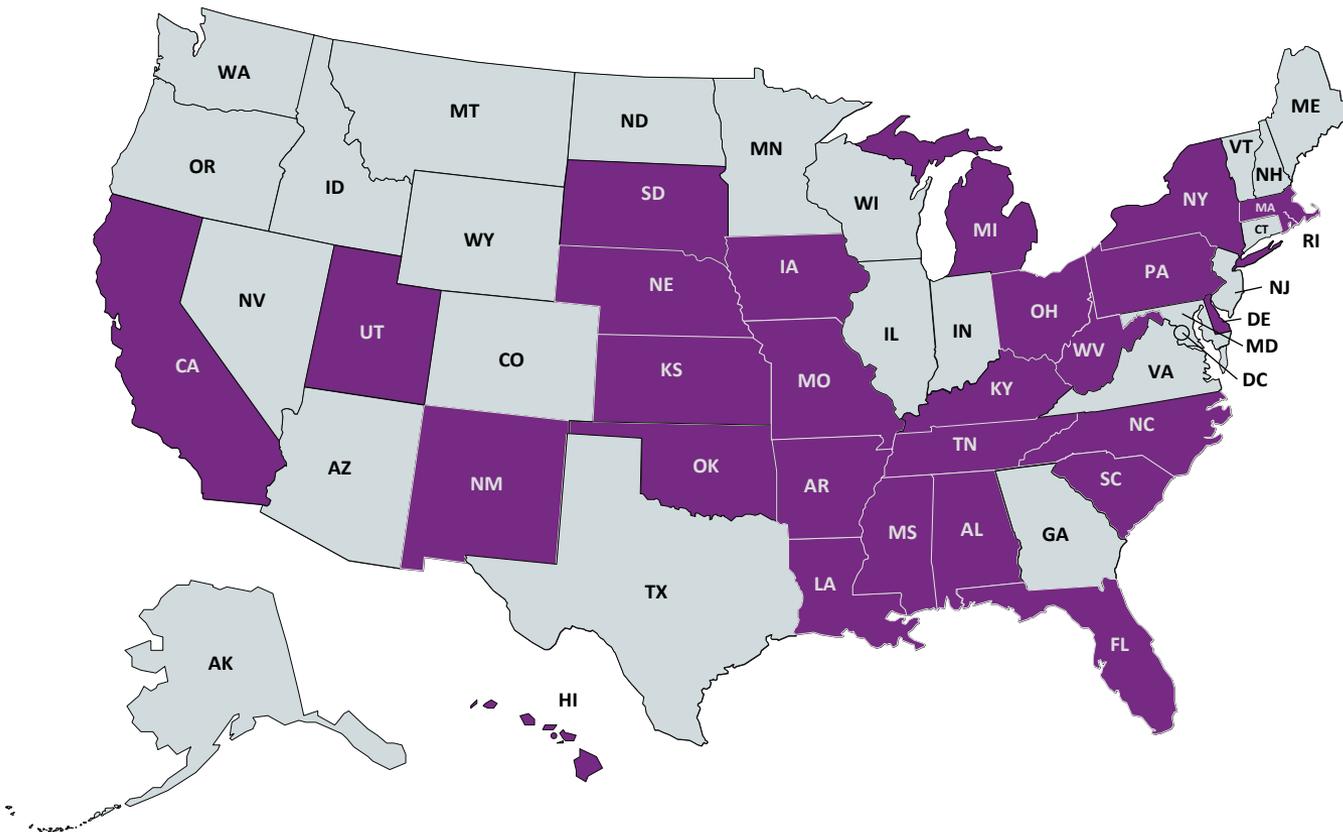
- Started in 1986
- 15 sites, mainly urban
- Currently involved in NOWS clinical trials

## OD/ECHO IDeA States Pediatric Clinical Trials Network (ISPCTN)



- Started in 2016
- 17 sites, many are rural
- Currently involved in NOWS clinical trials

# States currently participating in the ACT NOW Program

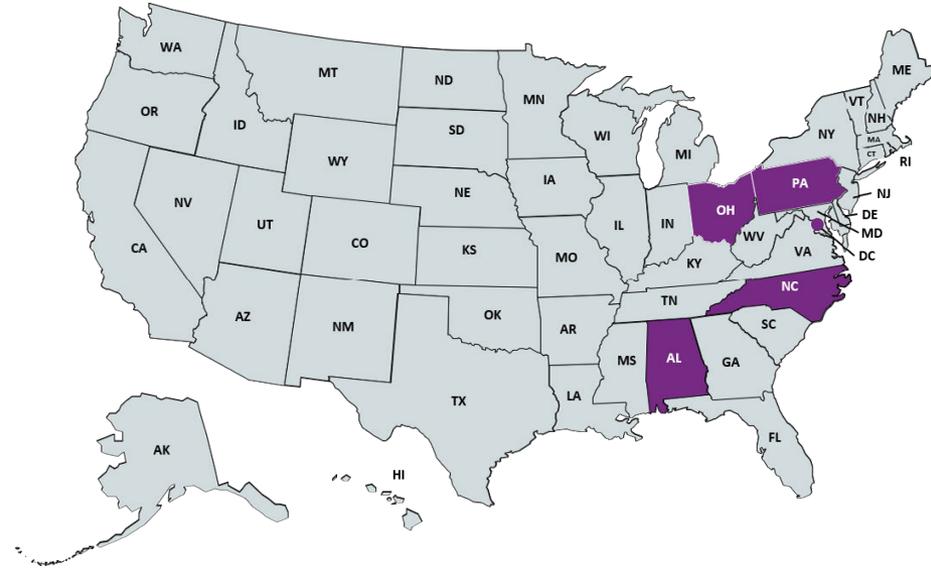


Weaning States	ESC States	Both ACT NOW Trials
AL	DE	AL
AR	FL	AR
CA	HI	CA
IA	KS	DE
LA	KY	FL
MA	LA	HI
MI	MA	IA
MO	MS	KS
NC	NC	KY
NM	NE	LA
OH	NM	MA
PA	NY	MI
RI	OH	MO
SD	OK	MS
TN	PA	NC
WV	SC	NE
	SD	NM
	UT	NY
		OH
		OK
		PA
		RI
		SC
		SD
		TN
		UT
		WV
16	18	27

# Summary of the ACT NOW Program (to date)

## ➤ ACT NOW Longitudinal Study

- Goal recruitment number: 375
  - 275 opioid-exposed infants
  - 100 unexposed infants
- Coordinating Center:
  - RTI International
- Neuroimaging Core:
  - Children's National Medical Center
- **Clinical Centers:**
  - The University of Alabama at Birmingham (AL)
  - The Children's Hospital of Philadelphia (PA)
  - Case Western Reserve University (OH)
  - Cincinnati Children's Hospital Medical Center (OH)

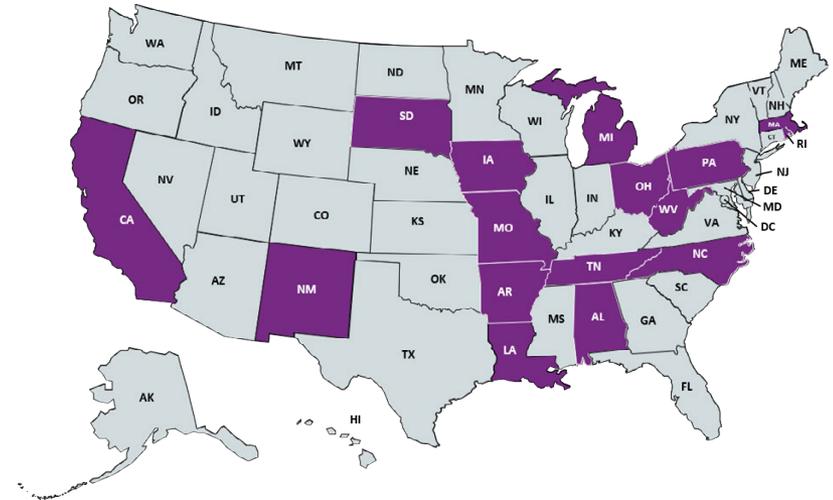




# Summary of the ACT NOW Program (to date)

## ➤ ACT NOW Weaning Clinical Trial

- Goal recruitment number: 502
- Coordinating Centers:
  - RTI International
  - Duke and Arkansas
- Clinical Centers:



### NRN:

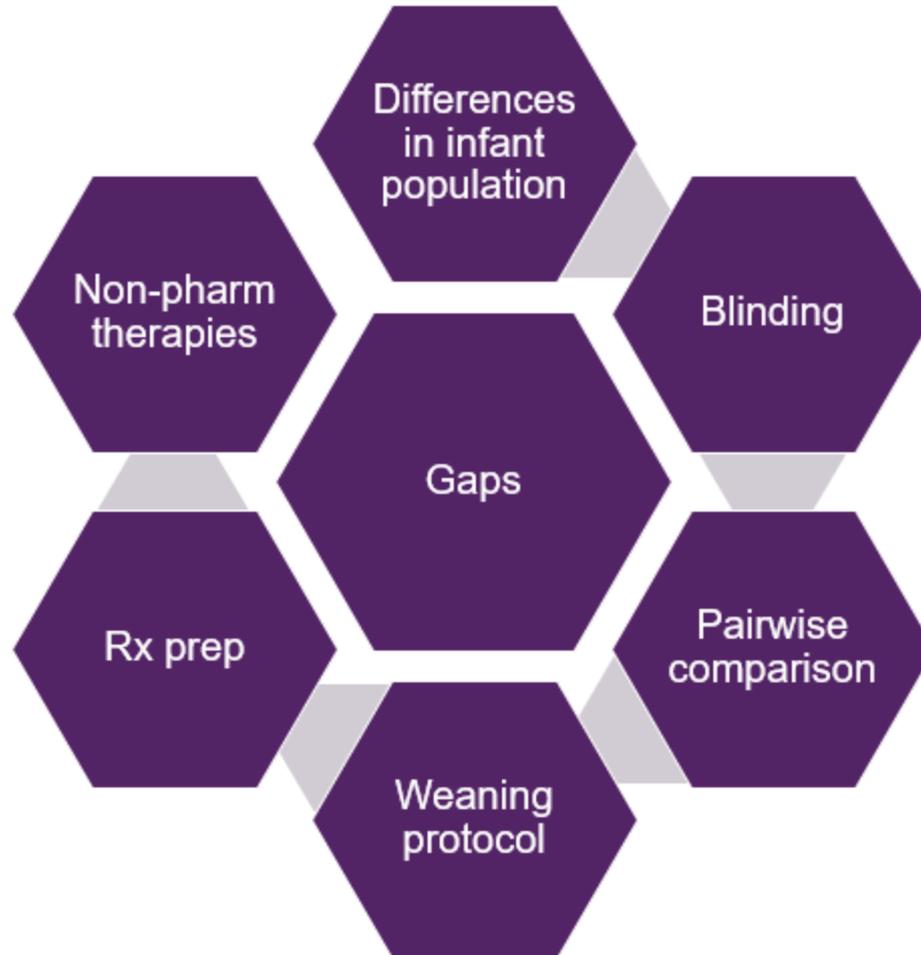
Nationwide Children's Hospital (OH)  
Ohio State University (OH)  
Sanford Health (SD)  
University of Alabama at Birmingham (AL)  
University of Iowa (IA)  
University of New Mexico, Health Sciences Center (NM)  
WakeMed Health & Hospitals (NC)  
Women and Infants Hospital Rhode Island (RI)

### ISPCTN:

Arkansas Children's Hospital (AK)  
Oschner Baptist Clinical Trials Unit (LA)  
Oschner Kenner Regional Hospital (LA)  
West Virginia University (WV)  
Tulane University Health Science Center (LA)  
Children's Mercy Hospital (KS)  
Loma Linda University Medical Center (CA)  
University of Tennessee Health Science Center (TN)  
Washington University School of Medicine (MO)  
Wayne State University School of Medicine (MI)  
University of Massachusetts (MA)  
Coastal Children's Services (NC)

# Neonatal Opioid Withdrawal Syndrome (NOWS)

## Scientific Gaps



# ACT NOW comparative-effectiveness trial preparation

- **Workshop (Aug 2020):** <https://heal.nih.gov/events/2020-buprenorphine-infants>
  - Discuss approaches to the use of buprenorphine in infants with NOWS
  - Discuss challenges with regard to the preparation of buprenorphine for infant use
  - Discuss how to address concomitant use of methamphetamine (or other drugs) with opioids in pregnant women
  - Discuss challenges keeping individuals with co-occurring substance use in treatment
  - ***Address the medical and social needs of children affected by opioids***
- **Study (expected to launch in 2021):**
  - Determine what is the most appropriate pharmacological treatment of an infant born to a mother using opioids who is experiencing NOWS?
    - Study will also record what treatment the mother received to evaluate how that influences the infants' symptoms and responses to treatment

# HEALthy Brain and Child Development Study

Michelle Freund, Ph.D.  
Division of Extramural Research, NIDA  
HEAL MDWG Meeting  
September 1, 2020



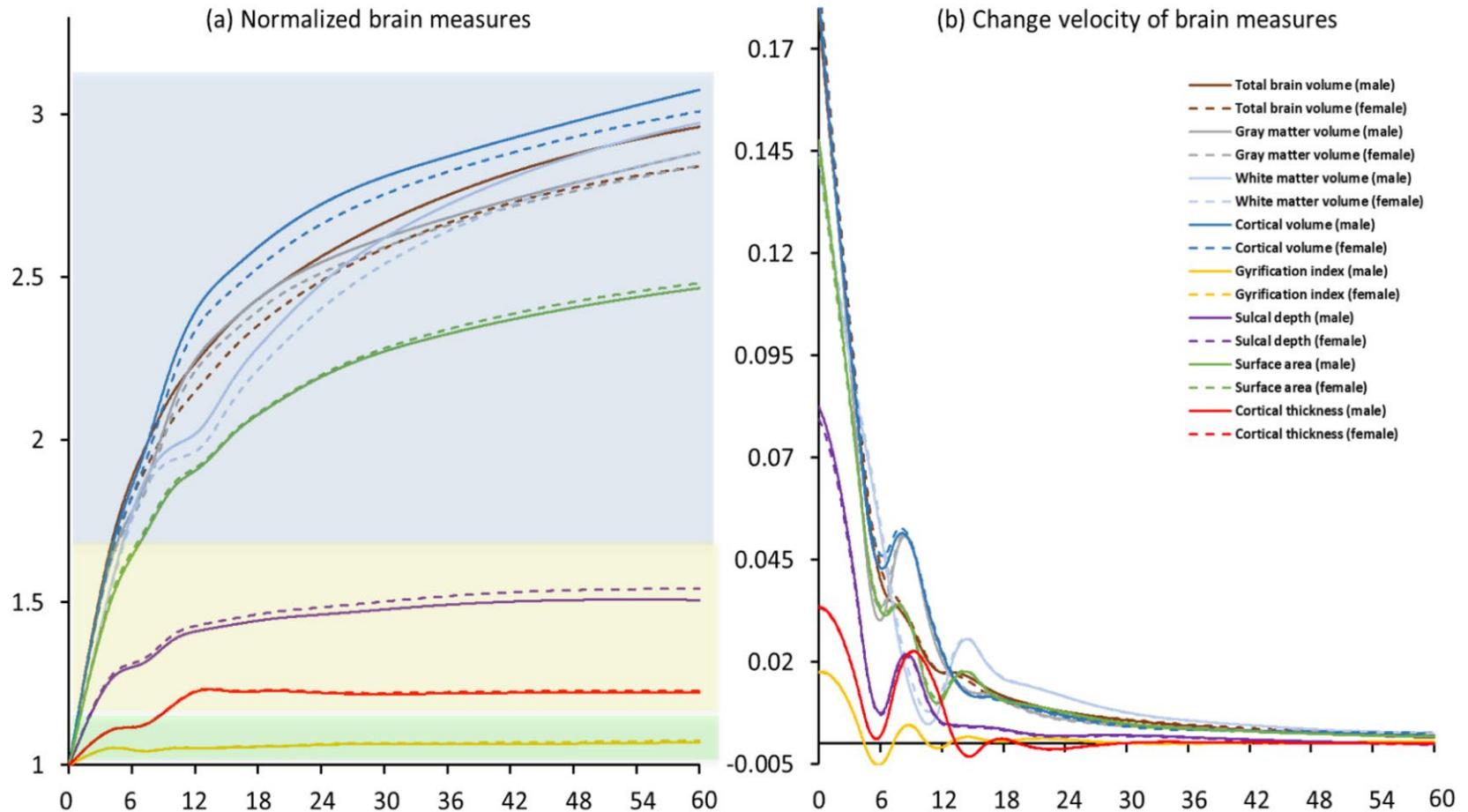
# HEALthy Brain and Child Development Study



A longitudinal observational study that aims to understand normative neurodevelopment from birth to 9-10 years with an emphasis on providing information on the impact of *in utero* exposures to potentially harmful substances and environments



# Rapid Changes in the first 2 years of life



These graphs depict dramatic changes in volume, thickness, and surface area of structures within the human brain in the first two years of life, with little change in these measures after 30 months of age. Source: Personal Communication, Weili Lin, Department of Radiology and BRIC, University of North Carolina at Chapel Hill, NC 27599, USA.

## TWO CENTRAL QUESTIONS

What are the developmental effects of prenatal opioid and other substance use exposures on children from birth through middle childhood?

**Q1: EXPOSURES** 

What are the “typical” or “normative” developmental trajectories for children from birth through middle childhood?

 **Q2: DEVELOPMENT**

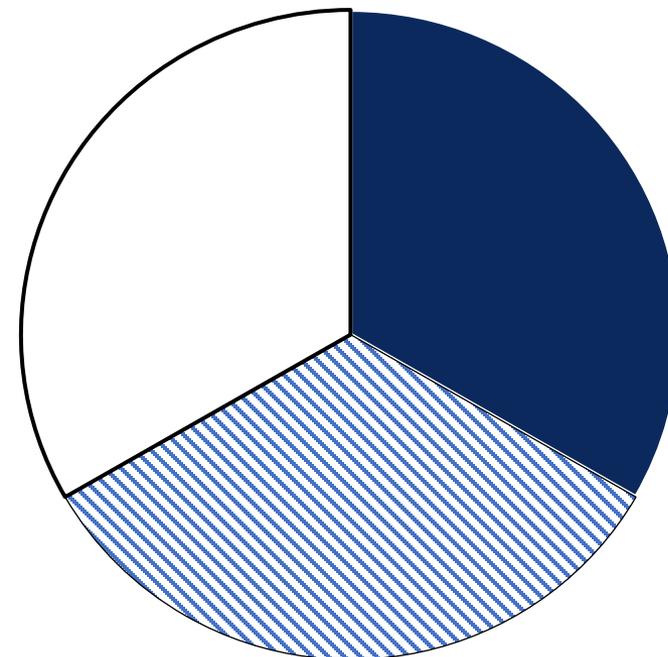
# Study Design

- **Sampling Strategy: Preliminary recommendations**

Clinic based recruitment  
Community engagement  
    SUD treatment programs  
    Recovery programs  
    Social media  
    State and local partners  
    Justice settings  
Respondent-driven sampling (chain referral)

Sample must be diverse  
    racial/ethnic  
    socioeconomic  
    rural/urban

**Target sample**



- High risk, opioid exposed
- ▨ High risk, unexposed
- Normative Control

# Planning for HEALthy Brain and Child Development Study



CENTER *for*  
BETTER BEGINNINGS  
Promoting Maternal Health And Child Development

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## Solving the Mysteries of the Baby Brain

Planning for the HEALthy Brain and Child Development Study



A baby's brain develops at a tremendous pace during the first few years of life. Yet we still know very little about what "typical" looks like and how it contributes to a child's cognitive, emotional, and physical functioning. We also don't know a whole lot about how this development is altered by things like exposures that may happen during a child's life, or other critical environmental influences. The HEALthy Brain and Child Development (HBCD) Study to answer these questions is as big and complex as this requires a whole lot of planning. The planning phase (Phase I) will help us make sure that we have the best possible data collection tools and methods to collect the data we have. We are proud to be involved in the Planning f

## Progress Highlights

- **sIRB and local reliance agreements**
- **Core assessment battery**
- **4 manuscripts *in prep*; special issue in Adversity and Resilience Science: Research and Practice**
- **Established a collaborative data transfer and use agreement**

# iOPEN Consortium—Recruitment and Retention Strategies

## Survey self-reported perinatal substance use across sites

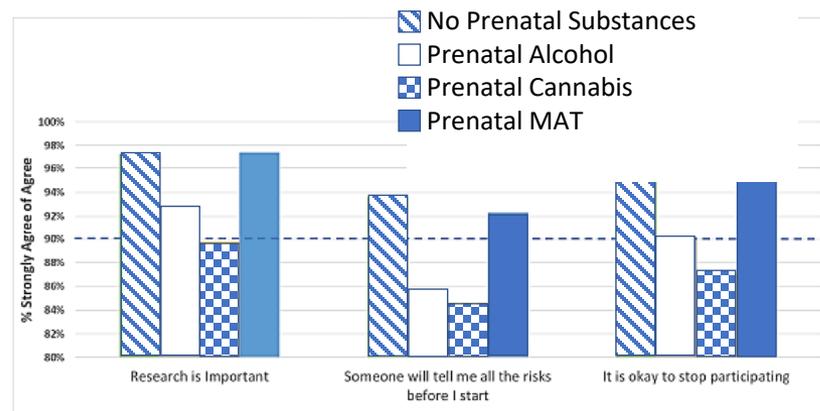
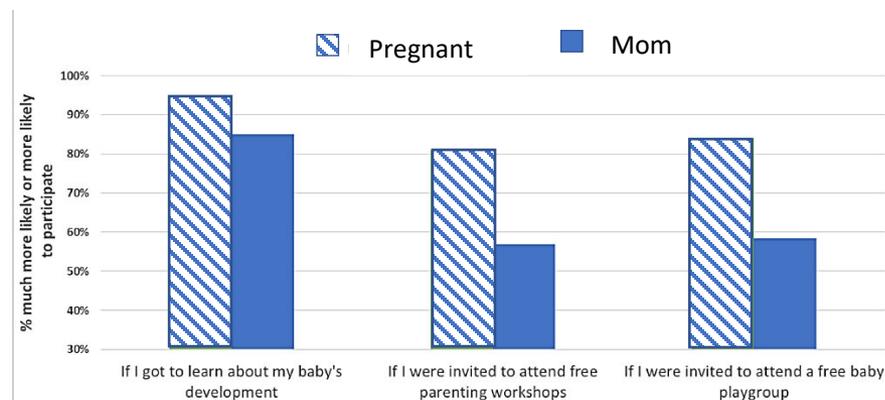
Have you ever been diagnosed with:			Are you currently being			
	Alcohol use disorder	Opioid use Disorder	Treated for a substance use disorder			
Clinic	<b>28%</b>	<b>18%</b>	<b>21%</b>			
Facebook	20%	11%	11%			
During your pregnancy did you use:						
	Nicotine	Alcohol	Cannabis	MAT	Illicit Opioid	Rx Opioid
Clinic	8%	14%	6%	5%	1%	3%
Facebook	<b>23%</b>	<b>21%</b>	<b>8%</b>	<b>5%</b>	<b>3%</b>	<b>6%</b>

## Demographics of Aim 1 Survey participants across all sites

	Pregnant Women	Partners	Moms of infants (<12 mos)	Dads of infants (<12 mos)
N(%)	535 (37%)	159 (11%)	616 (43%)	132 (9%)

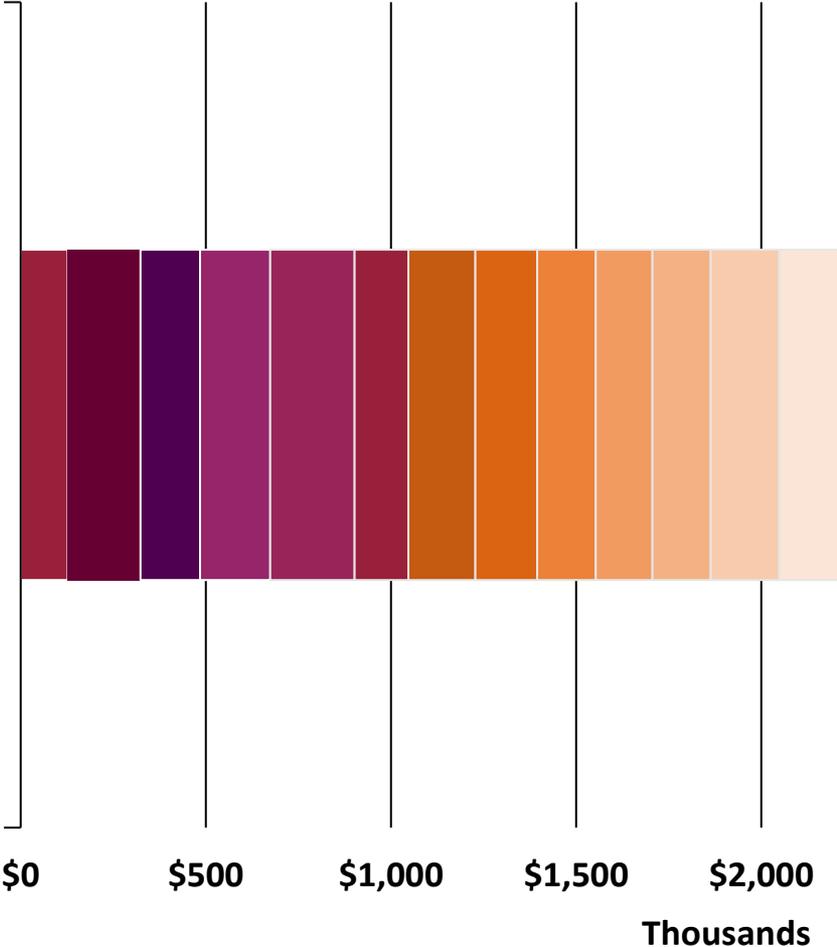
### Combined pregnant women and moms (n=1,151)

Age	<30	30–35	35–40	Over 40	
	37%	43%	16%	5%	
Race	White/Caucasian	Black/African American	More than one race	Other/Decline	
	82%	11%	4%	3%	
Education	HS/GED/Less (12%)	Some college (12%)	Assoc. (19%)	BA/BS (36%)	Advanced degree (21%)
Insurance	Medicaid 18%	Private 75%	Military 1%	None 1%	Other 5%



# COVID-19 Research Supplements

**Awarded**

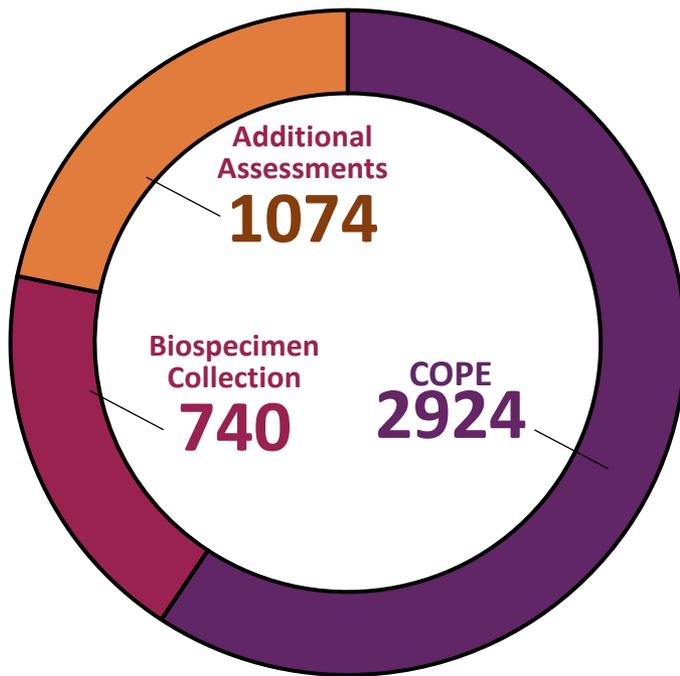


- \$126,699 PI: Deoni (Brown U)
- \$196,414 PI: Nelson (Harvard)
- \$161,000 PI: Singer (Case Western)
- \$189,329 PI: Gurka (U. Florida)
- \$228,033 PI: Chambers (UCSD)
- \$145,460 PI: Croff (OSU)
- \$180,332 PI: Fair (OHSU)
- \$167,000 PI: Gao (Cedars Sinai)

Total: \$2,207,484

# COVID-19 Research Supplements

## Approved/Awarded



### COVID-19 Perinatal Experiences (COPE): Longitudinal survey battery of parent & infant

- 2050 Untested Pregnant Women
- 473 COVID-19 Negative Pregnant Women
- 401 COVID-19 Positive Pregnant Women

### Biospecimen Collection:

#### Virus & antibody panels, stress, epigenetics

- 320 Untested Pregnant Women  
→ Saliva, Nasal Swab, Blood, Hair, Breastmilk
- 413 COVID-19 Negative Pregnant Women
- 341 COVID-19 Positive Pregnant Women  
→ Blood, Hair, Breastmilk, Fecal Matter

### Additional Assessments:

~ 275 -835 participants

- Substance Use, Anxiety, Depression, Stress
- Qualitative remote interviewing (n=50)
- In-home language assessment (n=136)
- MRI/EEG brain structure and function (n=121)

# HEALthy Brain and Child Development Study

## Notice of Intent to Publish a Funding Opportunity Announcement for HEALthy Brain and Child Development Study

**Notice Number:** NOT-DA-20-069

### Key Dates

**Release Date:** July 31, 2020

**Estimated Publication Date of Funding Opportunity Announcement:** November 01, 2020

**First Estimated Application Due Date:** March 01, 2021

**Earliest Estimated Award Date:** September 01, 2021

**Earliest Estimated Start Date:** October 01, 2021

### Related Announcements

None

### Issued by

National Institute on Drug Abuse ([NIDA](#))

### Purpose

The purpose of this Notice is to alert the community that NIH plans to publish a set of Funding Opportunity Announcements (FOAs) as part of the Helping to End Addiction Long-term<sup>SM</sup> (HEAL) Initiative to support research project sites, a Data Coordinating Center, and a Consortium Administrative Core for the HEALthy Brain and Child Development (HBCD) Study.

This Notice is being provided to allow potential applicants sufficient time to form meaningful collaborations and develop responsive applications.

# Discussion

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# Building the HEAL Research Community, Data Platform, and Virtual Engagement Series

# Engagement with HEAL Investigators and Research Dissemination

Investigators expressed strong desire to continue to connect with one another as studies get underway

## Steps Taken:

- HEAL PI listserv
- Website functionalities
- Central engagement platform

## Research Spotlights

Explore the projects helping to make a difference in the opioid crisis.



### The Search for New, More Targeted Pain Treatments

From surgery and drugs to cell-based therapies, researchers will test innovative, non-addictive approaches for treating pain.

## 2021 HEAL Investigators Meeting

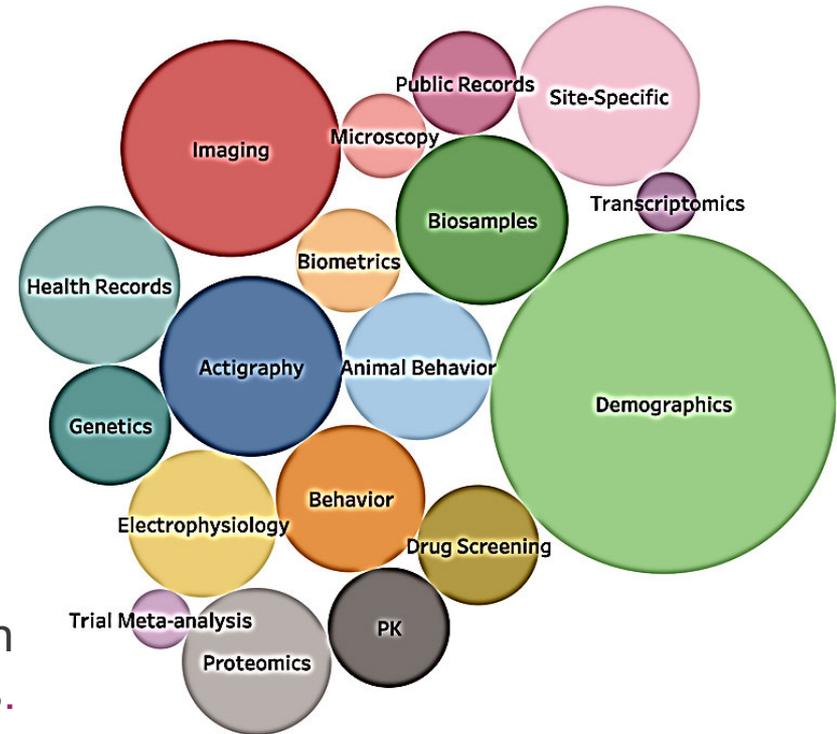
The Inaugural HEAL Investigator Meeting brought together more than 350 investigators. Plans for continued virtual engagement include:

- **2020-2021 Virtual Meeting Series**
  - Health disparities and vulnerable populations (race, ethnicity, sex, gender)
  - Patient engagement
  - Regulatory challenges and opportunities
  - Research collaboration needs, opportunities, and challenges
- **Ideascale online platform** to submit ideas about research for the HEAL Initiative

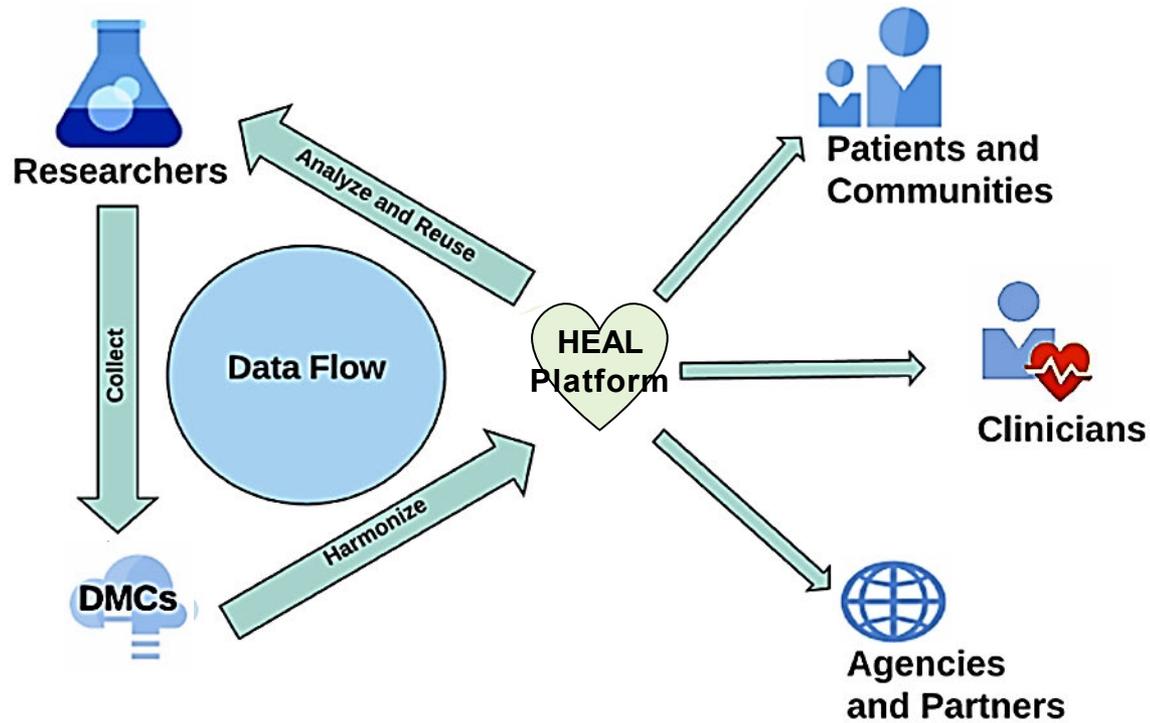


# Data Sharing and Harmonization Across HEAL

- HEAL to gather **diverse set of research data** drawing from an extraordinarily broad range of research domains in order to address the Opioid Crisis
  - Therapeutics, community-based treatment, pain neuroscience and detection, etc.
- The **HEAL Public Access and Data Sharing** plan has been well-received.
- Potential to **further “open science”** through data management and data sharing policies.



# HEAL Data Platform



5 million/year for 3 years



Figure 1. Schematic of a proposed HEAL Data Strategy.

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# General Discussion & Meeting Review

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**Next Steps**

**Adjourn**