Learning from Rapid Response, Innovation, and Adaptation to the COVID Crisis

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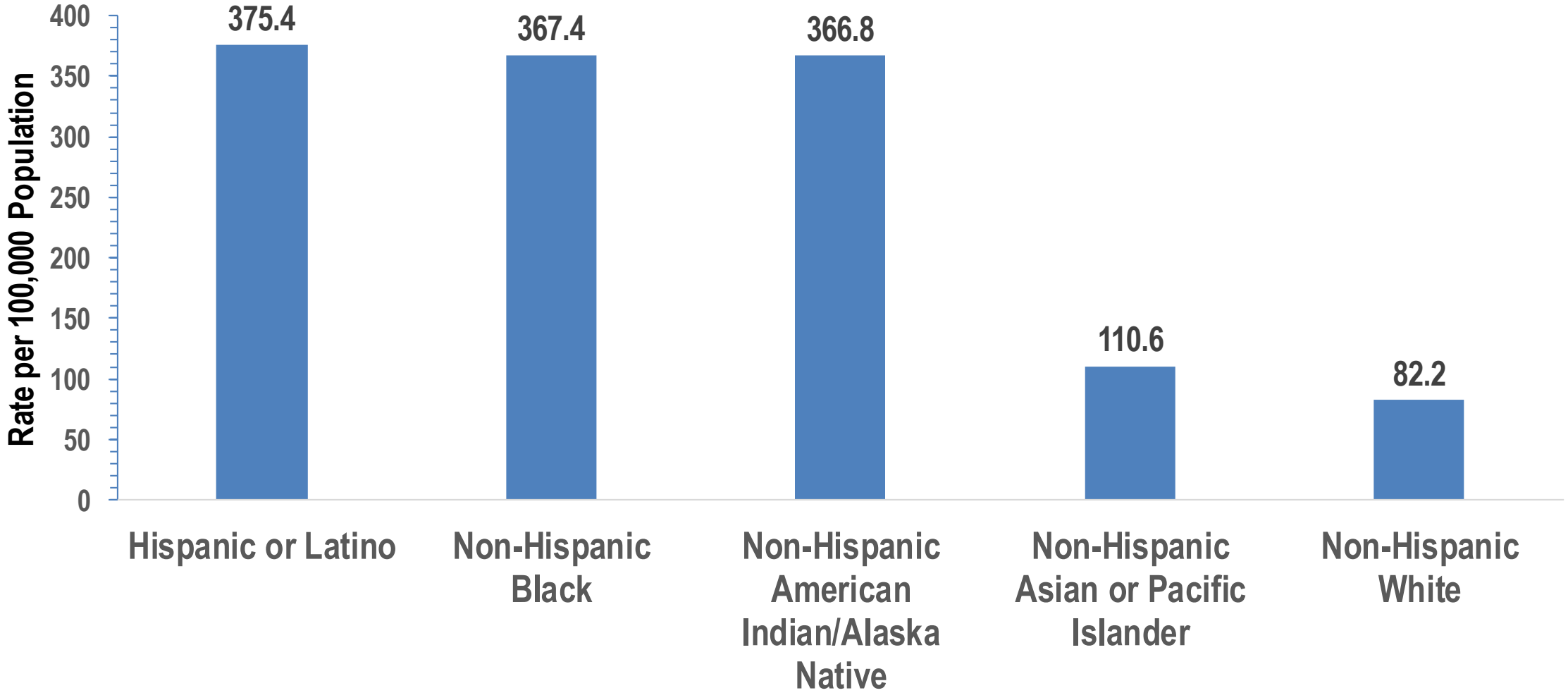
Disclaimer and Disclosure Statements

- I have no conflicts of interest to disclose.
- The contents of this presentation should not be construed as representing an official position of the NIH or the United States Department of Health and Human Services.

Presentation Outline

1. Evidence of COVID-19 disparities.
2. NIH's rapid response, innovation, and adaptation to COVID-19.
3. Implications for future pandemics and the public's health.

Age-adjusted COVID-19-associated hospitalization rates by race and ethnicity — COVID-NET, March 1–October 3, 2020; USA



Source: CDC. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

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COVID-19 CASES, HOSPITALIZATION, AND DEATH BY RACE/ETHNICITY

FACTORS THAT INCREASE COMMUNITY SPREAD AND INDIVIDUAL RISK


CROWDED SITUATIONS


CLOSE / PHYSICAL CONTACT


ENCLOSED SPACE

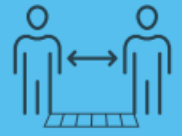

DURATION OF EXPOSURE

Rate ratios compared to White, Non-Hispanic Persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
CASES[1]	2.8x higher	1.1x higher	2.6x higher	2.8x higher
HOSPITALIZATION[2]	5.3x higher	1.3x higher	4.7x higher	4.6x higher
DEATH[3]	1.4x higher	No Increase	2.1x higher	1.1x higher

Race and ethnicity are risk markers for other underlying conditions that impact health — including socioeconomic status, access to health care, and increased exposure to the virus due to occupation (e.g., frontline, essential, and critical infrastructure workers).

ACTIONS TO REDUCE RISK OF COVID-19


WEARING A MASK


SOCIAL DISTANCING (6 FT GOAL)


HAND HYGIENE


CLEANING AND DISINFECTION

[1] Data source: COVID-19 case-level data reported by state and territorial jurisdictions. Case-level data include about 80% of total reported cases. Numbers are unadjusted rate ratios.

[2] Data source: COVID-NET (https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html, accessed 08/06/20). Numbers are ratios of age-adjusted rates.

[3] Data source: NCHS Provisional Death Counts (https://www.cdc.gov/nchs/nvss/vsrr/COVID19/index.htm, accessed 08/06/20). Numbers are unadjusted rate ratios.

cdc.gov/coronavirus

CS319360-A 08/08/2020

NIH-Wide Strategic Priority #5 to Address COVID-19 Disparities

PRIORITY 5

Prevent & Redress Poor COVID-19 Outcomes in **Health Disparity and Vulnerable Populations**

https://www.nih.gov/sites/default/files/research-training/initiatives/covid-19-strategic-plan/coronavirus-strategic-plan-20200713.pdf

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The NIH-Wide Response to the COVID-19 Pandemic

A focus on Underserved Populations & COVID-19 Disparities

1. **RADx-UP**: Rapid Acceleration of Diagnostics Initiative in Underserved Populations.

2. **ACTIV**: Accelerating COVID-19 Therapeutic Interventions and Vaccines: An Unprecedented Partnership for Unprecedented Times.

3. **CEAL**: Community Engagement Alliance Against COVID-19 Disparities.

Common Themes in the NIH Response to COVID-19

- **Rapid Response**:
  - Leveraged extant clinical trial network infrastructure to rapidly launch the ORCHID trial (**within 6 weeks** of proposal, instead of 6-12 months).
- **Adaptive Response**:
  - Created unprecedented **public-private partnership** (ACTIV model) and deployed multiple **Master Protocols** within a span of a few months.
- **Inclusive Participation**:
  - Active community engagement efforts using trusted voices and trusted messengers to promote diverse and inclusive participation.

Timeline of Important Events in Response to COVID-19 National Heart, Lung, and Blood Institute (NHLBI)

Feb 28 — **Clinical Characteristics of Coronavirus Disease 2019 in China**

Mar 17 — **NOSI supporting all COVID-19 research (NOT-HL-20-757)**

Mar 25 — **Roundtable: Randomized Controlled Trials in COVID-19 Patients**

Apr 3 — **Roundtable: Acute Care Cohort / Longitudinal Cohort / National Registry of COVID 19 Patients**

Mar 27 — **CARES Act passed**

NHLBI and trans-NIH COVID-19 strategy discussions

Apr 9 — **1st NHLBI Clinical Study Launched**

Apr 13 — **NOSI supporting COVID-19 observational research (NOT-OD-20-097)**

Apr 27 — **NOSI supporting COVID-19 clinical research (NOT-HL-20-782)**

Apr 29 — **ROA for Host-targeting Therapies for COVID-19 (OTA-20-11)**

- **ORCHID Trial** of hydroxychloroquine
  - **First patient recruited** April 9
- **COLCORONA Trial** on the effects of colchicine on cardiopulmary complications
- **CORAL Observational Cohort**
  - Network of health systems data
- **REDS Sero-Surveillance** & Biospecimen Repository

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NHLBI Response: Timeline of Important Events

- **June 2020**
  - CONNECTS launched: >30 networks, >1,000+ sites.
  - Suite of pre-clinical translation studies funded.
- **July 2020**
  - Community Engagement Roundtable.
  - Hydroxychloroquine RCT completed early
- **August 2020**
  - Convalescent plasma study (C3PO) launched.
  - ACTIV 4A study launched.
- **September 2020**
  - ACTIV 4 B launched
  - CEAL awards announced
  - Cohort of Cohorts (C4R) launched.

Collective Response to a Global Pandemic: Leveraging NHLBI Resources Through CONNECTS

"Collaborating Network of Networks for Evaluating COVID-19 and Therapeutic Strategies"

Integrate	Fully integrate major NHLBI networks under one organizational umbrella
Align	Align with NIH ACTIV and engage with OWS, BARDA, and FDA as partners
Adapt	Utilize adaptive trials with multiple active arms
Shift	Nimbly shift studies as needed, based on changing clinical landscape
Innovate	Utilize Master Protocol approach for LS/OS studies
Create	Develop COVID-19 CDEs and consensus-based outcomes measures
Share	Operate in a shared space as entities with common standardized cores: data & specimen repos., imaging centers, EDC technologies, etc.

Integrating Communities Within Longitudinal and Cohort Studies

Leverage long-established community relationships in clinical networks and longitudinal cohort studies to better define the clinical course of COVID-19 and identify predictive risk factors

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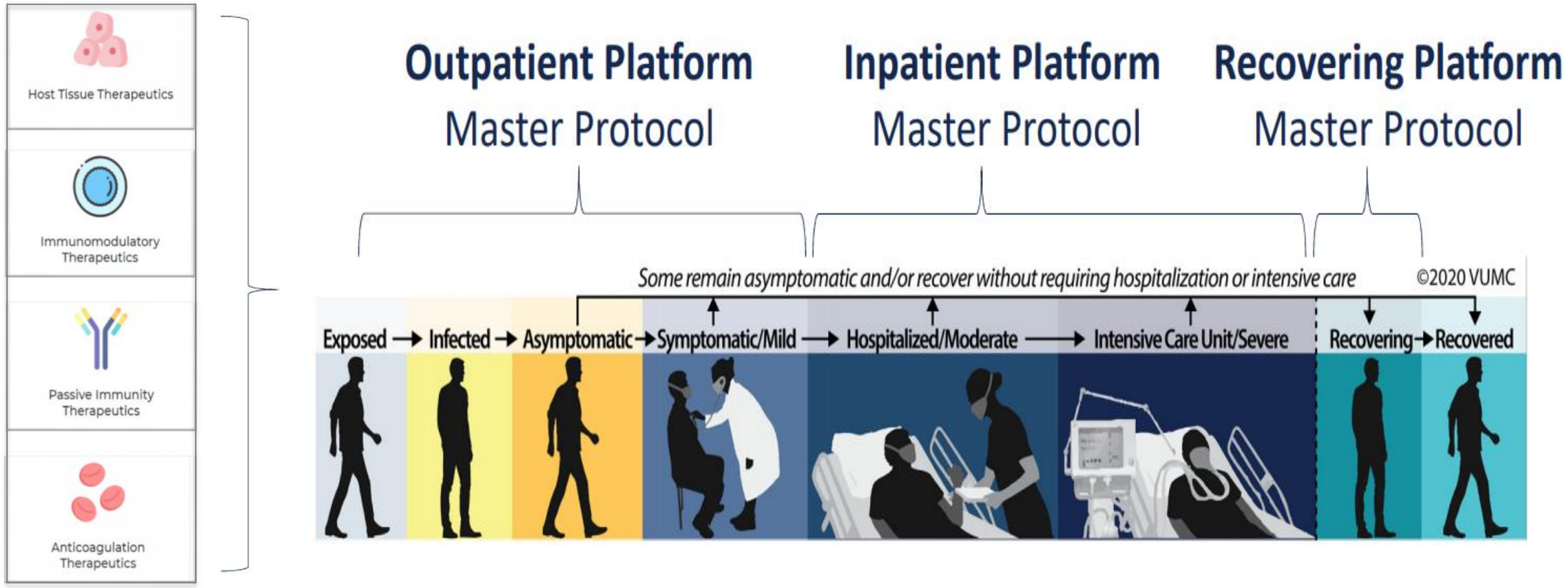
Innovative Master Protocol Driven Adaptive Clinical Trials



RADx-UP Overall Purpose

- Understand factors that have led to disproportionate COVID-19 burden so that interventions can be implemented to decrease these disparities.
- Determine baseline rates of testing and increase **reach, access, uptake**, and **impact** of COVID-19 testing in underserved and/or vulnerable populations.
- Create strategies to widely disseminate up-to-date FDA-authorized and/or approved testing.
- Test community engagement strategies to reduce barriers and increase access.
- Leverage community relationships to test strategies for adoption

NOT-OD-20-121 and NOT-OD-20-120

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Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Eisai, Eli Lilly, Evotec, Gilead, GlaxoSmithKline, Johnson & Johnson, KSQ Therapeutics, Merck, Novartis, Pfizer, Roche, Sanofi, Takeda, and Vir. Multiple NIH institutes, FDA, BARDA, CDC, the European Medicines Agency, Department of Defense, the VA, the Foundation for NIH

The Goals of ACTIV are to:

1. Develop a collaborative, streamlined forum to identify preclinical treatments.
2. Accelerate clinical testing of the most promising vaccines and treatments.
3. Improve clinical trial capacity and effectiveness.
4. Accelerate the evaluation of vaccine candidates to enable rapid authorization or approval.

Collins et al. *JAMA* 2020;323(24):2455-2457

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NIH-Wide Community Engagement Alliance Against COVID-19 Disparities

CEAL

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Adverse Impact of Misinformation and Distrust

- "Recruiting Black volunteers for vaccine trials during a period of severe mistrust of the federal government and heightened awareness of racial injustice is a formidable task."
- **"So far, only about 3 percent of the people who have signed up nationally are Black."** See footnote*

New York Times, October 7, 2020
https://www.nytimes.com/2020/10/07/health/coronavirus-vaccine-trials-african-americans.html?referringSource=articleShare

*For comparison, the NHLBI hydroxychloroquine trial (ORCHID) enrolled 24% African American and 37% Hispanic participants

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Two Black university leaders urged their campuses to join a Covid-19 vaccine trial. The backlash was swift!

BY NICHOLAS ST. FLEUR @SCIFLEUR; *STAT NEWS*; OCTOBER 12, 2020

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NIH Community Engagement Alliance (CEAL) Against COVID-19 Disparities

CEAL works with communities to respond to COVID-19 by addressing misinformation and promoting participation in clinical trials

CEAL Objective 1

Conduct urgent community engagement **research and outreach** focused on COVID-19 awareness and education to address **misinformation and mistrust**.

CEAL Objective 2

Promote and facilitate **inclusion of diverse racial and ethnic populations** in clinical trials (prevention, vaccine, therapeutics), reflective of the populations disproportionately affected by the pandemic.

CEAL Activities:

- Support and expand existing community outreach efforts by NIH COVID-19 trial networks, such as ACTIV (**treatments**), RADx (**diagnostic tests**), CoVPN (**vaccines**), and **CONNECTS** .
- Establish communication networks across multiple channels and through engagement with trusted organizations and trusted messengers in the communities.

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Community Engagement Alliance (CEAL) Against COVID-19 Disparities

Urgent, Creative, Adaptive Community Engagement Research & Outreach

- At NIH, the vetting process for a research concept to be approved as a funding announcement **can take between 6 - 12 months.**
- Once the funding announcement is released, the review and approval of specific applications leading to funding awards **can take another year.**
- This means that funding concepts conceived of today won't be announced until mid to late 2021 and won't be funded until mid-2022.
- **The entire process for CEAL took <u>less than 6 weeks</u>.**

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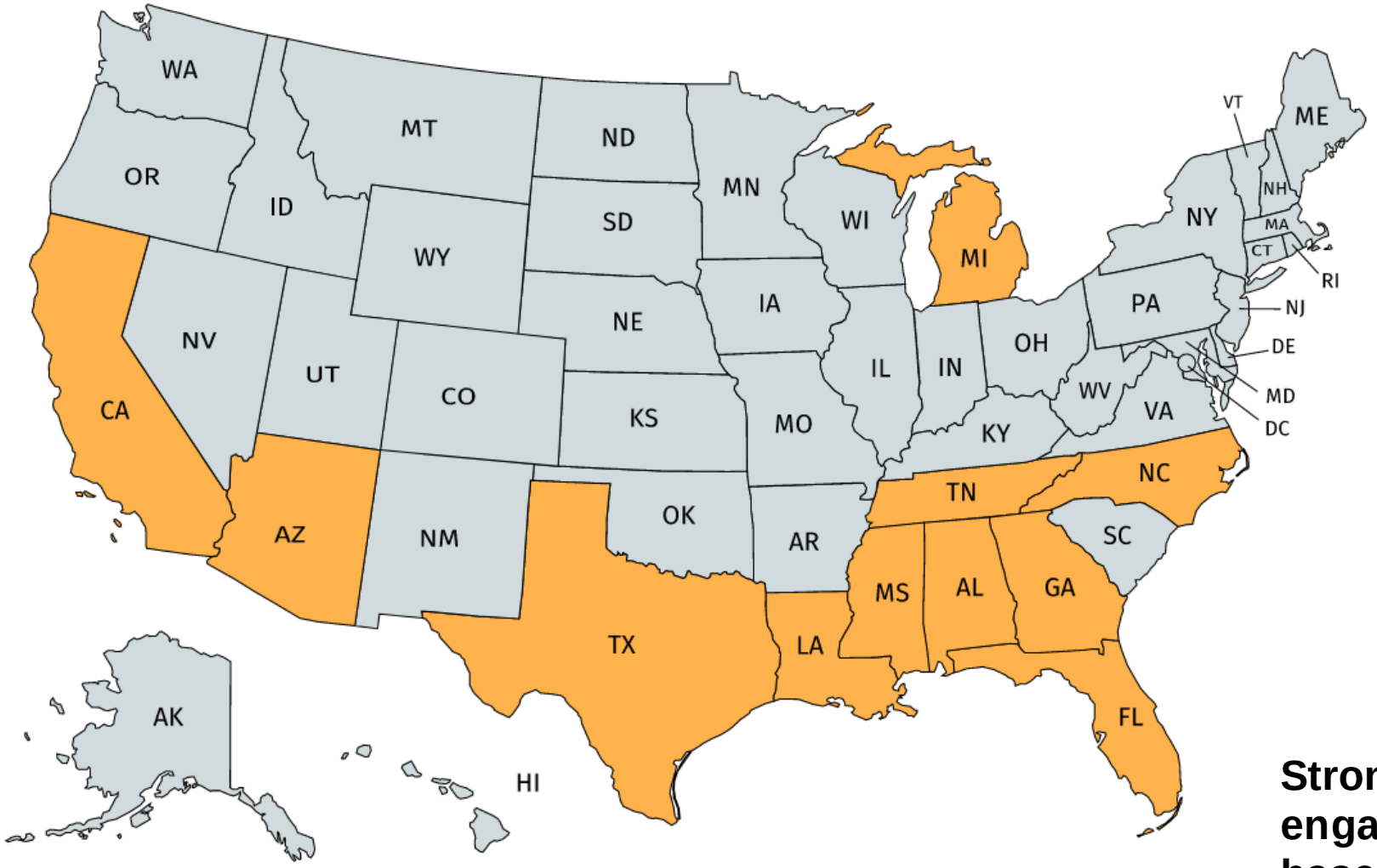
An NIH-wide Community Engagement Alliance (CEAL) Against COVID-19 Disparities to address Misinformation and Distrust



CEAL Teams

1. Alabama
2. Arizona
3. California
4. Florida
5. Georgia
6. Louisiana
7. Michigan
8. Mississippi
9. North Carolina
10. Tennessee
11. Texas

Strong partnerships between community engagement researchers and community-based organizations.

NIH. CEAL. https://covid19community.nih.gov/

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Informing, Educating, and Promoting Clinical Trial Participation

NIH COVID-19 Communities Responding Together

Download resources for use in talking to your communities about COVID-19, the vaccines under development, how they are developed, and the importance of being included in research studies.

Bookmark this page and return often for new resources to help you engage community organizations and individuals and encourage participation in clinical trials.

https://covid19community.nih.gov

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Implications for Clinical and Public Health Practice and Research

1. **Social determinants of health** play a crucial role in COVID-19 disparities. Attention to these factors is crucial for reducing disparities.
2. **Active community engagement** is needed to build and sustain **trusting relationships** with the hardest-hit, underserved communities.
3. In all actions to address disparities, **move at the speed of TRUST!**
4. Work with **trusted voices** and **trusted messengers** at the national and local levels. Forums that enable listening sessions are crucial.
5. **Innovative and strategic public-private partnerships** are crucial for accelerating the development of drugs and vaccines.

CONCLUSIONS

1. NIH has mounted an unprecedented, rapid, innovative, and adaptive response that includes:
   - **RADx-UP**: Rapid acceleration of diagnostics in underserved populations
   - **ACTIV**: Accelerating COVID-19 drug and vaccine development with emphasis on **safety**, **speed**, and **diverse & inclusive participation**.
   - **CEAL:** Supporting **urgent community engagement** and **outreach** to address misinformation and distrust in the hardest-hit communities.
2. Creative research designs that leverage **master protocols, network of extant clinical trial networks, and cohort of cohort studies** have enabled rapid execution of research with unprecedented speed and safety.
3. Strategic partnerships with the Industry, community-based organizations, and a coordinated federal response have been invaluable.

When the world was hurting, I did this ***one*** thing.

I volunteered and participated in research to put an end to COVID-19. I will look back and know we did something to make a difference.

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We can join **this** movement, too.

Decades of racial injustice have put the health of our communities at risk. We can stop this. We can stand up and be included in preventing and treating COVID-19.

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Your representation matters.

Will you participate?

Throughout history, medical research has not been inclusive of all groups of people. We want to be sure COVID vaccines protect **all of us**.

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