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

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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.

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

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Rate per 100,000 Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic or Latino</td>
<td>375.4</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>367.4</td>
</tr>
<tr>
<td>Non-Hispanic American Indian/Alaska Native</td>
<td>366.8</td>
</tr>
<tr>
<td>Non-Hispanic Asian or Pacific Islander</td>
<td>110.6</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>82.2</td>
</tr>
</tbody>
</table>

## COVID-19 Cases, Hospitalization, and Death by Race/Ethnicity

### Factors that Increase Community Spread and Individual Risk

<table>
<thead>
<tr>
<th></th>
<th>American Indian or Alaska Native, Non-Hispanic Persons</th>
<th>Asian, Non-Hispanic persons</th>
<th>Black or African American, Non-Hispanic persons</th>
<th>Hispanic or Latino persons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases</strong>¹</td>
<td>2.8x higher</td>
<td>1.1x higher</td>
<td>2.6x higher</td>
<td>2.8x higher</td>
</tr>
<tr>
<td><strong>Hospitalization</strong>²</td>
<td>5.3x higher</td>
<td>1.3x higher</td>
<td>4.7x higher</td>
<td>4.6x higher</td>
</tr>
<tr>
<td><strong>Death</strong>³</td>
<td>1.4x higher</td>
<td>No Increase</td>
<td>2.1x higher</td>
<td>1.1x higher</td>
</tr>
</tbody>
</table>

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

1. **Wearing a Mask**
2. **Social Distancing** (6 FT Goal)
3. **Hand Hygiene**
4. **Cleaning and Disinfection**

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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.


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.


3. **CEAL**: Community Engagement Alliance Against COVID-19 Disparities.
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.
Timline of Important Events in Response to COVID-19
National Heart, Lung, and Blood Institute (NHLBI)

- NHLBI and trans-NIH COVID-19 strategy discussions
- Mar 27: CARES Act passed
- Apr 9: 1st NHLBI Clinical Study Launched
- Apr 13: NOSI supporting COVID-19 observational research
- Apr 27: NOSI supporting COVID-19 clinical research

- Clinical Characteristics of Coronavirus Disease 2019 in China (NOT-HL-20-757)
- Roundtable: Randomized Controlled Trials in COVID-19 Patients
- Roundtable: Acute Care Cohort / Longitudinal Cohort / National Registry of COVID 19 Patients
- ORCHID Trial of hydroxychloroquine
  - First patient recruited April 9
- COLCORONA Trial on the effects of colchicine on cardiopulmonary complications
- CORAL Observational Cohort
  - Network of health systems data
- REDS Sero-Surveillance & Biospecimen Repository
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"

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

Outpatient Platform Master Protocol

Inpatient Platform Master Protocol

Recovering Platform Master Protocol

Exposed → Infected → Asymptomatic → Symptomatic/Mild → Hospitalized/Moderate → Intensive Care Unit/Severe → Recovering → Recovered

Some remain asymptomatic and/or recover without requiring hospitalization or intensive care
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.
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.
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*

*I Won’t Be Used as a Guinea Pig for White People*

Mistrust of vaccines runs deep in African-American communities. Against formidable odds, Father Paul Abernathy and his teams are trying to convince residents of Pittsburgh’s historic Black neighborhoods to volunteer for trials testing a Covid-19 shot.

*For comparison, the NHLBI hydroxychloroquine trial (ORCHID) enrolled 24% African American and 37% Hispanic participants*
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
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.
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 less than 6 weeks.
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/
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
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.
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.

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**CONCLUSIONS**

Center for Translation Research and Implementation Science
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.
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.
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.
Advancing science. Improving health.

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www.nhlbi.nih.gov