NCATS

COLLABORATE. INNOVATE. ACCELERATE.

Catalyzing Translational Innovation in the Age of COVID-19

Christopher P. Austin, M.D.

Director, NCATS

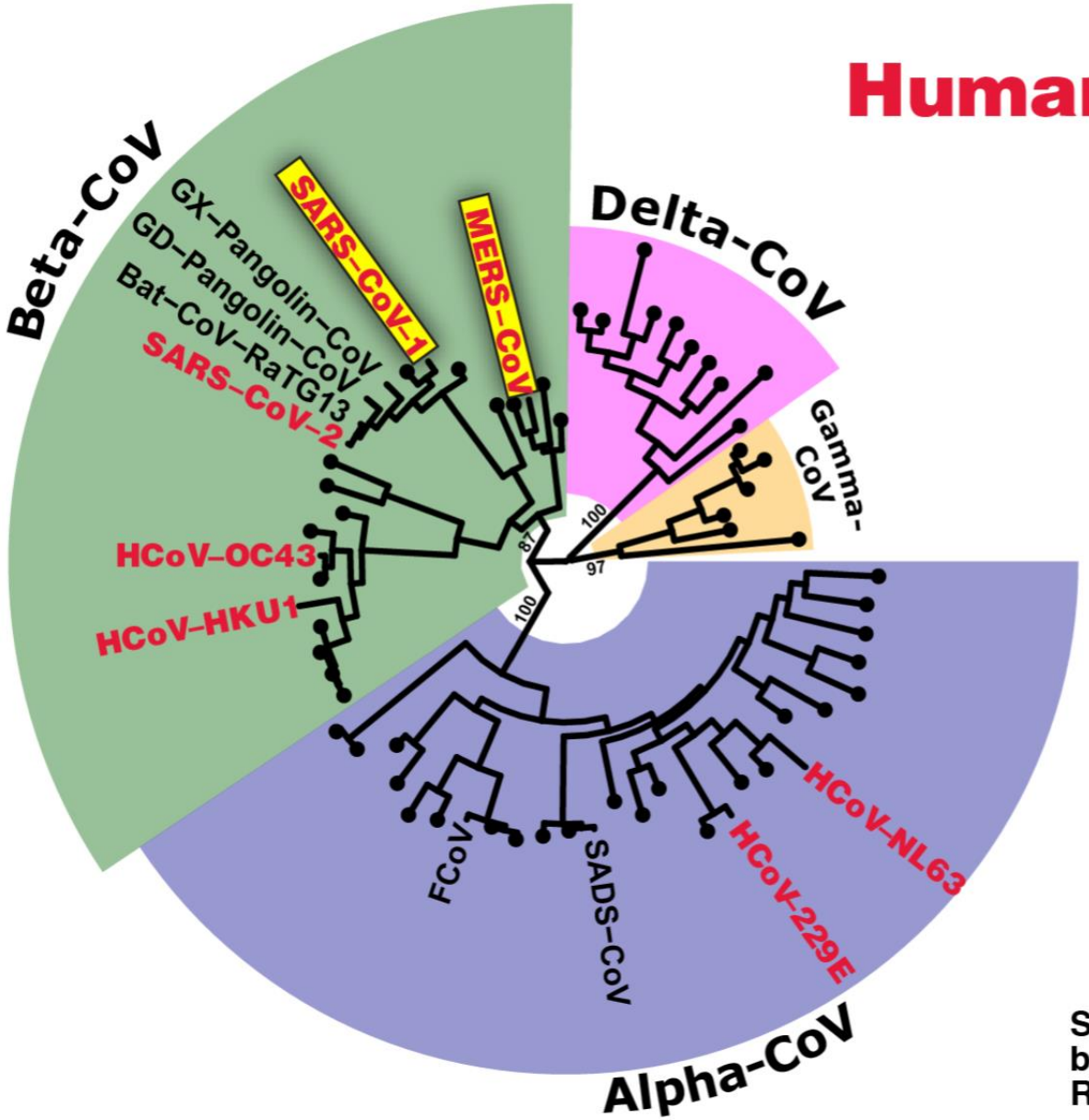
Virtual GUIRR Meeting Series:

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

October 14, 2020

National Center for Advancing Translational Sciences

Coronavirus Phylogenetic Tree



Human coronaviruses

Source: SM Gygil, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.

Coronavirus Phylogenetic Tree

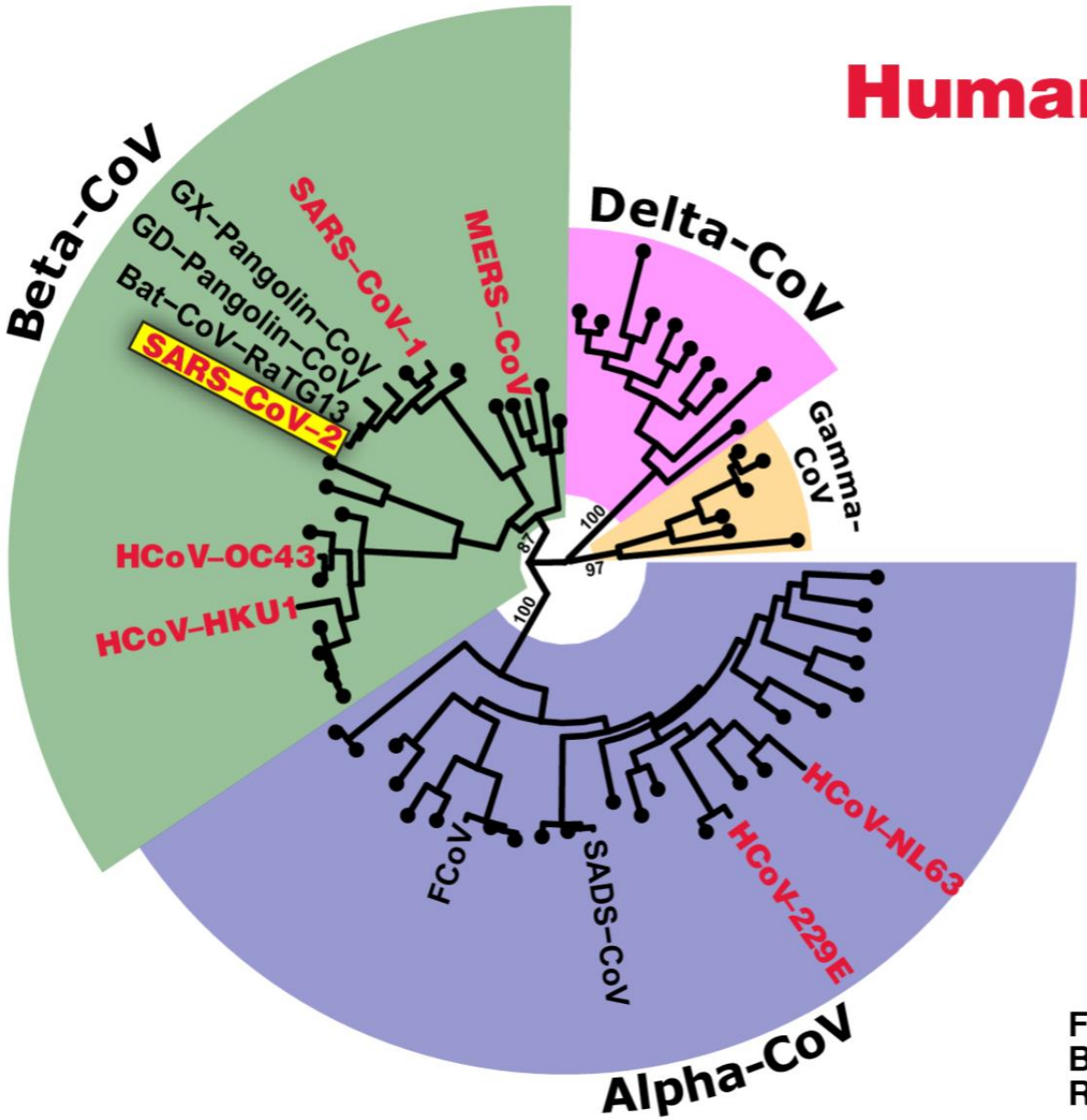
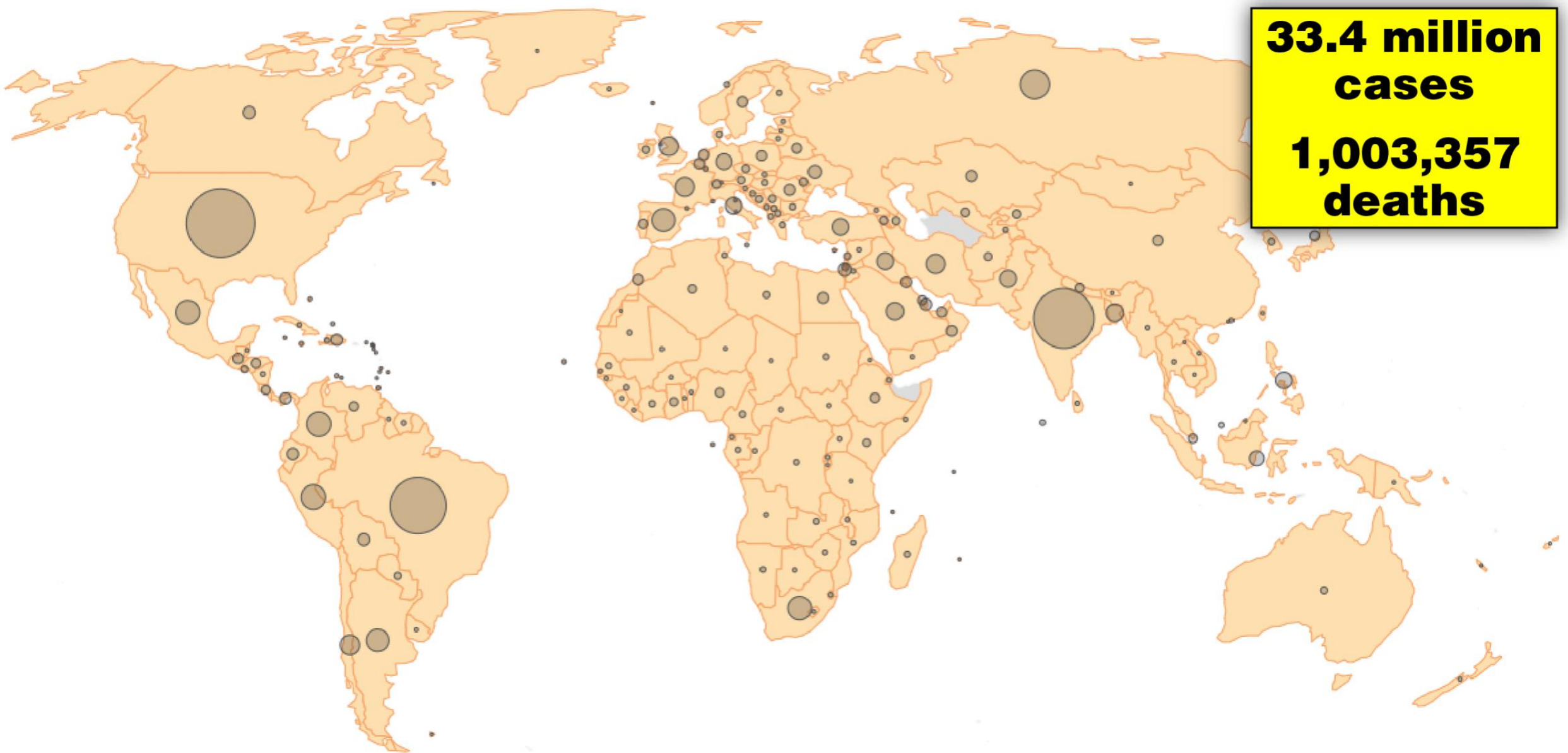


Figure courtesy of SM Gygli, PhD, NIAID.
Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.

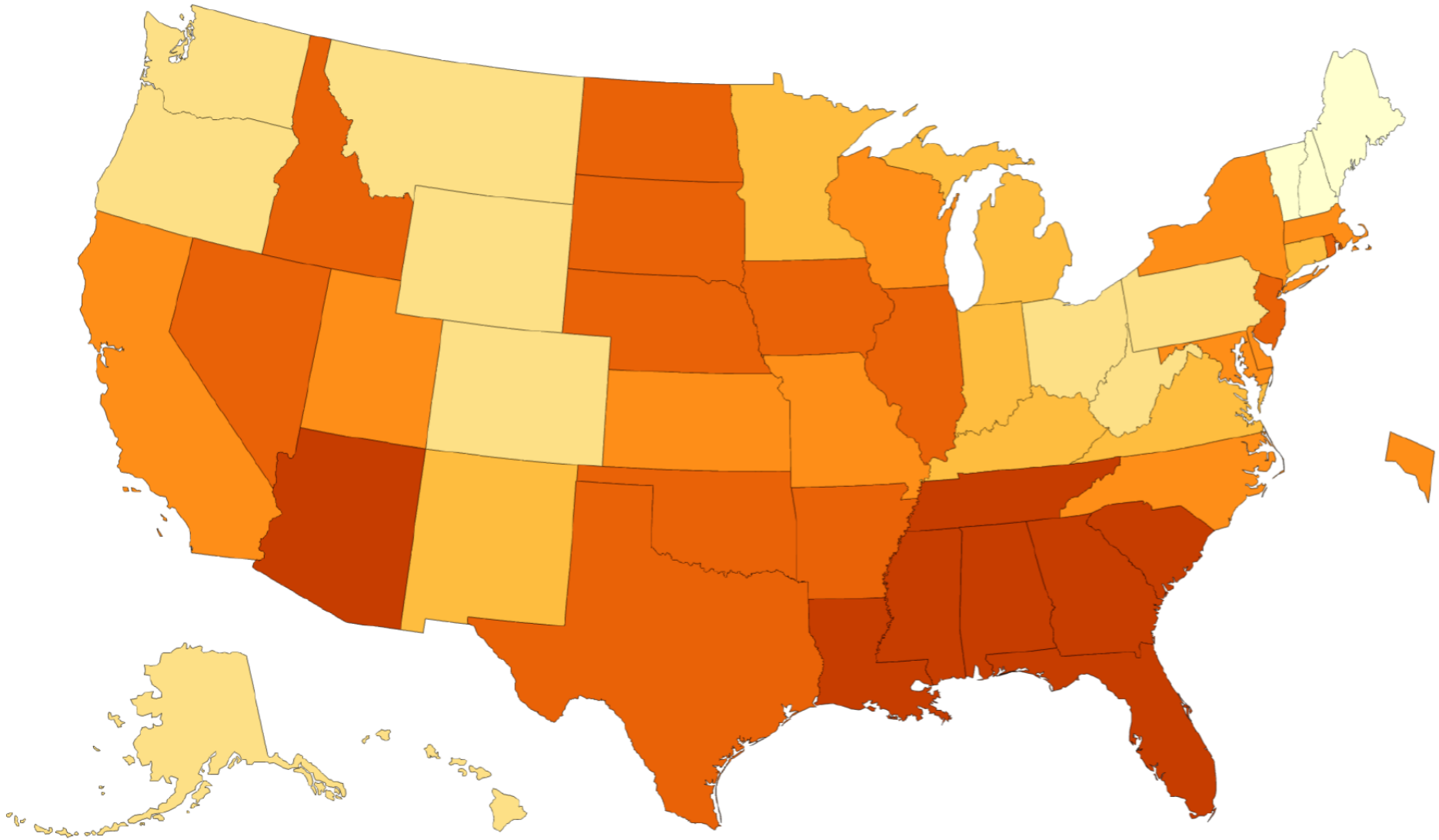
COVID-19 Globally



AS Fauci/NIAID

Sources: NPR.org; Worldometer. Data as of 9/28/2020

COVID-19 in the United States



7.1 million cases

204,033 deaths

Cases/100,000

- 0-599
- 778-1,283
- 1,346-1,742
- 1,906-2,200
- 2,260-2,727
- 2,820-3,544

Source: CDC. Data as of 9/28/2020.

AS Fauci/NIAID

COVID-19 Clinical Presentation

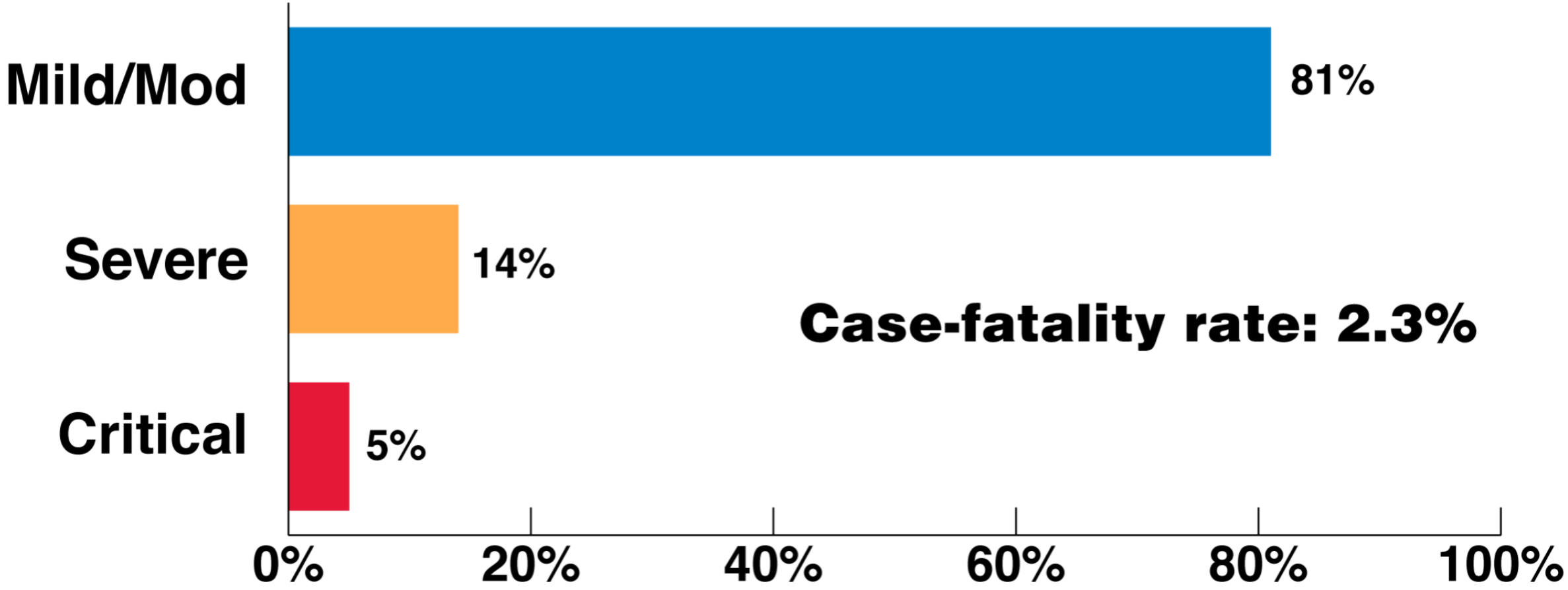
Fever	83–99%
Cough	59–82
Fatigue	44–70
Anorexia	40–84
Shortness of breath	31–40
Myalgias	11–35

Other non-specific symptoms reported

- Sore throat, nasal congestion, headache, diarrhea, nausea, vomiting. Loss of smell/taste preceding the onset of respiratory symptoms.

Source: WHO, 5/2020

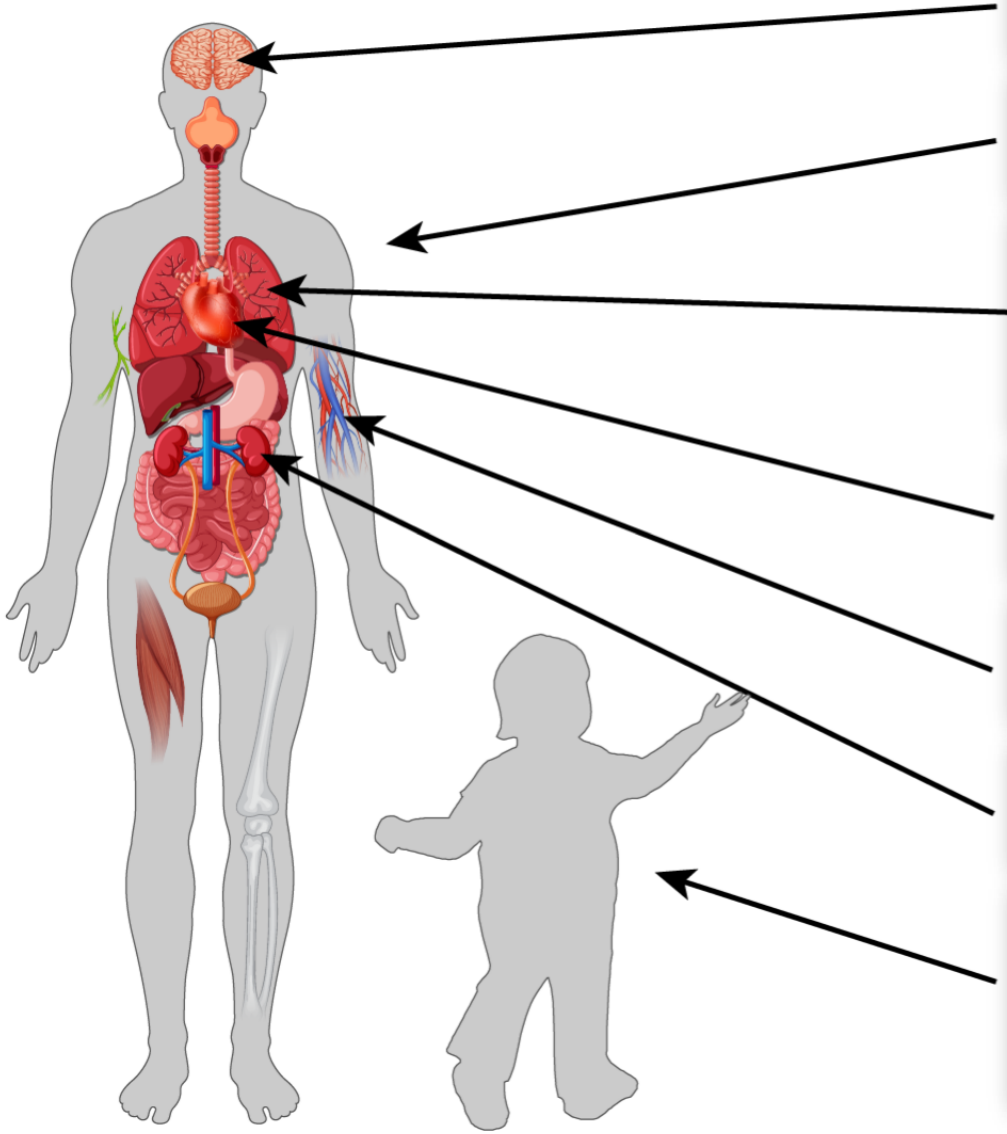
Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China



Source: Z Wu & JM McGoogan, *JAMA* 323:1239, 2020.

AS Fauci/NIAID

Manifestations of Severe COVID-19



- Neurological disorders
- Hyperinflammation
- Acute respiratory distress syndrome (ARDS)
- Cardiac dysfunction
- Hypercoagulability
- Acute kidney injury
- Multisystem inflammatory syndrome in children (MIS-C)

AS Fauci/NIAID

COVID “Long-Haulers”

From ‘Brain Fog’ to Heart Damage, COVID-19’s Lingering Problems Alarm Scientists

J Couzin-Frankel

August 12, 2020

STAT

Long After the Fire of a COVID-19 Infection, Mental and Neurological Effects Can Still Smolder

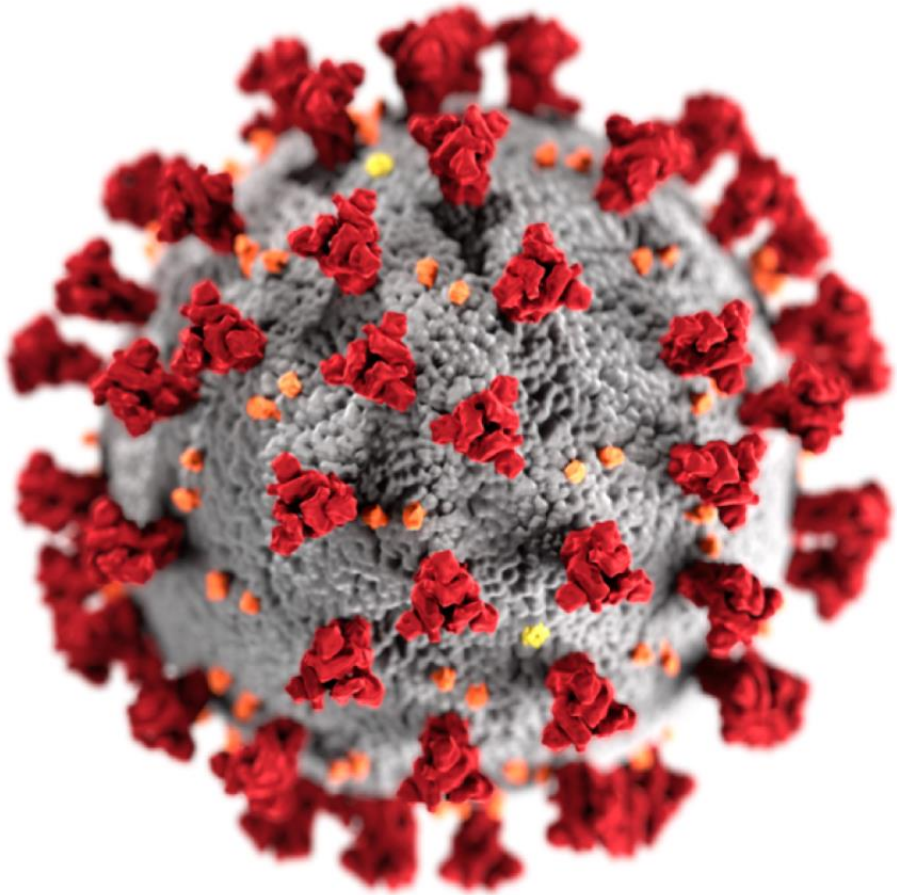
E Cooney

AS Fauci/NIAID

People at Increased Risk for Severe COVID-19 Illness

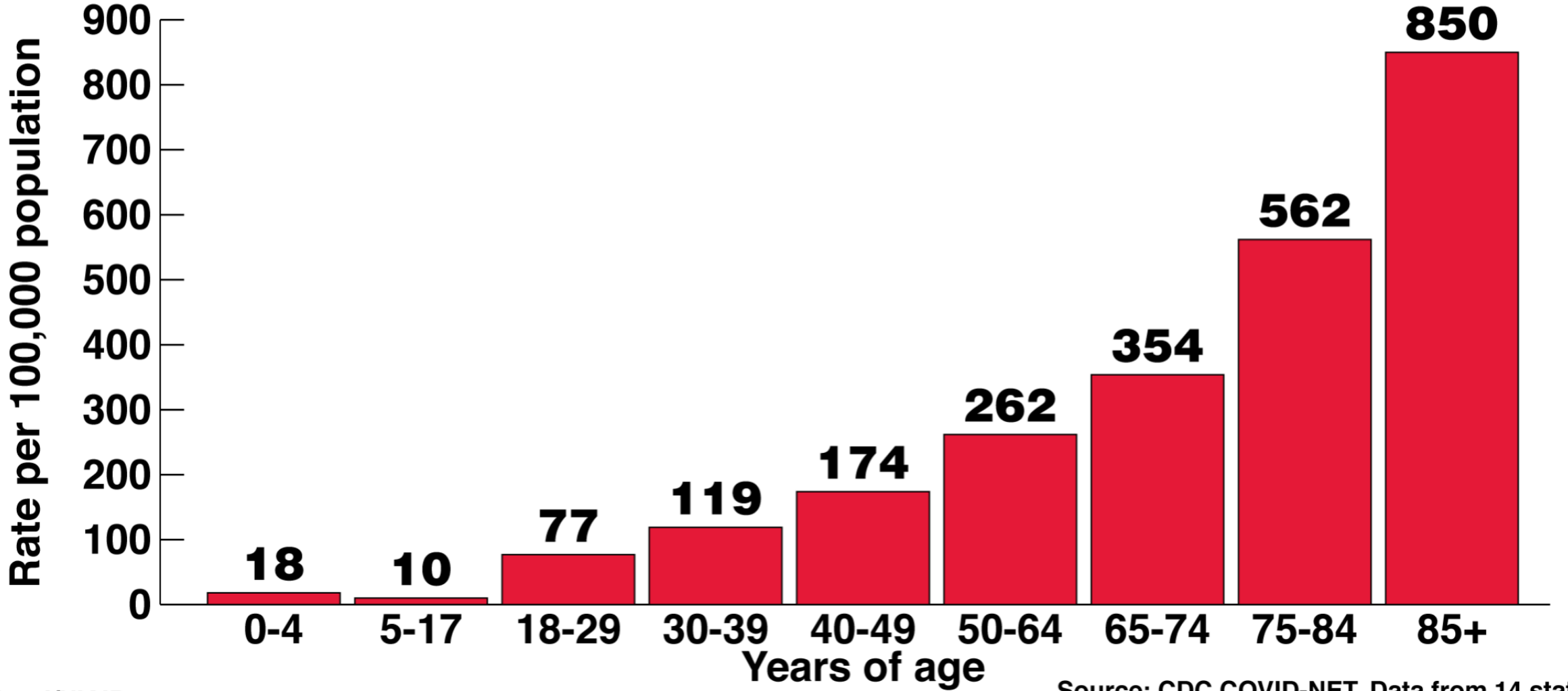
- Older adults

- People of any age with certain underlying medical conditions



Source: CDC, 6/25/2020

Cumulative Rates of Laboratory-Confirmed COVID-19-Associated Hospitalizations by Age, United States, March 1 – September 19, 2020



AS Fauci/NIAID

Source: CDC COVID-NET. Data from 14 states.

Underlying Medical Conditions Strongly Associated with Increased Risk for Severe COVID-19 Illness

- Serious heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)
- Chronic kidney disease
- Chronic obstructive pulmonary disease (COPD)
- Diabetes, type 2
- Obesity (BMI ≥ 30)
- Cancer
- Sickle cell disease
- Immunocompromised state from solid organ transplant

Source: CDC, 7/28/2020

May 11, 2020

JAMA

The Journal of the American Medical Association

Viewpoint

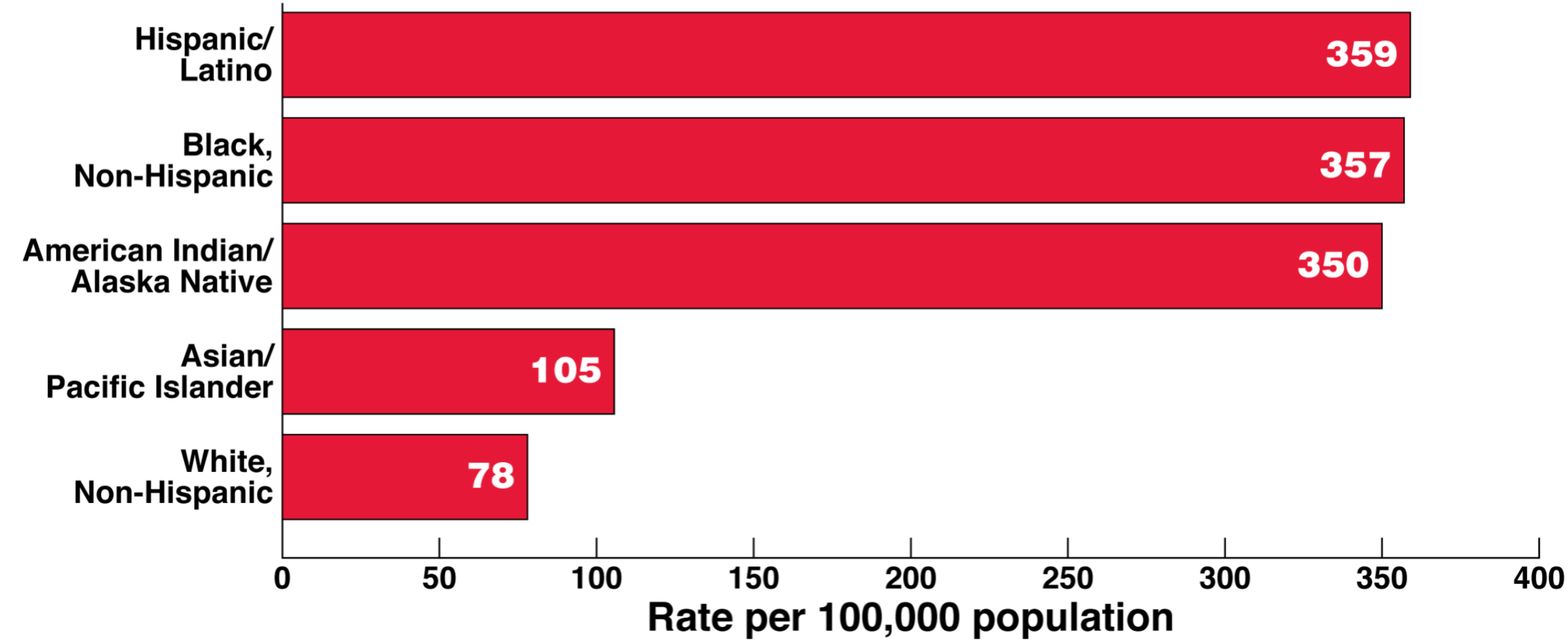
COVID-19 and Racial/Ethnic Disparities

MW Hooper, AM Nápoles and EJ Pérez-Stable

"The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations."

AS Fauci/NIAID

Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – September 19, 2020



AS Fauci/NIAID

Source: CDC COVID-NET. Data from 14 states.

National Institutes of Health
Turning Discovery Into Health

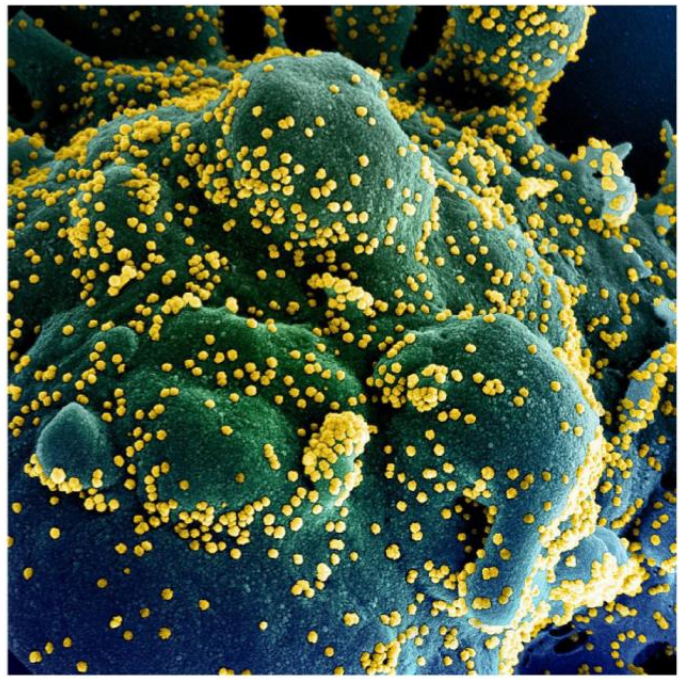
Tuesday, April 21, 2020

News Release

Expert U.S. Panel Develops NIH Treatment Guidelines for COVID-19

"Living document" expected to be updated often as new clinical data accrue

- **Covid19treatmentguidelines.nih.gov**



AS Fauci/NIAID

Therapeutics for COVID-19

Recommended by the NIH COVID-19 Treatment Guidelines Panel for Certain Patients

- Remdesivir (investigational antiviral)
- Dexamethasone (corticosteroid)

Examples of Other Investigational Therapies

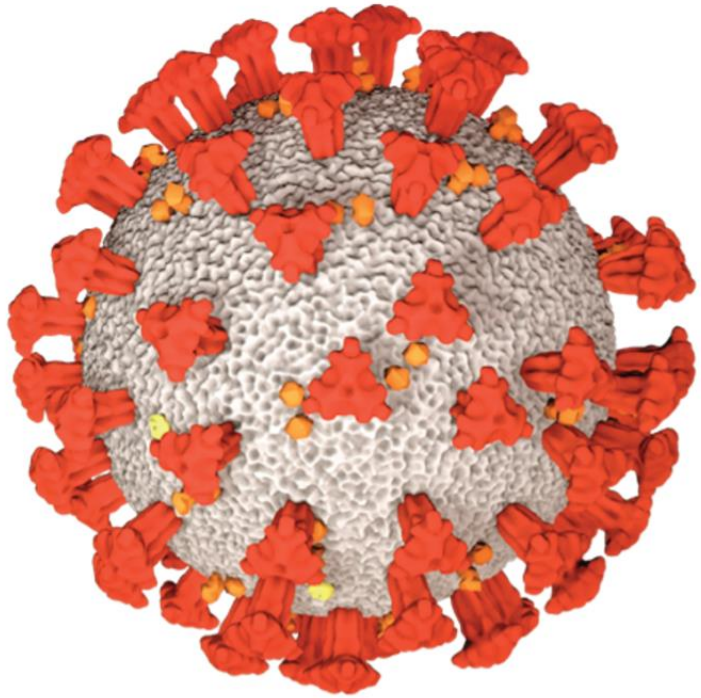
- Antivirals
- Blood-derived products, e.g., convalescent plasma, hyperimmune globulin
- Monoclonal antibodies against SARS-CoV-2
- Immunomodulators, e.g., cytokine inhibitors, interferons
- Adjunct therapies, e.g., anticoagulants

AS Fauci/NIAID

Selected COVID-19 Vaccine Candidates

Platform	Developer	Phase 1/2	Phase 2/3
Nucleic acid	moderna	Enrolled	Ongoing
	BIONTECH Pfizer	Enrolled	Ongoing
Viral vector	UNIVERSITY OF OXFORD AstraZeneca	Enrolled	Ongoing
	Janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson	Enrolled	Ongoing
	MERCK	Ongoing	--
Protein subunit	NOVAVAX Creating Tomorrow's Vaccines Today	Ongoing	Ongoing
	gsk SANOFI	Ongoing	--

AS Fauci/NIAID



COVID-19

Prevention Network

coronaviruspreventionnetwork.org

AS Fauci/NIAID

A Translational Approach to Addressing COVID-19

The process of developing new therapies and getting them to patients is long and difficult. During public health emergencies, science — and the process of turning observations into new therapies — must move faster than ever. That is where translational science comes in.

Translational science is focused on streamlining the process of moving ("translating") lab findings into medical practice and treatments to improve health and well-being. NCATS is focused on advancing the science of translation.

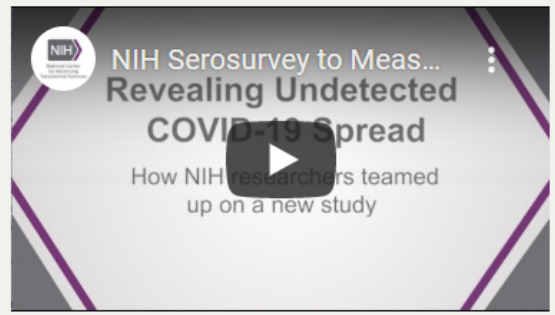
NCATS is supporting research activities **spanning the translational science spectrum** to address the novel coronavirus 2019 (SARS-CoV-2) and the disease it causes (COVID-19). With the aim of accelerating translational research across all diseases, NCATS has developed research tools, technologies, expertise and collaborative networks that can quickly pivot to address urgent public health issues.

In addition, by using its networks to draw together experts with necessary and complementary skills, knowledge and experience, NCATS is enabling projects to cut through operational roadblocks.

From the Director

Read Director's Messages from Christopher P. Austin, M.D., about NCATS' response to COVID-19.

Video Spotlight



Watch this video for a behind the scenes look at how a collaborative NIH study to measure undetected coronavirus cases came together or **read more about the study**.

Research Activities

- **Learn about NCATS projects that are leveraging existing platform approaches to help detect coronavirus cases and find ways to the treat infection**.
- **Learn about collaborations that are speeding research related to COVID-19**.

Additional Resources

Funding

Open NCATS opportunities: NCATS has issued several notices of special interest that highlight the urgent need for research on SARS-CoV-2 and COVID-19. **See all open NCATS funding opportunities**.

Collaborate and Share Information

NCATS and CLIC are partnering resources to facilitate discussions around COVID-19. Specific research or translational discussions should use the CTSA Program Response to COVID-19 Discussion Forum to discuss and identify efforts to manage the Coronavirus outbreak. **Learn more about how to join a Discussion Forum** and join in on the conversation on COVID-19. You can also **view the NCATS Getting Started** resource for using the DF.

Please share your hubs' events, news, educational content and other resources about COVID-19 by posting them on the CLIC website using the tag "COVID-19". **View all posted hub information about COVID-19 on the COVID-19 tag page**. For information on how to share content, please check out the CLIC Library video on Sharing Content. We have provided a comment section below for short inter-consortium communications about hub efforts around COVID-19.

NATIONAL CENTER FOR DATA TO HEALTH
COVID-19 Resources

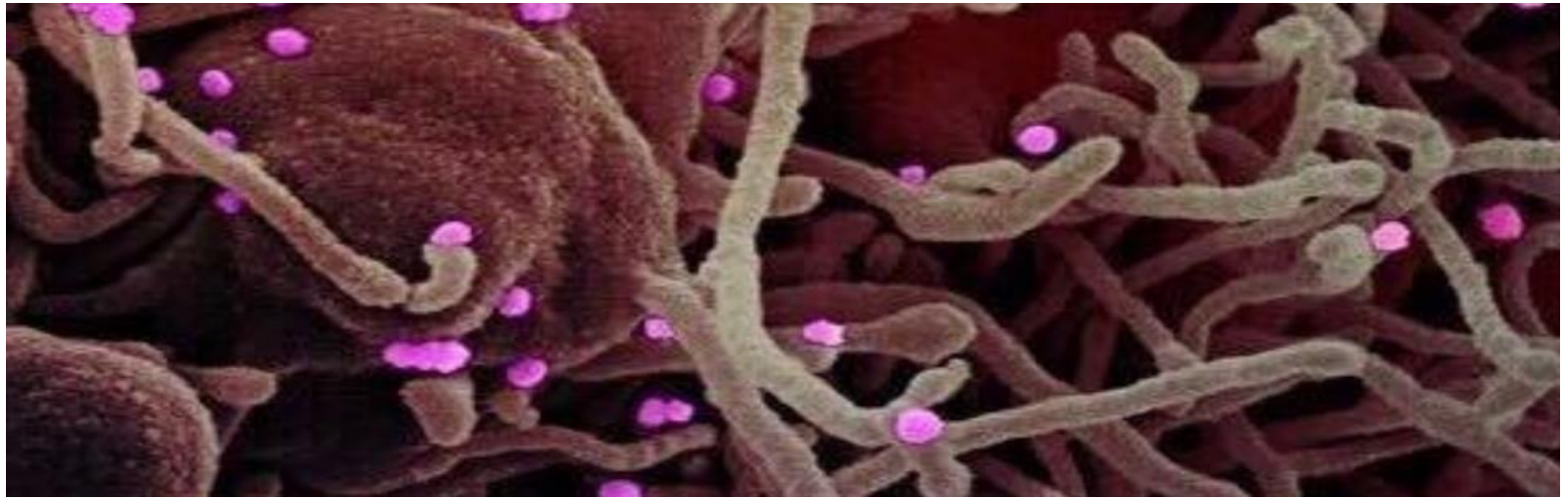
National COVID Cohort Collaborative

In collaboration with several HHS agencies, the CTSA program, and distributed clinical data networks, CD2H has created the (**National COVID Cohort Collaborative (N3C)**a centralized, secure, limited access portal to access COVID-19 clinical data. The N3C page and the accompanied CD2H-COVID portal has been established to provide the additional assets needed to rapidly develop the analytics that clinical centers and physicians need.

COVID Case Report Forms and Phenotyping Standards contains a list of known CRFs for triage, intake, and patient-focused phenotype/metadata collection efforts

NCATS OpenData Portal

Making drug screening data completely and immediately public

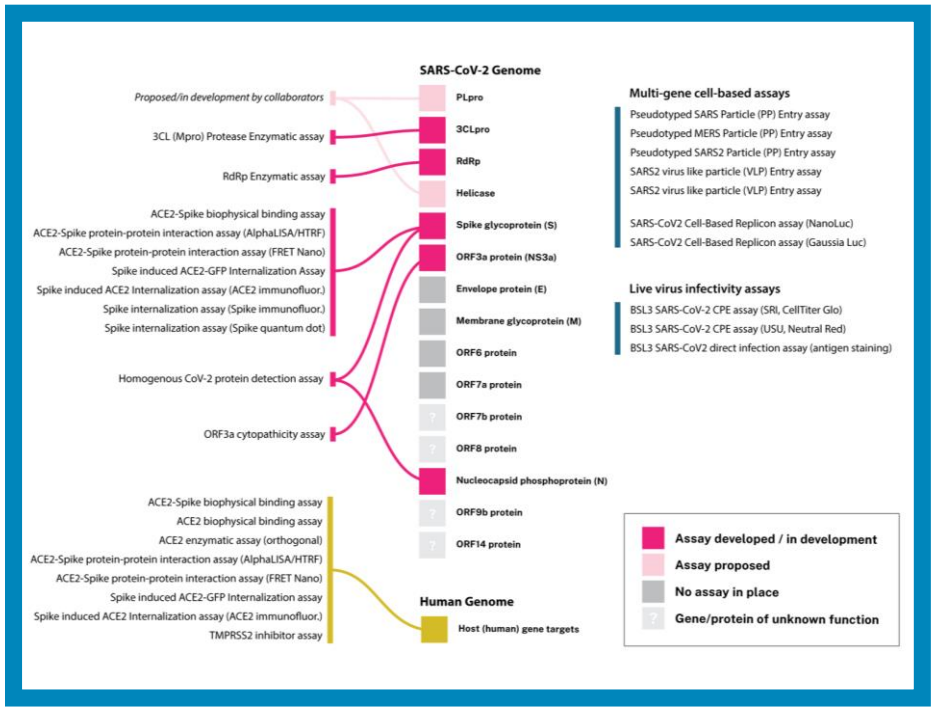


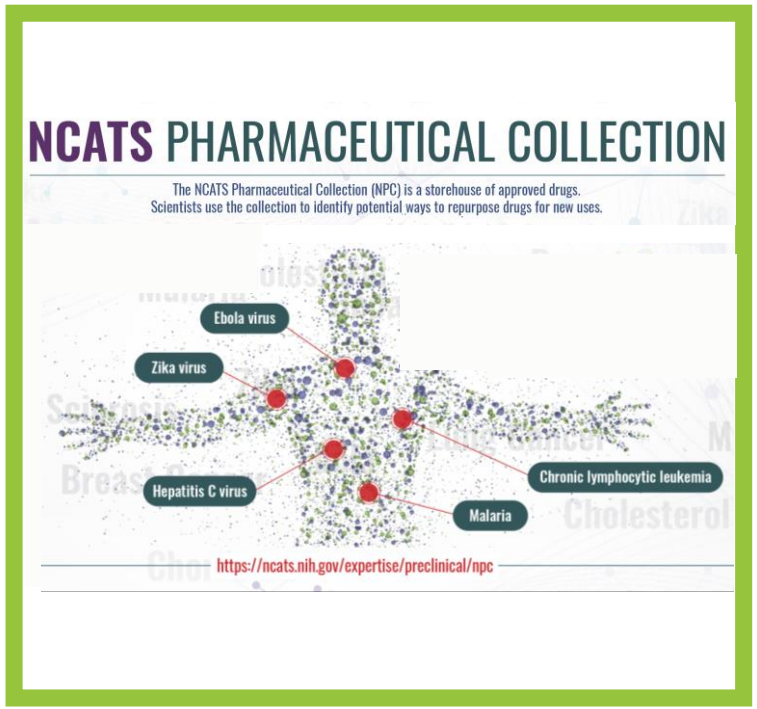
Problem:

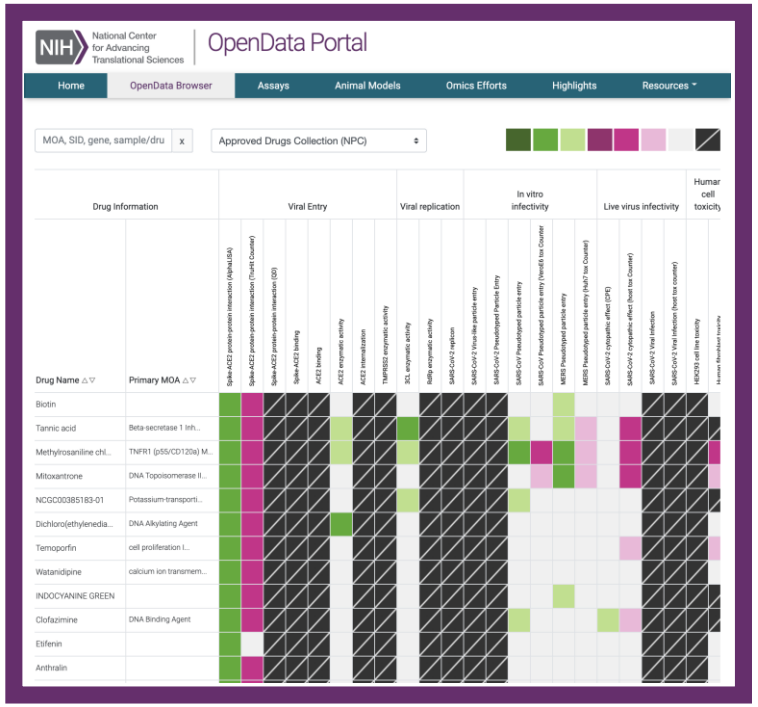
Many labs around the world running compound screens to find a potential treatment for COVID-19, but their results/methods aren't shared quickly or completely, and aren't easily available to the scientific community

This limits their impact and delays how quickly we can bring treatments to these patients

NCATS OpenData Portal

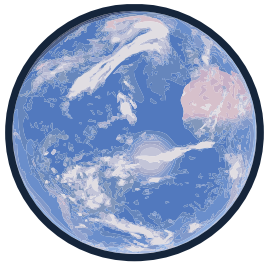






Run as many screens against as many COVID targets as NCATS can…

against all approved drugs…



and make our data immediately available to the world

Sharing clinician experience in real time: CURE ID

A mobile app that allows health care workers to share their clinical experience using approved drugs to treat diseases other than the one for which they are regulatorily indicated

Developed by FDA and NCATS

Allows health care workers* to

Contribute knowledge and expertise

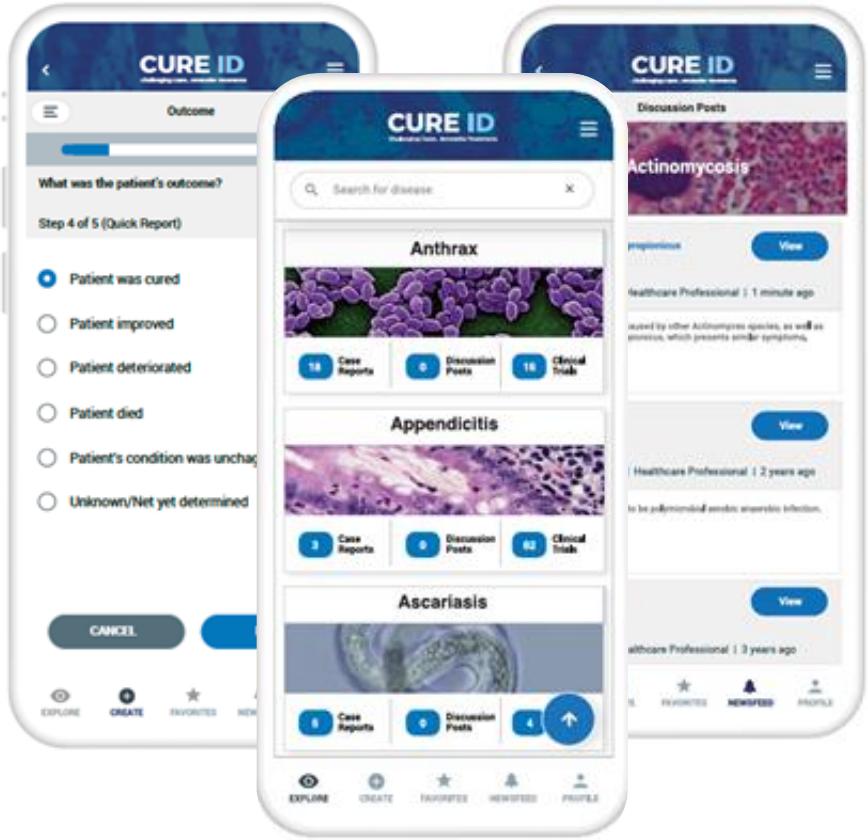
Explore experiences of clinicians globally

Discuss share challenging clinical cases and treatment questions

Available at http://cure.ncats.io, or

Download on the App Store

GET IT ON Google Play



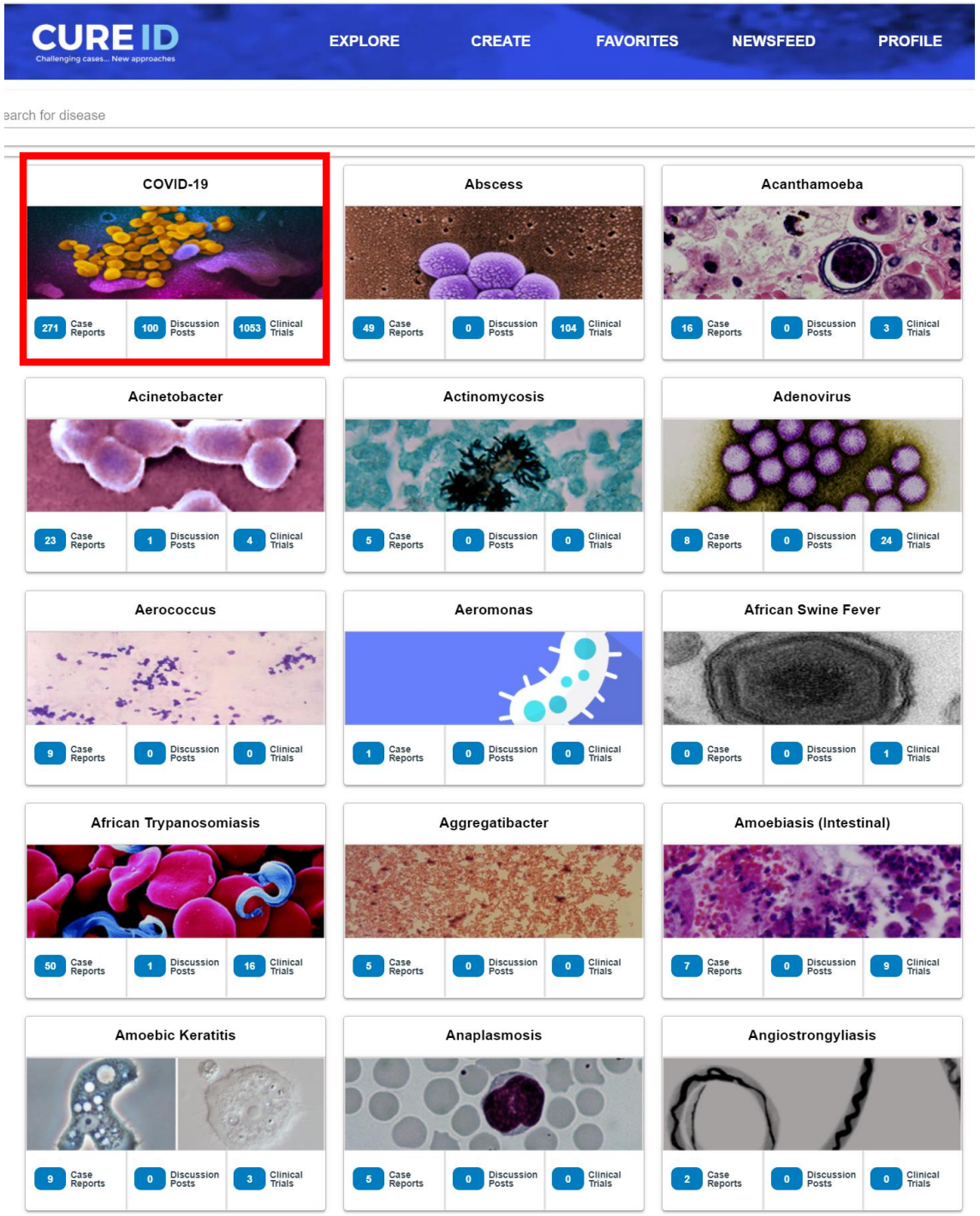
https://cure.ncats.io

**Must be a certified health care professional to use*

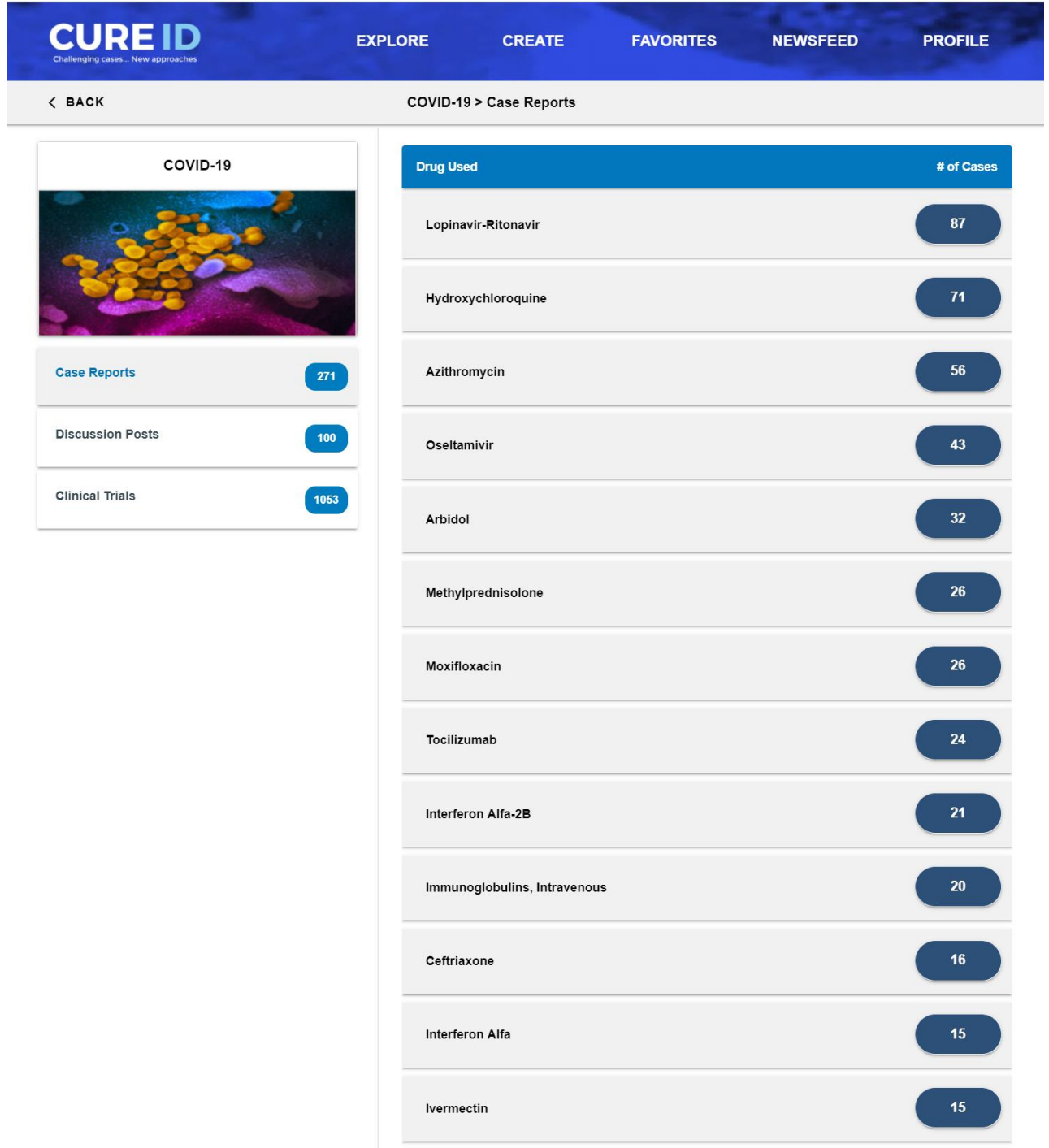
CURE-ID launched December 5, 2019

First COVID-19 case less than a month later

https://cure.ncats.io



National Center for Advancing Translational Sciences



https://cure.ncats.io/explore/cases/630

National Center for Advancing Translational Sciences

June 23, 2020

C-Path Launches CURE Drug Repurposing Collaboratory to Accelerate Identification of New Uses of Existing Drugs to Treat Infectious Diseases, Including COVID-19

Clinicians to report novel uses of existing drugs through FDA-NCATS CURE ID Mobile App.

TUCSON, Ariz., June 23, 2020 — As millions of patients struggle with diseases that lack adequate treatments, there is a critical need to understand how existing drugs can be used in new ways to improve clinical outcomes. Health care professionals use drugs in novel ways as a potential life-saving intervention when no specific approved therapies are available. However, without the ability to share these experiences in a systematic manner, the clinical and research communities cannot benefit from lessons learned.

To address the challenge, the Critical Path Institute (C-Path) today announced the launch of the CURE Drug Repurposing Collaboratory (CDRC) funded by the U.S. Food and Drug Administration (FDA), in collaboration with the National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health (NIH). A public-private partnership, CDRC will provide a forum for the exchange of clinical practice data to inform potential new uses of existing drugs for areas of high unmet medical need, advancing research in these areas. The Collaboratory will also create a network connecting major treatment centers, academic institutions and researchers, private practitioners, government facilities and health care professionals around the world.

CDRC
CURE DRUG REPURPOSING COLLABORATORY
CRITICAL PATH INSTITUTE

CURE ID
Challenging Cases... Innovative Treatments

NIH
National Center for Advancing Translational Sciences

SARS-CoV-2 Serosurvey

NIH National Center for Advancing Translational Sciences

NIH National Institute of Allergy and Infectious Diseases

NIH National Institute of Biomedical Imaging and Bioengineering

NIH NATIONAL CANCER INSTITUTE NCIatFrederick

What are we doing?

- Evaluating proportion of healthy population that has been exposed to SARS-CoV2 infection by measuring antibodies in blood serum

What will we learn?

- Extent of spread of SARS-CoV2 infection in population not been diagnosed with COVID-19
- Distribution of SARS-CoV2 cases across the U.S. geographically and demographically
- Will be useful as social distancing restrictions eased
- Assist with investigations of immunity and correlates of protection

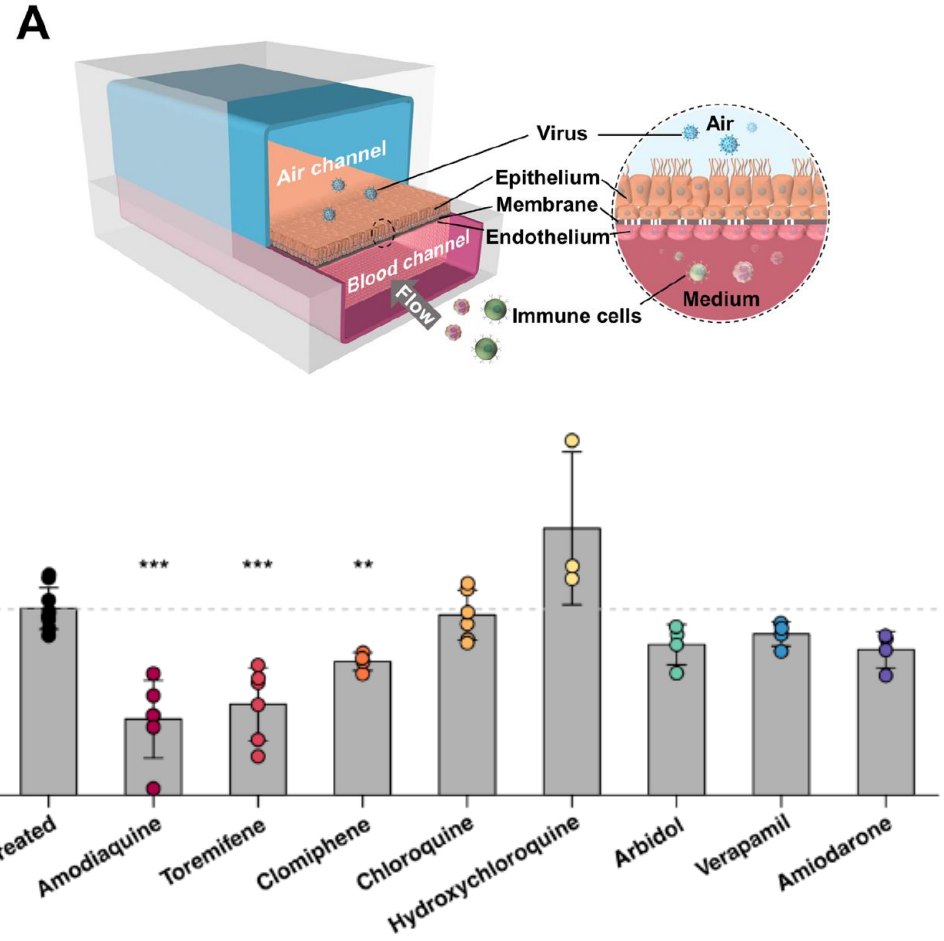
Current status

- Proper sampling of US population via CTSA hubs at UAB and U Pitt
- Rapid highly specific testing method
- **10K recruitment completed; >8.5K samples received and measured**
- Ongoing funding through NCI Serological Sciences Network

NIH National Center for Advancing Translational Sciences

COVID-19 Tissue Chips

- Don Ingber and team (Wyss Institute) previously funded by NCATS to model human lung-on-chip and response to influenza
- Chip used to model viral entry of SARS-CoV2 and test repurposed drugs
- Amodiaquine, toremifene, and clomiphene inhibit viral infection under physiological conditions
- Hydroxychloroquine, chloroquine and arbidol did not inhibit viral entry, consistent with clinical data
- **Proof-of-concept that tissue chips can help identify existing drugs that may be repurposed for pandemic viral applications.**



https://doi.org/10.1101/2020.04.13.039917 (bioRxiv)

National Center for Advancing Translational Sciences

CTSA-driven Convalescent Plasma Trials*

- **NYU/Einstein CONTAIN trial** (NCT04364737)
  - Begun April during peak of NYC caseload, target enrollment n=300
    - New cases declined dramatically in NYC, limiting further recruitment
  - Expanded in August to additional sites and target enrollment to n=1000
    - UT Houston: At least 6 Texas sites; n=400
    - U Miami: At least 2 Florida sites; n=360
    - Considering additional sites now
  - Current total enrollment: 315
- **Vanderbilt PassItOnII trial (Pass**ive **I**mmunity **T**rial **O**f **N**ashville II for COVID-19) (NCT04362176)
  - Also started in April, same dynamic as CONTAIN w decrease in caseload in Nashville limiting enrollment
  - Expanded in August to additional sites and target enrollment to n=1000
  - Up to 50 sites currently being activated
  - Current total enrollment: 85

*Supported with NCATS and Operation Warp Speed funds

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

ACTIV-1 Trial being run by NCATS though CTSA TIN and Hubs

Study Objectives

ACTIV-1 is a master protocol designed to evaluate **multiple therapeutic agents** for the treatment of **moderately or severely ill** patients infected with SARS-Cov-2.

The research objectives are to evaluate each agent with respect to **speed of recovery, mortality, illness severity, and hospital resource utilization**. Each agent will be evaluated as **add-on therapy to remdesivir (provided) plus the standard of care (SoC) in use at the local clinics**.

Patient Population

Hospitalized adults (≥18 years old) with COVID-19, including patients both in and out of the ICU.

CANDIDATES

TNF-alpha blocker
Elevated in several coronavirus infections

CTLA-4

Binds to Ag presenting cells limiting T-cell activation

CCR2/CCR5 antagonist

Increased in cytokine storm

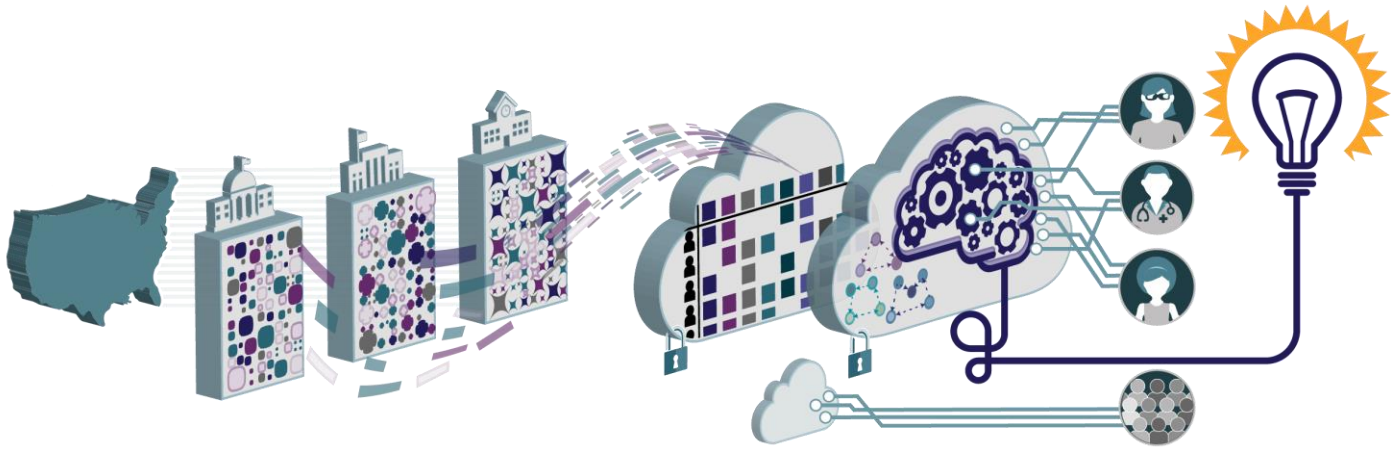
PRIMARY ENDPOINT

Time to Recovery by Day 29
Satisfies one of the following three categories from the ordinal scale:

- Hospitalized, not requiring supplemental oxygen – no longer requires ongoing medical care;
- Not hospitalized, limitation on activities and/or requiring home oxygen;
- Not hospitalized, no limitations on activities.

The National COVID-19 Cohort Collaborative (N3C)

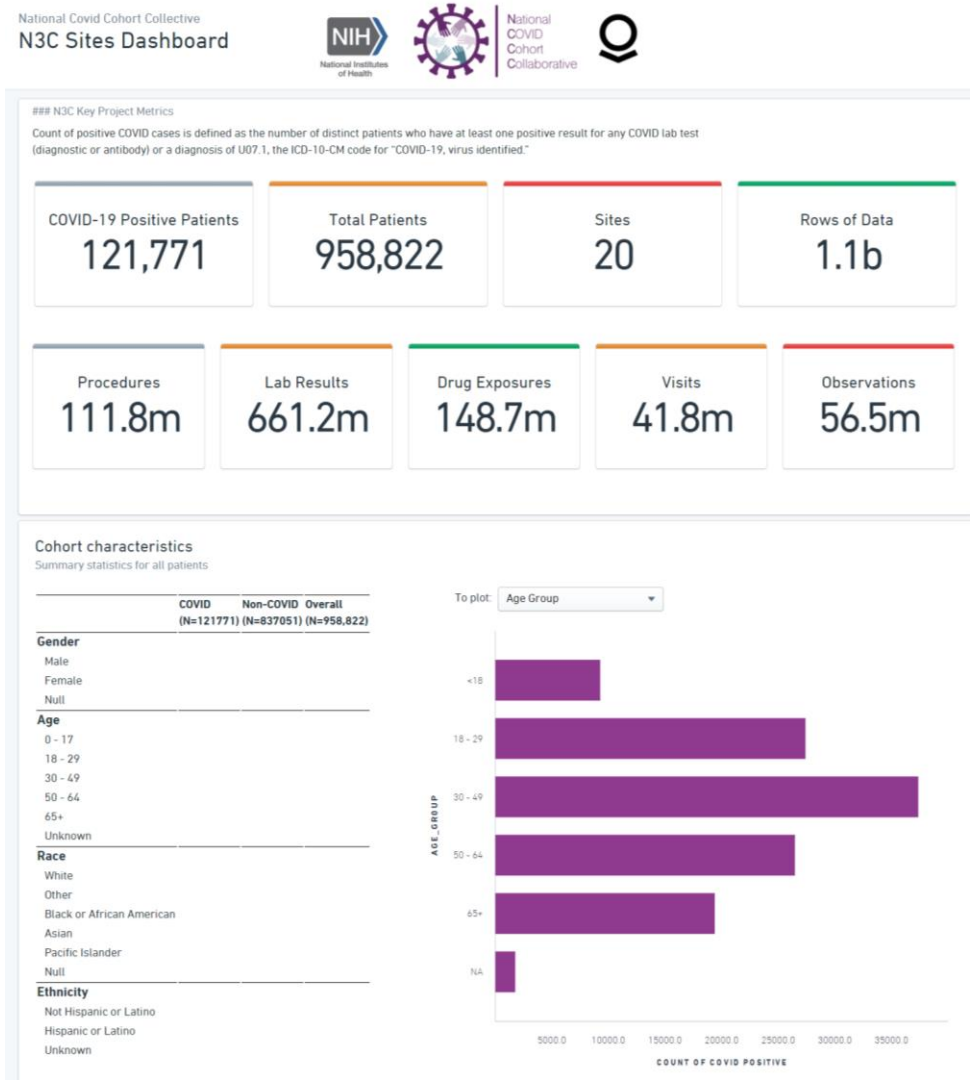
- Making available vast amounts of clinical EHR data for speeding COVID-19 research and improving patient care
- Centralized, secure data enclave that provides access to medical record data from people diagnosed with COVID-19 across the US



- Harnesses resources of Clinical and Translational Sciences Awards (CTSA) Program hubs and Center for Data to Health (CD2H)

What makes the N3C unique?

- **Robust Scale and Scope:** Includes demographics, symptoms, laboratory test results, procedures, medications, medical conditions, physical measurements
- **Harmonized Data**: Makes data from different types of medical records comparable
- **Collaborative Analytics**: enables team-based research, machine-learning and rigorous statistical analyses
- **Centralized and Secure**: data remain in NCATS' secure FedRAMP-certified cloud, provides standardized assessment, authorization and continuous monitoring

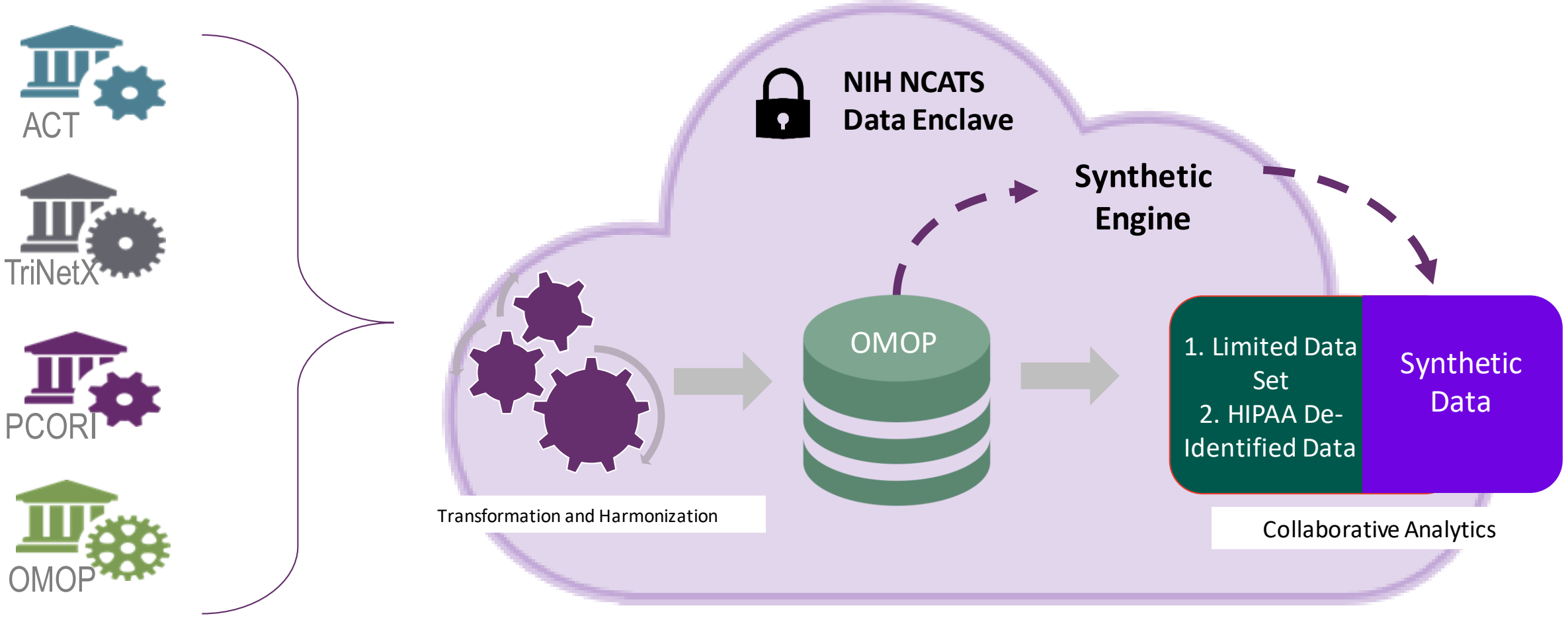


As of 10/13/20

https://ncats.nih.gov/n3c

National COVID Cohort Collaborative

N3C Data Pipeline



1	2	3	4
NCATS Data Transfer Agreement	**Data Acquisition**	**Data Harmonization**	**NCATS Data Use Agreement**

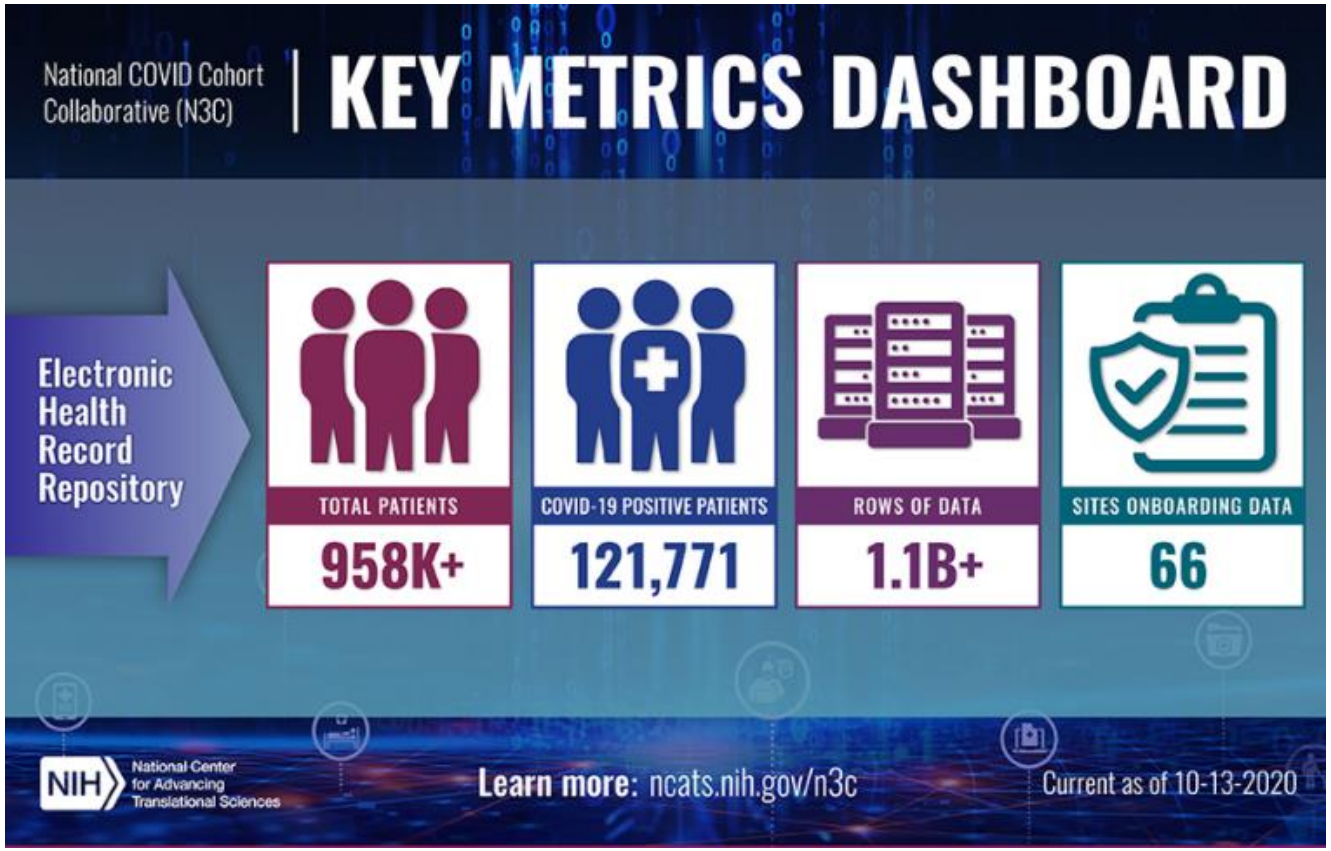
National Center for Advancing Translational Sciences

Is the N3C open for research?

YES!

The N3C Data Enclave opened for research on September 3, 2020

- 66 institutions or organizations have agreed to transfer their patient data to N3C.
- How to apply for N3C data access: https://ncats.nih.gov/n3c/about/applying-for-access



Watch N3C demo video at https://ncats.nih.gov/n3c/about

NIH National Center for Advancing Translational Sciences

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

LAUNCH

On April 17, NIH announced the launch of a public-private partnership, **Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)**

MISSION

Develop a coordinated research response to **speed COVID-19 treatment and vaccine options**

FNIH

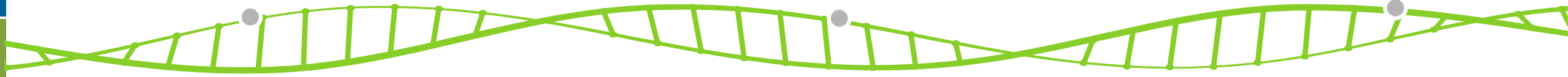
ACTIV Stakeholders

ACTIV is being coordinated by the Foundation for the National Institutes of Health (FNIH), and has brought together multiple partners from government, industry and non-profits.

8
Government Partners

20
Industry Partners

4
Non-Profits



BARDA
CDC
Department of Defense
European Medicines Agency
U.S. Food & Drug Administration
Operation Warp Speed
NIH
Department of Veterans Affairs
FNIH

abbvie
AMGEN
AstraZeneca
Bristol-Myers Squibb
Eisai
Lilly
evotec
gsk
Johnson & Johnson
MERCK
moderna
NOVARTIS
RHYTHM THERAPEUTICS
Roche Genentech
Pfizer
SANOFI
Takeda
NOVAVAX
VIR

Bill & Melinda Gates foundation
Fred Hutch Cures Start Here
RTI International
FNIH

ACTIV Fast-Track Focus Areas

The ACTIV partnership consists of four fast-track focus areas, consisting of Working Group membership of both public and private sector representatives:

Preclinical

Therapeutics – Clinical

Clinical Trial Capacity

Vaccines

Focus Area Objectives & Composition

Each focus area is a Working Group that contains several sub groups to oversee tactical operations :

Preclinical

Therapeutics – Clinical

Clinical Trial Capacity

Vaccines

	Preclinical	Therapeutics – Clinical	Clinical Trial Capacity	Vaccines
Objective	+ Develop a collaborative, streamlined forum to identify preclinical treatments	+ Accelerate clinical testing of the most promising vaccines and treatments	+ Improve clinical trial capacity and effectiveness	+ Accelerate the evaluation of vaccine candidates to enable rapid authorization or approval
Sub-Groups	+ Animal Models + In Vitro Assays	+ Agent Prioritization + Master Protocol	+ Survey Development + Clinical Trial Network Inventory + Innovations	+ Vaccines Clinical Trials + Protective Immune Responses + Vaccine-Associated Immune Enhancement

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ACTIV Governance

ACTIV Governance includes representation from key stakeholders in both the private and public sector.

ACTIV Executive Committee

Co-Chairs

Francis Collins, NIH
Paul Stoffels, J&J

Members

Anthony Fauci, NIAID
Gary Gibbons, NHLBI
Janet Woodcock, OWS
William Pao, Roche
Mikael Dolsten, Pfizer
Gary Disbrow, BARDA
Peter Marks, FDA
Andrew Plump, Takeda

ACTIV Leadership Team

Scientific leaders from all participating organizations

- Preclinical Working Group
- Therapeutics Clinical Working Group
- Clinical Trial Capacity Working Group
- Vaccines Working Group

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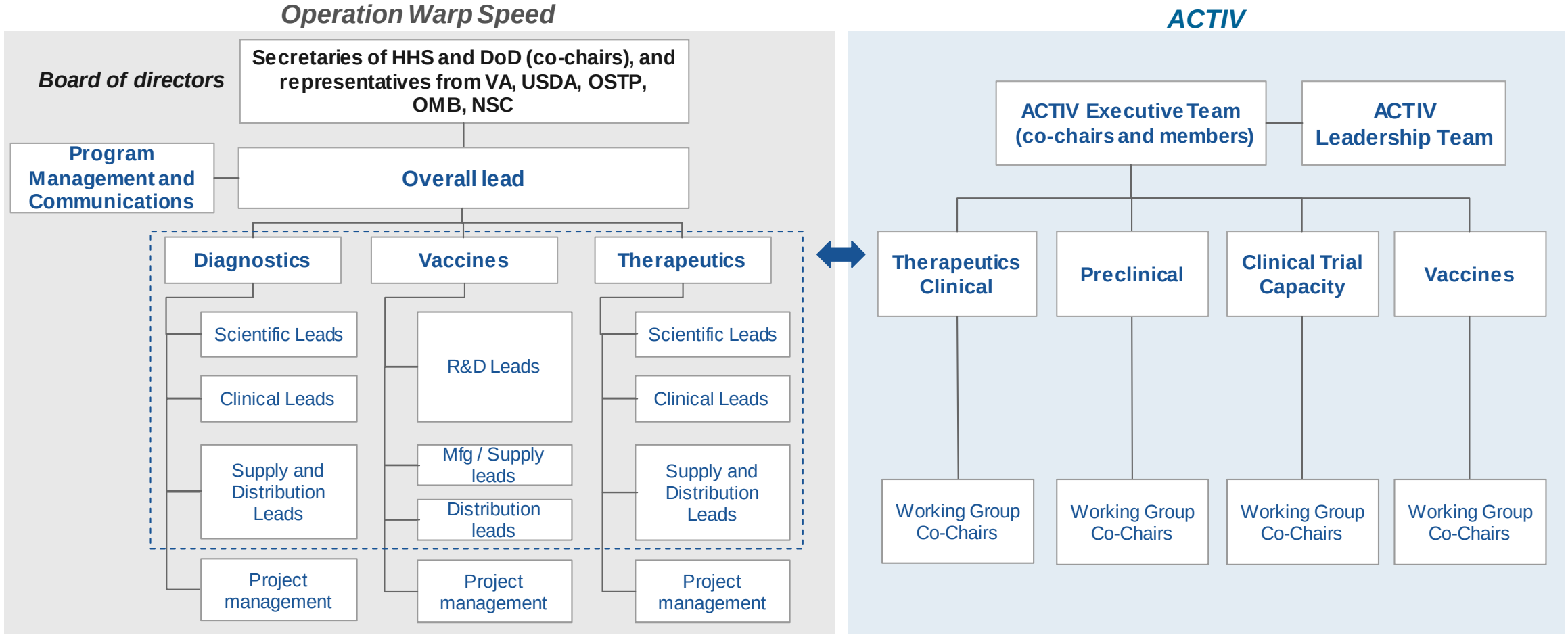
ACTIV Governance & Coordination with Operation Warp Speed

OWS and ACTIV working groups have been closely collaborating to ensure alignment across both efforts.



Preclinical Working Group

OBJECTIVE

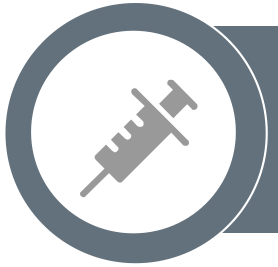
Standardize and share preclinical evaluation methods and sharing testing resources in an open forum that allows for effective validation and comparison of therapeutic candidates.

ACCOMPLISHMENTS TO DATE

- ✓ Developed a **master inventory of preclinical testing** resources
- ✓ Established SOPs for **accelerated preclinical agent development** in response to a pandemic
- ✓ **Developed a National Strategy for NHP Research** and a process to coordinate NHP studies centrally through NIH, and "field guides" for the use of small animal testing models
- ✓ Established a process for **prioritizing in vitro assays** and **evaluating preclinical compounds**
- ✓ Created a **public database** for sharing preclinical data (NCATS Open Science Portal)
- ✓ Established a **virtual preclinical in vitro and in vivo testing network** for therapeutic sponsors to streamline access to testing resources
- ❑ **Conducting a "matchmaking" process** to pair promising compounds with available preclinical resources and funding, on an ongoing basis

FNIH ✓ *Completed* ❑ *In progress*

Therapeutics – Clinical Working Group



OBJECTIVE

Prioritize promising therapeutic candidates and accelerate their clinical evaluation by establishing large-scale master protocol trials.

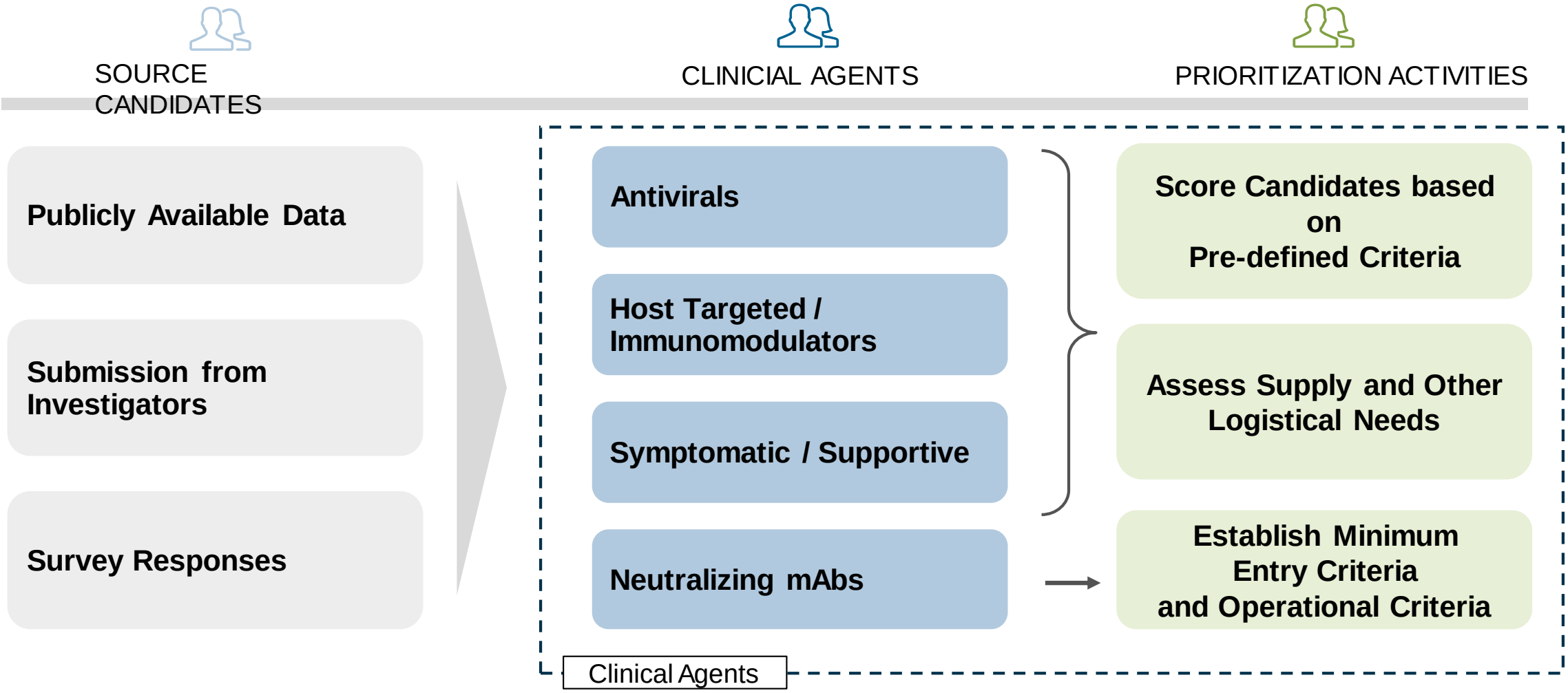
ACCOMPLISHMENTS TO DATE

- ✓ Developed and continuously enhanced a **world-class process for prioritizing clinical agents** for rapid testing
- ✓ Evaluated ~500+ available agents with potential relevance for COVID-19 therapies and **prioritized the most promising agents for further study** (agent prioritization continues on a rolling basis)
- ✓ **Assessed, designed, and harmonized five master protocols** for ACTIV clinical trials, focusing on candidates selected through the agent prioritization process
- ✓ **Selected clinical trial networks** best suited to execute these master protocols and supported NIH efforts to launch them; four protocols have been launched to date:
  - ACTIV-2, ACTIV-3, and ACTIV-4a/4b, ACTIV-5
- ❑ **Actively working with NIH and OWS across all five protocols** to ensure they are effectively coordinated, efficiently managed, and meet recruitment targets

FNIH ✓ *Completed* ❑ *In progress*

Prioritizing the most promising therapeutic agents for COVID-19

The Working Group continues to Identify agents that stop the virus or that treat its symptoms so they can be placed in a master protocol for a Phase II/II Progressive trial – so far ACTIV has reviewed more than 500 agents.



Current Portfolio of ACTIV Master Protocols

ACTIV Therapeutics has been taking a portfolio approach to address the dramatic health and economic challenges posed by the pandemic, with harmonized "master protocol" trials.

	DESIRED OUTCOMES	STATUS
ACTIV-1	• Phase III trial of 3 host-targeted immune modulators • Inpatient (hospitalized) patient population • NCATS networks + Duke CRI + CRO	• **Projected** to launch **October 15**
ACTIV-2	• Phase II/III trial of up to 5-7 Neutralizing Antibodies and Oral Antivirals • Outpatient population • NIAID network + CRO	• ***Trial launched on August 3*** • Initial agent: nAb from Lilly, onboarding other agents
ACTIV-3	• Phase III trial of 5-7 Neutralizing Antibodies and Oral Antivirals • Inpatient population • NIAID, NHLBI, VA networks +CRO	• ***Trial launched on August 4*** • Initial agent: nAb from Lilly, onboarding other agents
ACTIV-4	• Phase III trial of anticoagulants (heparin, aspirin) and antiplatelet drug • Three different populations: pre-hospitalized, hospitalized, & post-hospitalized • NHLBI-NINDS network	• Hospitalized and post-hospitalized ***trials launched on September 17*** • Post-hospitalized cohort **projected** to launch **mid-October**
ACTIV-5 *(Big Effect Trial)*	• Phase II "proof of concept" study to identify multiple promising treatments • Inpatient population • NIAID networks + CRO	• ***Trial launched on October 13*** • Two initial agents selected (anti-inflammatory and immune modulator)

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Clinical Trial Capacity Working Group

OBJECTIVE

Create tools to identify and connect existing networks of clinical trial sites across the U.S. and the world, and identify best practices for running effective COVID-19 trials.

ACCOMPLISHMENTS TO DATE

✓ Developed and conducted an ambitious set of **clinical trial capacity surveys**:

- Collected clinical capacity data for federal networks, industry, academic, Clinical Research Organizations (CROs) and Site Management Organizations (SMOs)

✓ **Identified best practice innovation "playbooks"** to enable safe and rapid execution of clinical trials

✓ **Shared data, insights, and recommendations** with the Therapeutics-Clinical and Vaccine Working Groups

FNIH ✓ *Completed* ❑ *In progress*

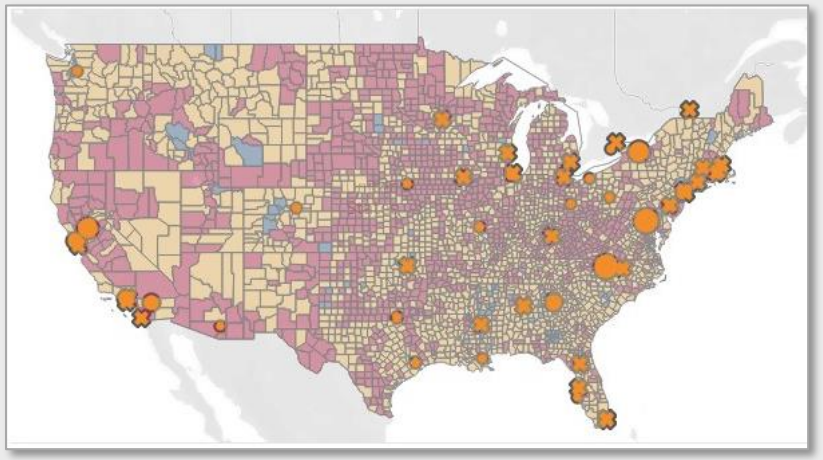
Clinical Trial Capacity Site Optimization Dashboard

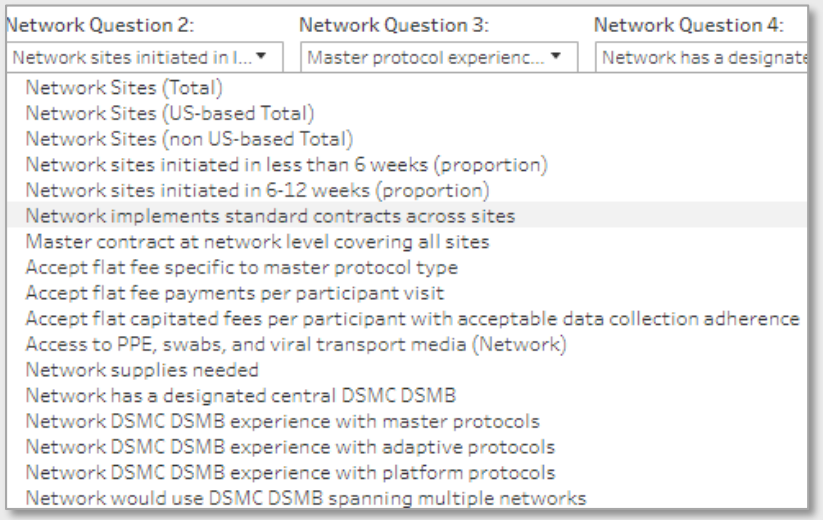
The Clinical Trial Capacity Site Optimization Dashboard was developed to help ACTIV maximize limited clinical trial sites and resources across a global network of clinical sites.

NOTABLE FEATURES INCLUDED

Dashboard includes overlay of data indicating:

- **1) days until peak hospitalization** from University of Pennsylvania
- **2) confirmed COVID cases**
- **3) confirmed COVID deaths** with clinical trial capacity survey data to optimize site selection for therapeutic and vaccine trials





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Vaccines Working Group

OBJECTIVE

Support the evaluation of vaccine candidates to enable rapid authorization and approval.

ACCOMPLISHMENTS TO DATE

- ✓ Developed **harmonized vaccine protocols** to enable analyses of correlates of protection across trials (these are being executed by OWS/NIH/BARDA)
- ✓ Assessed protective immune response evidence to support **accelerated use or approval of vaccine candidates** and provided perspective on many related regulatory issues
- ✓ Articulated scientific and operational **challenges of developing controlled human infection models** (published manuscript)
- ✓ Evaluated implications of evidence on **immune-associated disease enhancement** for COVID-19 vaccine development (published manuscript)
- ❑ Examining approaches to evaluating vaccine safety and efficacy in **pregnant and pediatric populations**

FNIH ✓ *Completed* ❑ *In progress*

Where do I go for more information on ACTIV?

For:	Page / Link
General information:	✓ NIH ACTIV Website: [https://www.nih.gov/research-training/medical-research-initiatives/activ]
	✓ FNIH Website: [https://fnih.org/news/press-releases/nih-launches-partnership-to-speed-covid19-vaccines-treatments]
To submit information for a diagnostic, vaccine, technology, or other information for the awareness of NIH:	✓ NIH COVID-19 Candidate and Technologies Portal: [https://grants.nih.gov/grants/rfi/rfi.cfm?ID=107]
Formal submission of agents for testing in ACTIV:	✓ ACTIV Preclinical and Clinical Asset Data Survey: [https://redcap.ncats.nih.gov/redcap/surveys/index.php?s=DAE87WPTE7]
Publications to date:	✓ Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV): An Unprecedented Partnership for Unprecedented Times [https://jamanetwork.com/journals/jama/fullarticle/2766371]
	✓ Accelerating Development of SARS-CoV-2 Vaccines — The Role for Controlled Human Infection Models [https://www.nejm.org/doi/full/10.1056/NEJMp2020076]
	✓ Bridging the Gap at Warp Speed — Delivering Options for Preventing and Treating Covid-19 [https://www.nejm.org/doi/full/10.1056/NEJMp2028535?query=TOC]
	✓ A strategic approach to COVID-19 vaccine R&D [https://science.sciencemag.org/content/368/6494/948]

What have we learned?

- It is possible to go from fundamental discovery to therapeutics and vaccines much more quickly than has historically occurred
- Ingredients for this are
  - Feeling of urgency in all participants in the research ecosystem
  - Recalculation of benefit:risk based on urgency
  - Willingness to share based on recalculation of benefit:risk
  - Proactive collaboration among public sector, private sector, and public-private orgs that derives from *desire* to share
- This is a potentially positively self-reinforcing cycle since increased efficiencies lead to increased productivity which has potential to increase return on investment despite sharing of credit/profits
- But many of the conditions, regulatory/policy exemptions, and additional funding will likely not continue without proactive steps by all participants in the university, industry, and government sectors

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