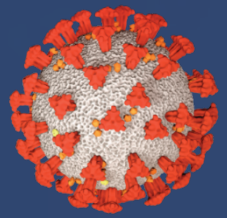
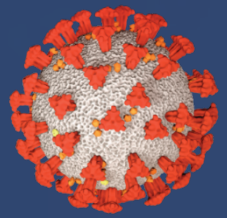


COVID-19
Prevention Network

The COVID-19 Prevention Network and Vaccine Efficacy Trials

October 21st, 2020

James G. Kublin, MD, MPH
Vaccine and Infectious Disease Division
Fred Hutch, and
Department of Global Health
University of Washington
Seattle, WA



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Outline

- The pandemic
- The virus
- Epidemiology and health disparities
- Vaccine platforms
- The COVID-19 Prevention Network (CoVPN)
- Randomized clinical trials and development pipelines
- Clinical trials operations
- Monitoring cases
- Community engagement and the CoVPN Volunteer Screening Registry
- What are we learning?

Coronavirus Timeline: The Beginning

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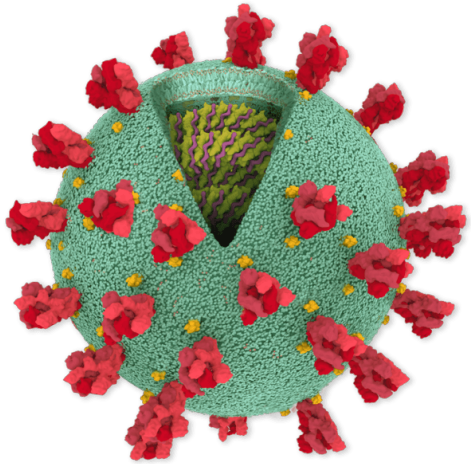
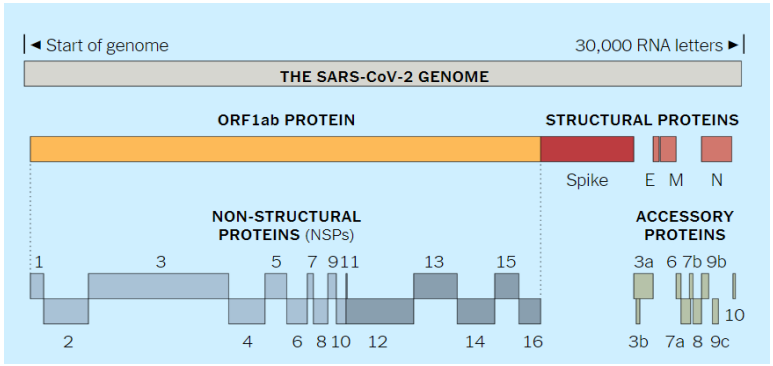
Image: Avetta

SARS-CoV-2: Bad News Wrapped in Protein



SOURCE CREDIT:
April 3, 2020 / New York Times
Jonathan Corum and Carl Zimmer



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The yellow protein is eventually split by two scissor proteins into 16 proteins

Human Coronaviruses

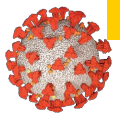
There are four non-SARS-like human coronaviruses.

- HCoV-229E; HCoV-OC43; HCoV-NL63 and HCoV-HKU-1

They generally cause mild respiratory illness, both naturally and with experimental challenge; occasionally cause lung disease in immunocompromised persons.

Seasonal activity (winter/early spring) - they tend to recur at two to four-year cycles; which suggest natural infection is not long-term protective.

This type of seasonal persistence is a worry for SARS-CoV-2; albeit the disease is quite different than the human respiratory coronavirus.



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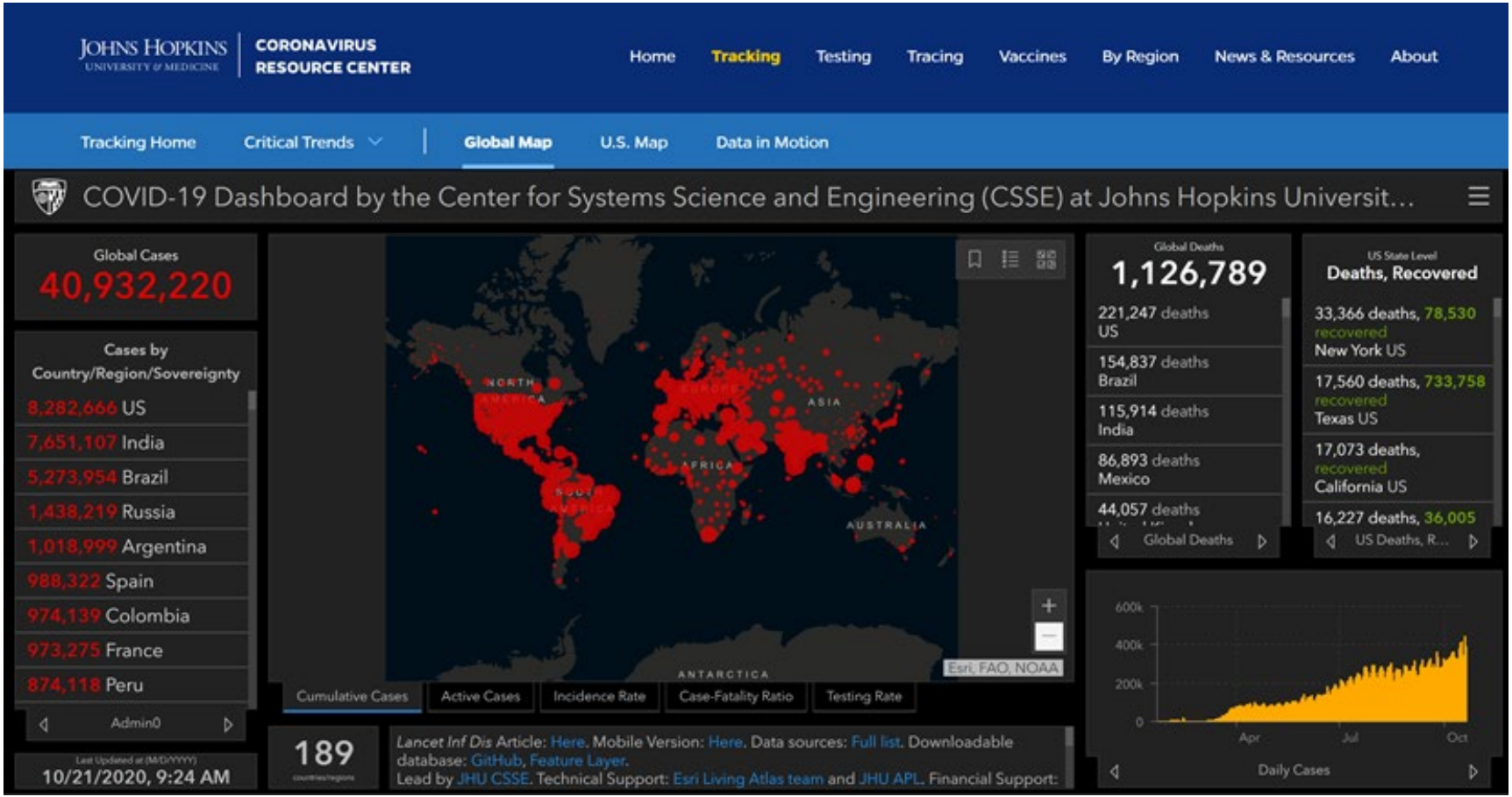

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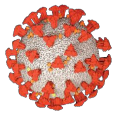
Social and structural factors impacting COVID Risk

- Minority populations are overrepresented in essential service industries with increased exposure
- Low wage jobs often do not provide:
  - Health insurance
  - Paid sick leave
  - Childcare
  - Options to work from home
  - Other benefits (e.g., retirement savings)
- Residential Segregation
  - Black/AA/Hispanic/Latinx are more likely to live in residentially segregated settings with high housing density
  - Poor access to healthy foods
  - More multigenerational households with limited space
- Increased levels of Chronic Stress
  - Resulting from structural racism, increased incidence of violence, everyday aggressions and trauma



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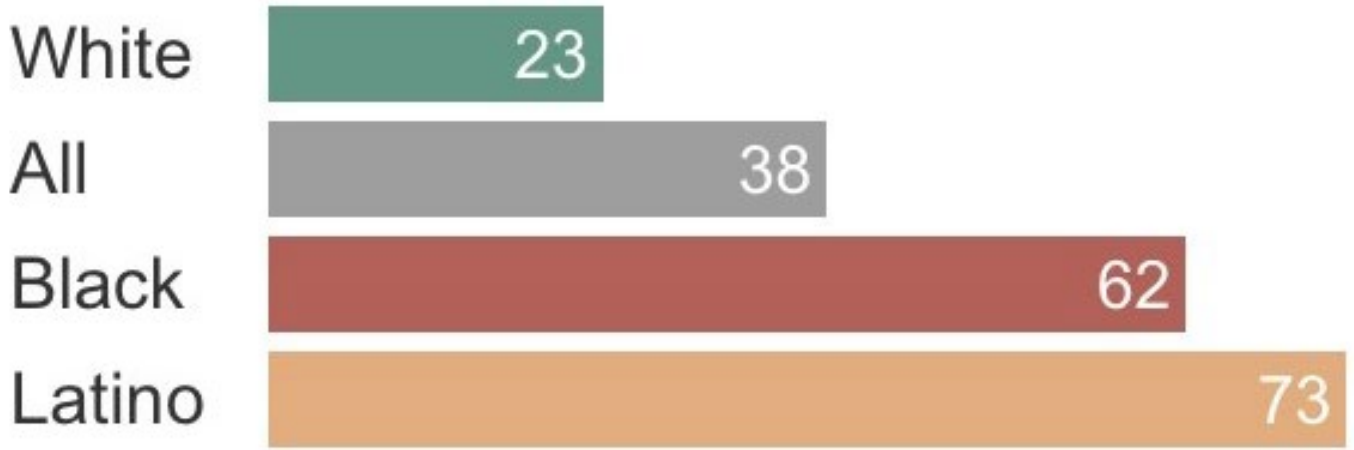
CDC, 2020; Poteat, Millet, Nelson and Beyrer, 2020; van Dorn A, Cooney R, Sabin ML, 2020; Yancy, 2020

Coronavirus cases per 10,000 people



Source: The Fullest Look Yet at the Racial Inequity of Coronavirus
By Richard A. Oppel Jr., Robert Gebeloff, K.K. Rebecca Lai, Will Wright and Mitch Smith
New York Times / July 5, 2020

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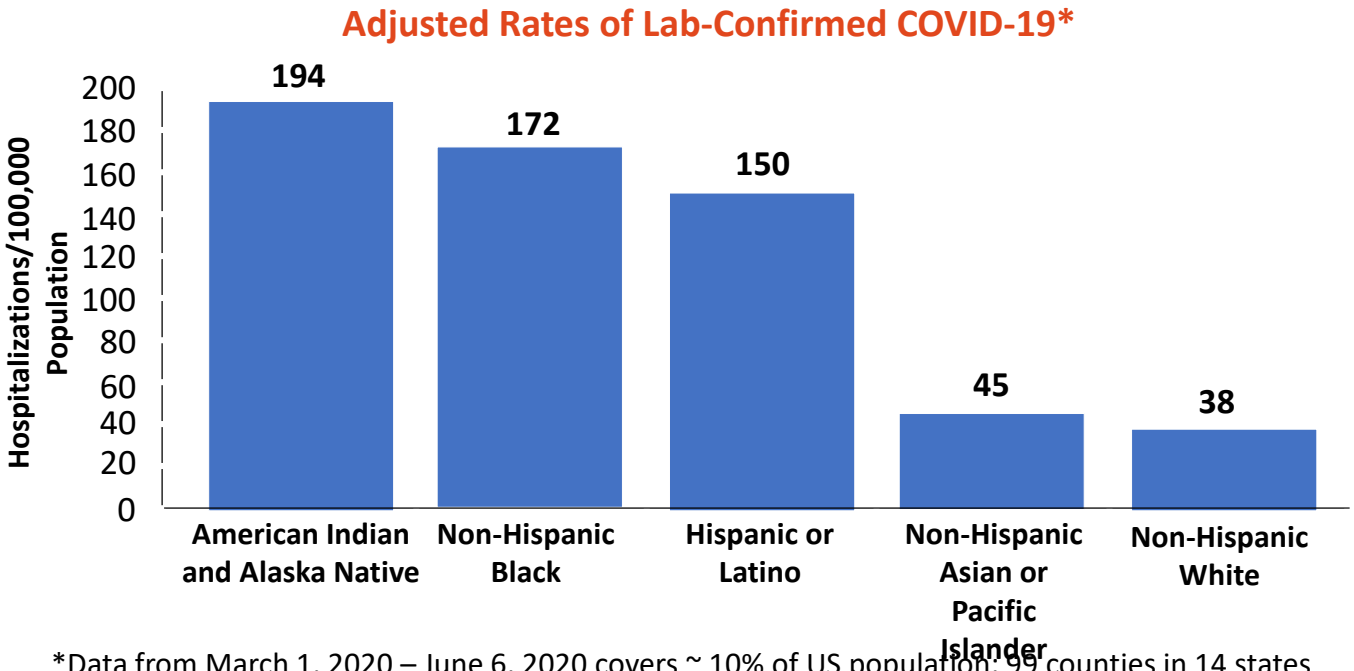
COVID-NET: COVID-19–Associated Hospitalization By Race and Ethnicity



*Data from March 1, 2020 – June 6, 2020 covers ~ 10% of US population: 99 counties in 14 states (CA, CO, CT, GA, IA, MD, MI, MN, NM, NY, OH, OR, TN, UT). Adjusted to account for differences in age distribution within race and ethnicity groups.

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/data-visualization.htm

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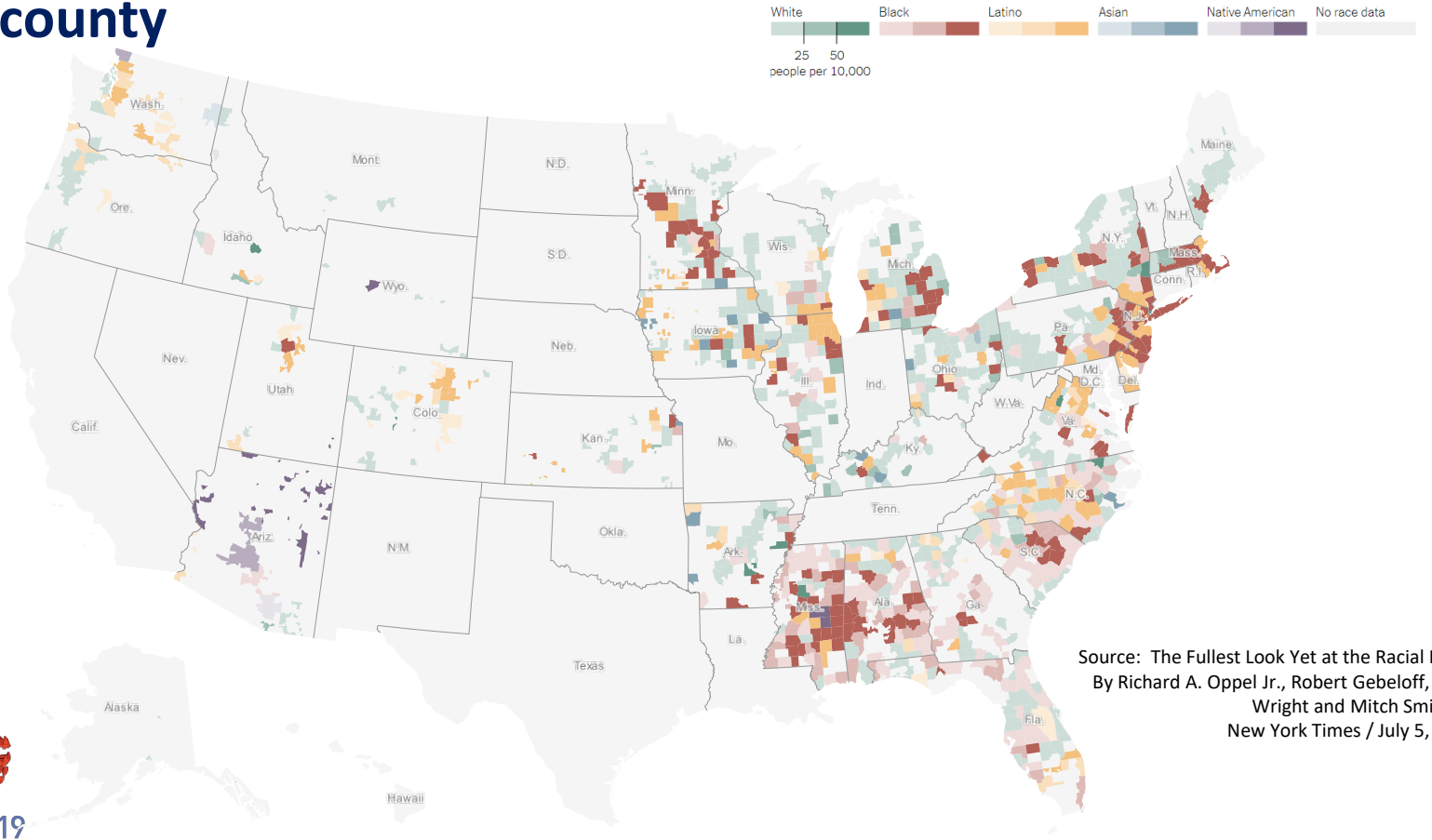
Slide credit: clinicaloptions.com

Race or ethnicity with the highest coronavirus rate in each county



Source: The Fullest Look Yet at the Racial Inequity of Coronavirus
By Richard A. Oppel Jr., Robert Gebeloff, K.K. Rebecca Lai, Will Wright and Mitch Smith
New York Times / July 5, 2020

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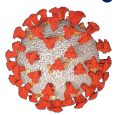
COVID-19 Fatalities and African Americans

- **Louisiana** – Black people are 33% of population, 70% of fatalities
  - Orleans Parish – Black people 60% of population, 70% of fatalities
- **Chicago, IL** – Black people are 29% of city's population, 70% of fatalities
- **Washington, DC** – Black people are 46% of population, 62.5% of fatalities
- **Michigan** – Black people are 14% of state's population, 40% of fatalities
- **Wisconsin**, Black people are 7% of state's population, 33% of fatalities
  - Milwaukee – 39% of population, 71% deaths
- **Mississippi** – Black people are 38% of state's population, 61% of fatalities
- **New York (state)** – Black people twice as likely to die as white people



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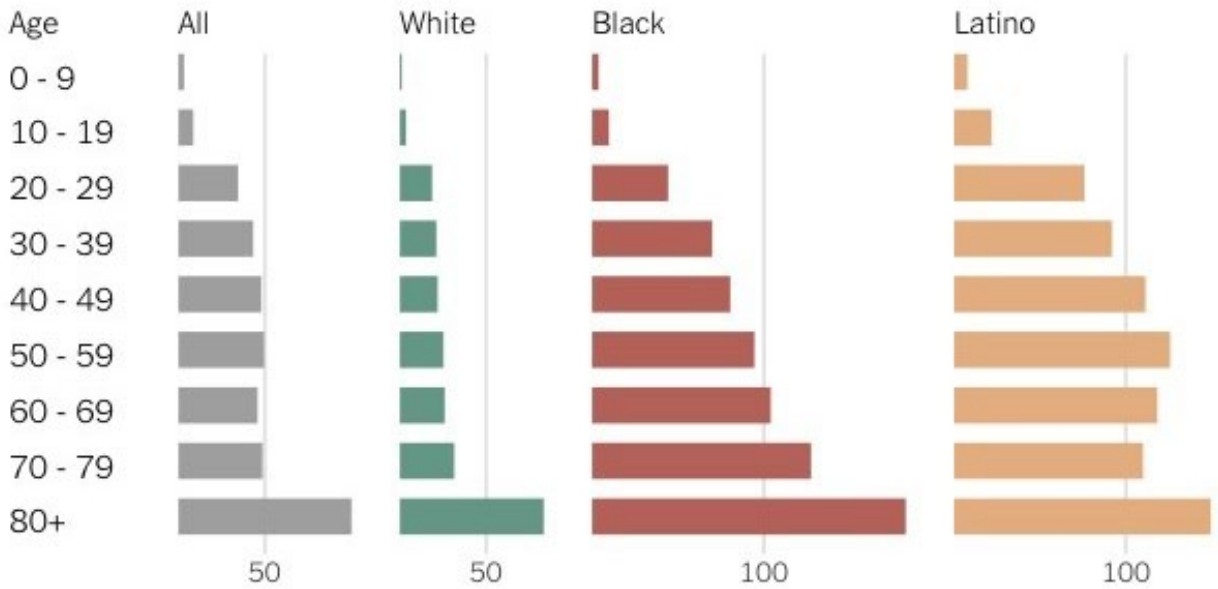
Perry AM, Harshbarger D, Romer C, 2020; van Dorn A, Cooney R, Sabin ML, 2020; Villarosa, 2020

Coronavirus cases per 10,000 people, by age and race



Source: Centers for Disease Control and Prevention | Note: Data is through May 28.

Oppel et al, 2020

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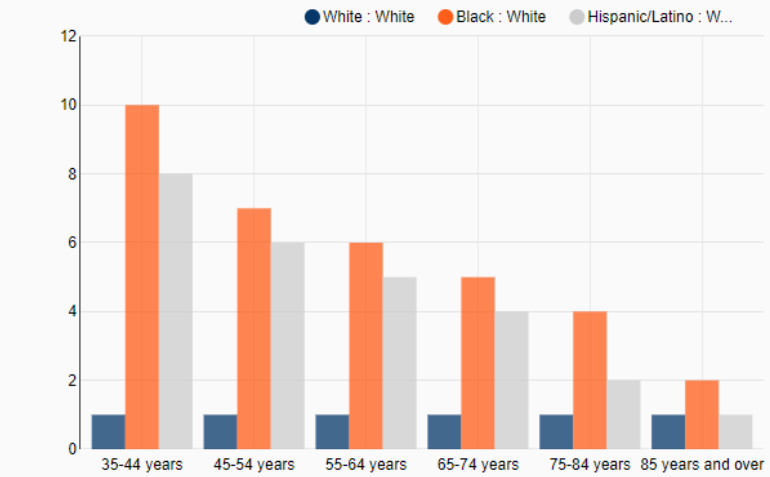
COVID-19 disease burden and outcome disparity are concentrated in sub-populations

COVID-19 Disease Burdens

- **Patients aged 60 and above** account for ~60% of hospital and ICU admissions and **~90% of deaths** while representing 20% of population
- **Patients with preexisting conditions** are 6-7 times more likely to be hospitalized and **more than 10 times more likely to die** than patients without preexisting conditions
- **Communities of color** are over-represented in cases and deaths by **~1.5-2x for Latinx and African American populations**, with huge disparities in outcomes for middle age

Figure 2. Huge race gaps in COVID-19 death rates, especially in middle age



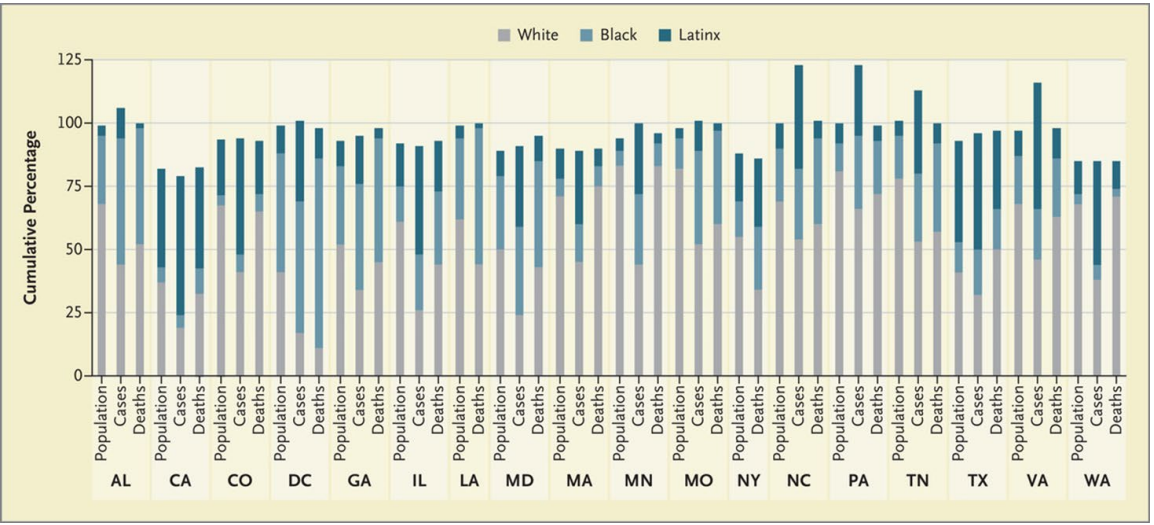
Source: CDC data from 2/1/20-6/6/20 and 2018 Census Population Estimates for USA

BROOKINGS

COVID-19 Prevention Network

Sources: CDC MMWR, 69 (24), p. 759; CDC Weekly Updates by Select Demographic and Geographic Characteristics, June 24, 2020; Brookings, Race gaps in COVID-19 deaths are even bigger than they appear, June 16, 2020

The NEW ENGLAND JOURNAL of MEDICINE



Perspective

AUGUST 27, 2020

Racial Disproportionality in Covid Clinical Trials

Daniel B. Chastain, Pharm.D., Sharmon P. Osae, Pharm.D., Andrés F. Henao-Martínez, M.D., Carlos Franco-Paredes, M.D., M.P.H., Joeanna S. Chastain, Pharm.D., and Henry N. Young, Ph.D.

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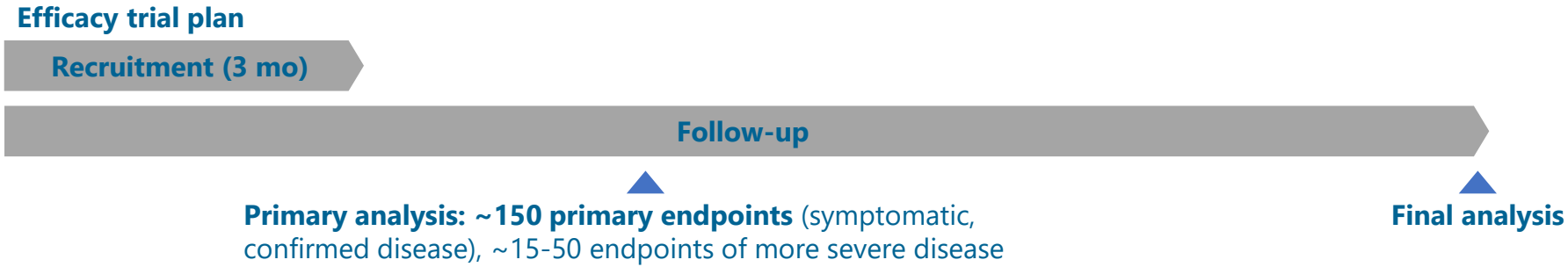
What are the implications of COVID-19 disparities by sub-population for clinical trial representation and recruitment?



Key questions	
	▪ **What representation of populations is important for the primary analysis? …for the final analysis?**
	▪ **What, if any, trade-offs in recruitment speed are justified to increase representation of sub-populations?**
	▪ **How can this group help accelerate recruitment of important sub-populations?**

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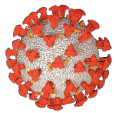
Summary and the Way Forward

- Communities most impacted by COVID-19 have long-standing experiences of social and structural inequities that negatively impact health and wellbeing
- Community Engagement efforts are critical to ensure:
  - Well-informed communities
  - Community support for research
  - Meaningful relationships
  - Reciprocal partnerships
  - Increased trust
- To promote equitable representation in COVID-19 trials, we must
  - Recognize the importance of enrolling Black, Native and Latinx participants
    - Studies must report demographics of trial enrollment while they are ongoing
  - Provide appropriate funding to trial sites to support diversity initiatives
    - Translations, reimbursement for transportation, diverse research workforce, etc.
  - Address research mistrust by engaging communities early and often throughout the process
  - Paying people back for trusting in medical research = equitable vaccine access once approved



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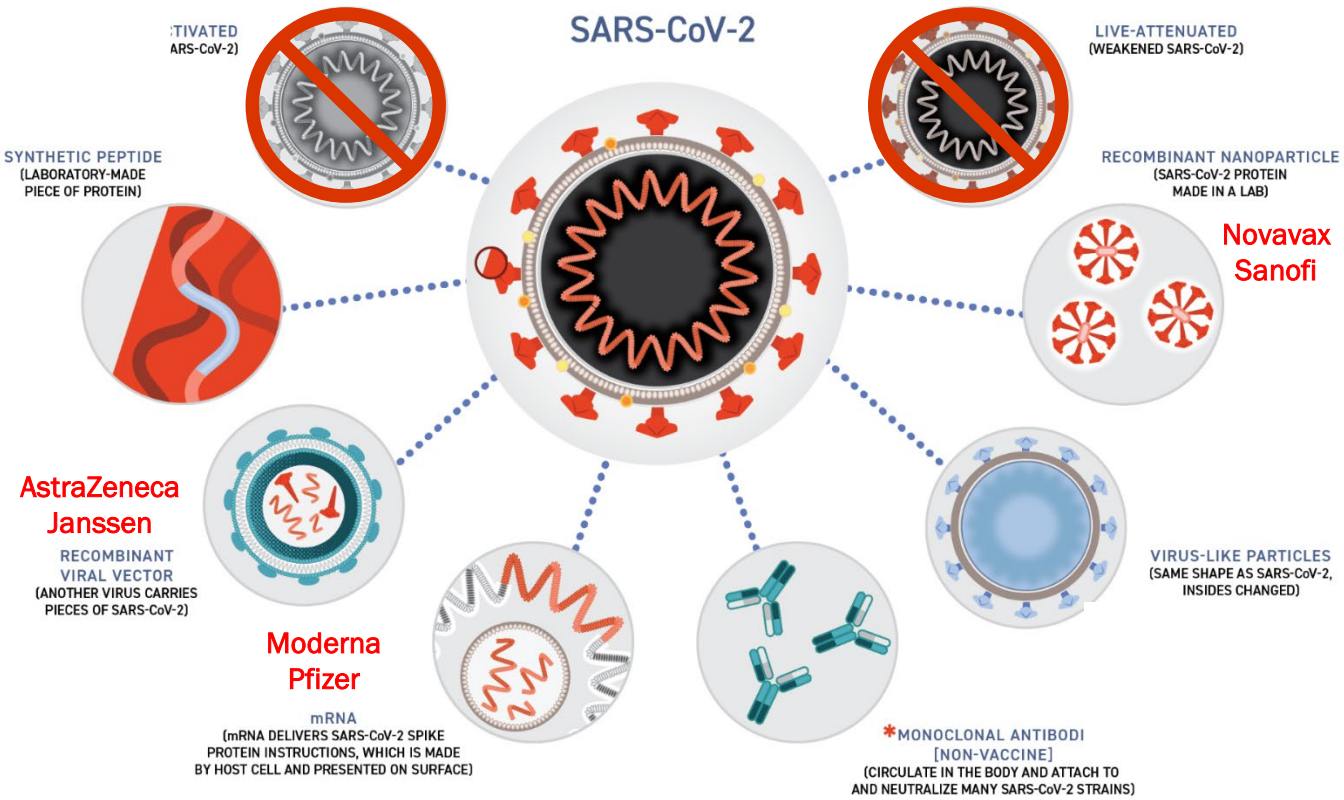
Stephenson & Bisola. 2020

Vaccine Designs



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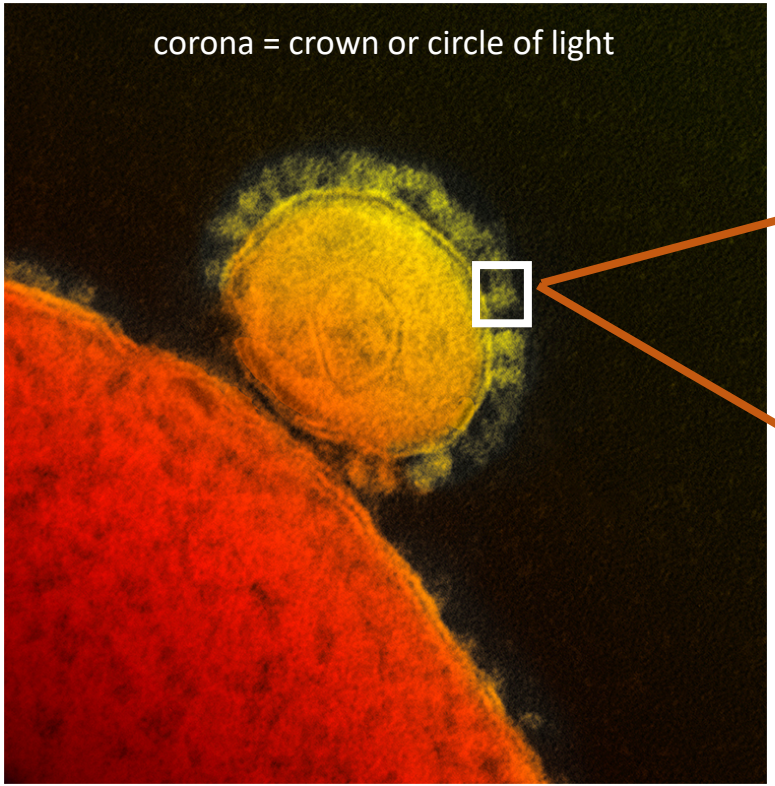
SARS-CoV-2 and its spike protein (the vaccine target)



Slide credit: Vaccine Research Center, NIAID

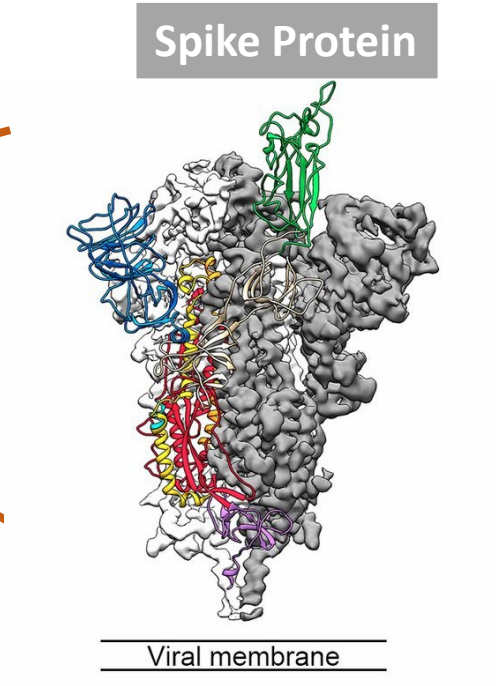


Image credit: Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, Graham BS, McLellan JS. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020 Feb 19:eabb2507. doi: 10.1126/science.abb2507.

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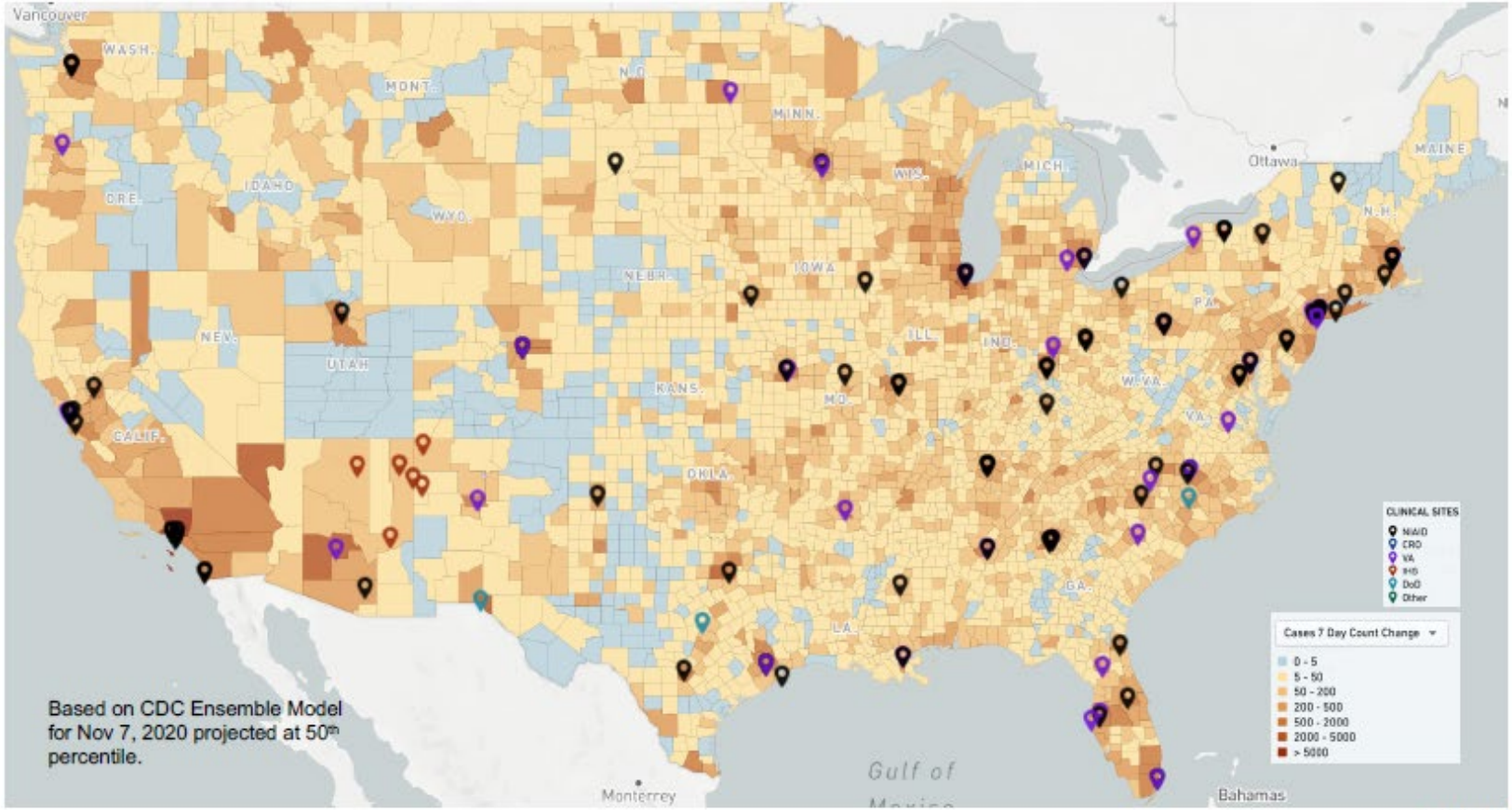
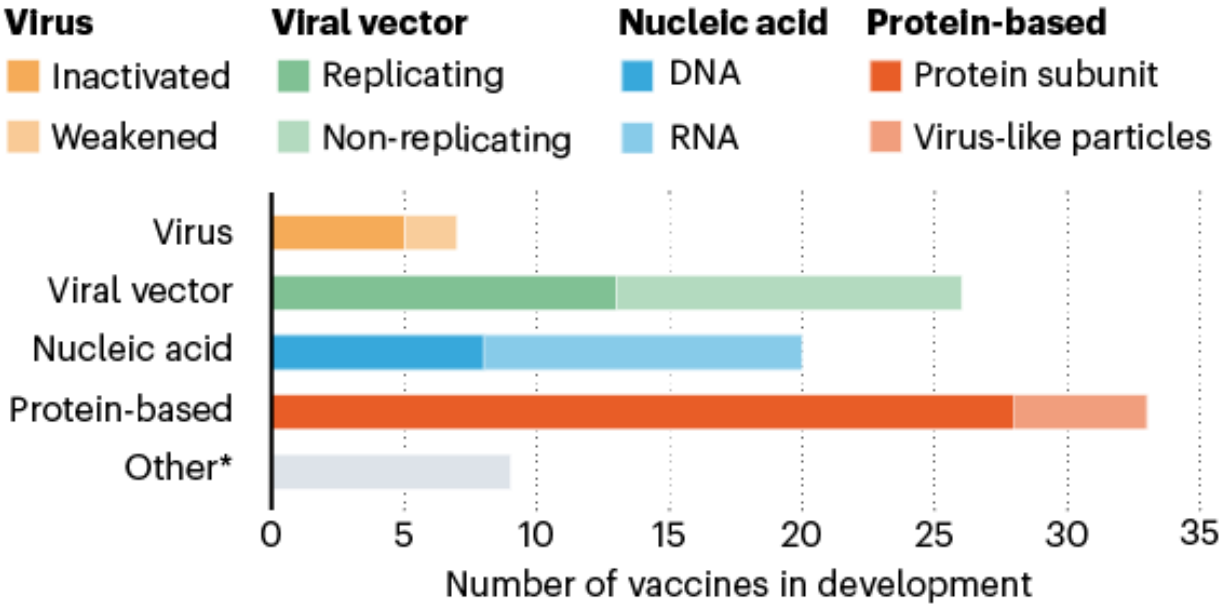
Projected US COVID-19 Cases by County Based on 7 Day Count Change and Trial Site Distribution for CoVPN



Source: HHS Protect
Data as of Oct 15, 2020

AN ARRAY OF VACCINES



* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

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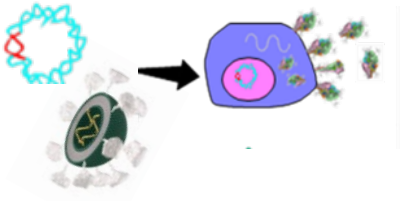
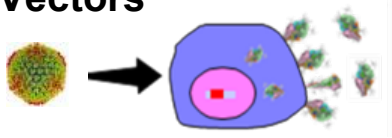
Nature analysis based on: WHO COVID-19 Vaccine Landscape/Milken Institute COVID-19 Treatment and Vaccine Tracker/T. Thanh Le et al. Nature Rev. Drug. Disc. http://doi.org/ggrnbr (2020)/F. Amanat & F. Krammer Immunity 52, 583–589 (2020)/W. Shang et al. npj Vaccines 5, 18 (2020).

Tailoring Immune Response by Vaccine Platform

	Antibody	CD4	CD8	Pros	Additional Considerations
Nucleic acid (mRNA or DNA) 	++	++	+	Rapid translation RNA can be modified No prior immunity	RNA-Requires formulation LNP DNA requires electroporation
Adenoviral Vectors 	++	++	+++	In clinical trials (Ebola, Malaria, HIV, Cancer) Most potent inducer CD8 T cells	Influenced by prior immunity from natural adenovirus exposure
Protein + adjuvant 	+++	++	-	Gold standard for high antibody titers	Adjuvant is critical Limited/no CD8

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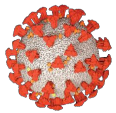
Optimism about developing a SARS Cov-2 Vaccine

- Immunity develops from infection, although the durability of protection is unknown
- Humans cure the infection >95% of the time
- No latent infection
- Produces a proinflammatory dysregulated immune response
- Known target for infection of epithelial and endothelial cells
- There is little variation in the spike protein – 2 base pairs per month
- Pre-clinical non-human-primate models display protection in SARS-CoV-2 challenge models with vaccines



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What is the COVID-19 PREVENTION NETWORK?

The network was formed 2 decades ago by Dr. Anthony Fauci of the **National Institute of Allergy and Infectious Diseases**, part of the **National Institutes of Health**, to address HIV, flu and other global vaccine needs. The network quickly pivoted to COVID-19 and studies to ensure a safe and effective COVID-19 vaccine. Comprised of the foremost infectious disease and vaccine experts in the country, the research network and its global partners are working hand in hand to address this urgent need in our fight against the pandemic.

Dr. Anthony Fauci, *Director of the National Institute of Allergy and Infectious Diseases*

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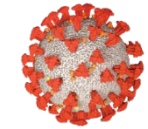
CoVPN Over-arching Engagement Effort



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NIH National Institute of Allergy and Infectious Diseases

U.S. Department of Veterans Affairs

WRAIR Walter Reed Army Institute of Research
Soldier Health • World Health

FRED HUTCH

hanc
HIV/AIDS Network Coordination

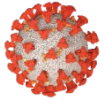
fhi360
THE SCIENCE OF IMPROVING LIVES

METRO

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

JOHNS HOPKINS UNIVERSITY

UNIVERSITY of WASHINGTON



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Prevention Network

Published online May 11, 2020

Science

A Strategic Approach to COVID-19 Vaccine R&D

L Corey, JR Mascola, AS Fauci & FS Collins

The full development pathway for an effective vaccine for SARS-CoV2 will require that industry, government, and academia collaborate in unprecedented ways, each adding their individual strengths. . . .We further discuss a collaborative platform for conducting harmonized, randomized controlled vaccine efficacy trials. This mechanism aims to generate essential safety and efficacy data for several candidate vaccines in parallel, so as to accelerate the licensure and distribution of multiple vaccine platforms and vaccines to protect against COVID-19

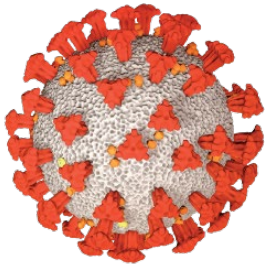
CoVPN:
NIH funded clinical trial network to conduct Ph3 trials

HIV VACCINE TRIALS NETWORK

IDCRC
Infectious Diseases Clinical Research Consortium

HPTN
HIV Prevention Trials Network

ACTG
AIDS CLINICAL TRIALS GROUP



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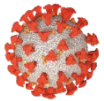
Vaccine Efficacy Trials
- Larry Corey and Kathy Neuzil

mAb Prevention Trials
- Mike Cohen and David Stephens



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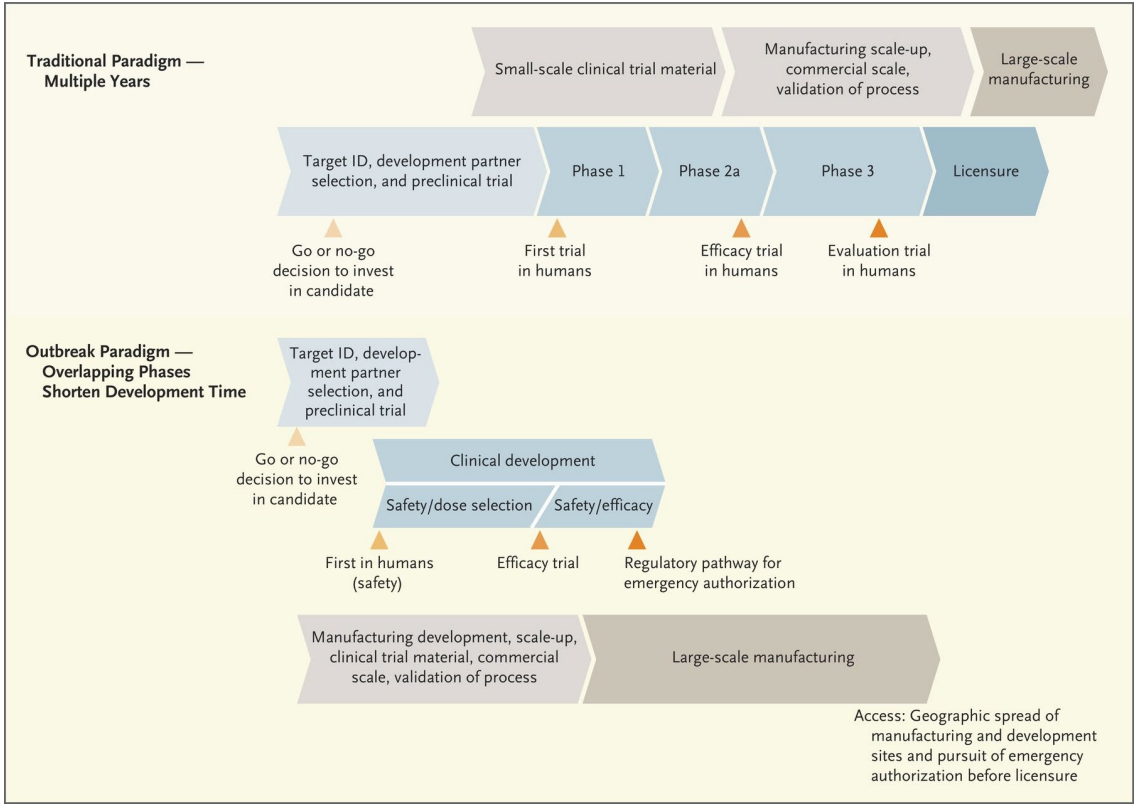
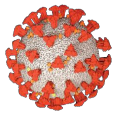
Difference between Traditional Vaccine Development and Development Using a Pandemic Paradigm



Lurie N, et al. Developing Covid-19 Vaccines at Pandemic Speed. May 21, 2020. N Engl J Med 2020; 382:1969-1973.

How do we organize ourselves to do this?

- Global effort, global cooperation and transparency are needed to maximize the speed, veracity and decision-making required to deliver scientific advances to the global population in a timely fashion.



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CoVPN Operations Center

- Built around structure of the HIV Vaccine Trials Network founded in 1999 at Fred Hutchinson Cancer Research Center
- Extensive clinical trials network with in early 2020 52 sites in US and Latin America, and another 56 sites in sub-Saharan Africa
- Academically based CRO
  - Operations Center (Corey and Kublin)
  - Statistical Data Management Center (Peter Gilbert)
  - Centralized world class immunology and virology labs (Julie McElrath)

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Conceptual Framework for COVID-19 Vaccine Development

We need to develop multiple vaccine platforms.

No single vaccine platform can be manufactured at enough scale to immunize the 4.4 billion adult population on the planet and 3 billion children

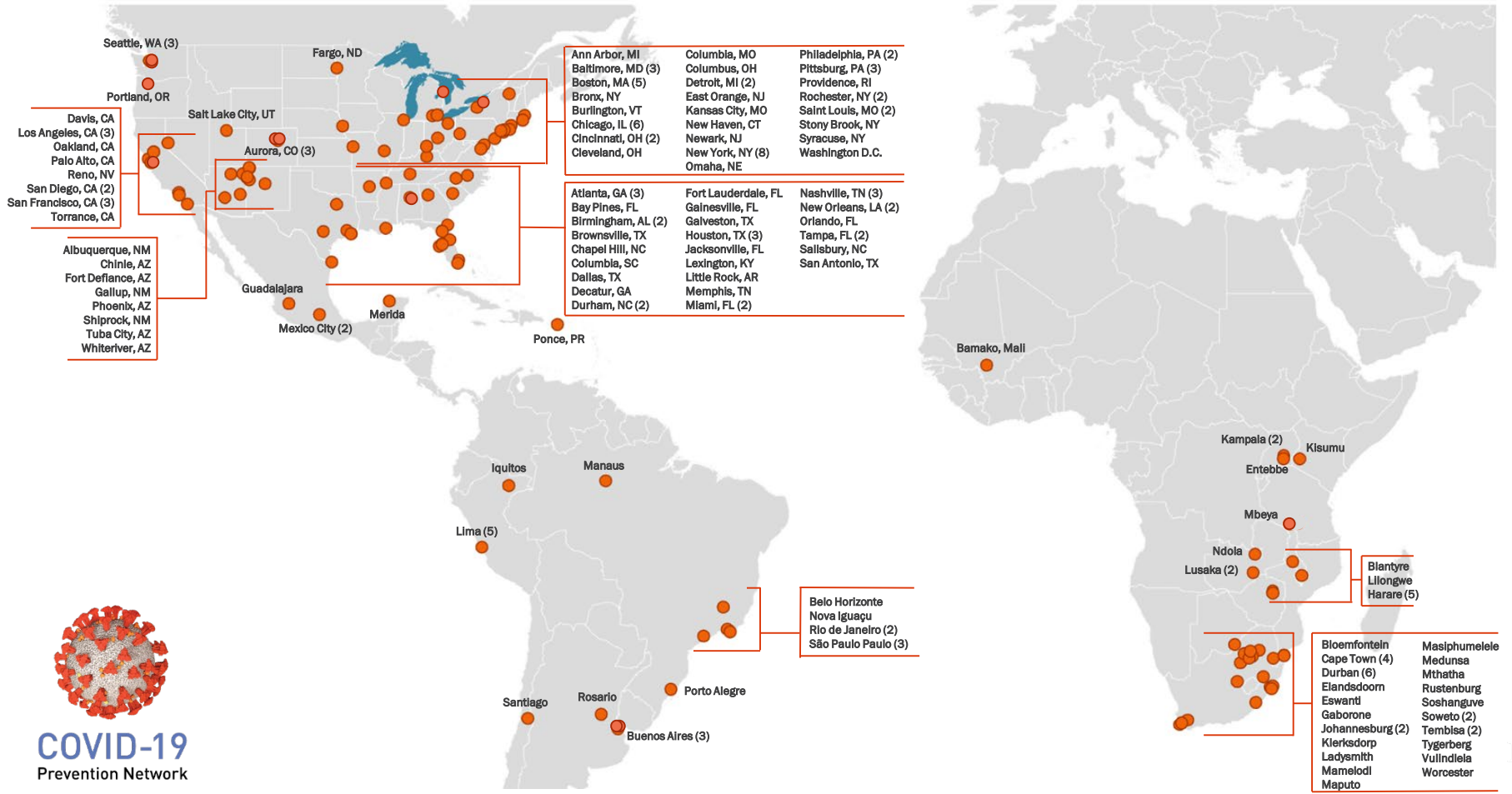
- 220 million adults in US alone

Use known platforms to cover the field scientifically. Manufacturing scalability is a key factor.

Coordinated USG effort to involve global vaccine manufacturing companies.

There must be an unprecedented coordinated approach to test, manufacture the vaccine at scale, and deliver the vaccine into peoples' arms throughout the world.

NIAID COVID-19 Prevention Network, N=189 (as of 8/1/2020)



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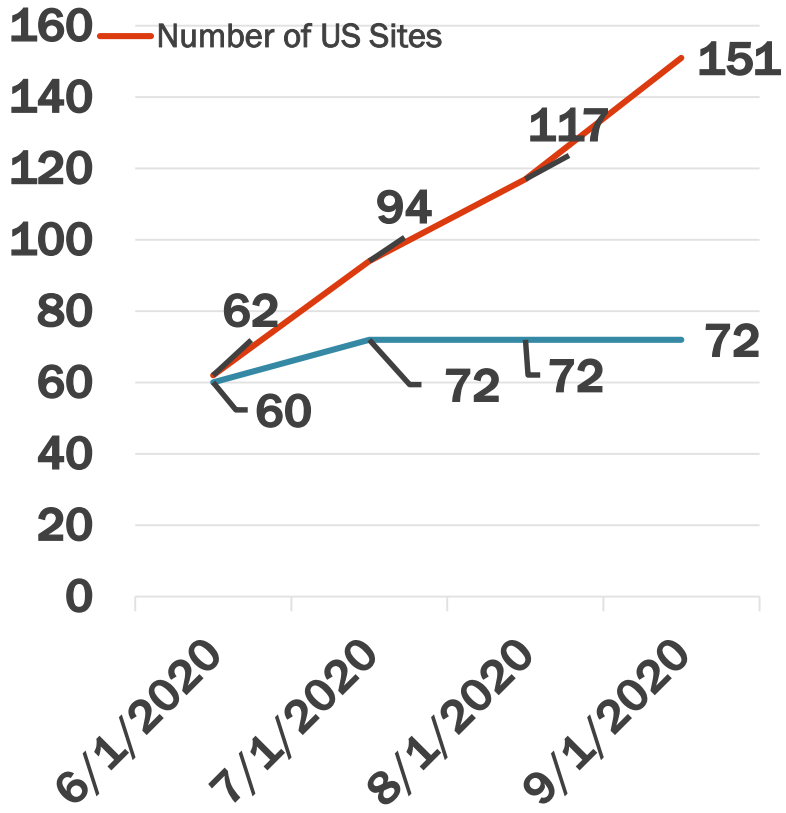
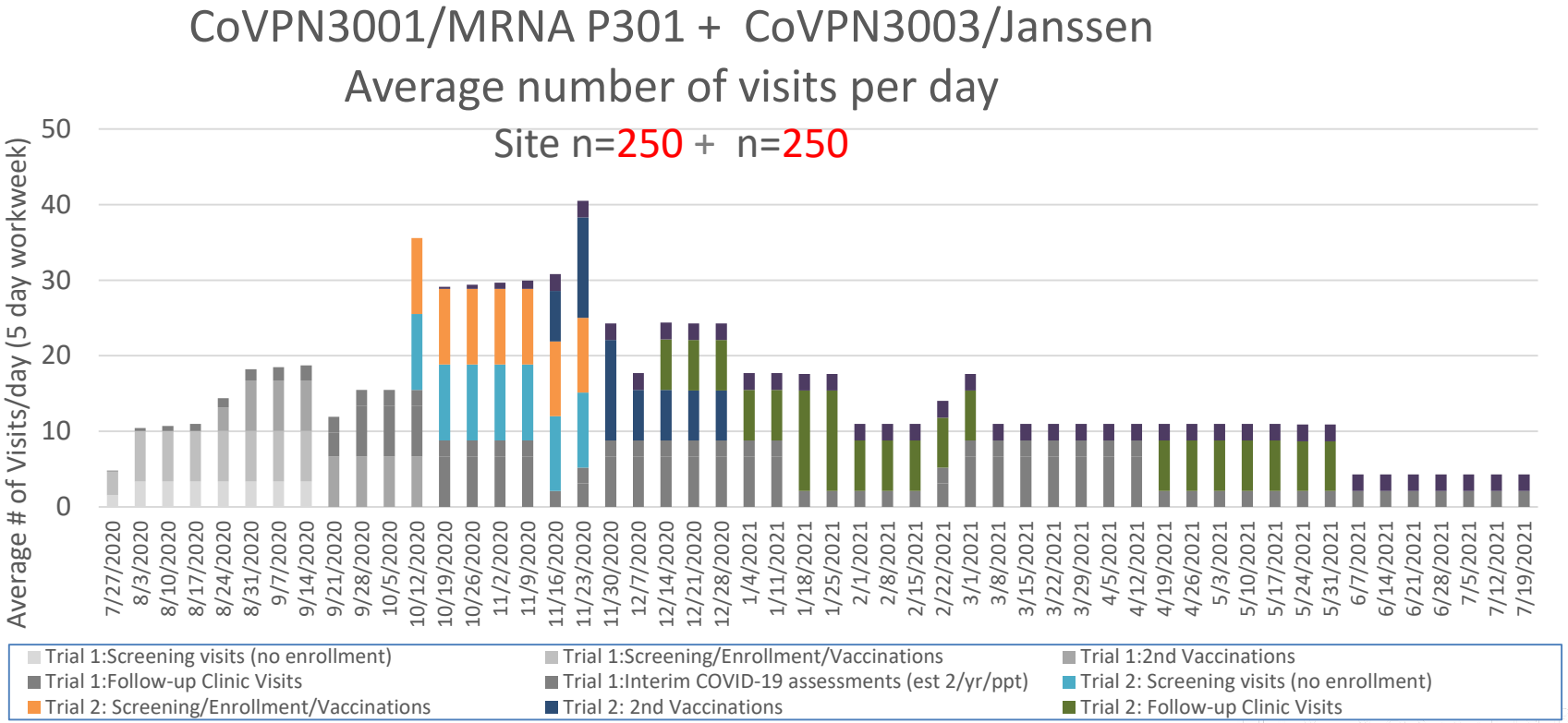
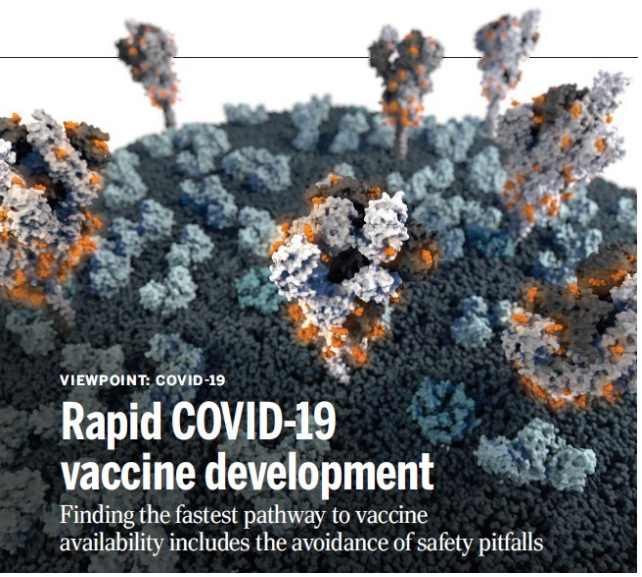
Monthly Expansion of CoVPN



Assisting investigators to predict capacity in sequential efficacy trials





VIEWPOINT: COVID-19

Rapid COVID-19 vaccine development

Finding the fastest pathway to vaccine availability includes the avoidance of safety pitfalls

Potential risks associated with vaccine development for COVID-19

Antibodies that bind virus without neutralizing infectivity can cause disease through increased viral replication or formation of immune complexes that deposit in tissue and activate complement pathways associated with inflammation. T helper 2 cell (T_H2)–biased responses have also been associated with ineffective vaccines that lead to enhanced disease after subsequent infection. Antibody-dependent enhancement (ADE) of viral replication has occurred in viruses with innate macrophage tropism. Virus-antibody immune complexes and T_H2-biased responses can both occur in vaccine-associated enhanced respiratory disease (VAERD).

	Antibody-mediated		T cell–mediated
	ADE	**VAERD**	**VAERD**
Mechanism	Fc-mediated increase in viral entry	Immune complex formation and complement deposition	T_H2-biased immune response
Effectors	Macrophage activation and inflammatory cytokines	Complement activation and inflammatory cytokines	Allergic inflammation and T_H2 cytokines
Mitigation	Conformationally correct antigens and high-quality neutralizing antibody		T_H1-biasing immunization and $CD8^+$ T cells

COVID-19
Prevention Network

Stages of clinical trials

PHASE 1

12 to 18 months

Trials to test safety and whether the body can tolerate the product. Often involves comparing against a placebo with no active ingredients. Usually less than 100 people.

PHASE 2

Up to 2 years

Identifying the maximum tolerated dose, the best dosing schedule, and if the immune system is having the desired responses. Usually a few hundred to a few thousand people.

PHASE 3

2+ years

“Does this product prevent infections, or help to reduce the severity of disease?” Involves thousands of people, including some at risk of infection.

With SARS-CoV-2, we are working as quickly as possible. No phases are skipped. Instead, we overlap the phases, starting the next phase as quickly as we have the necessary safety data collected and analyzed from the earlier phase. The new phase can start while the long-term follow-up of people in the earlier phase continues. Other steps can be done in parallel, instead of one after the other.

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ORIGINAL ARTICLE

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

L.A. Jackson, E.J. Anderson, N.G. Rouphael, P.C. Roberts, M. Makhene, R.N. Coler, M.P. McCullough, J.D. Chappell, M.R. Denison, L.J. Stevens, A.J. Pruijssers, A. McDermott, B. Flach, N.A. Doria-Rose, K.S. Corbett, K.M. Morabito, S. O'Dell, S.D. Schmidt, P.A. Swanson II, M. Padilla, J.R. Mascola, K.M. Neuzil, H. Bennett, W. Sun, E. Peters, M. Makowski, J. Albert, K. Cross, W. Buchanan, R. Pikaart-Tautges, J.E. Ledgerwood, B.S. Graham, and J.H. Beigel, for the mRNA-1273 Study Group*

ABSTRACT

BACKGROUND

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in late 2019 and spread globally, prompting an international effort to accelerate development of a vaccine. The candidate vaccine mRNA-1273 encodes the stabilized prefusion SARS-CoV-2 spike protein.

METHODS

We conducted a phase 1, dose-escalation, open-label trial including 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25 μg, 100 μg, or 250 μg. There were 15 participants in each dose group.

RESULTS

After the first vaccination, antibody responses were higher with higher dose (day 29 enzyme-linked immunosorbent assay anti–S-2P antibody geometric mean titer [GMT], 40,227 in the 25-μg group, 109,209 in the 100-μg group, and 213,526 in the 250-μg group). After the second vaccination, the titers increased (day 57 GMT, 299,751, 782,719, and 1,192,154, respectively). After the second vaccination, serum-neutralizing activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens. Solicited adverse events that occurred in more than half the participants included fatigue, chills, headache, myalgia, and pain at the injection site. Systemic adverse events were more common after the second vaccination, particularly with the highest dose, and three participants (21%) in the 250-μg dose group reported one or more severe adverse events.

CONCLUSIONS

The mRNA-1273 vaccine induced anti–SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. These findings support further development of this vaccine. (Funded by the National Institute of Allergy and Infectious Diseases and others; mRNA-1273 ClinicalTrials.gov number, NCT04283461).

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Jackson at Kaiser Permanente Washington Health Research Institute, 1730 Minor Ave., Suite 1600, Seattle, WA 98101, or at lisa.a.jackson@kp.org.

*The mRNA-1273 Study Group members are listed in the Supplementary Appendix, available at NEJM.org.

Drs. Graham and Beigel contributed equally to this article.

This article was published on July 14, 2020, and updated on August 25, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2022483

Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial

Pedro M Folegatti, Katie J Ewer*, Parvinder K Aley, Brian Angus, Stephan Becker, Sandra Belij-Rammerstorfer, Duncan Bellamy, Sagida Bibi, Mustapha Bittaye, Elizabeth A Clutterbuck, Christina Dold, Saul N Faust, Adam Finn, Amy L Flaxman, Bassam Hallis, Paul Heath, Daniel Jenkin, Rajeka Lazarus, Rebecca Makinson, Angela M Minassian, Katrina M Pollock, Maheshi Ramasamy, Hannah Robinson, Matthew Snape, Richard Tarrant, Merryn Voysey, Catherine Green*, Alexander D Douglas*, Adrian V S Hill*, Teresa Lambe*, Sarah C Gilbert*, Andrew J Pollard*, on behalf of the Oxford COVID Vaccine Trial Group†*

Summary

Background The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, reactogenicity, and immunogenicity of a viral vectored coronavirus vaccine that expresses the spike protein of SARS-CoV-2.

Methods We did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. Healthy adults aged 18–55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 at a dose of 5×10^{10} viral particles or MenACWY as a single intramuscular injection. A protocol amendment in two of the five sites allowed prophylactic paracetamol to be administered before vaccination. Ten participants assigned to a non-randomised, unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. Humoral responses at baseline and following vaccination were assessed using a standardised total IgG ELISA against trimeric SARS-CoV-2 spike protein, a multiplexed immunoassay, three live SARS-CoV-2 neutralisation assays (a 50% plaque reduction neutralisation assay [$PRNT_{50}$]; a microneutralisation assay [MNA_{80}, MNA_{90}, and MNA_{80}]; and Marburg VN), and a pseudovirus neutralisation assay. Cellular responses were assessed using an ex-vivo interferon-γ enzyme-linked immunospot assay. The co-primary outcomes are to assess efficacy, as measured by cases of symptomatic virologically confirmed COVID-19, and safety, as measured by the occurrence of serious adverse events. Analyses were done by group allocation in participants who received the vaccine. Safety was assessed over 28 days after vaccination. Here, we report the preliminary findings on safety, reactogenicity, and cellular and humoral immune responses. The study is ongoing, and was registered at ISRCTN, 15281137, and ClinicalTrials.gov, NCT04324606.

Findings Between April 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group. Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group and many were reduced by use of prophylactic paracetamol, including pain, feeling feverish, chills, muscle ache, headache, and malaise (all $p<0·05$). There were no serious adverse events related to ChAdOx1 nCoV-19. In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14 (median 856 spot-forming cells per million peripheral blood mononuclear cells, IQR 493–1802; n=43). Anti-spike IgG responses rose by day 28 (median 157 ELISA units [EU], 96–317; n=127), and were boosted following a second dose (639 EU, 360–792; n=10). Neutralising antibody responses against SARS-CoV-2 were detected in 32 (91%) of 35 participants after a single dose when measured in MNA_{80} and in 35 (100%) participants when measured in $PRNT_{50}$. After a booster dose, all participants had neutralising activity (nine of nine in MNA_{80} at day 42 and ten of ten in Marburg VN on day 56). Neutralising antibody responses correlated strongly with antibody levels measured by ELISA (R^2=0·67 by Marburg VN; $p<0·001$).

Interpretation ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.

Funding UK Research and Innovation, Coalition for Epidemic Preparedness Innovations, National Institute for Health Research (NIHR), NIHR Oxford Biomedical Research Centre, Thames Valley and South Midland's NIHR Clinical Research Network, and the German Center for Infection Research (DZIF), Partner site Gießen-Marburg-Langen.

Lancet 2020; 396: 467–78
Published Online July 20, 2020
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This online publication has been corrected. The corrected version first appeared at thelancet.com on August 13, 2020
See Comment page 448

*Contributed equally
†Members are listed in the appendix
The Jenner Institute (P M Folegatti MSc, K J Ewer PhD, S Belij-Rammerstorfer PhD, D Bellamy MSc, M Bittaye PhD, A L Flaxman DPhil, D Jenkin MRCP, R Makinson Mbiol, A M Minassian DPhil, A D Douglas DPhil, Prof A V S Hill FMedSci, T Lambe PhD, Prof S C Gilbert PhD) **and Clinical Biomanufacturing Facility** (R Tarrant PhD, C Green PhD), **Nuffield Department of Medicine** (B Angus MD); **and Oxford Vaccine Group, Department of Paediatrics** (P K Aley PhD, S Bibi PhD, E A Clutterbuck PhD, C Dold PhD, M Ramasamy DPhil, H Robinson DipHE, M Snape MD, M Voysey DPhil, Prof A J Pollard FMedSci)**; University of Oxford, Oxford, UK; NIHR Oxford Biomedical Research Centre, Oxford, UK** (P M Folegatti, K J Ewer, P K Aley, B Angus, S Belij-Rammerstorfer, D Bellamy, S Bibi, M Bittaye, E A Clutterbuck, C Dold, A L Flaxman, D Jenkin, R Makinson, A M Minassian, M Ramasamy, H Robinson, M Snape, M Voysey, A D Douglas, Prof A V S Hill, T Lambe, Prof S C Gilbert, Prof A J Pollard)**; Institute of Virology, Philipps University of Marburg, Marburg, Germany**

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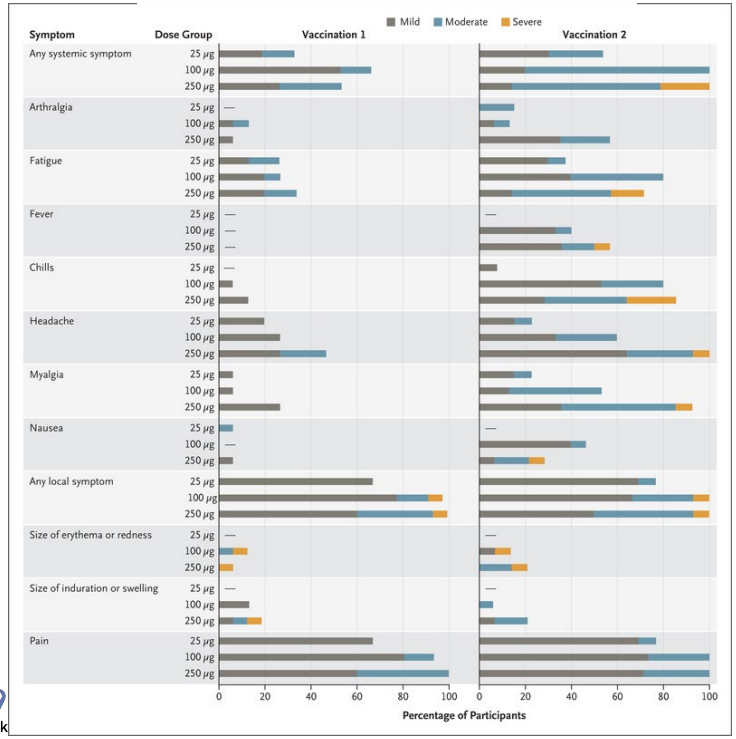

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Lancet 2020; 396: 467–78
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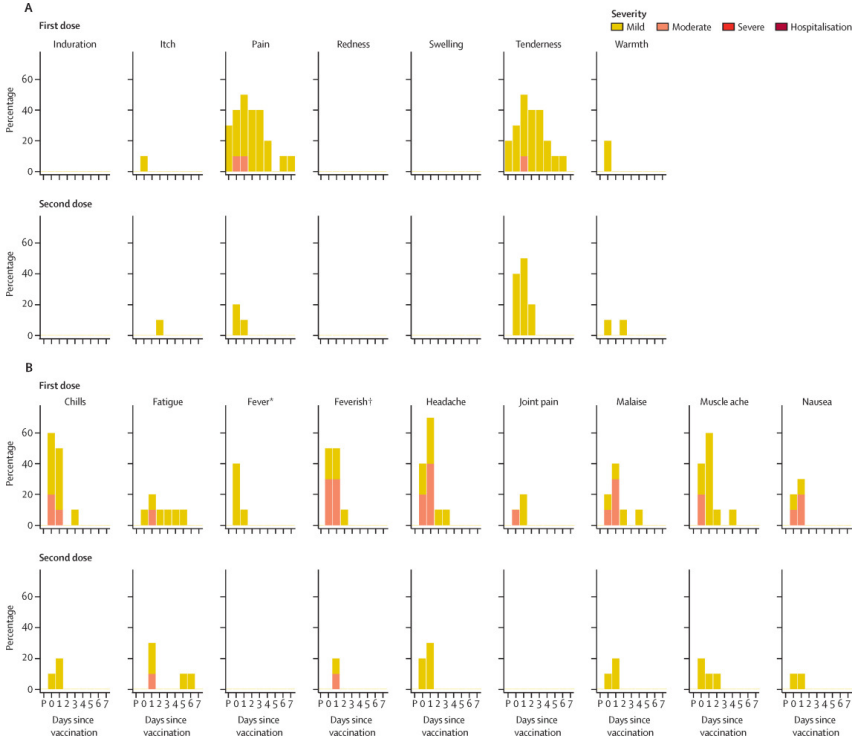

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ORIGINAL ARTICLE

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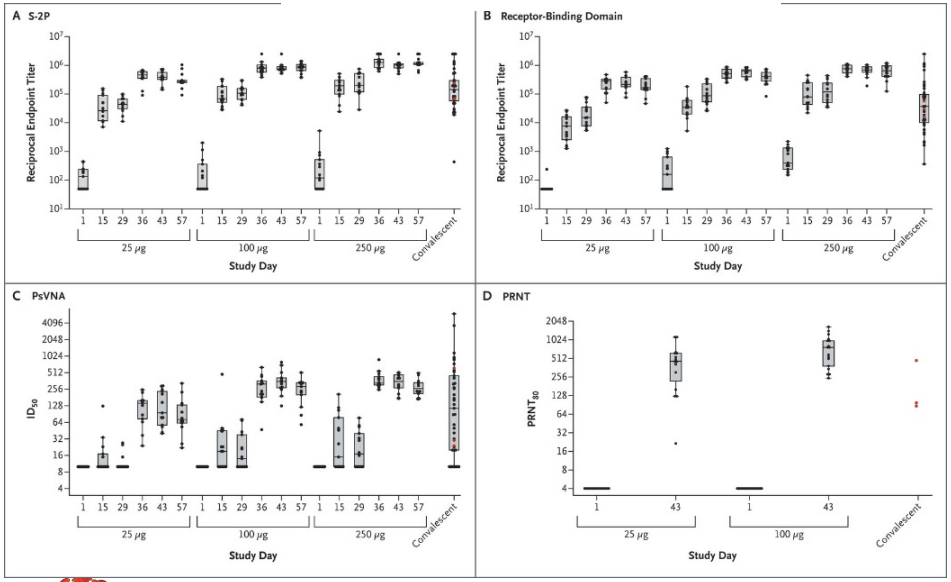

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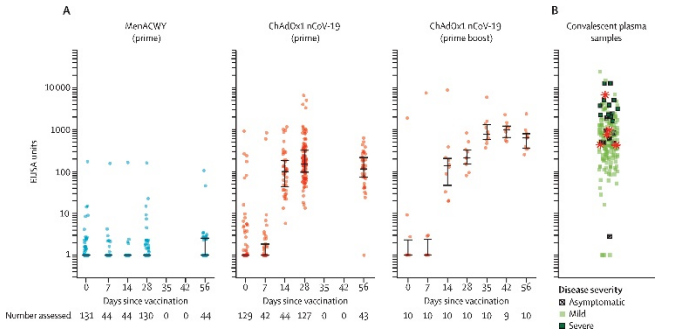

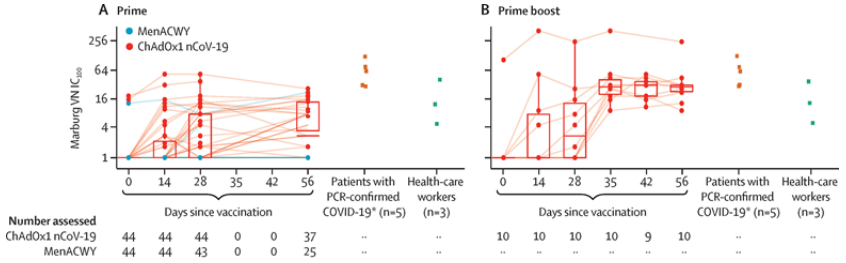

COVID-19 Prevention Network

Protocol pipeline: COVID-19 studies

Date data refreshed

October 21, 2020 7:05 AM

Protocol Name	Concept Name	Study N	Protocol Open
HVTN405/ HPTN1901	SARS-CoV-2 Immunity in Convalescents	800	5/6/2020
CoVPN 5001	Acute Immune Responses to SARS-CoV-2 Infection	800	6/11/2020
CoVPN 3001/ P301	Moderna phase 3	30000	7/27/2020
CoVPN 3002	AstraZeneca phase 3	30000	8/28/2020
CoVPN 3003	Janssen phase 3	60000	9/21/2020
CoVPN 3004	Novavax phase 3	30000	11/5/2020
CoVPN 3005 / VAT00002	Sanofi phase 3	34690	12/7/2020

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Monitoring Cases
Most Severe Disease Anticipated Due to Hypoxia

- Early Seattle ICU case-series: all had hypoxia and none due to shock alone (Bhattarju et al., NEJM 2020)
- Chinese series of 60 critically ill participants, all had hypoxia and none had shock on admission (Huang et al., Am J Med Sci 2020)
- In a cohort of patients with early COVID admitted to observation unit in S. Korea, 12% experienced disease progression; all on basis of hypoxia (J. Clin Med 2020)

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“Happy Hypoxics”: Feature of COVID-infection

Case:

- 74 year old without comorbidities.
- Asymptomatic.
- Sp02 62%, PaO2 36mmHg, SaO2 69%

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Tobin et al., AJRCCM 2020

Lamotte cnn.com May 7 2020

Novel Use of Home Pulse Oximetry Monitoring in COVID-19 Patients Discharged From the Emergency Department Identifies Need for Hospitalization

Sonia Shah, DO[1], Kaushal Majmudar, DO[2], Amy Stein, PhD[3], Nita Gupta, MD[1], Spencer Suppes, DO[1], Marina Karamanis, DO[1], Joseph Capannari, DO[1], Sanjay Sethi, MD[4], and Christine Patte, DO[1]

doi: 10.1111/acem.14053
ISSN 1553-2712

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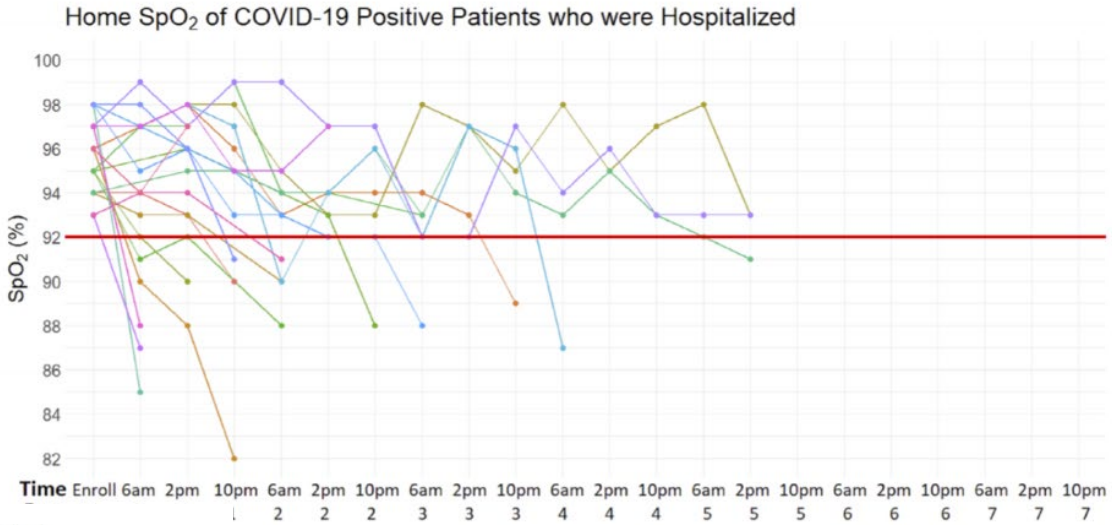
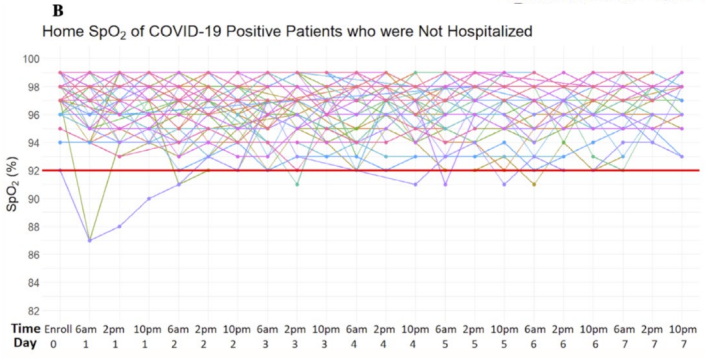
Finger pulse ox 3X/day; daily check-ins; repeat in 10 minutes if SpO2 <92%

Hypoxia Occurs Quickly During COVID Infection

- Home SPO2 monitoring in patients discharged from ER:

"Most patients who had SpO2 < 92% [after discharge] experienced an abrupt drop in SpO2 rather than a gradual decline"





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Shah et al., ACEM 20202

Interested in volunteering for a COVID-19 Prevention Clinical Study?

Thank you for your interest in our studies. Science can't move forward without your help!

Selecting the button below will take you to the CoVPN Volunteer Screening Registry.

The purpose of this screening registry is to create a list of potential volunteers who want to take part in current or future COVID-19 prevention clinical trials. You must be 18 years or older to participate. Participation involves completing a short online survey that includes some personal questions. Your participation is voluntary.

Volunteer Now!

Our studies enroll adults aged 18 and older, of all races and ethnicities, and of all gender identities.

Credit: iStock

www.coronaviruspreventionnetwork.org

COVID-19
Prevention Network

Volunteer | Clinical Studies | What to Expect | Science | FAQ | Locations

Success!

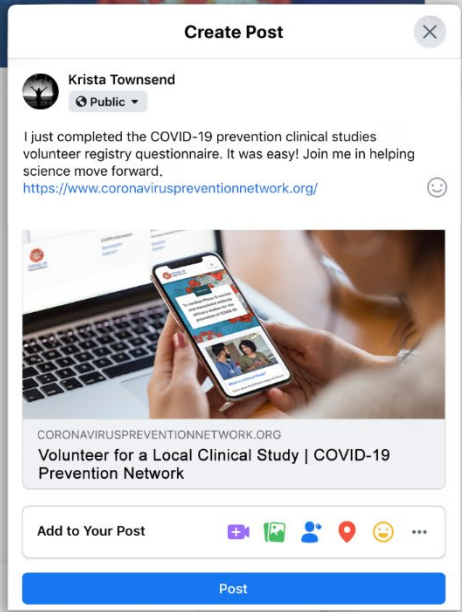
Thank you for your interest in participating in COVID-19 Prevention Network clinical studies. Our system does not send out an email confirmation message. If you are reading this, we have successfully received your information.

Please submit only one questionnaire unless you have a significant change in your information, such as a new job or new address. Your information will be provided to a study site closest to your location. If the study site thinks you may qualify for a particular study, they will reach out to you as soon as possible about participating. This could be soon, or it may be in several months, as there are several studies taking place over the next 6 months. We will never ask for your financial, credit, or bank account information. We will never ask for an ID number over the phone. If you have additional questions, please visit the FAQ page of the website.

Thank you for your interest in contributing to this important effort.

Science can't move forward without your help!

Share your participation in COVID-19 Prevention Network volunteer screening registry with your friends and family and encourage them to volunteer too.



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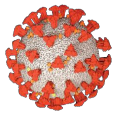
CoVPN Volunteer Screening Registry Overview

- The CoVPN registry is based on a pre-screening questionnaire accessible from the website:
  https://www.coronaviruspreventionnetwork.org/
  Or, www.preventcovid.org
- Data includes contact info/location, demographics, health conditions and other risk criteria.
- Registered users from each site access the registry using two-factor authentication for security.
- The intent is to grant access to only those staff needing it for recruitment efforts.



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CoVPN - Back Office Administration

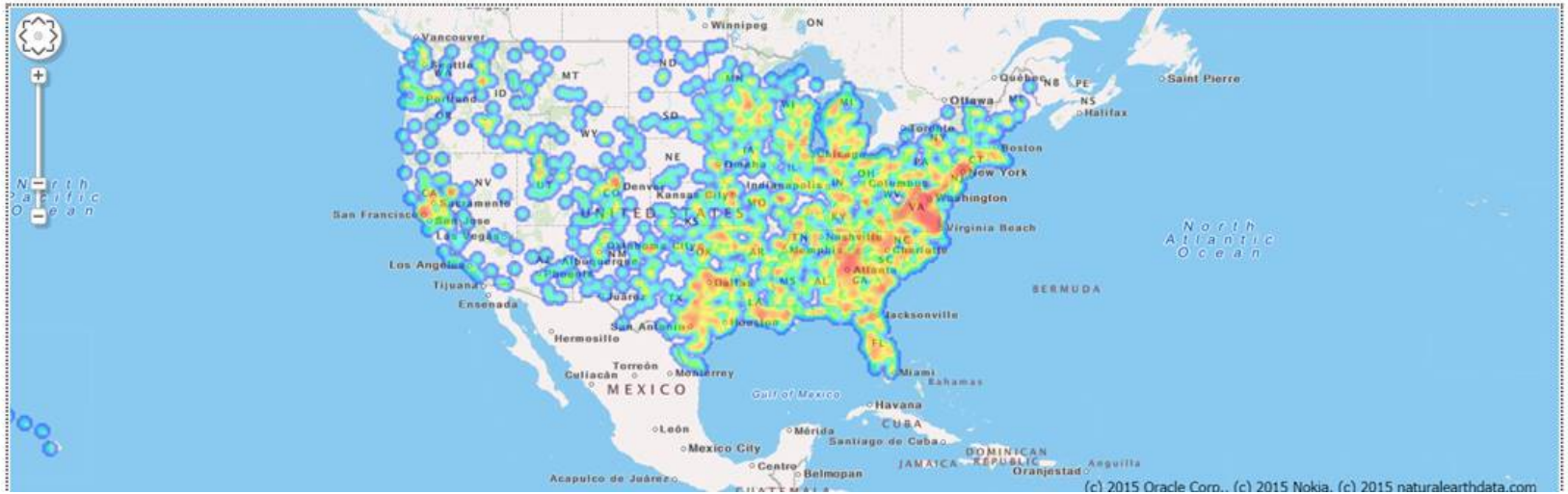
rebecca.laborde@oracle.com

Dashboard

This Week

1,899	250	0	0
Completed	Started	Completed	Started

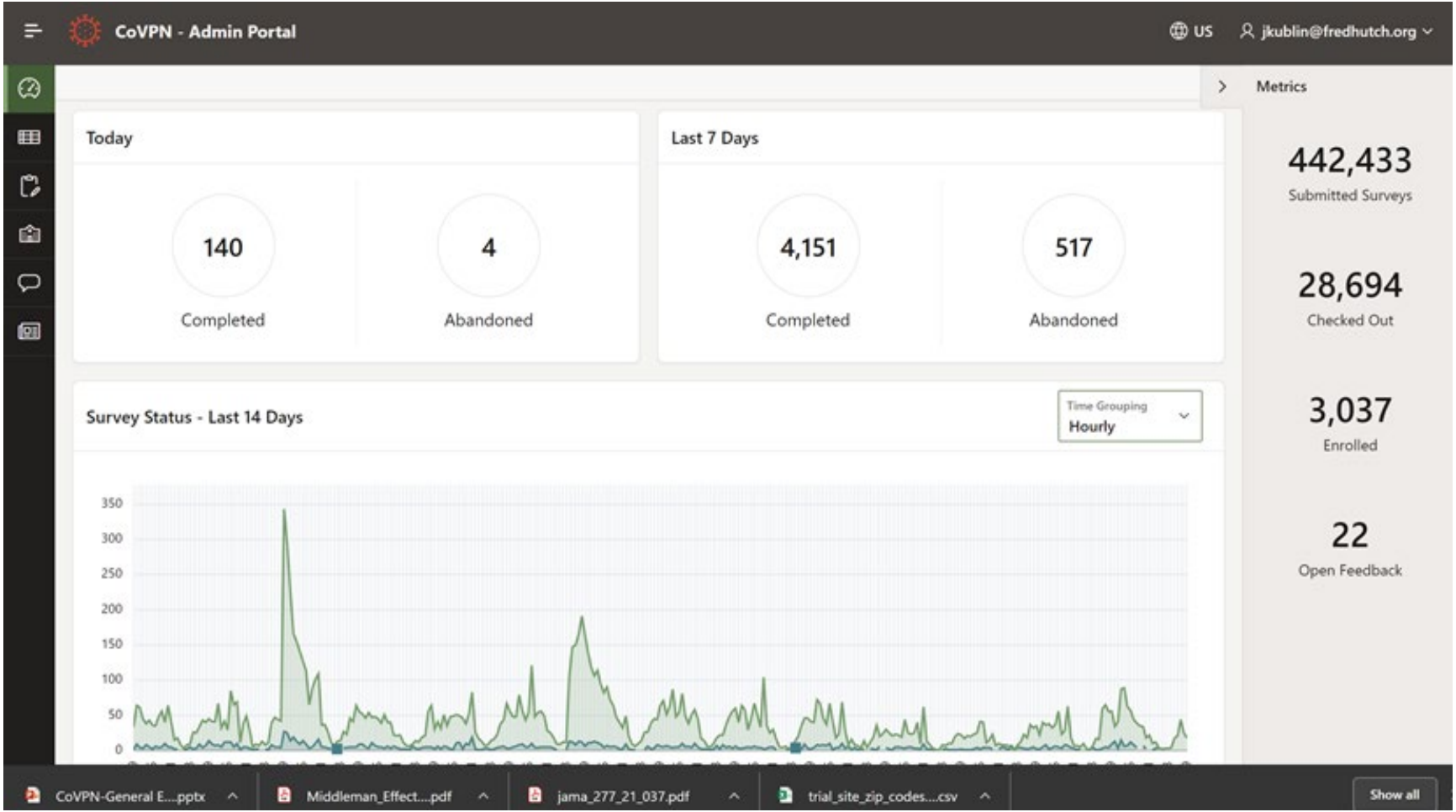
Completed Surveys Map



Metrics

3	2,465,800	98,836	12,179
Open Feedback	Page Views	Completed Surveys	Incomplete Surveys

COVID-19
Prevention Network



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Risk scores and other risk criteria

- To help you efficiently identify, characterize, and select potential enrollees, we are providing several risk scores* that predict:
  - Hospitalization (COVER-H)
  - Intensive care (COVER-I)
  - Fatality (COVER-F)
- We have also developed a composite score for the risk of exposure/infection and progression to disease.

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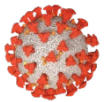
* Williams, Ross D., et al. "Seek COVER: Development and validation of a personalized risk calculator for COVID-19 outcomes in an international network." *medRxiv* (2020).

Updated Risk Score

- What is the likelihood that an individual in the CoVPN volunteer screening registry will become infected with SARS-CoV-2 and develop symptomatic COVID disease in the next 3 months?
- We developed an individual person-level cumulative endpoint risk score with four dimensions (home, community, work, transit), a relative risk of showing symptoms if infected, and a vaccine trial endpoint risk score that combines susceptibility, cumulative exposure, and risk of symptoms. This is currently being tested and will be deployed in the coming day(s).



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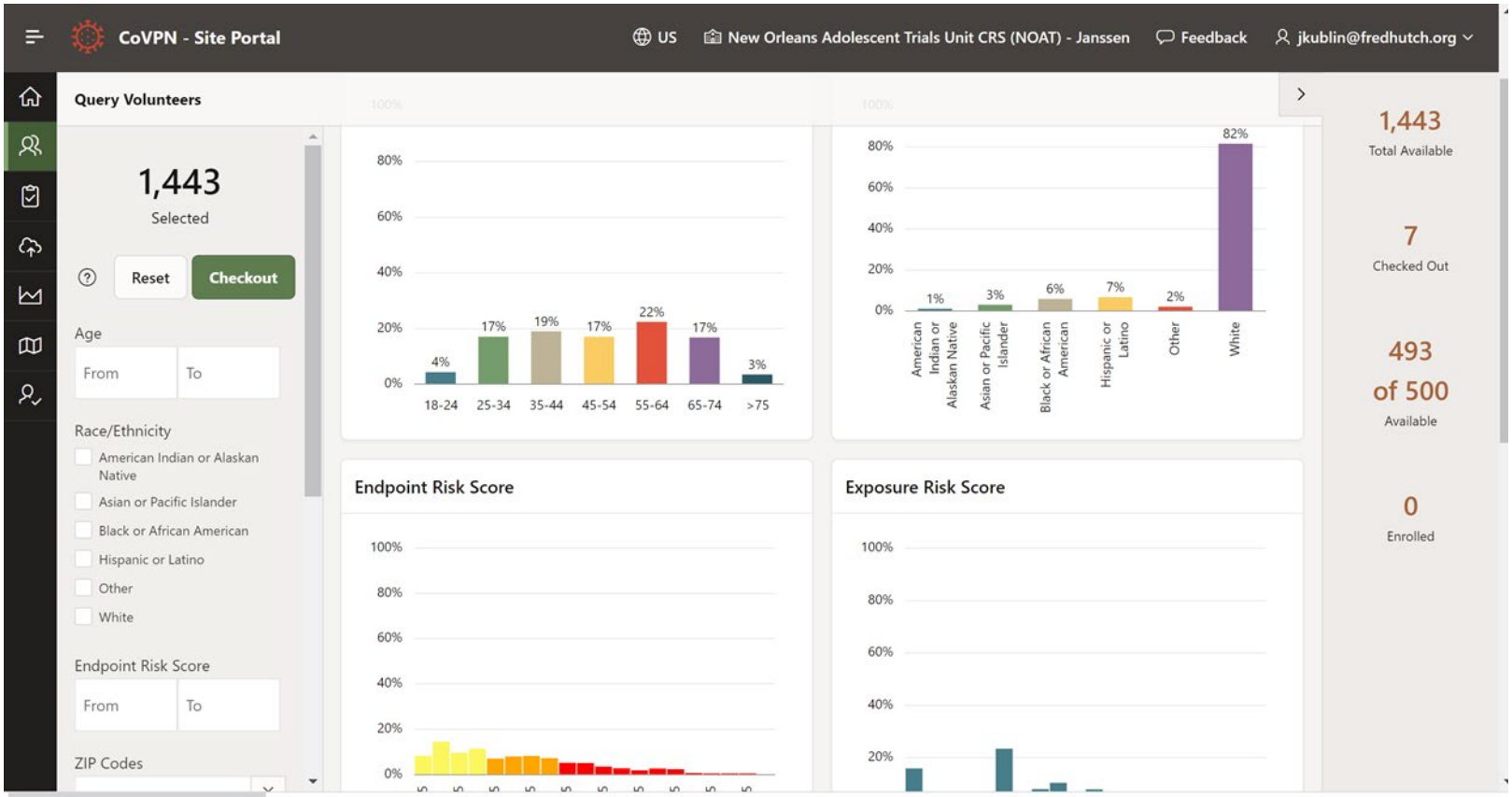

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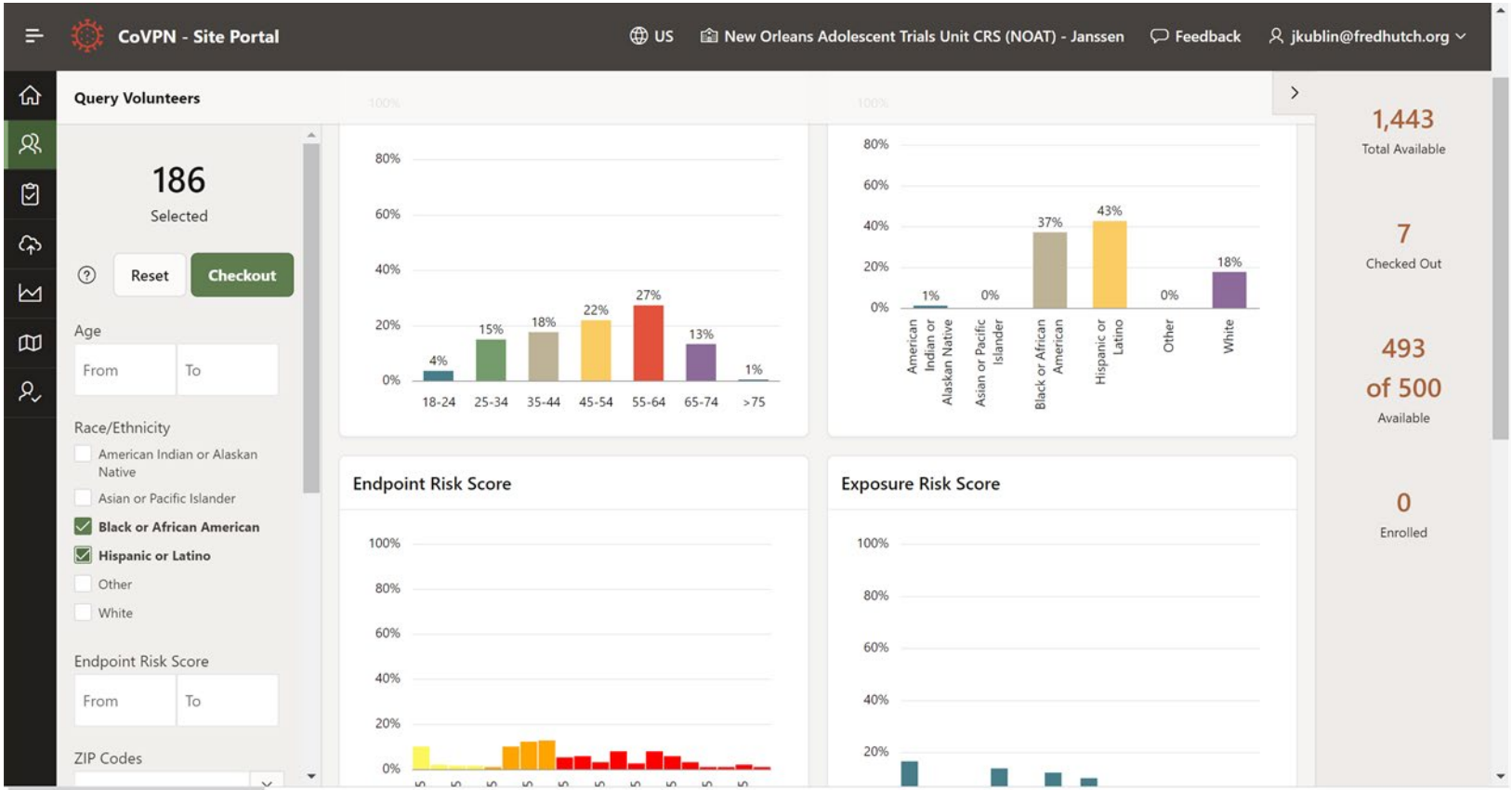

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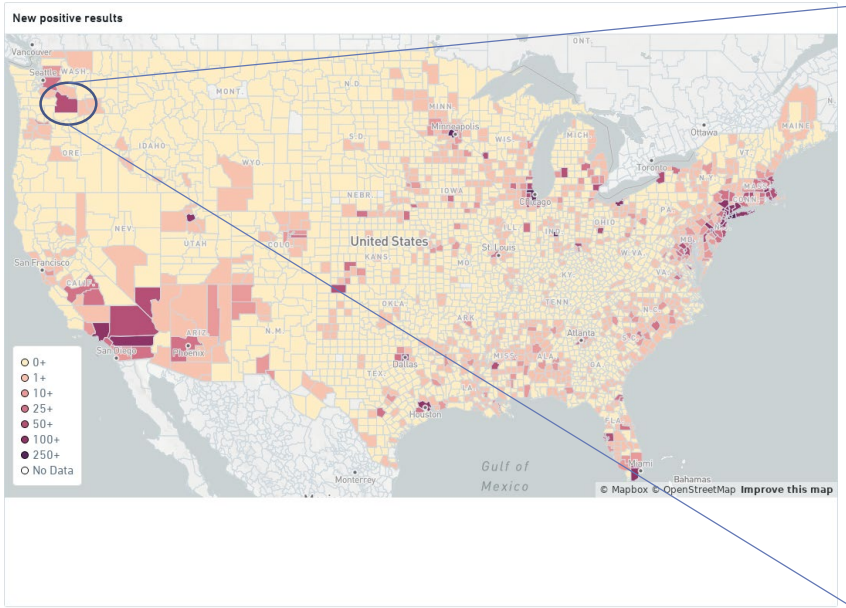


Data from state public health labs, commercial labs, and hospitals. Some data may still coming in for the most recent 3 days.

Agriculture | Health | Local Business | Local News | Nation | Northwest

Some agriculture workers walk off job in Yakima County over coronavirus concerns

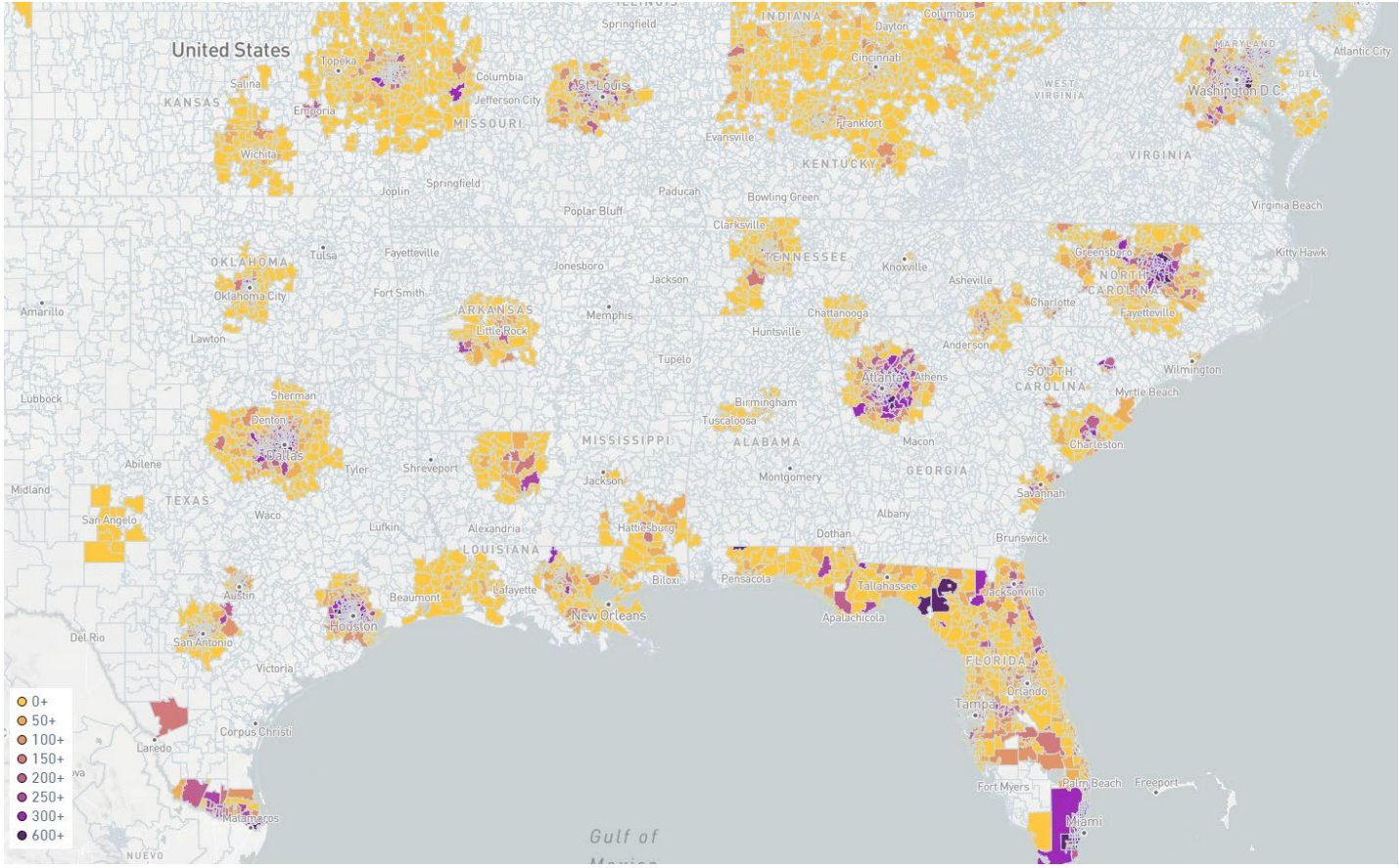
May 14, 2020 at 2:15 pm | *Updated May 14, 2020 at 3:03 pm*

1 of 2 | Monson Fruit Company workers strike on Wednesday in Selah. (Evan Abell / Yakima Herald-Republic)

By LEX TALAMO
Yakima Herald-Republic

COVID-19 Prevention Network

Regional Maps of Site Catchment Areas: # of positive lab results in the last month



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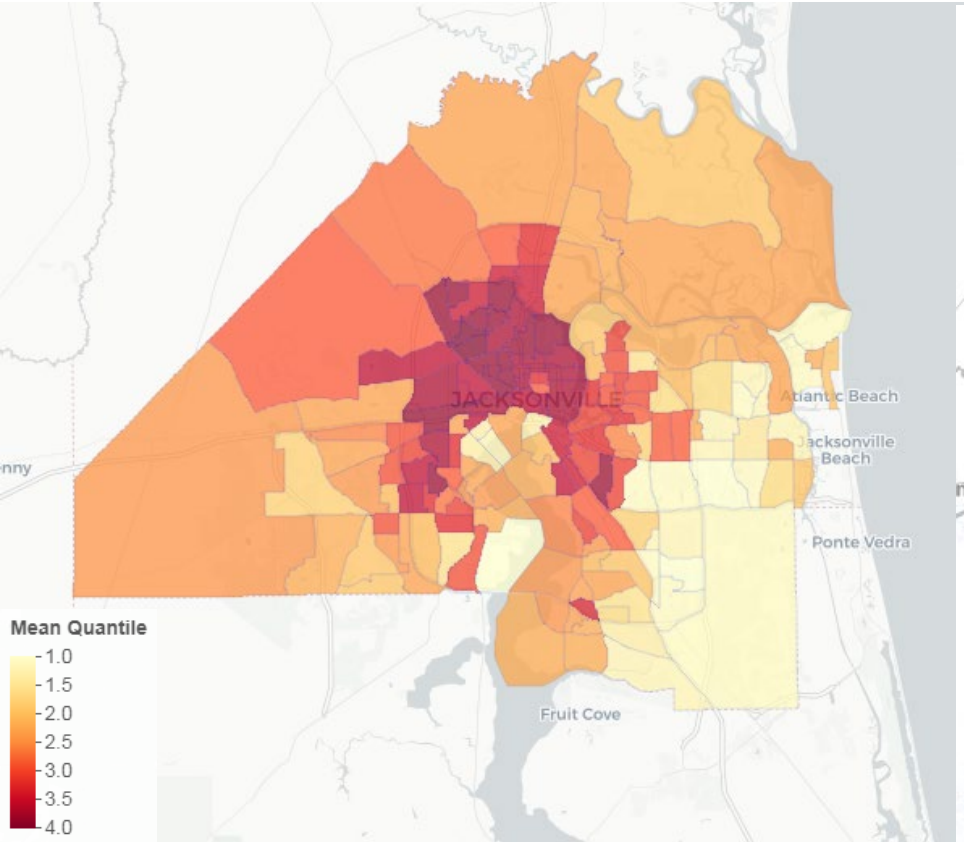
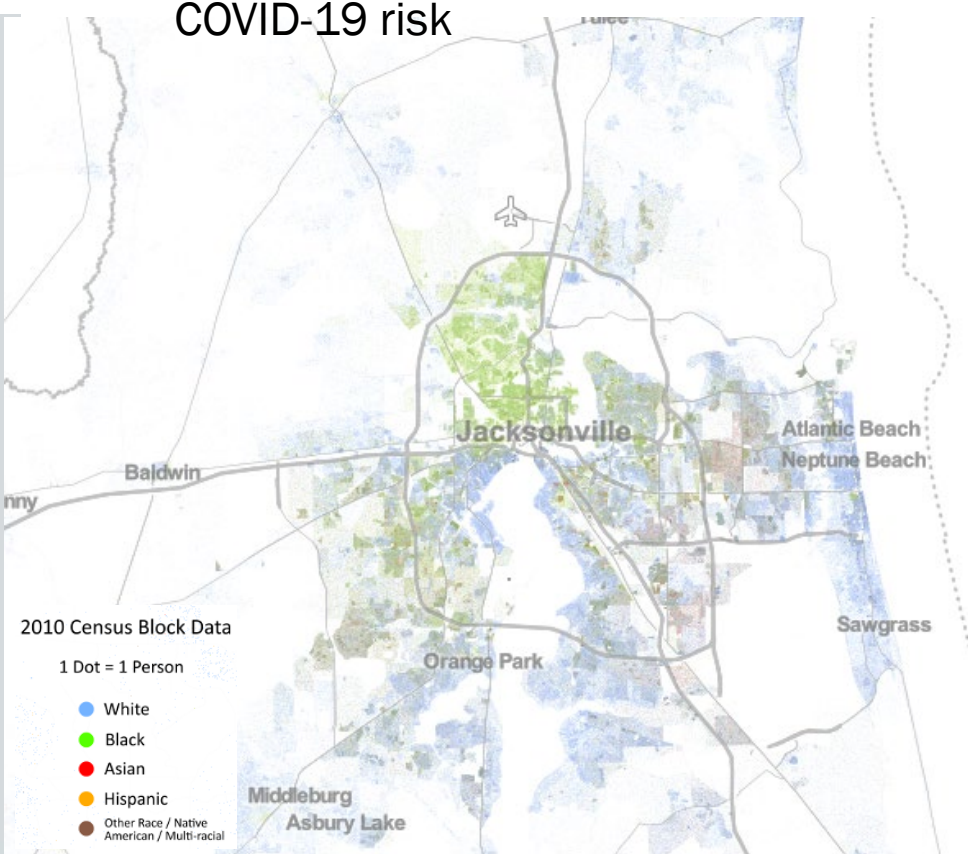
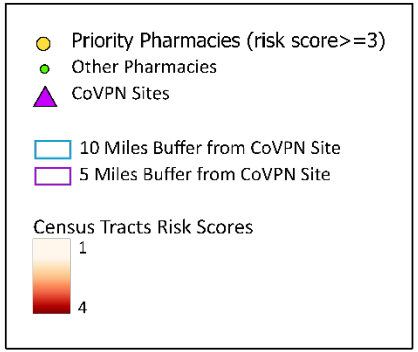
Risk maps - Jacksonville, FL

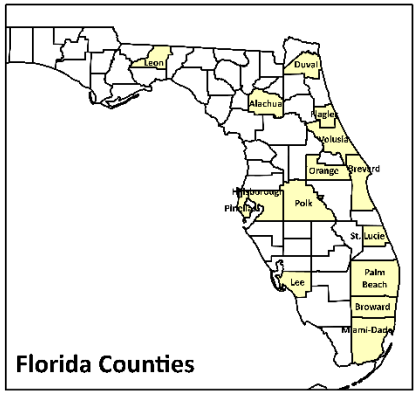
Pre-existing health disparities play a key role in exacerbating COVID-19 risk

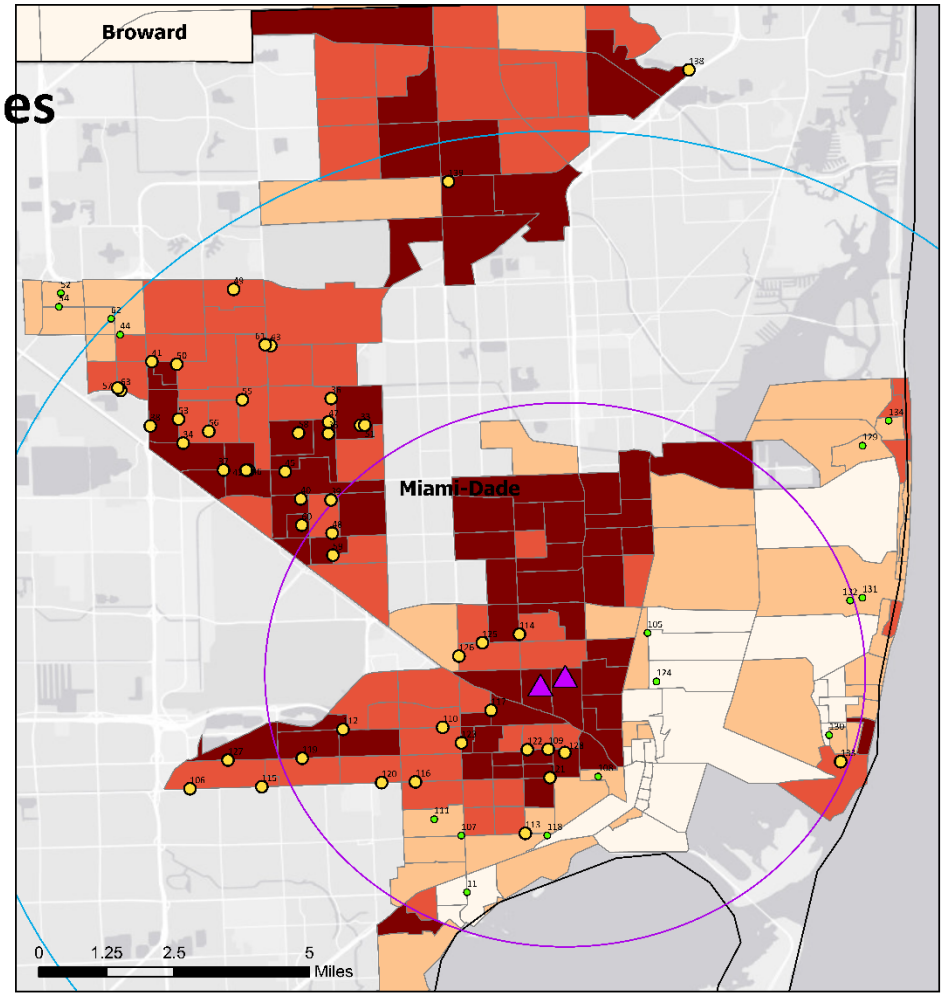




Miami-Dade County Pharmacies







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HELP
IS BETTER.
JOIN
THE FIGHT
AGAINST
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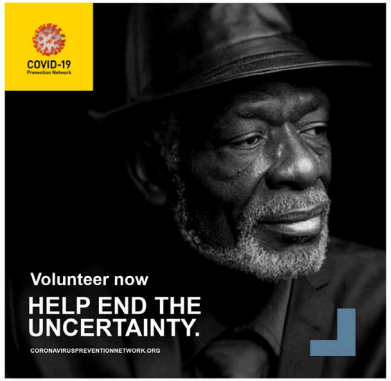

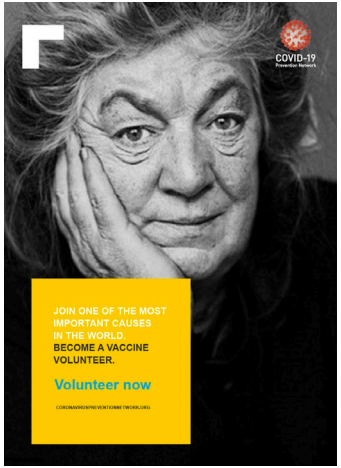

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WHAT STANDS IN OUR WAY?

People are bombarded with myths and misinformation

People who want to help don’t know how

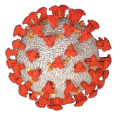
Volunteers may be stigmatized by a vocal anti-vax movement

A higher than normal number of US citizens are doubting the vaccine development process for COVID-19

Politics are interfering with science like never before

What have we learned?

- As predicted, global human pandemics resulting from trans-species transmission of virus pathogens, have and will continue to occur.
- Advanced technology makes opportunities for rapid vaccine development
- Advances in therapeutic options will reduce morbidity and mortality
- Transparency and scientific evidence should be guiding tenets to public health policy
- Community and the public trust demand a coordinated effort across society
- This pandemic highlights some of the weaknesses in our current healthcare system that require immediate and lasting changes
- Ultimately, effective vaccines may be the most efficient and effective means to controlling the pandemic with the greatest public health benefits.



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Thank You

COVPN Executive Committee

Larry Corey and Kathy Neuzil

David Stephens and Myron Cohen

Study Chairs

VRC

- John Mascola
- Barney Graham
- Julie Ledgerwood

CoVPN Staff

HHS

Oracle

Fred Hutch

NIH Executive Team

- Mary Marovich
- Emily Erbelding
- Carl Dieffenbach
- Hilary Marston
- Cliff Lane

NIH

- Tony Fauci
- Francis Collins
- Doug Lowy

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Thank You – Questions

Acknowledgement

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