

**COVID-19 VARIANTS
AND EVOLVING RESEARCH NEEDS**

HEARING
BEFORE THE
SUBCOMMITTEE ON INVESTIGATIONS
AND OVERSIGHT
OF THE
COMMITTEE ON SCIENCE, SPACE,
AND TECHNOLOGY
HOUSE OF REPRESENTATIVES
ONE HUNDRED SEVENTEENTH CONGRESS

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**COVID-19 VARIANTS
AND EVOLVING RESEARCH NEEDS**

WEDNESDAY, MAY 12, 2021

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
Washington, D.C.

The Subcommittee met, pursuant to notice, at 10:03 a.m., via Zoom, Hon. Bill Foster [Chairman of the Subcommittee] presiding.

**U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT**

HEARING CHARTER

COVID-19 Variants and Evolving Research Needs

Wednesday, May 12, 2021
10:00 a.m. EDT – 12:00 p.m. EDT
Zoom

PURPOSE

The purpose of this hearing is to discuss how variants develop, how researchers identify and sequence variants, and how this information can be utilized by public health officials, government agencies, and medical practitioners to make decisions. The hearing will examine the ways the Federal government can meet the research and forecasting needs that evolve as the virus continues to mutate. Members and witnesses will discuss how the federal government can better coordinate its approach to best serve the American people through this pandemic and beyond.

WITNESSES

- **Dr. Salim Abdool Karim**, Director of CAPRISA
- **Dr. Nathan Grubaugh**, Assistant Professor of Epidemiology, Yale School of Public Health
- **Dr. Stephen Streiffer**, Deputy Laboratory Director for Science and Technology, Argonne National Laboratory
- **Dr. Caitlin Rivers**, Senior Scholar, Johns Hopkins Center for Health Security

OVERARCHING QUESTIONS

- How do COVID-19 variants emerge and spread, and how do public health decisions influence the proliferation of variants?
- What is the state of data sharing among U.S. states and among countries regarding variants developing and spreading around the globe?
- Are existing tests and vaccines effective for the known COVID-19 variants? How do variant-specific tests bolster public health decision-making? What role do vaccines play in reducing the spread and emergence of variants?
- Have the models built to track and predict the spread of COVID-19 around the globe adapted with the emergence and spread of variants?
- How can the federal government serve as a resource during and between pandemics when it comes to information aggregation and accessibility and disease forecasting?

Variants in the United States

As viruses spread, small errors – called mutations – arise in the genetic material during replication. Many of these mutations are repaired or die off as the virus continues to move through a population. Mutations that enhance the virus’s ability to replicate, transmit, or survive in a host allow the virus to spread more quickly through a population, or become more resistant to immune system defenses, thereby increasing the mutations’ prevalence and creating a new strain of the virus.¹ Almost a year and a half into the global battle against COVID-19, the United States faces five known Variants of Concern (VOCs). According to the Centers for Disease Control², these are as follows:

- **B.1.1.7:** First identified in the U.K. in November 2020 and identified in the U.S. in December 2020. This variant increased transmissibility of the virus by about 50% and research suggests there is a potential – but not confirmed – increase in severity of cases.³
- **B.1.351:** First identified in South Africa in December 2020 and identified in the U.S. at the end of January 2021. This variant increased transmissibility of the virus by about 50%. Certain monoclonal antibody treatments and vaccine-induced immunity have been shown to be less effective against B.1.351.⁴
- **P.1:** First identified in Japan in early January 2021 among travelers from Brazil, where it likely originated in November 2020.⁵ Identified in the U.S. in January 2021. Research indicates P.1 is twice as transmissible as earlier strains and is less susceptible to immune defenses built by previous infections and vaccination.⁶
- **B.1.427 and B.1.429:** First identified in California in February 2021. This variant increased transmissibility of the virus by about 20%. Certain monoclonal antibody treatments and vaccine-induced immunity have been shown to be less effective against these variants.⁷

As variants of concern, these strains have evidence of an increase in transmissibility, more severe disease, significant reduction in susceptibility to infection- or vaccine-induced immunity, or diagnostic detection failures.⁸ These variants are closely monitored by federal health agencies and are analyzed to determine whether additional diagnostics, vaccines, or treatment are needed. If clear evidence of reduced effectiveness of prevention measures, vaccines, or approved therapeutics arises, a variant could be classified as a Variant of High Consequence. Currently, no COVID-19 variants rise to this level.

¹ <https://www.gavi.org/vaccineswork/patient-zero-understanding-how-new-coronavirus-variants-emerge>

² <https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html>

³ <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html>

⁴ Ibid.

⁵ <https://www.sciencenews.org/article/covid-coronavirus-p1-variant-brazil-strain-transmission-immunity>

⁶ Ibid.

⁷ <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html>

⁸ Ibid.

B.1.617 and the Importance of Vaccines in Squelching Variants

The variant currently dominating the news cycle was discovered in India. India is now experiencing the sharpest spike in coronavirus cases in the world, with a record of 400,000 new COVID-19 cases for the first time on May 1.⁹ One variant – B.1.617 – has become the dominant strain in some areas. Media coverage of this variant has dubbed it a “double mutant,” as it contains specific similarities to the mutation present in the California strain as well as one found in both the South African and Brazilian strains. However, this name implies that the strain has only two mutations, or that having two mutations is unusual; in fact, B.1.617 has about a dozen mutations, which is not uncommon.¹⁰

While B.1.617 is not the only mutation driving up infections in India, it appears that people who already had COVID-19 during an earlier surge are susceptible to reinfection with B.1.617. Existing vaccines appear to work against B.1.617, but could be slightly less effective.¹¹

Exacerbating this deadly wave in India is the country’s vaccine shortage. India is the largest vaccine manufacturer in the world, but just about 3 percent of the country – 30 million out of 1.3 billion people – had been fully vaccinated as of May 8.¹² Expanding vaccine access is not only imperative to save lives in India during this devastating wave, but to stem the spread of the virus and the inevitable mutations that will develop as it makes its way through the population. In late April, the Biden administration announced that it would share 60 million doses of the AstraZeneca vaccine – which is not authorized for use in the United States by the Food and Drug Administration (FDA) – with countries around the world.¹³

On May 5, 2021, the Administration announced that it supports the temporary lifting of intellectual property protections for COVID-19 vaccines.¹⁴ Lifting these protections would allow the production of generic versions of the vaccines to supplement the doses made available directly from brand-name pharmaceutical companies, from other countries, or through international programs such as COVAX, which aims to provide equitable access to tests, treatments, and vaccines.¹⁵ Pharmaceutical companies are opposed to lifting these protections, arguing that the increased competition for supplies could slow their production.

The more the virus circulates, the more variants will emerge, increasing the risk of a deadlier, more contagious strain of the disease. Though the exact effectiveness varies among vaccines and among variants, all approved vaccines appear to be effective in preventing infection from known variants. Last week, studies were published that showed the Pfizer-BioNTech vaccine to be 100 percent effective at preventing severe disease caused by B.1.351 (South African variant) and

⁹ <https://www.reuters.com/world/asia-pacific/india-posts-record-daily-rise-covid-19-cases-401993-2021-05-01/>

¹⁰ <https://www.npr.org/sections/goatsandsoda/2021/04/24/988744811/people-are-talking-about-a-double-mutant-variant-in-india-what-does-that-mean>

¹¹ *Ibid.*

¹² <https://www.nytimes.com/live/2021/05/06/world/covid-vaccine-coronavirus-cases>

¹³ https://www.washingtonpost.com/politics/us-to-share-up-to-60-million-doses-of-astrazeneca-coronavirus-vaccine-with-other-countries-official-says/2021/04/26/b2dab8a0-a694-11eb-bca5-048b2759a489_story.html

¹⁴ <https://twitter.com/ambassadortai/status/1390021205974003720?s=21>

¹⁵ <https://www.who.int/initiatives/act-accelerator/covax>

B.1.1.7 (U.K. variant), and 72-89.5 percent effective at preventing infection.¹⁶ Suppressing the spread and inevitable mutation of the coronavirus – especially as the world is opening back up – requires robust vaccination in the United States and abroad.¹⁷

Variant Testing

Though the tests used to detect the coronavirus were developed in the flurry of the early days of the pandemic, there is no evidence that they are less effective at detecting the newer strains of the virus.¹⁸ Polymerase chain reaction tests – or PCR tests – detect multiple sequences of the coronavirus genome. The detection of any one of these sequences will trigger a positive test result, meaning that the mutation of one gene target will not render the test ineffective. However, it is important that researchers, test manufacturers, and regulatory bodies remain vigilant in assessing the continued effectiveness of tests as the virus continues to mutate. The FDA maintains a list of EUA-authorized tests whose performance may be impacted by mutations¹⁹, and has issued policy guidance and recommendations for evaluating the impact of variants on tests.²⁰

Because certain variants are deadlier, more contagious, or respond differently to preventative measures or treatments, it is important that public health agencies understand where particular variants are emerging and circulating. While not in use diagnostically, genomic sequencing is used to identify specific strains of the coronavirus, after a sample comes back positive. PCR tests that identify which specific variant a patient is carrying have been developed to assess positive samples for a variety of known strains. But because different variants possess similar mutations, definitive PCR tests are difficult to develop, and full genomic sequencing is a more reliable way to detect what variant is present in a particular sample.

The FDA does not currently authorize the use of any variant-specific tests for diagnostic use. Commercial and public health entities that process PCR testing and genomic sequencing for the purpose of variant identification are bound by patient privacy rules. Therefore, virtually everything we know about the presence of variants is at the public, not individual, level. This means that medical practitioners do not make treatment decisions based on the particular strain of the virus a patient has contracted. Rather, an awareness of the variants circulating in a particular region can inform public health decisions at large.

Disease Modeling and Forecasting

Infectious disease models are critical planning tools for policymakers and healthcare providers. Officials use them to allocate resources, such as medical staff and supplies, forecast the spread or severity of a disease, and predict the effects and costs of different intervention options. Models can also be used to anticipate future outbreaks based on past experiences. Accurate models must

¹⁶ <https://www.nytimes.com/live/2021/05/05/world/covid-vaccine-coronavirus-cases#pfizer-vaccine-variants-covid>

¹⁷ <https://www.seattletimes.com/opinion/rise-of-variants-underlines-importance-of-covid-19-vaccination/>

¹⁸ <https://www.nytimes.com/2021/04/14/health/coronavirus-testing-variants.html>

¹⁹ <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests>

²⁰ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests>

incorporate what is known about the mechanics of the virus spread itself, how human behaviors adapt over the course of the pandemic, and, increasingly, how prevalent particular strains of the virus are in a given area.

Accurately and robustly incorporating variants into disease forecasting models would require an increased capacity for genomic surveillance and data sharing.²¹ At the end of 2020, the United States ranked 28th in percentage of coronavirus samples sequenced to detect variants – up from 43rd at the end of 2020²², but still far behind many of our global peers.²³ Genetic sequencing data is currently shared and accessed by researchers primarily on GISAID, a nonprofit started to share avian flu data.²⁴ Federal investments in data aggregation tools are necessary to ensure researchers, public health officials, and the American public have reliable models and forecasts through this pandemic and beyond.

Federal Activities on Variants²⁵

In 2014, the White House National Science and Technology Council (NSTC) chartered a new Pandemic Prediction and Forecasting Science and Technology Working Group to coordinate Federal outbreak prediction capabilities, including capabilities to predict variants. In late 2016, this Working Group issued a roadmap report, “Towards Epidemic Prediction: Federal Efforts and Opportunities in Outbreak Modeling.”²⁶ It included a list of 14 high-level policy recommendations for a coordinated multi-agency effort provide for robust data and information sharing, stronger outbreak model development and decision support tools, and a “One Health” strategy for integrating scientific information from various sources to more effectively predict infectious disease outbreaks. The report also presented a table of various activities in infectious disease modeling being conducted across 11 different federal agencies, such as modeling of foreign animal disease activities being conducted by USDA’s Animal and Plant Health Inspection Service (APHIS) and the Biosurveillance Ecosystem activities at DOE’s Los Alamos National Laboratory.

The ability to sequence the genome of a viral sample is critical to establishing what disease variant has led to a patient’s infection. In May 2020, the CDC’s Advanced Molecular Detection program established a new lab consortium called the SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance, or SPHERES, dedicated to collaborating on and aggregating results from genome sequencing of viral samples. SPHERES convenes scientists and data contributions from state and local public health laboratories, clinical laboratories, universities, and the private sector. Its objectives include identifying resource needs across the country so that genome sequencing can be more widely deployed, but also

²¹ <https://www.latimes.com/science/story/2021-02-07/how-the-u-s-plans-to-keep-tabs-on-the-coronavirus-variants-in-circulation-here>

²² <https://www.washingtonpost.com/world/2020/12/23/us-leads-world-coronavirus-cases-ranks-43rd-sequencing-check-variants/>

²³ https://covidcg.org/?tab=global_sequencing

²⁴ <https://www.gisaid.org/hcov19-variants/>

²⁵ <https://www.nytimes.com/2021/04/14/health/coronavirus-testing-variants.html>

²⁶ [towards_epidemic_prediction-federal_efforts_and_opportunities.pdf \(archives.gov\)](https://www.archives.gov/files/assets/epidemic-prediction-federal-efforts-and-opportunities.pdf)

championing principles of quick and open data sharing and the use of common data and analysis standards.²⁷

In a January 21, 2021 Executive Order, President Biden proposed a new interagency National Center for Epidemic Forecasting and Outbreak Analytics, which would support global efforts to prevent, detect, respond to, and recover from emerging biological threats.²⁸ In January 2021, CDC introduced the National SARS-CoV-2 Strain Surveillance (NS3) program, which asked state laboratories to remit viral sample data to CDC on a weekly basis in order to help establish a national picture of how variants are spreading and affecting patients.²⁹ On April 16, the Administration announced that the CDC will allocate \$1.7 billion to states to scale up science capabilities for tracking and monitoring COVID-19 variants.³⁰

²⁷ [SPHERES | CDC](#)

²⁸ [National Security Memorandum on United States Global Leadership to Strengthen the International COVID-19 Response and to Advance Global Health Security and Biological Preparedness | The White House](#)

²⁹ [FEB 2021 Revised NS3 FAQ_02052021 FNL.pdf \(aphl.org\)](#)

³⁰ <https://www.whitehouse.gov/briefing-room/statements-releases/2021/04/16/fact-sheet-biden-administration-announces-1-7-billion-investment-to-fight-covid-19-variants/>

Chairman FOSTER. This hearing will now come to order. Without objection, the Chair is authorized to declare a recess at any time.

Before I deliver my opening remarks, I wanted to note the circumstances under which we're meeting today. Pursuant to *House Resolution 8*, the Subcommittee is meeting virtually, and a couple of reminders for the Members about the conduct of this remote hearing. First, Members should keep their video feed on as long as they are present in the hearing. Members are responsible for their own microphones. Please also keep your microphones muted unless you're speaking. Finally, if Members have documents they wish to submit for the record, please email them to the Committee Clerk, whose email address was circulated prior to the hearing.

Well, good morning, and welcome to our Members and our panelists. Thank you for joining us for this hearing on COVID-19 variants. Over a year into the pandemic, we're all accustomed to a new normal: social distancing, mask wearing, and, of course, the virtual proceedings we're conducting today. Almost 60 percent of Americans have received at least one vaccination dose, and our ability to detect and monitor the spread of the virus puts us in a much better position than we were just one year ago.

But just as we've adapted to life in the pandemic, the virus has mutated as it continues to spread around the globe. Each new variant brings the potential for increased contagiousness, disease severity, and evasion of safety measures and vaccine-induced natural immunity. Today, most of the new variants seem to have evolved from national—natural evolutionary pressure, natural selection for infectiousness. One of the commonly expressed worries is about an escape variant of the virus, a superbug that is resistant to our vaccines and may—might evolve in a partially vaccinated population. In a worst-case scenario, such a variant would require us to start over from zero in our vaccine manufacturing, tests, and deployment.

One important policy decision that the United States faces is whether to hold in reserve vaccine manufacturing capacity for such a contingency or perhaps simply to reserve vaccine manufacturing capacity for possible booster shots, which may be required due to the waning of our immune response. This decision will be especially fraught if we conclude that we must use our manufacturing capacity to make booster shots for the U.S. at a time when the rest of the world may not be fully vaccinated.

To make those decisions, and many others, we need to evaluate the probability that new variants or escape variants, as well as what is known about the waning of our immune response from the vaccines, to the standard variants of the virus.

And, more broadly, we must ensure that the tools we use to detect, treat, and forecast the virus are keeping up with the emerging variants. Researchers, medical practitioners, and public health authorities have spent the last year standing up an unbelievably impressive network of testing, surveillance, treatment, and prevention tools. Thinking back to March 2020, it was unimaginable to many that by May 2021, more than half of Americans would be vaccinated against a virus that had just reached our shores. Disease monitoring tools require an unprecedented scale of data sharing and aggregation on an international level.

And, as the death rate in our country has been dropping for months, thanks to a better awareness of how to treat this disease, we must not lose any of the gains as this virus mutates, potentially increasing in contagiousness, severity, or its ability to escape our vaccines. It's important that we in the Federal Government support the efforts of researchers and public health agencies in conducting top-of-the-line research to inform health-protective policies.

Our witnesses here today will tell us about some of the amazing science that has come out of the work on the pandemic, and how we can best support their work now and into the future. The U.S. scientific enterprise has historically been equipped to answer those questions, and the Federal Government must continue to support and amplify this support.

In this fight, we must not lose sight of our Nation's place as a world leader and the importance of international collaboration. We have all seen the recent devastating news coming out of India, making this hearing all the more timely. Stories of overloaded hospitals, insufficient vaccine supplies, and mounting deaths. The more the virus spreads, the more mutations will occur, meaning more strains of virus will develop. No country is out of the woods until every country has the ability to reach herd immunity, or to paraphrase Dr. Rev. Martin Luther King, coronavirus anywhere is a threat to health everywhere.

The Biden Administration has committed to this global fight by rejoining the World Health Organization and the COVAX (COVID-19 Vaccines Global Access) program, pledging \$2 billion to support vaccine access in low- and middle-income countries. The United States is also sending 60 million doses of the AstraZeneca (AZ) vaccine overseas, but we must do more. All approved vaccines have shown to be efficacious in preventing severe forms of known variants, a triumph worth celebrating and something that we cannot take for granted into the future. Bolstering worldwide vaccine access must go hand-in-hand with continuing monitoring of vaccine efficacy in the face of new variants.

I look forward to hearing from our witnesses today about how we can best support the research that we need to end this pandemic and to prepare for the next.

[The prepared statement of Chairman Foster follows:]

Good morning, and welcome to our members and our panelists. Thank you for joining us for this hearing on COVID-19 variants. Over a year into the pandemic, we're all accustomed to a new normal—social distancing, mask wearing, hand sanitizing, and, of course, the virtual proceedings we're conducting today. Almost 60 percent of Americans have received at least one vaccination dose, and our ability to detect and monitor the spread of the virus puts us in a much better position than we were just one year ago. But just as we've adapted to life in a pandemic, the virus has mutated as it continues to spread around the globe. Each new variant brings the potential for increased contagiousness, disease severity, and evasion of safety measures and vaccine-induced and natural immunity. We must ensure that the tools we use to detect, treat, and forecast the virus are keeping up with emerging variants.

Researchers, medical practitioners, and public health authorities have spent the last year standing up an unbelievably impressive network of testing, surveillance, treatment, and prevention tools. Thinking back to March 2020, it was unimaginable to many that by May 2021, more than half of Americans would be vaccinated against a virus that had just reached our shores. Disease monitoring tools require an unprecedented scale of data sharing and aggregation on an international level. And the death rate in our country has been dropping for months, thanks in part to a better awareness of how to treat this disease. We must not lose any of these

gains as the virus mutates, potentially increasing its contagiousness and severity. It is imperative that we in the federal government support the efforts of researchers and public health agencies in conducting top-of-the-line research to inform health-protective policies.

Our witnesses here today will tell us about some of the amazing science that has come out of the pandemic, and how we can best support their work. Each time a new variant pops up on the CDC website, I'm sure we all have the same questions. How effective are existing tests and vaccines? How will masking and distancing guidelines be adjusted based on the contagiousness of this new strain? Will the virus cause more severe illness that requires different treatments? The U.S. scientific enterprise is equipped to answer these questions, and the federal government must continue to support and amplify this work.

In this fight, we must not lose sight of our nation's place as a world leader and the importance of international collaboration. We have all seen the recent devastating news coming out of India, making this hearing all the more timely. Stories of overloaded hospitals, insufficient vaccine supplies, and mounting deaths. The more the virus spreads, the more mutations will occur, meaning more strains of the virus will develop. No country is out of the woods until every country has the ability to reach herd immunity. The Biden Administration has committed to this global fight by rejoining the World Health Organization and the COVAX program, pledging \$2 billion to support vaccine access in low- and middle-income countries. The United States is also sending 60 million doses of the AstraZeneca vaccine overseas. All approved vaccines have shown to be efficacious in preventing severe disease from known variants—a triumph worth celebrating, and something we cannot take for granted. Bolstering worldwide vaccine access must go hand-in-hand with continued monitoring of vaccine efficacy in the face of new variants.

I look forward to hearing from our witnesses today about how we can best support the research we need to end this pandemic and prepare for the next.

I now yield to Ranking Member Obernolte for his remarks.

Chairman FOSTER. And I'll recognize my Ranking Member, Mr. Obernolte, for his—an opening statement.

Mr. OBERNOLTE. Thank you very much, Chairman Foster, and thank you for convening this very timely hearing on a very important topic. I am looking forward to hearing from our witnesses, and I'm particularly excited about this hearing because it gives us the opportunity to highlight the incredibly important role that our research community has had in fighting this epidemic. I believe that many of our Federal researchers are the unsung heroes of this epidemic, and I also believe that the development and deployment of the vaccines that have been accomplished in the last few months will go down as one of the greatest scientific achievements of mankind so far. So it can't be understated the incredible role that our research community has had in combatting this virus.

Unfortunately, though, it's clear that much more work needs to be done. If we look at the emergence of the different variants of COVID-19, it's clear that we need to invest more in research and development so that we understand a lot of the questions that are still unanswered, for example, the way that these variants emerge, whether or not these variants cause more or less severe illnesses, whether or not they're more or less transmissible, and the way that those variants respond to the various vaccines that have been developed and the way that we can develop vaccines in the future that anticipate those variants. So it's very important that we continue this investment in research into not only human biology but epidemiology and the spread of these variants.

I also want to highlight the important role that Congress has to play in stimulating this kind of research. The Federal Government is a natural—actually absolutely critical source of funding and of focusing attention on these efforts, and we need to continue that

investment. I know that the Science, Space, and Technology Committee is considering a number of different bills that will continue that investment, and I fully support those efforts. I want to highlight one in particular, H.R. 2153, the *Securing American Leadership in Science and Technology Act*, which authorizes Department of Energy (DOE) infectious disease research program. I think that that's incredibly important, and I hope that that's something that's going to get attention in this Committee.

So, Mr. Chairman, thank you very much again for convening the hearing, and I'm looking forward to hearing from our witnesses.

[The prepared statement of Mr. Obernolte follows:]

Thank you, Chairman Foster, for holding today's important and timely hearing. I would also like to thank our expert witnesses for their participation today.

I look forward to learning more about the important contributions the Department of Energy (DOE) Office of Science's National Laboratories are making to combat the COVID-19 virus, and what role they can play moving forward to combat other infectious diseases. Thank you, Dr. Streiffer for being here today and for all the important work you do at Argonne National Laboratory.

Our nation's research enterprise has demonstrated it has the expertise, resources, and talent to fight this pandemic. We have supercomputers, advanced manufacturing techniques, and even advanced photon sources being used to fight COVID-19.

The DOE National Labs have a history of using technical solutions to respond to national and international emergencies, and when the COVID-19 pandemic hit, the labs were prepared, ready, and willing to serve on the front lines. DOE received \$99.5M in the *CARES Act* to fund research at the National Labs to better understand COVID-19. This funding has since been fully expended.

At the start of the pandemic, DOE pivoted and launched the National Virtual Biotechnical Laboratory (NVBL) to mobilize the resources of the Department of Energy's 17 National Labs to engage in critical COVID-19 research. Projects within NVBL are focused on molecular design for medical therapeutics, development and evaluation of COVID-19 testing, epidemiological and transpiration modeling, and advanced manufacturing.

I would also like to highlight that decades of investment in basic scientific research involving the National Labs contributed to the unprecedented speed COVID-19 vaccines were developed and distributed. These investments have been truly life-saving.

The accomplishments made possible through the NVBL demonstrate the power of the U.S. innovation ecosystem, when you have DOE National labs, universities, and companies all working together to address a national and societal challenge.

As the original COVID-19 virus and new variants continue to spread across the globe, it is imperative that the United States continues to make critical investments in basic research for the health and safety of our nation. To date, the Centers for Disease Control and Prevention (CDC) have identified five COVID-19 Variants of Concern (VOCs) in the United States. Researchers are paying close attention to these VOCs as according to the CDC, they appear to spread more easily and quickly than other identified Variants of Interest (VOIs).

There remains a lot of information public health officials and researchers do not yet know about COVID-19 variants, and further studies are needed. For example, researchers still need to learn how easily emerging COVID-19 variants spread, if they cause milder or more severe illness, if they are detected by currently available viral tests, if they respond to medications currently being used to treat COVID-19, and whether existing authorized vaccines protect people from them. The DOE National Labs can build upon previous COVID-19 research work and get ahead in the race against COVID-19 mutations. The National Labs have existing infrastructure, resources, and experts ready to deploy, and can continue to play a leading role in addressing key concerns and challenges to confront the COVID-19 pandemic and beyond.

Before I close, I would like to highlight H.R. 2153, the *Securing American Leadership in Science and Technology Act (SALSTA)*, which was introduced by Full Committee Ranking Member Lucas in March, and which I am an original cosponsor of. This legislation includes an authorization for a DOE emerging infectious disease research program and high-performance computing research consortium.

I hope that today's hearing will continue an important dialogue on the role of Federal science agencies in supporting R&D to combat the COVID-19 virus and propose new and innovative solutions for infectious disease responses in the future.

Thank you, and I yield back.

Chairman FOSTER. Thank you. And we are honored to have the Full Committee Chairwoman, Ms. Johnson, with us today, and the Chair now recognizes the Chairwoman for an opening statement.

Chairwoman JOHNSON. Well, thank you very much, and good morning. Let me thank you for holding this hearing today and thank all of our witnesses for joining us this morning. Dr. Abdool Karim, I understand you are halfway around the world right now, so good evening to you.

Today's hearing could not be more timely. The United States has already made incredible strides in making safe, accessible vaccines available to all adults. Just this week, the FDA (Food and Drug Administration) extended an authorization for 12- to 15-year-olds to receive the Pfizer vaccine. And I understand that some of our basic science research was performed at one of our national laboratories, the home of one of our witness's laboratory. These scientific achievements were a gift to the world, and they've already saved millions of lives, and they will save millions more.

In the United States, every teenager and adult now has access to the tools they need to protect themselves and loved ones. We must not squander this gift. We have no time to waste because viral variants are threatening the progress the United States has made toward defeating COVID-19. In recent weeks, one variant has brought the entire nation of India to its knees. And the longer the COVID-19 persists around the globe, the more mutations will emerge. Pandemics know no borders. An emerging variant anywhere is a public health threat everywhere, as you have said, Mr. Chair.

Our witnesses today will help us understand how emerging variants make it even more urgent to vaccinate fast, not just in the United States, but across the globe. I also look forward to hearing about the scientific tools we can use to spot a variant. The Federal Government supports an impressive range of infectious diseases—disease modeling, data sharing, and surveillance activities. We know now that these programs should have been coordinating more closely before the pandemic. A 2016 White House report offered a roadmap for exactly that: stitching together science activities across a dozen different agencies to enable better models of how diseases spread and change. Unfortunately, we did not get far enough on implementing these recommendations before COVID-19 reached our shores.

But it isn't too late to continue to improve the Federal approach to disease forecasting and surveillance for this present-day crisis. We can deploy our best Federal science capabilities to detect and understand variants as early as possible. This helps public officials and healthcare providers have the quality information they need to protect and save lives.

Thank you, Subcommittee Chairman Foster and Ranking Member, for putting together this timely discussion, and I yield back.

[The prepared statement of Chairwoman Johnson follows:]

Good morning and thank you to our witnesses for joining us this morning. Dr. Abdool Karim, I understand you are halfway around the world right now, so good evening to you.

Today's hearing could not be more timely. The United States has already made incredible strides in making safe, accessible vaccines available to all adults. Just this week, the FDA extended an authorization for 12- to 15-year-olds to receive the Pfizer vaccine. I understand that some of the basic science research performed at Argonne National Laboratory, home to one of our witnesses today, was a foundational part of creating mRNA vaccines. These scientific achievements were a gift to the world. They have already saved millions of lives, and they will save millions more. In the United States, every teenager and adult now has access to the tools they need to protect ourselves and our loved ones.

But we must not squander this gift.

We have no time to waste, because viral variants are threatening the progress the United States has made toward defeating COVID-19. In recent weeks, one variant has brought the entire nation of India to its knees. And the longer COVID-19 persists around the globe, the more mutations will emerge. Pandemics know no borders; an emerging variant anywhere is a public health threat everywhere. Our witnesses today will help us understand how emerging variants make it even more urgent to vaccinate fast—not in just the United States, but across the globe.

I also look forward to hearing about all the scientific tools we can use to spot a variant. The federal government supports an impressive range of infectious disease modeling, data sharing, and surveillance activities. We know now that these programs should have been coordinating more closely before the pandemic. A 2016 White House report offered a roadmap for exactly this: stitching together science activities across a dozen different agencies to enable better models of how diseases spread and change. Unfortunately, we did not get far enough on implementing those recommendations before COVID-19 reached our shores.

But it isn't too late to continue to improve the federal approach to disease forecasting and surveillance for this present-day crisis. We can deploy our best federal science capabilities to detect and understand variants as early as possible. This helps public officials and healthcare providers have the quality information they need to protect the public and save lives.

Thank you Subcommittee Chairman Foster and Ranking Member Obernolte for putting together this timely discussion. I yield back.

Chairman FOSTER. Thank you. And if there are any Members who wish to submit additional opening statements, your statements will be added to the record at this point.

At this time, I'd like to introduce our witnesses. Our first witness is Dr. Salim Abdool Karim. Dr. Abdool Karim is a clinical infectious disease epidemiologist who has played a leading role in the global COVID-19 pandemic response. He is Director for the Center for AIDS—the AIDS Programme of Research in South Africa, CAPRISA, and CAPRISA Professor of Global Health at Columbia University. Dr. Abdool Karim is also one of the nine members of the World Health Organization's Science Council. His contributions during the pandemic have focused on the epidemiology of SARS-CoV-2 variants, including their impact on vaccine and natural immunity.

Next is Dr. Nathan Grubaugh, Associate Professor of Epidemiology at the Yale School of Public Health and head of the Grubaugh Lab where he studies virus emergence, transmission, and evolution. During disease outbreaks, his lab sequences viruses for epidemiological investigations, determines the disease phenotype and transmission fitness of novel virus mutations, and maps the evolutionary pathways that a virus may take to adapt.

Our third witness is Dr. Stephen Streiffer. Dr. Streiffer holds several positions at Argonne National Laboratory in the Illinois 11th District I might add, including Deputy Laboratory Director for Science and Technology. He is one of the founding Co-Chairs of the National Virtual Biotechnology Laboratory, or NVBL, a consortium

of DOE national labs founded to address the COVID-19 crisis. The NVBL has used their scientific and technical expertise to address medical supply shortages, discover potential drugs to fight the virus, develop and verify COVID-19 testing methods, model disease spread and impact across the Nation, and understand virus transport in buildings and in the environment.

Our final witness is Dr. Caitlin Rivers, Senior Scholar at the Johns Hopkins Center for Health Security and an Assistant Professor in the Department of Environmental Health and Engineering at Johns Hopkins Bloomberg School of Public Health. She's an epidemiologist specializing in emerging infectious diseases and has anchored or contributed to several reports on COVID-19 variants and the national pandemic strategy. Her research focuses broadly on improving public health preparedness and the response to large-scale events.

And, as our witnesses should know, you'll each have five minutes for your spoken testimony. Your written testimony will be included in the record for the hearing. And when you've all completed your spoken testimony, we will begin with questions and each Member will have five minutes to question the panel.

If time allows, we may have a second round of questioning. In addition, if there is interest in—among the Members at the close of the hearing, may—we may turn off the livestream and have an informal discussion with the panelists, something we do under normal circumstances and is possible also here.

We will now start with Dr. Abdool Karim, so you are now recognized for five minutes.

**TESTIMONY OF DR. SALIM ABDOOL KARIM,
DIRECTOR OF CAPRISA**

Dr. ABDOOL KARIM. Thank you very much, Chairman Johnson. It's indeed an honor for me to be here and provide some testimony. I submitted a slide set. I'm going to ask for that to be projected.
[Slide follows:]

SARS-CoV-2 variants: Implications for public health and the Covid-19 endgame

House Committee on Science, Space, and Technology, Subcommittee on Investigations & Oversight
Hearing on “COVID-19 Variants and Evolving Research Needs”, May 12, 2021

Salim S. Abdool Karim, FRS

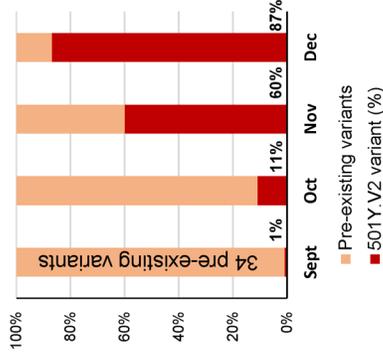
Director: CAPRISA – Center for the AIDS Program of Research in South Africa
CAPRISA Professor of Global Health, Mailman School of Public Health, Columbia University
Adjunct Professor in Immunology and Infectious Diseases, Harvard University
Adjunct Professor of Medicine: Cornell University
Pro Vice-Chancellor (Research): University of KwaZulu-Natal
Member: African Task Force for Coronavirus

Dr. ABDOOL KARIM. I speak to you from South Africa where I am based at—and the Nelson R. Mandela School of Medicine at an NIH- (National Institutes of Health-) funded research center. I'm actually at ground zero where one of the world's most concerning variants was first described. So I'm going to briefly touch on the variants. I want to talk about the implications for public health and the COVID-19 end game. Next slide.

[Slide follows:]

SAR-CoV-2 variants: why do they occur?

B. 1.351 becomes predominant within 3 months in South Africa



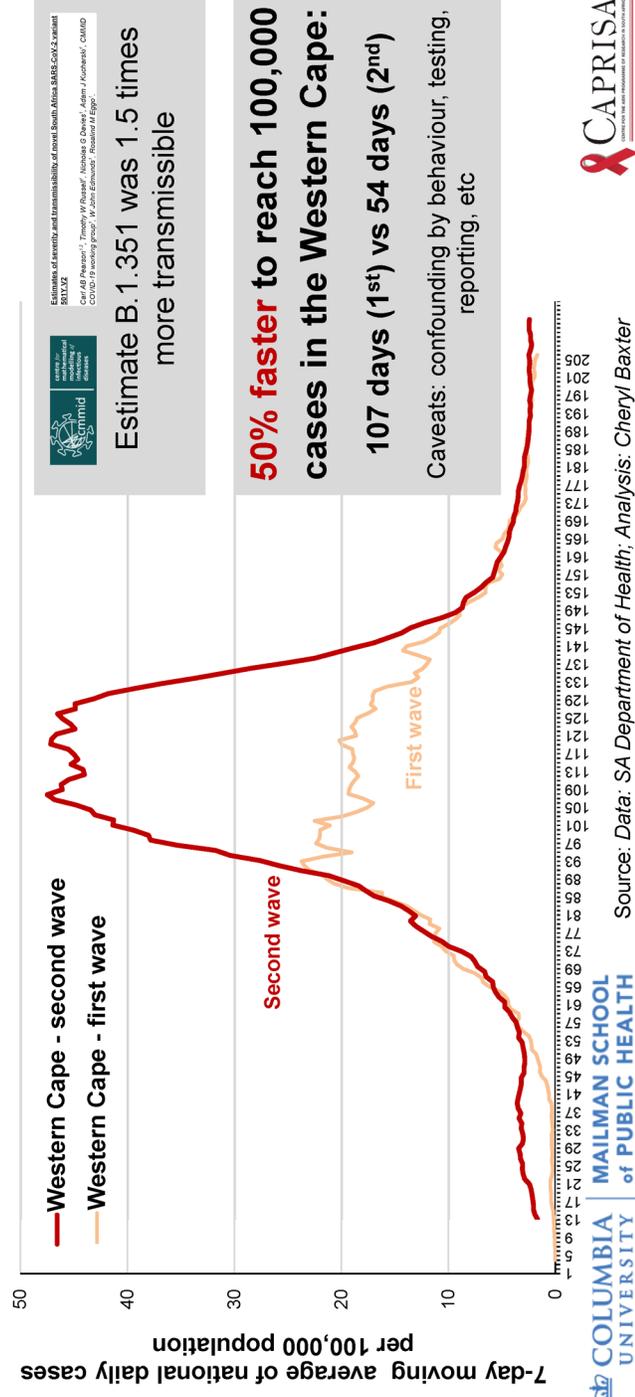
- SARS-CoV-2: slow genetic drift of 1-2 mutations per month
- Occasionally, a genetic shift with many mutations - leads to a new variant
- Persistent long-term active infection in immunocompromised individuals is an important source of new variants
- Immunocompromised individuals with past infection, Ab treatment or vaccination → variants with immune escape
- Most new variants have no functional advantage and die off
- Sometimes a new variant has a functional advantage such as higher transmissibility that enables it to become dominant

Dr. ABDOOL KARIM. So briefly, we know that all viruses mutate. That's in the nature of evolution, the way in which their genetic changes occur. SARS-CoV-2 shows slow genetic drifts pretty much one to two mutations per month. I've been monitoring in South Africa the epidemic and the viruses, and we see just a handful of mutations each month. But in November last year we saw something different, not just the slow antigenic drift but a shift, a major new mutant with 23 different mutations. And to give you some idea of its advantage and its functional advantage that it obtained, I point you to the graph on the left-hand side. Initially, in September, we had 34 pre-existing variants that were transmitted. The next month the new mutation referred to as B.1.351, constituted 11 percent of all the viruses. A month later, November, it was 60 percent, and by December, 87 percent of all the viruses transmitted were this new variant B.1.351.

Next slide, please.

[Slide follows:]

Variant B.1.351 spreads 50% faster SARS-Cov-2 cases in 1st and 2nd waves in Western Cape, South Africa

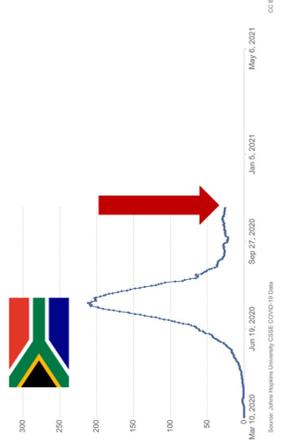
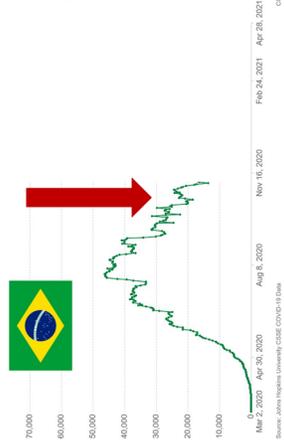
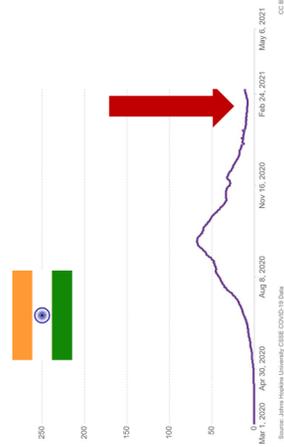


Dr. ABDOOL KARIM. And to give you some idea of what that has meant in comparing the first wave with pre-existing variants in the light yellow line you can see that the second wave, due to this new, more highly transmissible variant, the B.1.351 variant, is about 50 percent faster. If you just take one province in South Africa, Western Cape, it reached 100,000 cases within a matter of 54 days compared to the first wave where it took 107 days.

Next slide, please.

[Slide follows:]

Covid-19 1st wave in India, Brazil and South Africa



Dr. ABDOOL KARIM. And that translation of what we're seeing is if you take the three countries, India, Brazil, and South Africa, each of them in the first waves dealt with a pretty substantial wave, but what happened was as the epidemic settled, they all began to look at this epidemic in a different way.

Next slide.

[Slide follows:]

Misguided claims of “herd immunity” after the 1st wave

 **ARE SOUTH AFRICANS BECOMING IMMUNE TO COVID-19?**
14 September 2020

“...people in high-density areas have generated this immunity because of previous widespread exposure to common cold viruses....Professor xxx believes that between 40 and 45% of the population had already contracted the virus.... reaching the threshold required for herd immunity.”

23

 **Brazilian Amazon city of Manaus may have reached Covid-19 'herd immunity', study says**
25 September 2020

 **Herd Immunity in Sight for India's Capital?**
21 January 2021 2020
By Pavankumar Kamat

Dr. ABDOOL KARIM. And what we began to see was the—that each of these countries, they thought that they had conquered this virus. They had become immune, that they've developed some kind of protection from natural infection. We saw that in South Africa, we saw that in Brazil, we saw that in India.

Next slide.

[Slide follows:]

Covid-19 2nd wave with variants of concern in India, Brazil and South Africa



25

Past infection with pre-existing SARS-CoV-2 variants offers only limited protection against some new variants, possibly due to the 484 mutation.

Preliminary Covid-19 incidence (B.1.351 variant) in the South African Novavax trial: **5.3%** in 1,516 individuals with no past infection and **5.2%** in 674 individuals with past infection (seropositive at baseline)

Dr. ABDOOL KARIM. And what happened was complacency that set in, and this is what happened. In each of those settings, a new variant. In India, the B.1.617; in Brazil, the P.1 and P.2 variants; and in South Africa, the B.1.351 variant. And in South Africa the data we have shows quite clearly at this point that the B.1.351 variant was able to escape immunity that was acquired in the first wave. And so what we are seeing is reinfections occurring quite commonly in South Africa.

Next slide, please.

[Slide follows:]

Vaccine efficacy affected by variants

Clinical trials in:

USA / UK
Pre-existing variants

South Africa
B.1.351 variant

Substantial reduction in vaccine efficacy



NOVAVAX

70% (UK) → 89% (UK)



10% → 43%

Minimal reduction in vaccine efficacy



72% (USA) → 91-95% (USA)



64% → 100%

Qatar real world efficacy = 75%



Vaccine Breakthrough Infections with SARS-CoV-2 Variants

Ezgi Hacisuleyman, Ph.D., Caryn Hale, Ph.D., Yuhki Saito, Ph.D., Nathalie E. Blachere, Ph.D., Marissa Bergh, B.S.N., Erin C. Conlon, Ph.D., Punamit I. Chakrabarti, Ph.D., Thomas P. Flaxman, M.D., Emmanouil Mouton, Ph.D.



THE NEW ENGLAND JOURNAL OF MEDICINE



Source: Abdool Karim SS, et al. NEJM; 2021:10.1056/NEJMc2100362



B.1.1.7 doesn't impact vaccines.
Clinical studies on other variants and vaccine efficacy is ongoing.

Dr. ABDOOL KARIM. So if we look at where we are in terms of vaccines, that is perhaps the most concerning of the things that we see and that if you take the AstraZeneca vaccine with 70 percent efficacious in the U.K. but only 10 percent efficacious in South Africa. Novavax, 89 percent but only 43 percent. And we are seeing breakthrough variants. Fortunately, vaccines like the Johnson & Johnson (J&J) and the Pfizer vaccine have maintained their efficacy.

Next slide.

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Conclusion

- Expect more variants! No country is safe until every country is safe
- Maximal viral suppression needed to prevent the emergence and spread of new variants overcoming immunity from vaccination or past infection
- No single action is going to be sufficient to prevent the spread of the virus: Public health measures must be maintained in tandem with vaccination
- Need to strengthen genomic surveillance in many countries as the situation may be even more severe than it appears at present
- Next generation vaccines to elicit broadly neutralizing antibodies currently being developed are expected to overcome immune escape by variants

Dr. ABDOOL KARIM. And this is my last slide where I'll just make some parting comments that we should expect more variants, that no country is safe, as Chairman Johnson has pointed out so eloquently, until every country is safe, and that we need maximal suppression and that no single action is likely to be sufficient to prevent the spread of the virus. We're going to need our public health measures in addition to our vaccination programs. We need to strengthen genomic surveillance. And even though we are expecting next-generation vaccines to produce more broadly neutralizing antibodies and we expect they will impact on the escape variants, I suspect that we will continually see this virus finding ways to escape immunity.

Thank you very much, Chairman.

[The prepared statement of Dr. Abdool Karim follows:]

Testimonial for “COVID-19 Variants and Evolving Research Needs”

Salim S. Abdool Karim

Background

Currently there are multiple SARS-CoV-2 variants circulating across the world. These variants arise through natural variation, replication errors, cross-species transmission or immune pressure. Viruses with higher viral fitness and transmissibility are more likely to become dominant in the population. While most of variants are not a cause for concern, variants that acquire mutations in the functional parts of the virus, for example the receptor binding domain (RBD) of the spike protein, raise concerns. Accelerated changes leading to multiple mutations in the infecting virus have been observed in immunocompromised patients with persistent SARS-CoV-2 infection^{1,2}. In an immunosuppressed patient, who experienced persistent viral shedding over 154 days, the virus developed several genetic changes, especially in the spike gene and the RBD¹.

SARS-CoV-2 variants have been classified by the US Centers for Disease Control and Prevention (CDC) as variants of interest, variants of concern, and variants of high consequence. Until recently, there were three variants³ that had rapidly become dominant within their countries, that were classified as variants of concern; the B.1.1.7 (VOC-202012/01), B.1.351 (501Y.V2) and P.1 (B.1.1.28.1).

The B.1.1.7 variant (23 mutations with 17 amino acid changes) was first described in the UK on 14 December 2020, the B.1.351 variant (23 mutations with 17 amino acid changes) was initially reported in South Africa on 18 December 2020 while the P.1 variant (about 35 mutations with 17 amino acid changes) was reported on 12 January 2021 from Brazil. By 5 May 2021, the B.1.1.7, B.1.351 and P.1 variants have been reported in 114, 67 and 37 countries, respectively³. All three variants have the N501Y mutation that changes the amino acid asparagine (N) to tyrosine (Y) at position 501 in the RBD of the spike protein. Both the B.1.351 and P.1 variants have two additional RBD mutations K417N/T and E484K. These mutations increase binding affinity of RBD to the Angiotensin-converting enzyme 2 (ACE-2) receptor ACE2⁴.

In March 2021, another new variant, the CAL.20C (B.1.427 & B.1.429) variant, which was originally reported in California, was classified as the fourth variant of concern. The variant has one mutation in the RBD at position 452 (L452R) and 45% of current samples in California are this variant.

There are also several variants of interest, including: B1.525, B1.526, B.1.617 and P.2. The B.1.525 variant, which carries some of the same mutations as B.1.1.7, and the B.1.526 which carries the E484K or S477N mutation, has been spreading in New York. The B.1.617 is prevalent in India and carries the E484Q and L452R spike mutations, among its 13 other mutations. Emerging evidence from India suggests that B.1.617 spreads more rapidly and had been reported from 28 countries by May 3, 2021.

The emergence of these new variants raise four key concerns, viz. their impact on a) viral transmissibility, b) disease severity, c) reinfection rates (escape from natural immunity) and d) vaccine effectiveness (escape from vaccine-induced immunity).

Transmissibility

The variants of concern spread more easily and quickly than other variants, which may lead to more cases of Covid-19 in a shorter period. The B.1.351 variant has been estimated to be 50%⁵ more transmissible than pre-existing variants in South Africa, and B.1.1.7 to be between 43% and 82%⁶ more transmissible than pre-existing variants in the UK. The P.1 variant is estimated to be about 2.5 times more transmissible than pre-existing variants⁷, while the B.1.427 and B.1.429 variants are about 20% more transmissible⁸.

Disease severity

With regards to severity of the variants of concern, there is evidence in both directions. Hospital admission rates, clinical profile of admitted patients and hospital case fatality rates were similar in the first and second waves in South Africa. However, emerging evidence from the UK indicates that B.1.1.7 may be associated with an increased risk of death compared to pre-existing variants in the UK⁹. The variants may also indirectly increase mortality through their greater transmissibility, which rapidly overburdens health services, compromising access to, and quality of, hospital care. While there is no evidence that antivirals and anti-inflammatory treatments are affected, treatment with convalescent serum and monoclonal antibodies may no longer be effective¹⁰⁻¹².

Escape from natural immunity

With regard to escape from natural immunity, the B.1.1.7 variant showed a modest decrease in neutralization activity, by a factor of 1.5, whereas the B.1.351 variant showed complete escape from neutralizing antibodies in 48% of convalescent serum samples (21 of 44) obtained from patients who had previously had Covid-19¹³. A serendipitous finding from a vaccine trial in South Africa, in which 30% of the enrolled participants had previously been infected with SARS-CoV-2, was that the incidence of Covid-19, as confirmed on polymerase chain reaction, was 5.3% among seronegative enrollees and 5.2% among seropositive enrollees in the placebo group after 60 days of follow-up¹⁴. The P.1 variants also has reduced neutralization by convalescent sera¹⁵. For the B.1.427 and B.1.429 variants, antibody neutralization assays showed 4.0 to 6.7-fold decreases in neutralizing titres from convalescent patients¹⁶.

Escape from vaccine-induced immunity

Regarding escape from vaccine-induced immunity, the B.1.1.7, B.1.427 and B.1.429 variants showed modest decreases in neutralizing activity in serum samples obtained from vaccinated persons^{11,16-18}. The serum neutralizing activity for the B.1.351 variant among vaccinated persons was lower by a factor of 1.6 to 8.6 for the BBIBP-CorV vaccine¹⁹, the BNT162b2 vaccine¹⁷, and the mRNA-1273 vaccine²⁰ but was lower by a factor of up to 86, including complete immune escape, for the AZD1222 vaccine^{21,22}. Neutralizing activity for the P.1 variant among vaccinated persons was lower by a factor of 6.7 for the BNT162b2 vaccine²³ and by a factor of 4.5 for the mRNA-1273 vaccine. The clinical relevance of the lower neutralization activity for either mild or severe Covid-19 is not clear. Efficacy in clinical

trials was substantially lower for two of the four vaccines tested during transmission of the B.1.351 variant in South Africa than efficacy in trials conducted in countries with pre-existing variants.

Responses to questions from the committee

1. What is the state of data sharing among countries regarding variants developing and spreading across the globe?

There are a few different databases being used to load SARS-CoV-2 sequences onto the internet. The most widely used is a database known as GISAID. Since January 2020, more than 1.5 million SARS-CoV-2 sequences have been included in GISAID. Of the 93 countries that have had more than 100,000 Covid-19 cases, 19 countries have contributed more than 1% of their viral sequences, with 5 countries (Norway, Denmark, Japan, Switzerland and the UK) contributing more than 5% of their viral sequences.

GISAID doesn't allow sequences to be reshared publicly without due acknowledgement to the original source²⁴. While some researchers have regarded the GISAID processes of acknowledgement of sequence source as a hindrance, others consider it to be important acknowledgement of the scientific contributions of those who have provided the sequences. Other databases that also provide sequences on the internet such as the European Nucleotide Archive (ENA) and the NIH's *the* National Center for Biotechnology Information (NCBI) do not require acknowledgement of those who provided the original sequence. There are also websites that summarize data from these databases, such as <https://outbreak.info>, <https://covariants.org> and <https://cov-spectrum.ethz.ch>.

Researchers across the globe have free access to SARS-CoV-2 sequences from any of the databases providing genetic sequences on the internet. These databases are very widely used and provide a valuable repository for global information on the viruses; an essential requirement for future vaccine development.

2. Are existing vaccines efficacious in reducing the spread of known COVID-19 variants?

Some vaccines are highly effective against the variants of concern. For example, the efficacy of the Johnson & Johnson (J&J) vaccine was consistent across multiple variants including two variants of concern. It was 72% efficacious in the US (n=17,793; D614G variant), 68% efficacious in Brazil (n=6,666; P.2 variant) and 64% efficacious in South Africa (n=4,912; B.1.351 variant)²⁵. Similarly, the Pfizer–BioNTech vaccine, which was shown to be >90% effective against pre-existing variants, has been shown in a study in South Africa to also be >90% effective against the B.1.351 variant²⁶. Data from Qatar, which implemented a large-scale vaccination programme in the presence of the B.1.1.7 and B.1.351 variants shows that the Pfizer–BioNTech vaccine was 90% effective against the B.1.1.7 variant and 75% effective against the B.1.351 variant²⁷. Further, the Pfizer–BioNTech vaccine effectiveness in Qatar against the B.1.1.7 and B.1.351 variants for severe, critical, or fatal disease was very high, at 97.4%²⁷.

On the other hand, some vaccines have reduced efficacy in the presence of variants of concern. The efficacy of the AstraZeneca vaccine 70% in the UK (D614G variant) but only 10% efficacious against the B.1.351 variant in South Africa^{28,29}. Similarly, the Novavax vaccine was only half as efficacious against the B.1.351 variant as it was 89% efficacious in the UK compared to 43% in South Africa¹⁴. Unfortunately, the South African studies of the AstraZeneca and Novavax vaccines predominantly included young people and so had no cases of severe disease. Hence, there is no clinical evidence on whether these vaccines that have minimal, if any, efficacy for mild / moderate disease due to the B.1.351 variant of concern have any efficacy for severe disease. Some speculate, drawing upon indirect evidence, that even though some of the vaccines such as AstraZeneca are not effective in preventing asymptomatic, mild or moderate infections due to B.1.351, they may still prevent severe disease from B.1.351 infections, there is no clinical evidence for this conclusion.

3. What role do vaccines play in reducing the spread of existing variants and the emergence of new variants?

The vaccines play a critical role in suppressing viral replication which in turn reduces the risk of emergence of variants. However, the use of vaccines creates immune pressure on the virus, especially if there is persistent viral replication. In immunocompromised individuals there is the risk of new variants emerging². If these immunocompromised individuals were vaccinated or received monoclonal antibody treatments, their persistent viral replication may lead to immune escape mutations. If such mutations enhance escape from vaccine-induced immunity, the vaccines would be rendered less effective.

The Covid-19 pandemic has illustrated that no single action is sufficient to prevent the spread of the virus. Strong public health measures against the virus must be maintained in tandem with global vaccination programs to achieve the goal of maximum suppression (see Lancet commission on Covid-19 report "SARS-CoV-2 variants: the need for urgent public health action beyond vaccines" - Annexure 1).

For viruses to succeed in spreading in a highly vaccinated population, they would need to evade vaccine-induced immunity. The current variants with predominant mutations in the receptor binding domain at positions 501, 484, 417 and 452 predate widespread availability of vaccines as most originated between October and December 2020. Over the coming months we can reasonably expect new variants to emerge that are able to escape vaccine-induced immunity because the virus is being put under pressure from widescale vaccination at present. This creates a catch-22 situation; when vaccinations are being scaled-up while viral transmission is high, as is occurring in the US and Brazil, SARS-CoV-2 has a higher likelihood of acquiring escape mutations potentially undermining the vaccine efficacy. On the other hand, one of the most effective ways to decrease transmission is to scale-up vaccination. Within this catch-22 situation, slowing viral transmission and decreasing viral replication is paramount and supersedes concerns about variants. Hence, vaccination in the presence of high transmission is strongly recommended at this time.

4. What does the regular emergence of new COVID-19 variants tell us about the need to vaccinate the global population in order to protect the U.S.?

Although the development of these vaccines provides hope that we can begin to control the spread of SARS-CoV-2, the inequitable distribution and availability of vaccines across the world casts doubt on how rapidly, and even if, some measure of global epidemic control will be achievable. Currently, 77% of all vaccine doses have been administered in just 10 countries (the US, China, India, the UK, Brazil, Turkey, Germany, Indonesia, France and Russia), while some countries are yet to start their SARS-CoV-2 vaccination programs. From a policy and public health perspective, global equitable access to a vaccine, particularly prioritizing protection of healthcare workers and the elderly, is the key to mitigating the worldwide public health and economic impact of the pandemic. Unfortunately, vaccine nationalism has resulted in unequal distribution of and access to SARS-CoV-2 vaccines. The Director-General of the World Health Organization (WHO), Tedros A. Ghebreyesus, has cautioned about this issue, saying “the world is on the brink of a catastrophic moral failure”.

The spread of SARS-CoV-2 in one part of the world affects all parts of the world due to extensive global connections. Even for a country with high vaccination rates, if neighboring countries have ongoing high rates of viral transmission as they have not been able to vaccinate so widely or rapidly, new outbreaks could occur and new variants could spread when the populations interact. Defeating the pandemic requires global control, which can only be achieved through the equitable global distribution of vaccines.

In addressing this problem early in the pandemic, the WHO, in collaboration with its partners, launched the Access to Covid-19 Tools (ACT)-Accelerator partnership, which supports efforts to develop tools including diagnostics, treatment, vaccines and health system strengthening to fight Covid-19. The vaccine pillar of the ACT-Accelerator initiative is known as COVAX. Initiated in April 2020 by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI) and the WHO, COVAX is a global mechanism that invests in the development, manufacturing, procurement and distribution of Covid-19 vaccine candidates, offering member countries equitable access, regardless of income level, to successful vaccines as they become available. At present, the goal of COVAX is to provide countries with enough doses to cover 20% of their populations.

The inequitable distribution of resources significantly undermines the effective management and control of the pandemic. This concern is not hypothetical or theoretical; it was demonstrated by the actions of individual states in the US in March 2020 regarding PPE and ventilators. During that period, the absence of a centralized federal government procurement strategy for these items meant that US states were competing against each other, against the federal government and even against cities to procure the necessary equipment. This resulted in prices being driven up and PPE and ventilators being distributed on the basis of available resources, rather than need, and failure to ensure equitable and effective distribution. Such maldistribution of essential Covid-19 resources leads to the loss of lives.

Exactly the same is true of vaccines. At present there is a limited number of vaccines on the market. As such, supply is fixed, and current models predict that there will only be enough vaccines to cover the world's population by 2023. Countries that can afford to pay higher prices can enter bilateral deals with pharmaceutical companies and negotiate to jump the queue. By doing so, they remove vaccines from the available pool and end up limiting vaccine allocations to other countries, which undermines the objective of systematically vaccinating the highest number of people across the globe in the shortest period of time.

According to the Duke Global Health Innovation Center, to date high-income countries have secured 4.7 billion doses, upper-middle-income countries have secured 1.5 billion doses, lower-middle-income countries have secured 731 million doses and low-income countries have secured 770 million doses. Some low- and middle-income countries (LMICs) with vaccine manufacturing capacity, such as India and Brazil, and those with the infrastructure to host clinical trials, such as Peru, have used those assets as leverage to negotiate purchase deals. However, most LMICs have not been able to secure enough vaccines.

Pharmaceutical companies, with the exception of J&J, have not adopted a single exit price for their SARS-CoV-2 vaccines. The prices are therefore open to market forces, especially as the use of non-disclosure agreements means that these companies can prevent differential pricing from become public. More demand, especially from countries under significant pressure to buy vaccines, means higher prices. High-income countries with large buying capacity are able to pay higher prices, again pushing lower income countries out of the equation and furthering inequitable distribution.

Vaccine nationalism and the hoarding of vaccines is a consequence of limited supplies. Unfortunately, SARS-CoV-2 vaccines are currently manufactured by just a handful of companies. However, there are vast capabilities throughout the world to manufacture vaccines. For example, in Africa, companies like Biovac and Aspen in South Africa, Institute Pasteur in Senegal and Vacsera in Egypt could rapidly adapt to start making SARS-CoV-2 vaccines if provided with the funding, IP rights and know-how. The reliance of LMICs on others for the development of vaccines as well as diagnostic technologies has also highlighted the dire need for these countries to increase local investments in science and technology to build self-sufficiency and enhance their capacity to control pandemics.

There is a mistaken belief by some countries that they can vaccinate their populations and then they will be safe. This simply is not true. There is no endgame that sees one country achieving sustained control of the virus while the rest of the world is dealing with rampant spread. In the Covid-19 pandemic, no-one is safe until everyone is safe. This pandemic has highlighted the inter-dependence between individuals, between communities and between countries. Each person's risk of infection is influenced as much by the actions of others as it by their own actions. The antidote to vaccine nationalism is the recognition and appreciation of our mutual inter-dependence and the need to act with all our humanity to seek a just and equitable approach to vaccine access to overcome this pandemic.

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Annexure 1:

Lancet commission on Covid-19 report "SARS-CoV-2 variants:
the need for urgent public health action beyond vaccines"

THE *LANCET* COVID-19 COMMISSION
TASK FORCE ON PUBLIC HEALTH MEASURES
TO SUPPRESS THE PANDEMIC

SARS-CoV-2 variants: the need for urgent public health action beyond vaccines

MARCH 2021



The *Lancet* COVID-19 Commission

Task Force on Public Health Measures to Suppress the
Pandemic



THE *LANCET*
COVID-19 COMMISSION

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KEY POINTS

1. SARS-CoV-2 variants of concern have emerged simultaneously in many countries, including the highly transmissible variant B.1.351, now present in at least 46 countries.
 2. Lack of capacity for genomic surveillance in many countries, including some higher income countries, means that the situation may be even more serious than it appears.
 3. No one is safe until everyone is safe. We are in a race against time to get global transmission rates low enough to prevent the emergence and spread of new variants overcoming immunity conferred by vaccination and prior disease.
 4. Differences in the effectiveness of vaccines in providing immunity to variant B.1.351 raises the concern that current vaccines may be less effective against new and emerging variants.
 5. No single action is sufficient to prevent the spread of the virus: strong public health measures against the virus must be maintained in tandem with global vaccination programs.
 6. Conducting clinical trials of vaccines for every highly transmissible variant as it emerges is impracticable given the time needed to conduct them. We urgently need to identify biomarkers that can accurately predict vaccine protection against infection, disease and death.
- They are more easily passed from one individual to the next, which has potential implications for public health measures and for health system preparedness (given infections and hospitalizations occur more rapidly); and
 - They can lead to more severe disease, which has implications for health system preparedness.
- There are currently at least three documented SARS-CoV-2 variants of concern:
- B.1.351, first reported in South Africa in December 2020;
 - B.1.1.7, which was first reported in the U.K. in December 2020;
 - P.1, which was first reported in Brazil and Japan.
- Experience in South Africa suggests that:
- Past infection with SARS-CoV-2 offers no or only very weak protection against the B.1.351 variants;
 - The AstraZeneca vaccine-generated antibodies have up to an 86-fold reduction in neutralizing activity and 3.2-fold lower (70% vs 22%) clinical efficacy against mild to moderate illness for B.1.351; and
 - The B.1.351 variant is about 50% more transmissible compared to pre-existing variants.

which has significant potential implications for what current vaccination programs can achieve;

THE PROBLEM

At the end of 2020, there was strong hope that a global vaccination programme would render SARS-CoV-2 an endemic virus that could be contained at very low levels without further societal disruption or significant numbers of deaths. However, SARS-CoV-2 variants of concern have emerged and spread around the world, which means that current pandemic control efforts, including vaccination, are threatened.

Genetic mutations of viruses like SARS-CoV-2 emerge frequently, but some variants are labelled “variants of concern” because they have one or more of the following features:

- They can ‘re-infect’ people who already have antibodies from a previous infection and they can infect people who have already been vaccinated,

The B.1.351 variant has already been detected in at least 46 countries, including in the U.S.

If there are high levels of transmission and hence of replication of SARS-CoV-2 anywhere in the world, there will be more variants of concern, with the more infectious variants dominating. With international mobility, these variants will spread. Similar mutations are occurring in different countries simultaneously, meaning that not even border controls and high vaccination rates can protect individual countries from home-grown variants, including variants of concern, where there is substantial community transmission. Reducing community transmission is therefore paramount.

NEED FOR URGENT ACTION

1. **Maximum suppression:** Public health leaders should focus on efforts that maximally suppress viral infection rates and hence preventing the emergence of mutations that can become new variants of concern (each time the virus replicates there is an opportunity for a mutation to occur), through a combination of vaccination and continued public health and behavioural measures (such as facemasks and physical distancing).
2. **Global equity in vaccine access:** High-income countries should support multilateral mechanisms such as COVAX vaccines and donate excess vaccine to low and middle income countries. They should strengthen laboratory research globally, enable and accelerate knowledge transfer and sharing of intellectual property. While equitable access is an important global goal, there is an overarching imperative to reduce the emergence of viral variants of concern, and this may necessitate prioritising those countries or locations with highest disease prevalence and levels of transmission, where the selective pressure and the rate of mutation are likely to be greatest.
3. **Strengthen public health and behavioural interventions:** in all countries to reduce the risk of further dangerous variants.
4. **Capacity to accommodate surges in demand for healthcare:** Health system leaders need to mobilise and support health professionals and manage increased hospitalizations over shorter periods during surges, without reducing care for non-COVID patients.
5. **Preparedness:** Suppression of viral infection rates and health system efforts need to be accompanied by:
 - Genomic surveillance programmes to identify and quickly characterize emerging variants in as many countries as possible around the world;
 - Rapid large-scale 'second-generation' A vaccine programmes and increased production capacity that can support equity in vaccine distribution across and within countries;
 - Studies of vaccine effectiveness in relation to existing and new variants of concern (ideally using biomarkers in laboratory studies and rapid clinical studies that yield results quickly) and living syntheses of these studies that derive implications for vaccine choice, combinations and re-vaccination;
 - Monitoring of the ability of diagnostic tests to reliably identify new variants;
 - Evaluation studies that examine need for adaptation to public health measures (e.g., double masking, duration of quarantine, approach to and frequency of testing) and to health system arrangements (e.g., hospital and long-term care visitor policies, personal protective equipment (PPE), sharing of room or ward by two or more patients who are infected with the same microorganism, Heating Ventilation and Air Conditioning systems, and surge capacity).

Biography

Salim S. Abdool Karim, M.D., Ph.D., FRS

Salim S. Abdool Karim, MBChB, MMed, MS(Epi), FFPHM, DipData, PhD, DSc(hc) is a public health physician and clinical infectious diseases epidemiologist who has played a leading role in the global HIV and Covid-19 pandemic response. He is Director of the Center for the AIDS Program of Research in South Africa (CAPRISA), Durban, and CAPRISA Professor of Global Health at Columbia University, New York.

He is an Adjunct Professor of Immunology and Infectious Diseases at Harvard University, Adjunct Professor of Medicine at Cornell University, and Pro Vice-Chancellor (Research) at the University of KwaZulu-Natal, Durban, South Africa. He is an Associate Member of The Ragon Institute of Massachusetts General Hospital (MGH), Massachusetts Institute of Technology (MIT) and Harvard University. He previously served as President of the South African Medical Research Council (MRC).

He is one of the nine members of the World Health Organization's Science Council. He has been actively contributing to the mitigation of the COVID-19 epidemic in Africa, serving as a Member of the Africa Task Force for Coronavirus. He served as the Chair of the South African Ministerial Advisory Committee on COVID-19 for the first year of the epidemic. He is a Commissioner of the Lancet Commission on COVID-19.

He graduated as a medical doctor in 1983 from the University of Natal's medical school in Durban, South Africa. While at medical school he concurrently studied computer science and statistics by correspondence at the University of South Africa. He joined the Department of Virology at the University of Natal in 1986, to start his doctoral research on hepatitis B viral infection. In mid-1987, he went to New York on a Rockefeller fellowship to pursue a Masters in Epidemiology at Columbia University. During 1988, he also studied health economics at London School of Hygiene and Tropical Medicine and methods of epidemic investigations at the Centers for Disease Control (CDC) in Atlanta, USA. He completed his Fellowship in Public Health Medicine with the College of Medicine, South Africa and simultaneously graduated with a Masters in Medicine degree in Community Health from the University of Natal in 1992. He then joined the MRC and in 1993, was appointed as Director of the MRC's Centre for Epidemiological Research in South Africa (CERSA) and completed his PhD in 1999.

His main research interests are in HIV prevention, treatment of HIV-TB co-infection as well as Covid-19 prevention and treatment. His most impactful research contribution in HIV prevention was the CAPRISA 004 tenofovir gel trial, that he co-led, which provided the first evidence for the concept of antiretroviral pre-exposure prophylaxis against HIV infection. The finding has been heralded by UNAIDS and WHO in 2010 as one of the most significant scientific breakthroughs in the fight against AIDS and has been ranked among "The Top 10 Scientific Breakthroughs of 2010" by *Science*. This study also discovered that tenofovir gel prevents herpes simplex virus type 2 infection in women, the first biological prevention agent against genital herpes. He also led the team that provided the empiric evidence for the "Cycle of HIV Transmission" where young girls are most often infected by men about 10 years older. These findings provided the evidence for the UNAIDS Report "Get on the Fast-Track - The Life-Cycle approach to HIV", which has influenced the HIV response in several African countries and is listed as the highest priority in the current South African National AIDS Plan. In the field of HIV vaccines, he is co-inventor on patents which are part of HIV vaccine candidates and CAP256-VRC26.25, a highly potent broadly neutralizing antibody that is being developed for passive immunization as a prelude to future HIV vaccine development. His research on HIV-TB treatment was adopted in the WHO treatment guidelines of this co-infection and has been implemented in most countries. These significant findings have had a marked impact on HIV prevention and TB-HIV treatment in Africa and globally.

His contributions in Covid-19 have focused on the epidemiology of SARS-CoV-2 variants, including their impact on vaccine and natural immunity. His research has also assessed the impact of Covid-19 on HIV and tuberculosis.

Professor Abdool Karim's scientific contributions include over 400 peer-reviewed journal publications, including original contributions and editorials in *Science journals* (14), *Nature journals* (10), *New England Journal of Medicine* (8), and *The Lancet* (35). He is co-editor of an Epidemiology textbook (Oxford University Press), a book on HIV/AIDS in South Africa (Cambridge University Press) and a book on HIV Clinical Trials (Springer).

He is one of the world's most highly cited researchers – being listed on the Web of Science's Clarivate Analytics annual list of the world's six thousand most influential researchers by citations in the sciences and social sciences since 2018. He has 79 papers with more than 50 citations, 42 of which have been cited over 100 times – an H-index of 63. His most highly cited journal article, jointly first-authored with Quarraisha Abdool Karim (*Science* 2010; 329: 1168-1174), exceeds 1900 citations.

He is a member of the Editorial Board of the *New England Journal of Medicine*. He serves on the International Advisory Boards of *Lancet HIV* and *The Lancet - Global Health*. He is also a member of the Editorial Boards of *Journal of AIDS*, *AIDS Research and Human Retroviruses*, *HIV and Infectious Diseases*, and *AIDS Reviews*. He also previously served as a member of the Board of Reviewing Editors of *mBio*, *eLife*, as Associate Editor for *AIDS Clinical Care* and Corresponding Editor for the *International Journal of Infectious Diseases*. He has served as a Reviewer for more than 40 scientific journals.

He is an elected Fellow of the Royal Society. He is an elected Member of the US National Academy of Medicine. In addition, he is a Member / Fellow of the American Academy of Microbiology, Association of American Physicians (AAP), The World Academy of Sciences (TWAS), African Academy of Sciences (AAS), Academy of Science in South Africa (ASSA) and the Royal Society of South Africa (RSSA).

Salim S. Abdool Karim has made major contributions to global HIV policy and is actively involved in a range of initiatives that promote evidence-based science amongst policy makers as well to students and the general public. He has advised governments and international agencies in AIDS and global health such as the WHO, UNAIDS, PEPFAR and the Global Fund to fight AIDS, TB and Malaria. He served as the Chair of the UNAIDS Scientific Expert Panel and as a member of the UNAIDS-Lancet Commission on "Defeating AIDS" and co-authored the report, published in June 2015 in the *Lancet*, that mapped out a future direction for the global AIDS response. He is currently the Chair of the WHO Strategic and Technical Advisory Committee for HIV and Hepatitis, and a member of the WHO HIV-TB Task Force. He is a Member of the Board of the Population Council. He is a member of the Scientific Advisory Board for Global Health at the Bill and Melinda Gates Foundation.

His contributions in AIDS have been recognized nationally and internationally through several prestigious awards. He received the most prestigious scientific award in Africa - the African Union's "Kwame Nkrumah Continental Scientific Award". His other international awards include Kuwait's "Al-Sumait Prize" for research contributing to African development, the John Dirks Canada Gairdner Health Award, the "Lifetime Achievement Award" from the Institute of Human Virology, the DIA - Drug Information Association's "President's Award for Outstanding Achievement in World Health", the African Academy of Science's "Olusegun Obasanjo Prize for Scientific Discovery and Technological Innovation", Columbia University's "Allan Rosenfield Alumni Award", the "Outstanding Senior African Scientist Award" from the European Union – Developing Countries Partnership, and the "TWAS Prize in Medical Sciences" from The World Academy of Sciences (TWAS). He has also been awarded the "Distinguished Scholar Award" from the Biomedical HIV Prevention Forum of Nigeria, and the USAID "Science and Technology Pioneers Prize" (awarded to the CAPRISA 004 team) from US Agency for International

Development. In South Africa, he has received the MRC's "Platinum Medal Lifetime Achievement Award", "Gold Medal Award for Fellowship in the Art & Science of Medicine" from the South African Medical Association, the "John F. W. Herschel Medal" from the Royal Society of South Africa and the "Science for Society Gold Medal Award" from the Academy of Science in South Africa. He has been ranked as being among the 50 all-time "Legends of South African Science" by the Academy of Science of South Africa.

He has also been recognized for his broader contributions to society beyond his research through the "Hero in Medicine" Award from the International Association of Physicians for AIDS Care (IAPAC) and the "Men's Health Award" in the Science & Technology category from Men's Health magazine.

With regard to Covid-19, he was the joint recipient, with Dr Anthony Fauci, of the 2020 Sir John Maddox Prize (by Nature and Sense about Science) in recognition of his "achievements as going beyond the line of duty of government advisors on health policy, to communicate accurate medical advice to the public and policymakers during the Covid-19 pandemic – a contribution to society that surpasses even his work on HIV." Together with Dr Fauci (USA) and Dr Anders Tegnell (Sweden), he was one of the three chief government scientific advisors on Covid-19 profiled in the journal, Nature. He was invited to deliver a Keynote presentation at the Opening Special Session of the 1st International Covid-19 Conference in July 2020.

In summary, Professor Abdool Karim has had a profound impact through his HIV scientific discoveries and his leadership in both AIDS and Covid-19 in South Africa, Africa and globally.

Chairman FOSTER. Thank you. And next we will recognize Dr. Grubaugh for five minutes.

**TESTIMONY OF DR. NATHAN GRUBAUGH,
ASSISTANT PROFESSOR OF EPIDEMIOLOGY**

Dr. GRUBAUGH. Thank you, Chairman Foster and Members of the Subcommittee, for the invitation to discuss SARS CoV-2 variants. I am a virologist and molecular epidemiologist. That is, I use virus genome sequencing and molecular diagnostic assays to study the emergence and spread of infectious diseases. I helped to develop the SARS-CoV-2 genomic surveillance system for the State of Connecticut and I worked directly with the CDC (Centers for Disease Control and Prevention) and other regional and international partners to investigate the emergence of SARS-CoV-2 variants.

Surveillance is one of our most important tools for public health. Almost all major policy decisions rely on data informing the spread and incidence of an infectious disease. And it's not just local surveillance. We need global surveillance to inform as to what may be coming next. For example, surveillance from South Africa, Brazil, India, and the U.K. have provided critical information about what variants may be introduced into the United States, which is in addition to the variants that may emerge within our own borders.

While sequencing COVID-19 cases in the United States is increasing, there are still many regions in the world of which we have little or no SARS-CoV-2 genomic information. These gaps lead us into the dark what—as to what variants may be emerging in those locations and what could be a threat to the United States. Local surveillance systems detect variants by the pattern of specific mutation of each sequence virus, which we then use to assigned to a numbered lineage, such is B.1.1.7, B.1.351, P.1, et cetera. These data are then used to detect the introductions and track the frequencies of known or novel variants.

Our national and international surveillance systems are then reliant on SARS-CoV-2 genomic sequencing data to be submitted to public repositories. GISAID (Global Initiative on Sharing All Influenza Data) is the most popular repository which currently contains about 1.5 million sequences from around the world. From there, bioinformaticists and public health agencies and independent groups routinely poll the data to provide global, national, and regional reports on variants. This allows all of us to keep up-to-date on what is happening.

But there are some major challenges to variant surveillance. One is that it mostly requires the use of whole genome virus sequencing, a method that is far more expensive and technical than conventional clinical testing. There are some simpler tests, similar to what we use for clinical diagnostic testing, that are used to help us to track the frequency of variants. For example, a PCR (polymerase chain reaction) test has been used to track the rapid spread of B.1.1.7 in the United States. These simpler tests, however, are limited in what they can detect. It's hard for them to detect something that is novel. So while useful, they are not a replacement for sequencing.

Another challenge is the need for individual labs to share their data on public repositories. While data sharing is critical to our surveillance efforts, there are several barriers, especially in low-resource settings. These include technical barriers to data transfers to online repositories, lack of important information connected to the sequences needed for public health, lack of incentives to make expensive-to-generate genomic data available to the public versus keeping them for their own research, and international responses to publicly submitted data such as naming a variant after a location or the implementation of travel restrictions.

Here provides an opportunity for the U.S. Government to help. We need policies around pathogen genomic data sharing and usage for public health surveillance. These should include incentives to share and also protections for data generators to have the first right to publish. These policies should also be accompanied by standards for data generation, standards for data processing, and standards for analysis to help minimize sampling biases and eliminate data processing errors.

Finally, these policies should support the work of pathogen genomic surveillance of all types not just during a public health emergency. Without sustained support, the important work that we started here could fold. Rather, our genomic surveillance system should remain intact and only ramp up or ramp down depending on the need.

Thank you for your time, and I hope that I can answer any questions that you may have.

[The prepared statement of Dr. Grubaugh follows:]

Nathan D. Grubaugh, PhD
Assistant Professor of Epidemiology
Yale School of Public Health

Expert testimony presented to the House Committee on Science, Space, and Technology, Subcommittee on Investigations & Oversight during the remote hearing titled "COVID-19 Variants and Evolving Research Needs" on Wednesday, May 12, 2021 at 10:00 a.m. EDT.

Questions presented by the Subcommittee

1. What is the state of data sharing regarding variants developing and spreading across the globe? How are new variants detected and, once their genomes are sequenced, how is that information proliferated?

SARS-CoV-2 genomes from COVID-19 cases have been sequenced from around the globe since the beginning of pandemic. This process, however, is expensive and technical, and thus there are significant inequities in SARS-CoV-2 genomic data generation. **Figure 1** summarizes the percent of COVID-19 cases per week that have been sequenced and shared on a public repository across regions and countries. Australia (AUS), Japan (JPN), Denmark (DNK), and Great Britain (GBR) are some of the only counties that have been able to consistently sequence >5% of the COVID-19 cases, while there is little to no SARS-CoV-2 genomic data from many countries in Asia, Africa, and the Caribbean. The United States has so far sequenced 0.5-1% of the total COVID-19 cases, though sequencing has significantly increased in recent months. These global and national genomic surveillance gaps severely limit our ability to detect new and emerging SARS-CoV-2 variants, and should be considered as a threat to US public health.

SARS-CoV-2 genomic data is primarily shared via GISAID (gisaid.org), and to a lesser extent, other repositories like the National Center for Biotechnology Information (NCBI) Genbank (<https://www.ncbi.nlm.nih.gov/sars-cov-2/>). As of May 6, 2021, there were 1,432,306 SARS-CoV-2 genome submissions on GISAID, compared to 386,022 on Genbank. It is unclear, however, the percent of the total SARS-CoV-2 genomes that have been sequenced that these databases represent. There are some disincentives for laboratories to not publicly share their SARS-CoV-2 genomic data. This list is not exhaustive, but it includes:

- Technical barriers to data transfers to online repositories.
- Lack of complete metadata (collection date, location, patient information).
- Lack of incentives to make expensive-to-generate genomic data available to the public.
- Lack of protection for the researchers to have first rights to publishing their data.

- Inappropriate international responses to publicly submitted data, such as naming a variant after a location or the implementation of travel restrictions.

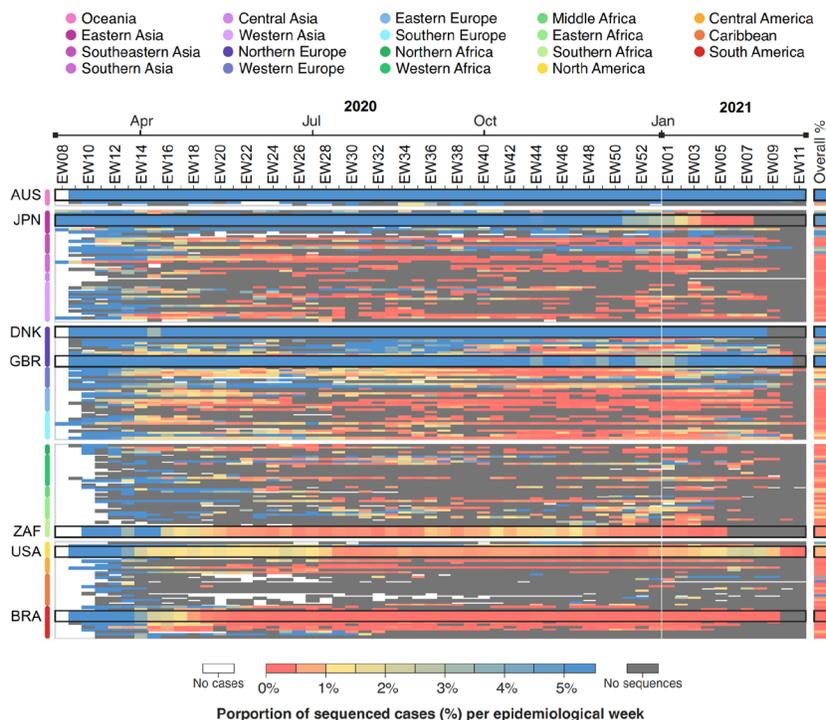


Figure 1. Proportion of sequenced cases per country per epidemiological week, 2020-2021 (up to April 16th, 2021). Few countries have capacity to sequence more than 5% of reported cases with genome coverage $\geq 70\%$, especially when COVID-19 incidence is high. When incidence is low, as in early phases of the pandemic, most countries were able to sequence high proportions of cases (3-5%, green and blue shades). However, with the aggravation of the pandemic, few countries were able to keep up, and in poor countries, despite cases being reported, many weeks had few (red) or no sequences (grey). Figure created by Anderson Brito, PhD (postdoctoral associate in the Grubaugh Laboratory at the Yale School of Public Health).

Most variants are initially detected by local laboratories or public health agencies. The SARS-CoV-2 genomic data are processed through open software like Pangolin (<https://pangolin.cog-uk.io/>) or Nextclade (<https://clades.nextstrain.org/>) that assign each sequenced to a specific lineage or clade based on the specific mutations in each sequence. This

provides an output such as “B.1.1.7” and a list of mutations. Many local laboratories or public health agencies are consistently monitoring the lineage assignments to (1) detect novel lineages that contain one or more mutations of interest, (2) detect the outside introduction of a known variant of concern or interest, and (3) track the frequencies of locally circulating variants.

There are also efforts to monitor for variants on national and global scales. There are now several programs, such as Outbreak.info (<https://outbreak.info/situation-reports>) and Nextstrain (<https://nextstrain.org/>), that pull data from GISAID daily to allow the user to generate custom variant tracking reports. Routine GISAID data retrievals are also used for many state and national surveillance programs to provide updates on the number of specific variants of concern or interest (e.g. <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>). The outputs of these reports are presented on various platforms, including press releases, traditional media, and social media.

2. Are existing COVID-19 tests effective at diagnosing infections of known variants? How are variant-specific tests use to bolster public health decision-making?

To my knowledge, all known SARS-CoV-2 variants can still be detected by the common clinical diagnostic assays. While some deletions or mutations can impact individual diagnostic assay targets, most clinical diagnostic assays target multiple parts of the genome to overcome this issue. **Thus there is not currently a significant issue with variants causing inconclusive or false negative results.** However, this is an area to continuously monitor, and there are several ongoing and parallel efforts to track mutations in diagnostic targets.

The primary issue is that **standard diagnostics cannot differentiate between SARS-CoV-2 variants.** While whole genome sequencing is the gold standard for variant identification, the additional time, expense, and laboratory equipment make sequencing not practical in all circumstances. PCR and other less complicated assays have the ability to detect a limited number of virus mutations, which can be indicative of a limited set of variants. These assays, which can be faster, cheaper, and less complicated, have an advantage of being able to generate information about variant frequencies with shorter turnaround times and at a larger scale than whole genome sequencing.

For example, the SARS-CoV-2 variant B.1.1.7 has a 6 nucleotide deletion in its spike protein, which causes a spike gene target failure (SGTF) result in one of the three targets with the ThermoFisher TaqPath COVID-19 Combo Kit. The result is still valid, but by comparing the

number of positive results with and without SGTF, we can get a relative picture of B.1.1.7 prevalence. This was valuable in tracking the increasing frequency of B.1.1.7 in the UK, and it is now being used in the US. National data about B.1.1.7 provenance based on TaqPath SGTF results are provided by Helix (<https://www.helix.com/pages/helix-covid-19-surveillance-dashboard>). My group also uses SGTF results to help track the frequency of B.1.1.7 in Connecticut (Figure 2; <https://covidtrackerct.com/variant-surveillance/>).

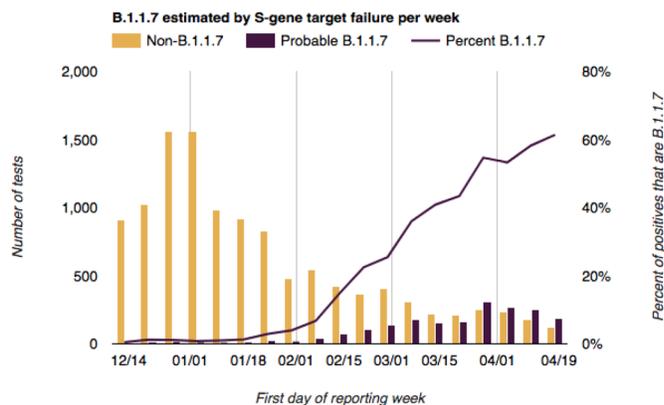


Figure 2. Presumed B.1.1.7 positivity (%). Tests performed by Yale-New Haven Hospital (primary catchment = New Haven and Fairfield Counties, CT) and Jackson Labs (primary catchment = New Haven and Hartford Counties, CT). Probable B.1.1.7 positivity defined as “spike gene target failure” (SGTF) frequency on the TaqPath SARS-CoV-2 diagnostic test. Figure from Covid Tracker CT (<https://covidtrackerct.com/variant-surveillance/>).

PCR assays specific to other variants have been developed, which can provide similar results to the above for B.1.1.7. These assays can be the most beneficial when they are used as the primary diagnostic test to immediately provide a SARS-CoV-2 test result and some information about the variant, rather than an add-on test. Variant-specific assays, however, cannot detect novel variants, and thus should only compliment whole genome sequencing, and not replace.

3. How can the federal government serve as a resource during and between pandemics when it comes to information aggregation and accessibility?

In my opinion, there are **three** primary ways that the federal government can facilitate data aggregation and accessibility during pandemics: policy, standards, and support.

The first is policy based. In my response to question 1, I outlined some barriers to pathogen data being shared on public repositories. It is not mandatory for data generated during pandemics that can benefit public health to be shared publicly. Furthermore, there are no policies in place to protect the rights of the data generators to have the first rights to publish the data. My group openly shares the genomic data that we generate in hopes that public health agencies can use it for decision making but also in hope that other academic labs will not scoop our data in their publication. Because some data (like sequencing data) can be very expensive to generate and publications are the “currency” for academic advancement, many groups are not open to sharing their data out of self preservation. Thus we often find data released upon a paper’s acceptance in a journal. While data sharing during the COVID-19 pandemic has been exceptional, these problems continue to exist. Thus finding resolutions around the legality of data sharing and usage to create an equitable framework would enhance data sharing during future pandemics.

Second, many forms of data useful for public health, including pathogen genomic sequencing, can be generated, processed, and analyzed by applying a variety of controls and methods. Then compiling data generated among different laboratories can create biases and inaccurate findings because they may represent different populations, include different intrinsic errors, or have different definitions/classifications of data fields. Thus standardization is critical, and is only likely to come from the national level. The federal government could create panels of field-specific experts to provide standards for sample selection, data generation, computational processing, and associated metadata.

Most importantly, public health surveillance - including all aspects from data collection, generation, storage, and dissemination - needs to be fully supported outside of outbreak/epidemic/pandemic times. We have seen many “pop-up” efforts created to fill critical needs, and some of this can be alleviated with consistent support. For example, many of the online tools mentioned above (e.g., outbreak.info) were created to assist with the pandemic response, and some of them may not be supported for long after the pandemic. If the national agencies can learn from the openness and innovation of the private and academic initiatives, they may be able to help preserve these tools and expand their use beyond SARS-CoV-2. As another example, the generation of and consistent support for NCBI means that there is a database to obtain access to records and data, which is fundamental for research and public health. Expanding these programs to include surveillance data which is notoriously difficult to

obtain would help to ensure that we have systems in place for when there are public health emergencies.

Dr. Nathan Grubaugh is Assistant Professor of Epidemiology at the Yale School of Public Health and head of the Grubaugh Lab studying virus emergence, transmission, and evolution. His lab uses genomics to determine the emergence risk and to track the spread of mosquito-borne viruses. Specifically, the lab sequences viruses during outbreaks for epidemiological investigations (genomic epidemiology), determines the disease phenotype and transmission fitness of novel virus mutations that occur during outbreaks (functional genomics), and maps the evolutionary pathways that a virus may take to adapt to a new environment (experimental evolution). Their goals are to integrate genomic data into surveillance and response programs to better prevent and control future mosquito-borne virus outbreaks.

Dr. Grubaugh earned his PhD in microbiology with a focus on West Nile virus evolution from Colorado State University in 2016 and went on to be a postdoctoral fellow at The Scripps Research Institute to study the 2015-2017 Zika virus epidemic. He also has a MS in biotechnology from Johns Hopkins University. Prior to graduate school, he spent around 7 years working in the biotech industry doing toxicology studies, monitoring food production lines for pathogens, and developing early phase vaccine candidates.

Chairman FOSTER. Thank you. And the Chair will now recognize Dr. Streiffer for five minutes.

**TESTIMONY OF DR. STEPHEN STREIFFER,
DEPUTY LABORATORY DIRECTOR
FOR SCIENCE AND TECHNOLOGY,
ARGONNE NATIONAL LABORATORY**

Dr. STREIFFER. Chairwoman Johnson, Chairman Foster, Ranking Member Obernolte, Members of the Subcommittee, thank you for the opportunity to testify today about the challenges presented by the COVID-19 variants and the important role the Department of Energy's national laboratories have played in combating COVID-19.

My name is Dr.—as Congressman Foster said, I'm Stephen Streiffer. I serve as Argonne's—National Laboratory's Deputy Laboratory Director for Science and Technology, as well as the Director of the lab's Advanced Photon Source (APS). For the last 15 months it's been my privilege to serve as the Co-Director of the DOE's National Virtual Biotechnology Laboratory.

As, again, Congressman Foster pointed out, the NVBL came together as a consortium of all 17 DOE national laboratories at the onset of the pandemic, supported by *CARES Act* funding. It brought together leading scientists and researchers from across the lab complex and leverages the Department of Energy's world-class experimental and computational facilities. Our state-of-the-art user facilities such as the APS, our capabilities in advanced computing and AI (artificial intelligence), structural and molecular biology and biotechnology, epidemiological and transportation modeling and advanced manufacturing, among others, uniquely position us to take on this challenge and lead the world in finding therapies to combat the virus.

If you'll allow me, I'll just go through several of the contributions that NVBL has made in the fight against COVID. I'll highlight just a few here, and there's more in my written testimony of course.

As the Nation initially grappled with testing, the lab supported the FDA, CDC, and DOD (Department of Defense) to establish national guidelines, identify diagnostic targets, and develop and prove out sample collection methodologies that were used in the administration of hundreds of millions of COVID-19 tests. We also worked to solve supply chain challenges that plagued the early days of the outbreak. Teams from the NVBL produced innovations in materials and advanced manufacturing that mitigated shortages and test kit components and personal protective equipment, leading to the creation of over 1,000 new jobs as we transferred development to the private sector. Our high-performance computing and AI capabilities have proven extremely effective in the molecular design of medical therapeutics and in epidemiological mobility modeling to support decisionmakers.

As far as we've come in the fight against COVID-19, as we're here today to discuss, the biggest threat right now are the variants that are emerging around the globe. An integrated approach that tracks and responds to the variants is what we need at this stage of the pandemic.

A four-step approach to this requires a whole-of-government approach to succeed. First, we need to sequence the genome of the virus collected from as many test results as possible nationally and, very importantly, globally. Second, we must maintain centralized inventories of collected viral sequences and build family trees that represent how they relate to each other. Third, we must use computational modeling and experimental methods to identify troublesome variants that can escape detection through current tests of current vaccines or resist current therapeutics. Fourth, as we discover those troublesome variants, we need to design new tests, vaccines, and treatments that target and work against variants as they continue to emerge.

Coupled with other strong public health measures, finding and rooting out the variants is what will get us to the finish line with the pandemic. However, a number of challenges remain. As you'll hear, we must improve upon the systematic sequencing of the viruses to identify and track new variants. The NIH is putting resources into this in the United States, but more is needed. And in fact, DOE has significant expertise that can support these efforts.

The issue of disinformation and vaccine hesitancy are highly concerning. DOE and the labs are playing a role combating disinformation and building scientific literacy among the American public and are actively engaged in outreach activities across communities, including the most underserved.

We need to speed the process of drug design by harnessing computational artificial intelligence tools that the DOE is very expert in to find potential therapeutics faster. DOE also has the capability to further develop, evaluate, and validate tools for less expensive, simpler testing and diagnostics. There is also a need for substantial work to incorporate the emergence of vaccine resistance variants into epidemiological modeling. DOE's expertise in AI is inspiring new ways of thinking about inputs into pandemic models, including data on mobility, health, behavior, and demographics.

And finally, we do need to enhance real-time standards and data sharing. Metropolitan and State-level models of COVID-19 variant penetration, immunity, transmission, and morbidity/mortality, broken down by geography and demographics, will continue to enhance the Nation's ability to proactively plan and to respond to the evolving landscape. These efforts will provide web-based tools and actionable information for a whole-of-government approach.

Let me conclude by saying that we appreciate the support that Congress has given to all the national laboratories, in particular to the NVBL. Thank you to the Subcommittee for your time and happy to answer questions through the hearing. Thank you.

[The prepared statement of Dr. Streiffer follows:]

Testimony of

Dr. Stephen Streiffer

Deputy Laboratory Director for Science and Technology

Argonne National Laboratory

House Committee on Science, Space, and Technology

Subcommittee on Investigations and Oversight

COVID-19 Variants and Evolving Research Needs

May 12, 2021

Chairman Foster, Ranking Member Obernolte, and Members of the Subcommittee, thank you for the invitation to testify before you today about the critical role of the U.S. Department of Energy (DOE) national laboratories in combatting the COVID-19 pandemic and the virus' emerging variants. My name is Stephen Streiffer and I serve as Argonne National Laboratory's deputy laboratory director for science and technology, as well as the director of the lab's Advanced Photon Source.

For the last 15 months I have also had the honor of serving as the co-director of the DOE's National Virtual Biotechnology Laboratory (NVBL). The NVBL is truly one of the unsung heroes in the nation's fight against this disease. It was formed at the beginning of the pandemic to put the broad capabilities of the DOE complex to the task of fighting COVID-19, including the expertise and facilities of all 17 DOE national laboratories. Our labs are home to scientists and researchers that lead the world in their areas of expertise. We also house unique and powerful "user facilities": experimental and computational tools used by researchers from universities, government laboratories, and companies from across the country and around the world.

The national laboratories have a long history of putting our groundbreaking discoveries and innovations to work responding to national and international emergencies. From the 2005 Hurricane Katrina disaster, to the 2010 Deepwater Horizon oil spill, to the 2011 Fukushima nuclear accident, we have been on the front lines, helping with immediate response and developing long-term technical solutions. When the COVID-19 pandemic hit, we were prepared, ready, and willing to support an whole-of-government effort to fight the disease.

ACCOMPLISHMENTS OF THE NVBL IN FIGHTING COVID-19

The creation of the NVBL allowed the laboratories' collective capabilities to be almost immediately transformed into key assets in the world's fight against COVID-19. With funding from the CARES Act, all 17 national laboratories, through the NVBL, addressed medical supply shortages, discovered potential drugs to fight the virus, developed and verified COVID-19 testing methods, modeled disease spread and impact locally and nationally, and helped officials understand virus transport in buildings and the

environment. Although NVBL CARES Act funding has been fully expended, this work sets the stage for ongoing work to identify, understand, track, and treat variants.

The national laboratory resources leveraged for this effort include a suite of world-leading facilities that are used by scientists from universities, industry, and other laboratories across the country and around the world:

- Light and neutron sources
- Nanoscale science research centers
- Sequencing and biocharacterization facilities
- High-performance computing centers
- Advanced manufacturing research facilities

Here are a few of the many contributions that the NVBL has made to the fight against COVID-19, through both the labs' discoveries and innovations and the support of their user facilities to the international scientific community.

Molecular Design for Medical Therapeutics

DOE's high-performance computers and light and neutron sources were used to identify promising candidates for antibodies and antivirals that universities and drug companies are now evaluating. These efforts were led by Oak Ridge, Lawrence Berkeley, and Lawrence Livermore National Laboratories with participation from six other laboratories. Specific examples include:

- Used artificial intelligence methods to screen 10^{40} (over a thousand-trillion-trillion-trillion) possible antibody variations, identifying the best matches against the SARS-CoV-2 spike protein.
- Computationally screened tens of millions of small molecules against SARS-CoV-2 viral proteins and then experimentally evaluated top contenders, greatly accelerating the search for new antiviral therapeutics.

Development and Evaluation of COVID-19 Testing

NVBL researchers developed new diagnostic targets and sample collection approaches and supported U.S. Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and Department of Defense (DoD) efforts to establish national guidelines used in administering hundreds of millions of COVID-19 tests. Led by Los Alamos, Sandia, and Lawrence Livermore National Laboratories, with significant contributions from eight other laboratories, projects included:

- Collaborated with DoD, CDC, and FDA to provide experimental data in support of national testing guidelines, assessing potential contamination in commercial kits, evaluating protocols such as for pooled samples, examining test kit viral transport media and protocols, and evaluating virus inactivation and extraction methods. These projects helped ensure that the nation was using effective tests and protocols and protecting frontline health care workers.
- Developed tools to analyze and assess how variants of the SARS-CoV-2 virus may affect the reliability of COVID-19 tests.

Epidemiological and Transportation Modeling

Researchers used artificial intelligence and high-performance computing to produce near real-time analysis of data to forecast disease transmission, stress on public health infrastructure, and impacts to the economy and transportation networks, supporting decision-makers at the local, state, and national levels. This work informed pandemic response with respect to underserved communities in Illinois, New Mexico, and Tennessee. Led by Oak Ridge National Laboratory with participation from six other laboratories (Argonne, Lawrence Berkeley, Livermore, Los Alamos, National Renewable Energy Laboratory, and Sandia), specific projects include:

- Created an approach to forecast COVID-19 case counts at state, county, and metropolitan scales using data-driven statistical models, enabling short-term planning of contact tracing, healthcare staffing, testing capacity, and vaccination strategies.
- Performed longer-term, scenario-based analysis and mitigation planning to support decision makers with information on effects of nonmedical interventions such as social distancing, masking, stay-at-home policies, and school closures before they are implemented.
- Collected and curated disease data, which created a unique national data resource to support epidemiological and pandemic modeling, including assessment of the impact of human behavior on infection spread and location and the availability of critical infrastructure.
- Developed an approach using cellular phone- and vehicle-derived data to reveal transportation patterns across industries, including bars and restaurants, as well as passenger, fleet, and heavy-duty vehicles.

Viral Fate and Transport

NVBL teams studied how to control indoor virus movement to minimize uptake and protect human health, designed materials to deactivate the virus, and developed models to track it in wastewater. This effort was led by Pacific Northwest National Laboratory with strong participation from Lawrence Berkeley, Livermore, and eight other laboratories. Examples include:

- Provided critical information about how behavioral, environmental, and operational conditions affect the risk of airborne virus transmission indoors, such as in classrooms, offices, and conference rooms, to mitigate viral spread in enclosed spaces.
- Designed new antiviral materials that can deactivate the virus.
- Produced and validated models for SARS-CoV-2 fate and transport in wastewater, enabling wastewater sampling as a means to provide early warning and hot-spot detection of localized COVID-19 outbreaks.

Advanced Manufacturing

Within just a few months, NVBL teams produced innovations in materials and advanced manufacturing that mitigated shortages in test kit components and personal protective equipment (PPE), creating over 1,000 new jobs. All 17 national laboratories contributed, and specific partnerships with industry include:

- Designed a system for mass producing N95 filter media, enabling Cummins Filtration (Nashville, TN) to produce material for more than 3 million masks per day, and worked with DemeTech (Miami Lakes, FL) to convert the N95 material to masks and respirators.

- Worked with the U.S. Department of Health and Human Services and Coca-Cola (Atlanta, GA), which produces 2 billion bottle preforms per week, to evaluate the use of these preforms to alleviate shortages of test tubes used to collect nasal swab samples.
- Developed an approach to 3D print the tooling needed to produce over 8 million sample collection tubes weekly by Thermo Fisher Scientific, Inc. (Lenexa, KS).
- Developed a new low-cost ventilator with BioMedInnovations (Denver, NC) that received FDA Emergency Use Authorization approval.

These accomplishments, made possible through the NVBL, demonstrate the game-changing resource represented by DOE's 17 national laboratories working together virtually, with a single focus on alleviating pandemic challenges. Going forward, the NVBL can bring these resources to bear on future national and international needs and emergencies.

BASIC RESEARCH UNDERLIES COVID-19 VACCINES

The speed with which effective COVID-19 vaccines were developed and disseminated has been unprecedented—and it wouldn't have happened without decades of investment in scientific research involving the national laboratories. I share two examples below.

First, the science behind the production of messenger RNA, or mRNA, that is used in the Pfizer/BioNTech and Moderna vaccines, is based on the building blocks of innovation that started at Brookhaven National Laboratory in the 1980s. At that time, a team led by F. William Studier was studying a virus that attacks *E. coli* bacteria. They created the first complete sequence of that virus' genome, which allowed them to understand how it produced many copies of itself. Studier and his team learned how to direct this copying capability toward making other things: specifically, copious amounts of RNA. This RNA could be delivered to the ribosomes in cells to be translated into proteins—or used directly in mRNA-based vaccines. Thus, Studier's pivotal discovery almost four decades ago enabled the production of today's life-saving treatments.

Second, five of the vaccines now in use—including those developed by Pfizer/BioNTech, Moderna, and Johnson & Johnson—leverage a technique developed from more than a decade of research at Argonne's Advanced Photon Source (APS). This technique, which increases the effectiveness of the vaccines, was developed by researchers now at the University of Texas at Austin and the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH). Their current work on COVID-19 vaccines is based on their research into an entirely different disease: respiratory syncytial virus (RSV), which affects thousands of individuals per year. In their work to develop a vaccine for RSV, they used data from the APS to design a version of an RSV viral protein that would provide an effective target for the immune system, helping it build immunity against the virus. They realized that the technique could be applied to coronaviruses as well, and in 2013 began work on a vaccine for the Middle East Respiratory Syndrome coronavirus (MERS-CoV). They reported success in 2017, which again was supported by their use of the APS. When SARS-CoV-2 emerged, they joined with other researchers to successfully apply the same technique to vaccines against it.

COVID-19 VARIANTS: STRATEGY AND CHALLENGES

Having made great strides in combatting the original SARS-CoV-2 virus, the U.S. and the world is in the midst of a race between human ingenuity and the evolving coronavirus. The growing number of vaccines that have received the FDA's Emergency Use Authorization offer real hope for increasing rates of immunity. However, community prevalence of COVID-19 conversely enables the rise of new virus variants, such as the B.1.1.7 variant first identified in the UK or the B.1.351 variant first identified in South Africa. The DOE national laboratories can build on previously mentioned contributions and continue to drive innovation and information for the sustained, multi-pronged approach necessary to stay ahead in the race against coronavirus mutation.

The SARS-CoV-2 virus, as with any biological entity, is essentially a moving target. As the virus replicates within its host, it will frequently make mistakes – spelling errors – as it copies its genetic code, creating new variants. Many of these mistakes are inconsequential, akin to spelling differences between American English and British English (e.g., “color” versus “colour”). You can still understand the underlying meaning of the word. Most mutations are benign, although occasionally a spelling mistake is made that is more profound (e.g., “fowl” to “foul”). Thus, some mutations can compound and create a situation where not only has the word's meaning changed but that of the entire sentence as well. At this stage, the virus might not be “readable” by diagnostic tests, and, in the worst case scenario, the vaccine target and therapeutic target might no longer be recognizable.

Protecting our communities from COVID-19 variants can be summarized in four steps. Each of these steps is a complex, research- and technology-intensive process that requires a whole-of-government approach to succeed.

1. Sequence the genome of the virus collected from as many samples as possible, with testing distributed equally across the country.
2. Provide a centralized inventory of collected viral sequences and build a “family tree” that represents how they relate to each other. This large-scale analysis enables us to understand what variants are arising, where they are arising, and when they are arising.
3. Use computational modeling and experimental assessments to identify which variants may escape detection through currently available tests, can evade current vaccines, may be more dangerous, or resist current medical therapeutics.
4. Design new tests, vaccines, and treatments that target and work against variants as they continue to emerge.

Through the NVBL, DOE national laboratories are leveraging their resources to provide solutions to all four of these critical steps.

Sequencing and Monitoring Viral Variants

What helps us monitor and identify variants that evade vaccines and therapies is to sequence as many samples of the virus as we can from as many communities as possible, either from testing or from wastewater – in a broad and consistent effort – that allows us to effectively track these changes. We can make our specialized scientific facilities available to our partners at the NIH, CDC and other agencies to improve and speed up current virus sequencing. We also have expertise in large-scale sampling that can be put to work to support testing across the country.

Analyzing the Virus' "Family Tree"

A framework for comparing, classifying, and analyzing the genome sequences of all of these variants is crucial. This framework is already in place by using phylogenetic trees ("family trees") to represent how the variants are related to one another. Each leaf on the tree represents a variant. Leaves attached to the same twig are very similar, whereas leaves on different branches are less similar. Having this framework in place allows us to understand how certain variants arise and what series of mutations create the path to a certain outcome, such as increased virulence. Although this analogy appears quite simple, the underlying calculations for representing these relationships when considering all of the leaves in the tree is extremely complex. DOE supercomputing resources have historically been a critical component for this type of large-scale bioinformatic analytical work, and they will continue to support this work moving forward. An NIH-funded Bioinformatics Resource Center supported by supercomputing at Argonne provides an ongoing analysis of all emerging variants based on available SARS-CoV-2 genome sequences. As these sequences become available, specific variants of concern are tracked, as are the corresponding discrete changes in their genome sequence that differentiate them.

Identifying Variants of Concern

The DOE national laboratories also play a major role in identifying variants that may escape detection or be resistant to vaccines or treatment. Having the above framework in place in order to identify, classify, and track variants of SARS-CoV-2 also means that this information can be used to understand the implications of these changes on the human body.

We have unique, large-scale scientific facilities – such as the aforementioned light sources – and the corresponding expertise for structural biology work that can identify the actual physical changes in the shape of variant components. If the virus is considered as a set of LEGO bricks, we have the tools to literally manufacture and then inspect each individual brick at the scale of its individual atoms. These bricks are viral proteins. Any change in shape of one of those bricks means that we can predict how it interacts with other bricks, including those that stick to surfaces of human cells. Visualizing the changes in shapes of viral proteins provides insight into how they interact with and function in the human body.

Once we can predict how the changed viral proteins interact in the body, our large-scale computing and data management facilities can quickly assess if existing tests, vaccines, and therapeutics might fail against a new variant.

Mitigating Impacts of New Variants

For the fourth step, designing new testing, protocols, and treatment, the DOE laboratories collectively bring significant resources and expertise to the table. We support computational modeling, data analysis, and artificial intelligence techniques that accelerate the discovery of drugs that can successfully treat COVID variants. Our structural and experimental biology expertise and facilities can help national laboratory and university researchers refine or, if necessary, completely redesign therapeutic antibodies and small molecules in response to variations in the virus.

We can develop new tests for rapid detection of variants in clinical and environmental samples. We can also help decision-makers understand how the virus is transported, so that physical and administrative protocols can be developed and implemented that protect people against variants.

We can provide epidemiological modeling for near real-time forecasts and predictions. These forecasts help officials at all levels plan for different intervention options to prevent COVID variants from spreading, allowing them to make the best decisions regarding how to use their resources to keep our communities healthy. At Argonne, we have supported elected officials from the City of Chicago and the State of Illinois with forecasts and predictions since the start of the COVID pandemic, and stand ready to continue this support for COVID variants.

Lastly, to support both the ongoing response to the pandemic caused by the original SARS-CoV-2 virus, and the new variants, we will continue to develop innovative materials and manufacturing processes that address critical supply chain issues and support domestic production of key supplies.

CHALLENGES AND HURDLES

We have come a long way in the last year but we still have far to go both in confronting the current pandemic and preparing the nation for the next one. DOE and the NVBL can play a leading role addressing key concerns including virus sequencing, vaccine hesitancy, speed of drug design, testing and diagnostic development, enhancing epidemiology models, and real-time data sharing.

1. *Virus sequencing.* The U.S. has not performed much in the way of systematic sequencing of the virus in the country's population to identify and track the emergence of variants, and what we have conducted has predominately been done on a regional basis. A national, uniform sequencing of the virus across the whole country is needed to track these emerging variants. Fortunately, the NIH is putting resources into this effort, but more is needed.
2. *Vaccine hesitancy.* Improved public education about the efficacy of vaccines and the pivotal role they play in curtailing the extent and length of the pandemic would go a long way towards instilling confidence among the American people and decrease their skepticism about taking the vaccine. The DOE plays an important role in building scientific literacy among the American public, and the laboratories are actively engaged in STEM outreach across communities, including the most underserved. In addition, vaccine uptake/hesitancy is one variable the labs' epidemiological models can address, helping government and public health leaders better understand the likely evolution of the pandemic.
3. *Computational modeling and drug design.* The national laboratories' computational and artificial intelligence tools can accelerate the process of drug and vaccine development, and narrow the field of effective existing treatments. NVBL sponsored projects built computational discovery platforms that leveraged investments from multiple agencies and had demonstrable success in finding potential therapeutics that can enable faster response to future variations.
4. *Testing and diagnostic tool development.* DOE has the capabilities to further evaluate and validate existing or experimental tools for testing and diagnostics. DOE has a long history of experience in large-scale sampling and DNA sequencing and can deploy efforts to lower the cost and introduce simpler diagnostics.
5. *Continued epidemiology work.* Artificial intelligence inspired new ways of thinking about data inputs into pandemic models, including data on mobility, health, behavior, and demographics.

Future work can incorporate the emergence of vaccine-resistant variants, the analysis of societal impacts, the effects of international travel, and the potential benefits of vaccination to inform long-term planning efforts to mitigate effects of COVID-19.

6. *Standards and data sharing.* Metropolitan and state-level models of COVID-19 variant-penetration, immunity, transmission, and morbidity/mortality—broken down by geography and demographics—will continue to enhance the nation’s ability to proactively plan and near real-time respond to the evolving landscape. These efforts would build on multiple agency investments for a dynamic, accurate, and multi-modal operational picture and provide web-based tools and actionable information for a whole of government approach.

CONCLUSION

For these reasons, Congress should consider continuing to strongly support the DOE complex and the NVBL as part of the nation’s continued response to COVID-19 and future pandemics. At the national laboratories, we have infrastructure, networks, and teams of experts ready to deploy. Together, our national labs were able to develop vaccines, mitigation strategies, and solutions in record time due to Congress’s robust and consistent support for the past several decades. Our all-hands approach—marshalling the talent and resources of the national laboratories, other government agencies, pharmaceutical industries, and universities from across the country—was instrumental to the impact we’ve demonstrated.

We were fortunate that we had a head start on research and modeling of coronaviruses. We were able to develop potential vaccines within weeks of the release of the original virus genomic code (most of the time to the authorization of the vaccines was taken up by Phase 1, 2, and 3 clinical testing). This will not always be the case. In the future, we may be confronted with more complex, less understood, more deadly viruses—diseases that can spread from different species and more effectively evade current treatments.

I am proud of the accomplishments of the NVBL and the national laboratories in responding to the COVID-19 pandemic, and feel confident these resources will be available to respond to future national challenges.

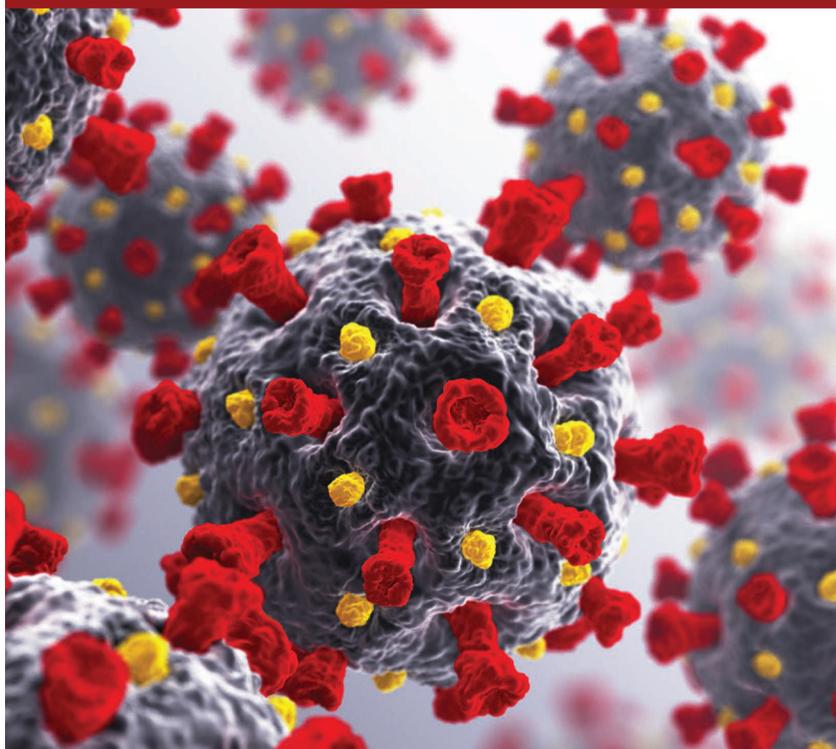
At Argonne, as we celebrate our 75th year as a national lab, we look forward to confronting the next 75 years of complex challenges facing society like the current pandemic. The scale of our facilities, the depth of our experience, and our collaborative approach, which are hallmarks of our national laboratories, match the scale of the pandemic we collectively face, and whatever the future holds.

Thank you to the Subcommittee for your time and consideration. I am happy to answer any questions.

U.S. Department of Energy

National Virtual Biotechnology Laboratory

R&D for Rapid Response to the COVID-19 Crisis



U.S. DEPARTMENT OF
ENERGY

Office of
Science

January 2021

National Virtual Biotechnology Laboratory

A Game-Changing Framework for Responding to the Nation's Needs

With funding from the CARES Act, the U.S. Department of Energy (DOE) established the National Virtual Biotechnology Laboratory (NVBL) in March 2020 to address key challenges associated with the COVID-19 crisis. The NVBL brought together the broad scientific and technical expertise and resources of DOE's 17 national laboratories to address medical supply shortages, discover potential drugs to fight the virus, develop and verify COVID-19 testing methods, model disease spread and impact across the nation, and understand virus transport in buildings and the environment. National laboratory resources leveraged for this effort include a suite of world-leading user facilities broadly available to the research community, such as light and neutron sources, nanoscale science research centers, sequencing and biocharacterization facilities, and high-performance computing facilities.

Within just a few months, NVBL teams produced innovations in materials and advanced manufacturing that mitigated shortages in test kits and personal protective equipment (PPE), creating nearly 1,000 new jobs. They used DOE's high-performance computers and light and neutron sources to identify promising candidates for antibodies and antivirals that universities and drug companies are now evaluating. NVBL researchers also developed new diagnostic targets and sample collection approaches and supported U.S. Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and Department of Defense (DoD) efforts to establish national guidelines used in administering millions of tests. Researchers used artificial intelligence and high-performance computing to produce near-real-time analysis of data to forecast disease transmission, stress on public health infrastructure, and economic impact, supporting decision-makers at the local, state, and national levels. NVBL teams also studied how to control indoor virus movement to minimize uptake and protect human health.

Through its NVBL framework, DOE has contributed significantly to the nation's COVID response, demonstrating in only a few months the critical impact of the national laboratories. The NVBL serves as an outstanding model for developing and sustaining capabilities to respond to future national needs or emergencies. Examples of NVBL COVID-19 accomplishments are outlined below, and more details are available at science.osti.gov/nvbl.

NVBL Accomplishments

Materials and Manufacturing for Critical Supplies

- Designed a system for mass producing N95 filter media, enabling Cummins Filtration (Nashville, Tenn.) to produce material for more than 3 million masks per day, and worked with DemeTech (Miami Lakes, Fla.) to convert the N95 material to masks and respirators, creating over 1,000 new manufacturing jobs.
- Worked with the U.S. Department of Health and Human Services and Coca-Cola (Atlanta, Ga.), which produces 2 billion bottle preforms per week, to evaluate the use of these preforms to alleviate shortages of test tubes used to collect nasal swab samples.



Materials and Manufacturing for Critical Supplies. NVBL teams developed a mechanism to 3D print the tooling needed to mass produce sample collection tubes for COVID-19 test kits. [Courtesy Thermo Fisher Scientific Inc.]

- Developed an approach to 3D print the tooling needed to produce over 8 million sample collection tubes weekly by Thermo Fisher Scientific, Inc. (Lenexa, Kan.), creating more than 300 jobs.
- Developed a new low-cost ventilator with BioMedInnovations (Denver, N.C.) that received FDA Emergency Use Authorization approval.

Molecular Design for Medical Therapeutics

- Used artificial intelligence methods to computationally screen 10^{40} possible antibody variations, identifying the best hits that could be used as an antiviral against the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spike protein.
- Computationally screened tens of millions of small molecules against SARS-CoV-2 viral proteins and then experimentally evaluated top hits, greatly accelerating the search for antiviral therapeutics.

Development and Evaluation of COVID-19 Testing

- Collaborated with DoD, CDC, and FDA to provide experimental data in support of national testing guidelines, assessing potential contamination in commercial kits, evaluating sample pooling approaches, examining viral transport media and protocols, and evaluating virus inactivation and extraction methods to assure test efficacy and protect frontline health care workers.
- Developed analysis tools to assess global evolution of the SARS-CoV-2 RNA genome, as it relates to nucleic acid-based assays.
- Identified distinguishing signatures in the SARS-CoV-2 RNA genome that can be used to rapidly detect this pathogen and other co-infecting pathogens in multiplexed assays.
- Developed a small nucleic acid test instrument to rapidly detect SARS-CoV-2 with high sensitivity.

Epidemiological Modeling

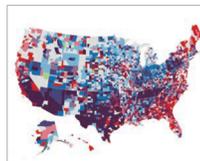
- Created an approach to forecast COVID-19 case counts at state, county, and metropolis scales using data-driven statistical models, enabling short-term planning of contact tracing, staffing, and testing capacity needs.
- Created the ability to perform longer-term, scenario-based analysis and mitigation planning to support decision-makers with information on effects of interventions before they are implemented.



Molecular Design for Medical Therapeutics. Scientists used computational modeling and simulation approaches as well as molecular dynamics to design and optimize small molecules that are experimentally confirmed to inhibit viral proteins, such as the 3CLpro cysteine protease shown here. [Courtesy Oak Ridge National Laboratory]



Development and Evaluation of COVID-19 Testing. NVBL researchers provided experimental data that helped inform national guidelines used in millions of tests. [Courtesy Los Alamos National Laboratory]

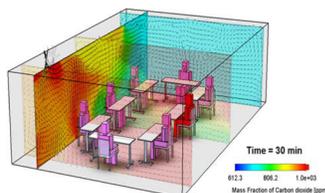


Epidemiological Modeling. Data scientists developed tools to forecast and visualize in near-real time COVID-19 transmission rates and dynamics at the county level. [Courtesy Oak Ridge National Laboratory]

- Produced a platform with comprehensive data access and visualization capabilities to process near-real-time, multi-modal, and multi-source data to support informed decision-making and monitor potential recovery efforts.
- Collected and curated disease data, creating a unique national data resource to support epidemiological and pandemic modeling, including assessment of the impact of human dynamics on infection spread and location and the availability of critical infrastructure.
- Developed an approach to assess mobility behavior changes in response to COVID-19 using cellular phone- and vehicle-derived data to reveal travel patterns for commercial activity by type and across industries, including bars and restaurants, as well as passenger, fleet, and heavy-duty vehicles.
- Established a novel epidemiological modeling approach to quantify contact tracing, testing, and vaccination strategies in resource-constrained environments and to help identify optimal vaccination strategies for states and large metropolitan areas.

Viral Fate and Transport

- Provided critical information about how behavioral, environmental, and operational conditions affect the risk of airborne virus transmission indoors, such as in classrooms, offices, and conference rooms, to mitigate viral spread in enclosed spaces.
- Designed new antiviral materials that can adsorb SARS-CoV-2 virus and deactivate the pathogen.
- Produced and validated models for SARS-CoV-2 fate and transport in wastewater and groundwater arising from seepage of sewer water or septic tanks into groundwater and the associated transport through the subsurface and potential exposure routes and risks to the population.



Viral Fate and Transport. NVBL researchers used computational fluid dynamics simulations to examine airborne transport of the virus indoors. Shown here is a simulation of the airflow and distribution of expelled respiratory aerosols within a classroom or office configuration. [Courtesy Sandia National Laboratories]

Summary

DOE's NVBL has proven to be an exceptionally effective contributor to the nation's COVID response, quickly marshaling unique national laboratory expertise and capabilities to meet the most critical needs. For example, the NVBL supported manufacturers to address key shortages in medical supply chains, creating nearly 1,000 new medical manufacturing jobs. Working closely with other federal agencies and state and regional decision-makers, the NVBL provided solutions across a range of COVID challenges. These accomplishments demonstrate the game-changing resource represented by DOE's 17 national laboratories working together within the integrated NVBL framework. Going forward, the NVBL can bring these resources to bear on future national and international needs and emergencies.

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**STEPHEN STREIFFER**

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Stephen Streiffer is the Deputy Laboratory Director for Science and Technology, Interim Associate Laboratory Director for Photon Sciences directorate, and Director of the Advanced Photon Source at Argonne. The Photon Sciences directorate consists of the X-ray Science, Accelerator Systems and Advanced Photon Source Engineering Support divisions, which comprise the Advanced Photon Source (APS); and the Argonne Accelerator Institute.

The APS is the brightest source of high-energy X-rays in the Western Hemisphere and is used to study the structures of materials and processes at the atomic scale. It is also one of the largest scientific user facility in the North America, with more than 5,500 users visiting each year.

He has also served as interim director of Argonne's Center for Nanoscale Materials, a national user facility that provides capabilities explicitly tailored to the creation and characterization of new functional materials on the nanoscale. The center's portfolio includes research on electronic and magnetic materials and devices, nanobio interfaces, nanofabrication, nanophotonics, theory and modeling, and X-ray microscopy.

Streiffer's scientific expertise is in structural characterization of materials particularly using transmission electron microscopy and X-ray scattering techniques. He has authored or co-authored more than 150 scientific publications and holds one patent.

He is one of the founding co-chairs of the National Virtual Biotechnology Laboratory (NVBL). The NVBL is a consortium of all seventeen Department of Energy National Laboratories founded in March 2020 to address key challenges associated with the COVID-19 crisis. The NVBL brought together the broad scientific and technical expertise and resources of the National Laboratories to address medical supply shortages, discover potential drugs to fight the virus, develop and verify COVID-19 testing methods, model disease spread and impact across the nation, and understand virus transport in buildings and the environment.

Streiffer holds a PhD degree in materials science and engineering from Stanford University and a BS degree in materials science and engineering from Rice University.

Chairman FOSTER. Thank you. And we will now recognize Dr. Rivers for five minutes.

**TESTIMONY OF DR. CAITLIN RIVERS, SENIOR SCHOLAR,
JOHNS HOPKINS CENTER FOR HEALTH SECURITY**

Dr. RIVERS. Chairman Foster, Ranking Member Obernolte, Chairwoman Johnson, and Members of the Subcommittee, thank you for the opportunity to speak to you today about variants and evolving research needs.

In the United States we have entered a new phase of the pandemic. Nearly 60 percent of American adults have begun vaccination, including more than 80 percent of adults over age 65. However, in the last 14 months, over 575,000 Americans have died and 32 million cases have been reported. Beyond the direct impacts, we've endured severe economic consequences, disruption to education, and strain on our healthcare systems. We've collectively suffered an enormous loss, and that grief will not be easily overcome.

The situation in some other countries is much worse, and the pandemic is far from over. Case counts globally are reaching new highs. India is in the midst of a terrible wave and reports suggest that in some communities the situation is dire. A variant of interest, B.1.617, may be contributing to the surge. As our own domestic outlook improves, we must turn our attention to helping the world.

And as we continue the work of ending the pandemic both at home and abroad, we must also identify the changes necessary to ensure we are never caught in this position again. In doing so, we should recognize that we were caught unprepared more than once. We were unprepared to manage the emergence and swift global spread of the novel coronavirus, and we were late to recognize when it reached our shores. Those delays set us on a worse trajectory than we might have otherwise faced.

But so, too, were we unprepared for variants. Although genomics experts had warned of the threat, it was not until the United Kingdom suffered a severe wave attributed to the B.1.1.7 variant that public health officials worldwide sharpened their focus. B.1.1.7 is now understood to be perhaps 50 percent more transmissible than other variants, and it may also cause more severe illness. The U.K. was able to identify and track this variant over time because they invested heavily in genomic surveillance. That capability yielded important information they needed to guide their response, and they provided warning to the world about what was to come. We did not have that level of genomic surveillance in the United States, and that was a gap.

The United States currently recognizes five variants of concern and several variants of interest. The most concerning possibility with some of these variants is that they may exhibit some degree of immune escape, meaning that vaccines and therapeutics may be somewhat less effective. Future variants may drift even further from the protection existing vaccines can provide, cause more severe illness, or impact diagnostic testing. If we do need to update our vaccines or diagnostics to be a better match, we must know that as early as possible so that we can begin the work—that work before the variant becomes widespread. We must not again be caught unprepared.

The American Rescue Plan includes \$1.7 billion for genomic surveillance, as well as additional funds for biological research, expansion of the public health workforce, and a suite of other important public health initiatives that will improve our preparedness, including for variants. Looking ahead, given that SARS CoV-2 is likely to continue to circulate and in anticipation of the next viral threat that we will almost certainly face, Congress should provide long-term, sustainable support for this expansion in our public health infrastructure so that we will be in a better position to respond next time.

As we advance our genomic surveillance infrastructure, we should also further develop the modeling and analytics infrastructure that will allow us to make even better use of that data. With the exception of a few small groups within the Department of Health and Human Services, most modelers work in academia and volunteer to support the public health response when an urgent need arises. This arrangement is not well-suited to either party. The Federal Government would benefit from a permanent capability with infectious disease modelers working to advance the state of the science and support public health decisionmaking both between and during emergencies.

The Biden Administration announced a National Security Directive 1, an intention to create a National Center for Epidemic Forecasting and Outbreak Analytics, and the American Rescue Plan appropriated \$500 million to CDC for disease forecasting and data modernization. These are promising steps toward modernizing our response capabilities, and I believe they will serve the Nation well. Congress could help by appropriating annual funding and authorizing language so that the forecasting center can endure as a permanent capability.

In conclusion, although the currently circulating variants complicated our course through the spring months, we are now on track to regain control of the pandemic in the United States. Continued vigilance to current and future variants is essential to ensuring that we maintain our current encouraging trajectory. We must expand our genomic surveillance efforts domestically and work with partners and allies abroad to ensure global coverage. The United States is a world leader in science and technology, and we have the opportunity using those capabilities to lead the world through the rest of the pandemic. Thank you.

[The prepared statement of Dr. Rivers follows:]

United States House of Representatives Committee on Science, Space and Technology
Subcommittee on Investigations and Oversight

COVID-19 Variants and Evolving Research Needs

May 12, 2021

Caitlin Rivers, PhD, MPH

Senior Scholar, Johns Hopkins Center for Health Security
Assistant Professor, Environmental Health and Engineering
Johns Hopkins Bloomberg School of Public Health

Current situation

In the United States, we have entered a new phase of the pandemic. Nearly 60% of American adults have begun vaccination, including more than 80% of adults over age 65. Community transmission is declining, and I believe that by summer we will be able to resume most normal activities. However, in the last 14 months over 575,000 Americans have died and 32 million cases have been reported, with more likely unrecognized. Beyond the direct impacts, we have also endured severe economic consequences, disruption to education, strain on our healthcare systems, and we have missed time with loved ones. We have collectively suffered an enormous loss, and that grief will not be easily overcome. The toll of this pandemic is profound.

The situation in some other countries is much worse, and the pandemic is far from over. Case counts are reaching new highs, with some recent days exceeding 800,000 reported cases and 13,000 deaths. India is in the midst of a terrible wave, and reports suggest that in some communities the situation is dire. A variant of interest, B.1.617, may be contributing to the surge. As our own domestic outbreak improves, we must turn our attention to helping the world.

As we continue the work of ending the pandemic both at home and around the world, we must also identify the changes necessary to ensure we are never in this position again. In doing so, we should recognize that we were caught unprepared more than once. We were unprepared to manage the emergence and swift global spread of the novel coronavirus, and we were late to recognize when it reached our shores. Those delays set us on a worse trajectory than we might have otherwise faced. Strengthening those early-response capabilities will likely feature heavily in reforms.

But so, too, were we unprepared for variants. Although genomics experts had warned of the threat, it was not until the United Kingdom suffered a severe wave attributed to the B.1.1.7 variant that public health officials worldwide sharpened their focus. B.1.1.7 is now understood to be perhaps 50% more transmissible than other variants, and it may also cause more severe illness. The UK was able to identify and track this variant over time because they invested heavily in genomic surveillance, aiming to sequence 10% of their positive cases. That capability yielded important information needed to guide their domestic response. It also provided warning to the world about what was to come. We did not have that level of genomic surveillance in the United States, and that is a gap.

As anticipated, B.1.1.7 has gone on to become dominant in the United States, constituting perhaps 60% of our current cases. Its increased transmissibility gives it an advantage that allows it to outcompete other variants. The increased transmissibility also makes it more difficult to control the virus using standard public health interventions like masks, social distancing, and ventilation. Adherence to those measures must be even higher to counter the variant's ease of spread. Fortunately, the performance of the vaccines authorized for use in the U.S. is not substantially impacted, and they still provide very high levels of protection against this variant.

B.1.1.7 is now joined by four others designated as "variants of concern" and several "variants of interest." The most concerning characteristic of these other variants is that they exhibit some degree of immune escape, meaning that vaccines and therapeutics may be somewhat less effective. Future variants may drift even further from the protection existing vaccines can provide, cause more severe illness, or impact diagnostic testing. These possibilities underscore the importance of careful surveillance and characterization of emerging variants. If we do need to update our vaccines or diagnostics to be a better match, we must know that as early as possible so we can begin that work before the variant becomes widespread. We must not again be unprepared.

The American Rescue Plan includes \$1.7B for genomic surveillance, which the Biden Administration has announced will be spent on expanding sequencing, establishing Centers of Excellence in Genomic Epidemiology, and building a National Bioinformatics Infrastructure. These endeavors would be bolstered by the development of a national strategy that could enumerate near term and long-term priorities for advancing our genomic surveillance infrastructure, drawing on lessons from similar, successful efforts for influenza and foodborne illness. The development and

implementation of the strategy could be led by the Department of Health and Human Services and supported by interagency and academic experts.

The American Rescue Plan also includes additional funds for biological research, expansion of the public health workforce, and a suite of other important public health initiatives that will improve our preparedness. Given that SARS-CoV-2 is likely to circulate both here and abroad for the foreseeable future, and in anticipation of the next viral threat, Congress should provide long-term, sustainable support for this expansion in public health infrastructure so that we will be in a position to better respond to the next threat.

Data Sharing

Timely collection and sharing of accurate, detailed public health data have long been a challenge during outbreaks. Public health data infrastructure is underdeveloped and out of date in many places around the world, including in the United States. Both the CARES Act and the American Rescue Plan contain funding for Centers for Disease Control and Prevention's (CDC) Data Modernization Initiative (DMI). DMI is an important plan to bring together state, tribal, local, and territorial public health jurisdictions as well as stakeholders from the public and private sectors to upgrade our national public health data infrastructure.

Genomic surveillance data should be included in the efforts of DMI. In some respects, sharing of viral genome data is more common than for other kinds of public health data. Although far from perfect, many scientists do share sequence data publicly, allowing others to analyze and learn from those data. Several public repositories exist and are widely used, including GISAID and GenBank. The GISAID repository includes over 1.4M submissions of SARS-CoV-2 sequences, including over 380,000 from the United States. Following the experience of the United Kingdom and the B.1.1.7 variant, sharing of sequence data has accelerated rapidly, and I expect that trend to continue.

However, several gaps in data sharing remain. Right now, most sharing is concentrated around individual sequences. But to determine whether a mutation or variant has clinical or public health consequences, we must be able to observe how the variant behaves in individuals and populations. To do that, researchers must know about the demographics, symptoms, clinical course and history, and outcomes of the person infected. Additional information about the circumstances of infection, including the number of secondary cases, is also valuable. For example, the United Kingdom was able to characterize the B.1.1.7 variant by analyzing case data linked with testing data. The New York City Department of Health and Mental Hygiene recently accomplished

something similar with the B.1.526 variant, finding that it likely does not cause more severe disease.

The kind of data infrastructure that allows for analyses that combine sequence data with case data is not common in the United States. This gap limits our ability to understand whether new variants have changed in ways that are meaningful to public health, or whether they are simply benign variations. To remedy this, we should work toward the examples set by the United Kingdom and New York City by developing research partnerships between public health departments, laboratories and hospital systems, which is an effort that could be coordinated by the National Institutes of Health and CDC.

Modeling & Analytics

As we advance our genomic surveillance infrastructure, we should also further develop the modeling and analytics infrastructure that will allow us to make even better use of that data. Epidemiological modeling has played an important role both in the Covid-19 response and in previous epidemics, but that capability is not yet fully developed. With the exception of a few small groups within the Department of Health and Human Services, most modelers work in academia and volunteer to support the public health response when an urgent need arises. This arrangement is not well suited for either party.

The Federal government would benefit from a permanent capability, with infectious disease modelers working to advance the state of the science and support public health decision-making both between and during emergencies. Efforts along those lines are newly underway. The Biden Administration announced in National Security Directive-1 an intention to create a National Center for Epidemic Forecasting and Outbreak Analytics, and the American Rescue Plan appropriated \$500M to CDC for disease forecasting and data modernization. These are promising steps towards modernizing our response capabilities, and I believe they will serve the nation well. Congress could help by appropriating annual funding for the forecasting center so that it can endure as a permanent program.

Future Preparedness

The challenges we face in setting up and maintaining genomic surveillance infrastructure are not unique to SARS-CoV-2. We have faced these challenges before with influenza surveillance, and we will at some point face them again with the next emerging pathogen. The lessons we learn and the investments we make to navigate

through this crisis can also serve as an opportunity to fortify our preparedness and response infrastructure for other infectious disease threats that we face.

It is also in our interest to ensure that countries around the world are similarly equipped to conduct genomic surveillance in their communities. Although the United States is already achieving widespread vaccination which will slow circulation of the virus, that will not be the case in much of the world in the short or medium term. Continued transmission will facilitate the emergence of new variants, including potentially those that are not well matched for the vaccines. Bolstering surveillance globally will give warning to the world and allow medical countermeasures to be updated accordingly. The United States could offer technical assistance and funding to other research and public health institutions that wish to develop and expand genomic surveillance.

In conclusion, although the currently circulating variants complicated our course through the spring months, we are now on track to regain control of the pandemic in the U.S. Continued vigilance to current and future variants is essential to ensuring that we maintain our encouraging trajectory. We must expand our genomic surveillance efforts domestically, and work with partners and allies abroad to ensure global coverage. The United States is a world leader in science and technology, and we have the opportunity, using those capabilities, to lead the world through the rest of the pandemic.

Dr. Caitlin Rivers, PhD, MPH is a Senior Scholar at the Johns Hopkins Center for Health Security and an Assistant Professor in the Department of Environmental Health and Engineering at the Johns Hopkins Bloomberg School of Public Health. She is an epidemiologist specializing in emerging infectious diseases. Her research focuses on improving public health preparedness and response to large-scale events.

Dr. Rivers recently co-authored a report [Staying Ahead of the Variants: Policy Recommendations to Identify and Manage Current and Future Variants of Concern](#). She has also participated as author or contributor in influential reports that are guiding the US response to COVID-19, including National Coronavirus Response: A Roadmap to Reopening; A National COVID-19 Surveillance System: Achieving Containment; Filling in the Blanks: National Research Needs to Guide Decisions about Reopening Schools in the United States; and A National Plan to Enable Comprehensive COVID-19 Case Finding and Contact Tracing in the US. She is the lead author on the report Public Health Principles for a Phased Reopening During COVID-19: Guidance for Governors which was used by the National Governors Association, the state of Maryland, and the District of Columbia to guide reopening plans.

Prior to joining Johns Hopkins in 2017, Dr. Rivers worked as an epidemiologist for the US Army Public Health Center. Dr. Rivers has been awarded the Johns Hopkins Bloomberg School of Public Health Faculty Award for Excellence in US Public Health Practice; the Department of the Army Achievement Medal for Civilian Service; and a Department of Defense Science, Engineering, Mathematics and Research Transformation Scholarship. She received a PhD and MPH from Virginia Tech, and a BA from the University of New Hampshire.

Chairman FOSTER. Thank you. And at this point we will now begin our first round of questions. So the Chair will recognize himself for five minutes.

The first question is what I hope is sort of a simple question on the public health significance of new viral strains. Dr. Rivers, you note in your testimony that B.1.1.7 has gone on to become dominant in the United States, constituting perhaps 60 percent of our current cases. So my question is does that mean that if this variant had never existed that we would have 60 percent fewer cases in the United States today or is it more complicated than that? You know, should we think about these as, you know, each new strain is a whole new disease circulating in our population or are there things like, you know, cross-immunity that really muddy the picture here? And how should we think about this?

Dr. RIVERS. Yes, thank you for that question. It's not the case that we would have 60 percent fewer cases. What it means for a variant to be more transmissible is the tools we have, particularly around masking, distancing, ventilation, have to be adhered to even more closely in order to be effective because the virus passes more easily between people. The increased transmissibility is seen across a number of variants of concern and interest, and it makes it more difficult for the variants to be—the virus to be controlled and slowed.

Chairman FOSTER. OK. And so in the modeling do you model it as just one virus with a range of infectiousness or do you independently model the frequency of each strain in the population? I guess maybe that gets at my question.

Dr. RIVERS. There are several different approaches depending on the question you would like to answer. When producing a forecast, you would increase the infectiousness or the transmissibility, and so you would have a better sense of the new trajectory given the variant. If you would like to know how competing variants might unfold over time, it would be a different approach, but that is also a question that can be answered using modeling approaches.

Chairman FOSTER. Thank you. Dr. Abdool Karim, in your prepared testimony you gave a great overview of how the known variants have affected disease severity, transmissibility, and treatment efficacy, and as well as natural and vaccine-induced immunity. I think that addressed a lot of questions and concerns that I have as we see new variants pop up, but, you know, how—could you say a little bit about the difference between how variants will evolve before you have the population vaccinated or at least partially vaccinated versus after you've got a big part of the population vaccinated? You know, what fraction of the danger from a vaccine-induced mutation, what fraction of the woods are we out of in that—in regards to that?

Dr. ABDOOL KARIM. Thank you very much for that question. I think you're getting to one of the difficult areas that we don't have data, and so I what I'm going to tell you is speculation to some extent. What we understand now is immunocompromised individuals are playing an important role in the generation of variants, and so as the virus is spreading at a higher rate, we are enhancing the risk of seeing new variants.

When we have a vaccinated population, if a vaccinated individual or an individual who has had past infection or an individual who is receiving monoclonal antibodies has a virus that's evolving to create a variant, then that variant has a higher likelihood of escaping that immunity, and so that's our concern that as we get to higher levels of vaccination, the individuals who are immunocompromised that may lead to the emergence of new variants would be those at risk of creating variants with vaccine escape—ability to escape vaccine immunity.

Chairman FOSTER. And are we in a situation now at least in the United States that when we see what are called these breakthrough cases where you get vaccinated and nonetheless get COVID, are those of enough special interest that at least those are completely sequenced to see if we're seeing those as the source of new vaccine-resistant variants?

Dr. ABDOOL KARIM. So there are several programs underway, and many of the companies themselves as part of their clinical trials have been sequencing the viruses that constitute escape and also they want to measure the antibody levels at which escape is occurring. And the most recent published paper in the *New England Journal of Medicine* showed that two of the variants that had been sequenced and studied in detail that caused breakthrough infections, that they were variants with escaped mutations. So I think what we're going to see in breakthrough infections is a combination of normal viruses that are just escaping because immunity is low and others that have escaped mutations that enable them to bypass the immunity or at least partially bypass it.

Chairman FOSTER. And beautiful timing on ending your remarks as the timer goes to zero, and I will now recognize our Ranking Member, Mr. Obernolte, for five minutes.

Mr. OBERNOLTE. Well, thank you, Mr. Chairman, and thank you to all of our panelists. It's been a fascinating hearing.

I am very interested in what we can do as a Federal Government to change policy to make the process of identifying these variants and combating them more cost-effective and efficient. So, Dr. Grubaugh, I had a question for you because you talked about different policy changes that can be contemplated along those lines. And one of the things that you mentioned is giving data generators the first right to publish, which seems to me to be counterintuitive because, you know, wouldn't that slow the spread of information? We want to speed that up. So what could we do to help that?

Dr. GRUBAUGH. Yes, thank you for that question. It's a really complex area in public health. I think if data being generated by a public health lab and for the sole purpose of public health, then it makes sense just to make that free and open. In the United States we have a lot of data that are not being generated by public health labs but by academic labs that cost somewhere between, you know, \$100 and \$200 to sequence a virus genome. And when you have an academic lab whose first order of business is to support students and postdocs that need to publish to go on with their careers, if they're spending a lot of that time then giving the data away for free, then that can become problematic for those who actually need it.

Now, in my lab I am open data, open resource, open everything, and we're sort of in a privileged situation that we can make everything available. And if we get scooped on that, then we have other things to help make sure that our students get papers. But other people may not be in those privileged situations, especially in the low-resource countries where maybe they can't quite survive—a lab may not be able to survive having their data be poached by high-income countries. So it becomes a really complicated scenario, one that there's a national and global debate right now, and I hope that I answered your question.

Mr. OBERNOLTE. OK. Thank you. I would hope—we all would hope that at some point the greater good of sharing information to combat something which is an existential threat to humanity, you know, could prevail over parochial interests, and so anything that we can do as a government to stimulate that I think would be a good thing.

Dr. Karim, I found your testimony particularly interesting, and I wonder, you've testified that some variants such as the recent B.1.351 variant have proven to be problematic for some vaccines. And so, for example, vaccine efficacy of vaccines like AstraZeneca has been much lower whereas vaccines like the Pfizer vaccine and the Johnson & Johnson have not been as effective. So could you tell us a little bit more about why that is, why some vaccines are affected more than others and what we can do to improve that?

Dr. ABDOL KARIM. Yes, thank you for that. So we don't fully understand why some vaccines are differentially affected and others are not, but I'll give you one of the possible reasons that might explain that. The mutation that occurs in position 484 is a particularly important mutation. Naturally when—in the pre-existing variants the position 484 has an amino acid that is negatively charged. The human cell at that point is also negatively charged, so the pre-existing variants have a bit of propulsion because of negative versus negative. However, when the mutation occurs, the virus becomes positively charged, so that enhances the ability of the virus to attach to the cell so it becomes more difficult for antibodies to displace it. It's what we refer to as electrostatic charge is impacting on that.

So the way in which the vaccine immunity can displace one that has more affinity is differential by the different vaccines, and that's probably the key explanation why the AstraZeneca vaccine is pretty much—has no efficacy against mild to moderate disease against B.1.351, whereas Pfizer at this point has 100 percent efficacy. And we only know this because both the trials were done in South Africa.

Mr. OBERNOLTE. Right. Well, thank you very much. I find that fascinating. One last question for Dr. Streiffer. A couple of our panelists have expressed the need for faster and less expensive whole-virus genome sequencing. What can we do as a Federal Government to make that faster and less expensive? Because it seems very central to our ability to fight these virus variants.

Dr. STREIFFER. You know, one example of that is really fascinating right now is actually wastewater testing. So a lot of the genetic information is actually coming from patient samples where you're tying that back to a specific patient. What's actually been

very efficacious at least in high-income countries is the idea of actually doing pooled sampling from wastewater and then sequencing everything in that wastewater. And that gives you more of a shotgun approach to be able to understand everything that's coming out of the community and the ability to be able to detect variants well before they present through clinical patient testing. And it's got some limitations, but that's one way in which we could do something that's much cheaper.

I think Dr. Grubaugh also indicated some ways where you can actually design diagnostic tests that are simpler than the full genome sequencing but still allow you to sample variants in a way that gives you more visibility than the standard clinical testing, and that's a very important area to pursue.

Mr. OBERNOLTE. Well, great. Well, thank you. I've got about a dozen other questions, but I see my time's expired, so thank you to all of our panelists. And, Mr. Chairman, I yield back.

Chairman FOSTER. All right. It looks like we will have a shot at another—second set of questions if there—if interest is retained.

And I'll now recognize the Chairwoman of the Full Committee, Ms. Johnson, for five minutes.

Chairwoman JOHNSON. Thank you very much. Dr. Karim Abdool—Abdool Karim, the rollout of the vaccine to many and the much-needed light at the end of the tunnel of course we think after a year waiting and hoping that we've gotten there, the CDC has gradually upgraded its guidance on measures such as social distancing, mask wearing as vaccine uptake in the United States increases. However, we are still falling short of achieving herd immunity in this country and globally. How important are the behavioral measures in preventing the spread of the virus while we remain under the threshold for herd immunity? And what current state of science regarding the ability of the vaccinated individuals to asymptotically infect nonvaccinated people?

Dr. ABDOL KARIM. Thank you very much, Chairwoman Johnson. So let me try and answer the first question, which is that we vaccinate individuals for two reasons. The first is for individual benefit. I get a vaccine so I benefit in that I don't get severe disease or I don't get infected at all when I'm exposed. The second reason we vaccinate is we want population benefit. We want to slow the transmission of the virus. Now, we can only do that with vaccines if a person who's vaccinated does not transmit the virus because if a person who is vaccinated who gets infected then transmits the virus, then we undermine our ability to achieve herd immunity. So far, the preliminary data—and it's pretty—it's very preliminary—suggests that transmission rates are dropped in individuals who are vaccinated, but we do not yet have definitive evidence because those studies are hard to do.

The second issue—the second question you asked me is about how important it is that we maintain our nonpharmaceutical prevention measures while we are vaccinating. It is critical because vaccines on their own are not able to achieve herd immunity or to slow transmission on their own. We do need to maintain those.

When we start nearing levels of herd immunity with vaccine coverage only, I think what we will then see is a change in the number of restrictions that will be required, and many of the individual

restrictions will be replaced by broader restrictions such as avoiding mass gatherings where the risk is high, but for the individual restrictions, we can expect that some of those will be eased, and the CDC has been doing that in a systematic, slow way at the moment.

Chairwoman JOHNSON. Thank you very much. Mr. Chairman, I yield back.

Chairman FOSTER. Thank you, and I will now recognize our colleague from Florida, Mr. Posey, for five minutes.

Mr. POSEY. Thank you very much, Chairman Foster and Ranking Member Obernolte, for holding this hearing.

Discussing the variants of COVID-19 is very important to our work of defeating this virus and understanding its dangers and history. Dr. Streiffer, in 2003 it appears the first SARS epidemic, SARS-CoV, was beginning to spread, and the virus was mutating rapidly as it adapted to humans. But it appears once it became more contagious, it became more stable and stopped mutating so quickly.

COVID-19 or SARS-CoV-2, appears to have been remarkably stable since it first emerged in 2019 in Wuhan. It never appears to have had the same period of rapid mutation that was seen in the 2003 SARS outbreak. Each witness obviously is very interested in the variants, but I wonder if we are as curious about the missing links for earlier variants of COVID-19 that we would have expected to have seen just after the emergence of a new virus. Can staff bring my pictures up now?

[Slide follows:]

Figure 2

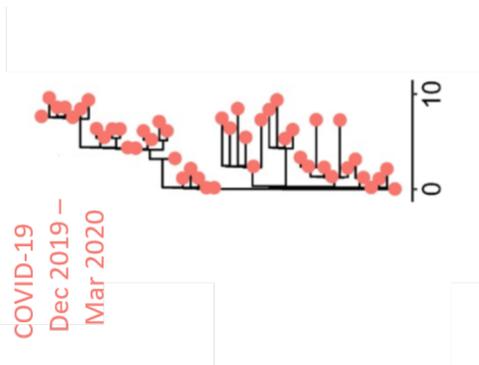
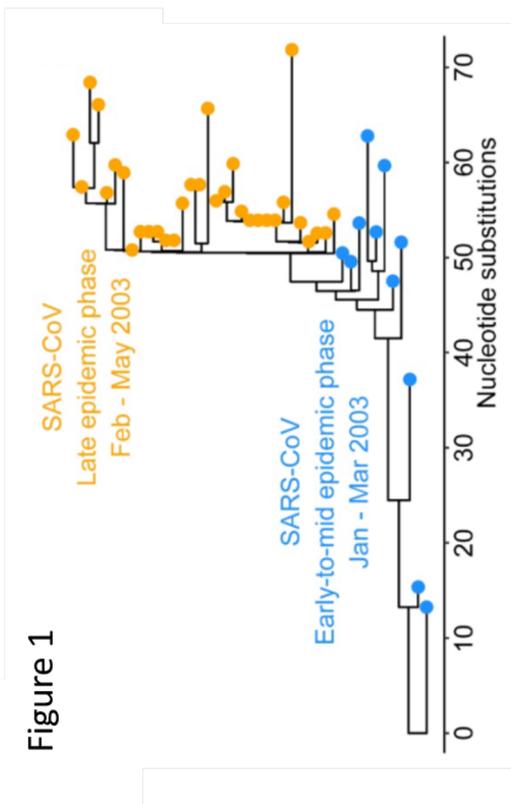


Figure 1



Mr. POSEY. This is from a preprint paper, and figure 1 shows mutations in early stage SARS in blue and then the late-stage SARS in yellow. Figure 2 shows the mutations in COVID-19. Bigger spaces between those dots would appear to this layperson to indicate greater mutations in the virus. And obviously, the two figures are very different from each other, and in fact the red COVID, COVID-19 looks a lot more like the yellow late-stage SARS. The original SARS is known to be a nationally emerging virus, and it mutated rapidly when it did emerge. COVID-19 on the other hand did not have the same rapid mutations. So my question, Dr. Streiffer, based on your expertise, how would you explain why figure 2 does not have the early mutations that we see in figure 1?

Dr. STREIFFER. So just to jump in—and sorry, I apologize, I moving screens around so I can actually see the figure. I'm actually paying attention. So I think virus evolution is always a careful balance between trying to infect the host, replicate, and do that in a way which is efficient but not actually kill the host. And one of the things that you'll find is that vaccine—viruses rather are actually too aggressive they cause too much fatality and will actually damp out very quickly, so you do see an enormous amount of difference in the rate at which viruses mutate and the patterns that you see in those mutations.

And I think that's reflected here. I think these are both natural viruses. I think the difference in the mutation rates is a reflection of the different epidemiology, the way in which the initial pandemic's played out, and then just the natural differences in the virus.

And Dr. Abdool Karim and Dr.—excuse me, I'm going to get my name wrong—Dr. Grubaugh could probably comment very eloquently on this if they'd like to follow up with that, although, of course, it's the Member's prerogative.

Mr. POSEY. I'd be delighted for the follow-up. Thank you. I yield.

Chairman FOSTER. Thank you. The gentleman has yielded his time for—

Mr. POSEY. I was going to yield to the witness to answer that Dr. Streiffer recommended.

Dr. GRUBAUGH. I can answer for a minute. So, one, each virus is a little bit different, and especially when we have viruses that emerge from animals and to people that they're at different stages of being able to adapt and spread within people. And so there's—it's always hard to compare apples to apples when you have different events that are happening.

Also, evolution is not just dependent on adapting to the host. There's other things in play such as the re-transmission, some other inherent factors, the types of therapeutics that are used, so it's a really complicated factor.

And I would say that with SARS CoV-2 we did see early adaptation to humans. We had the D614G mutation that rapidly spread around the world, and then now we are seeing the emergence of many new variants that are happening. And also just to say that the pandemic with SARS-CoV-2 is really unprecedented in terms of the number of infections. It's evolutionary patterns with the emergence of several variants that have many mutations that are acquired in a very short period that I would just say it's very dif-

difficult to compare this to really anything else because we haven't seen anything quite like this.

Mr. POSEY. Thank you very much. Mr. Chairman, thank you. I yield back.

Chairman FOSTER. Thank you. And, yes, the—I believe the gentleman's line of questioning touched on a very important issue, which is trying to understand what we can about the origins of this virus. And, you know, this is a subject of very serious scientific debate among serious scientists about what constitutes evidence in various directions. This Subcommittee on Investigations and Oversight does intend to have a hearing on the origins of the SARS-CoV-2 virus in the near future.

And I will now recognize our colleague from California, Dr. Bera, for five minutes.

Mr. BERA. Thank you, Chairman Foster.

I know that, you know, that tracking variants and making sure we're data sharing is something that we've been incredibly interested in—along with Senator Tammy Baldwin from Wisconsin, we introduced the *Tracking COVID-19 Variants Act* asking for \$2 billion to go to CDC. We were able to get \$1.75 billion into the American Rescue Plan, so hopefully, that's a first step, as well as indicating to the CDC to talk about the issue that I know—I think we've talked to Dr. Rivers about data sharing and how we, you know, link public health and academia and data sharing.

I'm going to put my doctor hat on and just, you know, when I think about the variants that we're seeing in India, you know, also some of the variants that we're seeing in Michigan or some of the cases that we're seeing, it does seem like, you know, younger people are now being infected more rapidly, as well as being hospitalized. And I don't know if that's just epidemiology that younger folks are less vaccinated and thus are susceptible, and maybe, Dr. Karim, you know, since you're on the frontline in South Africa, you could tell us what you're seeing on the ground in terms of hospitalizations of who is being infected right now.

Dr. ABDOL KARIM. Thank you for the question. Yes, you're quite right. It's a matter of epidemiology. And we saw that certainly in the second wave in Brazil, South Africa, and in India, that in the second wave, because the virus has a higher transmissibility, it infects a lot more people quickly. The number of younger people in those populations is high, and so even though it's a smaller fraction that will actually get to a hospital, so many of them became infected that disproportionately there were larger numbers of young people in hospitals, so it's just a function of the way in which the rapid transmissibility infects such a high proportion of young people that we begin to see more young people in hospitals. And that's been described quite well in all three settings. And it's a similar issue with the B.1.1.7 variant, that it causes many young people to get infected, so that's why disproportionately we start seeing more young people in hospital. You're quite right.

Mr. BERA. And, you know, for any of the panelists, as we think about that then, you know, I think many of us in the medical community were surprised that India, Sub-Saharan Africa, et cetera, weren't severely impacted in the first wave a year ago, and some of us thought that, well, it's a younger population so they had sub-

clinical infections, et cetera. Now our concern is that we're seeing these variants spread more rapidly with younger population, what this may do in Sub-Saharan Africa that also speaks to a younger population. Is that a legitimate concern? And, you know, obviously we're seeing the overwhelming infections in India. And how should we—outside of rapidly getting vaccinations to these populations, how else should we think about it? And, again, I'm happy to let—or Dr. Karim, if you want to answer that one as well.

Dr. ABDOL KARIM. Sure, I'll start with an answer. I have spent the last several months trying to answer that question. That's because we all predicted that Africa would have a really severe epidemic, but it didn't come to pass, and so there was some hypotheses that were proposed. And I have looked at nine of the different hypotheses, including temperature, including age, and so on.

I think in summary I have found that there is no specific protection that Africans have. There's nothing in their lifestyle, there's nothing that they've got genetically that gives them any protection that I have been able to find.

What is most clear is that the young populations that we see in Africa, the very small fractions of the population that are above 60 means that a large number of people who are getting infected are getting infected asymptotically, and so the reporting has been—you know, they don't report those cases because they don't know about those cases. In addition, most of the countries in Africa went into very severe lockdowns initially, so that's why the first waves weren't that bad. But now they're being caught in the second wave and the variants where many countries in Africa have much more severe epidemics. So variants, age, and implementing nonpharmaceutical interventions early played that role in why I think Africa did not see a severe epidemic. And I'm sure my colleagues may have something to add. Thank you.

Mr. BERA. I see I'm out of time. Hopefully, we'll have that second round of questions.

Chairman FOSTER. And we plan to. And now, despite the fact that he is not a doctor but merely holds a master's degree in biochemical engineering, the Chair will now recognize our colleague from Illinois, Mr. Casten, for five minutes.

Mr. CASTEN. Oh, you're far too kind. It's nice to be one of the non-nerds in this group.

I really want to thank you all for being here. Thank you to our Chairman for pulling this hearing together.

The—Dr. Abdool Karim, I want to start with you and I think just give us a chance to have a little bit of a—just a few quick public service announcements. The—you know, we are fortunately going from a point in our country where we shifted from having more demand than supply for vaccine to, you know, starting to see the opposite and, you know, daily doses administered have fallen off in the last month or so and starting to sort of get to that harder more vaccine-hesitant community.

I want to start with a public service announcement of my own. My 16-year-old daughter is getting her second dose in two weeks, and my 14-year-old daughter has just registered for her first dose

tomorrow, so what's good for us is good for—and hopefully everyone will follow.

But, Dr. Abdool Karim—and you mentioned this before, but just a couple quick yes or noes. To the best of your knowledge are the Moderna, Pfizer, and J&J vaccines currently available to Americans effective at preventing the worst aspects of COVID-19?

Dr. ABDOOL KARIM. Yes.

Mr. CASTEN. To your knowledge are they all generally safe?

Dr. ABDOOL KARIM. Yes.

Mr. CASTEN. To your knowledge are they broadly effective against all of the common variants of COVID-19 that are circulating in the United States?

Dr. ABDOOL KARIM. I can't answer that exactly, but they are effective against most of the common variants. They haven't been tested against, for example, the Indian variant yet, the variant in India.

Mr. CASTEN. OK. Well, there's—is there any good reason for any American, unless their doctor tells them otherwise, not to go get a vaccine?

Dr. ABDOOL KARIM. No.

Mr. CASTEN. OK. Well, that's an easy one.

Let me then move on to something a little bit more deep in the weeds. And you alluded to some of this in your conversation with Chairwoman Johnson. Early on I think we were all concerned about what is the likelihood of asymptomatic spread and how do we know about that and how do we think through that. Have you seen anything in the data to suggest that the risk of asymptomatic spread is—excuse me—asymptomatic spread is substantially different between vaccinated and nonvaccinated populations?

Dr. ABDOOL KARIM. We don't have empiric data, so I'm going to speculate based on what we have been seeing in terms of the viral load that's in the swabs that are taken from the nose. When we look at the swab—the amount of virus that's in the swab, vaccinated individuals who do get infected have lower levels of the virus in those swabs. So we would think that that translates into lower transmission, but I don't have clinical evidence. That laboratory evidence is certainly suggestive that vaccination means lower levels of transmission.

Mr. CASTEN. And what about for folks who have, you know, tested positive for COVID and may have developed some degree of natural immunity? How would you put that population in amongst the vaccinated versus nonvaccinated?

Dr. ABDOOL KARIM. So individuals who have had prior infection generally have some level of protection to new infections even if they are variants. And the level of protection that's provided is at this point most likely in terms of the severity of infection, so they may be able to transmit, but we think that they get less severe disease. The empiric data for that is still preliminary. Only—there's only one study I've seen it, and that's of a small number that suggests that.

But in terms of transmission, an individual who's been infected gets reinfection, we don't know about their risk of transmission. I can't answer that question.

Mr. CASTEN. So I—and I realize I may be getting into small subsets of data, but if—you talked about viral loading as being your sort of estimate of why this might change. If you have experienced COVID but not been vaccinated versus experienced COVID and have been vaccinated, is there a difference in the viral loading of those two populations? I mean, what I'm trying to get at is do we expand herd immunity more greatly by making sure that even if you've had a bad case of COVID and you still get vaccinated, do you reduce your risk of asymptomatic spread at least theoretically?

Dr. ABDOOL KARIM. There's a big difference. If we look at vaccinated individuals, especially when they've been vaccinated with an mRNA vaccine, the antibody levels are really high. They are extremely high. They are at the highest levels that we see with natural infection, as opposed to natural infection where the antibodies are much lower. And when you deal with variants, higher antibodies are really important, higher levels of these antibodies, so there's no question that vaccination is a big advantage compared to natural infection in terms of risk of reinfection.

Also, that when you've had natural infection, if you've had asymptomatic natural infection, the antibodies disappear quite early, within three, to four, five months, and so we see lower levels of antibodies with asymptomatic infections in natural infections, but with vaccines, it's consistent. Everybody gets high levels of antibodies.

Mr. CASTEN. It's fascinating. And I'm unfortunately out of time. I have more questions, but I really appreciate your time. I yield back.

Chairman FOSTER. Thank you. And I will now recognize our colleague from Colorado, Mr. Perlmutter, for five minutes.

Mr. PERLMUTTER. Thank you, Dr. Foster. And I guess I want to start with a question that was posed early on in this process, and that was sort of Sweden's approach toward herd immunity by, you know, just sort of going on with their lives compared to surrounding Scandinavian countries. And this is to the whole panel. You know, I haven't seen much in the news about Sweden and its herd immunity and whether or not it's facing any new challenges given these variations. So, Dr. Rivers, why don't I start with you if you have any—or anybody who wants to jump in on that one.

Dr. RIVERS. Sure. I can't speak to the latest situation in Sweden as I haven't followed up on their current status, but I will note that their early strategy of allowing the infection to spread in hopes of achieving naturally acquired herd immunity was changed over time, and they did go on to adapt more restrictive measures in order to slow the spread because they saw that their hospitals were becoming overwhelmed. And so I think that our early perception of how Sweden managed the pandemic was something that evolved to look more in line with the measures that many other countries took. But I'll see if any of my colleagues know the latest on Sweden.

Mr. PERLMUTTER. Anybody else?

Dr. ABDOOL KARIM. I can perhaps just comment briefly. I just did a webinar with Anders Tegnell, who is the chief COVID scientist in Sweden, my equivalent there, and he went with this initial approach, which is—actually was promoted by a group of scientists

in—across the oceans both in the United States and the U.K. under something called the Great Barrington Declaration. And their hypothesis was if you let the virus run wild in younger populations, natural infection will provide immunity and herd immunity. Well, it's been shown now that that simply is not true, that in fact what happens is when you end up with large numbers of infections like that, the older people do get infected and you get the situation of high numbers of death. And Sweden saw that and so had to make those changes. And Sweden, by the way, still doesn't promote mask wearing, but that's a separate discussion. It's not related to this.

Mr. PERLMUTTER. All right, thank you. Yes, I mean, what—you saw the initial, you know, reports was, you know, Norway had a much smaller incidence than Sweden as Sweden was trying to, you know, develop herd immunity. They were having a lot sicker people and deaths compared to their next-door neighbor. So—OK. Thank you.

Now I'm going to ask more personal questions because, Dr. Rivers, I'm one of those 32 million who was infected. And, you know, my curiosity is more in these variations. You know, we've talked about two things, how transmissible it is and how severe the new variations may be. So, you know, one thing we haven't talked and I'd ask the Chair and the Ranking Member that we also take a look at sort of the long-term effects of this disease. And, you know, we do know that there are issues that linger. So in terms of the severity of some of these new, more transmissible viruses, what are we seeing in terms of the effect on people's health? Is there something that, say, in the South African variation is more dangerous in terms of health or is it just because it's more transmissible? So, Dr. Grubaugh, why don't you—I don't know if you want to jump in on that or if that's something you've been thinking about or anybody else.

Dr. GRUBAUGH. I'll just quickly start, and I believe Dr. Rivers probably has some points to make here, too. There is some data from the U.K. that would indicate that the B.1.1.7 variant can cause more severe disease. It's not just more transmissible. It's a really difficult thing to actually answer because when you're—there's—you know, what has the most impact on disease is actually host factors, age, comorbidities. These sorts of things impact whether or not you're going to be—you know, have more severe disease or not, much more than the virus. So the virus could have some small impacts on that, but we need really large studies to be able to measure these sort of small changes.

Mr. PERLMUTTER. OK. Dr. Rivers?

Dr. RIVERS. Thank you. I'll just add that there are three levels of variant classification in the United States, variants of interest, variants of concern, and the third is a variant of high consequence. And the variant that causes more severe disease would be classified as a variant of high consequence. There are currently no variants that carry that designation, and so that's not something that is currently circulating or has been identified.

Mr. PERLMUTTER. Thank you. My time is expired. I yield back.

Chairman FOSTER. Well, thank you. And at this point we will now begin our second round of questions, and the Chair will recognize himself for five minutes.

Dr. Streiffer, it was I guess about a year ago last week the Science Committee held its first roundtable about the Federal research enterprise and its response to COVID-19. And we talked about the natural—National Virtual Biotechnology Laboratory with Michelle Buchanan of Oak Ridge. And at the time NVBL was only a few weeks old, and now with a year of experience behind you, you know, there are serious efforts to consider a permanent reauthorization of the NVBL both by—on the part of our former colleague, now Senator Ben Ray Lujan, as well as efforts in the House. And so with that year of experience behind you, what are the observations that you might have about the best practices on how to coordinate all of the diverse Federal capabilities that were brought together in the NVBL?

Dr. STREIFFER. Thank you, Dr. Foster. It's a very good question. I think some of the lessons learned from that is that the coordination across the 17 laboratories through a central body was actually very effective. And coordinating that directly with the Department of Energy and then with each of the agencies that's been involved in the national response is crucially important. And I think one thing that's very gratifying is the increased level of coordination that we're seeing over the last several months in the Nation's response to COVID-19.

I think also very importantly is that the National Virtual Biotechnology Laboratory created a model that was very flexible, very adaptive, and very fast to respond to the issues, much different than we often think of the national response framework, particularly when research and development is concerned where those timescales are quite long. And with that adaptability I think we're able to quickly pivot to the most important problems at hand, maintain a focus on issues that they—as they developed and move on from issues like designing new ventilators as it became apparent that those were not going to be as of a concern as they initially appeared to be.

Chairman FOSTER. Thank you. And I guess my next question is for any of the witnesses that might want to get to it. Do we really have a complete picture of how this disease spreads? You know, is it—for example, if it's airborne, is it a few large droplets that someone sprays at you while we're talking and gets inhaled deeply into the lungs or is it the ambient concentration of very small viral particles when you walk into a bar that's just had people in it for hours? How important is direct ingestion of the virus compared to inhalation both through the nose and directly into lungs? You know, what's the model here? Is it every virus that gets into your respiratory tract has the same probability, or are there certain configurations that are dangerous? What's understood about that?

Dr. RIVERS. I can perhaps start. This is one of the areas of our understanding of the virus that has changed substantially over time. We—particularly because it's difficult when people are in close contact to determine which mode of transmission was actually the one that infected them, but there's a growing understanding that the virus can buildup in the air and that crowded environments, even if you are not within 6 feet of someone, can be particularly risky. On the other hand, our perception of fomite transmission or contaminated services has gone down in the list and it

is no longer considered one of the primary modes of transmission. And I would put even below that ingestion. So airborne and respiratory are—excuse me, airborne and droplet transmission are at the top of the list.

Chairman FOSTER. Any other comments? You know, one of the reasons I bring it up is that the British are now apparently going to go ahead and do experiments in controlled human infection where they're going to be testing the efficacy directly of several candidate vaccines, which is one of the applications to very quickly get accurate measurements of the efficacy, you know, months faster than you can with standard clinical trials but also to get a better understanding of the methods of spread. And this is one of the tools that, you know, many people wish were available. You know, had we understood the role—the small role of fomites compared to inhalations on—early in the pandemic, we would be in a position to save hundreds of thousands of lives. If you can have some questions answered through those sort of experiments of direct human infection, what are the questions you'd really like to have answered in that kind of thing, or do you think that they won't really in the end be that useful?

Dr. ABDOOL KARIM. Perhaps I'll just add a quick comment if I might. I think Dr. Rivers really captured the issues quite well. We were initially taken with the wide spread of infection on the cruise liners, and we thought that fomites were important, but now it's becoming clearer and certainly in mice experiments, mice in different cages are infecting each other, showing the importance of aerosol transmissions, the very small droplets that carry the virus. But I think the droplet spread I think still remains probably, you know, the most important or, together with aerosols, is the most important. So I think that still remains our main focus, that having direct infection is still quite important, and then aerosols and then fomites being much more less important.

Chairman FOSTER. Well, thank you. And if there is some best state-of-the-knowledge document that you could forward to our offices, it would be very valuable for any of the witnesses because it's—it matters a lot for policy obviously.

My time is up. I will now recognize the Ranking Member, Mr. Obernolte, for five minutes.

Mr. OBERNOLTE. Thank you, Mr. Chairman. This has been a fascinating discussion, and I want to continue the discussion along the lines of our ability to combat this kind of crisis in the future because I think that when the dust settles, we put this crisis behind us, and we do a postmortem, we're going to realize how extraordinarily fortunate we were that the level of antigenic drift of COVID-19 was not higher. So to prepare ourselves for the future I think we need to really focus on the lessons that we've learned here, on how the virus is transmitted, and, more importantly, how it mutates and how those mutations affect immune escape and the ability of the vaccines we develop to react to it.

So to any of our panelists that want to comment on this, how can the U.S. Government catalyze that kind of spread of information? Because I think it's going to be vital to our future ability to respond to these kind of crises.

Dr. STREIFFER. So I'll jump in here. I'd also add in addition to that one of the things we need to do is a much better job of what you would refer to as international zoonotic surveillance. So by the best scientific knowledge available to us, this disease came to mankind originally from bats. What we need to do is a much better job of understanding the viruses that are out there that could cross the species barrier, sample those, understand their threat, and track them as they move through potentially the wildlife populations and into contact with humans. That's something we need to invest much more in globally.

Dr. GRUBAUGH. I'll jump in here, too, with this question. So of course we—you know, the hope is that, you know, with continued evolution and, you know, some level of transmission of this virus likely for years to come, that we don't have significant antigenic drift where this would significantly impact our vaccines, but I think we need to be prepared for that worst-case scenario. And the goal here would then be to sequence, you know, first, you know, as many of the vaccine breakthroughs as possible. I think these are really important to do, and then maintaining this general surveillance that we have on a yearly basis similar to what has already been done for flu for a long time to help inform vaccines. I think this is going to be one of the most critical areas as we go forward and have some level where there's always going to be some pockets of transmission probably at least for the next several years and being able to stay on top of how the virus is evolving and not having to respond from behind like we did starting at the beginning of this year.

Mr. OBERNOLTE. Right. Well, thank you very much to everyone, and let me restate my opinion that more funding into this kind of research is vitally important for us. I mean, it might be a case of existential survival for us as a species to make sure that we understand the threat that's out there and the way that we as governments and as a world health community can respond to it. So thank you very much, Mr. Chairman, and thank you to our witnesses. I yield back.

Chairman FOSTER. Thank you. And we'll now recognize Dr. Bera for five minutes.

Mr. BERA. Great, thank you. You know, maybe this is a question for Dr. Karim. When we talk about the vaccines, obviously, we talk about the efficacy of the vaccines. But each of the vaccines, including AstraZeneca, seem to be efficacious at preventing severe illness, hospitalization, and death. Is that a correct statement?

Dr. ABDOL KARIM. Yes, against the D614G variant, pretty much all the vaccines seem to be doing quite well in preventing severe disease both in the clinical trials but more importantly in the real world data that's now being collected.

Mr. BERA. OK. So, you know, while the AstraZeneca vaccine is not as effective at preventing illness necessarily, it's still, you know, an important component of our arsenal as we try to vaccinate the entire world. Is that—

Dr. ABDOL KARIM. So that's a little bit more difficult. So the studies that have been done with other variants, not the D614G variant, so if you take, for example—I'll just—to simplify just focus on the variant that was first described in South Africa by us, the

B.1.351, that variant, the studies that have been done only included younger people in South Africa with the AstraZeneca vaccine, so we know it doesn't work for mild and moderate infections in the South African setting against the B.1.351. The problem is we don't know if it prevents and ameliorates severe disease because there were no severe infections in the study itself.

And so there's only indirect evidence. There's only speculation and, you know, using laboratory evidence to suggest that maybe it will protect against severe disease, but there is no clinical evidence. And so on that basis—

Mr. BERA. If I were to ask Dr. Rivers or any of the other panelists—because obviously there's real-world evidence. You know, many people have gotten the AstraZeneca vaccine. Are we seeing those that have been vaccinated with AZ, let's say, in the United Kingdom and Britain being hospitalized or dying? Again, I have not seen anecdotal evidence that folks that have been vaccinated with the AZ even in places where there's a high prevalence of variants ending up dying? Is that—again, you know, Dr. Rivers?

Dr. RIVERS. I'm not sure that there is data available describing what Dr. Abdool Karim is sharing about the clinical evidence, but there are many places in the world where the immune escape variants are not circulating. The B.1.351 to my knowledge is not prevalent in many countries, and so the AZ and similar platforms would still have value there.

Mr. BERA. OK. Shifting—a question that's, you know, certainly—that I've been pondering since the beginning of the pandemic is, you know, when I think about how hard New York City was hit and then I think about Tokyo and how Japan, you know, approached the pandemic, you know, with the older population in Japan with mass transit systems, et cetera, you know, it was quite remarkable that they escaped, you know, at least in the first phase, you know, a similar impact that New York City potentially possessed. And I would just be curious, again, you know, this is the opinions of folks, obviously, mask wearing has a significant impact and culturally, you know, that's not taboo in Japan, and that was an issue—you know, the politics around mask wearing in the United States clearly had some impact. But is there a cross-immunity? You know, Japan, Korea, other places probably did get exposed to SARS and other coronaviruses in previous pandemics, and I would just be curious, you know, why Japan or, you know, or some of the Asian nations, you know, skirted the first phase of this, whereas we got hit quite hard? Maybe Dr. Rivers or any of the panelists.

Dr. RIVERS. The number of people infected by the SARS pandemic in 2003 was quite small, and so I don't expect it would contribute meaningfully to population immunity really anywhere in the world. Several of the Asian countries were much swifter and more aggressive in their response with—after the emergence of the novel coronavirus, and I think that contributed to their success. Japan focused very heavily on contact tracing, particularly backwards contact tracing, and I think that lent itself well to early containment. South Korea was also very successful, Singapore. They focused very heavily on diagnostic testing. They had a testing volume many times over what the United States was doing at the

time, which allowed them to find cases. And so the overarching lesson for me is that we need to be prepared to respond very quickly even before we really can characterize and feel confident that the threat is severe. If you fall behind, it's very difficult to catch up.

Mr. BERA. And the impact of wearing masks in Asia versus the United States?

Dr. RIVERS. Certainly in many countries in Asia after the 2003 pandemic it became common to wear masks in the community, and I—and many countries not only did they have them stockpiled but people had them in their homes, and I think that was very helpful as well.

Mr. BERA. Great. I'll yield back.

Chairman FOSTER. Yes, thank you. And I should also say in my one experience on Tokyo subways, it was very crowded but people were not talking, and I have never been on a New York subway where there weren't multiple people mouthing off in various ways.

And we will now recognize our colleague, Representative Posey, for five minutes.

Mr. POSEY. Thank you very much, Mr. Chairman.

The thing that alarmed me the most about COVID-19 in the very beginning is when we got our first TV reports. They said the damage to your lungs from this virus is unlike any others that we've ever seen before, and it will not heal itself. It's irreversible damage like neurological damage. You might stop it from progressing, but you can never reverse all the damage it's done. Of course, we've heard an awful lot of people have fully recovered.

I remember talking to NASA (National Aeronautics and Space Administration) Administrator Jim Bridenstine right after he got tested, and he was sick at the time he got tested. And he said the doctor called him and said what do you want first, the good news or the bad news? And he said, well, give me the good news. He said, well, you don't have COVID. He said, well, then what's the bad news? He said, well, you've got the other virus that's already killed 80,000 people. But I guess that other virus didn't kill anybody after COVID came out. I guess it was stopped in its tracks.

I was wondering, Dr. Streiffer, if the answer to my question that I asked before, you mentioned that you would expect to see this natural evolution, yet no one has presented any evidence of the evolution of COVID in animals or humans prior to the December 2019 outbreak. What do you make of that?

Dr. STREIFFER. I think there's a general understanding about the time that COVID-19 emerged as a disease in China. You know, as we've discussed previously, I think there's still some details about its origin that we don't quite understand. But I think the path of the virus upon its initial detection and its propagation around the world has followed more or less what we would expect for a virus that at some level has hit that sweet spot of being just infectious enough to spread, dangerous enough that it's caught our attention, but not so dangerous to kill so many hosts that it tamps itself down.

So, again, I would respectfully ask the Member to perhaps call on Dr. Rivers or Dr. Karim or Dr. Grubaugh to add some additional perspective on this. But I think we're seeing a progression in the genetic evolution of the virus under the pressures that we would

expect from both nonpharmaceutical interventions and how the vaccines are taking hold that is within the spectrum that we would anticipate as scientists.

Mr. POSEY. You know, I've had a lot of—and I'll direct this to Dr. Karim. I've had a lot of constituents question about taking the vaccination. You know, you mentioned a blanket statement absolutely everybody should and there's no good reason for anybody not to, but I've had people, well, what if my sister has pneumonia? I mean, should she take it then? Well, I mean, common sense would dictate no, but I'm not a doctor, and there are people that have contacted my office, we've had bad outcomes from vaccines before, and I'm sure you're probably familiar with that. And I've just told people talk to your physician about it. Your physician knows best of all if you should get it, and I've had some sort of vaccine—hey, my physician said not to do it. Well, I'm not going to argue with your physician about that.

You know, I'm aware of the vaccine injury trust fund. I don't know if you all are familiar with it or not, but when people make these statements that vaccines are 100 percent safe for everybody without exception, end of subject, you're an idiot if you don't get vaccinated, the public is in large part unaware of the vaccine injury trust fund, which is very hard to access, has a 2-year statute of limitations on it. Most pediatricians tell people they're crazy if they think their kids were injured or whatever. That vaccine injury trust fund has paid out \$4.5 billion and hasn't paid for a lot of the common bad outcomes that people suffer. So, Dr. Karim, just your thoughts briefly on that?

Dr. ABDUOL KARIM. Yes, thank you for that question. So I think all vaccines carry some side effects, and so that's part and parcel of what we live with. It's a question of the benefits and risks. In my own clinic I have had two severe reactions, one of which was very severe. The patient hospitalized, demyelinating disease, and she happened to have lupus, systemic lupus erythematosus. So she has a history of this kind of problem, and she didn't do well with the vaccine. I'm not sure if she actually got COVID, you know, she would probably also have quite a severe form of COVID, but we can never say that vaccines are 100 percent safe. There will always be those effects, and we've seen with some of the vaccines, clotting disorders. We've seen a range of others—I see them in my clinic. But I also see all of the many patients with severe COVID in my clinic, and I've got, you know, several patients with long COVID, and I can't tell you how debilitating it is. I'd rather you put up with the side effects and, you know, the antigenicity of the vaccine than have to deal with long COVID. I watch it and I shudder.

Mr. POSEY. I see my time is up. Mr. Chairman, thank you very much. I yield back.

Chairman FOSTER. Thank you. And we will—finally, we will now recognize our colleague from Colorado, Mr. Perlmutter, for five minutes.

Mr. PERLMUTTER. Thanks. And what Dr. Karim was just talking about is—I think should be another panel on the long-term effects of this and the potential costs associated with it because they do exist, and they are debilitating and—for some.

So my question is—let's start with Dr. Karim. When you were talking about immunoescape, you also mentioned people who are immunocompromised were more likely to have the virus do an immunoescape. And so can you tell me what you mean by immunocompromised and then the immunoescape? I wasn't quite sure I got it.

Dr. ABDOL KARIM. Sure. So when the person gets naturally infected, the body's immune system goes through three steps—well, there's many steps but just to make it simple, an innate immunity and then you get the B cells and the T cells responding, so those are the three parts. In somebody who is immunocompromised, let's say, somebody who has got cancer and is on immunosuppressive treatment, they don't follow those three steps, and so they can't bring the virus under quick control. Their innate response is first and foremost your first line of defense, and it brings the virus under some control quickly. So if you don't do that, the virus continues to replicate for months and months and months. And it remains viable all those months. And as it's replicating in the presence of antibodies against the virus, the virus itself will start mutating. So these antibodies are not killing the virus, but they are exposing this virus to what it needs to bypass. And so that's what the problem is.

And so when we see—there's a superb paper in the *New England Journal of Medicine*, and that paper shows in the cancer patient over a period of four months how the virus systematically evolves and changes itself to bypass the immune response. And so that's—those are the individuals seem to be an important group in creating these shifts where these new variants are emerging.

Mr. PERLMUTTER. Thank you. Anybody else? Or I'm happy to yield back to the Chair. I appreciate that answer. Dr. Grubaugh?

Dr. GRUBAUGH. Yes, I'll just add onto that. I think Dr. Abdool Karim's explanation was really fantastic. And from the evolutionary perspective when we see natural infections and transmission so acute infections and then you transmit to somebody else and you look at that over the course of four months or so, there's about one to two mutations that are incorporated into the virus per month. When we look at some of these long infections, either, you know, some level of immunocompromised, obviously, that's a huge sort of range of things, it could be somebody who had an organ transplant and they're on immunosuppressive drugs, it could get somebody who has AIDS, cancer, right, a lot of different ways. And when the immune system can't quickly just clear the virus and it's left in some sort of middle state, it provides a great selective advantage. And that's where we see these new mutations rising quicker than what we would have in just natural—you know, a person-to-person acute transmission.

The other thing that happens that we see is the virus responds really quickly to some of our drugs and monoclonal antibodies. And if they're not completely suppressing the virus, it gives an opportunity again for the virus to adapt. So we end up with these—during these prolonged infections in immunocompromised individuals we see some of those exact same mutations that we find in variants of interest and variants of concern.

And so one of the hypotheses is that some of these variants that all of a sudden acquire, you know, 10, 20 different mutations and many of those occurring in the spike protein where we're really concerned with, that some period of time later in infection when you have the viremia that goes up, they might be transmitting to other people, and therefore, you have these sort of jumps then of viruses that are adapted to humans. I mean, that's one of the hypotheses here. And then, you know, these events are still probably pretty rare overall, but when you have millions and millions and millions of infections that have happened that—and these jump and then they're more transmissible, I think that's one of the explanations for what we're seeing for the rise of many of these variants.

Mr. PERLMUTTER. Thank you to this panel. You guys really are—have been educating me, and I appreciate it. I yield back to the Chair.

Chairman FOSTER. Thank you. And before we bring this hearing to a close, I want to myself thank our witnesses for testifying before the Committee today. And for those Members and witnesses with time, at the close of the hearing we can just hang around for some informal discussions as we often do following in-person hearings.

The record will remain open for two weeks for additional statements from the Members and for any additional questions that the Committee may ask of the witnesses. And this hearing is now adjourned.

[Whereupon, at 11:41 a.m., the Subcommittee was adjourned.]

Appendix

ANSWERS TO POST-HEARING QUESTIONS

ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Stephen Streiffner

Question for the Record to:

Dr. Stephen Streiffner

Deputy Laboratory Director for Science and Technology

Argonne National Laboratory

House Committee on Science, Space, and Technology

Subcommittee on Investigations and Oversight

COVID-19 Variants and Evolving Research Needs

May 12, 2021

Submitted by: Representative Sean Casten (IL-06)

What distinguishes DOE's role from that of other agencies in conducting research on COVID -19 variants?

The DOE and its 17 National Laboratories are distinguished by unique capabilities that are applicable to the threats posed by COVID-19, that are leveraged directly from core missions in fundamental research (including its scientific user facilities), applied energy, and national security, and that complement the role and expertise of other agencies. This includes a significant portfolio in biological and environmental research and bioenergy production, underscoring the concept of the energy-environment-climate nexus. More specifically, DOE's state-of-the-art user facilities and capabilities in advanced computing and artificial intelligence (AI), genomics, structural and molecular biology and biotechnology, systems modeling and decision analysis, and advanced manufacturing, among others, built up to serve the core missions, have been directly utilized by DOE national laboratories to pivot almost instantaneously to take on certain roles in the fight against COVID-19. Expertise in all of these domain science areas coupled with the DOE's nuclear security mission also leads directly to strengths in biosecurity and bioinformatics. Additionally, laboratory stewardship of DOE user facilities results in national laboratory scientists often being the strongest and most knowledgeable in applying those facilities to emerging research challenges, such as the COVID-19 pandemic.

This overarching framework has long served as the basis for strong cooperation between DOE and other federal agencies, including the National Institutes of Health (NIH), Department of Homeland Security (DHS), and Department of Defense (DoD). An example of this is that DOE is the steward of the x-ray light sources on behalf of the entire science and technology community. NIH has partnered with DOE by providing substantial NIH investment in both experimental capabilities (both capital and operations support for structural biology beamlines) at the light sources as well as research support for the structural biology community that uses those capabilities, hand-in-glove with DOE support for development and global operation of the facilities. A second example is the long-term development of extremely advanced epidemiological models at several national laboratories in cooperation with NIH

and DoD, using DOE's world-leading expertise in computational science and high-performance computing, that have been rapidly adapted to COVID-19.

Taken together, DOE and its laboratories maintain as part of their on-going mission the cyber infrastructure, computational platforms, and next-generation experimental research capabilities within a single portal allowing distributed networks of scientists to work together on national emergency challenges such as COVID-19 variants. This set of platforms supports understanding the structure and function of biological systems such as SARS-CoV-2 and its variants, effectively integrating knowledge from distributed datasets, individual process components, and individual component models in an AI/machine learning-enabled, open access environment. DOE develops and maintains capabilities at user facilities that allow characterization and response to biological threats, and develops advanced instrumentation to address these research challenges. No other agency fills this role in the specific areas discussed for DOE.

