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COVID-19 Variants and Evolving Research Needs

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## 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.