26 February 2021

BRIEF19

A daily review of covid-19 research and policy

SPECIAL BRIEFING

When will the pandemic be over? Thinking towards a post-pandemic world.

As vaccinations continue to ramp up across the country, many people are starting to seriously think about when the pandemic may be over. The most acute phase of the emergency won't be over until most of the elderly and those with chronic medical conditions—who are at the highest risk for severe disease, hospitalization, and death—have been vaccinated. As the elderly population skews White, it is essential that we also get people with chronic medical conditions vaccinated, too, as this will capture most of the high-risk persons of color, who've been hit so hard by this pandemic. We should have enough vaccine supply for every American who wants to get vaccinated to do so by the end of July, if not sooner. While we are unsure of the exact threshold needed for herd immunity, our best guess right now is around 75-85 percent of the population needs some degree of protection—preferably from vaccination, though antibodies from natural infection will also contribute to this.

First, let's take stock of where we stand in the United States. While things have improved as of late, we are still seeing about 2,000 deaths per day, down from about 4,000 deaths per day following the winter holidays. This is on par with March and April of last year. Hospitals and healthcare workers are still stretched too thin in some places and don't have enough personal protective equipment.

As a result, we should also be vaccinating people in high-risk workplaces (e.g. meatpacking, food processing, jails/prisons) and improving administrative infection controls (e.g. screening/testing), environmental infection controls (e.g. ventilation) and providing appropriate personal protective equipment. Outbreaks in these settings still pose substantial threats and would be devastating.

That said, it's not too soon to think about the post-pandemic world. Once the emergency is over, we need to focus on preventing the next one. One way to achieve this is by scaling up our ability to test for new coronavirus variants, and other possible emerging threats. One important way to do this is by having scientists collect and study the sequences of various viruses, which is called genomic surveillance. The US Centers for Disease Control and Prevention has ramped this up since President Biden took office, but we need to invest more and enlarge the efforts. We need to know what new variants are emerging, what might be driving their emergence, and to characterize those new variants. We also need to use this information to start thinking about developing what are known as "multivalent vaccines." These vaccines would protect against the original strains of SARS-CoV-2 as well as any emerging variants. This will be difficult at first. Because of how much virus is circulating at the present time, mutations are more likely. That means more diverse mutations are likely ("viral heterogeneity") now than they will be in the future.

When will life return to normal? That depends on what "normal" is." We may have a "new normal" in which we don't shake hands anymore (or at least without hand sanitizer at the ready) and wear masks in the winter months, as many do in East Asia.

We also need to acknowledge that new infections are emerging with greater frequency—driven by climate change, environmental degradation, deforestation, and overpopulation—in other words, anything that brings people in closer contact with wildlife habitats. And that means that we really do need to adopt a new normal to better insulate ourselves against the next SARS-CoV-2.

Once the vast majority of people have been vaccinated, coronavirus vaccination will likely become one of the essential childhood vaccinations (assuming we don't need frequent boosters for variant strains). At some point, newborns will constitute the majority of persons entering the population who are susceptible. Realistically, SARS-CoV-2 will likely become "endemic" in much of the world, meaning the virus is permanently among us, though at lower levels.

—Céline Gounder MD, ScM
Brief19 Thread-of-the-Week

POLICY BRIEFING

FDA issues new guidance on developing vaccines that cover variants.

This week the US Food and Drug Administration (FDA) issued a new policy for companies who manufacture tests, therapies, and any preventive medications that applies to companies submitting changes to existing products in response to the emerging coronavirus variants. Under normal circumstances, new submissions require submission of extensive clinical data and production plans, but in response to the mounting and potentially pandemic-elongating mutations, the FDA has published an expedited review pathways for public opinion and contribution.

For pharmaceutical companies producing vaccines, there are no anticipated changes to manufacturing requirements should changes need to be made to cover variants, but additional clinical information in the form of "immunogenicity studies" will need to support any changes. Unlike a full clinical trial, such studies are designed to demonstrate patients' immune response to new formulations compared to authorized vaccines, similar to how annual influenza vaccines are evaluated. Applicants are also being encouraged to compare the response of unvaccinated individuals and those who have been previously inoculated against the virus.

Monoclonal antibodies, which despite mixed evidence still have potential to help some patients, have been shown to be less effective in targeting variant strains. The FDA guidelines provide a pathway for expedited generation of the required clinical and non-clinical data required for approval of modified submissions. Similarly, the recommendations for the broader therapeutics market focused on the composition of Phase II and Phase III clinical trials and the changing variables of vaccine availability and viral makeup.

Tests are also a concern. With the accuracy of many tests relying on the genetic makeup of the virus for adequate detection, the FDA included a list of products known to be affected by existing mutations. This portion of the publication focused on the Administration's efforts to study and catalogue the variants. It also highlights the importance of monitoring how any variants in the future may affect the reliability of existing products.

Collectively this report aims to empower companies to continue developing products related to combatting the pandemic with prevention, detection, and treatment, by providing guidance on an evolving enemy and how to swiftly and effectively respond to changing response requirements. *The Food and Drug Administration*

—Brief19 Policy Team

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