VIEWPOINT

COVID-19: BEYOND TOMORROW

The Potential Future of the COVID-19 Pandemic
Will SARS-CoV-2 Become a Recurrent Seasonal Infection?

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There is growing optimism and hope that by virtue of ongoing immunization efforts, seasonality (declining infections through August), and naturally acquired immunity, by spring and early summer 2021 in the US there will be a substantial decline in the number of deaths and hospitalizations related to COVID-19. However, this optimism must be tempered by several important factors. The likelihood of achieving herd immunity against SARS-CoV-2 is low simply because not all individuals in the US are eligible to be vaccinated and a quarter of eligible individuals will likely decline to be immunized. Moreover, the vaccines do not provide full immunity against infection, and the currently available vaccines are less effective against variant B.1.351, and possibly other variants. Accordingly, the public and health systems need to plan for the possibility that COVID-19 will persist and become a recurrent seasonal disease.

Herd immunity is a theoretical construct from infectious disease modeling that posits that in a population in which every individual is equally likely to encounter every other individual, transmission will not be sustained when immunity through past infection, vaccination, or both reaches the level of $1 - (1/R)$, where R is the number of infections caused by a single infection in a population in which everyone is susceptible.[1] Reality diverges from this simple notion. First, because COVID-19 is clearly seasonal, like other coronaviruses, the herd immunity level will be lower in the summer and higher in the winter. Second, herd immunity depends on how much interaction individuals have with one another, which will vary by state or city after social distancing mandates are lifted. Third, nonrandom mixing (individuals are not equally likely to interact with one another) can lead to modifications of the level of immunity required to stop transmission. Despite these factors, some public health officials suggest that achieving winter herd immunity in the presence of new more contagious variants will require more than 70% to 80% of individuals to be immune.

Three key considerations will make achieving herd immunity against COVID-19 challenging. First, vaccines will have a reduced effect on preventing infection from the B.1.351 variant. Moderna and Pfizer vaccines have an overall effectiveness against symptomatic disease of approximately 95% for wild-type variants, whereas adenovirus vector vaccines, such as the Janssen/Johnson & Johnson vaccine, have effectiveness closer to 70%. Evidence on vaccine efficacy for preventing infection, however, comes only from 1 group in the AstraZeneca trial that showed 55% protection against infection as measured through weekly nasal swabs vs 70% protection for symptomatic disease.[2] Furthermore, for the 3 vaccines tested against the B.1.351 variant, Janssen, Novavax, and AstraZeneca reported effectiveness estimates for symptomatic disease of 57%,[3] 49%,[4] and a statistically nonsignificant percentage, respectively. If the B.1.351 variant becomes dominant, a simple calculation suggests that the aggregate effectiveness of vaccines for preventing B.1.351 transmission in the US could be only 50% (ie, based on current effectiveness of 90% to prevent symptomatic disease × 20% reduction of efficacy for preventing infection compared with symptomatic disease and assuming an average reduction in efficacy for B.1.351 of 33% [excluding the statistically insignificant protection from the AstraZeneca vaccine]).

Second, not enough individuals will receive the vaccine. Because the vaccines are currently not authorized for use in children, only approximately 75% of US individuals are eligible to be immunized. Perhaps more important in the long run, not all individuals are willing be immunized. Data collected daily through Facebook's Data for Good initiative provide timely information on the proportion of individuals who respond yes or "yes, probably" to the question, Will you take the vaccine if offered it? These positive responses regarding likelihood of vaccine receipt increased in January 2021 and have reached 71%,[5] similar to the 72% response in a nationally representative sample.[6] Even with an effective approved vaccine for children, if B.1.351 or some other variant becomes dominant, the US can expect vaccine-derived immunity to reach only 37.5% (the estimated potential 50% aggregate efficacy for transmission × 75% of individuals receiving the vaccine) in 2021 if all supply and administration difficulties are overcome.

Third, there is concern about the extent to which previous infections from one variant protect individuals from reinfection with some new variants. Novavax reported that in a phase 2b clinical trial in South Africa, the COVID-19 incidence rate in the placebo group, predominantly from variant B.1.351, was 3.9% both among individuals with COVID-19 seropositivity and those who were COVID-19 seronegative.[7] The interpretation by Novavax of this finding has been that past infection provides no immunity against new variants. If that is true, herd immunity can be achieved only through vaccination. But if B.1.351 spreads widely, vaccine-derived immunity will likely be much lower than the levels required to reach herd immunity by the 2021-2022 northern hemisphere winter.

Various models suggest continuing COVID-19 surges are possible even without B.1.351 dominance.[8] A winter surge of infection with B.1.351 dominance may occur in 2021-2022. Hospitalization and death rates, however, may be expected to be lower, assuming vaccines remain more effective for preventing symptomatic disease and remain effective for preventing severe disease and death. For example, the Janssen vaccine was more than 85% effective against severe disease, even in South Africa, with no hospitalizations or deaths reported in the trial, albeit with

a very wide CI for these outcomes.[3] If transmission remained similar to what occurred this winter, hospitalizations and deaths should be less in winter 2021-2022. But the magnitude of the winter surge also depends on behavior. Through mask wearing and social distancing, only an estimated 19% of US residents have been infected so far. In the next winter, it will be problematic to maintain social distancing mandates due to public fatigue and the potential lasting effect of the pandemic on the economy. Despite the protection from vaccination, effective *R* in the absence of concerted social distancing and low levels of mask use could be higher next winter than this winter.

If new variants continue to appear, winter surges may become the norm. This prospect requires advance planning and consideration of a range of strategies to mitigate the consequences for communities and health systems. Five strategies should be considered and vigorously debated in the months ahead.

1. Intensify global vaccination efforts. New variants can appear anywhere and more transmission will increase the likelihood of their emergence. Intensified expansion of vaccination in low- and middle-income countries along with high-income countries could help reduce the harm of recurrent seasonal COVID-19 and could reduce the frequency of new variants.

2. Monitor the epidemic and the emergence of new variants and accelerate the modification of vaccines to enhance their efficacy for emerging high-risk variants if they are shown to significantly reduce vaccine protection. The US, European Union, and other high-income countries should invest in global surveillance, including with genome sequencing, to facilitate early detection of variants and track trends at the local level. Strategies of creating multivalent vaccines and adapting vaccines to new variants through boosters will need to be deployed rapidly to maintain overall vaccine efficacy. If variants continue to emerge, it is possible that annual vaccination will be needed, similar to that for seasonal influenza. However, Centers for Disease Control and Prevention data indicate that seasonal influenza vaccine uptake averaged 50% and estimated vaccine efficacy averaged 35% from 2014 to 2019.[9] For COVID-19, the identification of new variants and modification of vaccines to be efficacious for these variants would need to be more effective.

3. Manage and finance winter hospital surges. COVID-19 has burdened intensive care units (ICUs) in the US this winter. Social distancing measures have reduced COVID-19 transmission and substantially reduced influenza transmission. US hospitals have avoided the double pressure on bed availability from both influenza and COVID-19 infection. A shift to recurrent seasonal COVID-19 makes it unlikely governments would adopt social distancing mandates every winter, potentially leading to hospitalizations for influenza and COVID-19. ICU bed availability pressure could require halting elective procedures in peak months such as December and January. Hospitals may need to develop greater capacity to respond to surges with sufficient bed capacity and personnel, and anticipate associated financial implications. Financing mechanisms that address that currently hospital income is driven by elective procedures would need to be considered.

4. Reduce transmission in peak months through employer and educational institution action. Although it is unlikely that the federal government or state governments will use social distancing mandates every winter, employers and educational institutions could adopt certain measures. Actions could include establishing mandatory vaccination, requiring masks during peak transmission months, and avoiding superspreader events by moving meetings or classes with attendance above a certain number to digital platforms. Requiring vaccination where legally allowed could help increase vaccination rates. Requiring mask use in the winter months could contribute both to reduced transmission in those settings and cultural change toward accepting mask use as normal.

5. Modify behavior of at-risk individuals. Increased risk of death in a winter surge may be large enough to motivate at-risk individuals to change their behavior. Higher-risk individuals (eg, aged ≥65 years or with comorbidities) would need to consider winter behavioral modification such as mask wearing and avoiding congregate settings such as bars, indoor dining, concerts, and sports events, and any setting in which transmission risk is high.

It is not clear whether COVID-19 will become a chronic seasonal disease. There is too much uncertainty about the probability and frequency of emergence of new variants, the reduction in vaccine efficacy for each variant, the critical question of cross-variant immunity, and the consistency of safe human behavior. However, the prospect of persistent and seasonal COVID-19 is real. If immunity from infection for the same SARS-CoV-2 variant or vaccine-derived immunity wanes, the prospect would increase further. There is much to learn in the coming months about variants, vaccines, and immunity. Recurrent seasonal COVID-19 could require both health system change and profound cultural adjustment for the life of high-risk individuals in the winter months. There is an urgent need to prepare for such a scenario by aligning surveillance, medical response, public health response, and socioeconomic programs.

ARTICLE INFORMATION

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REFERENCES

1. Fine P, Eames K, Heymann DL. "Herd immunity": a rough guide. *Clin Infect Dis*. 2011;52(7):911-916.

2. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2. *Lancet*. 2021;397(10269):99-111.

3. Johnson & Johnson announces single-shot Janssen COVID-19 vaccine candidate met primary endpoints in interim analysis of its phase 3 ENSEMBLE trial. January 29, 2021. Accessed February 10, 2021. https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial

4. Novavax COVID-19 vaccine demonstrates 89.3% efficacy in UK phase 3 trial. News release. January 28, 2021. https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3

5. CMU Delphi Research Group. COVID symptom survey. Accessed February 10, 2021. https://cmu-delphi.github.io/delphi-epidata/symptom-survey/

6. Loomba S, de Figueiredo A, Piatek SJ, et al. Measuring the impact of COVID-19 vaccine misinformation on vaccination intent in the UK and USA. *Nat Hum Behav*. Published online February 5, 2021. doi:10.1038/s41562-021-01056-1

7. Efficacy data updates from Novavax' protein-based vaccine candidate. February 2, 2021. https://www.novavax.com/sites/default/files/2021-02/20210202-NYAS-Novavax-Final.pdf

8. Saad-Roy CM, Wagner CE, Baker RE, et al. Immune life history, vaccination, and the dynamics of SARS-CoV-2 over the next 5 years. *Science*. 2020;370(6518):811-818. doi:10.1126/science.abd7343

9. CDC seasonal flu vaccine effectiveness studies. Accessed February 10, 2021. https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm