

## VIEWPOINT

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Viewpoint



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# Confronting the Delta Variant of SARS-CoV-2, Summer 2021

**Availability** of safe and highly effective SARS-CoV-2 vaccines increased the possibility of durable control of COVID-19 both in the US and worldwide. After initial challenges in vaccine supply and delivery, there was substantial progress in vaccinating US residents. The arrival of spring 2021 and increasing vaccination rates, particularly among individuals at high risk for severe infection and complications, was followed by a steady decline in cases, hospitalizations, and deaths.

As of August 16, 2021, the US Centers for Disease Control and Prevention (CDC) estimates that 168.7 million people have been fully vaccinated in the US, which represents 50.8% of the population and 59.4% of the vaccine-eligible population.<sup>1</sup> However, there are large variations in vaccination rates by state, with a high of 76.9% in Vermont to a low of 44% in Alabama. Moreover, immunization rates have plateaued, largely due to a lack of focus on the various behavioral aspects of vaccine uptake, especially a new vaccine that would need to be given to virtually every eligible person in the US.

## Delta Variant

This latest wave of infections has been closely associated with the emergence of the Delta variant of SARS-CoV-2. Like other RNA viruses, SARS-CoV-2 constantly mutates with new variants emerging as long as ongoing transmission persists. A variant can become more common if it provides a selective advantage to the virus.<sup>2</sup>

The US Department of Health and Human Services established a SARS-CoV-2 Interagency Group that created a classification system that includes variants of interest, variants of concern, and variants of high consequence. The B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta) variants are all "variants of concern," which is a variant with 1 or more mutations that allow the virus to transmit more easily, make the virus less responsive to treatments, or affect how well vaccines work against the virus.<sup>3</sup>

The Delta variant, first identified in India in December 2020, spread rapidly throughout a mostly unvaccinated country and caused massive numbers of cases, hospitalizations, and deaths. In the UK, the Delta variant also spread rapidly despite high vaccination coverage, although there was a much slower increase in hospitalizations and deaths. Some public health experts have speculated that this rapid spread was at least partially explained by the country's decision to delay second doses of vaccine. In the US, the Delta variant was first identified in March 2021. Since then, Delta has become the predominant variant in the US and has caused an expansive wave of new infections, especially in the Southeastern US in places where community vaccination rates are low. In fact, the spread of Delta is largely a reflection of the uneven vaccination coverage in the US, with substantially higher numbers of cases, hospitalizations, and deaths among states with low vaccination rates and limited public health mitigation measures.

The Delta variant is highly transmissible, estimated to be about 60% more transmissible than the Alpha variant, and the CDC has suggested its basic reproduction rate ( $R_0$ ; ie, the estimated number of secondary cases of infections that are transmitted from an infected person to a susceptible population) is somewhere between 5 and 8. A simple calculation can help illustrate the effect of this increase in the  $R_0$ . If a virus with an  $R_0$  of 2.5 spreads among a completely susceptible population, an estimated 9536 infections would result after 10 cycles of transmission. However, for a virus with an  $R_0$  of 6, 10 cycles of transmission could result in an estimated 60 466 176 infections. While the current focus is on Delta variants, other variants will undoubtedly emerge as long as uncontrolled transmission is occurring within the US and globally.

## Vaccines and the Delta Variant

The protection offered by the available vaccines against the Delta variant is beginning to be understood. Data from the UK suggest that 1 dose of either the Pfizer-BioNTech BNT162b2 or the AstraZeneca-Oxford ChAdOx1 nCoV-19 vaccine is insufficient to protect against symptomatic infection with the Delta variant, but 2 vaccine doses increases effectiveness to 88% and 67%, respectively, which is still lower than the protection against the Alpha variant offered by both vaccines.<sup>4</sup> Similar findings have been reported for the Janssen/Johnson & Johnson vaccine, but these data have not yet been published.<sup>5</sup> What is increasingly clear is that breakthrough infections remain infrequent but are occurring with the Delta variant; however, the currently available vaccines remain highly effective against severe disease, hospitalization, and death. The overwhelming majority of severe cases occurring in the US are among unvaccinated individuals.

As a result of the emergence of the Delta variant, and preliminary and inconsistent evidence of waning immunity, decision makers in different countries have developed different policy recommendations. For example, Germany and Israel have announced plans for an additional vaccine dose for previously vaccinated individuals. Other countries, such as the United Arab Emirates, have already implemented programs to give additional vaccine doses primarily to those previously immunized with the Sinovac and SinoPharm vaccines. At this point, the most robust data on additional doses comes from solid organ transplant recipients, in whom an additional dose of an mRNA vaccine increased levels of anti-SARS-CoV-2 antibodies among 55% of individuals.<sup>6</sup> Based on these and other data, on August 13, 2021, the US Food and Drug Administration (FDA) modified the current Emergency Use Authorization and the CDC now recommends administering a third dose of an mRNA vaccine to immunocompromised individuals 28 days after the second dose.<sup>7</sup> Even though an estimated 10 million people in the US may be considered immunocompromised, this recommenda-

tion applies to only a small subset of them, including the following:

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid organ transplant and taking immunosuppressive therapy
- Receipt of CAR T-cell or hematopoietic stem cell transplant (within 2 years of transplant or taking immunosuppressive therapy)
- Moderate or severe primary immunodeficiency (eg, DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids, alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory

### Vaccination Rates

While many unknowns remain, what is abundantly clear is the only way to contain and eventually end the coronavirus pandemic is for more people to get vaccinated. In US, states with high vaccination rates (>70% of the population) are reporting lower numbers of vaccine breakthrough cases as well as hospitalizations and deaths from COVID-19. However, the decision to get vaccinated has become highly politicized and along with widespread misinformation has resulted in the US having a large vaccine supply with low vaccine demand. An uptick in vaccinations has occurred in recent weeks, likely due to surging case counts due to the Delta variant. While this is welcome news, vaccination will not have an immediate effect given that it requires several weeks (5-6 weeks with the mRNA vaccines) to achieve full protection.

With an  $R_0$  of 6, it will be extremely difficult to slow the spread of the Delta variant because the herd immunity threshold (ie, the proportion of persons who would need to be fully vaccinated, infected, or both, to interrupt endemic transmission) would need to be greater than 85%.<sup>8</sup> However, even this level of vaccination may not be enough in many situations. For example, in Iceland, nearly all the eligible population is vaccinated; 96% of females and 90% of males 16 years and older have received at least 1 dose of a SARS-CoV-2 vaccine, making it one of the most highly vaccinated populations in the world. However, even in Iceland there has been an increase in COVID-19 cases because of the Delta variant. But despite the increase in cases there has not been an increase in COVID-19-related deaths, and vaccinated individuals who become infected generally have recovered without serious illness.<sup>9</sup> These data suggest that even if herd immunity is not achieved for COVID-19 (given the Delta variant), high levels of vaccination will help prevent hospitalizations and deaths as SARS-CoV-2 moves toward endemicity.

### Vaccine Mandates

Vaccine mandates are becoming increasingly common, and it is unlikely that high vaccination levels in the US can be achieved without them. Vaccine mandates are not new; vaccination requirements have been in place for health care workers, members of the military, and schoolchildren in all 50 states. Many states allow exemptions for religious, personal, and medical reasons but California revoked personal and religious exemptions to vaccination in 2019. Employers can require vaccines and some are already doing so, but many are holding off until the FDA grants full approval of the COVID-19 vaccines. Reassuringly, courts have, so far, upheld institutional vaccine mandates and to date more than 700 colleges and universities have adopted COVID-19 vaccine requirements.

Research on effectiveness of vaccine mandates suggests that a "middle-of-the road" approach to crafting a vaccine requirement may be most optimal.<sup>10</sup> If it is too easy to opt out of vaccine mandates, these mandates are not very effective; however, if it is nearly impossible to obtain an exemption, even for strongly held beliefs, people will find loopholes to avoid the requirements altogether.<sup>10</sup>

As the immunization efforts move on from the mass vaccination model, physicians and other health care professionals will be vital to increasing vaccine acceptance. Several decades of research on vaccine acceptance and hesitancy identify clinicians as the most trusted source of vaccine information. This remains true for COVID-19 vaccines. Fortunately, there has been increased focus on evidence-based approaches for health care professionals to communicate about vaccines with patients. Until recently this evidence has not been translated into skills-based training, but this too is occurring.

### Conclusions

The Delta variant presents a serious challenge to controlling the COVID-19 pandemic in the US and worldwide. Effectively responding to this formidable variant will require an evidence-based response that, unfortunately, has not been the case for many US states. Vaccines are the only way forward that will preserve the health care infrastructure and the economy, and eventually contain the pandemic. Increasing uptake among vaccine-hesitant populations will require full participation and complete commitment by everyone, including government officials, clinicians, public health practitioners, and members of the community. Elected officials and other policy makers can do their part now by lending strong support to vaccination and public health mitigation strategies.

#### ARTICLE INFORMATION

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