COVID-19 vaccines: acting on the evidence

Diverging from tested vaccination regimens without scientific evidence could undermine public confidence in vaccines against COVID-19 and the success of a global vaccination strategy to curtail the pandemic.

The development, approval and rollout of safe and effective vaccines against SARS-CoV-2 is cause for celebration and provides a glimmer of hope that the end of the global pandemic could be within grasp. It is an unprecedented scientific achievement that several vaccines, including the vaccines from Pfizer–BioNTech, NIH–Moderna and Oxford–AstraZeneca, among others, have attained approval by regulatory bodies in multiple countries in under one year. Each vaccine has been rigorously evaluated for efficacy and safety in preclinical and clinical studies, culminating in tightly controlled, successful phase 3 clinical trials. In contrast to their sluggish responses in the early phases of the epidemic, worldwide, governments are now moving rapidly to implement national and state-wide vaccination programs, largely focused on prioritizing healthcare and essential workers and vulnerable populations. However, in an attempt to maximize population coverage with limited availability of vaccines, coupled with the threat of surges in case numbers fueled by the emergence of new, potentially more-transmissible strains of SARS-CoV-2, some governments have opted to modify vaccine dosing strategies—albeit in a vacuum of hard evidence.

The UK government, for example, has extended the interval between doses of the Pfizer–BioNTech mRNA vaccine from a regime of two doses scheduled 21 days apart, as tested in clinical trials, to two doses no more than 12 weeks apart. While this might be indicative of a pragmatic government keen to harness the resources available, it is deeply troubling that this risky departure from the specified schedule has become national policy on the basis of scant, untested evidence. According to a statement released by the Joint Committee on Vaccination and Immunisation in the UK, the published efficacy of the Pfizer–BioNTech vaccine was determined to be 52% between the first dose and second dose; however, post-hoc analyses using case data restricted to 15–21 days after the first dose estimated the efficacy at 89%. It is important to note that these estimates have not been derived from pre-specified analyses or specifically tested in dedicated phase 3 trials. Thus, vast gaps remain in concrete knowledge about how effective a second dose will be when administered at the longer 12-week interval, or whether a single dose can confer sufficient protection among vulnerable populations to alleviate the burden on already overstretched critical-care facilities. In Israel, for example, where case numbers are currently surging and around 2 million people have already received a first dose of the Pfizer–BioNTech vaccine, but only 400,000 have received a second dose, some health officials have suggested that a single dose alone might not offer as much protection as initially thought.

The justification for this seemingly egregious deviation from the evidence in the UK is to curb the spread of the newly characterized variant of SARS-CoV-2, B.1.1.7, which is proposed to spread more rapidly than other forms of the virus. Real-time genomic sequencing during the pandemic has enabled researchers to understand how the virus mutates and to track the spread of variants over time, as well as geographically. However, the power of this approach is hamstrung by limited availability of global sequence data.

Globally, almost 100 million cases of COVID-19 have been identified, yet at the time of this writing, only 400,000 SARS-CoV-2 genomic sequences have been deposited in the GISAID database, and of those, nearly half (175,000) are from the UK alone. And of the over 20,000 new SARS-CoV-2 sequences deposited in GISAID in the period of 1–19 January 2021, over three quarters are from European countries, with only 142 from South America, where a new strain from Brazil with potential increased transmissibility has recently been reported. In contrast, a total of around 3,000 isolates have been sequenced in South Africa since February 2020, but only a handful have been characterized. The USA, too, has come under criticism for a lack of a national genomics surveillance program. Of the 1.4 million new cases identified in the USA each week over recent months, fewer than 3,000 have been sequenced. Although countries such as the UK and South Africa have substantially ramped up their sequencing capacity, on a global scale it is unknown if other variants with increased transmissibility or infectivity exist in other regions. Furthermore, it remains unknown if the SARS-CoV-2 coronavirus could spontaneously mutate in such a way that new variants could evade current vaccines or if alternative vaccination regimens such as that in the UK could apply selective pressure on the virus to induce escape.

In the early months of the pandemic, very little was known about the novel SARS-CoV-2 coronavirus. Immediate health policies had to be implemented on the basis of experience and evidence from past epidemics, including the SARS-CoV epidemic that originated in China in 2003 and the Ebola virus outbreak in West Africa in 2014. Nearly a year later, a large volume of data has been generated that has allowed better understanding of SARS-CoV-2, its epidemiology, the host immune response and clinical aspects of COVID-19. There are still gaps in knowledge that need to be addressed—including understanding the impact of the emergence of potentially more-transmissible or more-virulent variants of the virus.

The global toll from COVID-19 has surpassed the grim milestone of 2 million deaths. Over one fifth of these deaths have occurred in the USA, with the highest per-capita mortality rate being in the UK. While these troubling statistics justify rapid action to vaccinate as many people as possible, deviating from a data-driven, clinically validated vaccine regimen is a risky approach that could derail current vaccination efforts, undermine public confidence in the vaccines and result in unintended long-term untoward consequences. Vaccination policies firmly grounded in scientific evidence must remain the mainstay of the global COVID-19 exit strategy. ❐

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