The new bivalent COVID vaccine boosters: The withering of the vaccine-only strategy

Benjamin Mateus
21 August 2022

Last week the British Medicines and Healthcare Products Regulatory Agency (MHRA) announced the approval of the first bivalent COVID-19 booster vaccines for adults, with endorsement by the government's independent expert scientific advisory body, the Commission on Human Medicines.

Manufactured by Moderna under the name Spikevax (mRNA-1273.214) for those 18 years and older, the bivalent vaccine will be promoted as part of the coming autumn booster program. Only those individuals who have completed the initial vaccination series will be eligible for the bivalent vaccines, but it remains unclear when the booster will be available to the British public.

A bivalent vaccine combines two separate elements derived from two different variants of a disease. Each dose of the new Moderna booster dose contains 25 micrograms of vaccine that targets the spike protein from the original Wuhan strain and 25 micrograms targeted against the BA.1 subvariant of the Omicron strain.

Evidence for using the bivalent vaccine was based on a phase 2/3 clinical trial with 437 study participants. The vaccine maker announced results in late June that found neutralizing antibodies against the BA.4/BA.5 subvariants were boosted "5.4-fold above baseline in all participants regardless of prior infection, and by 6.3-fold in the subset of seronegative participants." (Seronegative participants are those with no serum antibodies, indicating no previous vaccination or exposure to a disease).

Furthermore, "One month after an mRNA-1273.214 booster, neutralizing geometric mean titers (GMT) against BA.4/BA.5 were 941 in all participants, and 727 in seronegative participants. For context, prior studies of a third dose of the prototype booster induced neutralizing GMT against BA.1 of 629 and against Delta of 828. A third dose of the prototype booster was shown to be effective against Delta and BA.1 infection and hospitalization in observational studies."

Though safety data were similar to Moderna's initial mRNA COVID vaccines, the neutralizing antibody levels against BA.4/BA.5 were only 1.7 times higher than those receiving the booster against the original strain of the virus. As some have noted, these differences are slight and offer uncertain benefits in clinical terms.

Health officials also emphasize that the current vaccines offer considerable protection against severe disease and death. Still, the obligatory statements of support congratulating the progress in the next generation of vaccines by leading officials were quickly printed in all the mainstream press.

Dr. June Raine, MHRA chief executive, said, "The first generation of COVID-19 vaccines being used in the UK continues to provide important protection against the disease and save lives. What this bivalent vaccine gives us is a sharpened tool in our armory to help protect us against this disease as the virus continues to evolve."

Professor Sir Munir Pirmohamed, Chair of the Commission on Human Medicines, added, "The virus, SARS-CoV-2, is continually evolving in order to evade the immunity provided by vaccines. This novel bivalent vaccine represents the next step in the development of vaccines to combat the virus, with its ability to lead to a broader immune response than the original vaccine."

Stephane Bancel, CEO of Moderna, declared, "We are delighted with the MHRA's authorization of Spikevax Bivalent Original/Omicron, our next-generation COVID-19 vaccine. This represents the first authorization of an Omicron-containing bivalent vaccine, further highlighting the dedication and leadership of the UK public health authorities in helping to end the COVID-19 pandemic." The vaccine maker is also advancing a second bivalent booster based on the BA.4/BA.5 strain (mRNA 1273.222) and has completed regulatory submissions with Australia, Canada, and the European Union.

The US is following suit with promises that the bivalent booster shots will be publicly available by September. However, unlike the UK, the Biden administration is betting on the boosters that target the BA.4/BA.5 Omicron strains.

At the end of July, the US Department of Health and Human Services (HHS) released a press statement stating that in collaboration with the US Department of Defense (DOD), they had agreed to purchase 66 million doses of Moderna's bivalent COVID-19 vaccine booster candidate with the caveat that the vaccine manufacturer updates their vaccine to target BA.4/BA.5 which were becoming dominant across the country. Data on these versions aren't expected until around mid-September. The purchase agreement is on top of the 105 million doses of bivalent COVID-19 vaccine booster purchased from Pfizer.

Pfizer's bivalent vaccines had previously targeted BA.1 or BA.2 subvariants, providing 30 and 60 microgram doses of one of two bivalent vaccine candidates. Though a monovalent vaccine limited to just the Omicron variant produced a more robust immune response, regulators hope the bivalent vaccines offer broader protection. One month after administering the Omicron-adapted bivalent candidates, they conferred a nine- to 11-fold increase in neutralizing GMTs against Omicron BA.1. However, the titers were three-fold lower against BA.4/BA.5. Pfizer's boosters will be available for those 12 years and older. Whether the 30 or 60 microgram doses will be used remains to be determined.

Though the Biden administration has the options for a total of 600 million doses—300 million from each vaccine maker—the current allotment of vaccines was purchased through the reallocation of critical COVID-19 response funds. The promised 171 million vaccine boosters are insufficient to cover the US population, and it isn't very likely that Congress will provide funding for additional doses. US regulators considered these calculations in not authorizing a second booster for adults under 50 this summer.

White House COVID-19 response coordinator Dr. Ashish Jha recently admitted the US is ill-prepared to face more waves of COVID infections. He said, "We have taken money from other really important priorities like having a stockpile of tests and having a stockpile of personal protective

equipment. We took those dollars and put them into buying vaccines for the fall and winter because time was running out. We need to get in there and ensure that America is not way behind every other country in the world … I would like to get to a point where every adult in America who wants a vaccine can get one. I'm hopeful. We will be there. We're not quite there yet. In terms of how many vaccine doses we've been able to buy, what's really limited us is a lack of resources."

Abandoning any effort to stem the spread of COVID-19

The recent declaration by the Biden administration that COVID is now a permanent feature of American life and the Centers for Disease Control and Prevention's (CDC) abrogation of almost all pandemic mitigation measures also imply a forthcoming end to the official COVID-19 public health emergency.

Earlier this month, HHS updated its COVID-19 guidance for hospital reporting. It has changed reporting recommendations for psychiatric hospitals and rehabilitation facilities to once per year, from October to October.

The Centers for Medicare & Medicaid Services (CMS) Chief Operating Officer Jonathan Blum recently wrote:

> Throughout the COVID-19 public health emergency (PHE), CMS has used a combination of emergency authority waivers, regulations, enforcement discretion, and sub-regulatory guidance to ensure access to care and give healthcare providers the flexibilities needed to respond to COVID-19, and help keep people safer. Many of these waivers and broad flexibilities will terminate at the eventual end of the PHE, as they were intended to address the acute and extraordinary circumstances of a rapidly evolving pandemic and not replace existing requirements. To minimize any disruptions, including potential coverage losses, following the end of PHE, HHS Secretary Becerra has committed to giving states and the health care community writ large 60 days' notice before ending the PHE. *In the meantime, CMS encourages healthcare providers to prepare for the end of these flexibilities as soon as possible and to begin moving forward to reestablishing previous health and safety standards and billing practices.* [emphasis added]

As Blum's statement makes it clear, the shift to normalcy is underway. Even CNN observed that the Biden administration is attempting to extricate from the crisis phase of the pandemic and is looking to discontinue the purchase of future vaccines.

While, on the one hand, Jha has incessantly promoted the idea that "we have all the tools we need" to face the pandemic, out of the other side of his mouth, he casually explained at an event sponsored by the US Chamber of Commerce Foundation that the administration was working diligently to get "out of the acute emergency phase where the US government is buying the vaccines, buying the treatments, buying the diagnostic test."

He added, "My hope is that in 2023, you're going to see the commercialization of almost all of these products. Some of that is actually going to begin this fall, in the days and weeks ahead."

Those without health insurance and the under-insured will either pay out of pocket for vaccines and therapeutics or face the consequences of repeat infections. And for the current academic year, children in schools and daycare centers will once more function as a major vector for community transmission of the coronavirus.

According to the latest report by the COVID-19 Scenario Modeling Hub, under various scenarios, including the emergence of new variants and the autumn booster campaign, in the nine months between August 2022 and May 2023, 111,000 to 181,000 cumulative deaths could be expected. Their assumptions include high vaccine efficacy and rapid ramp-up. However, given the current lack of funding and anemic vaccination rates of barely 200,000 per day, the vaccine-only strategy is withering, and the dangers posed by allowing indefinite life to COVID loom.

It bears reviewing a report published in the Journal of the American Medical Association in July 2022 looking at life expectancy in California by census tract median household income. The poorest deciles already had a ten-year lower survival compared to the wealthiest deciles in the pre-pandemic years. Two years into the pandemic, they faced an additional five-year loss in life expectancy. In contrast, the richest saw their projected lifespan of over 85 years remain untouched. Given the nature of COVID and long-term complications caused to the immune system and various organ systems, the implication couldn't be more apparent as to the long-term impact of COVID on the working class.

A news update published in JAMA in early July reviewing the June 28, 2022, virtual FDA advisory committee meeting about updating COVID-19 vaccines cited Dr. Paul Offit, a pediatric infectious disease specialist and the director of the vaccine education center at Children's Hospital of Philadelphia. He noted that at the time when BA.4/BA.5 were evolving as the dominant strains, "It is not reasonable to assume that data generated for an Omicron BA.1 vaccine can easily be extrapolated to BA.4 and BA.5. These new Omicron subvariants are highly transmissible. Therefore, they will require a very high level of neutralizing antibodies present at the time of exposure to prevent symptomatic infection." Given that the BA.1 component of the vaccine only offered a modest rise in neutralizing antibodies, he added, "Why would we think using BA.4 and BA.5 would be any different?"

Waning efficacy of vaccines and the threat of new variants

Dr. Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine and co-director of the Texas Children's Hospital Center for Vaccine Development, said, "By fall, it's likely that Omicron will be in the rearview mirror. From my point, there's no advantage to giving an Omicron booster." He then added, "We need an overarching coronavirus vaccination strategy for the country. What we're doing is we're allowing the pharma companies to push their own agenda."

In another recent report published in *Nature*, microbiologist John Moore at Weill Cornell Medicine in New York City explained, "The underwhelming results for the bivalent vaccines are probably due to a phenomenon known as immune imprinting. By now, much of the population has either been vaccinated or infected with an earlier variant of SARS-CoV-2. The immune system has been trained to remember this variant—and a dose of vaccine, even one with Omicron-specific components, will tend to boost those earlier immunological memories. The degree of Omicron-specific response will be relatively small."

Indeed, in a critical scientific report published in *the New England Journal of Medicine* in April 2022, vaccine effectiveness rapidly declined after a few weeks for the Omicron subvariants due to their immune evasive qualities, making suboptimal and ephemeral the current vaccine-only strategy.

The notion that variant-specific boosters will be given annually to those

who will accept them, like the flu vaccines, means that vaccine immunity will be non-existent in the population for a significant portion of the year. Additionally, concerns over coronavirus resistance to Paxlovid imply that the promised tools to live with COVID are also fading in efficacy. And by reliable accounts, rosy estimates of producing a viable universal or mucosal vaccine against SARS-CoV-2 are one to two years away, and depend on considerable funding and mobilization of resources for success.

Despite this, no scholarship on elimination and eradication has ever been taken up to address the effectiveness of this strategy. This alternative, whose effectiveness has been demonstrated again and again in China, has been repeatedly dismissed as too late, too far gone, too onerous, and politically impossible. However, in the final analysis, the failure to pursue this strategy has been deliberate and based on the policy that prioritizes “the economy”—that is, corporate profit.

Clinical real-world experience, however, has proven such a strategy feasible and expeditious. China’s Zero-COVID policy effectively halted the Omicron wave that passed over the country, particularly Shanghai, in March 2022. Since the end of May, there have been zero deaths across that huge country due to COVID. In the same timeframe, the policy of forever COVID has seen another 30,000 Americans die from this preventable disease.