Four Vaccine Doses Prevented Severe Omicron COVID-19 Better Than 3

Older patients in Israel who received a fourth dose of the BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 vaccine were more than 3 times less likely to develop severe COVID-19 than those who received only 3 doses. But while protection against severe disease did not wane during the testing period, protection against confirmed infection appeared short-lived.

Conducted in early 2022 when Omicron was the dominant SARS-CoV-2 variant, the study, reported in the *New England Journal of Medicine*, examined more than 1.25 million persons aged 60 years or older. Each had received a third dose at least 4 months before the study period ended on March 2.

Among patients who had their fourth dose at least 8 days earlier, the unadjusted rate of severe COVID-19 disease was 1.5 per 100 000 person-days. The rate was 3.9 in the 3-dose control group and 4.2 in a second internal control group that received a fourth dose 3 to 7 days earlier.

Adjusting for demographic and exposure differences, the rate of severe COVID-19 among patients during the fourth week after the fourth dose was 3.5 times less than the 3-dose group, and 2.3 times less than the internal control group. Protection against severe illness hadn’t waned during the 6 weeks after the fourth dose.

As for confirmed infections, the unadjusted rate 4 weeks after receiving a fourth dose was 177 per 100 000 person-days compared with 361 in the 3-dose and 388 in the internal control groups. Although the adjusted rate of confirmed infection in the 4-dose group was 2 times less than the 3-dose and 1.8 times less than the internal control groups, this protection declined in later weeks.

New Brain Charts Could Become Clinical Benchmarks

Physicians may one day be able to track brain development across the human lifespan much as they do height and weight in children. Preliminary brain charts based on magnetic resonance imaging (MRI) scans are now available online.

Assembled using more than 120,000 MRI scans of more than 100,000 patients from 100-plus studies, the charts represent the largest number of brain images used in such an analysis. The charts track brain development and aging from 16 weeks after conception through age 100 years, according to a *Nature* article. They will be updated continuously as more scans are added to the data set.

While these preliminary charts are for research rather than diagnostic use, they enable visualization of both brain development trajectory and deviations from patient control populations, stratified by age and sex. They uncover new neurodevelopmental milestones as well as some structural features associated with neurological and psychiatric disorders, the authors wrote.

The charts reveal rapid growth in mean cortical thickness, peaking at about age 2 years, and gray matter volume, peaking at about age 6 years, before slowly declining. White matter volume grows more slowly, peaking at about age 30 years before decling. Conversely, cerebrospinal fluid volume increases slowly from birth until about age 40 years, then increases rapidly after age 60 years, indicating brain shrinkage.

Limitations of the study include a lack of diversity among the participants, with bias toward White, urban, and affluent participants from North America and Europe. While not yet ready for precise clinical diagnosis, “the present work proves the principle that building normative charts to benchmark individual differences in brain structure is already achievable,” the authors wrote.

Two mRNA COVID-19 Vaccines Stimulate Different Immune Responses

Subtle variations in immune responses to the mRNA-1273 (Moderna) and BNT162b2 (Pfizer-BioNTech) COVID-19 vaccines suggest that each may confer somewhat different protection, according to a study in *Science Translational Medicine*. This could mean that a mix-and-match booster strategy might increase protection against future variants and could have implications for future therapy development.

Both vaccines induce robust antibodies that neutralize the SARS-CoV-2 virus, making them highly effective against the early D614G strain of SARS-CoV-2. However, while both induce robust humoral responses, differences, particularly in certain Fc-mediated effector functions, may account for observed differences in effectiveness against more recent variants, which better evade neutralization.

In the study involving 73 fully immunized hospital workers, the 28 who received mRNA-1273 had elevated IgA concentrations and greater antibody-dependent neutrophil phagocytosis and antibody-dependent natural killer cell activation compared with the 45 BNT162b2 recipients. Binding by receptor binding domain–specific IgA1 and IgG2, as well as N-terminal domain–specific IgA1, FcγR2A, and FcγR2B all were enhanced with mRNA-1273. Some IgM levels were higher with BNT162b2.

While these effector functions may not prevent disease spread, they may help clear infections more quickly. “Thus, understanding the differences in disease attenuating, and not simply blocking antibodies, elicited by BNT162b2 and mRNA-1273 may provide new clues for the redesign of vaccines and monoclonal therapeutics able to offer a durable barrier of protection against the virus,” the authors wrote. — Howard D. Larkin

*Note:* Source references are available through embedded hyperlinks in the article text online.