

The pros and cons of the second booster dose of the COVID-19 vaccine

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Received: July 2022, Accepted: July 2022

Keywords: Booster dose; Vaccine; COVID-19

INTRODUCTION

Vaccination against COVID-19 remains the most effective way to prevent severe forms of this disease during the pandemic. During the two and a half years since the start of pandemic and the one and a half since the vaccine became available in the world, two primary doses of the vaccine and one booster dose have been recommended in almost every country in the world. approximately 65% of the world's population has received two doses of the vaccine and around 25% have received the third dose (first booster dose). However, the distribution of vaccine protection is not stable, and in Africa, only about 20% of individuals have received two doses of the vaccine.

Now the question is how effective the second booster dose of COVID-19 vaccine (the second booster dose) is given the conditions in the world.

There is clear evidence that a third dose of the vaccine is essential to ensure a strong immune response to the Omicron variant for all age groups. This is partly because the immune response diminishes over time, and partly because Omicron is reasonably effective at bypassing immunity to existing COVID-19 vaccines and previous infections. The question, however, is how long the acquired immunity of the first booster dose of the vaccine will last.

Some of the best data tracking vaccine effectiveness over time have been collected in the United Kingdom, and follow-up data are available for 15

weeks after the third dose of vaccine. In this study, it was found that the vaccine effectiveness against infections, hospitalizations, and deaths decreased significantly after the third dose (1).

In another study, the stability of the third dose of the Moderna vaccine was evaluated after six months and it was found that the level of neutralizing antibodies decreased significantly (2). The US Center for Disease Control and Prevention also reported a significant decrease in protection five months after the first dose of the vaccine (3).

In the aforementioned studies, data were collected from all age groups. However, researchers know that adults, especially those 65 and older, and people with underlying medical conditions do not have a stable immune response as young people. A recent study published in the Lancet examined the duration of the third dose in people aged 76 to 96 years and showed that the third dose improved neutralizing antibodies, but the amount of neutralizing antibodies in this group decreased significantly 3.5 months after receiving the third dose (4).

The European Medicines Agency (EMA) and the European Centers for Disease Control and Prevention (ECDC) have stated that it is early to use the 2nd booster dose of the COVID-19 vaccine in the general population. For the general population, all 30 countries have recommended 1st booster doses to different age groups. However, the second booster dose of the COVID-19 mRNA vaccine (Pfizer or Moderna)

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can be used for the age group over 80 years (5).

According to the two agencies, there is currently no clear evidence in the EU that there is a significant decline in vaccine protection against severe COVID 19 diseases in adults with normal immune systems aged 60 to 79 years, and therefore there is no clear evidence to support the immediate use of the second booster dose. If the current epidemiologic situation changes and new signals emerge, a second booster dose may need to be considered in this age group. For adults younger than 60 years with a normal immune system, there is currently no conclusive evidence that the vaccine's protection against severe disease is reduced or that the second booster dose provides additional benefit (5).

In late March 2022, the U.S. Food and Drug Administration (FDA), approved a second booster dose of the COVID-19 vaccine for vulnerable populations, immediately following approval by the Centers for Disease Control and Prevention (CDC). People over age 50 and some immunocompromised individuals who are at higher risk for serious illness, hospitalization and death are eligible four months after receiving the first booster dose. The second booster vaccination is equivalent to the fourth dose for people who received the Pfizer or Moderna series, or the third dose for people who received the Johnson & Johnson vaccine (6).

The US Food and Drug Administration has approved Pfizer and Moderna for the second booster dose as follows: The second booster dose is administered to persons who have had received the third dose for at least four months and who are at least 50 years of age. In addition, an immunodeficient person (organ transplant and similar conditions) may receive the second booster dose of Pfizer when at least 12 years of age and Pfizer or Moderna when at least 18 years of age (6).

The most recent COVID-19 vaccine guidelines from the Canadian National Advisory Committee on Immunization strongly recommend receiving a second booster dose of COVID-19 vaccine (7). The combination of vaccination and infection with COVID-19 is called "hybrid immunity." More than 35 studies have shown that hybrid immunity provides comprehensive protection. This is because immunization by vaccines targets the spike protein, while immunity by infection targets the entire virus more broadly (8). Therefore, it is not necessary to recommend the second booster dose in the case of confirmed Omicron

infection. This does not mean that individuals should be specifically exposed to the virus, but it is clear that hybrid immunity is a good way to protect oneself (9).

Now that the second booster dose has been injected in some countries for several months, researchers have data to evaluate the effectiveness of this vaccine dose. For example, in a paper published in the *New England Journal*, a study of more than 2 million people over the age of 60 showed that the second booster dose reduced severe disease as well as COVID 19 disease by nearly four- and two-fold, respectively than people who received only three doses (10). In another study, injection of a second booster dose of the vaccine in the over-60 age group demonstrated a 78% and 64% reduction in deaths and hospitalizations due to COVID-19, respectively (11). A clinical trial showed that the highest immunogenic response of the COVID-19 mRNA vaccine occurred after the third dose. However, as immunity declined over time, the second booster dose was able to restore this immune response to the peak level after the third dose. Similar neutralizing antibody response against Omicron was observed after the third dose (12).

CONCLUSION

Fourth-dose injections are now licensed to specific groups in all developed countries and some developing countries that have adequate access to the vaccine.

After reviewing the available documentation on how the immune system changes over time after each dose, there is now strong evidence that the second booster dose of the vaccine provides significant protection among vulnerable populations, including those over 60 years of age and this issue is mentioned in the guidelines of most countries. At the same time, no serious side effects attributed to the vaccine after the second booster dose were seen more than in previous doses. Therefore, it makes sense to suggest a second booster dose, especially for vulnerable groups in society.

While administering the second booster dose is beneficial to the vulnerable group, it is very important that other members of the community also receive their first, second, and third doses, and implementing the second booster dose injection program in the vulnerable groups should not lead us to ignore people who have not received the first three full doses.

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