



## Letter of Editor-in-Chief

# COVID-19 vaccination and long COVID-19

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We are now living in a pandemic with the coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). By September 30, 2024, there are more than 704 million infected and 7 million deaths from COVID-19. It is well established that acute COVID-19 is associated with notable morbidity and mortality. However, there are concerns about the sequelae of COVID-19 in adults and children, which may persist for weeks or even months after recovery from acute COVID-19 infection (1).

Prolonged COVID-19 is characterized by persistent symptoms for at least 4 to 12 weeks after 3 months of initial SARS-CoV-2 infection, which is rapidly rising as a global health priority (1, 2). About 10-30% of patients with acute COVID-19 develop to prolonged COVID-19, which affects multiple organs with persistent symptoms e.g. fatigue, dyspnea, cough, chest pain, diarrhea, headache, insomnia, joint pain, myalgia, weakness, neurocognitive issues, palpitations, pins and needles, rash, hair loss, and also imbalance in walking (2, 3).

Despite the effect of COVID-19 vaccines on reducing SARS-CoV-2 infection, as well as COVID-19-related problems such as hospitalization, admission to the intensive care unit (ICU), and death in both children and adults, there are no clear evidence regarding the clinical relevance of COVID-19 vaccine protection against long COVID-19 (4). There is no specific treatment for long COVID-19; people with long-term COVID-19 have been exposed to re-infection with SARS-CoV-2 due to dysregulation of the immune system (2, 4). Thus, further studies are needed to investigate the clinical effectiveness of COVID-19 vaccines against long COVID-19. Taken together, the present

document discusses about the clinical safety and efficacy of COVID-19 vaccine in preventing the development of long COVID-19 using evidences from real-world human trials.

In this regard, Gao et al. examined the efficacy of COVID-19 vaccines for the protection against long COVID-19 using eighteen included trials; they found that the incidence of long COVID-19 in vaccinated group was 29% lower than controls (RR: 0.71; 95% CI: 0.58–0.87). In addition, the authors elucidated that vaccination was effective against long COVID-19 phenomenon in both situations, before (RR: 0.82, 95% CI: 0.74–0.91) and after (RR: 0.83, 95% CI: 0.74–0.92) SARS-CoV-2 infection. However, based on their findings, COVID-19 vaccine was protective against long COVID-19 only in individuals vaccinated with two doses (RR: 0.83, 95% CI: 0.74–0.94) (5). Ceban et al. also investigated COVID-19 vaccination for the prevention of long COVID-19. There were 6 human trials in this document which at least one dose of COVID-19 vaccine was significantly protective against long COVID-19 (OR: 0.53, 95% CI 0.295–0.987) (6). Watanabe et al. assessed data of six observational studies including 536,291 unvaccinated and 84,603 vaccinated adults to find the clinical efficacy of COVID-19 vaccines against long COVID-19. They showed that two-dose vaccination was associated with a lower risk of long COVID-19 than other modes: no vaccination (OR: 0.64; 95% CI 0.45–0.92) and one-dose vaccination (OR: 0.60; 95% CI 0.43–0.83). Furthermore, the authors suggested that 20.3% of individuals with long COVID-19 symptomatically improved after two weeks to six months of COVID-19 vaccination (7).

According to the literature, COVID-19 vaccines reduce long COVID-19 symptoms such as cognitive dysfunction, kidney diseases, myalgia,

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and sleeping disorders (5-7). Therefore, the results of the meta-analysis support the clinical safety and efficacy of SARS-CoV-2 vaccines against long COVID-19. However, the available studies have several limitations: 1) there were individuals that exhibited natural improvement of long COVID-19 symptoms which may have been underestimated as vaccination in clinical setting; 2) studies used wide range of COVID-19 vaccines including both inactivated vaccines and mRNA COVID-19 vaccines. Thus, findings should be interpreted with caution. Since booster vaccines show great promise in both prevention of infection and progression, further research on boosters and omicron-specific vaccination is needed to be performed.

Consequently, the current comprehensive literature recommends SARS-CoV-2 vaccine to reduce the risk of long COVID-19 in cases of progression. There are no findings of a negative effect of COVID-19 vaccination on worsening symptoms of COVID-19. Therefore, SARS-CoV-2 vaccination should be improved as soon as possible, especially offering a full course of vaccination. More research is needed to discover the mechanism of action of the COVID-19 vaccines on long COVID-19 in the future.

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