

The Potential Effects of COVID Vaccination as a Protective Measure against Long COVID

Jenna La, Nicole Lay, Mariah Lapierre
Medical Laboratory Sciences

Research Question

Does full vaccination (at least 2 doses of any COVID-19 vaccine) offer protection from developing Long COVID in individuals (adults 18+) who have contracted COVID-19?

The **P**opulation for our question is adults (18+) who have contracted COVID-19. Our **I**ntervention is fully vaccinated (at least 2 doses of any COVID-19 vaccine) adults. Our **C**omparison is unvaccinated adults. Our **O**utcome is a decreased risk of developing Long COVID. Long COVID in this question will be defined as: “physical or psychological symptoms more than 12 weeks after contracting the virus”.¹

Introduction & Background

Long COVID, or post-acute sequelae of COVID-19 (PASC), is a phenomenon where some individuals have persistent symptoms that last 12 weeks or longer even after apparent recovery from an initial COVID infection.¹ The mechanisms as to why this occurs, and the potential long-term health consequences are unknown. Increased awareness of the burden persistent COVID infections may place on our healthcare system is necessary. One of the few preventative methods used in preventing SARS-CoV-2 infections is vaccination. However, there is contradicting evidence as to whether vaccination can protect against PASC when breakthrough infections occur.

Methods

The literature search was conducted using PubMed (2299 results), EBSCO MedLine (1829 results), Cochrane Library (145 results), and Cochrane COVID-19 Study Register (204 results) between Sept. 29 to Oct. 4, 2022. Keywords include “Long COVID”, “vaccination”, “Long COVID protection”, “PASC”, “Incidence Post COVID-19 symptoms” which were used on their own or in combination with each other using the Boolean operator “AND” to filter results. A number of inclusion and exclusion criteria were used which can be found in the detailed literature search report.²

Summary of Literature

The ten articles used in our literature search include: 5 prospective cohort studies^{3,4,6,8,11}, 1 cross-sectional study⁵, 1 retrospective cohort study¹², 2 reviews^{7,9}, and 1 systematic review¹⁰. The reviews^{7,9} were used to provide context on the current knowledge of Long COVID. Vaccination was shown to reduce the risk of some Long COVID symptoms^{3-5,8,10} while other studies indicated vaccination has no statistically significant effect on the reduction of symptoms.^{6,11,12}

Table 1	Ayoubkhani et al. ⁴ (Prospective Cohort Study)	Kuodi et al. ⁸ (Prospective Cohort Study)	Taquet et al. ¹² (Retrospective Cohort Study)
PICO/Question	P: 6180 individuals aged 18+ I: individuals who had received two or more doses of any COVID-19 vaccine at least two weeks prior to infection C: Unvaccinated individuals infected with COVID-19 O: At least two doses of any COVID-19 vaccine reduced the risk of developing Long Covid compared to having no vaccinations	P: 3572 individuals aged 18+ I: Infected individuals and those with no previous infection who are vaccinated with 2+ doses of BNT162b2 (Pfizer) C: Infected individuals and those with no previous infection who are unvaccinated and those vaccinated with 1 dose of Pfizer O: Individuals who are vaccinated with 2+ doses of Pfizer report no more symptoms of Long COVID than those who have never been infected	P: 10,024 individuals aged 18+ I: Individuals who had received 1+ shot of COVID-19 vaccine at least 14 days before onset of infection with COVID-19 C: Individuals who were not vaccinated against COVID-19 but received an influenza vaccine O: There was no significant difference between the cohorts for Long COVID symptoms, but those who received 2 doses of COVID-19 vaccines had lower risk for some COVID sequelae
Methods	Matched prospective cohort study using in-person interviews regarding persistent COVID-19 symptoms which were conducted by trained study workers. Swabs were taken to test for COVID-19 infection.	Cross-sectional and prospective longitudinal cohort study using an online questionnaire sent to individuals who PCR-tested for COVID-19 at participating hospitals in Northern Israel between March 2020 and November 2021.	Matched retrospective cohort study using anonymous data obtained from 59 healthcare organizations using TriNetX Analytics (an electronic health record network)
Results	Adjusted odds ratios (aOR) for developing Long Covid symptoms in double-vaccinated individuals compared to unvaccinated participants were estimated using the logistic regression method. For individuals who had two doses of either adenovirus or mRNA vaccines, the aOR for developing Long Covid symptoms of any severity was 0.59 (95% CI, 0.50-0.69) and the aOR for activity limiting symptoms was also 0.59 (95% CI, 0.48-0.73).	Using binomial regression (Risk Ratio=RR, those who were vaccinated with 2+ doses were less likely to report the symptoms of fatigue (RR 0.38, 95% CI, p< 0.04), headache (RR 0.50, 95% CI, p< 0.04), weakness of limbs (RR 0.38, 95% CI, p< 0.04), persistent muscle pain (RR 0.34, 95% CI, p< 0.04) than unvaccinated individuals. The likelihood of vaccinated individuals reporting symptoms was comparable to those who had never been infected with COVID-19.	Using the Kaplan-Meier estimator (Hazard Ratio = HR), the various outcomes were compared for individuals with at least 1 COVID-19 vaccine and those with the influenza vaccine. The risk of Long COVID symptoms was not statistically significant between the cohorts (HR 1.01, 95% CI 0.96 - 1.05, p = 0.83, Bonferroni-corrected p= 1.0). Individuals with 2 doses had lower risks in certain COVID sequelae than those with 1 dose, the results for Long COVID were not statistically significant.
Validity	Random selection from the UK COVID-19 Infection Survey minimized selection bias. Participants were also tested during the follow-up visits allowing the study to include both asymptomatic and symptomatic infections.	Weak internal validity and underpowered analysis as the frequency of 29/39 symptoms and diagnoses were too low to meaningfully include in the regression model hence not used in analysis. Weak external validity as most of the participants experienced milder symptoms of COVID-19 and were not hospitalized; results cannot be applied to those who experience more serious symptoms of COVID-19.	Due to the use of electronic health records, patients with untreated symptoms of Long COVID but did not receive medical care were not included in the study. Due to the nature of a retrospective study, the duration of Long COVID symptoms could not be analyzed.
Benefit	Two doses of any vaccination against COVID-19 is an effective method to reduce the risk of long-term symptoms associated with COVID-19 infection.	2+ doses of Pfizer were shown to reduce some Long COVID symptoms however the results can only be applied to the Pfizer vaccine.	1 dose of a COVID-19 vaccine can help mitigate some of the COVID-19 sequelae and the protection increases against certain outcomes with 2 doses, however COVID-19 vaccination does not provide protection against Long COVID.

Summary & Discussion

Our literature review illustrates the contradicting evidence on vaccination and Long COVID where some studies suggest vaccination reduces the risk of developing some PASC symptoms while other studies suggest there is no statistically significant effect. To fill in gaps in the current understanding of vaccination and its preventive role in Long COVID, more data is needed on whether vaccines protect against newer variants such as Omicron, if specific types of vaccinations (mRNA vs. adenovirus) provide more protection than others, and whether boosters provide additional protection or prolong protection against Long COVID. Future research should include longer studies to determine if vaccination provides short-term or long-term protections against Long COVID. Mechanistic studies should also be conducted to understand why Long COVID occurs and how vaccines could protect against it.