Vaccination and Its Effects on Long COVID-19 Prevalence, Severity, and Clinical Outcomes: A Literature Review

Klevis Caushaj
Department of Public Health, University of Medicine, Tirana, Albania

Aldo Shpuza
Department of Public Health, University of Medicine, Tirana, Albania

Enver Roshi
Department of Public Health, University of Medicine, Tirana, Albania

Abstract

Long COVID is a heterogeneous condition characterized by persistent symptoms following SARS-CoV-2 infection and represents an important public health concern. COVID-19 vaccination has been widely implemented, yet its association with long-term post-COVID outcomes remains incompletely understood. This narrative review summarizes current evidence on the relationship between COVID-19 vaccination and Long COVID, focusing on prevalence, symptom severity, and clinical outcomes. Available studies suggest that vaccination may be associated with a lower risk of Long COVID and reduced symptom burden in breakthrough infections, although findings are variable across populations and study designs. Age and pre-existing comorbidities consistently emerge as relevant factors that may influence observed associations. Overall, existing evidence supports a potential protective association of vaccination with Long COVID outcomes, while emphasizing the need for further longitudinal studies with standardized definitions and outcome measures.

Keywords: Long COVID; SARS-CoV-2; COVID-19 vaccination; symptom severity; clinical outcomes

Introduction

According to the CDC, Long COVID is a chronic condition occurring after SARS-CoV-2 infection, persisting for at least three months, and characterized by a wide range of symptoms that may fluctuate over time, affecting individuals of

all ages regardless of the severity of the initial illness (1). Consequently, Long COVID represents a major global health challenge with medical, social, and economic implications, while its estimated prevalence varies widely due to the lack of specific diagnostic biomarkers or standardized criteria (2). Recent global meta-analytic evidence indicates that the pooled prevalence of Long COVID is approximately 36% following SARS-CoV-2 infection worldwide, with marked heterogeneity across geographic regions, symptom subtypes, and follow-up duration (3). COVID-19 vaccination has been widely implemented and remains ongoing, with U.S. data from the 2025–2026 season indicating uptake of 16.7% among adults and 34.7% among those aged ≥65 years (4). A systematic review of observational studies suggests that COVID-19 vaccination may be associated with a reduced risk of Long COVID when administered before or after SARS-CoV-2 infection, although the overall certainty of evidence is low (5). This literature review aims to evaluate the effect of COVID-19 vaccination on the prevalence, severity, and clinical outcomes of Long COVID. This narrative review aims to describe and discuss the existing literature on the association between COVID-19 vaccination and Long COVID, with a focus on reported effects on prevalence, symptom severity, and clinical outcomes.

Methods

A narrative literature review was conducted to examine the relationship between COVID-19 vaccination and Long COVID. The PubMed database was searched using Boolean combinations of terms related to COVID-19, Long COVID, post-acute sequelae of SARS-CoV-2 infection, and vaccination. Relevant peer-reviewed articles published from 2021 onwards were identified and reviewed. The selected literature was used to provide a descriptive synthesis of current evidence regarding the potential effects of vaccination on Long COVID prevalence, symptom severity, and clinical outcomes.

As this review was based exclusively on previously published studies, formal ethical approval was not required, and all sources were appropriately cited and acknowledged.

Results and Discussion

Results from the studies demonstrated that, despite geographical variations, approximately one in three COVID-19-positive patients might have developed symptoms of Long COVID-19 (3). Evidence also suggests that vaccination may lower the risk and severity of Long COVID-19; however, findings remain heterogeneous, with variations observed based on vaccine type, booster status, timing of vaccination relative to infection, and the predominant SARS-CoV-2 variant (6–9). Factors such as age, comorbidities, immune response variability, and differences in study design may explain the inconsistencies in findings. In a 2-year follow-up cohort study, individuals aged over 65 years had a significantly higher risk of Long COVID, confirming age as an independent risk factor for persistent post-COVID sequelae (10). Age may therefore confound or modify the observed effect of vaccination on Long COVID, as older individuals differ in baseline risk, immune response, and vaccination patterns compared with younger populations. Evidence from a large meta-analysis indicates that pre-existing comorbidities more than doubled the risk of post-COVID-19 condition, whereas prior COVID-19 vaccination was associated with a significant protective effect against PCC development (11). Beyond reducing the risk of Long COVID, accumulating evidence suggests that COVID-19 vaccination is associated with reduced disease severity, including a lower burden of persistent physical and neuropsychological symptoms, improved functional status, and more favorable long-term clinical outcomes among infected individuals (12). Taken together, these findings highlight the multifactorial nature of Long COVID and suggest that observed associations between vaccination and long-term outcomes should be interpreted within the context of individual risk profiles, population heterogeneity, and methodological variability across studies.

Conclusion

While current evidence suggests a potential protective role of vaccination against Long COVID-19, further research is needed to establish definitive causal relationships. Future studies should focus on identifying the specific mechanisms through which vaccination influences Long COVID-19 and addressing inconsistencies in existing findings by incorporating diverse population and standardized outcome measures.

References

1. CDC. Long COVID. 2025 [cited 2026 Jan 13]. Long COVID Basics. Available from: https://www.cdc.gov/long-covid/about/index.html

2. National Academies of Sciences E, Division H and M, Health B on G, Policy B on HS, Covid C on E the WD for L, Goldowitz I, et al. Introduction. In: A Long COVID Definition: A Chronic, Systemic Disease State with Profound Consequences [Internet]. National Academies

Press (US); 2024 [cited 2026 Jan 13]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK605678/

3. Hou Y, Gu T, Ni Z, Shi X, Ranney ML, Mukherjee B. Global Prevalence of Long COVID, Its Subtypes, and Risk Factors: An Updated Systematic Review and Meta-analysis. Open Forum Infect Dis. 2025 Sep 1;12(9):ofaf533.

4. CDC. Respiratory Illnesses. 2026 [cited 2026 Jan 13]. Vaccination Trends. Available from: https://www.cdc.gov/respiratory-viruses/data/vaccination-trends.html

5. Byambasuren O, Stehlik P, Clark J, Alcorn K, Glasziou P. Effect of covid-19 vaccination on long covid: systematic review. BMJ Med. 2023 Feb 1;2(1):e000385.

6. Kim Y, Bae S, Chang HH, Kim SW. Characteristics of long COVID and the impact of COVID-19 vaccination on long COVID 2 years following COVID-19 infection: prospective cohort study. Sci Rep. 2024 Jan 9;14(1):854.

7. Tofarides AG, Christaki E, Milionis H, Nikolopoulos GK. Effect of Vaccination against SARS-CoV-2 on Long COVID-19: A Narrative Review. Life. 2022 Dec 8;12(12):2057.

8. Patel V, Korsun M, Cervia J. Protective effects of booster dose of SARS-COV-2 vaccination against post-acute COVID-19 syndrome: A systematic review. J Investig Med Off Publ Am Fed Clin Res. 2025 Dec;73(8):606–13.

9. Guimarães GN, Brunetti NS, De Lima DG, Proenca-Modena JL, Farias AS. Vaccination and COVID-19: impact on long-COVID. Front Immunol. 2025;16:1686572.

10. Zhang D, Chen C, Xie Y, Zhou S, Li D, Zeng F, et al. Prevalence and risk factors of long COVID-19 persisting for 2 years in Hainan Province: a population-based prospective study. Sci Rep. 2025 Jan 2;15(1):369.

11. Tsampasian V, Elghazaly H, Chattopadhyay R, Debski M, Naing TKP, Garg P, et al. Risk Factors Associated With Post-COVID-19 Condition: A Systematic Review and Meta-analysis. JAMA Intern Med. 2023 Jun 1;183(6):566–80.

12. Guimarães GN, Brunetti NS, De Lima DG, Proenca-Modena JL, Farias AS. Vaccination and COVID-19: impact on long-COVID. Front Immunol [Internet]. 2025 Nov 19 [cited 2026 Jan 26];16. Available from: https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2025.1686572/full