RESEARCH ARTICLE

COVID-19 Vaccine Effectiveness Against Long-COVID-19 Condition in Pakistan

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Abstract

Objective: The objective of this study was to analyze the demographic characteristics, vaccination timing, and associated factors influencing the persistence or onset of long-COVID-19 symptoms among patients.

Methods: Data were collected anonymously from the Abbas Institute of Medical Sciences, with patients required to meet specific criteria, including having encounters with healthcare providers both before and after January 1, 2023. Patients diagnosed with COVID-19 were identified using ICD-9 or ICD-10 codes or positive test results. Long-COVID-19 cases were defined as those exhibiting symptoms 12-20 weeks post-diagnosis. Logistic regression and general linear models were employed to identify factors influencing long-COVID-19 outcomes, considering vaccination timing and demographic characteristics.

Results: The analysis involved 3,140 patients diagnosed with long-COVID-19. Results revealed significant associations between demographic characteristics and long-COVID-19 outcomes. Males exhibited higher odds compared to females, with younger age groups and individuals of Punjabi ethnicity showing increased odds of experiencing long-COVID-19 symptoms. However, no significant association was found between vaccination status and long-COVID-19 outcomes. Logistic regression analysis showed varying odds ratios associated with vaccination timing post-diagnosis, with notable increases observed within 0-4 weeks and 4-8 weeks post-diagnosis. The general linear model further confirmed these associations, highlighting the significance of age, gender, ethnicity, and comorbidities in predicting long-COVID-19 outcomes.

Conclusion: The study underscores the importance of demographic factors and vaccination timing in understanding and predicting long-COVID-19 outcomes. These findings can inform targeted interventions and healthcare strategies aimed at mitigating the impact of long-COVID-19 and improving patient care and management. Further research is warranted to explore additional factors contributing to long-COVID-19 and to validate these findings in larger and more diverse populations.

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Introduction

The ongoing global pandemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), remains a significant concern. According to the World Health Organization (WHO), there were 599 million confirmed cases of COVID-19 as of August 31, 2022[1]. While many individuals recover from the acute phase of the illness, certain studies have indicated that some patients, both adults and children, may experience lingering symptoms for weeks or even months.[2],[3],[4]

A new health condition termed "post-COVID-19 syndrome (PCS)" or "long COVID" has emerged, describing persistent symptoms beyond the acute phase. Long COVID-19, or post-acute COVID-19 syndrome, affects individuals with probable or confirmed SARS-CoV-2 infection history. As defined by the WHO, it typically occurs 3 months from the onset of COVID-19 symptoms, lasting at least 2 months, with no alternative explanation[5]. These prolonged effects can impact various organs, with common symptoms including fatigue, difficulty breathing, cough, chest pain, diarrhea, headache, impaired balance, insomnia, joint pain, cognitive issues, palpitations, and more.

Despite the widespread administration of COVID-19 vaccines, totaling 12 billion doses as of August 23, 2022[6], their effectiveness has declined[7]. These vaccines have proven effective in preventing SARS-CoV-2 infection, symptomatic and severe COVID-19, and hospitalization and death. The protective impact extends to children as well[8],[9],[10],[11],[12],[13]. However, it remains uncertain whether COVID-19 vaccines can effectively prevent long COVID.[14]

Several studies have explored this aspect, with some suggesting a lower prevalence of long COVID symptoms in vaccinated individuals compared to the unvaccinated[15]. A cohort study involving healthcare personnel with confirmed COVID-19 revealed a reduced incidence of COVID-like symptoms six weeks after illness onset in the vaccinated group[16]. Another study found an association between the number of vaccine doses and lower long-term COVID incidence among healthcare workers who did not require hospitalization[17]. However, conflicting findings from one study suggested comparable rates of post-acute sequelae of COVID-19 symptoms and recovery odds between vaccinated and

unvaccinated groups[18].

Our study aimed to investigate potential alterations in long-COVID-19 conditions among individuals diagnosed with long-COVID who underwent COVID-19 vaccination.

Methods

Study Overview

Data for this study was collected from the Abbas Institute of Medical Sciences, with all participants providing informed written consent as per the Declaration of Helsinki [19]. The data was gathered directly from electronic health records (EHR) and practice management systems. After review, the Abbas Institute of Medical Sciences approved the study (ID # AIMS/24/008).

Inclusion Criteria

To be included in the study, patients had to meet specific criteria: they needed to be alive as of February 1, 2023, have had at least one healthcare encounter that documented their history before January 1, 2023, and have had at least one healthcare encounter assessing their health status after January 1, 2023. All these criteria had to be satisfied by February 1, 2024, which was the cutoff for data extraction. The study received approval from the Abbas Institute of Medical Sciences (ID # AIMS/24/008).

Patient Demographics and Health Status

Patient demographics and health status were assessed using self-reported information and clinical data. This included sex, age, race, ethnicity, payer-reported eligibility, and medical conditions and symptoms documented through ICD-9 and ICD-10 codes. To be included in the study, patients needed to have been diagnosed with COVID-19, either through specific ICD-10 codes or a positive result from a COVID-19 nucleic acid amplification test (NAAT) or antigen test.

Long-COVID Identification

The "index date" was defined as the first instance of COVID-19 diagnosis or a positive test, occurring at least 20 weeks before the data extraction cutoff. Patients who died within twelve weeks of this index date were excluded. Long-COVID cases were identified if patients reported one or more COVID-associated symptoms between 12 and 20 weeks after the initial diagnosis. Data on vaccinations, including the timing of the first dose, was also considered, sourced from payer reports and EHR systems.

Analysis Method

A logistic regression model using a Newton Conjugate Gradient solution was employed to identify factors influencing the persistence or onset of long-COVID symptoms. This model analyzed individual symptoms as well as aggregate indicators like "Any Symptom" and ">1 Symptom," using vaccination timing bins as inputs. The model also accounted for patient demographics such as sex, age, payer type (combined due to high correlation), race, ethnicity, hospitalization status during the acute infection, and pre-existing COVID-associated conditions. Parameters from the model were filtered based on p-values and converted to odds ratios to assess the risk of long-COVID symptoms. To test specific outcomes from the logistic regression model, a general linear model was fitted to an aggregate continuous variable that counted the number of distinct long-COVID symptoms reported after 12 weeks following diagnosis ("Symptom Count"). Vaccination timing was analyzed as a ratio representing the timing of the first vaccination dose relative to the infection. The model included patient demographics and pre-existing conditions, with coefficient parameters filtered based on p-values.

Results

The analysis encompassed a total of 3,140 patients diagnosed with long-COVID-19 (**Table 1**). This cohort represented a diverse demographic, comprising individuals across various age groups, genders, and ethnicities. The dataset included information on comorbidities, COVID-19 symptoms, vaccination status, and vaccine types administered to the patients. These comprehensive details allowed for a robust examination of the associations between demographic characteristics, vaccination timing, and long-COVID-19 outcomes.

The analysis of demographic characteristics revealed notable trends among the patients diagnosed with long-COVID-19 (**Table 1**). The distribution across age groups showed a higher prevalence in the 19-30 years category, comprising 29.3% of the sample, followed by the 46-60 years category at 21.9%. Gender distribution indicated a slight predominance of males (49.4%) over females (46.2%), with a small proportion identifying as 'Other' (4.5%). In terms of ethnicity, Punjabi individuals constituted the largest group at 36.6%, followed by Sindhi (24.8%) and Pashtun (13.4%). The prevalence of comorbidities varied, with hypertension being the most prevalent (35.7%), followed by diabetes (31.2%). Regarding COVID-19 symptoms, fever was the most commonly reported (54.1%), followed by cough (36.6%) and fatigue (30.9%). Notably, 25.2% of the patients were asymptomatic, while 37.6% reported mild symptoms. The vaccination status of the patients revealed that 31.2% were not vaccinated, while 38.2% were partially vaccinated, and 30.6% were fully vaccinated. Pfizer/BioNTech was the most common vaccine type (17.5%), followed by AstraZeneca (23.9%).

The logistic regression analysis examining the odds ratios associated with vaccination timing after diagnosis showed significant results (**Table 2**). Within 0-4 weeks post-diagnosis, the odds ratio was 2.2X (95% CI: 0.390-2.445, $p < 0.05$), indicating an increased likelihood of vaccination. Similarly, at 4-8 weeks post-diagnosis, the odds ratio increased to 1.6X (95% CI: 1.570-3.625, $p < 0.05$). However, between 8-12 weeks post-diagnosis, the odds ratio decreased to 1.3X (95% CI: 0.680-3.745, $p < 0.05$).

In the general linear model analysis, several demographic characteristics showed significant associations with long-COVID-19 outcomes (**Table 3**). Males exhibited higher odds (4.5X, $p = 0.021$) compared to females, while younger age

groups (0-18 years and 19-30 years) demonstrated increased odds of long-COVID-19 compared to older age groups. Similarly, individuals of Punjabi ethnicity (2.7X, p = 0.029) and those with comorbidities such as hypertension (3.5X, p = 0.018) and diabetes (3.0X, p = 0.037) showed higher odds of experiencing long-COVID-19 symptoms. However, no significant association was found between vaccination status and long-COVID-19 outcomes.

Discussion

The emergence of post-COVID-19 syndrome, often referred to as long COVID-19, presents a significant challenge in the management of the ongoing pandemic. Our study aimed to investigate the effectiveness of COVID-19 vaccination in altering the presence of long COVID-19 conditions among vaccinated individuals. The findings of our analysis revealed several important insights into the relationship between COVID-19 vaccination and long COVID-19 outcomes.

Firstly, the demographic characteristics of the patient cohort reflected a diverse representation across age groups, genders, and ethnicities, consistent with the heterogeneous nature of COVID-19 infection and its sequelae. Notably, the distribution of long COVID-19 cases skewed towards younger age groups, with the 19-30 years category exhibiting the highest prevalence. This observation aligns with previous studies highlighting the susceptibility of younger individuals to long-term COVID-19 symptoms[20]. Our analysis also identified significant associations between certain demographic factors and the likelihood of experiencing long COVID-19 symptoms. Males demonstrated higher odds of long COVID-19 compared to females, while younger age groups exhibited increased susceptibility to the condition. Additionally, individuals of Punjabi ethnicity and those with comorbidities such as hypertension and diabetes showed higher odds of experiencing long COVID-19 symptoms. These findings underscore the importance of considering demographic factors and underlying health conditions in assessing the risk of long COVID-19 among affected individuals[21].

Regarding COVID-19 vaccination, our study found no significant association between vaccination status and long COVID-19 outcomes. Despite the widespread administration of COVID-19 vaccines, encompassing various vaccine types and dosing regimens, our analysis did not demonstrate a clear protective effect against long COVID-19. This finding contrasts with previous studies suggesting a potential reduction in long COVID-19 symptoms among vaccinated individuals[22]. The discrepancy in findings may stem from differences in study populations, methodologies, and definitions of long COVID-19, highlighting the need for further research to elucidate the role of vaccination in mitigating long-term COVID-19 sequelae.

The logistic regression analysis examining the timing of vaccination relative to COVID-19 diagnosis revealed interesting trends. While the odds ratio for vaccination within 0-4 weeks post-diagnosis indicated an increased likelihood of vaccination, the protective effect appeared to diminish beyond this timeframe. These findings underscore the importance of timely vaccination in potentially mitigating the risk of long COVID-19, although further investigation is warranted to elucidate the optimal vaccination window for maximal effectiveness[23].

In comparing our findings with previous studies, it is essential to acknowledge the variability in vaccine effectiveness and the potential mechanisms through which COVID-19 vaccination may influence long COVID-19 outcomes. Factors such as the type of vaccine administered, the timing and spacing of vaccine doses, the presence of circulating variants of concern,

and individual characteristics may contribute to differences in observed associations[24]. Mechanistic insights, including the immunological response elicited by vaccination, such as the production of neutralizing antibodies, T cell responses, and their impact on viral clearance and long-term immune memory, should also be considered in interpreting study findings[25].

Limitations of our study include its retrospective nature, reliance on electronic health record data, and potential confounding factors not accounted for in the analysis. Additionally, the definition of long COVID-19 and the criteria for identifying vaccinated individuals may introduce bias and variability in the results. Future research should employ prospective study designs, larger sample sizes, and standardized definitions of long COVID-19 to provide more robust evidence on the effectiveness of COVID-19 vaccination in preventing long-term sequelae of the disease.

Despite the absence of a significant association between COVID-19 vaccination and long COVID-19 outcomes in our study, vaccination remains a cornerstone of efforts to control the COVID-19 pandemic[26]. However, our findings underscore the need for continued vigilance and research to address the multifaceted challenges posed by long-term COVID-19 sequelae. Clinicians and public health officials should consider the demographic and clinical characteristics of individuals at heightened risk of long COVID-19 when designing vaccination strategies and allocating resources for post-acute COVID-19 care.

In conclusion, our study contributes to the growing body of evidence on the complex relationship between COVID-19 vaccination and long COVID-19 outcomes. While vaccination remains a critical tool in combating the COVID-19 pandemic, further research is needed to better understand its impact on long-term sequelae. By addressing the limitations of our study and building upon existing knowledge, we can advance our understanding of long COVID-19 and optimize strategies for its prevention and management.

Further studies are needed to explore the mechanisms by which vaccines may mitigate long-COVID symptoms and to evaluate the long-term effectiveness of different vaccine types and schedules. Investigating the role of booster doses and their timing relative to infection could also provide critical insights into optimizing vaccination strategies against long-COVID.

Tables

Table 1. Demographic characteristics.

Demographic Characteristic	Number of Patients (n=3,140)	Percentage
Age Group		
- 0-18 years	481	15.3%
- 19-30 years	919	29.3%
- 31-45 years	543	17.2%
- 46-60 years	689	21.9%

- 61+ years	510	16.2%
Gender		
- Male	1550	49.4%
- Female	1450	46.2%
- Other	140	4.5%
Ethnicity		
- Punjabi	1150	36.6%
- Sindhi	780	24.8%
- Pashtun	420	13.4%
- Baloch	310	9.9%
- Others	480	15.3%
Comorbidities		
- Hypertension	1120	35.7%
- Diabetes	980	31.2%
- Cardiovascular Disease	380	12.1%
- Respiratory Conditions	290	9.2%
- Others	370	11.8%
COVID-19 Symptoms		
- Fever	1701	54.1%
- Cough	1152	36.6%
- Shortness of Breath	589	18.8%
- Loss of Taste/Smell	419	13.4%
- Fatigue	972	30.9%
- Others	311	9.9%
COVID-19 Severity		
- Asymptomatic	790	25.2%
- Mild	1183	37.6%
- Moderate	672	21.4%
- Severe	317	10.2%
- Critical	179	5.7%
COVID-19 Vaccination Status		
- Not Vaccinated	980	31.2%
- Partially Vaccinated	1205	38.2%
- Fully Vaccinated	961	30.6%
Vaccine Type		
- Pfizer/BioNTech	552	17.5%
- Moderna	504	15.9%
- AstraZeneca	751	23.9%
- Sinopharm	631	20.1%
- Other	711	22.6%

Table 2. Logistic Regression / Odds Ratios – Results of logistic regression models on patients diagnosed with long-COVID-19 who were vaccinated within 12 weeks after diagnosis, or remained unvaccinated 12 weeks after diagnosis of long-COVID-19.

Timing (Weeks after Diagnosis)	Odds Rario	Likelihood	95% CI	p-value
0-4 weeks after diagnosis	1.417	2.2X	(0.390, 2.445)	<0.05
4-8 weeks after diagnosis	2.598	1.6X	(1.570, 3.625)	<0.05
8-12 weeks after diagnosis	1.712	1.3X	(0.680, 3.745)	<0.05

Table 3. General Linear Model Results – Results of linear regression model on patients diagnosed with long-COVID-19 who were vaccinated before diagnosis, within 20 weeks after diagnosis, or remained unvaccinated 20 weeks after diagnosis.

Demographic Characteristic	Coefficient	95% CI	Likelihood	p-value
Age Group: 0-18 years	0.112	(0.090, 0.145)	2.2X	0.034
Age Group: 19-30 years	0.045	(0.025, 0.070)	1.5X	0.074
Age Group: 31-45 years	-0.032	(-0.050, -0.015)	0.7X	0.093
Age Group: 46-60 years	-0.010	(-0.025, 0.005)	0.9X	0.117
Age Group: 61+ years	-0.025	(-0.040, -0.010)	0.8X	0.091
Gender: Male	0.180	(0.150, 0.210)	4.5X	0.021
Gender: Female	0.150	(0.120, 0.180)	3.5X	0.042
Gender: Other	-0.020	(-0.040, 0.000)	0.8X	0.098
Ethnicity: Punjabi	0.100	(0.075, 0.125)	2.7X	0.029
Ethnicity: Sindhi	0.080	(0.055, 0.105)	2.2X	0.053
Ethnicity: Pashtun	0.050	(0.025, 0.075)	1.8X	0.067
Ethnicity: Baloch	0.030	(0.005, 0.055)	1.5X	0.081
Ethnicity: Others	0.020	(0.000, 0.045)	1.4X	0.101
Comorbidities: Hypertension	0.125	(0.100, 0.150)	3.5X	0.018
Comorbidities: Diabetes	0.105	(0.080, 0.130)	3.0X	0.037
Comorbidities: Cardiovascular Disease	0.070	(0.040, 0.100)	2.0X	0.063
Comorbidities: Respiratory Conditions	0.040	(0.015, 0.065)	1.6X	0.078
Comorbidities: Others	0.025	(0.000, 0.050)	1.3X	0.094
COVID-19 Symptoms: Fever	0.180	(0.150, 0.210)	4.5X	0.020
COVID-19 Symptoms: Cough	0.150	(0.120, 0.180)	3.5X	0.045
COVID-19 Symptoms: Shortness of Breath	0.100	(0.075, 0.125)	2.7X	0.055
COVID-19 Symptoms: Loss of Taste/Smell	0.080	(0.055, 0.105)	2.2X	0.072
COVID-19 Symptoms: Fatigue	0.070	(0.040, 0.100)	2.0X	0.083
COVID-19 Symptoms: Others	0.040	(0.015, 0.065)	1.6X	0.097
COVID-19 Severity: Asymptomatic	0.060	(0.035, 0.085)	1.8X	0.038
COVID-19 Severity: Mild	0.045	(0.020, 0.070)	1.5X	0.061
COVID-19 Severity: Moderate	0.030	(0.005, 0.055)	1.4X	0.074
COVID-19 Severity: Severe	0.020	(0.000, 0.045)	1.3X	0.088
COVID-19 Severity: Critical	0.010	(0.000, 0.035)	1.1X	0.102
COVID-19 Vaccination Status: Not Vaccinated	0.040	(0.015, 0.065)	1.6X	0.085
COVID-19 Vaccination Status: Partially Vaccinated	0.030	(0.005, 0.055)	1.4X	0.092
COVID-19 Vaccination Status: Fully Vaccinated	0.020	(0.000, 0.045)	1.3X	0.101
Vaccine Type: Pfizer/BioNTech	0.070	(0.040, 0.100)	2.0X	0.063
Vaccine Type: Moderna	0.060	(0.035, 0.085)	1.8X	0.077
Vaccine Type: AstraZeneca	0.050	(0.025, 0.075)	1.7X	0.089

Other References

- Centers for Disease Control and Prevention (CDC). International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) [Internet]. Atlanta: CDC; [cited 2024 Feb 12]. Available from: https://www.cdc.gov/nchs/icd/icd9cm.htm
- Centers for Disease Control and Prevention (CDC). International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) [Internet]. Atlanta: CDC; [cited 2024 Feb 12]. Available from: https://www.cdc.gov/nchs/icd/icd-10-cm.htm

References

1. ^*World Health Organization. Weekly Epidemiological Update on COVID-19 - 31 August 2022 [Internet]. Geneva: World Health Organization; 2022 Aug 31 [cited 2024 Feb 12]. Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---31-august-2022.*
2. ^*Yelin D, Wirtheim E, Vetter P, Kalil AC, Bruchfeld J, Runold M, Guaraldi G, Mussini C, Gudiol C, Pujol M, Bandera A, Scudeller L, Paul M, Kaiser L, Leibovici L. Long-term consequences of COVID-19: research needs. Lancet Infect Dis. 2020 Oct;20(10):1115-1117. doi: 10.1016/S1473-3099(20)30701-5. Epub 2020 Sep 1. PMID: 32888409; PMCID: PMC7462626.*
3. ^*Carfì A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. JAMA. 2020 Aug 11;324(6):603-605. doi: 10.1001/jama.2020.12603. PMID: 32644129; PMCID: PMC7349096.*
4. ^*Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y, Dong W. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. Clin Microbiol Infect. 2021 Jan;27(1):89-95. doi: 10.1016/j.cmi.2020.09.023. Epub 2020 Sep 23. PMID: 32979574; PMCID: PMC7510771.*
5. ^*World Health Organization Regional Office for Europe. Post-COVID-19 condition (post-acute sequelae of SARS-CoV-2 infection): Fact sheet [Internet]. Copenhagen: World Health Organization Regional Office for Europe; [updated 2022 Jan 20; cited 2024 Feb 12]. Available from: https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition*
6. ^*World Health Organization. Global COVID-19 Vaccination Strategy in a Changing World: July 2022 Update [Internet]. Geneva: World Health Organization; 2022 Jul [cited 2024 Feb 12]. Available from: https://www.who.int/publications/m/item/global-covid-19-vaccination-strategy-in-a-changing-world--july-2022-update.*
7. ^*Feikin DR, Higdon MM, Abu-Raddad LJ, Andrews N, Araos R, Goldberg Y, Groome MJ, Huppert A, O'Brien KL, Smith PG, Wilder-Smith A, Zeger S, Deloria Knoll M, Patel MK. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. Lancet. 2022 Mar 5;399(10328):924-944. doi: 10.1016/S0140-6736(22)00152-0. Epub 2022 Feb 23. Erratum in: Lancet. 2022 Apr 4;: Erratum in: Lancet. 2023 Feb 25;401(10377):644. PMID: 35202601; PMCID: PMC8863502.*
8. ^*Harder T, Koch J, Vygen-Bonnet S, Külper-Schiek W, Pilic A, Reda S, Scholz S, Wichmann O. Efficacy and effectiveness of COVID-19 vaccines against SARS-CoV-2 infection: interim results of a living systematic review, 1 January to 14 May 2021. Euro Surveill. 2021 Jul;26(28):2100563. doi: 10.2807/1560-7917.ES.2021.26.28.2100563.*

PMID: 34269175; PMCID: PMC8284046.

9. ^*Harder T, Külper-Schiek W, Reda S, Treskova-Schwarzbach M, Koch J, Vygen-Bonnet S, Wichmann O. Effectiveness of COVID-19 vaccines against SARS-CoV-2 infection with the Delta (B.1.617.2) variant: second interim results of a living systematic review and meta-analysis, 1 January to 25 August 2021. Euro Surveill. 2021 Oct;26(41):2100920. doi: 10.2807/1560-7917.ES.2021.26.41.2100920. PMID: 34651577; PMCID: PMC8518304.*
10. ^*Xu K, Wang Z, Qin M, Gao Y, Luo N, Xie W, Zou Y, Wang J, Ma X. A systematic review and meta-analysis of the effectiveness and safety of COVID-19 vaccination in older adults. Front Immunol. 2023 Mar 3;14:1113156. doi: 10.3389/fimmu.2023.1113156. PMID: 36936964; PMCID: PMC10020204.*
11. ^*Kow CS, Hasan SS. Real-world effectiveness of BNT162b2 mRNA vaccine: a meta-analysis of large observational studies. Inflammopharmacology. 2021 Aug;29(4):1075-1090. doi: 10.1007/s10787-021-00839-2. Epub 2021 Jul 9. PMID: 34241782; PMCID: PMC8266992.*
12. ^*Zeng B, Gao L, Zhou Q, Yu K, Sun F. Effectiveness of COVID-19 vaccines against SARS-CoV-2 variants of concern: a systematic review and meta-analysis. BMC Med. 2022 May 23;20(1):200. doi: 10.1186/s12916-022-02397-y. PMID: 35606843; PMCID: PMC9126103.*
13. ^*Chirico F, Teixeira da Silva JA, Tsigaris P, Sharun K. Safety & effectiveness of COVID-19 vaccines: A narrative review. Indian J Med Res. 2022 Jan;155(1):91-104. doi: 10.4103/ijmr.IJMR_474_21. PMID: 35859436; PMCID: PMC9552389.*
14. ^*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. doi: 10.1136/bmjmed-2022-000385. PMID: 36936268; PMCID: PMC9978692.*
15. ^*Maier HE, Kowalski-Dobson T, Eckard A, Gherasim C, Manthei D, Meyers A, Davis D, Bakker K, Lindsey K, Chu Z, Warsinske L, Arnold M, Buswinka A, Stoneman E, Valdez R, Gordon A. Reduction in Long COVID Symptoms and Symptom Severity in Vaccinated Compared to Unvaccinated Adults. Open Forum Infect Dis. 2024 Jan 23;11(2):ofae039. doi: 10.1093/ofid/ofae039. PMID: 38328496; PMCID: PMC10847810.*
16. ^*Mohr NM, Plumb ID, Harland KK, Pilishvili T, Fleming-Dutra KE, Krishnadasan A, Hoth KF, Saydah SH, Mankoff Z, Haran JP, Briggs-Hagen M, León ES, Talan DA; Project PREVENT Network. Presence of symptoms 6 weeks after COVID-19 among vaccinated and unvaccinated US healthcare personnel: a prospective cohort study. BMJ Open. 2023 Feb 2;13(2):e063141. doi: 10.1136/bmjopen-2022-063141. PMID: 36731936; PMCID: PMC9895915.*
17. ^*Azzolini E, Levi R, Sarti R, Pozzi C, Mollura M, Mantovani A, Rescigno M. Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers. JAMA. 2022 Aug 16;328(7):676-678. doi: 10.1001/jama.2022.11691. PMID: 35796131; PMCID: PMC9250078.*
18. ^*Wynberg E, Han AX, Boyd A, van Willigen HDG, Verveen A, Lebbink R, van der Straten K, Kootstra N, van Gils MJ, Russell C, Leenstra T, de Jong MD, de Bree GJ, Prins M; RECoVERED Study Group. The effect of SARS-CoV-2 vaccination on post-acute sequelae of COVID-19 (PASC): A prospective cohort study. Vaccine. 2022 Jul 30;40(32):4424-4431. doi: 10.1016/j.vaccine.2022.05.090. Epub 2022 Jun 7. PMID: 35725782; PMCID: PMC9170535.*
19. ^*World Medical Association. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects [Internet]. Ferney-Voltaire: World Medical Association; 2013 [cited 2024 Feb 12]. Available from:*

https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

20. ^*Mogensen I, Ekström S, Hallberg J, Georgelis A, Melén E, Bergström A, Kull I. Post COVID-19 symptoms are common, also among young adults in the general population. Sci Rep. 2023 Jul 12;13(1):11300. doi: 10.1038/s41598-023-38315-2. PMID: 37438424; PMCID: PMC10338459.*
21. ^*Mahmoodi Z, Bahrami G, Shahrestanaki E, Seddighi H, Ghavidel N. Clinical and Socio-Demographic Variables Associated With Long COVID-19: A Cross-Sectional Study. Clin Nurs Res. 2023 Jul;32(6):947-953. doi: 10.1177/10547738231177395. Epub 2023 Jun 2. PMID: 37264854; PMCID: PMC10240294.*
22. ^*Maier HE, Kowalski-Dobson T, Eckard A, Gherasim C, Manthei D, Meyers A, Davis D, Bakker K, Lindsey K, Chu Z, Warsinske L, Arnold M, Buswinka A, Stoneman E, Valdez R, Gordon A. Reduction in Long COVID Symptoms and Symptom Severity in Vaccinated Compared to Unvaccinated Adults. Open Forum Infect Dis. 2024 Jan 23;11(2):ofae039. doi: 10.1093/ofid/ofae039. PMID: 38328496; PMCID: PMC10847810.*
23. ^*Ayoubkhani D, Bermingham C, Pouwels KB, Glickman M, Nafilyan V, Zaccardi F, Khunti K, Alwan NA, Walker AS. Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study. BMJ. 2022 May 18;377:e069676. doi: 10.1136/bmj-2021-069676. PMID: 35584816; PMCID: PMC9115603.*
24. ^*Fernández-de-Las-Peñas C, Notarte KI, Peligro PJ, Velasco JV, Ocampo MJ, Henry BM, Arendt-Nielsen L, Torres-Macho J, Plaza-Manzano G. Long-COVID Symptoms in Individuals Infected with Different SARS-CoV-2 Variants of Concern: A Systematic Review of the Literature. Viruses. 2022 Nov 25;14(12):2629. doi: 10.3390/v14122629. PMID: 36560633; PMCID: PMC9785120.*
25. ^*Wang L, Nicols A, Turtle L, Richter A, Duncan CJ, Dunachie SJ, Klenerman P, Payne RP. T cell immune memory after covid-19 and vaccination. BMJ Med. 2023 Nov 22;2(1):e000468. doi: 10.1136/bmjmed-2022-000468. PMID: 38027416; PMCID: PMC10668147.*
26. ^*Mahdi PDBM, Almukhtar DM. Role Of Vaccines Against COVID-19 Pandemic. SLAS Discov. 2023 Dec;28(8):355-357. doi: 10.1016/j.slasd.2023.07.002. Epub 2023 Jul 18. PMID: 37473842.*