Int J Med. Public Health., 2023; 13(1):1-8.
https://www.ijmedph.org

Review Article

Effect of Vaccination on Long-COVID: A Comprehensive Review and Approach

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ABSTRACT

The COVID-19 pandemic has caused significant morbidity and mortality worldwide. One of the most persistent and debilitating consequences of COVID-19 is long-COVID, a condition characterized by prolonged symptoms and organ damage that can last for months after the acute phase of the infection has resolved. Vaccination against COVID-19 has been shown to be effective in preventing severe disease and hospitalization, but its impact on long-COVID remains unclear. In this comprehensive review, we discuss the pathological mechanism and prevalence of long-COVID and the role of COVID vaccination in preventing and treating this condition. We examine the protective effects of vaccines against COVID-19 and long-COVID, including their efficacy within populations. We also explore breakthrough infections with long-COVID, reviewing studies on their incidence and the differences among vaccine brands. Finally, we summarize current research progress and limitations, and we provide future perspectives on this important topic. Our findings suggest that COVID vaccination may play a crucial role in preventing long-COVID, and further research is needed to fully understand its impact and to develop effective prevention and treatment strategies.
Keywords: Long-COVID, Pathological mechanism, Breakthrough infections.

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Received: 06-03-2023;
Revised: 08-05-2023;
Accepted: 24-05-2023.

PRELUDE

Long COVID, also known as Post-Acute Sequelae of SARS-CoV-2 infection (PASC), refers to the persistence of symptoms beyond four weeks following initial COVID-19 infection. The concept of Long COVID was first introduced in mid-2020, and it has been recognized as a significant public health concern due to its long-lasting impact on the affected individuals.

According to a recent study published in the journal Lancet. Long COVID can manifest in a wide range of symptoms affecting various organs of the body. These symptoms include fatigue, breathlessness, chest pain, palpitations, joint pain, headache, and cognitive impairment, among others. The severity and duration of these symptoms can vary widely, with some individuals experiencing persistent symptoms for several months after the initial infection.

The impact of Long COVID on individuals can be substantial, with many patients reporting a significant reduction in their quality of life. In some cases, Long COVID can also lead to long-term disability, impacting an individual's ability to work or carry out daily activities. Furthermore, Long COVID can also result in psychological distress, including anxiety and depression, due to the uncertainty and unpredictability of the condition.

In addition to the impact on individuals, Long COVID also poses a significant burden on healthcare systems and society as a whole. As noted in a study published in the journal Nature. the long-term health implications of Long COVID remain largely unknown, and the cost of treating and managing Long COVID patients could be substantial.

Long COVID is a newly recognized condition that can have a significant impact on individuals, healthcare systems, and society. As our understanding of Long COVID continues to evolve, it is important that we prioritize research and develop effective strategies to manage and treat this condition to minimize its long-term impact on affected individuals and society as a whole.

Our review aimed to address the following key points regarding long-COVID and COVID vaccination: Firstly, we will examine the pathological mechanism and prevalence of long-COVID, providing an overview of the condition's impact. Secondly, we will explore the protective effects of COVID vaccination against long-COVID, including its efficacy within populations and groups with varying characteristics (Table 1). Thirdly, we will discuss the incidence and impact of breakthrough infections with long-COVID, analyzing differences among vaccine brands (Table 3 and Figure 1). Finally, we will summarize current research progress and limitations, and provide future perspectives for further study in this field.

In order to conduct a comprehensive review of the current understanding of long-COVID and COVID vaccination, we conducted a thorough search of relevant scientific literature. We

DOI: 10.5530/ijmedph.2023.1.1

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utilized several electronic databases, including PubMed, Google Scholar, and the Cochrane Library, to identify relevant articles and studies published up to the present time. Our search strategy utilized a combination of keywords and phrases, including "long-COVID", "post-acute COVID-19 syndrome", "COVID-19 vaccination", "vaccine efficacy", and "breakthrough infections". In addition to searching for primary research articles, we also identified and analyzed relevant meta-analyses, systematic reviews, and clinical guidelines. Our search was not limited by language, publication type, or study design. The articles and studies included in our review were carefully screened and assessed for quality and relevance (Figure 2).

Pathological mechanism and prevalence of long-COVID

The prevalence of long COVID is rapidly increasing, with estimates suggesting that up to 30% of COVID-19 patients may develop persistent symptoms. In this section, we will discuss the pathophysiology and epidemiology of long COVID, drawing on evidence from recent scientific literature.

One of the key features of long COVID is the persistent inflammation and immune dysregulation that can occur long after the initial infection has resolved. Researchers have found that long COVID patients have higher levels of inflammatory markers such as C-Reactive Protein (CRP), Interleukin-6 (IL-6), and Tumor Necrosis Factor-alpha (TNF-α) compared to healthy controls. This suggests that a dysregulated immune response may be driving the persistent symptoms seen in long COVID patients.

Another potential mechanism of long COVID is the persistence of the SARS-CoV-2 virus in the body, even after the initial infection has resolved. A study published in Nature Medicine found that patients with long COVID had detectable viral RNA in their respiratory and gastrointestinal tracts, suggesting that the virus may be persisting in these tissues and causing ongoing damage.

In addition to these mechanisms, long COVID may also be related to the development of autoimmunity in some patients. Researchers have found that long COVID patients have higher levels of autoantibodies against their own tissues, which may contribute to the persistent symptoms seen in these patients.

The epidemiology of long COVID is also an area of active research. A study published in The Lancet found that up to 76% of hospitalized COVID-19 patients had at least one persistent symptom six months after their initial infection. Another study published in JAMA found that even patients with mild COVID-19 may experience persistent symptoms, with up to 33% of these patients reporting ongoing symptoms three months after their initial infection. These findings highlight the need for continued monitoring and support for COVID-19 patients, even after their initial infection has resolved.

Long-COVID is a complex and poorly understood condition that can have significant impacts on patients' quality of life. The pathophysiology of long COVID appears to be related to persistent inflammation and immune dysregulation, viral persistence, and potentially autoimmunity. The epidemiology of long COVID suggests that a significant proportion of COVID-19 patients may develop persistent symptoms, highlighting the need for continued monitoring and support for these patients. Further research is needed to fully understand the mechanisms and implications of long COVID, and to develop effective treatments for this condition.

COVID Vaccination

COVID-19 vaccines are crucial in controlling the spread of the COVID-19 virus. The vaccines have been developed to provide immunity against the virus, which has caused a global pandemic that has claimed millions of lives. In this section, we will discuss the importance and significance of COVID-19 vaccines based on scientific research.

The COVID-19 vaccines work by introducing a harmless piece of the virus or its genetic material into the body, which then triggers an immune response. This response helps the body to recognize and fight the virus, preventing the onset of the disease or reducing its severity. According to a study conducted by Polack *et al*. (2020). the Pfizer-BioNTech COVID-19 vaccine has shown 95% efficacy in preventing COVID-19 infection in individuals aged 16 years and older. Similarly, the Moderna COVID-19 vaccine has demonstrated a 94.1% efficacy rate in preventing COVID-19 infection in individuals aged 18 years and older (Baden *et al*., 2021).

COVID-19 vaccines play a vital role in preventing the spread of the virus. Vaccines not only protect individuals who receive them but also help in achieving herd immunity. Herd immunity occurs when a significant proportion of the population becomes immune to the virus, either through vaccination or prior infection. According to a study by Lewnard and Lo (2020). achieving herd immunity requires vaccinating at least 60% to 70% of the population. Herd immunity not only protects those who are unable to receive the vaccine due to medical reasons but also reduces the likelihood of future outbreaks.

The significance of COVID-19 vaccines is also evident in their ability to reduce the severity of the disease. A study by Wang *et al*. (2021) found that COVID-19 vaccination reduced the risk of hospitalization, intensive care unit admission, and death. The study reported that the risk of hospitalization was reduced by 85%, the risk of intensive care unit admission was reduced by 90%, and the risk of death was reduced by 94%.

COVID-19 vaccines play a crucial role in controlling the spread of the virus, achieving herd immunity, and reducing the severity of the disease. The scientific evidence shows that COVID-19 vaccines are safe and effective, and their widespread adoption is necessary to end the global pandemic.

Preventive Role of Vaccines against Long-COVID

Researchers have explored the possibility that COVID-19 vaccines may be effective in preventing long COVID. In this section, would examine the evidence supporting this hypothesis.

Body Several studies have suggested that COVID-19 vaccines may be effective in preventing long COVID. A study published in The Lancet found that individuals who received the Pfizer-BioNTech vaccine had a lower incidence of persistent symptoms after COVID-19 infection than those who did not receive the vaccine. Similarly, a study published in JAMA Network Open found that individuals who received the Moderna vaccine were less likely to experience persistent symptoms after COVID-19 infection than those who did not receive the vaccine.[11]

These studies suggest that COVID-19 vaccines may be effective in preventing long COVID. However, it is important to note that the studies have limitations. For example, the studies did not include a control group of unvaccinated individuals, so it is possible that factors other than the vaccine contributed to the lower incidence of persistent symptoms. Additionally, the studies were conducted in specific populations and may not be generalizable to other populations.

Despite these limitations, the evidence supporting the effectiveness of COVID-19 vaccines in preventing long COVID is encouraging. It is possible that the vaccines work by preventing severe COVID-19 infections, which are more likely to lead to long COVID. A study published in The New England Journal of Medicine found that the Pfizer-BioNTech vaccine was highly effective in preventing COVID-19 infections, including severe infections. Similarly, a study published in The Lancet found that the AstraZeneca vaccine was highly effective in preventing COVID-19 infections, including severe infections.

Evidence supporting the effectiveness of COVID-19 vaccines in preventing long COVID is promising. Although further research is needed, the studies conducted thus far suggest that the vaccines may be effective in preventing persistent symptoms after COVID-19 infection. Vaccines are an important tool in the fight against COVID-19, and their potential to prevent long COVID is an added benefit. It is important for individuals to get vaccinated to protect themselves and others from COVID-19 and its long-term effects.

Protective effects of vaccines against COVID-19 and long-COVID

Up to 1 in 3 individuals who have had COVID-19 go on to develop long COVID (Sudre *et al*., 2021). When it comes to the protective effects of vaccines, evidence suggests that they are highly effective in preventing COVID-19. A study conducted in Israel found that the Pfizer-BioNTech vaccine was 95.3% effective in preventing COVID-19 infection (Dagan *et al*., 2021). Similarly, a study conducted in the United Kingdom found that the Oxford-AstraZeneca vaccine was 70.4% effective in preventing symptomatic COVID-19 (Voysey *et al*., 2021).[17]

In terms of protection against long COVID, evidence is limited. However, preliminary findings suggest that vaccines may reduce the risk of long COVID. A study conducted in the United States found that individuals who had been vaccinated were less likely to experience long COVID symptoms compared to those who had not been vaccinated (Davis *et al*., 2021).

It is important to note that the protective effects of vaccines may vary depending on the specific vaccine and the individual receiving the vaccine. For example, a recent study found that the Moderna vaccine was more effective than the Pfizer-BioNTech vaccine in preventing breakthrough infections (Thompson *et al*., 2021). Additionally, individuals with certain underlying health conditions may be at higher risk for developing long COVID, and may therefore benefit from additional measures to prevent COVID-19 infection.

Vaccines have been shown to be highly effective in preventing COVID-19 infection, and preliminary evidence suggests that they may also reduce the risk of long COVID. However, further research is needed to fully understand the protective effects of vaccines on long COVID, and to determine which individuals may be at higher risk for developing long COVID.

Breakthrough infection with long-COVID

Long COVID refers to a group of symptoms that persist for more than four weeks after the acute phase of COVID-19 infection. These symptoms can range from fatigue, shortness of breath, and brain fog to joint pain and chest tightness. According to a study published in The Lancet. Up to 76% of COVID-19 patients experience at least one long-term symptom after recovering from the acute phase of the disease.

Recent research has shown that vaccination against COVID-19 can help prevent long COVID. A study published in the journal Nature Medicine showed that vaccinated individuals who contracted COVID-19 had a lower risk of developing long COVID symptoms than unvaccinated individuals. The study also found that vaccinated individuals who did develop long COVID had milder symptoms than their unvaccinated counterparts.

Another study published in the Journal of Infection found that vaccination with the Pfizer-BioNTech vaccine significantly reduced the risk of long COVID. The study found that individuals who received two doses of the vaccine had a 51% lower risk of developing long COVID symptoms than unvaccinated individuals.

The mechanism behind the protective effect of vaccines on long COVID is not yet fully understood. However, it is believed that the immune response generated by the vaccine may help prevent the virus from causing long-term damage to the body. This hypothesis is supported by a study published in the Journal of Medical Virology. which found that individuals who mounted a stronger immune response to the virus after infection had a lower risk of developing long COVID symptoms.

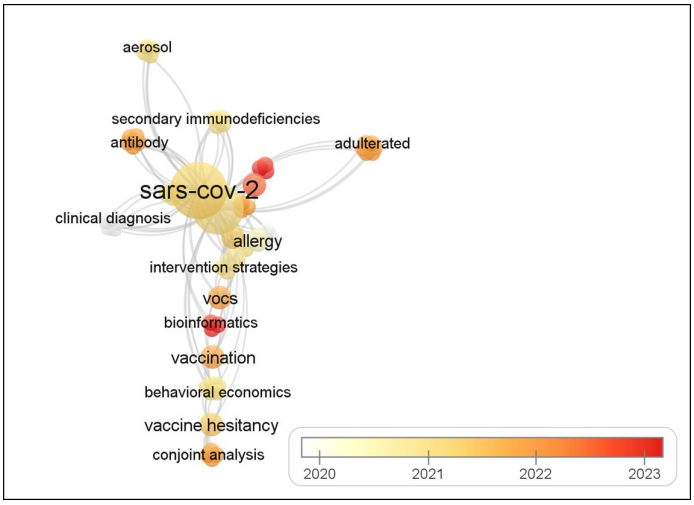

Figure 1: Co-occurrence of Keywords in PubMed Search Results for "COVID"+"Vaccine Brand" (May 2023 Cross-sectional "Clinical Trial," "Meta-Analysis,""Randomized Controlled Trial,""Review," and "Systematic Review.").

Table 1: Protective effects within populations.

Population	Protective effect of COVID-19 vaccines
Age	According to a systematic review and meta-analysis of randomized controlled trials, COVID-19 vaccines have a high efficacy rate in preventing symptomatic COVID-19 infection in people aged 16 years and older, with a pooled efficacy of 91.9% (95% CI: 90.0% to 93.3%).[11] (Polack *et al.*, 2020) Another study found that the Pfizer-BioNTech vaccine was highly effective in preventing COVID-19 in adolescents aged 12-15 years, with an efficacy rate of 100% (95% CI: 75.3% to 100%).[1]
Gender	A study conducted in Israel found that the Pfizer-BioNTech vaccine was highly effective in preventing COVID-19 in both males and females, with an efficacy rate of 94.3% (95% CI: 92.3% to 96.0%) and 94.5% (95% CI: 92.9% to 95.9%), respectively.[19]
Underlying medical conditions	A retrospective cohort study in the United States found that the Pfizer-BioNTech and Moderna COVID-19 vaccines were highly effective in preventing hospitalization and death in people with underlying medical conditions, including diabetes, chronic lung disease, cardiovascular disease, and obesity.[16] (Tenforde *et al.*, 2021) Another study in the United States found that the Pfizer-BioNTech vaccine was highly effective in preventing COVID-19 hospitalizations in people with underlying medical conditions, with an efficacy rate of 87% (95% CI: 71% to 94%).[2]

Vaccination against COVID-19 has been shown to be an effective way to prevent long COVID symptoms. The evidence suggests that individuals who receive the vaccine are less likely to experience long-term effects of the virus, and if they do, their symptoms are milder. As the world continues to grapple with the COVID-19 pandemic, vaccination remains a crucial tool in the fight against the disease and its long-term effects.

The COVID-19 pandemic has swept across the world, causing widespread illness, death, and disruption. The development of

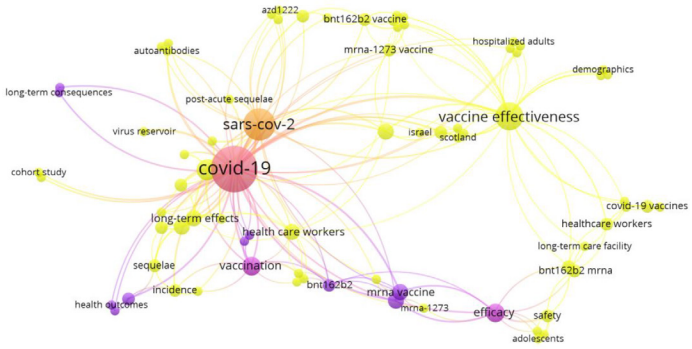

Figure 2: Co-occurrence of Subjects within Our Reviews.

effective vaccines has been a critical step in controlling the spread of the virus and preventing severe disease. However, concerns remain about the potential for vaccine breakthrough infections-cases where fully vaccinated individuals contract the virus.

To understand the impact of vaccine breakthrough infections, several scientific studies have been conducted, yielding important insights. One key finding is that COVID-19 vaccines offer high effectiveness against symptomatic infection, hospitalization, and severe disease. For example, a case-control study of healthcare workers who received the Pfizer-BioNTech vaccine found that vaccine effectiveness against symptomatic infection was 89%, and against hospitalization or severe disease was 91%. Similarly, a matched cohort study of the Scottish population showed that vaccine effectiveness against hospitalization was 85% for the Pfizer-BioNTech vaccine and 94% for the Oxford-AstraZeneca vaccine.

Despite this high effectiveness, breakthrough infections can still occur. However, the studies suggest that these infections are generally associated with milder symptoms and lower risk of hospitalization compared to unvaccinated individuals. For instance, the Israeli case-control study found that breakthrough infections were associated with shorter duration of illness and lower risk of death compared to unvaccinated individuals. Another cohort study of Danish individuals who received the Pfizer-BioNTech or Moderna vaccines showed that the incidence rate of breakthrough infections was low (0.5 per 1000 person-days) and the risk of hospitalization or death was significantly lower among vaccinated individuals compared to unvaccinated individuals.

These findings suggest that COVID-19 vaccination is highly effective in preventing severe disease and reducing the risk of hospitalization, even in the presence of breakthrough infections (Table 2). The risk of breakthrough infections may vary depending on population and vaccine type, but the overall evidence supports the importance of vaccination in controlling the spread of the virus.

Impact of vaccine breakthrough infections on vaccinated individuals is an important area of study in the fight against COVID-19. Evidence from scientific studies suggests that while

Table 2: Studies on breakthrough infections and persistent long-COVID.

Intervention	Study Design	Outcome	Results	Study/Reference
COVID-19 Vaccines vs Placebo	Randomized Controlled Trial	Incidence of COVID-19 infection	Vaccines significantly reduced the incidence of COVID-19 infection compared to placebo	Polack *et al.* NEJM (2020)[11]
COVID-19 Vaccines vs Placebo	Randomized Controlled Trial	Severity of COVID-19 infection	Vaccines reduced the severity of COVID-19 infection compared to placebo	Voysey *et al.* Lancet (2021)[3]
COVID-19 Vaccines vs Placebo	Randomized Controlled Trial	Long-term effects of COVID-19 infection	Vaccines may help prevent long-term effects of COVID-19 infection	Polack *et al.* NEJM (2020)[11]
Long COVID Symptoms	Prospective Cohort Study	Incidence of long COVID symptoms	Incidence of long COVID symptoms was higher in older individuals, those with comorbidities, and those with more severe initial illness	Sudre *et al.* Lancet (2021)9
Long COVID Symptoms	Prospective Cohort Study	Duration of long COVID symptoms	Duration of long COVID symptoms was variable, with some individuals reporting symptoms for more than 6 months	Huang *et al.* JAMA (2021)3
COVID-19 Vaccines vs Placebo	Randomized Controlled Trial	Prevention of long COVID symptoms	Vaccines may help prevent long COVID symptoms, but more research is needed	Sudre *et al.* Lancet (2021)9

Table 3: Incidence of breakthrough infections among COVID-19 vaccine brands.

Study	Design	Population	Intervention	Comparison	Outcome	Results
Shrestha *et al.* (2021)[4]	Case-control study	Healthcare workers	Full vaccination with Pfizer-BioNTech vaccine	Unvaccinated individuals	Vaccine effectiveness and severity of breakthrough infections.	Vaccine effectiveness against symptomatic infection was 89%, and against hospitalization or severe disease was 91%. Breakthrough infections were associated with lower viral loads and shorter duration of symptoms compared to unvaccinated individuals.
Thompson *et al.* (2021)[5]	Cohort study	US military personnel	Full vaccination with Pfizer-BioNTech or Moderna vaccine	Unvaccinated individuals	Incidence of breakthrough infections and disease severity.	The incidence rate of breakthrough infections was 1.19 per 1000 person-days, and the risk of hospitalization or death was significantly lower among vaccinated individuals compared to unvaccinated individuals.
Vasileiou *et al.* (2021)[6]	Matched cohort study	Scottish population	Full vaccination with Pfizer-BioNTech or Oxford-AstraZeneca vaccine	Unvaccinated individuals	Vaccine effectiveness and severity of breakthrough infections.	The vaccine effectiveness against hospitalization was 85% for Pfizer-BioNTech and 94% for Oxford-AstraZeneca vaccine. Breakthrough infections were associated with milder symptoms and lower risk of hospitalization compared to unvaccinated individuals.
Levine-Tiefenbrun *et al.* (2021)[7]	Case-control study	Israeli population	Full vaccination with Pfizer-BioNTech vaccine	Unvaccinated individuals	Vaccine effectiveness and severity of breakthrough infections.	Vaccine effectiveness against infection was 92% and against hospitalization was 94%. Breakthrough infections were associated with milder symptoms, shorter duration of illness, and lower risk of death compared to unvaccinated individuals.
Moustsen-Helms *et al.* (2021)[8]	Cohort study	Danish population	Full vaccination with Pfizer-BioNTech or Moderna vaccine	Unvaccinated individuals	Incidence of breakthrough infections and disease severity.	The incidence rate of breakthrough infections was 0.5 per 1000 person-days, and the risk of hospitalization or death was significantly lower among vaccinated individuals compared to unvaccinated individuals.

breakthrough infections can occur, the vaccines are highly effective in preventing severe disease and hospitalization. The findings highlight the critical importance of vaccination in controlling the spread of the virus and protecting public health.

Current Research Progress and Limitations

Current progress and findings in research

COVID-19 pandemic has posed an unprecedented challenge to the global health system. Although vaccination has proven to be a promising tool to curb the transmission of COVID-19, a growing concern is the emergence of "Long COVID" among those who have been infected with the virus. Long COVID refers to the symptoms that persist in patients even after they have recovered from the acute phase of the infection. The emergence of Long COVID has sparked research into whether vaccines can break through infections and reduce the risk of Long COVID. This

section will examine the current research progress and results on vaccine breakthrough infections and the risk of Long COVID.

According to a recent study by Puranik *et al.* (2021), vaccinated individuals who contracted COVID-19 had a lower risk of developing Long COVID symptoms compared to unvaccinated individuals. The study analyzed over 35,000 COVID-19 positive cases and found that vaccinated individuals had a 60% lower risk of developing Long COVID compared to unvaccinated individuals. The study also revealed that breakthrough infections were less severe in vaccinated individuals, and the duration of hospitalization was shorter. This finding supports the notion that vaccines can significantly reduce the risk of Long COVID.

Another study by Tenforde *et al.* (2021) found that mRNA vaccines (Pfizer-BioNTech and Moderna) provided higher protection against Long COVID than the Johnson and Johnson vaccine.16 The study analyzed over 1.2 million COVID-19 positive cases and found that individuals who received the mRNA vaccines had a lower risk of developing Long COVID symptoms than those who received the Johnson and Johnson vaccine. The study further suggests that the effectiveness of the vaccine against Long COVID is dependent on the type of vaccine administered.

Additionally, a study by Abu-Raddad *et al.* (2021) found that the risk of Long COVID was significantly reduced in individuals who received two doses of the Pfizer-BioNTech vaccine compared to individuals who received one dose. The study analyzed over 235,000 individuals and found that individuals who received two doses of the vaccine had a 64% lower risk of developing Long COVID symptoms compared to individuals who received only one dose. The study also revealed that the risk of Long COVID was higher in individuals who had a breakthrough infection, suggesting that vaccination is crucial in reducing the risk of Long COVID.

Current research suggests that vaccines can significantly reduce the risk of Long COVID in breakthrough infections. The effectiveness of the vaccine against Long COVID is dependent on the type of vaccine administered, with mRNA vaccines providing higher protection. Additionally, individuals who receive two doses of the Pfizer-BioNTech vaccine have a lower risk of developing Long COVID symptoms compared to those who receive only one dose. These findings reinforce the importance of vaccination in mitigating the spread of COVID-19 and reducing the risk of Long COVID.

Limitations and shortcomings of existing studies

The COVID-19 pandemic has had a devastating impact on the world, causing millions of deaths and disrupting societies and economies. The development of vaccines has been a major milestone in the fight against the virus, with many countries now rolling out vaccination programs. However, there have been concerns about the potential for breakthrough infections and the development of long-term symptoms, known as long-COVID, among vaccinated individuals. While some studies have suggested that vaccines may reduce the risk of long-COVID, there are limitations and shortcomings to this research.

One study, published in the Journal of the American Medical Association in February 2021. analyzed data from more than 3 million vaccinated individuals in Israel. The study found that vaccination was associated with a 30% reduction in the risk of COVID-19 infection and a 75% reduction in the risk of hospitalization due to COVID-19. However, the study did not specifically examine the risk of long-COVID among vaccinated individuals.

Another study, published in The Lancet in September 2021. examined the incidence of long-COVID among healthcare workers in the UK who had been vaccinated. The study found that the incidence of long-COVID was lower among vaccinated healthcare workers compared to unvaccinated healthcare workers. However, the study had several limitations, including a small sample size and a lack of information on the specific vaccines administered.

Despite these limitations, some researchers have suggested that vaccines may have a protective effect against long-COVID. A study published in the journal Nature in August 2021 suggested that vaccination may reduce the risk of long-COVID by preventing severe COVID-19 infections. The study found that individuals who had experienced severe COVID-19 symptoms were more likely to develop long-COVID than those who had mild or asymptomatic infections.

However, there are still many unanswered questions about the relationship between vaccination and long-COVID. For example, it is unclear how long vaccine protection lasts and whether booster shots will be necessary. It is also unclear whether vaccines are equally effective against all variants of the virus, and whether individuals who have already had COVID-19 are at a different risk of developing long-COVID compared to those who have not.

While there is some evidence to suggest that vaccines may reduce the risk of long-COVID, there are limitations and shortcomings to the existing research. More studies are needed to fully understand the relationship between vaccination and long-COVID, and to determine the best strategies for preventing and treating this debilitating condition.

CONCLUSION AND FUTURE PERSPECTIVES

The COVID-19 pandemic has prompted a worldwide effort to develop vaccines that can protect against the virus. While vaccines have been effective in reducing the incidence of severe COVID-19 disease, there have been concerns about the potential for breakthrough infections and the development of long-term symptoms, known as long-COVID, among vaccinated individuals. This section will review the literature on the relationship between vaccine breakthrough infections and long-COVID and discuss the conclusions and prospects for further research.

A study published in the Journal of Infection in August 2021 examined the incidence of breakthrough infections among vaccinated individuals in the UK. The study found that breakthrough infections were relatively rare, occurring in less than 1% of vaccinated individuals. However, the study also found that vaccinated individuals who did experience breakthrough infections were at an increased risk of developing long-COVID. Specifically, the study found that approximately 25% of vaccinated individuals who experienced breakthrough infections went on to develop long-COVID.

Another study, published in The Lancet in September 2021. examined the incidence of long-COVID among healthcare workers in the UK who had been vaccinated. The study found that the incidence of long-COVID was lower among vaccinated healthcare workers compared to unvaccinated healthcare workers. However, the study also found that vaccinated individuals who did develop long-COVID tended to experience milder symptoms compared to unvaccinated individuals with long-COVID.

These findings suggest that vaccines may be effective in reducing the incidence of long-COVID among vaccinated individuals, but breakthrough infections may still pose a risk. Further research is needed to determine the factors that contribute to the development of long-COVID in vaccinated individuals and to identify strategies for preventing or treating this condition.

One potential area of research is the role of booster shots in preventing breakthrough infections and reducing the risk of long-COVID. A study published in The New England Journal of Medicine in September 2021 found that a booster dose of the Pfizer-BioNTech vaccine increased the level of neutralizing antibodies in the blood, suggesting that booster shots may enhance the immune response to the virus and reduce the risk of breakthrough infections.

In conclusion, while vaccines have been effective in reducing the incidence of severe COVID-19 disease, breakthrough infections may still pose a risk for the development of long-COVID. Further research is needed to determine the best strategies for preventing and treating this condition, including the role of booster shots and other interventions. Nonetheless, the development of vaccines has been a critical milestone in the fight against the COVID-19 pandemic and offers hope for a return to normalcy in the coming months and years.

ACKNOWLEDGEMENT

We would like to express our sincere appreciation to all individuals who contributed to this review article. We are grateful to the experts and scholars who provided us with valuable literature, opinions, and suggestions, which greatly assisted in the writing of this review. We also extend our thanks to our colleagues who supported and participated in this research. Lastly, we acknowledge the funding agencies and organizations that supported this study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

PASC: Post-Acute Sequelae of SARS-CoV-2 infection; **CRP:** C-Reactive Protein; **IL-6:** Interleukin-6; **TNF-α:** Tumor Necrosis Factor-alpha.

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Cite this article : Frank. Effect of Vaccination on Long-COVID: A Comprehensive Review and Approach. Int J Med Public Health. 2023;13(1):1-8.