How Effective are Vaccines in Preventing Long Covid After Infection? Living Evidence Synthesis (January 15, 2025)

What questions did we want to answer?

 How effective are COVID-19 vaccines in preventing <u>Long Covid</u> outcomes caused by variants of concern? How does this vary based on (1) the number of doses received; and (2) type of <u>Variant of Concern</u> (VOC)?

Why is it important to summarize all the evidence on this?

- According to the World Health Organization, around 10 to 20 percent of individuals who contract COVID-19 may experience long-term symptoms.
- We need to gather this evidence so that people can make informed decisions about vaccination.

How have we done this living evidence synthesis?

- A living evidence synthesis is a summary of research on a topic that is regularly updated as new studies come out.
- We identified published literature by searching various electronic databases (e.g., MEDLINE, Cochrane) and preprints through COVID-19 Evidence Alerts from McMaster PLUSTM.
- We compared the likelihood of developing Long Covid among vaccinated people who have been infected vs. unvaccinated people who have been infected.
- We evaluated the studies carefully and assessed the level of certainty of the evidence as low, moderate, or high certainty evidence.
- In this report, we included multiple analyses from 10 studies that examined Long Covid outcomes, of which nine were published and one was a preprint.
- Combined estimates across brands are shown in Table 1. Brand-specific estimates are presented in Table 2 when available.
 - Underlined terms are defined on page 3







Table 1. Vaccine Effectiveness in Preventing Long Covid				
Outcomes				
Developing Long Covid Outcome such as:	<u>Comparators</u>	Vaccine effectiveness (%) (Results here represent estimates measured 3 to 24 months since infection)		
Overall Long Covid	Primary series vs Unvaccinated	Combined estimate from eighteen <u>analyses</u> showed that the primary series was 26% less likely than unvaccinated (this ranged from the primary series being 55% less likely to the unvaccinated being 17% less likely).		
	Booster dose(s) vs Unvaccinated	Combined estimate from eight analyses showed that booster dose(s) were 36% less likely than unvaccinated (this ranged from the primary series being 95% less likely to the unvaccinated being 84% less likely).		
Cardiovascular conditions	Primary series vs Unvaccinated	Combined estimate from eighteen analyses showed that the primary series was 14% less likely than unvaccinated (this ranged from the primary series being 95% less likely to the unvaccinated being 7% less likely).		
Respiratory functioning, symptoms, and conditions	Primary series vs Unvaccinated	Combined estimate from twelve analyses showed that the primary series was 43% less likely than unvaccinated (this ranged from the primary series being 11% to 66% less likely than unvaccinated).		

Table 1 continues to the next page.

What are the main results?

 When we combine all the estimates in the studies, they indicate that compared to unvaccinated individuals, those who received the primary dose series were up to 43% less likely, and those who received booster dose(s) were up to 64% less likely, to develop Long Covid outcomes. These outcomes include cardiovascular issues, respiratory problems, fatigue, pain, nervous system dysfunction, cognitive impairment (for example, memory loss, trouble concentrating or completing tasks), and mental health issues.

How confident are we in the results?

- Low Certainty of Evidence: This means our confidence in the study results is low. There are aspects of the studies that lead us to believe the results may not be the same in future studies.
- The results varied widely due to differences across studies in the definition and diagnosis of Long Covid, the symptoms assessed, as well as variations in how the studies were designed and the characteristics of the research participants.

What are the gaps in what we know?

- At this time, there is limited evidence about the effectiveness of the vaccine in preventing Long Covid outcomes from VOC infection.
- To increase confidence in our results, we need higher-certainty evidence.

Table 1, continued.			
Fatigue or exhaustion conditions	Primary series vs Unvaccinated	Combined estimate from four analyses showed that the primary series was 21% less likely than unvaccinated (this ranged from the primary series being 13% to 28% less likely than unvaccinated).	
Pain symptoms and conditions	Primary series vs Unvaccinated	Combined estimate from eight analyses showed that the primary series was 10% less likely than unvaccinated (this ranged from the primary series being 24% less likely to the unvaccinated being 5% less likely).	
Nervous system functioning, symptoms, and conditions	Primary series vs Unvaccinated	Combined estimate from fifteen analyses showed that the primary series was 20% less likely than unvaccinated (this ranged from the primary series being 37% less likely to the unvaccinated being 2% less likely).	
Cognitive functioning, symptoms, and conditions	Primary series vs Unvaccinated	Primary series 13% less likely than unvaccinated.	
Mental functioning, symptoms, and conditions	Primary series vs Unvaccinated	Combined estimate from twelve analyses showed that the primary series was 11% less likely than unvaccinated (this ranged from the primary series being 37% less likely to the unvaccinated being 3% less likely).	

See glossary on page 3 for definition of underlined terms. Combined estimates are bolded.

> For a visual summary of these results, visit: https://www.ksau.ca/ve-voc-long-covid-infographic

Table 2. Vaccine Effectiveness in Preventing Long Covid by VOC		
Developing Long Covid from	Comparators	Vaccine effectiveness (%) (Results here represent estimates measured 3 to 12 months since infection)
Delta	Primary series vs Unvaccinated Booster	Combined estimate from three analyses showed that the primary series was 18% less likely than unvaccinated (this ranged from the primary series being 35% less likely to the unvaccinated being 3% less likely). Booster dose(s) 40% less likely
	dose(s) vs Unvaccinated	than unvaccinated. Unvaccinated 84% less likely than primary series.
Omicron	Primary series vs Unvaccinated	Primary series 18% to 40% less likely than unvaccinated.
	Booster dose(s) vs Unvaccinated	Combined estimate from three analyses showed that booster dose(s) were 51% less likely than unvaccinated (this ranged from the primary series being 28% to 70% less likely than unvaccinated).
Vaccine Effectiveness in Preventing Long Covid by Vaccine Brand		
Vaccine Effect	tiveness in Preve	enting Long Covid by Vaccine Brand
Vaccine Effect Vaccine Type/Brand	tiveness in Preve Comparators	enting Long Covid by Vaccine Brand Vaccine effectiveness (%) (Results here represent estimates measured 3 to 12 months since infection)
Vaccine Effect Vaccine Type/Brand mRNA vaccines (Pfizer, Moderna)	Comparators Primary series vs Unvaccinated	enting Long Covid by Vaccine Brand Vaccine effectiveness (%) (Results here represent estimates measured 3 to 12 months since infection) Combined estimate from ten analyses showed that the primary series was 22% less likely than unvaccinated (this ranged from the primary series being 55% less likely to the unvaccinated being 3% less likely).
Vaccine Effect Vaccine Type/Brand mRNA vaccines (Pfizer, Moderna)	Comparators Comparators Primary series vs Unvaccinated Booster dose(s) vs Unvaccinated	enting Long Covid by Vaccine Brand Vaccine effectiveness (%) (Results here represent estimates measured 3 to 12 months since infection) Combined estimate from ten analyses showed that the primary series was 22% less likely than unvaccinated (this ranged from the primary series being 55% less likely to the unvaccinated being 3% less likely). Combined estimate from three analyses showed that booster dose(s) were 64% less likely than unvaccinated (this ranged from the primary series being 70% less likely to the unvaccinated being 3% less likely).

Definitions of terms

Analysis: In research, an analysis refers to the process of examining data to draw meaningful conclusions. Some studies conduct multiple analyses, whereby researchers look at the same data in different ways to explore various patterns.

Booster doses: Additional doses of a vaccine that are given after the initial primary series to help maintain and extend the protection provided by the vaccine.

Comparators: The different groups or options being compared in a study to see how they affect the outcomes. In this report, we're comparing different numbers of vaccine doses. **Long Covid:** New or persistent symptoms more than 12 weeks after COVID-19 infection. Long Covid is also referred to as Post-COVID Condition (PCC) or Post-Acute Sequelae of SARS-CoV-2 Infection (PASC).

Primary series: Refers to the initial sequence of vaccine doses that are required to provide full protection. Depending on the vaccine, the primary series may consist of one or two doses. **Vaccine Effectiveness:** In this report, vaccine effectiveness is a measure of how well vaccines protect against Long COVID outcomes between fully vaccinated versus unvaccinated and booster versus primary series.

Variant of Concern (VOC): A virus variant that increases disease spread or severity, or decreases the effectiveness of diagnostic tests, vaccines, and therapeutics, compared to previous variants.

Table 2 continues to the next page.

Table	2,	continued.
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Vaccine Effectiveness in Preventing Long Covid in Vaccinated				
Pre-or Post-Infection				
Individuals	Vaccinated	Combined estimate from twenty-		
Vaccinated	(Primary	six analyses showed that		
Pre-	series &	vaccinated were 28% less likely		
Infection	Booster	than unvaccinated (this ranged		
	dose(s) vs	from vaccinated being 95% less		
	Unvaccinated	likely to the unvaccinated being		
		84% less likely).		
Individuals	Vaccinated	Primary series 2% to 7% less likely		
Vaccinated	(Primary	than unvaccinated.		
Post-	series &			
Infection	Booster			
	dose(s) vs			
	Unvaccinated			

See glossary on page 3 for definition of underlined terms. Combined estimates are bolded.

Citation

Dahroug, L., Shaver, N., Katz, M., Asamoah, G. D., McGuire, M., Linkins, L. A., Abdelkader, W., Bennett, A., Hughes, S. E., Smith, M., Begin, M., Coyle, D., Piggott, T., Kagina, B., Welch, V., Colijn, C., Earn, D., El Emam, K., Heffernan, J., O'Brien, S., Wilson, K., Collins, E., Navarro, T., Beyene, J., Boutron, I., Bowdish, D., Cooper, C., Costa, A., Curran, J., Griffith, L., Hsu, A., Grimshaw, J., Langlois, M. A., Li, X., Pham-Huy, A., Raina, P., Rubini, M., Thabane, L., Wang, H., Xu, L., Brouwers, M., Horsley, T., Lavis, J., Iorio, A., Little, J. Living evidence synthesis on variants of concern and COVID-19 vaccine effectiveness.

What are the main takeaways from citizen partners?

- Although evidence about the effectiveness of primary and booster dose(s) is constantly being updated with new findings, to date, there is some evidence that they can be effective in preventing Long Covid.
- People who are vaccinated and develop Long Covid might have fewer or less severe symptoms compared to those who are unvaccinated. The vaccine can be more effective at protecting people from certain symptoms than others.

If you're interested in learning more about vaccine effectiveness against specific Long Covid symptoms, read the full report here: <u>https://osf.io/yuh3d</u>

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