COVID-19 vaccination before infection strongly linked to reduced risk of developing long COVID

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Receiving at least one dose of a COVID-19 vaccine before the first infection is strongly associated with a reduced risk of developing post-

COVID-19 condition, commonly known as long COVID, finds a study published by *The BMJ* today (Nov. 22).

The findings, based on data for more than half a million Swedish adults, show that unvaccinated individuals were almost four times as likely to be diagnosed with long COVID than those who were vaccinated before first infection.

The researchers stress that causality cannot be directly inferred from this observational evidence, but say their results "highlight the importance of primary vaccination against COVID-19 to reduce the burden of post-COVID-19 condition in the population."

The effectiveness of COVID-19 vaccines against SARS-CoV-2 infection and severe complications of acute COVID-19 are already known, but their effectiveness against long COVID is less clear because most previous studies have relied on self-reported symptoms.

To address this, researchers investigated the effectiveness of primary COVID-19 vaccination (the first two doses and the first booster dose within the recommended schedule) against post-COVID-19 conditions using data from the SCIFI-PEARL project, a register-based study of the COVID-19 pandemic in Sweden.

Their findings are based on 589,722 adults (aged 18 and over) from the two largest regions of Sweden with a first COVID-19 infection registered between 27 December 2020 and 9 February 2022.

Individuals were followed from a first COVID-19 infection until a diagnosis of post-COVID-19 condition, vaccination, reinfection, death, emigration or end of follow-up (30 November 2022), whichever came first. The average follow-up was 129 days in the total study population (vaccinated: 197 days, not vaccinated: 112 days).

Individuals who had received at least one COVID-19 vaccine dose before infection were considered vaccinated.

A range of factors including age, sex, existing conditions, number of health care contacts during 2019, education level, employment status, and dominant virus variant at time of infection were also accounted for in the analysis.

Of 299,692 vaccinated individuals with COVID-19, 1,201 (0.4%) were diagnosed with post-COVID-19 condition during follow-up, compared with 4,118 (1.4%) of 290,030 unvaccinated individuals.

Those who received one or more COVID-19 vaccines before the first infection were 58% less likely to receive a diagnosis of post-COVID-19 condition than unvaccinated individuals.

And vaccine effectiveness increased with each successive dose before infection (a dose-response effect). For example, the first dose reduced the risk of post-COVID-19 condition by 21%, two doses by 59%, and three or more doses by 73%.

This is an observational study, which provides less conclusive evidence of causality, and the researchers point to several limitations such as limited data on post-COVID-19 condition symptoms and that the diagnosis code is not yet validated, the potential impact of reinfections on vaccine effectiveness, and expectations about the protective effect of vaccination.

However, this was a large, well-designed study based on high-quality, individual-level registry data with a low risk of self-reporting bias, suggesting that the results are robust.

As such, the authors conclude, "The results from this study highlight the

importance of complete primary vaccination coverage against COVID-19, not only to reduce the risk of severe acute COVID-19 infection but also the burden of post-COVID-19 condition in the population."

These findings, combined with evidence from other studies, highlight the association between the immune system and the development of post-viral conditions, and underline the importance of timely vaccination during pandemics, say researchers in a linked editorial.

They call for continued investigation into the evolution of long-term residual symptoms of COVID-19 and other viral illnesses as well as steps to "improve the accuracy of recording both recovery and continued illness after infection, and in quantifying key family, social, financial, and economic outcomes."

"Such estimates are fundamental to unlocking the funding required for future research and increased investment in specialist clinical services offering treatment and rehabilitation to support patients with post-viral conditions," they conclude.

More information: COVID-19 vaccine effectiveness against post-COVID-19 condition among 589,722 individuals in Sweden: population based cohort study, *The BMJ* (2023). DOI: 10.1136/bmj-2023-076990

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