

COVID-19 Vaccine Effectiveness Against Long Covid

What is Long COVID? Long COVID describes symptoms persisting long after the acute effects of infection with the COVID-19 virus, called SARS-CoV-2, which can affect almost any part of the body and can vary from person to person. The World Health Organization (WHO) defines Long COVID as *the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation*. Long COVID is also known as post-acute sequelae of COVID-19 (PASC) or post-COVID conditions (PCC). Researchers have found that people with Long COVID can experience many different symptoms across multiple parts of the body. The heart, lungs, liver, kidneys, pancreas, spleen, gastrointestinal tract, neurological system, blood system, reproductive system, and immune system have all been reported to be affected in people with Long COVID.¹ Due to this wide range in symptomology, a pathognomonic definition of Long COVID has not been established.

Millions of people experience symptoms of Long COVID globally. Estimates of the incidence of Long COVID among persons infected with SARS-CoV-2 range widely due to differences in the definition and study design used, and the population studied. Around 10-20% of persons infected with SARS-CoV-2 will go on to develop symptoms that can be defined as Long COVID, although some estimates are higher.¹⁻³ The lower estimate would mean that some 77 million people around the world have experienced Long COVID given that 767 million SARS-CoV-2 infections have been documented globally up until July 2023.⁴ As many as 50-70% of hospitalized cases can go on to develop Long COVID, but many of the persisting medical problems are comparable to those following hospitalizations with influenza and sepsis. This suggests that a high proportion of the lasting symptoms may be due to the severity of the infection rather than being infected with SARS-CoV-2 specifically. There are, however, additional health risks with severe COVID-19 disease: [a study](#) by the United States Department of Veterans Affairs found that the risk of death after the first 30 days of illness among people hospitalized with COVID-19 was 1.5 times higher than that of people hospitalized with influenza. Hospitalized COVID-19 patients are also much more likely to experience neurological, mental health, metabolic, cardiovascular, gastrointestinal, and coagulation disorders, such as pulmonary embolisms. [Another US study](#) found that the risk of venous thromboembolic disease was 1.8 times higher in people with COVID-19 than for those with influenza.

Long COVID is difficult to study. Because some Long COVID symptoms – such as headache, fatigue, dizziness, heart palpitations - are common in non-COVID patients, it can be difficult to know if they are due to Long COVID or to another condition. Researchers have used people without SARS-CoV-2 infection as a control group to understand which symptoms are likely to be due to Long COVID. For example, a large US study of 10,000 people found that 12 symptoms most distinguished those with Long COVID from those without: malaise after exertion or exercise, fatigue, brain fog, dizziness, gastrointestinal symptoms, heart palpitations, issues with sexual desire or capacity, loss of smell or taste, thirst, chronic

¹ Davis HE, McCorkell L, Vogel JM, et al. Long COVID: major findings, mechanisms and recommendations. *Nat Rev Microbiol* 21, 133–146 (2023). doi: 10.1038/s41579-023-00896-0.

² National Center for Health Statistics. U.S. Census Bureau, Household Pulse Survey, 2022–2023. Long COVID. Generated interactively: from <https://www.cdc.gov/nchs/covid19/pulse/Long-covid.htm>.

³ Thaweethai T, Jolley SE, Karlson EW, et al. Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection. *JAMA*. 2023;329(22):1934–1946. doi:10.1001/jama.2023.8823

⁴ WHO: <https://covid19.who.int/>

cough, chest pain, and abnormal movements.² Despite the challenges in studying Long COVID, it is clear that Long COVID is a substantial public health issue, and reducing the prevalence and duration of Long COVID are important public health goals.

Vaccination prior to SARS-CoV-2 infection provides protection against Long COVID. Several studies provide evidence that COVID-19 vaccination prior to infection can help prevent or reduce the symptoms of Long COVID. A [systematic review](#) of studies conducted before the emergence of the Omicron variant found that while a primary vaccination series plus a booster dose prevents Long COVID a single dose does not. Most (6 of 8) studies that examined the impact of a complete primary series of a COVID-19 vaccine on Long COVID found reductions in Long COVID of between 22% and 75%. A single study evaluated a third dose and reported an even greater reduction of 84% (95% CI: 15-97%). Vaccination *after* infection may also reduce the subsequent risk of Long COVID, but studies have so far been inconsistent and too small to detect an effect.

The few studies to evaluate the protection provided by vaccines against Long COVID following an infection with the Omicron variant also suggest that vaccination is beneficial. [A study](#) in Switzerland found that people who completed a primary series or booster vaccination before being infected were 46% less likely to experience Long COVID symptoms compared to those who were unvaccinated or partially vaccinated (i.e., received just 1 dose of a 2-dose vaccine course). [A study](#) in the United States found that people who completed the primary vaccination series and then were infected with SARS-CoV-2 when Omicron or Delta variants were common were 33% (95% CI: 21-44%) less likely to experience symptoms of Long COVID compared to unvaccinated persons.

Studies so far provide encouraging evidence that COVID-19 vaccination prior to infection reduces the risk of acquiring Long COVID, but many questions remain. The most important gap in our knowledge is the exact cause(s) of Long COVID. Theories include that it is due to lingering SARS-CoV-2 virus, reactivation of non-SARS-CoV-2 dormant viruses, tiny blood clots that prevent the movement of oxygen throughout the body, and immune system dysregulation. Questions also remain about the role of reinfection and whether certain populations are more vulnerable, and whether Long COVID is less severe and less common in those infected with Omicron compared to earlier variants.⁵ Addressing these knowledge gaps could help to improve diagnosis, identify effective treatments, and understand how vaccines might prevent Long COVID. Regarding the preventive effect of vaccines for Long COVID, we don't know if this effect differs by the type of vaccine (e.g., vaccine that target specific variants such as bivalent Omicron vaccines) or by the number of doses or the time since last dose (i.e., waning protection). The impact of vaccination *after* infection in reducing symptoms of Long COVID is also not well understood. Nevertheless, the evidence to date suggests that vaccination against COVID-19 prior to infection does prevent and/or reduce the severity or number of symptoms of Long COVID. Improving vaccine coverage in populations yet to be fully immunized could therefore substantially reduce the impact of Long COVID on public health systems globally.

⁵ Thaweethai T, Jolley SE, Karlson EW, et al. Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection. *JAMA*. 2023;329(22):1934–1946. doi:10.1001/jama.2023.8823