

Overview of Long-COVID Studies From November 2022 to April 2023

This document provides an overview of relevant research studies the COVID Patient Alliance has identified as part of our daily intel scans. While this document is a high-level overview, we publish our monthly trackers to the website, [linked here](#), which include more detailed information and additional studies that may be of interest. Further, the Appendix D of the [National Research Action Plan](#) lists ongoing studies various government agencies are undertaking and which topics they are researching.

Prevalence				
Date	Article	Publication	Author	Key Takeaways
4/16/2023	Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review - PMC (nih.gov)	Journal of Infectious Diseases	Chen C. et al	A meta-analysis 41 studies found that the global estimated pooled prevalence of post “COVID-19 condition was 0.43 (95% CI: 0.39,0.46). Hospitalized and non-hospitalized patients have estimates of 0.54 (95% CI: 0.44,0.63) and 0.34 (95% CI: 0.25,0.46), respectively. Regional prevalence estimates were Asia— 0.51 (95% CI: 0.37,0.65), Europe— 0.44 (95% CI: 0.32,0.56), and North America— 0.31 (95% CI: 0.21,0.43) . Global prevalence for 30, 60, 90, and 120 days after infection were estimated to be 0.37 (95% CI: 0.26,0.49), 0.25 (95% CI: 0.15,0.38), 0.32 (95% CI: 0.14,0.57) and 0.49 (95% CI: 0.40,0.59), respectively. Fatigue was the most common symptom reported with a prevalence of 0.23 (95% CI: 0.17,0.30), followed by memory problems (0.14 [95% CI: 0.10,0.19]).” It was also concluded that long COVID will have prolong stressful effects on the healthcare system globally.
3/7/2023	Prevalence and risk factor for long COVID in children and adolescents: A meta-analysis and systematic review - PubMed (nih.gov)	Journal of Infection and Public Health	Zheng Y. et al	A meta-analysis found that among children the estimated prevalence point of long COVID 23.36 percent (95 % CI 15.27-32.53). Of the population examined being older, female, having poor physical or mental health, or having has a severe infection led to an increase in risk for long COVID. “The generalized symptom (19.57 %, [95 % CI 9.85-31.52]) was reported most commonly, followed by respiratory (14.76 %, [95 % CI 7.22-24.27]), neurologic (13.51 %, [95 % CI 6.52-22.40]), and psychiatric (12.30 %, [95% CI 5.38-21.37]). Dyspnea (22.75 %, [95% CI 9.38-39.54]), fatigue (20.22 %, [95% CI 9.19-34.09]), and headache (15.88 %, [95 % CI 6.85-27.57]) were most widely reported specific symptoms. The prevalence of any symptom during 3-6, 6-12, and > 12 months were 26.41 % ([95 % CI 14.33-40.59]), 20.64 % ([95 % CI 17.06-24.46]), and 14.89 % ([95 % CI 6.09-26.51]), respectively.”

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Prevalence				
Date	Article	Publication	Author	Key Takeaways
1/24/2023	Long Covid Is Keeping Significant Numbers of People Out of Work, Study Finds - The New York Times (nytimes.com)	New York Times	Belluck P.	Long Covid is causing a significant percentage of Americans to not withdraw from the workforce. "New York's largest workers' compensation insurer, found that during the first two years of the pandemic, about 71 percent of people the fund classified as experiencing long Covid either required continuing medical treatment or were unable to work for six months or more." The brooking institute estimates that nationally 500,000 individuals are currently not working due to long COVID.
12/14/2022	CDC says long Covid has contributed to thousands of U.S. deaths - POLITICO	Politico	Mahr K.	The CDC has noted that long COVID has become a significant cause of death among Americans, specifically 3,544 death certificates list long COVID as a cause of death from January 2020 to June 2022. White patients make up 78.5 percent of these death and are more likely to have long COVID listed as a cause of death than other patients.

Risk Factors/Co-Morbidities				
Date	Article	Publication	Author	Key Takeaways
4/28/2023	Long COVID Is Disabling. So Is It a 'Disability'? - The Atlantic	The Atlantic	Ryan L.	The complicated nature of classing long COVID as a disability is explored through interviews conducted with patients that have long COVID. It also examines the larger disabled communities response to those with long COVID reaching out for guidance.
4/17/2023	Prevalence and characteristics of long COVID in elderly patients: An observational cohort study of over 2 million adults in the US PLOS Medicine	PLOS Medicine	Fung K. et al	A symptom-based definition was utilized to estimate the prevalence of long COVID in patients and compared this estimate to the estimate provided by only capturing cases coded, using ICD-10 codes, as long COVID. Based on symptom-based definition it is estimated that 29.2 percent of hospitalized COVID-19 patients and 16.6 percent of non-hospitalized COVID-19 patients develop long COVID. This is a higher estimate than that derived from capturing only patients coded as having long covid (non-hospitalized, .49%; hospitalized 2.6%). The significant difference between these estimates means pervious prevalence rates of how many patients have long COVID are most likely inaccurate.

COVID-19 Patient Recovery Alliance Research Tracker

Risk Factors/Co-Morbidities				
Date	Article	Publication	Author	Key Takeaways
3/23/2023	Risk Factors Associated With Post-COVID-19 Condition: A Systematic Review and Meta-analysis Infectious Diseases JAMA Internal Medicine JAMA Network	JAMA Internal Medicine	Tsampsian V. et al	A meta-analysis of 41 different studies (n=860,783) found that patients are at an increase risk of developing long covid if they are female (OR, 1.56; 95% CI, 1.41-1.73), older (OR, 1.21; 95% CI, 1.11-1.33), smokers (OR, 1.10; 95% CI, 1.07-1.13), or have a high BMI (OR, 1.15; 95% CI, 1.08-1.23). Patients with comorbidities (OR, 2.48; 95% CI, 1.97-3.13) and previous hospitalization or ICU admission (OR, 2.37; 95% CI, 2.18-2.56) were also found to be of higher risk.
2/9/2023	Long COVID in cancer patients: preponderance of symptoms in majority of patients over long time period eLife (elifesciences.org)	eLife	Dager H. et al	It was found that more than one in two cancer patients (n=312) develop long COVID. Females were more likely to develop long COVID symptoms.
1/2023	Long COVID: mechanisms, risk factors and recovery - PubMed (nih.gov)	Experimental Physiology	Astin, R. et al.	The group of patients who developed long-COVID had the following characteristics: Higher percentage of severe COVID-19 cases (odds ratio 3.87; p=0.001), more often required hospitalization (odds ratio 2,55; p=0.014), More COVID-19-related symptoms during initial infection (odds ratio 1.81; p=0.001), decreased levels of two immunoglobulins, IgM and IgG3, at the time of infection and at 6-month follow up, asthmatic, and higher age (odds ratio 1.67; p=0.008). “94% of individuals with a history of asthma bronchiale developed PACS (long-COVID) and 71% developed post-COVID-19 syndrome, defined as prolonged symptoms for more than 12 weeks after symptom onset. 59% of individuals without a history of asthma bronchiale developing PACS and 42% developing post-COVID-19 syndrome” These findings were translated into a model, termed PACS score, which, when applied to our cohort comprising 134 followed-up and extensively characterized COVID-19 patients, the PACS score performed better than a symptom-based score, was independent of timepoint of testing and sex, and only required broadly available Ig measurements rather than specialized tests, such as SARS-CoV-2-specific immunoassays.”
12/2022	Risk of incident diabetes after COVID-19 infection: A systematic review and meta-analysis - PubMed (nih.gov)	Metabolism	Lai H. et al	A meta-analysis of 47.1 million patients (4.5 million with COVID-19) concluded that there is a 64 percent greater risk factor of diabetes in patients with COVID-19 (RR = 1.64, 95 % confidence interval: 1.51 to 1.79; absolute risk difference = 701 more per 10,000 persons, 558 more to 865 more; I2 = 91.1 %). It also states that type 2 diabetes is more likely in this population than type 1.

COVID-19 Patient Recovery Alliance Research Tracker

COVID-19 Variants and Long-COVID				
Date	Article	Publication	Author	Key Takeaways
4/5/2023	Cleveland Clinic Researchers Find Sleep Disturbances Prevalent in Long COVID – Cleveland Clinic Newsroom	Cleveland Clinic	Reale-Cooney A.	Cleveland Clinic researchers found that 41 percent of long COVID patients have moderate to severe sleep disturbances. “More than two-thirds of patients (67.2%) reported moderate to severe fatigue, while 21.8% reported severe fatigue. More than half of the patients (58%) reported normal to mild disturbances, while 41.3% indicated moderate to severe sleep disturbances.”
3/2023	Blood-brain barrier penetration of non-replicating SARS-CoV-2 and S1 variants of concern induce neuroinflammation which is accentuated in a mouse model of Alzheimer’s disease – ScienceDirect	Brain, Behavior, and Immunity	Erickson M. et al	Two different non-infective mice models of COVID-19 demonstrated that the virus can cross the blood brain barrier and cause neuroinflammation. The neuroinflammation would account for the some of the neurological symptoms seen in long COVID such as brain fog. It was found that the Delta and Omicron variants cross the barrier quicker than other variants. How quickly the virus is able to enter the peripheral tissue also differs by variant. Finally, aged SAMP8 mice models, mice breed to exhibit Alzheimer’s, had significantly greater neuroinflammation.
1/11/2023	Long Covid symptoms ease for most within a year, new research finds (nbcnews.com)	NBC News	Edward E	A report by KI Research Institute and Maccabi Healthcare Services in Israel found that after a year most patients (n= ~2 million) experiencing long COVID symptoms from a mild COVID-19 infection had reduced symptoms after a year. The study did not consider patients that were infected with the Omicron variant or its sub-variants.
11/30/2022	Comparison of Long COVID-19 Caused by Different SARS-CoV-2 Strains: A Systematic Review and Meta-Analysis – PubMed (nih.gov)	International Journal of Environmental Research and Public Health	Du M. et al	Overall, this study concludes that there is not a significant difference in the symptoms of long COVID experienced by patients by strain. “The highest pooled estimate of long COVID-19 was found in the CT abnormalities (60.5%; 95% CI: 40.4%, 80.6%) for the wild-type strain; fatigue (66.1%; 95% CI: 42.2%, 89.9%) for the Alpha variant; and ≥1 general symptoms (28.4%; 95% CI: 7.9%, 49.0%) for the Omicron variant. The pooled estimates of ≥1 general symptoms (65.8%; 95% CI: 47.7%, 83.9%) and fatigue were the highest symptoms found among patients infected with the Alpha variant, followed by the wild-type strain, and then the Omicron variant. The pooled estimate of myalgia was highest among patients infected with the Omicron variant (11.7%; 95%: 8.3%, 15.1%), compared with those infected with the wild-type strain (9.4%; 95%: 6.3%, 12.5%). The pooled estimate of sleep difficulty was lowest among the patients infected with the Delta variant (2.5%; 95%: 0.2%, 4.9%) when compared with those infected with the wild-type strain (24.5%; 95%: 17.5%, 31.5%) and the Omicron variant (18.7%; 95%: 1.0%, 36.5%).”

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Vaccination and Long-COVID

Date	Article	Publication	Author	Key Takeaways
2/8/2023	Protective effect of COVID-19 vaccination against long COVID syndrome: A systematic review and meta-analysis - PubMed (nih.gov)	Vaccine	Watanabe A. et al	A comparative meta-analysis of 12 studies involving unvaccinated (n=536,291), vaccinated before infection (n=84,603), vaccinated after infect and have long COVID (n=8,199) patients demonstrated that a two dose vaccination and a one dose vaccination reduces the risk of long COVID compared to unvaccinated individuals (OR, 0.64; 95% confidence interval [CI], 0.45-0.92; OR, 0.60; 95% CI, 0.43-0.83). "Two-dose vaccination compared to no vaccination was associated with a lower risk of persistent fatigue (OR, 0.62; 95% CI, 0.41-0.93) and pulmonary disorder (OR, 0.50; 95% CI, 0.47-0.52). Among those with ongoing long COVID symptoms, 54.4% (95% CI, 34.3-73.1%) did not report symptomatic changes following vaccination, while 20.3% (95% CI, 8.1-42.4%) experienced symptomatic improvement after two weeks to six months of COVID-19 vaccination."

Treatments for Patients with Long-COVID

Date	Article	Publication	Author	Key Takeaways
11/29/22	Can Paxlovid Treat the Symptoms of Long COVID? Time	Time	Ducharme J.	A patient presentation demonstrates that Paxlovid taken after the initial infection may be able to treat long COVID symptoms, but more research is needed to establish a firm link. The patient was still testing positive months after an initial COVID-19 infection took a five-day course of Paxlovid, and found it eased her symptoms. It should be noted this is not the current standard of care.
11/2022	Effects of L-Arginine Plus Vitamin C Supplementation on Physical Performance, Endothelial Function, and Persistent Fatigue in Adults with Long COVID: A Single-Blind Randomized Controlled Trial - PubMed (nih.gov)	Nutrients	Tosato M. et al	This study demonstrated that a combination of L-arginine and liposomal vitamin C may improve endothelial and muscle function by stimulating nitric oxide synthesis in long COVID patients. Ultimately, this may result in patients seeing improved physical performance, for instance being able to walk farther without becoming tired quickly.