

CURRENT AWARENESS BULLETIN

LONG COVID

December 2025

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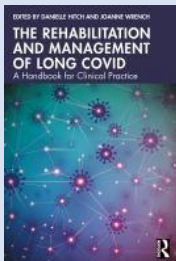
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NEW BOOK

Available to loan from MPH Library

[The rehabilitation and management of Long COVID : a handbook for clinical practice](#)

/ edited by Danielle Hitch, Joanne Wrench. 2025.

London : Routledge, 2025.

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EPIDEMIOLOGY OF LONG COVID

Asghar, A. F., Enderle, J., Salazar, J. H., & Esani, M. (2025). [Predictors of post-acute sequelae of coronavirus disease 2019 and long COVID in adults and children: A retrospective cohort study using US electronic health record data](#). *Journal of Public Health*,

OBJECTIVE: This study examined the incidence and predictors of post-acute sequelae of COVID-19 (PASC) and Long COVID in adults and children with confirmed Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. Associations assessed included demographic factors, comorbidities, lab markers, and patient clinical complications. **CONCLUSIONS AND PUBLIC HEALTH IMPLICATIONS:** Protocols that include targeted follow-up and early intervention are needed for post-COVID conditions in high-risk individuals across age groups. Integrating predictive markers into routine care could enhance preparedness and resilience against future waves of post-viral syndromes.

Cai, E., Kouznetsova, V. L., & Tsigelny, I. F. (2025). [Metabolomics-based machine learning diagnostics of post-acute sequelae of SARS-CoV-2 infection](#). *Metabolites*, 15(12)

Background: COVID-19 has taken millions of lives and continues to affect people worldwide. Post-Acute Sequelae of SARS-CoV-2 Infection (also known as Post-Acute Sequelae of COVID-19 (PASC) or more commonly, Long COVID) occurs in the aftermath of COVID-19 and is poorly understood despite its widespread effects. **Conclusions:** By creating and testing models pairwise on each of these diseases, we elucidated the unique strength of the similarity between FM and PASC relative to other PASC-similar diseases. Our approach is unique to PASC diagnosis, and our use of molecular descriptors enables our model to work with any metabolite where molecular descriptors can be identified, as these descriptors can be generated and compared for any metabolite. Our study presents a novel approach to PASC diagnosis that partially circumvents the lengthy process of exclusion, potentially facilitating faster interventions and improved patient outcomes.

Peng, B., Zhang, Y., Dalhuisen, T., Rogers, A., Estevez, J., Davies, H. E., . . . Qian, Y. (2025). [Machine learning analysis of post-acute COVID symptoms identifies distinct clusters and severity groups](#). *MedRxiv : The Preprint Server for Health Sciences*

Questionnaires that capture patient-reported symptomatology provide low-cost but potentially high-value data for the de novo discovery of disease phenotype, severity, and responsiveness to intervention groupings within an umbrella condition. The availability of comprehensive electronic health records (EHRs) has nonetheless overshadowed the use of questionnaire data for symptom analysis in the context of COVID-19. We analyzed de-identified questionnaires from post-acute COVID-19 cohorts at the University of California, San Francisco (UCSF, n = 669), Icahn School of Medicine at Mount Sinai (ISMMS, n = 615), Emory University (Emory, n = 60), and the University Hospital of Wales (Cardiff, n = 317). Using topic modeling followed by unsupervised clustering, we identified distinct symptom clusters and their corresponding symptom signatures. Mapping these signatures to organ systems revealed nine to twelve endotypes per cohort, capturing the heterogeneity of post-COVID-19 symptoms. Some clusters were associated with pre-existing conditions, including a female-predominant severity cluster with neurological and hormonal symptoms. Longitudinal analysis distinguished three symptom trajectories: acute then resolving, persistent but attenuated, and progressive disease. Across all cohorts, three severity levels, namely, mild, moderate, and severe, were evident from symptoms alone. Symptom-based severity scores correlated with patient-reported health status (EQ-5D) and SARS-CoV-2-specific antibody responses in plasmablasts, validating the prediction. Cluster-level analyses further stratified patients into recovered and non-recovered subgroups, identifying endotypes associated with different recovery trajectories. Finally, meta-analysis integrating cohort-specific clusters defined ten global endotypes and a unified map of severity scores, highlighting cohort-specific patterns, sex differences, and relationships among organ systems. These findings demonstrate that machine learning-assisted screening of questionnaire data can robustly identify symptom clusters, endotypes, and severity groups, providing a framework for stratifying long COVID patients for precision medicine trial design.

Pinero, S., Li, X., Zhang, J., Winter, M., Lee, S. H., Nguyen, T., . . . Le, T. D. (2025). [Omics-based computational approaches for biomarker identification, prediction, and treatment of long COVID](#). *Critical Reviews in Clinical Laboratory Sciences*, 1-27

Long COVID, or post-acute sequelae of COVID-19 (PASC), is a major global health problem, with cumulative estimates suggesting that around 400 million people worldwide have been affected. It is characterized by persistent or new symptoms such as fatigue, cognitive impairment, and breathlessness lasting beyond four weeks after acute infection. Diverse clinical manifestations, chronic course, and incompletely understood pathophysiology—including hypotheses involving viral persistence, immune dysregulation, autoimmunity, endothelial dysfunction, and metabolic reprogramming—impede the development of diagnostic criteria, biomarkers, and targeted therapies. We conducted a critical review of 101 Long COVID omics studies, focusing on the computational methods used and their methodological quality. Using standardized criteria, we evaluated study design, statistical rigor, reproducibility, and clinical relevance across genomics, epigenomics, transcriptomics, proteomics, metabolomics, and multiomics integration, and mapped these findings onto regulatory and translational frameworks. Despite substantial methodological heterogeneity, convergent biological signals emerged. Genomic studies implicate risk loci in immune and cardiopulmonary pathways. Epigenomic analyses identify differentially methylated regions in immune and circadian genes. Transcriptomic studies reveal persistent dysregulation of innate immune and coagulation pathways, as well as reproducible molecular endotypes. Proteomic studies consistently show abnormalities in the complement cascade and coagulation, with a small panel of complement proteins showing highly reproducible changes across independent cohorts. Metabolomic studies demonstrate sustained mitochondrial dysfunction and altered cellular bioenergetics for up to two years after infection. Multiomics integration supports at least two major endotypes, characterized by predominant inflammatory versus metabolic dysregulation, and provides a basis for patient stratification and computational treatment discovery. Machine learning models frequently achieve high classification performance, but are rarely externally validated. Critical limitations restrict clinical translation. Most studies are underpowered relative to analytical complexity, use heterogeneous case definitions and controls, and report platform-specific signatures with limited overlap. External validation, preregistered analysis plans, and regulatory-aligned assay development are uncommon. To date, no regulatory-approved diagnostic assay or evidence-based therapeutic intervention has directly emerged from these computational findings. Future progress requires harmonized phenotyping protocols, adequately powered longitudinal cohorts with external validation, integration of spatial omics and explainable artificial intelligence, and early engagement with regulatory and health-technology assessment pathways. This review provides a critical assessment and a translational roadmap, outlining how methodologically robust computational omics can be advanced toward clinically actionable tools for Long COVID.

Sinclair, J. E., Mayfield, H. J., Lu, H., Brown, S. J., Moghaddam, T., Waller, M., . . . Lau, C. L. (2025). [Estimating risk of long COVID using a bayesian network-based decision support tool](#). *Vaccine*, 72, 128127.

IMPORTANCE: Long COVID causes substantial health burden globally, affecting over 30 % of adults who have ever had symptomatic COVID-19. Individuals at continued risk of long COVID need better and more accessible information to make choices about vaccines and treatments. **OBJECTIVE:** To quantify modifiable risk factors for having long COVID six months post-infection, and develop a decision support tool for managing the risk factors. **CONCLUSIONS AND RELEVANCE:** The decision-support tool can be used by individuals or in conjunction with clinicians for shared decision-making on vaccination, pursuing early drug treatment during acute infection, and continuing protective behaviors such as masking and social distancing. The model can also generate population-level estimates of outcomes to assist public health decision-makers to design better-informed public health policies.

VACCINATION

El-Akkad, S., Shao, S., Tran, K. C., Naik, H., Janjua, N., Sbihi, H., . . . Wong, A. W. (2025). [Association between COVID-19 vaccination, SARS-CoV-2 variants, and post COVID-19 condition: A cross-sectional study](#). *PLoS ONE [Electronic Resource]*, 20(12), e0336929.

BACKGROUND: Individuals may experience persistent symptoms after recovering from coronavirus disease 2019 (COVID-19), a condition referred to as post COVID-19 condition (PCC). Patient-reported outcome measures (PROMs) evaluate a patient's health status and can be used to quantify symptom severity from the patient's perspective. The impact of COVID-19 vaccination and variant of infection on PCC is not well understood. We therefore sought to explore vaccination and variant trends among individuals with PCC and investigate their association with abnormal PROMs. **CONCLUSIONS:** Patients who were partially or fully vaccinated did not have increased risk of reporting common PCC symptoms. Infection with the alpha and delta variants was associated with increased likelihood of reporting dyspnea, which may be related to the severity of acute illness and associated impairments in lung function.

Guimaraes, G. N., Brunetti, N. S., De Lima, D. G., Proenca-Modena, J. L., & Farias, A. S. (2025). [Vaccination and COVID-19: Impact on long-COVID](#). *Frontiers in Immunology*, 16, 1686572.

Long- and post-COVID-19 syndromes have emerged as a significant global health challenge, with millions of individuals experiencing persistent or the development of new symptoms after a long period of an initial SARS-CoV-2 infection. These symptoms are multisystemic and may indicate changes in the respiratory, neurological, cardiovascular and gastrointestinal systems, in addition to prolonged fatigue. Vaccination has played a crucial role in reducing severe disease and mortality, but the impact of the different vaccine combinations on the development and resolution of Long COVID remains a topic of debate. This review synthesizes current evidence on how different vaccine platforms, dosing strategies and booster doses influence the immunological response, protection, incidence, severity, and persistence of Long COVID symptoms. We discuss key immunological mechanisms by which vaccination may modulate and protect post-COVID syndrome outcomes, including its effects on viral clearance, immune response reprogramming, inflammation, and autoimmunity, seeking to combat misinformation and concepts spread by fake news. The review also highlights controversies and research gaps, such as variability in vaccine response among different populations and the role in the selection of more transmissible and virulent SARS-CoV-2 variants, as well as the potential differences between vaccine-induced and infection-induced immunity, and the role of pre-existing immune conditions in this scenario.

McClymont, E., Blitz, S., Forward, L., Cole, S., Alton, G. D., Boucoiran, I., . . . Money, D. (2025). [The role of vaccination in maternal and perinatal outcomes associated with COVID-19 in pregnancy](#). *JAMA*,

Gaps in knowledge exist about the impact of COVID-19 and vaccination on pregnancy outcomes. To investigate the impact of vaccination on maternal and perinatal outcomes associated with SARS-CoV-2 infection in pregnancy. Population-level surveillance of pregnant individuals infected with SARS-CoV-2 and their infants using the CANCOVID-Preg database between April 5, 2021 (beginning of the Delta variant time period and initiation of recommendations for vaccination in pregnancy in Canada), and December 31, 2022. Cases were identified based on COVID-19 diagnoses in pregnancy in 9 of 13 Canadian provinces/territories. Cases occurring through 2022 were followed up into 2023 for pregnancy conclusion and infant outcomes. SARS-CoV-2 infection in pregnancy, with or without prior vaccination. COVID-19-associated hospitalization, critical care unit admission, and preterm birth. Of 26 584 cases identified, 19 899 cases were eligible for analysis. Among these, most infections occurred among those aged 30 to 35 years (46.3%) and among those of White race (55.9%). A total of 72% (n = 14 367) of cases were vaccinated and 28% (n = 5532) were unvaccinated prior to their COVID-19 diagnosis. Among those vaccinated prior to COVID-19 diagnosis, 80% (n = 11 425) were vaccinated prior

to pregnancy and 20% (n = 2942) were vaccinated during pregnancy. Cases occurred during both Delta (n = 6120) and Omicron (n = 13 799) variant time periods. Vaccination was associated with lower risk of hospitalization (Delta: relative risk [RR], 0.38 [95% CI, 0.30-0.48]; absolute risk difference [ARD], 8.7% [95% CI, 7.3%-10.2%]; Omicron: RR, 0.38 [95% CI, 0.27-0.53]; ARD, 3.8% [95% CI, 2.4%-5.2%]), critical care unit admission (Delta: RR, 0.10 [95% CI, 0.04-0.26]; ARD, 2.4% [95% CI, 1.8%-2.9%]; Omicron: RR, 0.10 [95% CI, 0.03-0.29]; ARD, 0.85% [95% CI, 0.27%-1.44%]), and preterm birth (Delta: RR, 0.80 [95% CI, 0.66-0.98]; ARD, 1.8% [95% CI, 0.3%-3.4%]; Omicron: RR, 0.64 [95% CI, 0.52-0.77]; ARD, 4.1% [95% CI, 2.0%-6.2%]). In multivariable analyses, vaccination was still associated with lower hospitalization risk in both variant time periods after controlling for comorbid conditions. In Omicron, compared with the vaccinated group, those unvaccinated had an adjusted RR of hospitalization of 2.43 (95% CI, 1.72-3.43). In Delta, those unvaccinated had an adjusted RR of hospitalization of 3.82 (95% CI, 2.38-6.14). Vaccination against SARS-CoV-2 prior to and during pregnancy, before COVID-19 diagnosis, was associated with a lower risk of severe maternal disease and preterm birth regardless of variant time period.

PATHOPHYSIOLOGY

Keller, C., Mascarenhas, L., Reyes, J. L., Duval, S., & Benditt, D. G. (2025). [Association of autonomic dysfunction with long COVID: Evaluation using quantitative autonomic testing](#). *Journal of the American College of Cardiology*,

BACKGROUND: Persistent symptoms (eg, heart palpitations, lightheadedness, fatigue) despite resolution of acute COVID-19 infection is termed "long COVID syndrome" or simply "long COVID." Long COVID is believed to be associated with autonomic dysfunction, but the nature and severity of any autonomic disturbances are not well understood. **CONCLUSIONS:** When adjusted for age and sex, patients with long COVID may demonstrate persistent autonomic dysfunction that is similar to patients with pure autonomic failure.

Zuniga-Jimenez, C. T., Rojas-Esguerra, D. F., Munoz-Martinez, A. P., Mendoza-Guzman, D. C., & Daza-Arana, J. E. (2025). [Musculoskeletal sequelae of post-COVID-19 syndrome: A systematic review](#). *Diseases*, 13(12)

Background/Objectives: COVID-19 infection is a respiratory illness that affects multiple body systems, including the musculoskeletal system. In August 2024, Colombia reported 6 million infections and a 2.2% mortality rate related to COVID-19. Post-COVID-19 syndrome (PCS) is a chronic condition occurring after the acute infection, typically characterized by fatigue, weakness, pain, and sarcopenia, impacting the patient's quality of life (QoL). This systematic review aimed to identify musculoskeletal sequelae, including peripheral muscle strength, fatigue, and QoL, in patients with PCS. **Conclusions:** Patients with PCS who required mechanical ventilation showed reduced muscle strength and poor physical performance, especially older adults. Inactive individuals had worse musculoskeletal sequelae, while physical activity was associated with better strength levels. Although QoL improved after 12 months, the combination of aerobic exercise with adequate nutrition is essential to promote muscle recovery, reduce fatigue, and improve overall functional capacity in post-COVID-19 patients.

Cardiology & Pulmonary

Kvandova, M., Balis, P., Kalocayova, B., Vlkovicova, J., Dobrodenkova, S., & Puzserova, A. (2025). [Cardiovascular damage and comorbidities related to long COVID: Pathomechanisms, prevention, and therapy](#). *Frontiers in Cardiovascular Medicine*, 12, 1671951.

Long COVID (LC) is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection-associated chronic condition and is present for at least 3 months as a continuous, relapsing and remitting, or progressive disease state that affects one or more organ systems, including cardiovascular.

Extensive literature supports an association between SARS-CoV-2 infection and cardiovascular complications and increased cardiovascular risk after infection. The cardiovascular sequelae after SARS-CoV-2 infection have not yet been comprehensively characterized. A growing body of evidence suggests that endothelial dysfunction is a central mechanism in COVID-19 and has also been identified as a key pathogenic mechanism in LC. Although considerable progress has been made in characterizing the epidemiology, clinical course, and biology of LC, many questions remain unanswered. The incomplete understanding of the pathomechanisms of LC has hampered the development of targeted therapies to date. Further research and data are needed to develop effective therapeutic and preventive tools. Based on current literature this review aims to provide an up-to-date overview of the pathomechanisms affecting the cardiovascular system and the potential role of selected micronutrients, vitamins and minerals, and flavonoids as preventive and therapeutic strategies in LC.

Laszlo, S., Ianosi, E., Vasiesiu, A., Szathmary, M., Ianosi, M. B., Rachis, D., . . . Jimborean, G. (2025). [COVID-19 and lung cancer interactions: A literature review](#). *Medical Sciences*, 13(4)

This review aims to discuss the apparent reduction in pulmonary cancer incidence in the general population during and shortly after the COVID-19 pandemic from a biological and pathophysiological mechanistic point of view. While the epidemiological evidence points to a disruption in the early- and mid-stage diagnostic process, which causes a shift to late-stage lung cancer discovery with no impact on its actual prevalence, an alternative hypothesis based on the intersection of viral and cancer biology could have a real effect on lung carcinogenesis as an independent phenomenon. By weaving together population-level trends, mechanistic insights, and translational oncology, we discuss whether the pandemic-associated decline in lung cancer diagnoses reflects primarily a temporary diagnostic artifact or whether it also reveals biologically relevant intersections between SARS-CoV-2 and pulmonary oncogenesis. We conclude that the "diagnostic deficit" phenomenon was a reality during and immediately post-pandemic. However, a definitive answer to the questions related to the impact of the infection as an independent phenomenon would require advanced research information covering the biology of the viral infection and lung cancer oncogenesis: processes that are not currently implemented in routine clinical laboratory investigations.

CFS/ME/MS/CF

Herman, M. E. (2025). [How pandemics reshape our brain: Common links and targets between long-haul COVID-19, myalgic encephalomyelitis/chronic fatigue syndrome \(ME/CFS\), oxidative stress, and neurodegeneration](#). *Neuroprotection*, 3(3), 280–287.

Fatiguing syndromes affect millions of patients in the United States and globally, but are grossly underserved in the clinic and in the contemplative design of basic research. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a complex multisystem metabolic-immune-inflammatory disorder. Although research on this condition is in its infancy, it appears to involve the immune system and central nervous system malfunction, with cellular oxidative stress as a predominant feature. Approximately half of the cases of long-haul coronavirus disease 2019 meet the diagnostic criteria for ME/CFS, burgeoning the number of affected individuals. Recent strides in neurobiology have yet to transfer the understanding of the neurodegenerative aspects, and potential for neuroprotection, of ME/CFS. ME/CFS may represent a useful paradigm and research model for the study of the impact of sustained oxidative stress on the central nervous system and the body at large.

Michael, H. U., Aste, F. G., Brouillette, M., Fellows, L. K., & Mayo, N. E. (2025). [How do fatigue, cognitive dysfunction, activity and role functioning, and mental health inter-relate in adults with post-COVID-19 syndrome? A structural equation model analysis](#). *Quality of Life Research*, 35(1), 3.
PURPOSE: Post-COVID-19 Syndrome (PCS) is associated with persistent fatigue and cognitive symptoms that may disrupt daily functioning and mental health. This study examined interrelationships among fatigue, cognitive function, activity and role functioning, and mental health in individuals with PCS.

CONCLUSION: Fatigue and self-reported cognitive concerns were associated with mental health symptoms in PCS. These findings highlight the value of symptom cluster-based screening to inform referral pathways for cognitive, psychological, and functional support. Longitudinal research is needed to clarify temporal ordering.

Cognitive/psychological/neurological

Furevik, L. L., Lapina, O., Lindland, E. S., Hogestol, E. A., Geier, O. M., Devik, K., . . . Bolding, M. I. (2025). [Brain MRI findings in patients with post COVID-19 condition: Frequency and longitudinal changes in a nationwide cohort study](#). *Frontiers in Neurology [Electronic Resource]*, *16*, 1662263.

Background: Prolonged neurological symptoms following COVID-19 are common, yet few longitudinal studies describe brain MRI findings in this patient group. The use of contrast enhanced sequences is particularly lacking. We address this knowledge gap by reporting the frequency and longitudinal changes in brain MRI findings among patients with post COVID-19 condition exhibiting neurological symptoms. **Conclusion:** Our findings indicate that brain MRI primarily serves to exclude differential diagnoses in post COVID-19 condition, with limited clinical benefit of repeated imaging in the absence of new symptoms. However, signs of long-term inflammatory processes can be observed, and detection is improved by contrast enhanced sequences.

Ryu, S., Slocum, E. M., Whittington, B., Arciniega, L. Z., Ahmed, S., & Fleischer, N. L. (2025). [Prospective associations of long COVID with sleep health nearly 3 years after SARS-CoV-2 infection: A statewide representative cohort study](#). *Sleep*,

STUDY OBJECTIVES: While many adults with Long COVID experience sleep problems, the long-term relationship between Long COVID and sleep remains poorly understood. We investigated how Long COVID is prospectively associated with sleep duration, sleep quality, and sleep disturbance using a population-based cohort of Michigan adults with COVID-19 (n=2,406). **CONCLUSION:** Long COVID was prospectively associated with unhealthy sleep outcomes 3 years after onset. There is a need to enhance sleep health among individuals with Long COVID.

Thapaliya, K., Marshall-Gradisnik, S., Inderyas, M., & Barnden, L. (2025). [Altered brain tissue microstructure and neurochemical profiles in long COVID and recovered COVID-19 individuals: A multimodal MRI study](#). *Brain, Behavior, & Immunity Health*, *50*, 101142.

Background: Diverse neurological symptoms are experienced by long COVID and COVID-19 recovered individuals. However, the long-term effects of SARS-CoV-2 in the brain of both groups are underexplored. This study aimed to investigate changes in tissue microstructural and brain neurochemical levels in long COVID and recovered COVID-19 patients compared to healthy controls. **Interpretation:** This is one of the first studies to report different myelin signal and brain neurochemical changes between long COVID, COVID-recovered-healthy controls, and healthy controls without SARS-CoV-2 infection. These brain changes provide compelling evidence for the long-term effects of SARS-CoV-2 on brain function.

Wilson, J. C., Liu, K. Y., Mittelman, E., Bareke, P., Shleifer, E., & Howard, R. (2025). [Brain fog with long covid and chemotherapy: Systematic review and meta-analysis](#). *BMJ Mental Health*, *28*(1)

QUESTION: What are the cognitive, functional and affective characteristics of brain fog in individuals with long covid and following chemotherapy, and how are these features assessed across studies? **STUDY SELECTION AND ANALYSIS:** In March 2024, we conducted a systematic review and meta-analysis of peer-reviewed studies assessing cognition, function or mood in adults (>=18 years) with brain fog after COVID-19 or chemotherapy. PubMed, Embase and Web of Science were searched systematically according to eligibility criteria to March 2024, with an update in May 2025. Random-effects meta-analyses using the 'dmetar' package (V.0.0.9000) in R V.4.3.1 were performed for studies comparing individuals with and without brain fog. Bias was assessed using the National Institutes of Health Study Quality Assessment Tools. **CONCLUSIONS:** Brain fog in long covid and chemotherapy

populations is associated with cognitive complaints, fatigue and mood disturbance, though assessment methods differ widely. To improve comparability and clinical understanding, we propose adoption of consistent tools and definitions in future studies. This will be a crucial step in generating findings that can be meaningfully compared across populations.

Wilson, J. E., Gurdasani, D., Helbok, R., Ozturk, S., Fraser, D. D., Filipovic, S. R., . . . Wesley Ely, E. (2025). [COVID-19-associated neurological and psychological manifestations](#). *Nature Reviews.Disease Primers*, 11(1), 91.

Long COVID is an infection-associated chronic condition that typically occurs within 3 months of acute COVID-19 infection in which symptoms are intermittently or continuously present for at least 3 months. Long COVID is estimated to affect between 80 and 400 million people globally, with an incidence of 5-20% in the community and up to 50% among hospitalized patients following acute SARS-CoV-2 infection. Common neuropsychiatric and mental health symptoms of long COVID include memory deficits, executive dysfunction, anxiety, depression, recurring headaches, sleep disturbances, neuropathies, problems with taste and smell, and dizziness that accompanies erratic heart rates and severe post-exertional malaise. Underlying pathophysiological mechanisms includes SARS-CoV-2 viral persistence, herpesvirus reactivation, microbiota dysbiosis, autoimmunity, clotting and endothelial abnormalities, and chronic immune activation. Owing to the variability in the clinical presentation, management must be tailored based on a patient's presenting symptoms.

PSYCHO-SOCIAL IMPACTS OF LONG COVID (INC. WORK, EDUCATION, QOL)

Al-Oraibi, A., Martin, C. A., Woolf, K., Nellums, L. B., Tarrant, C., & Pareek, M. (2025). [Patterns of long COVID symptoms among healthcare workers in the UK and variations by sociodemographic, clinical and occupational factors: A cross-sectional analysis of a nationwide study \(UK-REACH\)](#). *Journal of the Royal Society of Medicine*, 118(12), 387–406.

OBJECTIVES: This study aimed to examine symptom patterns between healthcare workers (HCWs) with and without long COVID, identify the most common long COVID symptom groups and investigate how these symptom profiles vary across different ethnic groups, demographic characteristics, clinical factors and occupational roles in UK HCWS. **CONCLUSIONS:** Our findings are the first to reveal distinct patterns in long COVID symptoms among HCWs with significant variations by ethnicity, sex and occupational role. These findings emphasise the need for targeted support strategies and workplace adjustments that consider both occupation-specific risks and individual sociodemographic factors.

Ballouz, T., Kerksieck, P., Haile, S. R., Dressel, H., Hammig, O., Bauer, G. F., . . . Menges, D. (2026). [Work ability trajectories and sick leave in individuals with post COVID-19 condition: 3-year follow-up of a population-based cohort](#). *The Lancet Regional Health.Europe*, 61, 101536.

Background: Data on the longer-term impact of post COVID-19 condition (PCC) on work-related functioning is limited, despite evidence on the persistence of PCC for years after infection. This study aimed to describe changes in work ability and sick leave associated with PCC up to three years post-infection. **Interpretation:** The study highlights the prolonged impact of PCC on work-related functioning and underscores the need for targeted occupational, clinical and social measures for those affected. **Funding:** Federal Office of Public Health, Department of Health of the Canton of Zurich, University of Zurich Foundation, Switzerland; Horizon Europe.

De Matteis, S., Consonni, D., Espinosa, A., de Cid, R., Magrina, N. B., Castano-Vinyals, G., . . . Straif, K. (2025). [Occupational determinants of long COVID in the population-based COVICAT cohort](#). *Occupational & Environmental Medicine*,

OBJECTIVES: Occupational factors affect SARS-CoV-2 infection risk, but the occupational factors

associated with Long COVID (LC) are unknown. We aimed to address this issue using individual data in a population-based cohort. **CONCLUSIONS:** In a population-based cohort, several occupational factors increased LC risk. Focused preventive strategies are warranted to avoid the associated public health burden. LC should be recognised and compensated as an occupational disease.

Delano, P., Serra-Sutton, V., Rodriguez-Arjona, D., Benavides, F. G., Vives, A., & Utzet, M. (2025). [Long COVID and its impact on healthcare worker's job performance. A qualitative study in Spain.](#) *Journal of Occupational & Environmental Medicine,*

OBJECTIVE: To explore the experiences of healthcare workers (HCWs) in Spain with long COVID and its impact on their job performance, from the perspectives of affected HCWs, healthcare providers, and key stakeholders. **CONCLUSIONS:** Long COVID significantly impacts affected HCWs job performance, highlighting a need for recognition, support and workplace adaptation.

Igarashi, Y., Tateishi, S., Sawajima, T., Harada, A., Matsuoka, J., Kawasumi, M., & Mori, K. (2025). [Occupational physicians' practices in supporting employees with long COVID: A mixed-methods study.](#) *Journal of Occupational Health,*

OBJECTIVES: This study examined the support provided by occupational physicians (OPs) in Japan to employees with Long COVID, a condition that has significantly affected workforce health during the pandemic. **CONCLUSIONS:** This study clarified how OPs in Japan supported workers with Long COVID through diverse, context-dependent practices. The identified Main OH Responses and Advice for Employers provide a framework for understanding current practices. Developing practical case examples, structured assessment tools, and workplace guidelines, together with further research grounded in real-world practice, will enhance OPs' ability to provide appropriate support and strengthen preparedness for future health crises.

Sisti, J. S., Packard, S. E., & Metzler, J. (2025). [Long COVID symptoms and loneliness: Findings from the World Trade Center health registry.](#) *BMC Public Health,*

BACKGROUND: Symptoms of long COVID can profoundly impact affected individuals' functioning, including their ability to participate in social activities. While individuals experiencing long COVID symptoms frequently report loneliness, few studies to date have investigated whether loneliness is more common among those with symptoms compared to those without. We examined associations between long COVID symptoms and loneliness among World Trade Center Health Registry (WTCHR) enrollees. **CONCLUSION:** Long COVID symptoms were associated with prevalence of loneliness in a sample of primarily older adults. As loneliness itself is associated with subsequent adverse health outcomes, addressing loneliness among people living with long COVID may help prevent further reductions in quality of life.

Wei, H., Daniels, S., Wiggans, R., Coleman, A., Bramwell, D., McElvenny, D., . . . van Tongeren, M. (2025). [Long COVID and work in the UK: Challenges, support and perspectives.](#) *Archives of Public Health, 83(1), 297.*

AIM: Long COVID (LC) presents significant challenges for working age individuals, leading to major inequalities in access to work, employment and relevant support. This study investigates the workplace support provided to people with Long COVID (PwLC) in the UK, focusing on their return-to-work (RTW) experiences. It encompasses perspectives from both PwLC and managers of PwLC. **CONCLUSION:** This qualitative study highlights potential barriers, challenges and gaps in supporting PwLC's RTW. To ensure equitable access to work for PwLC, a flexible and personalised approach is crucial, given the variability in LC symptoms and recovery rates. RTW support that fails to accommodate these characteristics may exacerbate symptoms or cause relapses. A supportive work environment is essential, as LC symptoms can be invisible and concerns about stigma may prevent PwLC from communicating openly and seeking support. Lack of resources is a major barrier for managers in supporting PwLC. Effective government support can potentially fill this gap but must be well-designed and implemented to reduce the burden on

applicants.

SERVICE DESIGN & PATHWAYS

Buettikofer, T., Maher, A., Johnson, M., Hartono, S., Rainbird, V., Nickels, M., . . . Bissett, B. (2025). [Safety and physical outcomes of a novel Australian multidisciplinary long COVID clinic that incorporates exercise: A prospective observational study](#). *Journal of Multidisciplinary Healthcare*, **18, 7827–7838.**

Few studies in Australia have investigated the impact of exercise in people with Long COVID. This observational study describes the safety and physical outcomes of 72 adults who completed an Australian multidisciplinary Long COVID clinic that incorporates supervised cardiovascular and strength training over several weeks. For those who completed the program, there were no adverse events, while multiple physical outcome measures improved relative to baseline. This study shows that exercise can be safely incorporated in a multidisciplinary clinic for people recovering from Long COVID.

Kamdem, O. L., Guyot, J., Dupre, C., Gouttefarde, P., Vericel, M. P., Fanget, M., . . . Bongue, B. (2025). [Management of patients with post covid-19 condition in France: A qualitative study exploring nurses' contributions to care pathways](#). *Journal of Public Health Research*, **14(4), 22799036251390963.**

Objective: To investigate the different contributions made by nurses in the management of patients with post covid-19 condition (PCC) within the French healthcare context. **Conclusion:** The results offer important perspectives for the organization of the healthcare system and for the nursing profession in the management of chronic diseases. An important aspect of our findings concerns the coordination of care pathways, which raises the issue of task delegation to nurses, particularly in a context of healthcare professional shortages.

Leighton, J., Heldmann, I., Van de Ven, K., Reis, L., Vijayakumar, A., Simpson, R., . . . Wasilewski, M. B. (2025). [Rehabilitation providers' experiences with long COVID care in Canada: A qualitative study](#). *Disability & Rehabilitation*, **1-12**

Rehabilitation professionals are recommending individualized and flexible care approaches focused on symptom validation and energy conservation, due to the diverse and unpredictable nature of Long COVID. In the absence of formal guidelines, rehabilitation professionals have adapted practices in real time, emphasizing the urgent need for standardized, evidence-informed Long COVID rehabilitation frameworks. Effective Long COVID rehabilitation includes patient and caregiver education, integration of peer support, and the promotion of self-management strategies to enhance recovery and reduce isolation. Interdisciplinary collaboration and system-level integration are critical to ensure continuity of care and to build sustainable rehabilitation pathways for emerging chronic conditions like Long COVID.

Uecker, C., Schlee, C., Utz, S., Schmid, S., & Langhorst, J. (2025). [Integrative multimodal treatment approach for patients suffering from post-COVID syndrome: A study based on qualitative interviews with individuals participating in an 11-weekday clinic program](#). *Frontiers in Public Health*, **13, 1688592.**

Background: Post-COVID syndrome is a complex condition affecting patients after SARS-CoV-2 infection. It is characterized by fatigue, pain, reduced resilience, and quality of life. Severe cases resemble myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), associated with post-exertional malaise (PEM). Due to the unknown etiology and lack of curative options, multimodal therapy

offers a particularly promising approach to symptom management. **Conclusion:** Post-COVID syndrome poses ongoing challenges for individuals and healthcare systems. Multimodal integrative treatment can effectively reduce symptoms, enhance coping strategies, and promote sustainable self-care. Clinical trial registration: [Clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT05630378), identifier NCT05630378.

INTERVENTIONS/RESEARCH

Interventions

Debie, V. H. J., Peters, L. H. L., van Schayck, O. C. P., Burgers, J. S., Ottenheijm, R. P. G., & Gidding-Slok, A. H. M. (2025). [Patient perspectives on the usability and content validity of the assessment of burden of chronic conditions tool for post-COVID in the Netherlands: A qualitative study](#). *BMJ Open*, *15*(12), e109201.

BACKGROUND: Post-COVID syndrome manifests with a diverse array of symptoms for which no standard care plan currently exists. Many questions were raised by patients, which underscored the need for a validated patient-reported outcome measure (PROM). Therefore, a post-COVID module was developed to be included in the Assessment of Burden of Chronic Conditions (ABCC-) tool. The ABCC-tool evaluates and visualises the perceived physical, emotional and social burden of one or multiple chronic disease(s) using a balloon diagram and aims to facilitate person-centred care and structured discussions between patients and healthcare professionals. This study explores the patients' perspective on the content of the ABCC-tool for post-COVID and the tool's usability in a home-based setting. **CONCLUSIONS:** The ABCC-tool is a promising instrument for post-COVID patients, offering a structured way to monitor and communicate experienced burden in addition to standard healthcare consultations. Refinements addressing usability and comprehensiveness are recommended to facilitate its integration into clinical practices.

Leavesley, M. R., Dugen-Williams, C., Dobel-Ober, D., & Carson, A. (2025). [PCE-CfD and long covid: An NHS service evaluation on the benefits of using person-centred experiential counselling for depression with people with long covid](#). *Health Expectations*, *28*(6), e70517.

OBJECTIVE: This NHS service evaluation investigated outcomes from clients with Long Covid who received PCE-CfD, specifically the impact on reduced depression and anxiety symptoms, and improved social and occupational functioning. It analysed pre- and post-treatment client/patient self-reported data using routine outcome measures, including the PHQ-9, GAD-7 and WSAS. **CONCLUSION:** This NHS service evaluation underscores the effectiveness of PCE-CfD in reducing symptoms of depression and anxiety, as well as improving social and occupational functioning. These improvements observed in routine outcome measures highlight the benefits of offering a humanistic approach to people with Long Covid. These small but significant findings offer valuable insights into future service delivery and research in managing mental health challenges associated with chronic health conditions. **PATIENT OR PUBLIC INVOLVEMENT AND ENGAGEMENT (PPIE) CONTRIBUTION:** This NHS service evaluation uses secondary data analysis, meaning PPIE did not take place in advance. However, PPIE discussions could arise when disseminating its findings that could lead to further research in this area.

Nielsen, T. B., Oestergaard, L. G., Hawkins, J., Nielsen, C. V., Leth, S., Laursen, C. H., & Sorensen, D. (2025). [How a long COVID rehabilitation intervention works: Refining its programme theory through a realist-informed qualitative study](#). *BMC Health Services Research*,

BACKGROUND: Although the majority of individuals infected with SARS-CoV-2 recover without treatment, some individuals experience persistent symptoms (long COVID), which may negatively affect their activities and roles of everyday life, leaving them with a profound rehabilitation need. In response to

the emergence of long COVID patients, a Danish municipality developed and implemented a structured, out-patient long COVID rehabilitation intervention (The Long COVID Rehabilitation Intervention). To understand how, why and for whom the intervention works, and its functioning, an exploration of the underlying programme theory is required. We thus aimed to explore the interactions between the intervention mechanisms of change, the implementation context and the expected outcomes of The Long COVID Rehabilitation Intervention to confirm or refine the initial programme theory. **CONCLUSION:** Overall, the initial programme theory was confirmed but required refinement to contexts and mechanisms. The theorisation of The Long COVID Intervention clarified how, why, and for whom it worked, informing the development of future long COVID and post-viral rehabilitation interventions.

Yet, M., Teo, H. S., Kwa, H., Yeo, J., & Wang, S. S. Y. (2025). [Long COVID: A review of mechanisms and treatment modalities](#). *Inflammopharmacology*,

Long COVID is defined by the World Health Organisation (WHO) as a condition arising within 3 months of an acute COVID infection with symptoms lasting for a minimum of 2 weeks. However, this syndrome is poorly understood and has been recorded to include many systemic manifestations, including neurological, respiratory, cardiovascular, gastrointestinal, dermatological, psychosocial, and metabolic systems. Constitutional symptoms also include fatigue, insomnia, body weight changes, poor attention span, hair loss, sexual dysfunction, myalgia, and joint pain, with fatigue being the most common. Given the various proposed mechanisms published in the literature, the postulated mechanisms and pathways are discussed in this paper to contribute to the understanding of defining this syndrome. In this review article, the authors first explored how endothelial damage from COVID infection can lead to a hypercoagulable state. In addition, the effects of an insufficient initial immune response can lead to viral persistence alongside a potentially prolonged hyperactive immune response that includes a cytokine storm and mast cell activation syndrome. Furthermore, the viral persistence can be exacerbated by antibody-dependent enhancement or complicated by molecular mimicry. Current pharmacological therapies are explored and evaluated to investigate their efficacy in addressing this complex and chronic presentation. This review article has been written after an extensive literature review to increase the understanding and awareness regarding Long COVID, as a sincere effort to direct further research for an effective diagnosis and management.

Zahiriharsini, A., Rostami, M., Hurd, C., Vakilian, F., Brar, G., Wang, T., . . . Manhas, K. P. (2025). [Evaluating medical and rehabilitation programs for long COVID: Utilization, health outcomes, and healthcare costs](#). *American Journal of the Medical Sciences*,

BACKGROUND: Long COVID presents a substantial and evolving challenge to individuals and health systems. Despite growing interest in interdisciplinary care models, empirical evidence on their structure, utilization, and effectiveness remains limited. This study examined the delivery and outcomes of specialized outpatient programs for long COVID in Alberta, Canada, focusing on: (a) patterns of program utilization; (b) patient-reported health outcomes; and (c) impacts on healthcare system utilization and costs. **CONCLUSIONS:** In this observational analysis, program participation was associated with small improvements in patient-reported health status and modest cost patterns. Because natural recovery, regression to the mean, and concurrent system changes may also explain these trends, the findings should be interpreted as preliminary associations rather than causal effects. Prospective controlled studies are needed to confirm effectiveness and economic value.

Research

Guo, Z., Wei, Y., Lin, G., Jia, K. M., Boyer, C., Wang, H., . . . Chong, K. C. (2025). [Effectiveness of nirmatrelvir/ritonavir and molnupiravir in reducing the risk of short-term and long-term cardiovascular complications of COVID-19: A target trial emulation study](#). *Nature*

Communications.

Harrois, A., Jouffroy, R., Ayed, S., Bruel, C., Savale, L., Devaux, M., . . . Duranteau, J. (2025). [Awake prone positioning in patients with COVID-19 respiratory failure: A randomized clinical trial](#). *JAMA Network Open*, 8(12), e2548201

Jornada Ben, A., Varga, A. N., de Bruijn, S., Dekker, W. B., van den Wijngaard, C. C., Verburg, A. C., . . . van Dongen, J. M. (2025). [A comparison of allied healthcare versus no allied healthcare on participation, fatigue, physical functioning and health-related quality of life for patients with persistent complaints after a COVID-19 infection](#). *Annals of Medicine*, 57(1), 2600139.

Oostwouder, C., Vos, K., Lutke Schipholt, I. J., Merkus, M. R., Telders, T., van Deursen, D. F. A., . . . Scholten-Peeters, G. G. M. (2025). [Effect of subcutaneous lidocaine-hydroxypropyl-beta-cyclodextrin \(HP-beta-CD\) on quality of life in patients with post-COVID condition: A 36-week observational interrupted time series study](#). *EClinicalMedicine*, 90, 103681.

Riste, L., Perrin, R., Mulholland, T., Hann, M., McDonald, O., & Heald, A. (2025). [Testing the feasibility of a self-help intervention that includes lymphatic drainage to reduce fatigue-related symptoms among patients with long COVID in general practice: Experiences from our randomized controlled trial \(RCT\)](#). *Infectious Diseases & Therapy*.

Rizvi, G. S., Ullah, R., Khalid, M., Talha, M., & Waafira, A. (2025). [Circadian rhythm disruption and melatonin dysregulation as overlooked drivers of immune imbalance and multiorgan failure in post-COVID syndrome: A call for chronotherapy-based interventions](#). *Annals of Medicine & Surgery*, 87(12), 9069–9070.

Soares, L., Davis, H., Spier, E., Walker, T., Davenport, T., Putrino, D., . . . Vogel, J. M. (2025). [Recommended long COVID outcome measures and their implications for clinical trial design, with a focus on post-exertional malaise](#). *EBioMedicine*, 123, 106083.

Tura, N. C., da Silva Pereira, F., Fogaca, B., Pang, A. S., do Amaral, L. A., & Barbosa, R. I. (2025). [Efficacy of synchronous vs. asynchronous telerehabilitation for musculoskeletal symptoms in post-covid-19 syndrome: A randomized clinical trial](#). *International Journal of Telerehabilitation*, 17(2), 6716

Livia Arcencio do Amaral, Rafael Inacio Barbosa.

Vandersteen, C., Plonka, A., Derreumaux, A., Ramette, M., Payne, M., Castillo, L., . . . Gros, A. (2025). [Kinematic handwriting impairments in olfactory dysfunction-related post-acute covid syndrome: Short and long-term neurophysiological considerations](#). *Brain & Cognition*, 193, 106383.

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