COVID PATIENT RECOVERY ALLIANCE

The COVID Patient Recovery Alliance is a multi-sector collaboration with the mission to support the energy and innovation of government and private-sector leaders as they care for individuals with long-COVID. The Alliance is developing national solutions that link diverse data sources, improve clinical care pathways, and ensure sustainable federal financial support for the care of these patients. The Alliance is particularly interested in those patients who served their communities and nation when called to duty; whose COVID-19-related costs are extraordinary and burdensome; or who are underserved by existing programs, including racial and ethnic minorities and communities experiencing health disparities.

For more information, please visit our website at COVID19PatientRecovery.org.

PURPOSE OF RESEARCH TRACKER

The research, news, and knowledge of long-COVID is quickly evolving. To stay up-to-date and informed on long-COVID, the Patient Recovery Alliance is performing routine intel scans from a variety of sources – from peer-reviewed publications to various news websites – and on variety of long-COVID-related topics, including health care coverage, workers' compensation, impacted populations, symptoms, and prevalence. The outputs of these intel scans are compiled in this document, which will be periodically updated.

Date	Article	Publication	Key Takeaways
August 2022			
8/2/2022	Profiling post-COVID syndrome across different variants of SARS-CoV-2 | medRxiv	medRxiv (preprint)	Three main clusters of post-COVID syndrome, evident across all variants: (1) Those with neurological symptoms including fatigue, brain fog and headache – most commonly found among those who became infected when the most dominant strains were alpha and delta. (2) A second group who experienced respiratory symptoms, including chest pain and shortness of breath. This was found more commonly among those infected during the first wave of the virus. (3) A final group experiencing a range of symptoms including heart palpitations, muscle ache and pain, and changes in skin and hair.
8/2/2022	Axcella long COVID treatment helps some patients in small trial | Reuters	Reuters	41-patient pilot study, 21 of whom received the drug, AXA1125. For 3 of the 21 patients who received AXA1125, their physical fatigue scores returned to normal levels after 28 days of treatment. Others who received the drug also reported physical and mental improvements that were deemed to be statistically significant as shown on a scale developed to measure chronic fatigue, according to the preliminary results, and the drug was shown to be safe and well tolerated. AXA1125 failed on the small study's main goal of restoring the normal function of mitochondria.
Aug-22	Long COVID in the Long Run—23-Month Follow-up Study of Persistent Symptoms	Open Forum Infectious Diseases	N=170. Symptoms of long-COVID were found in 38% of participants followed for a median of 22.6 months. The most prevalent symptoms were fatigue, affected taste and smell, and difficulties remembering and concentrating. Predictors for long COVID were older age and number of symptoms in the acute phase.
7/29/2022	Rates and Factors Associated With Documentation of Diagnostic Codes for Long COVID in the National Veterans Affairs Health Care System	JAMA	N=198,601 persons with a positive SARS-CoV-2 test. Three or more months after infection, COVID-19 care was documented in the electronic health records of 13.5%; mean follow-up of 13.5 months. More common in older persons, those with higher comorbidity burden, those with more severe acute COVID-19 presentation, and those who were unvaccinated at the time of infection. Long-COVID care was documented in a wide variety of clinics, most commonly primary care and general internal medicine (33.1%), pulmonary (13.1%), and geriatrics (9.7%).
8/3/2022	Services and Supports for Longer-Term Impacts of COVID-19	HHS	This report outlines the federally funded supports and services currently available to individuals experiencing the longer-term effects of COVID-19. COVID-19 has affected all aspects of life.
8/3/2022	National Research Action Plan (covid.gov)	HHS	This plan introduces the first U.S. government–wide national research agenda focused on advancing prevention, diagnosis, treatment, and provision of services and supports for individuals and families experiencing Long COVID. It proposes an effective, comprehensive, and equitable research strategy to inform our national response to Long COVID.
8/5/2022	Post–COVID-19 Symptoms and Conditions Among Children and Adolescents — United States, March 1, 2020–January 31, 2022	CDC	N=781,419 patients aged 0–17 years with COVID-19; N=2,344,257 patients aged 0–17 years without COVID-19. Compared with patients aged 0–17 years without previous COVID-19, those with previous COVID-19 had higher rates of acute pulmonary embolism (adjusted hazard ratio = 2.01), myocarditis and cardiomyopathy (1.99), venous thromboembolic event (1.87), acute and unspecified renal failure (1.32), and type 1 diabetes (1.23).Patients with COVID-19 were also more likely than were those without to develop smell and taste disturbances (aHR = 1.17), circulatory signs and symptoms (1.07), malaise and fatigue (1.05), and musculoskeletal pain (1.02).
8/8/2022	Tim Kaine has long Covid. That's not moving Congress to act. - POLITICO	Politico	"But after months of efforts, Kaine's experience sounds a lot like his constituents': a frustrating and so far fruitless exercise. While he and other Democrats in the House and Senate are pushing for action, they have failed to gain meaningful momentum due to lack of GOP support and a congressional leadership bogged down in battles around spending, inflation, foreign policy and reproductive rights."

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8/6/2022	Prevalence of symptoms, comorbidities, fibrin amyloid microclots and platelet pathology in individuals with Long COVID/Post-Acute Sequelae of COVID-19 (PASC)	Cardiovascular Diabetology	N=845 South African Long COVID/PASC patients Analyzed blood samples from 80 patients using g a previously published scoring system for fibrin amyloid microclots and platelet pathology. Hypertension, high cholesterol levels, cardiovascular disease, and type 2 diabetes were found to be the most important comorbidities. The gender balance (70% female) and the most commonly reported Long COVID/PASC symptoms (fatigue, brain fog, loss of concentration and forgetfulness, shortness of breath, as well as joint and muscle pains) were comparable to those reported elsewhere. Microclot and platelet pathologies were associated with Long COVID/PASC symptoms that persisted after the recovery from acute COVID-19.
8/4/2022	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is common in post-acute sequelae of SARS-CoV-2 infection (PASC): Results from a post-COVID-19 multidisciplinary clinic	medRxiv (preprint)	Participants: N=134 adults with a history of COVID-19 who were referred to the multidisciplinary Stanford PACS clinic from May 18, 2021, to February 1, 2022. Functional limitations were noted in 109 patients, including 45 subjects with significantly compromised wellbeing. The median duration of symptoms at the initial clinic visit was 285.5 days, and the median number of symptoms was 12 per patient. Fatigue, post-exertional malaise, unrefreshing sleep, brain fog, and sleepiness during the day were common. The median number of symptoms was greater in females than males, with fatigue, dysgeusia, and insomnia being more frequent among females. The authors found a significant correlation between the severity and frequency of symptoms. Symptoms persisted longer than six months for 105 patients, with fatigue, brain fog, post-exertional malaise, insomnia, daytime sleepiness, and unrefreshing sleep being the most common and severe. Most patients referred to the PASC clinic had not been hospitalized or supported with oxygen during acute COVID-19. 43% of patients with PASC and symptoms for longer than six months met the criteria for ME/CFS. The ME/CFS-PASC phenotype, like ME/CFS, was more prevalent in non-hospitalized females.
8/9/2022	Long-COVID treatments: why the world is still waiting (nature.com)	Nature	“Researchers are narrowing in on the pathology that underlies long-COVID. In the next year, key trials could yield results for drugs that target the immune system, blood clots or lurking fragments of the coronavirus itself. A key barrier to developing long-COVID treatments has been uncertainty about the condition’s root cause; current hypotheses are not mutually exclusive. The large number of symptoms associated with long-COVID, coupled with the uncertainty of root cause, complicates clinical trial design. Several trials try to tame errant immune responses. Some of these rely on familiar drugs, such as colchicine, an anti-inflammatory drug that treats gout and is often prescribed to people with long-COVID. Other trials are using drugs that have shown some success in treating severe acute COVID-19, including steroids and other immunosuppressants, such as sirolimus, which is used to prevent organ rejection after a transplant. Small trials and anecdotal reports suggest that antihistamines show some promise, providing a “band-aid solution.” Other approaches aim to manage symptoms, such as extreme fatigue, muscle weakness and memory and concentration difficulties. There are still no registered studies looking at whether the two FDA-approved antivirals ease long-COVID symptoms.
8/10/2022	Distinguishing features of Long COVID identified through immune profiling | medRxiv	Nature (Preprint at medRxiv)	Exploratory analyses identified key significant immunological differences relative to demographically matched control populations at >400 days post infection. A number of significant changes in circulating leukocytes, including increases in non-classical monocytes, activated B cells, double-negative B cells, exhausted T cells, and IL-4/IL-6 secreting CD4 T cells, and decreases in conventional DC1 and central memory CD4 T cells were identified. In addition, antibodies to SARS-CoV-2 antigens and herpesvirus lytic antigens were elevated in participants with long-COVID. In contrast, no significant differences were found for autoantibodies to human exoproteome. Most strikingly among participants with long-COVID, levels of plasma cortisol were roughly half of

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			those found in healthy or convalescent controls. Based on machine learning, cortisol levels alone were the most significant predictor for long-COVID classification, as well as for estimation of Long-COVID Propensity Score. Data suggest the involvement of persistent antigen, reactivation of latent herpesviruses, and chronic inflammation, and are less consistent with the autoantibodies to extracellular antigens.
8/6/2022	Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study - The Lancet	The Lancet	N=4,231 with a history of COVID infection, matched with 8,462 controls. Longitudinal dynamics of 23 somatic symptoms surrounding COVID-19 diagnoses (due to SARS-CoV-2 alpha variant or previous variants) were assessed using 24 repeated measurements between March 31, 2020, and Aug 2, 2021. At 90-150 days post-acute infection, persistent symptoms in COVID-19-positive participants – compared with before COVID-19 and compared with matched controls – included chest pain, difficulties with breathing, pain when breathing, painful muscles, ageusia or anosmia, tingling extremities, lump in throat, feeling hot and cold alternately, heavy arms or legs, and general tiredness. In 12.7% of patients, these symptoms could be attributed to COVID-19. 21.4% of COVID-19-positive participants versus 8.7% of COVID-19-negative controls had at least one of these core symptoms substantially increase (to at least moderate severity) at 90–150 days after COVID-19 diagnosis or matched timepoint.
8/12/2022	The US Now Has a Research Plan for Long COVID—Is It Enough? | Neurology | JAMA | JAMA Network	JAMA	Angela Meriquez Vázquez, MSW, who has had post-COVID symptoms since March 2020 and is president of Body Politic, a global COVID-19 patient support group with 11 000 members, praised the establishment of the federal long-COVID office but pointed out that it still needs congressional funding. She called the plan otherwise "underwhelming." "There's definitely growing frustration that the information that does exist on these conditions is not being readily disseminated by public health out to clinicians, especially primary care. For the most part big investments like the RECOVER Initiative are largely observational and not necessarily driving new research on ME/CFS, or POTS, or MCAS, which is really where I think the patient community wants the research to go in a much bigger way." Yale cardiologist and health policy professor Harlan Krumholz, MD, SM, who was an external advisor on the new plan, said that although this definition is likely to evolve over time, setting it was important. "One of the principal problems is that there are a lot of competing ideas about what exactly Long COVID is." By establishing a broad definition, the government is "giving license to saying that there are lots of different forms of this, and that part of our job on the research side is to begin to organize our knowledge about all these different subgroups."
8/16/2022	MediciNova Reaches Agreement to Participate in Grant-Funded Clinical Trial to Evaluate MN-166 (ibudilast) for the Treatment of Long COVID (yahoo.com)	Yahoo Finance	Biopharmaceutical company MediciNova announced that it plans to participate in RECLAIM (Recovering from COVID-19 Lingering Symptoms Adaptive Integrative Medicine Trial), a grant-funded, multi-center, randomized, clinical trial to evaluate MN-166 (ibudilast) and other therapies for the treatment of long-COVID. MediciNova will collaborate with the University Health Network, an academic health sciences center located in Toronto, which has the largest hospital-based research program in Canada. The trial is funded by the Canadian government through the Canadian Institutes of Health Research (CIHR). The initiation of this trial is pending protocol finalization and regulatory review. MN-166 (ibudilast) is a small molecule compound that inhibits phosphodiesterase type-4 (PDE4) and inflammatory cytokines, including macrophage migration inhibitory factor (MIF). It is in late-stage clinical development for the treatment of neurodegenerative diseases such as ALS, progressive MS, and degenerative cervical myelopathy; as well as for glioblastoma, chemotherapy-induced

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			peripheral neuropathy, and substance use disorder. In addition, MN-166 (ibudilast) was evaluated in patients that are at risk for developing acute respiratory distress syndrome (ARDS).
8/14/2022	'Left to rot': The lonely plight of long Covid sufferers	Politico	At least 90 long-COVID groups exist around the world in 34 countries. Most are pushing for more research, improved clinical treatments and increased access to disability benefits, while others offer support and advice. "We are just left to rot," said Chantal Britt, founder and president of Long Covid Switzerland. "That's why all those organizations are popping up: There is no official help." "Increasingly, the government just wants to move on. Everything's about, 'We must live with COVID now,'" said Jo House, an advocate in the U.K. "There isn't that same sense of urgency, which I think is tragic given the vast number of people who are ill with this." "The government must inform its citizens about this risk so you can make informed choices," said Emma Moderato, a long-COVID advocate in Sweden. "We're often not seen as part of the pandemic."
8/17/2022	Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1,284 ,437 patients	The Lancet Psychiatry	N= 1,284,437 (185,748 children, 856,588 adults, and 242,101 older adults) patients with a recorded history of COVID-19 infection, matched with an equal number of patients with another respiratory infection. Children with a history of COVID-19 infection were twice as likely to suffer from epilepsy or a seizure, and three times as likely to develop a psychotic disorder compared with those recovering from other respiratory illnesses, even if the overall risk of the conditions remain low. Adults aged between 18 and 64 who had recovered from COVID-19 suffered from brain fog at a rate 16 percent higher than patients with other respiratory diseases. In those aged over 65, increased risk was also found for psychosis and dementia. While most outcomes had significantly elevated hazard ratios after 6 months, their risk horizons and time to equal incidence varied greatly. Risks of the common psychiatric disorders returned to baseline after 1–2 months (mood disorders at 43 days, anxiety disorders at 58 days) and subsequently reached an equal overall incidence to the matched comparison group (mood disorders at 457 days, anxiety disorders at 417 days). Risks of cognitive deficit (known as brain fog), dementia, psychotic disorders, and epilepsy or seizures were still increased at the end of the 2-year follow-up period. The risk of neurological and psychiatric diagnoses of COVID-19 was greater with the emergence of the delta variant (e.g., for cognitive deficit, epilepsy or seizures, and ischemic strokes) than just before its emergence. With omicron (N=39,845 in each cohort), there was a lower death rate than just before emergence of the variant, but the risks of neurological and psychiatric outcomes remained similar.

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8/12/2022	Health Care Utilization in the 6 Months Following SARS-CoV-2 Infection	JAMA	This matched retrospective cohort study included 127,859 patients with positive SARS-CoV-2 test results matched to 127,859 patients with negative SARS-CoV-2 test results from 8 large integrated health care systems across the United States who completed a SARS-CoV-2 diagnostic test during March 1 to November 1, 2020. SARS-CoV-2 infection was associated with a 4% increase in health care utilization over 6 months, predominantly for virtual encounters (RRR, 1.14), followed by emergency department visits (RRR, 1.08). COVID-19–associated utilization for 18 post-COVID conditions (PCCs) remained elevated 6 months from the acute stage of infection, with the largest increase in COVID-19–associated utilization observed for infectious disease sequelae (RRR, 86.00), COVID-19 (RRR, 19.47) alopecia (RRR, 2.52), bronchitis (RRR, 1.85), pulmonary embolism or deep vein thrombosis (RRR, 1.74), and dyspnea (RRR, 1.73). In total, COVID-19-associated excess health care utilization amounted to an estimated 27,217 additional medical encounters over 6 months (212.9 visits per 1000 patients).
8/20/2022	Prevalence, trajectory over time, and risk factor of post-COVID-19 fatigue - PMC (nih.gov)	Journal of Psychiatric Research	N=495 acute-COVID-recovered patients. Researchers evaluated fatigue severity at one, three, six, and twelve-months according to Fatigue Severity Scale (FSS) and explored the potential predictor of long-term post-COVID fatigue (six or twelve months FSS). Found that 22%, 27%, 30%, and 34% of patients self-rated fatigue symptoms in the pathological range at one, three, six, and twelve months; detected a worsening of fatigue symptomatology over time. From the elastic net regression results, only depressive symptomatology at one month predicted the presence of post-COVID-19 long-term fatigue. No other clinical or demographic variable was found to predict post-COVID fatigue. The researchers suggest that, rather independent of COVID-19 severity, depression after COVID-19 is associated with persistent fatigue. Clarifying mechanisms and risk factors of post-COVID fatigue will allow to identify the target population and to tailor specific treatment and rehabilitation interventions to foster recovery.
8/22/2022	Long COVID-19 study identifies novel blood markers as potential diagnostic and therapeutic targets (apnews.com)	Associated Press	First study utilizing Somalogic SomaScan® to assess blood samples that had been collected from long-COVID patients who had not been hospitalized (focused on those with neurological symptoms including brain fog, where blood immune cell changes were observed). The samples were used to generate data on up to 7,000 proteins in the blood utilizing a large-scale protein analysis known as proteomics. The analyzed data has identified a number of proteins that are significantly modulated in the blood of Neuro long-COVID patients when compared to convalescent subjects who had recovered from COVID-19 infection with no persistent symptoms and to healthy subjects. This data has been included in recently filed patent applications as potential diagnostic and therapeutic targets for the treatment of long-COVID. Certain targets when combined (as few as 5) identified all 48 Neuro long-COVID patients and the 42 of 44 subjects who were convalescent or healthy controls suggestive of these targets' diagnostic potential. A number of targets (<15) have been identified as potentially amenable to treatment by currently available drugs or other therapeutic approaches on the market. Provisional patent applications have been filed in the US to seek protection for these new inventions. A potential therapeutic marker known to be modulated by ATL1102 in DMD patients has been identified as suggestive of its therapeutic potential as a treatment for long-COVID. Antisense Therapeutics plans to review its new patent applications with targeted pharmaceutical and diagnostic companies for potential commercial discussions.

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8/25/2022	Long COVID in Children Appears Less Common Than Early Fears Suggested - Scientific American	Scientific American	"At that time, some papers were starting to report on pandemic symptoms—children suffering from the 'new normal': the new everyday life with lockdowns and social isolation and a world that was afraid of disease," Berg says. A study published in February in the *Lancet Child & Adolescent Health* offered crucial information about the pandemic's mental health toll on children, regardless of whether they had personally been infected with SARS-CoV-2. An alarming 40 percent of children surveyed—both those who had COVID three months prior and those who had not had it—reported feeling worried, sad or unhappy. Taken together, many recent studies have found the odds of children developing long COVID are low, and other factors—including different respiratory viruses and the pandemic itself—could be to blame for many long-COVID-like symptoms. The welcome news, however, does not negate the fact that debilitating COVID symptoms can persist for months in a small percentage of children, likely because of lingering effects of infection and the body's immune response to it. Even if only a small percentage of children develop long COVID, the sheer number of those who are being infected with SARS-CoV-2 means a significant amount of children are suffering. Freedman argues that vaccination likely helps prevent long COVID in children by lowering the risk of hospitalization. Yonts agrees that the jab is crucial. "Every time you get COVID, it's a gamble," she says. "So anything to do to maximize your protection from that, including vaccination, is kind of no-brainer. At least tip the odds a little bit more in your favor."
8/24/2022	New data shows long Covid is keeping as many as 4 million people out of work (brookings.edu)	Brookings	This report uses data from the Census Bureau's Household Pulse Survey (HPS), which added four questions about long-COVID to the survey in June. Findings: Around 16 million working-age Americans (those aged 18 to 65) have long-COVID today – this represents roughly 8% of working-age Americans. Of those 16 million, two to four million are out of work due to long-COVID. The annual cost of those lost wages alone is around $170 billion a year (and potentially as high as $230 billion). The speed at which this economic burden grows will depend on three factors: (1) The availability and accessibility of improved treatment options that increase the long-COVID recovery rate or move people from "severely ill" to "moderately" or "mildly" ill; (2) Whether vaccines reduce the odds of getting long-COVID; and (3) Whether repeat infections carry additional long -COVID risk