

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.

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Date	Article	Publication	Key Takeaways
May 2022			
5/1/2022	Post-acute COVID-19 is characterized by gut viral antigen persistence in inflammatory bowel diseases - PMC (nih.gov)	Journal of Gastroenterology	<ul style="list-style-type: none"> • Endoscopy study with 46 inflammatory bowel disease (IBD) patients 219 days (range: 94-257) after a confirmed COVID-19 infection. • Findings: Expression of SARS-CoV-2 RNA in the gut mucosa ~7 months after mild acute COVID-19 in 32 of 46 patients with IBD. Viral nucleocapsid protein persisted in 24 of 46 patients in gut epithelium and CD8+ T cells. • Expression of SARS-CoV-2 antigens was not detectable in stool and viral antigen persistence was unrelated to severity of acute COVID-19, immunosuppressive therapy and gut inflammation. • Post-acute sequelae of COVID-19 were reported from the majority of patients with viral antigen persistence, but not from patients without viral antigen persistence. • Conclusion: Results indicate that SARS-CoV-2 antigen persistence in infected tissues serves as a basis for post-acute COVID-19. The concept that viral antigen persistence instigates immune perturbation and post-acute COVID-19 requires validation in controlled clinical trials.
5/4/2022	The Children Left Behind by Long Covid	Bloomberg	<ul style="list-style-type: none"> • “More cases will mean more long-Covid, including pediatric long Covid. Estimates of the number of children who face long-term symptoms are far from precise, but they probably range from 5% to 10% of those infected with the virus, says Daniel Griffin, an infectious diseases expert at Columbia University who treats Covid patients...even at the lower end of the estimates, that translates to more than a half-million children of the 13 million so far infected.” • Even when doctors are attentive, children often can’t or don’t know how to articulate their symptoms. Fatigue is the most prevalent complaint, followed by pain. Difficulty paying attention and altered taste or smell are also common. • “Many children slip through the cracks, though, especially those from Black and Hispanic families. At Children’s National, the clinic primarily sees “affluent, medically literate, White families,” Yonts says, even though Black

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			<p>and Hispanic people in Washington are more likely to have had Covid than Whites. A report out at the end of March, The State of Black America and Covid-19, said there is “already evidence of disparities in diagnosis and access to treatment” regarding long Covid. The group that released the report, the Black Coalition Against Covid, says more efforts are needed to include Black people in trials and treatment programs.”</p>
5/5/2022	Evidence mounts for need to study Pfizer's Paxlovid for long COVID - researchers say Reuters	Reuters	<ul style="list-style-type: none"> • Three new case studies follow earlier reports of long-COVID patients who experienced relief of their symptoms after taking the treatment, which is currently only authorized for high-risk people early after onset of COVID symptoms. • In two of the cases, the patients "were able to access Paxlovid antiviral therapy and feel that their long COVID symptoms improved substantially." • In the third, a patient was given the drug as prescribed to treat an acute infection. While his symptoms improved at first, they rebounded shortly after he stopped taking the drug, and the man later developed long COVID. • All three patients, who were in their 40s and had previously been vaccinated against COVID-19, were enrolled in the UCSF long COVID trial known as LIINC. • "There's been a lot of hope that early antiviral therapy, in addition to preventing severe COVID, will prevent long COVID. And that might be true, but this case suggests that it won't be true 100% of the time," said Dr. Michael Peluso. "It provides evidence that we really need to study this soon, and ... systematically, which means randomized trials." • Pfizer spokesman Kit Longley said company does not have any current long COVID studies underway but was monitoring data from ongoing clinical studies and real-world evidence and may explore the issue further.
5/12/2022	Frontiers The Impact of Initial COVID-19 Episode Inflammation Among Adults on Mortality Within 12 Months Post-hospital Discharge	Frontiers in Medicine	<ul style="list-style-type: none"> • “Hyperinflammation present with severe COVID-19 is associated with an increased mortality risk after hospital discharge. Although suggestive, treatment with anti-inflammatory medications like steroids upon hospital discharge is associated with a decreased post-acute COVID-19 mortality risk. • This suggests that treating inflammation may also benefit other post-acute sequelae like long COVID. A reconceptualization of COVID-19 as both an acute and chronic condition may be useful.”

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5/11/2022	Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study	The Lancet Respiratory Medicine	<ul style="list-style-type: none"> • N=1192. Longitudinal cohort study of individuals who had survived hospitalization with COVID-19 and who had been discharged from hospital between January 7 and May 29, 2020. • Measured health outcomes 6 months, 12 months, and 2 years after symptom onset with a 6-min walking distance (6MWD) test, laboratory tests, and a series of questionnaires on symptoms, mental health, modified British Medical Research Council (mMRC) dyspnea scale, health-related quality of life (HRQoL), return to work, and health-care use after discharge. • The proportion of COVID-19 survivors with at least one sequelae symptom decreased from 68% at 6 months to 55% at 2 years, with fatigue or muscle weakness always being the most frequent. • The proportion of COVID-19 survivors with an mMRC dyspnea score of at least 1 was 14% of 1191 at 2 years, compared to 26% at 6 months. HRQoL continued to improve in almost all domains, especially in terms of anxiety or depression: the proportion of individuals with symptoms of anxiety or depression decreased from 23% at 6 months to 12% at 2 years. Survivors with long-COVID symptoms at 2 years had lower HRQoL, worse exercise capacity, more mental health abnormality, and increased health-care use after discharge than survivors without long COVID symptoms. • COVID-19 survivors still had more prevalent symptoms and more problems in pain or discomfort, as well as anxiety or depression, at 2 years than did controls. • Compared to controls, a significantly higher proportion of survivors who had received higher-level respiratory support during hospitalization had lung diffusion impairment, reduced residual volume, and total lung capacity than did controls.

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5/9/2022	Scientists Discover Genetic Cause Of Lupus, Findings May Help Research On Long Covid. (forbes.com)	Forbes	<ul style="list-style-type: none"> • Toll-like receptor 7 (TLR7), one of the 10 different types found in humans, is in charge of detecting single-stranded RNA in the endosomes of cells — endosomes are “sorting stations”, located within the cytoplasm of cells, that help send important proteins to various destinations within the cell • Although an important component of the antiviral immune response, TLR7 has also been associated with autoimmune disorders. • This is in large part because of its role in regulating inflammation and B cell survival via NF-κB. There appear to be some parallels between the TLR7-driven autoimmunity seen in lupus and the autoimmune aspects of long-COVID. Being a single-stranded RNA virus, SARS-CoV-2 also induces TLR7 activation. • This has been confirmed by studies showing that individuals with TLR7 deficiencies are more likely to develop severe COVID-19. • Like lupus, SARS-CoV-2 infection is accompanied by a proliferation of B cells that have not passed through germinal centers, and therefore maintain the capacity for self-recognition – both lupus and long-COVID are characterized by the persistence of such auto/antibodies. Both lupus and long-COVID are more prevalent in women than in men • Given the results of their latest study, Brown et al. suggest that, in lupus, this may be because the TLR7 gene is found on the X chromosome, and females have two X chromosomes where males have one X and one Y chromosome. • Although one X chromosome is usually inactive in women, silencing of the section of the chromosome on which the TLR7 gene sits is often incomplete. • Dr. Carola Vinuesa, senior author of the study, mentions that “There are other systemic autoimmune diseases, like rheumatoid arthritis and dermatomyositis, which fit within the same broad family as lupus. TLR7 may also play a role in these conditions.” “Perhaps TLR7 may also be to blame for the autoimmune aspects of long-COVID; at the very least, the many parallels between the two suggest it may be worth taking a closer look.”

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5/25/2022	Long COVID after breakthrough SARS-CoV-2 infection	Nature Medicine	<ul style="list-style-type: none"> • Used US Department of Veterans Affairs national healthcare databases to build a cohort of 33,940 individuals with breakthrough infections (BTI) and several controls of people without evidence of SARS-CoV-2 infection, including contemporary ($n=4,983,491$), historical ($n=5,785,273$) and vaccinated ($n=2,566,369$) controls. • At 6 months after infection, the study shows that, beyond the first 30 days of illness, compared to contemporary controls, people with BTI exhibited a higher risk of death (hazard ratio (HR)=1.75) and incident post-acute sequelae (HR=1.50), including cardiovascular, coagulation and hematologic, gastrointestinal, kidney, mental health, metabolic, musculoskeletal and neurologic disorders. • The results were consistent in comparisons versus the historical and vaccinated controls. Compared to people with SARS-CoV-2 infection who were not previously vaccinated ($n=113,474$), people with BTI exhibited lower risks of death (HR=0.66) and incident post-acute sequelae (HR=0.85) • Altogether, the findings suggest that vaccination before infection confers only partial protection in the post-acute phase of the disease; hence, reliance on it as a sole mitigation strategy may not optimally reduce long-term health consequences of SARS-CoV-2 infection. The findings emphasize the need for continued optimization of strategies for primary prevention of BTI and will guide development of post-acute care pathways for people with BTI.

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5/24/2022	Post-COVID Conditions Among Adult COVID-19 Survivors Aged 18–64 and ≥65 Years — United States, March 2020–November 2021	CDC	<ul style="list-style-type: none"> • Case-patients=353,164; Control patients=1,640,776. Patients were followed for 30–365 days after the index encounter until the first occurrence of an incident condition or until October 31, 2021, whichever occurred first. • One in five adult COVID survivors under the age of 65 in the United States has experienced at least one health condition that could be considered long-COVID; one in four for patients 65 and older. • In both age groups, COVID patients had twice the risk of uninfected people of developing respiratory symptoms and lung problems, including pulmonary embolism. • Post-COVID patients aged 65 or older were at greater risk than the younger group of developing kidney failure, neurological conditions and most mental health conditions. • The most common post-COVID conditions, regardless of age, were respiratory problems and musculoskeletal pain. • The risk of post-COVID patients aged 65 and older developing the 26 health conditions the study evaluated was between 20 percent and 120 percent greater than people who didn't get COVID. • Those aged 18 to 64 had a 10 percent to 110 percent greater risk than uninfected people of developing 22 of the health conditions. Between 30 days and 365 days after their COVID diagnosis, 38 percent of the patients experienced one or more new health problems, compared to 16 percent of the non-COVID patients. • The younger age group, 18-to-64, was somewhat less likely to have those problems — 35 percent developed long-COVID issues, compared with 15 percent of uninfected people. In the 65-and-older group, 45 percent had new health conditions, compared with 19 percent of uninfected people. Concluded that nearly 21 percent of the younger group and nearly 27 percent of the older group developed health problems that could be attributed to long-COVID.

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5/24/2022	Evolution of neurologic symptoms in non-hospitalized COVID-19 “long haulers”	Annals of Clinical and Translational Neurology	<ul style="list-style-type: none"> • Follow-up study on non-hospitalized COVID patients evaluated at Northwestern’s Neuro-COVID-19 clinic between May and November 2020. • Patients completed phone questionnaires on their neurologic symptoms, subjective impression of recovery, and quality of life. N=52 patients: 27 SARS-CoV-2+, 25 SARS-CoV-2-. Follow-up occurred at a median 14.8 months after symptom onset. • Mean age was 42.8years, 73% were female, and 77% were vaccinated for SARS-CoV-2. • Overall, there was no significant change in the frequency of most neurologic symptoms between first and follow-up evaluations, including “brain fog” (81 vs. 71%), numbness/tingling (69 vs. 65%), headache (67 vs. 54%), dizziness (50 vs. 54%), blurred vision (34 vs. 44%), tinnitus (33 vs. 42%), and fatigue (87 vs. 81%). • Dysgeusia (63 vs. 27%) and anosmia decreased overall (58 vs. 21%). Heart rate and blood pressure variation (35 vs. 56%) and gastrointestinal symptoms (27 vs. 48%) increased at follow-up. • Patients reported improvements in their recovery, cognitive function, and fatigue, but quality of life measures remained lower than the US normative population. SARS-CoV-2 vaccination did not have a positive or detrimental impact on cognitive function or fatigue • Interpretation: “Non-hospitalized COVID-19 “long haulers” continue to experience neurologic symptoms, fatigue, and compromised quality of life 14.8 months after initial infection.”
5/21/2022	Long Covid Symptoms and Treatment: What We Know So Far	New York Times	<ul style="list-style-type: none"> • Mentioned the Alliance: “Several groups, such as Body Politic, Long Covid Alliance and Survivor Corps, provide emotional support, as well as resources for seeking treatment, disability benefits and patient advocacy.”
5/18/2022	Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study	BMJ	<ul style="list-style-type: none"> • N=28,356 aged 18-69 years who received at least one dose of an adenovirus vector or mRNA COVID-19 vaccine after testing positive for SARS-CoV-2 infection. A first vaccine dose was associated with an initial 12.8% decrease (in the odds of long-COVID). • A second dose was associated with an initial 8.8% decrease in the odds of long-COVID, with a subsequent decrease by 0.8% per week. • Heterogeneity was not found in associations between vaccination and long-COVID by sociodemographic characteristics, health status, hospital admission with

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			<p>acute COVID-19, vaccine type (adenovirus vector or mRNA), or duration from SARS-CoV-2 infection to vaccination.</p> <ul style="list-style-type: none">• Conclusion: " The likelihood of long-COVID symptoms was observed to decrease after COVID-19 vaccination and evidence suggested sustained improvement after a second dose, at least over the median follow-up of 67 days. Vaccination may contribute to a reduction in the population health burden of long covid, although longer follow-up is needed."