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
March 2022			
3/4/2022	Almost a third of people report lingering symptom 6-12 months after COVID-19 -study	Reuters	N=151,880 tested for COVID-19 between September 2020 and April 2021. 61,002 who had tested positive for COVID-19 6, 9, or 12 months before the survey (96% non-hospitalized; 15.6% asymptomatic); 91,878 people who had tested negative. 29.6% of the respondents who had tested positive reported at least one ongoing physical symptom 6 to 12 months after infection, compared to 13% in the control group. The largest risk differences between test-positive and test-negative groups were observed for: dyssomnia (RD = 10.92%); dysgeusia (RD=8.68%); fatigue/exhaustion (RD=8.43%); dyspnea (RD=4.87%); and reduced strength in arms/legs (RD=4.68%). 53.1% of those with positive tests said they had experienced either mental or physical exhaustion, sleep problems or cognitive problems within the 6 to 12 months after infection, compared to 11.5% in the control group. At least one diagnosis of depression, anxiety, chronic fatigue symptom, fibromyalgia, or post-traumatic stress disorder with new onset within the first 6, 9 or 12 months after the test was reported by 7.2% of test-positives, compared to 3.3% of test-negatives. The risk for all symptoms, except for dysgeusia, dyssomnia and runny nose were higher among hospitalized than non-hospitalized individuals. Test-positives reported higher rates of part-time and full-time sick leave than test-negative participants, from 4 weeks after COVID test until completing questionnaire.
3/7/2022	SARS-CoV-2 is associated with changes in brain structure in UK Biobank	Nature	N=785; Aged 51-81; 401 participants in the test-positive group (tested positive between the first and second scans); 384 controls – matched with the test-positive group's rates of obesity, blood pressure, smoking, and diabetes, as well as their socioeconomic status, age and sex. Average of 3 years between scans. Average of 141 days between diagnosis and second scan, for the test-positive group. Compared to controls, test-positive participants were found to have (i) greater reduction in grey matter thickness and tissue-contrast in the orbitofrontal cortex and parahippocampal gyrus, (ii) greater changes in markers of tissue damage in regions functionally connected to the primary olfactory cortex, and (iii) greater reduction in global brain size. The infected participants also showed on average larger cognitive decline between the two timepoints. Importantly, these imaging and cognitive longitudinal effects were still seen after excluding the 15 cases who had been hospitalized.
3/7/2022	Researchers Are Getting Closer to Understanding Long COVID. But Treatments Are Likely Still a Ways Off	TIME	One researcher says the autoantibody finding was the most important, in part because it showed a possible similarity between Long-COVID and the autoimmune disease lupus. While there's no cure for lupus, "there are treatments out there that can be effective, so those would be a line of things that are worth looking at". Another researcher who co-authored a study finding that older people, those with a history of asthma, and people with low levels of certain immunoglobulins were at increased risk of developing Long COVID said "If you have patients who are of older age and/or have a history of asthma, then you could measure their immunoglobulin levels. If those are also relatively low, then you would know this individual has a particularly high risk of developing Long COVID," "You can make sure that individual is very well vaccinated," perhaps getting more regular booster shots than the average person. If researchers learn more about how chronic disease works, it could over time lead to improvements for people who live with a variety of different ailments, says myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) advocate Rivka Solomon. Research is "not really just about Long COVID. It's

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			about the triggers that can lead to the development of chronic diseases." Long-COVID seems to overlap especially significantly with ME/CFS—a condition that can follow viral illnesses and leads to debilitating exhaustion—to the point that some Long COVID patients meet the diagnostic criteria for ME/CFS.
3/8/2022	Toward Unbiased Evaluation of Postacute Sequelae of SARS-CoV-2 Infection: Challenges and Solutions for the Long Haul Ahead	Annals of Internal Medicine	"The first challenge when studying any disease is knowing how to diagnose it, and although we have seen serious medical consequences stemming from COVID-19, we do not yet have definitive diagnostic criteria." "We believe that as more high-quality data emerges, the current list of symptoms will become better refined, and the timing and duration of symptoms will become clearer. So far, however, these have remained elusive." "Now more than ever, we must implement robust, standardized, longitudinal assessments of health and well-being across systems and settings, including premorbid evaluation, to facilitate real-time monitoring of trends." Recommendations: (1) coalesce around a well-delineated and measurable PASC case definition that can be consistently applied, (2) implement similarly robust and standardized measures of potential risk factors and outcomes, (3) consider risk of bias in study designs and provide thorough descriptions of ascertainment methodology and assessment tools to facilitate cross-study comparison of published reports, and (4) be judicious in application of this evolving evidence as we all strive to provide effective and efficient care that reduces prior inequities.
3/9/2022	Association of Vaccination with the Persistence of Post-COVID Symptoms	Journal of General Internal Medicine	N= 453; 324 of whom were vaccinated between baseline and 6-month follow-up. Used data from a cohort of COVID-19 patients enrolled into a prospective registry established at a tertiary care health system in New York City. Participants underwent a baseline evaluation before COVID-19 vaccines were available and were followed 6 months later. Unadjusted analyses did not show significant differences in the baseline to 6-month change in anosmia, respiratory symptoms, depression, anxiety, PTSD, or quality of life among vaccinated vs. unvaccinated patients. Similar results were found in propensity-adjusted comparisons and in secondary analyses based on the number of vaccine doses received.
3/15/2022	Quantitative Chest CT Assessment of Small Airways Disease in Post-Acute SARS-CoV-2 Infection	Radiology	Participants: 100 adults with confirmed COVID-19 who had remained symptomatic more than 30 days following diagnosis; 106 healthy, non-infected individuals. Of the 100 COVID-19 participants: Median age=48; 67 non-hospitalized; 17 hospitalized; 16 ICU. Researchers detected air trapping on expiratory chest CT images in the COVID-19 group. The percentage of lung affected by air trapping was similar across COVID-19 severity groups: Non-hospitalized: 25.4%; Hospitalized: 34.6%, Requiring intensive care: 27.3%, Healthy controls: 7.2%. The median time from diagnosis to chest CT imaging was approximately 75 days. Air trapping persisted in 8 of the 9 participants who underwent imaging more than 200 days after diagnosis

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3/13/2022	Long COVID in Children and Adolescents: A Systematic Review and Meta-analyses	medRxiv (preprint)	N=80,071 children who had been infected with COVID-19. A systematic review and meta-analyses of 21 studies that met the inclusion criteria. Inclusion criteria: 1) a minimum of 30 patients, 2) ages ranged from 0 to 18 years, 3) published in English, 4) published before February 10th, 2022, and 5) meets the National Institute for Healthcare Excellence (NICE) definition of long-COVID, which consists of both ongoing (4 to 12 weeks) and post-COVID-19 (≥12 weeks) symptoms. The prevalence of long-COVID was 25.24%, and the most prevalent clinical manifestations were mood symptoms (16.50%) fatigue (9.66%), and sleep disorders (8.42%). When compared to controls, children infected by SARS-CoV-2 had a higher risk of persistent dyspnea (OR 2.69), anosmia/ageusia (OR 10.68), and/or fever (OR 2.23). The main limitation of these meta-analyses is the probability of bias, which includes lack of standardized definitions, recall, selection, misclassification, nonresponse and/or loss of follow-up, and the high level of heterogeneity.
3/11/2022	The Pandemic After the Pandemic	The Atlantic	"But for all we know now about long-COVID, it is still not enough. Researchers still don't know who's most at risk, or how long the condition might last; whether certain variants might cause it more frequently, or the extent to which vaccines might sweep it away. We do not have a way to fully prevent it. We do not have a way to cure it. We don't even have a way to really quantify it: There still isn't consensus on how common long-COVID actually is. Its danger feels both amorphous and unavoidable." "It's going to continue to affect people, even people who are protected from severe illness during the acute phase of infection." – Michael Peluso, an infectious-disease physician and long-COVID researcher at UC San Francisco
3/17/2022	COVCOG 2: Cognitive and Memory Deficits in Long COVID: A Second Publication From the COVID and Cognition Study	Frontiers in Aging Neuroscience	181 long-COVID patients; 185 healthy, non-infected controls. Study participants were recruited between October 2020 and March 2021; the majority suffered COVID-19 at least six months before the study began. Very few participants had been ill enough with COVID-19 to be hospitalized. Found that, among the long-COVID group: 78% reported difficulty concentrating; 69% reported brain fog; 68% reported forgetfulness; and 60% reported problems finding the right word in speech.
3/16/2022	Long Covid Could Reveal Clues to Alzheimer's, Lyme Disease	The Washington Post via Bloomberg	"A recent brain scanning study showed that people who had tested positive showed tiny but statistically significant changes in the brain regions that govern smell, which Albers says suggests that Covid could lead to inflammation of this part of the brain — the same part that's associated with early Alzheimer's disease." "The brain imaging study shouldn't be interpreted to mean that Covid-19 causes dementia. The changes measured were minuscule and not linked to any lingering symptoms, and there's a certain expected natural fluctuation in people's brain images." "Levy says funding research into long Covid could help people who suffer from other maladies. "There's definitely an urgent need to learn more about long Covid for the hundreds of thousands or millions of people that are experiencing it. I would also say that there is much to learn from long Covid that may translate to other conditions."" "The majority of people who get Covid are fine, but even if only 5 or 6% have long-term symptoms, that still adds up to a lot of people. With tens of millions of people having been infected, that's many, many people "who are still bearing the wounds and scars from it."" "Funding more research is essential for making sure we're channeling resources toward measures that work."

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3/21/2022	Risks and burdens of incident diabetes in long COVID: a cohort study	The Lancet Diabetes & Endocrinology	Cohort of 181,280 participants who had a positive COVID-19 test between March 1, 2020, and Sept 30, 2021, and survived the first 30 days of COVID-19; a contemporary control (n=4,118,441) that enrolled participants between March 1, 2020, and Sept 30, 2021; and a historical control (n=4,286,911) that enrolled participants between March 1, 2018, and Sept 30, 2019. Participants in all three comparison groups were free of diabetes before cohort entry and were followed up for a median of 352 days. Compared with the contemporary control group, people with COVID-19 exhibited an increased risk (hazard ratio: 1.40) and excess burden (13.46 per 1000 people at 12 months) of incident diabetes; and an increased risk (HR 1.85) and excess burden (12.35 per 1000 people at 12 months) of incident antihyperglycemic use. Risks and burdens of post-acute outcomes increased in a graded fashion according to the severity of the acute phase of COVID-19 (whether patients were non-hospitalized, hospitalized, or admitted to intensive care). All the results were consistent in analyses using the historical control as the reference category.
3/16/2022	Post-COVID-19 syndrome: assessment of short- and long-term post-recovery symptoms in recovered cases in Saudi Arabia	Infection	N=744 individuals with initial COVID-19 infections between April 2020 and December 2021. 47.5% of patients had ongoing symptoms and, of that group, more than half had two or more symptoms.Three most common symptoms: fatigue (25.4%), headache (15.9%), and myalgia (8.5%).
3/14/2022	Assessing the impact of COVID-19 at 1 year using the SF-12 questionnaire: Data from the Anticipate longitudinal cohort study	International Journal of Infectious Diseases	Prospective, single center observational cohort study. N=155 COVID-19 patients; aged 31-52 years; mix of hospitalized and non-hospitalized. Participants were seen at a dedicated long-COVID clinic twice, at 2-4 months and 7-14 months post-infection. The main objectives of this study are to assess the longitudinal impact of COVID-19 in patients using the 12-item Short Form Survey (SF-12) score, a Health-Related Quality of Life tool, and to identify predictors of developing long-COVID The overall cohort had significantly reduced Physical Composite Score (PCS) of the SF-12. Participants with long-COVID had significantly lower (worse) scores than those without symptoms at 1 year follow up, and scores for these patients did not improve over the two timepoints. Fatigue was the most common symptom. Those with five or more symptoms at initial diagnosis had lower physical composite and mental composite scores at 1 year. Predictors of long-COVID at 1-year were lower physical composite score and higher baseline heart rate at clinic review median 3 months after COVID-19.
3/24/2022	Evidence grows that vaccines lower the risk of getting long COVID	NPR	"…there is now a growing body of research that's offering at least some reassurance for those who do end up getting infected — being fully vaccinated seems to substantially cut the risk of later developing the persistent symptoms that characterize long COVID. While many of the findings are still preliminary, the handful of studies that have emerged in the past half year are telling a relatively consistent story." "It may not eradicate the symptoms of long COVID, but the protective effect seems to be very strong," says epidemiology professor Michael Edelstein, of Bar-Ilan University in Israel, who's studying long COVID.

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3/23/2022	Visual interpretation of brain hypometabolism related to neurological long COVID: a French multicentric experience	European Journal of Nuclear Medicine and Molecular Imaging	From the beginning of August 2021 to the end of October 2021, F-FDG PET scans of patients referred for suspected neurological long COVID with positive RT-PCR and/or serology tests for SARS-CoV-2 infection were retrospectively reviewed in three French nuclear medicine departments. On average, PET scans were performed at 10.9 months from symptom onset. N= 143 patients; median age = 47.4 years old; 98 women. 53% of the scans were visually interpreted as normal, 21% as mildly to moderately or incompletely affected, and 26% as severely affected according to the COVID hypometabolic pattern.
3/23/2022	Long Covid could create a generation affected by disability, expert warns	The Guardian	"It's kind of an anathema to me that we've kind of thrown in the towel on control of omicron wave infections and have said 'it's endemic, and we don't care anymore, because it's very benign'," he said. "It just isn't. And there are new people joining the long-COVID support groups all the time with their disabilities. It's really not OK, and it's heartbreaking." "This is a global problem," said Altmann. "We've got at least 5 million people on the planet with long-COVID – [that is] very much a lower limit estimate. And they've all got a wide array of problems and they are big problems. It's going to drive people out of housing, out of work and in some cases, to suicide."
3/21/2022	Official U.S. Long Covid-19 Data Two Years Away, Hurts Research	Bloomberg Law	Reps. Don Beyer (D-Va.) and Ayanna Pressley (D-Mass.) asked the CDC in a January letter to publicly release their findings on how many people have long-COVID and to break that data down by race, ethnicity, age, gender, previous disability, and other demographic characteristics. Aaron Fritschner, a spokesman for Beyer, said his office got a briefing from the agency in response and were told the CDC "would not internally have a dataset from which they could publicly post disaggregated data for two years." The lawmakers' aides weren't provided any data at all.
3/25/2022	Drugmakers, scientists begin the hunt for long COVID treatments	Reuters	Leading drugmakers, including those who have launched antiviral pills and monoclonal antibodies for COVID-19, are having early discussions with researchers about how to target long-COVID. GlaxoSmithKline (GSK.L), Vir Biotechnology (VIR.O) and Humanigen (HGEN.O) confirmed they had spoken to researchers on trials using their current treatments against long-COVID. Others including Pfizer (PFE.N) and Roche (ROG.S) said they are interested but would not elaborate on plans. There are fewer than 20 clinical trials underway testing drugs, a handful of which have moved beyond early stages, according to interviews with more than a dozen independent and government-backed scientists and a Reuters review of a global clinical trials database.
3/23/2022	Post-COVID-19 syndrome and humoral response association after one year in vaccinated and unvaccinated patients	Clinical Microbiology and Infection	Interviews investigated post-COVID-19 syndrome 6 and 12 months after the disease onset of all adult in- and outpatients with COVID-19 attending Udine Hospital (March–May 2020). N=479; median age: 53 years. Post-COVID-19 syndrome was observed in 47.2% (226/479) of patients after one year. There were no significant differences in the worsening of post-COVID 19 symptoms among vaccinated (n=132) and unvaccinated (n=347) patients. The presence of non-RBD SARS-CoV-2 IgG induced by natural infection showed a significant association with post-COVID-19 syndrome, and median non-RBD SARS-CoV-2 IgG titres were significantly higher in long-haulers than in patients without symptoms 22 after one year. In contrast, the presence of RBD SARS-CoV-2 IgG (vaccine immunity) was not associated with the occurrence of post-COVID-19 syndrome and RBD SARS-CoV-2 IgG titres were similar in long-haulers, compared to patients without symptoms. The results of this prospective study indicate that: (a) post-COVID-19 syndrome rates are high up to one year after acute infection; (b) receiving the SARS-CoV-2 vaccination is not associated with worsening post-COVID-19 symptoms; and (c) the persistence of a high titre

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			serological response induced by natural infection, but not by vaccination, may play a role in long-COVID.
3/25/2022	Understanding Long Covid	New York Times	Discusses prevalence, theories of causation, risk factors, protective effect of vaccines. Causation: "There are different theories, but one of the leading theories has to do with the body's inflammatory reaction."; "Another theory is that the body's immune response didn't shut down after the acute threat from the virus was defeated." Risk factors: latent Epstein-Barr, high viral load at initial infection, autoantibodies, and certain comorbidities like diabetes. "A couple of studies have suggested that if you've been vaccinated and are then infected with COVID, it might make you less likely to have lingering symptoms, but at least one study suggested that vaccination didn't make any difference. If you consider that vaccines, generally put you at lower risk for acute outcomes like hospitalization, then it makes sense that there might be some positive effect on reducing long-term symptoms. But having a mild COVID infection definitely doesn't prevent long-COVID— many people with long-COVID did not get very sick initially or might even have had an asymptomatic COVID infection." "There has been some skepticism about long Covid, including from primary physicians, and a lot of throwing up of hands. People may find that they go to their primary physician, and they get a scan, and nothing shows up. A lot of times there isn't anything physically that an X-ray or blood test can show…It may be better to try to seek help from a long-COVID clinic at that point where at least you will get recognition that what you're going through is a real thing and needs attention."
3/24/2022	Different SARS-CoV-2 variants may give rise to different long COVID symptoms, study suggests	European Society of Clinical Microbiology and Infectious Diseases	Research to be presented at the European Congress of Clinical Microbiology & Infectious Diseases on April 23-26. Researchers did a retrospective observational study of 428 patients treated at the Careggi University Hospital's post-COVID outpatient service between June 2020 and June 2021, when the original form of SARS-CoV-2 and the Alpha variant were circulating in the population. Patients had been hospitalized with COVID-19 and discharged 4-12 weeks before attending a clinical visit at the outpatient service and completing a questionnaire on persistent symptoms; median time between discharge and study participation = 53 days. 76% of patients reported at least one persistent symptom. The most common reported symptoms were shortness of breath (37%) and chronic fatigue (36%), sleep problems (16%), vision problems (13%), and brain fog (13%). Analyses suggest that people with more severe forms, who required immunosuppressant drugs such as tocilizumab, were six times as likely to report long-COVID symptoms, while those who received high flow oxygen support were 40% more likely to experience ongoing problems. Women were almost twice as likely to report symptoms of long-COVID. Researchers performed a more detailed evaluation comparing the symptoms reported by patients infected between March and December 2020 (when the

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			original SARS-COV-2 was dominant) with those reported by patients infected between January and April 2021 (when Alpha was the dominant variant).
3/27/2022	How covid brain fog may overlap with 'chemo brain' and Alzheimer's	The Washington Post	"There is humongous overlap" between long-COVID and other long-studied brain conditions, including "chemo brain," Alzheimer's and other post-viral syndromes following infections with influenza, Epstein-Barr, HIV or Ebola. – Avindra Nath, intramural clinical director of the neurological disorders and stroke unit of the National Institutes of Health. She's optimistic that some of the symptoms people are experiencing post-covid are reversible, and there's already talk about testing drugs in clinical trials to treat "chemo brain" for those suffering from severe covid brain fog. "We are not starting from nothing," she said, "and I think that's very hopeful."
3/28/2022	Back-to-Office Pressure Is Creating a Crisis for Long COVID Patients	TIME	"Many people with long-COVID symptoms are unable to work or must do their jobs through extreme discomfort. Other long-haulers have been unable to secure disability benefits, in many cases because their symptoms defy easy explanation or documentation, making it difficult to prove they meet the standard for disability." "Millions of people in the U.S. have chronic illnesses or physical disabilities, and advocates have been calling for better workplace accommodations and federal disability policies since well before the pandemic. But two big changes in the workforce—an alarming number of newly disabled adults in the U.S. (many of them likely long-haulers) and millions of open jobs that need to be filled—may finally force companies to become more accommodating."
3/31/2022	The Long Covid Puzzle Is Getting More Complicated	Bloomberg	"Much information has been gathered about long-COVID since the pandemic's first wave in 2020, yet less is known about whether its symptoms are attenuated by various treatments, vaccination, pre-existing immunity and newer virus strains, including delta and omicron." "There are a lot of variations that may explain differences in long-COVID features over time — the variant that caused the infection is only one of them," said Ziyad Al-Aly, a clinical epidemiologist at Washington University in St. Louis who has been researching the long-term impacts of Covid for more than a year. "The complexity lies in the myriad of symptomatology — and it's immense," says Cliff Rosen, a professor of medicine at Tufts University School of Medicine and the director of clinical and translational research at Maine Medical Center's Research Institute in Scarborough, who is involved in the NIH research, known as the Recover initiative. "It was easy when we had one viral strain at the beginning and then people got symptoms afterwards. Now we've had three more strains and people are vaccinated." Rosen isn't optimistic that meaningful results will come anytime soon. "It's going to be a while before we figure this out," he said.

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3/29/2022	Long Covid May Become a Crisis for Black Americans, Experts Say	The New York Times	"But health experts warn that crucial data is missing: Black Americans have not been sufficiently included in long-COVID trials, treatment programs and registries, according to the authors of a new report released on Tuesday." "We expect there are going to be greater barriers to access the resources and services available for long-COVID," said one of the authors, Dr. Marcella Nunez-Smith, who is the director of Yale University's health equity office and a former chair of President Biden's health equity task force. "So much of even getting a long-COVID diagnosis is tied to having had a positive test right at the beginning," said Dr. Nunez-Smith, adding that early on in the pandemic, many Black Americans "weren't able to secure a test and in some cases, were denied testing." She emphasized the importance of investing adequate resources into studying long-COVID. "Like everything else, without intentionality, we're not going to get to equity there," she said.
3/28/2022	Associations between persistent symptoms after mild COVID-19 and long-term health status, quality of life, and psychological distress	Influenza and Other Respiratory Viruses	This study characterized the trajectories of COVID-19 symptoms before, during, and 6 to 11 months post-acute and mild COVID-19 infection and evaluated the long-term self-reported aspects of health, quality of life (QoL), and psychological distress. N= 397 non-hospitalized adults who tested positive for COVID between April and June of 2020. 44% had persistent COVID-19 symptoms at the time of long-term follow-up, and 56% had no persistent symptoms. Among the 176 who had persistent symptoms and completed Part 1 of the study, the symptoms most frequently reported as the most severe among all eight potential persistent symptoms were: fatigue (31%), shortness of breath (20%), difficulty with concentration (9%), and loss of smell (9%). Of 221 participants who did not have persistent symptoms at long-term follow-up, 55% of participants recovered in less than a month after COVID-19 diagnosis, 33% in 1 to 3 months, 9% in 3 to 6 months, 2% after 6 months. The median attributable persistent COVID-19 symptom burden score was 2 (on a 0-4 scale); higher scores were associated with lower overall health