Long COVID: Rapid Evidence Review

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Postacute sequelae of COVID-19, also known as long COVID, affects approximately 10% to 30% of the hundreds of millions of people who have had acute COVID-19. The Centers for Disease Control and Prevention defines long COVID as the presence of new, returning, or ongoing symptoms associated with acute COVID-19 that persist beyond 28 days. The diagnosis of long COVID can be based on a previous clinical diagnosis of COVID-19 and does not require a prior positive polymerase chain reaction or antigen test result to confirm infection. Patients with long COVID report a broad range of symptoms, including abdominal pain, anosmia, chest pain, cognitive impairment (brain fog), dizziness, dyspnea, fatigue, headache, insomnia, mood changes, palpitations, paresthesias, and postexertional malaise. The presentation is variable, and symptoms can fluctuate or persist and relapse and remit. The diagnostic approach is to differentiate long COVID from acute seguelae of COVID-19, previous comorbidities, unmasking of preexisting health conditions, reinfections, new acute concerns, and complications of prolonged illness, hospitalization, or isolation. Many presenting symptoms of long COVID are commonly seen in a primary care practice, and management can be improved by using established treatment paradigms and supportive care. Although several medications have been suggested for the treatment of fatigue related to long COVID, the evidence for their use is currently lacking. Holistic treatment strategies for long COVID include discussion of pacing and energy conservation; individualized, symptom-guided, phased return to activity programs; maintaining adequate hydration and a healthy diet; and treatment of underlying medical conditions. (Am Fam Physician. 2022;106(5):523-532. Copyright © 2022 American Academy of Family Physicians.)

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This article summarizes the best available evidence for the diagnosis and management of postacute sequelae of COVID-19 (PASC), also called long COVID, in adults. Proposed etiologies for long COVID include residual damage from acute infection, ongoing viral activity within an intrahost viral reservoir, complications from a

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See related editorial on page 488.

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 494.

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Patient information: A handout on this topic, written by the authors of this article, is available with the online version of this article.

hyperinflammatory state, immune dysfunction, and unmasking of preexisting health conditions.^{1,2}

Epidemiology

- Data show that long COVID affects approximately 10% to 30% of the hundreds of millions of people who have had acute COVID-19.^{3,4} The Centers for Disease Control and Prevention reports that 19% of adults who had COVID-19 in the past are still experiencing symptoms.⁵
- Reliable data on long COVID in children are lacking. 1,6
- Illness from COVID-19 has immediate and long-term consequences that can be conceptualized in three phases. Patients do not routinely develop all three.⁷
 - Phase 1. An acute illness with varying degrees of severity caused by viral replication and initial immune response lasts days to weeks. Asymptomatic patients can also progress to later phases of the illness.⁷
 - Phase 2. A rare hyperinflammatory illness known as multisystem inflammatory syndrome may occur two to five weeks after onset

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
COVID-19 vaccination is recommended to reduce the risk of acute infection and serious illness. ¹⁴	Α	Multiple ran- domized trials
COVID-19 vaccination is recommended to reduce the risk of long COVID. ¹⁴	В	Observationa study
A basic laboratory panel, including complete blood count, comprehensive metabolic panel, C-reactive protein, erythrocyte sedimentation rate, ferritin, thyroid stimulating hormone, vitamin D, and vitamin B_{12} , should be obtained to identify treatable conditions. Directed diagnostic testing should be offered based on history and physical examination findings and the persistence and severity of symptoms. 1	С	Consensus, expert opinio
An individualized, structured, symptom-guided, phased return to activity program is recommended for patients with fatigue or postexertional malaise. ²⁰	С	Consensus, expert opinio
Patients with cognitive impairment from long COVID should be referred to a specialist with expertise in formal cognitive assessment and remediation. ³⁸	С	Consensus, expert opinio
Energy conservation strategies such as the four P's framework (pacing, prioritizing, positioning, and planning) and the stop, rest, pace strategy, and avoiding relapsing triggers are recommended to help patients with fatigue related to COVID-19. ^{20,28}	С	Consensus, expert opinio
Patients should be counseled that most individuals experience resolution of some or all symptoms over time; however, there are varying rates of recovery, outcomes differ among patients, and the long-term prognosis of long COVID is unclear. ^{1,3,24,46}	С	Consensus, expert opinio
A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-qu C = consensus, disease-oriented evidence, usual practice, expert opinion, or case se SORT evidence rating system, go to https://www.aafp.org/afpsort.		

of the infection.7-10 Multisystem inflammatory syndrome can affect children and adults and is caused by a dysregulated immune response with signs and symptoms similar to Kawasaki disease.7,8

- Phase 3. Long COVID may develop and can last for months.1-4
- A 2022 study identified type 2 diabetes mellitus, SARS-CoV-2 viremia, Epstein-Barr virus viremia, and specific autoantibodies as risk factors for long COVID.11 Additional risk factors suggested by other studies include age older than 50 years, female sex, more severe acute infection, more than five symptoms in the first week of acute infection, immunosuppressive conditions, underlying health conditions (e.g., hypertension, obesity, psychiatric condition), and partial or no vaccination. 12-17
- In a large community-based sample, the risk of long COVID in fully vaccinated individuals with breakthrough COVID-19 is less than in partially or unvaccinated individuals. 14,18
- Patients with long COVID report decreased quality of life on standardized testing.17

Diagnosis

- The Centers for Disease Control and Prevention defines long COVID as the presence of new, returning, or ongoing symptoms associated with acute COVID-19 that persist beyond 28 days,18 whereas the World Health Organization defines long COVID as symptoms that last for at least two months.19
- The diagnosis of long COVID can be based on a prior clinical diagnosis of COVID-19 with ongoing symptoms. A prior positive polymerase chain

reaction or antigen test result to confirm SARS-CoV-2 infection is not required.¹ People with COVID-19 may have been asymptomatic or may not have had access to testing, and 10% to 20% do not produce detectable antibodies.^{1,20,21}

- The differential diagnosis includes acute sequelae of COVID-19, previous comorbidities, unmasking of preexisting health conditions, reinfection, new acute concerns, and complications of prolonged illness, hospitalization, or isolation.^{1,15,22}
- Review of the patient's medical history should assess for conditions that could impact severity of COVID-19, including asthma, chronic fatigue, chronic kidney disease, diabetes, heart conditions, pulmonary disease, mood disorders, and trauma.¹
- Physicians should advise patients that long COVID is not fully understood and be sensitive to patient concerns that symptoms could be misattributed to psychiatric causes.¹

SIGNS AND SYMPTOMS

• Patients with long COVID report a broad range of symptoms, most of which are common presentations in primary care. 1,23,24

- Presentation is variable, and symptoms can fluctuate or persist and relapse and remit. 17,20,22,23
- Common symptoms include abdominal pain, anosmia, chest pain, cognitive impairment (brain fog), dyspnea, fatigue, headache, insomnia, dizziness, mood changes, palpitations, paresthesias, and postexertional malaise (*Table 1*^{17,25-27}). The severity of these symptoms may not be consistent with objective findings.¹
- A comprehensive review of symptom prevalence and trajectory found that in patients who recovered within 90 days, symptoms peaked during the second week. In patients who did not recover before 90 days, symptoms peaked at two months.²³
- The most common symptoms after six months are fatigue, postexertional malaise, and cognitive dysfunction.²³
- A survey showed that 85.9% of patients with symptoms of long COVID lasting for more than six months experienced relapses, triggered mainly by physical activity, stress, exercise, or mental activity.²³
- Postexertional malaise, a hallmark of long COVID, is a disabling, often delayed exhaustion

TABLE 1

Prevalence of Common Signs and Symptoms of Long COVID

Cardiac

Chest pain (5% to 16%)

Palpitations (5% to 14%)

Hypertension (1%)

Dermatologic

Alopecia (7% to 25%)

Flushing (5%)

Rash, such as urticaria or livedo reticularis (3%)

Ear, nose, and throat

Ageusia/parageusia (4% to 23%)

Anosmia/parosmia (6% to 21%)

Voice changes (8%)

Nasal congestion (5%)

Throat pain (2% to 5%)

Gastrointestinal

Appetite changes (6% to 17%)

Nausea/vomiting (6% to 8%)

Diarrhea (4% to 8%)

Abdominal pain (2% to 6%)

Neurologic

Difficulty concentrating (18% to 27%)

Insomnia/sleep disorders (11% to 27%)

113011111a/3(ccp disorders (11% to 27%)

Cognitive impairments (17% to 26%) Memory deficits (16% to 19%)

Headaches (5% to 12%)

Dizziness (3% to 4%)

Paresthesias, including focal, diffuse, and changing locations (9%)

Vision changes (5%)

Psychiatric

Anxiety (13% to 30%)

Depression (8% to 23%)

Posttraumatic stress disorder (1% to 13%)

Dyspnea (18% to 30%)

Cough, new or progressive (5% to 15%)

Systemic

Fatigue (28% to 58%)

Night sweats (17% to 24%)

Weight loss (12% to 21%)

Mobility decline (14% to 20%)

Decreased exercise tolerance (15%)

Fever (0.3% to 11%)

Rheumatologic

Arthralgia (9% to 14%) Myalgia (8% to 13%)

Note: Percentages represent median prevalence in systematic reviews.

Information from references 17 and 25-27.

disproportionate to the effort exerted. It is characterized by improvement followed by severe exhaustion and worsening of symptoms requiring several days or weeks of recovery.^{1,20,28} Similar to other relapsing symptoms, postexertional malaise can be triggered by routine physical activities (e.g., bathing), cognitive activities, and emotional stress.^{1,20,23,28} The onset of symptoms is often delayed (12 to 72 hours after activity) with unpredictable severity.^{1,28} Postexertional malaise is distinct from fatigue, which is a feeling of weariness, tiredness, or lack of energy.²⁰

- The fatigue experienced in long COVID is often multifactorial and may appear similar to myalgic encephalomyelitis (chronic fatigue syndrome). Myalgic encephalomyelitis is a complex, severe, multisystem syndrome characterized by postexertional malaise that often follows a viral illness. 20,28,29 Although patients with long COVID can meet criteria for myalgic encephalomyelitis, more data are needed to better understand if fatigue related to long COVID represents a distinct process or is a manifestation of myalgic encephalomyelitis. 20
- Autonomic dysfunction (dysautonomia) such as postural orthostatic tachycardia syndrome (POTS) commonly occurs in long COVID and may include abdominal pain, bloating, blurry or tunnel vision, constipation or loose stools, dizziness, fatigue, labile blood pressures, light-headedness, orthostatic intolerance, palpitations, peripheral vasoconstriction, nausea, night sweats, tachycardia, and temperature intolerance.^{2,30,31} See *Table 2* for diagnostic criteria of POTS.³²

DIAGNOSTIC TESTING

- A basic laboratory panel, including complete blood count, comprehensive metabolic panel, C-reactive protein, erythrocyte sedimentation rate, ferritin, thyroid stimulating hormone, vitamin D, and vitamin B₁₂, should be obtained to identify treatable conditions.¹
- Further diagnostic testing is guided by specific history and physical examination findings, persistence and severity of symptoms, the possibility of other post-COVID complications, and a shared understanding of the risks and benefits. 1,3,22,24,33
- Targeted evaluation and management for symptom complexes associated with long COVID are summarized in *Table 3*. ^{1,3,20,24,31,34-42}

- Although laboratory and diagnostic test results are commonly normal in patients with long COVID, clinicians should not disregard the impact of symptoms on a patient's daily functioning, quality of life, and ability to return to school or work.^{1,17}
- Clinical assessment tools and survey instruments for long COVID are listed in *eTable A*. These tools can be considered to evaluate a patient's functional ability and monitor symptoms in various domains. *Figure 1* is an algorithm for determining a patient's self-reported functional status.⁴³

Treatment

- Treatment recommendations for long COVID are based on expert opinion and consensus guidelines in the absence of clinical trials. 1,20,22,24,38,44 The goal of treatment is to optimize function and improve quality of life. 1
- A comprehensive plan of care requires a whole-patient perspective representative of the patient's presenting symptoms, underlying conditions, psychological well-being, personal and social situations, and treatment goals.^{1,3}
- An individualized, symptom-guided, phased return to activity program is recommended for patients with fatigue or postexertional malaise (*Table 4*).²⁰ This is different from graded exercise therapy, which is controversial in the management of myalgic encephalomyelitis. Before initiating a program, patients should be assessed for fatigue patterns throughout the day and advised to avoid

TABLE 2

Diagnostic Criteria for Postural Orthostatic Tachycardia Syndrome

Heart rate increase of 30 beats per minute or more, or more than 120 beats per minute within the first 10 minutes of standing, in the absence of orthostatic hypotension; in children and adolescents, the standard is a heart rate increase of 40 beats per minute or more

Symptoms of orthostatic intolerance

Note: Postural orthostatic tachycardia syndrome is commonly diagnosed by a tilt table test; however, it can also be diagnosed with heart rate and blood pressure measurements taken in the supine position and then in the standing position at two-, five-, and 10-minute intervals

Information from reference 32.

- activities that trigger postexertional malaise. The appropriate range of activities used in the program is highly dependent on the patient. Guidelines also recommend assessing a patient's response to initiating and escalating activities.20
- Patients with cognitive impairment as a result of long COVID should be referred to a specialist with expertise in formal cognitive assessment and remediation (e.g., neuropsychologist, speech-language pathologist, occupational therapist).38

- · Clinicians should address polypharmacy and, if possible, discontinue medications that may impact cognition.38
- Patients with ongoing cough and dyspnea may benefit from breathing exercises that focus on optimal body position and posture (see patient handout with the online version of this article), pulmonary rehabilitation for pulmonary disease, and a phased return to activity program. 15,22,39
- The recommended treatment for dysautonomia (e.g., POTS) includes dietary and behavior

TABLE 3

Evaluation and Management of Symptom Complexes Associated With Long COVID

Symptom complex	Differential diagnosis	Initial evaluation*	Treatment†
Anosmia/ parosmia ²⁴	Allergies, postnasal drip	Consider allergy testing	Smell training (see patient handout with the online version of this article) Consider intranasal steroids
Autonomic dysfunction/dysau- tonomia ^{24,31,34-37}	POTS, deconditioning, dehydration, mast cell activation syndrome, inappropriate sinus tachycardia, Sjögren syndrome, systemic lupus erythematosus, paraneoplastic syndrome, arrhythmia due to cardiac or pulmonary disease, thyrotoxicosis, celiac disease	CBC, complete metabolic panel, thyroid stimulating hormone Orthostatic vital signs (Table 2), ECG, autonomic reflex testing Consider vitamin B ₁₂ , celiac panel, ambulatory heart rate monitoring, echocardiography	Fluid and salt repletion, compression garments Sleeping in the head-up position Isometric exercises Small, more frequent meals Physical reconditioning program (when stable) Avoidance of triggers Medications: propranolol, fludrocortisone, pyridostigmine, midodrine
Brain fog (e.g., difficulty concen- trating, memory deficits, cognitive impairment) ³⁸	Stroke, progressive neurologic illness (e.g., multiple sclerosis, dementia), sleep disorder, encephalop- athy, mood disorders, fatigue, traumatic brain injury, endocrine and autoimmune disorders	Montreal Cognitive Assessment CBC, vitamin B ₁₂ , vitamin D, thiamine, folate, homocysteine, magnesium, complete metabolic panel, liver function tests, thyroid function tests Consider neuropsychological testing (CT or magnetic resonance imaging of the head)	Referral to specialist with expertise in formal cognitive assessment and remediation Paced return to activity Polypharmacy reduction Discontinuation of medications that may impact cognition, if possible Sleep hygiene

Note: For a broader listing of symptoms and guidance, refer to reference 24. For links to functional capacity tests and survey instruments for long COVID, see eTable A with the online version of this article.

CBC = complete blood count; CT = computed tomography; ECG = electrocardiography; POTS = postural orthostatic tachycardia syndrome; STOP-BANG = snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck circumference, and gender.

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^{*—}These are testing options to consider if symptoms are concerning or persistent and do not represent a listing of required studies, which should be directed by the history, examination, and other objective findings.

^{†—}Consider specialty referrals if patients do not respond to initial treatment, for complex or severe presentations, or for new abnormalities on imaging or procedural studies. Underlying conditions should be treated when indicated.

TABLE 3 (continued)

Evaluation and Management of Symptom Complexes Associated With Long COVID

		·		
Symptom complex	Differential diagnosis	Initial evaluation*	Treatment†	
Breathing discomfort ^{1,3,24,39}	Anemia, asthma, heart failure, pneumonia, pulmonary fibrosis, myocarditis, coronary artery disease, venous thromboembolism	Modified Medical Research Council dyspnea scale, STOP-BANG questionnaire for obstructive sleep apnea B-type natriuretic peptide, CBC Chest radiography, ECG, functional capacity testing, pulmonary function tests Consider D-dimer, ferritin, chest CT, echocardiography, home pulse oximetry	Breathing exercises Paced return to activity Pulmonary rehabilitation	
Chronic fatigue (e.g., myalgic encephalomyelitis/ chronic fatigue syndrome) ^{20,24}	Autoimmune, cardio- vascular, endocrine, mood, pulmonary, and sleep disorders	Fatigue severity scale, Patient Health Questionnaire-9, STOP-BANG CBC, complete metabolic panel, thyroid stimulating hormone Functional capacity testing Consider antinuclear antibody, B-type natriuretic peptide, C-reactive protein, p-dimer, erythrocyte sedimentation rate, cortisol, ferritin, chest radiography, ECG, pulmonary function tests, chest CT, echocardiography	Energy conservation strategies Paced return to activity Healthy diet, hydration	
Mast cell activation syndrome (anxiety, conjunctivitis, hypotension, palpitations, rashes, rhinitis, sore throat, urticaria, and wheezing) ^{37,40-42}	POTS, multisys- tem inflammatory syndrome, diabetes mellitus, endocrine tumors, porphyria, thyrotoxicosis, para- sitic infections, celiac disease, vasculitis	Tryptase (baseline and less than four hours from onset of flare-up), 24-hour urine collection to test for N-methylhistamine and prostaglandin $\rm D_2$	Medications: cromolyn, H_1 and H_2 histamine antagonists, mass cell stabilizers	

Note: For a broader listing of symptoms and guidance, refer to reference 24. For links to functional capacity tests and survey instruments for long COVID, see eTable A with the online version of this article.

CBC = complete blood count; CT = computed tomography; ECG = electrocardiography; POTS = postural orthostatic tachycardia syndrome; STOP-BANG = snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck circumference, and gender.

Information from references 1, 3, 20, 24, 31, and 34-42.

modifications such as ensuring fluid and salt repletion; wearing compression garments; performing isometric exercises; eating small, more frequent meals; implementing physical reconditioning programs in nonupright positions (when stable); and avoiding exacerbating factors (e.g., alcohol use, warm environments).^{30,31,35}

• For symptoms of dysautonomia that persist despite conservative measures, first-line pharmacologic agents include propranolol, fludrocortisone,

pyridostigmine, and midodrine. 31,34 Patients with POTS are highly sensitive to the effects of medical management, and the lowest dose should be used first. 45

• Recommended initial treatments for symptoms suggestive of mast cell activation syndrome (anxiety, conjunctivitis, hypotension, palpitations, rashes, rhinitis, sore throat, urticaria, and wheezing) include $\rm H_1$ and $\rm H_2$ histamine antagonists, cromolyn, and leukotriene inhibitors.

^{*—}These are testing options to consider if symptoms are concerning or persistent and do not represent a listing of required studies, which should be directed by the history, examination, and other objective findings.

^{†—}Consider specialty referrals if patients do not respond to initial treatment, for complex or severe presentations, or for new abnormalities on imaging or procedural studies. Underlying conditions should be treated when indicated.

FIGURE 1 Α Can you live alone without any assistance from another person (e.g., independently able to eat, walk, use the toilet, and manage daily hygiene)? Nο I have no limitations in my everyday life Yes and no symptoms, pain, depression, or anxiety related to the infection. Are there any duties/activities at home or at work that you are no longer able to perform yourself? I have negligible limitations in my every-1 day life as I can perform all usual duties/ activities, although I still have persistent No Yes symptoms, pain, depression, or anxiety. I suffer from limitations in my everyday Do you suffer from symptoms, life as I occasionally need to avoid or pain, depression, or anxiety? reduce usual duties/activities or need to spread these over time due to symptoms, pain, depression, or anxiety. I am, No Yes however, able to perform all activities without any assistance. Do you need to avoid or reduce duties/ activities or spread these over time? I suffer from limitations in my everyday life as I am able to perform all usual duties/activities due to symptoms, pain, depression, or anxiety. I am, however, No Yes able to take care of myself without any assistance. Grade 0 I suffer from severe limitations in my everyday life: I am not able to take care of myself and therefore I am dependent on nursing care and/or assistance from

Patient self-report methods for the Post-COVID-19 Functional Status (PCFS) scale. (A) Flowchart. (B) Patient questionnaire. Instructions for use: (1) to assess recovery after SARS-CoV-2 infection, this PCFS scale covers the entire range of functional limitations, including changes in lifestyle, sports, and social activities; (2) assignment of a PCFS scale grade concerns the average situation of the past week (exception: when assessed at discharge, it concerns the situation of the day of discharge); (3) symptoms include (but are not limited to) dyspnea, pain, fatigue, muscle weakness, memory loss, depression, and anxiety; (4) in case two grades seem to be appropriate, always choose the highest grade with the most limitations; (5) measuring functional status before the infection is optional; (6) alternatively to this flowchart and patient questionnaire, an extensive structured interview is available. The full manual for patients and physicians or study personnel is available from https://osf.io/ggpdv/ (free of charge).

Reprinted with permission from Klok FA, Boon GJAM, Barco S, et al. The post-COVID-19 functional status scale: a tool to measure functional status over time after COVID-19. Eur Respir J. 2020;56(1):2001494.

- Many presenting symptoms and conditions associated with long COVID are commonly seen in primary care practice and can be managed using established treatment paradigms and supportive care. 1,22,24 Examples include renal disease, chronic pain, hyperglycemia, insomnia, mood disorders, paresthesias, pulmonary infections, small fiber neuropathy, and thromboembolism.
- Several medications commonly used to treat fatigue in other conditions (e.g., myalgic encephalomyelitis, multiple sclerosis, cancer) have been suggested for the treatment of fatigue related to COVID-19, including modafinil (Provigil),

methylphenidate (Ritalin), and amantadine. 20,24 However, evidence for this use is insufficient.²⁰

another person due to symptoms, pain,

depression, or anxiety.

- Follow-up visits are patient-specific but can be considered every two to three months.1
- · Although an in-person visit may have advantages for physiologic evaluation and other assessments, telemedicine approaches with phone calls or virtual visits can be helpful for follow-up and lessen the burden on patients. 20,44

LIFESTYLE AND BEHAVIOR INTERVENTIONS

• Energy conservation strategies such as the four P's framework (planning, pacing, prioritizing,

positioning) and the stop, rest, pace strategy, and avoiding relapsing triggers may help patients mitigate fatigue. 3,15,20,24,28,38

- Patients should be supported in maintaining adequate hydration and a healthy diet.^{1,3,20}
- Information on peer support resources should be provided (see patient handout with the online version of this article).¹

REFERRAL, CONSULTATION, AND HOSPITALIZATION

- \bullet Structured coordination of care and connection to social services can benefit vulnerable populations with long COVID. 20
- Primary care clinicians can manage most patients with long COVID, but almost every state has specialized clinics that can be used for more complex cases. Physicians can find post-COVID care centers in their state at https://www.survivorcorps.com/pccc.

TABLE 4

General Attributes of an Individualized, Symptom-Guided, Phased Return to Activity Program for Patients With Fatigue

The goal is to restore previous levels of activity and improve quality of life.

If the program is advanced too quickly, it can worsen symptoms and trigger postexertional malaise.

Patients are directed to perform activities at submaximal levels

Activities are adjusted in response to symptoms that develop during and after activity.

Patients are educated on how to recognize perceived exertion and use other metrics such as heart rate or validated exertion scales.

Activity recommendations depend on level of symptom severity and progress according to symptom tolerance.

Until goals are achieved, patients should not initiate high-intensity aerobic exercises or heavy weight training.

An example of program progression could be bedside mobilization, range of motion exercises, tolerated household activities, stretching of extremities, limited community activities, submaximal exercise, and eventual higher-intensity activities.

Consider referral to a physiatrist or physical therapist who is knowledgeable in caring for patients with long COVID and can monitor the course of the program.

Information from reference 20.

• Specialty referral should be considered if initial treatment is unsuccessful, for complex or severe presentations, or for new concerning findings on imaging or other studies.^{3,24,39}

Prognosis

- Most patients can expect gradual improvement in functional status with a relapsing and remitting course, aided by careful pacing, prioritization, and goal setting.^{3,24}
- Although many individuals may experience resolution of some or all symptoms over time, the ultimate long-term prognosis of long COVID is unclear.^{24,46}
- Clinicians should set expectations for patients, advising that there are varying outcomes and rates of recovery.¹
- One study found a progressive decline in the average number of symptoms after seven months; however, 65.2% of patients still had symptoms after six months. Those with continued postexertional malaise experienced a higher number of average symptoms.²³
- Most individuals with long-term breathing difficulties do not develop permanent or chronic lung injury.¹⁵
- Most people will gradually recover from cognitive impairment after a severe illness.¹⁵
- Long COVID is now a recognized disability under the Americans With Disabilities Act, sections 504 and 1557.47

Data Sources: A search of PubMed was completed using the key terms long COVID and post-acute symptoms of COVID-19. The search included government and professional organization websites such as the Centers for Disease Control and Prevention. The Essential Evidence Plus library was also searched. A reference library was curated by the Oregon Health and Science University School of Medicine COVID-19 Inquiry Group and through professional collaborative networks. Search dates: August 2021 through August 2022.

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BONUS DIGITAL CONTENT

LONG COVID

eTABLE A

Functional Capacity Tests and Survey Instruments for Long COVID

Functional capacity tests

1-minute sit-to-stand test^{A1}

https://www.rbht.nhs.uk/sites/nhs/files/Leaflets/One%20minute%20sit%20to%20stand%20test%20instructions%20-%20April%202021.pdf

2-minute step test^{A1}

https://geriatrictoolkit.missouri.edu/cv/2min-step-rikli-jones.doc

10-meter walk test^{A2}

https://geriatrictoolkit.missouri.edu/gaitspeed/10mWalkTest.pdf

6-minute walk test^{A3}

https://www.mdcalc.com/6-minute-walk-distance

Survey instruments

Modified Medical Research Council dyspnea scale^{A4}

https://www.mdcalc.com/mmrc-modified-medical-research-council-dyspnea-scale

Montreal Cognitive Assessment^{A5}

https://www.mdcalc.com/montreal-cognitive-assessment-moca

Patient Health Questionnaire-9^{A6}

https://www.mdcalc.com/phq-9-patient-health-questionnaire-9

Generalized Anxiety Disorder-7^{A7}

https://www.mdcalc.com/gad-7-general-anxiety-disorder-7

Fatigue Severity Scale^{A8}

https://www.sralab.org/sites/default/files/2017-06/sleep-Fatigue-Severity-Scale.pdf

Insomnia Severity Index^{A9}

https://www.ons.org/sites/default/files/InsomniaSeverityIndex_ISI.pdf

STOP-BANG score for obstructive sleep apnea^{A10}

https://www.mdcalc.com/stop-bang-score-obstructive-sleep-apnea

Note: Tests should be selected based on the patient's tolerance.

STOP-BANG = snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck circumference, gender. *Information from*:

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