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Long COVID Treatment Guide

A Collaboration between Patient-Led Research Collaborative and RTHM

March 2026

About This Guide

This Long COVID treatment guide is meant to spark meaningful conversations with patients and their clinicians about potential treatment options that could become part of a personalized care plan. The guide is not an exhaustive list, nor is it intended as individualized medical advice. Instead, it offers thoughtfully selected options clinicians and patients can explore together, based on the unique symptoms, needs, and goals of each patient.

We chose the treatments in this guide using a combination of clinical evidence (reviewed up until Nov 2025), observed real-world effectiveness, and experience treating people with Long COVID. We focused on treatment options from the Harvard/Stanford TREATME Study (PMID: 40627388) that at least 20% of participants with Long COVID reported moderate to substantial benefit. The Harvard/Stanford TREATME Study is a comprehensive assessment of efficacy of 150 treatments for Long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). It's important to highlight that while these treatment interventions benefited some, others reported no effect or even a worsening of symptoms. Additionally, we included treatments that show meaningful promise in clinical practice, or that have shown benefit in other infection-associated chronic conditions. The guide is focused on medications, but does include a few supplements, procedures, and lifestyle strategies to reflect the diverse nature of Long COVID care options.

You won't find recommendations in this guide for conditions like diabetes, migraines, or specific autoimmune diseases that developed or worsened following COVID-19 — those are best guided by established clinical care guidance for each specific condition. Instead, this guide zeroes in on therapies that address the other complex, often overlapping symptoms seen in Long COVID itself.

Please Remember

- This guide is for educational purposes only. It is not medical advice, and is not designed to diagnose or prescribe. Every person's experience with Long COVID is unique, and it's essential to consult your healthcare provider before making changes to your treatment.
- Your clinician will need to do standard assessments for safety and appropriateness on a case by case basis, looking into risks, contraindications, medication interactions, and side effects for each treatment - and weighing risks vs. benefits with each patient before prescribing.

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Medications

Low Dose Naltrexone (LDN)

Especially Helpful For

Fatigue, post-exertional malaise (PEM), cognitive impairment, insomnia, aches and pains, symptoms related to inflammation, poor mood

Notes

Needs a gradual increase in dose. Can start as low as 0.25-0.5mg or as high as 1-1.5mg, and taper up gradually to 3-4.5mg as tolerated. Doses can go higher than 4.5mg. Usually dosed before bed, but can be taken in the AM if interfering with sleep.

Summary

Across multiple cohort studies (36–852 patients), LDN was linked to significant improvements in fatigue, pain, energy levels, and overall quality of life in 34-58% of Long COVID patients. People taking LDN were more likely to improve compared to those doing physical therapy alone (HR=5.04; 95% CI=1.22–20.77; P = 0.02). In ME/CFS, improvement in symptoms was observed in 73.9% of 218 patients taking LDN in one study, with moderate to significant improvement in 26% of another study. In vitro research further showed that naltrexone restores TRPM3 calcium channel function and natural killer cell activity in Long COVID. A randomized controlled trial of LDN in Long COVID is currently underway in Canada. LDN is recommended for the treatment of neuroinflammation and sleep quality, PEM, cognitive dysfunction and small fiber polyneuropathy in the Bateman Horne Center Clinical Care Guide for managing ME/CFS, Long COVID, & IACCs, as well as the clinical care guidelines from 2021 ME/CFS Clinician Coalition, Mayo Clinic Proceedings of ME/CFS, and AAPM&R.

The Harvard/Stanford TREATME Study

34% of individuals with Long COVID who tried LDN (n=287) reported "moderate to much better" symptom improvement.

References

PMIDs 35814187, 37804660, 38267326, 38813984, 38352659, 38765011, 38740499, 40627388 DOI: 10.1080/21641846.2019.1692770

⚠ Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Medications

Beta Blockers

> **Non-Cardioselective, No Vasodilatory Activity** Propranolol/Nadolol/Sotalol/Pindolol
> **Non-Cardioselective, Yes Vasodilatory Activity** Carvedilol
> **Cardioselective, No Vasodilatory Activity** Atenolol/Metoprolol
> **Cardioselective, Yes Vasodilatory Activity** Nebivolol/Bisoprolol

Especially Helpful For

Postural orthostatic tachycardia syndrome (POTS), inappropriate sinus tachycardia (IST), heart failure, essential tremors, autonomic symptoms, anxiety, migraines

Notes

Low doses (often ¼-½ of lowest hypertension dose) can be effective. Older beta blockers tend to have more risk of weight gain in the first 2-3 months. Avoid beta blockers in people with anaphylactic allergies needing epi-pens, avoid nonselective beta blockers in people with asthma, COPD or other lung disease. Beta blockers can be helpful if a patient has a comorbid condition for which beta blockers are otherwise helpful - migraines, essential tremor, heart failure, etc.

Summary

Low dose propranolol has the most studies supporting its use in POTS, particularly hyperadrenergic POTS or where tachycardia is the predominant symptom. If a patient doesn't respond well to low dose propranolol, other beta blockers can be tried. POTS patients taking propranolol in low doses (20mg daily) experience reduced heart rate and orthostatic intolerance symptom alleviation, as well as increased exercise capacity. Lower dose propranolol doesn't lower blood pressure as much, and higher doses of propranolol don't add additional benefit and may increase side effects. Low dose propranolol is recommended for management of POTS in the consensus guidance statement on the assessment and treatment of autonomic dysfunction in Long COVID in the 2021 ME/CFS Clinician Coalition treatment recommendations, as well as in the clinical care guidelines from 2015 Heart Rhythm Society, Mayo Clinic Proceedings of ME/CFS, AAPM&R, and the Bateman Horne Center, especially those with excessive tachycardia and hyperadrenergic features. Atenolol is an alternative for patients that have fatigue, brain fog, depression or other neurocognitive symptoms as it doesn't cross the blood brain barrier as much.

Medications

Beta Blockers (continued)

The Harvard/Stanford TREATME Study

51% of individuals with Long COVID who tried cardioselective beta blockers (atenolol, metoprolol, nebivolol, or bisoprolol) (n=195) reported "moderate to much better" symptom improvement. 40% of individuals with Long COVID who tried non-cardioselective beta blockers (propranolol or carvedilol) (n=169) reported “moderate to much better” symptom improvement.

References

PMID: 19687359, 23616163, 29500811, 3616154, 25980576, 38958137, 6115665, 40627388

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual’s tolerance.

Medications

Ivabradine

Especially Helpful For

Postural orthostatic tachycardia syndrome (POTS), inappropriate sinus tachycardia (IST), diastolic heart failure

Notes

Often better than beta blockers especially in those with hyperadrenergic POTS. Dosed at 2.5mg daily up to 7.5 mg twice daily.

Summary

Ivabradine may help Long COVID patients presenting with POTS, as it can control heart rate without significantly affecting blood pressure. A randomized, double-blind placebo-controlled trial showed ivabradine significantly improved heart rate and quality of life with no significant side effects in hyperadrenergic POTS. Studies have demonstrated ivabradine improves symptoms in 60-78% of POTS patients. It is recommended for management of POTS in the consensus guidance statement on the assessment and treatment of autonomic dysfunction in Long COVID in the 2021 ME/CFS Clinician Coalition treatment recommendations, as well as in the clinical care guidelines from 2015 Heart Rhythm Society, Mayo Clinic Proceedings of ME/CFS, and the Bateman Horne Center,

The Harvard/Stanford TREATME Study

49% of individuals with Long COVID who tried ivabradine (n=100) reported "moderate to much better" symptom improvement.

References

PMID: 33602468, 37469536, 28846151, 21062792, 40627388 DOI: 10.1136/bcr-2021-243585, 10.1016/j.mayocp.2021.07.004

⚠ Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Medications

Midodrine

Especially Helpful For

Orthostatic Hypotension (OH), Postural Orthostatic Tachycardia Syndrome (POTS)

Notes

2.5-15 mg up to Q4 hours while upright. Avoid doses within 4 hours of bedtime to reduce supine hypertension. For orthostatic intolerance, low blood pressure, orthostatic hypotension start very low (2.5mg QAM) and adjust based on tolerance, and response. Consider serial orthostatic vitals (active stand or NASA Lean) testing and check for supine hypertension in response to medication.

Summary

It can effectively treat orthostatic hypotension and tachycardia in patients who have a baseline normal or low-normal blood pressure. Watch for supine hypertension. A double-blind placebo-controlled cross-over study study of 20 patients aged 12–20 y/o found that midodrine improved postural tachycardia in neuropathic POTS but not in hyperadrenergic POTS. A study found that 10 mg midodrine, taken three times daily, significantly improved standing systolic blood pressure in those with neurogenic orthostatic hypotension. Midodrine is recommended for management of POTS in the consensus guidance statement on the assessment and treatment of autonomic dysfunction in Long COVID in the 2021 ME/CFS Clinician Coalition treatment recommendations, as well as in the clinical care guidelines from the 2015 Heart Rhythm Society Expert Consensus, AAPM&R and the Bateman Horne Center.

The Harvard/Stanford TREATME Study

26.5% of individuals with Long COVID who tried midodrine (n=49) reported "moderate to much better" symptom improvement.

References

PMID: 23978222, 9091692, 35025999, 33243837, 37419532, 34144933, 38813984, 40627388; DOI: 10.1002/pmrj.13397, 10.1111/joim.13652

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Medications

Pyridostigmine (Mestinon)

Especially Helpful For

Postural orthostatic tachycardia syndrome (POTS), orthostatic hypotension (OH), autonomic neuropathy (AN), myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), post-exertional malaise (PEM), myasthenia gravis

Notes

Drug should be carefully titrated from 15 mg 1-3x daily up to 60 mg 3x daily as tolerated, doses can go higher. GI symptoms are common adverse effects since the drug increases bowel motility.

Summary

Pyridostigmine may help Long COVID patients presenting with POTS, ME/CFS, and post-exertional malaise. A randomized, placebo-controlled trial in 45 ME/CFS patients found pyridostigmine improved exercise capacity. Of 203 POTS patients on pyridostigmine, 43% experienced significant improvement in orthostatic intolerance, with notable relief in fatigue, palpitations, presyncope, and syncope. Pyridostigmine is recommended for management of POTS, OH, and AN in the consensus guidance statement on the assessment and treatment of autonomic dysfunction in Long COVID in the 2021 ME/CFS Clinician Coalition treatment recommendations, as well as in the clinical care guidelines from the 2015 Heart Rhythm Society Expert Consensus, AAPM&R, Bateman Horne Center and Mayo Clinic Proceedings of ME/CFS.

The Harvard/Stanford TREATME Study

34% of individuals with Long COVID who tried pyridostigmine (n=56) reported "moderate to much better" symptom improvement.

References

PMID: 35526605, 21410722, 38813984, 40627388; DOI: 10.1183/13993003.congress-2023.PA4639, 10.1002/pmrj.13397

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Medications

Oral Ketotifen

Especially Helpful For

Cognitive impairment, gastrointestinal symptoms, sleep, allergic reactions, mast cell activation, autonomic dysfunction, irritable bowel syndrome (IBS), other inflammation related symptoms

Notes

Oral ketotifen has to be compounded in the US. Dosing can start at 0.5-1mg nightly, taper up as tolerated. Doses can get up to 6 mg per day in divided doses (i.e. 2mg 3 times per day, or 3mg two times per day). Watch for sedation, weight gain.

Summary

Ketotifen is superior to other antihistamines due to its dual mechanism of stabilizing mast cells and being an H1 receptor blocker. Studies have shown ketotifen can help manage skin, gastrointestinal, and neuropsychiatric symptoms in mast cell activation syndrome (MCAS) and Long COVID. A 2023 study suggests ketotifen may reduce COVID-related brain fog by stabilizing mast cells and inhibiting Kv1.3 channels, suppressing neuro-inflammation and immune overactivation. Ketotifen relieves gastrointestinal symptoms in irritable bowel syndrome disease by decreasing mast cell activity in the intestines. As of 11/17/25, prescriptions through RTHM Direct show that 42.4% of the total number of patients prescribed ketotifen returned for a renewal of the prescription and reported a benefit, with 36.5% reporting moderate or great improvement. The RTHM Direct patients had a variety of IACC diagnoses including Long COVID, ME/CFS, and MCAS. Of those reporting benefits 72% had improved allergic symptoms, 56% had improved food tolerance, 61% had improved sleep, 36% had decreased GI symptoms, 34% had increased exertional tolerance, and 33% had PEM improvement. Ketotifen is recognized as a mast cell stabilizer and is mentioned in the Bateman Horne Center Clinical Care Guide for managing ME/CFS, Long COVID, & IACCs for treating MCAS symptoms seen in those with ME/CFS and Long COVID.

⚠ Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Medications

Oral Ketotifen (continued)

The Harvard/Stanford TREATME Study

24% of individuals with Long COVID who tried oral ketotifen (n=50) reported "moderate to much better" symptom improvement.

References

PMID: 37389095, 36952147, 32317585, 36169154, 40627388;

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Medications

Cromolyn Sodium

Especially Helpful For

Gastrointestinal symptoms, cognitive impairment, allergic reactions, mast cell activation, autonomic dysfunction, irritable bowel syndrome (IBS), other inflammation related symptoms

Notes

Oral liquid vials (100mg/5mL) are most common, but dosing is difficult (often starting at ¼ or ⅛ a vial stirred in a glass of water). Can be compounded into capsules that can be opened, dumped into water and stirred. Multiple delivery options are available depending on symptoms (eye drops, inhaler, can be put into shampoo for scalp/rashes, topical gel/cream for rashes). May need to increase the dose over time due to tachyphylaxis.

Summary

Long COVID patients exhibit activated mast cells and high occurrence of mast cell activation syndrome (MCAS); cromolyn sodium is an effective mast cell stabilizer that alleviates symptoms and reduces hyperinflammation. Cromolyn sodium stabilizes mast cells, reducing inflammatory substance release to help manage symptoms like brain fog, gastrointestinal issues, and skin reactions. Cromolyn sodium is recognized as a mast cell stabilizer and is mentioned in the Bateman Horne Center Clinical Care Guide for managing ME/CFS, Long COVID, & IACCs for treating MCAS symptoms seen in those with ME/CFS and Long COVID.

The Harvard/Stanford TREATME Study

36% of individuals with Long COVID who tried oral cromolyn (n=33) reported "moderate to much better" symptom improvement. Notably, only 10.5% of individuals with Long COVID who tried intranasal cromolyn (n=38) reported “moderate to much better” symptom improvement.

References

PMID: 37389095, 34563706, 37389095, 36169154, 40627388

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Medications

Antivirals against Herpesvirus Reactivations

Especially Helpful For

EBV reactivation, other herpes viral reactivations, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

Notes

There are multiple herpesviruses that can be reactivated after COVID. The commonly reactivated ones include EBV, VZV, CMV, and HHV-6. In one study, EBV DNA was detected in 27% of people who had COVID versus 13% who did not. In another study, people over 50 were 15% more likely to develop herpes zoster after COVID. There is a lot of nuance in testing for herpesvirus reactivations that is beyond the scope of this document, so if unfamiliar with the testing, one could empirically trial antivirals without testing.

PMID: 37364815, 37748514, 36639608, 35392454, 40696312, 39207648, 36146679 40627388.

Acyclovir (Zovirax)

is used to treat herpesvirus infections and has shown some promise in treating encephalopathy and coagulopathy in Long COVID. In the Harvard/Stanford **TREATME study, 19%** of individuals with Long COVID who tried acyclovir (n=21) reported “moderate to much better” symptom improvement.

PMID: 37228547, 40627388

Valacyclovir (Valtrex)

has shown promise in treating ME/CFS and is being trialed in Long COVID. In a recent preprint case series, Long COVID patients taking a combo of Valtrex, Celebrex, and 15 days of Paxlovid had a fatigue improvement of 55% greater than patients taking Valtrex and Celebrex alone (though both groups improved), with improvements persisting at least 600 days. In the Harvard/Stanford **TREATME study, 22.5%** of individuals with Long COVID (n=49) or 26.5% of individuals with ME/CFS (n=147) who tried valacyclovir reported “moderate to much better” symptom improvement.

PMID: 35102619, 12582420, 40627388; DOI: 10.21203/rs.3.rs-7500476/v1; Trial ID: NCT06316843

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Medications

Antivirals against Herpesvirus Reactivations (continued)

Tenofovir

(both its TDF and TAF forms) strongly inhibit lytic reactivation of EBV in vitro. Truvada is commonly used for HIV PrEP and includes TDF and emtricitabine, therefore patients may respond differently to Truvada vs Tenofovir. In the Harvard/Stanford **TREATME study, 25%** of individuals with Long COVID who tried Truvada (n=12) reported "moderate to much better" symptom improvement. Watch for bone loss and phosphorus wasting with extended Truvada use. A clinical trial for Truvada in Long COVID is currently underway.

PMID: 32409608, 40627388. Trial ID: NCT06511063

Valganciclovir (Valcyte)

has shown effectiveness in the case of known CMV reactivations and HHV-6 + EBV reactivations in ME/CFS. In the Harvard/Stanford **TREATME study, 21%** of individuals with ME/CFS who tried valgancyclovir (n=52) reported "moderate to much better" symptom improvement.

PMID: 35116025, 23959519, 35102619, 40627388

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Medications

Antivirals against SARS-CoV2 (Paxlovid, Ensitrelvir)

Especially Helpful For

Possible SARS-CoV2 persistence or antigen persistence

Extended Courses of Paxlovid

have shown promise in a case series and large RCT trials are ongoing; however, 2 trials with courses as long as 15 days did not demonstrate significant benefit over placebo. It is possible only a subset benefits or a longer course is needed. In a recent preprint case series, Long COVID patients taking a combo of Valtrex, Celebrex, and 15 days of Paxlovid had a VAS fatigue improvement of 55% greater than patients taking Valtrex and Celebrex alone (though both groups improved), with improvements persisting 600 days beyond the initial 120 days of treatment

Ensitrelvir

was demonstrated to reduce risk of Long COVID when taken during acute COVID. A clinical trial in Long COVID is underway.

The Harvard/Stanford TREATME Study

39% of the 23 individuals with Long COVID who tried Paxlovid for 10 or more days, reported "moderate to much" symptom improvement, whereas 28% out of the 127 individuals who tried Paxlovid for less than 10 days reported "moderate to much" symptom improvement.

References

PMID: 39762640, 38848477, 40188838, 38972603, 40627388; DOI: 10.21203/rs.3.rs-7500476/v1; Trial ID: NCT05965726, NCT06161688,

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Medications

Maraviroc

Especially Helpful For

Cognitive impairment, fatigue, post-exertional malaise (PEM), other inflammation related conditions

Notes

300mg 2x/day; can start at 150mg 2x/day depending on tolerance. The original protocol combined it with 10mg daily pravastatin (but other statins can be used instead).

Summary

Maraviroc and pravastatin may improve Long COVID by targeting immune dysregulation via the monocytic-endothelial-platelet axis, with significantly improved neurological, autonomic, respiratory, cardiac and fatigue scores and vascular markers. In a patient survey, 64% reported slight to significant improvement with maraviroc. A clinical trial is underway at Mount Sinai (NY). In HIV patients, maraviroc showed significant improvements in several cardiovascular parameters that have also been found to be abnormal in a proportion of Long COVID patients, including endothelial dysfunction, arterial stiffness, vascular competence, and overall cardiovascular risk.

The Harvard/Stanford TREATME Study

42% of individuals with Long COVID who tried maraviroc (n=50) reported "moderate to much better" symptom improvement.

References

PMID: 36844201, 40627388, 30968058; Trial ID: NCT06511063, NCT06974084

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Medications

Clopidogrel (Plavix)

Especially Helpful For

Dyspnea, chest pain, fatigue, cognitive impairment

Notes

Clopidogrel 75mg is typically dosed once daily, and may be combined with aspirin and/or apixaban after very careful consideration of the risks associated with dual or triple therapy.

Summary

In a study of 24 Long COVID patients with microthrombi markers, dual antiplatelet therapy with aspirin (75 mg) and clopidogrel (75 mg) daily led to improvements in a variety of symptoms, particularly fatigue, and reduced microclots in all participants. In another study (in preprint), 91 Long COVID patients received triple therapy with clopidogrel, aspirin and apixaban, and symptom resolution was experienced by 25.6% of patients with cognitive dysfunction, 22% with fatigue, and 23% with pain.

The Harvard/Stanford TREATME Study

30% of individuals with Long COVID who tried clopidogrel or Brilinta +/- aspirin (n=53) reported “moderate to much better” symptom improvement.

References

PMID: 36969241, 40627388, DOI: 10.21203/rs.3.rs-1205453/v1, 10.21203/rs.3.rs-2697680/v1

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual’s tolerance.

Medications

Intravenous Immunoglobulin (IVIG) and Subcutaneous Immunoglobulin (SCIG)

Especially Helpful For

Neuropathy including small fiber neuropathy, immune deficiency, autoimmune diseases, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), autonomic dysfunction, non-responders to other therapies

Notes

In the outpatient setting, immunoglobulin therapy (IVIG and SCIG) for autoimmune diseases is typically dosed at 1–2 g/kg per month, whereas primary immune deficiency dosing is typically 0.4g/kg/month. IVIG is usually administered every 3–4 weeks and the SCIG is divided into weekly self-administered doses. Proper hydration and premedication—commonly acetaminophen or an NSAID, an antihistamine like diphenhydramine or cetirizine, with optional H2 blocker and steroids—are key to minimizing infusion reactions. Infusion rate greatly determines tolerability: starting slowly and ramping up gradually can markedly reduce side effects such as headache, fever, or malaise. For IVIG, saline infusion before or during treatment often improves comfort, and splitting the total IVIG dose across several days or weeks can improve tolerability. SCIG tends to cause fewer systemic side effects than IV but may lead to local site reactions. Adjusting the number of sites, infusion rate, or using topical numbing agents can help. Thin patients may find SCIG more difficult to tolerate. Use care with IG in hypercoagulable patients as there can be active clotting factors in IG products.

Summary

Across all reviewed data, IVIG demonstrates consistent therapeutic potential for post-viral and immune-mediated syndromes. Specifically, there are five papers on post-COVID small fiber neuropathy (SFN) showing 60–100% response rates, and two studies on autoimmune dysautonomia, both reporting 40–80% functional improvement. In ME/CFS, three studies reported positive outcomes, and three mechanistic or review papers supported IVIG's immunomodulatory rationale. The NIH RECOVER IVIG study aims to confirm efficacy. IVIG is listed as a treatment option for Long COVID and ME/CFS in the clinical care guidelines from the Mayo Clinic Proceedings of ME/CFS, the Bateman Horne Center, and 2021 ME/CFS Clinician Coalition.

Medications

Intravenous Immunoglobulin (IVIG) and Subcutaneous Immunoglobulin (SCIG) (continued)

The Harvard/Stanford TREATME Study

42% out of 91 individuals with ME/CFS (n=78) or Long COVID (n=13) who tried IVIG/SCIG reported "moderate to much better" symptom improvement.

References

PMID: 38630952, 36818469, 40093251, 29781817l, 39389388, 37179564, 36414570, 35232750, 33382525, 38910072, 34828592, 34072494, 40627388; Trial ID: NCT06305780, NCT05350774

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Medications

Rapamycin

Especially Helpful For

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), fatigue, post-exertional malaise (PEM)

Notes

Titrate from 1mg 1x weekly up to 6mg 1x weekly. Good to get baseline markers of CMP, CBC, lipids, fasting glucose, A1C and fasting insulin before starting. Not all markers are required, but it can cause some insulin resistance and elevated lipids and LFTs in some people, particularly early on.

Summary

Findings from a phase one trial on ME/CFS patients found that weekly rapamycin doses of up to 6 mg significantly improved fatigue, sleep, and orthostatic intolerance over three months. These findings suggest rapamycin's potential as a treatment, likely due to its autophagy-promoting and mTOR-inhibiting properties, with further analyses expected to provide deeper insights. A trial for low-dose rapamycin is currently underway.

The Harvard/Stanford TREATME Study

22% of individuals with Long COVID or ME/CFS who tried rapamycin (n=18) reported "moderate to much better" symptom improvement.

References

PMID: 40627388, DOI: 10.21203/rs.3.rs-6596158/v1; Trial ID: NCT06960928

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Medications

Low Dose Aripiprazole (Abilify)

Especially Helpful For

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), cognitive impairment, fatigue, post-exertional malaise (PEM)

Notes

Dosage starts at 0.1 to 0.25 mg/day and titrated up or down based on each patient's response to a dose of 0.25 to 2.0 mg/day (mean 1.1 mg/day).

Summary

A retrospective Stanford study of 101 ME/CFS patients found that 74% experienced improvements in symptoms such as fatigue, brain fog, unrefreshing sleep, and post-exertional malaise while taking low-dose aripiprazole. It is listed in the Mayo Clinic Review for the management of ME/CFS and the Mayo Clinic proceedings for post-COVID conditions. Dopamine D2 receptor agonists have been shown to mediate neuroinflammation, microglial activation, and cell death in animal models and humans.

The Harvard/Stanford TREATME Study

32% of 133 individuals with ME/CFS (n=123) or Long COVID (n=13) who tried a </=2 mg dose of aripiprazole reported “moderate to much better” symptom improvement. 9% of 33 individuals with ME/CFS (n=31) or Long COVID (n=2) who tried a >2 mg dose of aripiprazole reported “moderate to much better” symptom improvement.

References

PMID: 33536023, 36969241, 38813984, 40627388, 37793728, 37419575

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Medications

Modafinil (Provigil)

Especially Helpful For

Somnolence, cognitive impairment, daytime fatigue

Notes

Start at a small dose and increase slowly up to the most effective dose in the 100-200mg/day range. Can disrupt sleep. Stimulants are most helpful when anxiety scores are low and the Epworth Sleepiness Scale is greater than 10. Watch out for post-exertional malaise (PEM) exacerbations.

Summary

Modafinil is a wakefulness-promoting agent that has shown promise for Long COVID fatigue and neurocognitive deficits through its anti-inflammatory and neuroprotective mechanisms. It is listed as a treatment recommendation for managing cognitive issues in ME/CFS and Long COVID in the clinical care guidelines from the Bateman Horne Center, Mayo Clinic Proceedings of ME/CFS, 2021 ME/CFS Clinician Coalition, as well as for cognitive issues in POTS in the guidelines from the 2015 Heart Rhythm Society. The NIH RECOVER Initiative is currently testing modafinil in clinical trials for Long COVID hypersomnia. The medication works by inhibiting inflammatory pathways and microglial activation that disrupt neuronal energy metabolism, potentially addressing the neuroinflammation underlying Long COVID symptoms.

The Harvard/Stanford TREATME Study

33% of individuals with Long COVID who tried modafinil or armodafinil (n=39) reported “moderate to much better” symptom improvement.

References

PMID: 34454716, 40627388; DOI: 10.1176/appi.ajp-rj.2022.170402

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual’s tolerance.

Medications

Guanfacine +/- NAC

Especially Helpful For

Cognitive impairment, attention deficit hyperactivity disorder (ADHD), hyperadrenergic postural orthostatic tachycardia syndrome (POTS)

Notes

Can cause sedation, lower blood pressure, and lower heart rate. Start low on the dose 0.5mg-1mg nightly, and taper up every 2 weeks, only as tolerated. Combined with N-acetylcysteine (NAC) in a case series, it showed brain fog improvements.

Summary

Guanfacine, a selective α2A-adrenoceptor agonist, has shown potential in improving cognitive function and frontotemporal brain activity in Long COVID patients experiencing cognitive impairment. A case series found that combined treatment with guanfacine and NAC improved cognitive function in eight out of twelve Long COVID patients, with benefits in memory, concentration, and executive function, though some experienced hypotension-related side effects. While placebo-controlled trials are needed to confirm efficacy, the established safety of these treatments suggests the use of guanfacine for addressing Long COVID-related cognitive deficits. Guanfacine is listed as a therapeutic option for cognitive impairment in the Long COVID clinical care guidelines Bateman Horne Center Clinical Care Guide for managing ME/CFS, Long COVID, & IACCs, and for orthostatic intolerance and autonomic dysfunction in the clinical care guidelines from the 2021 ME/CFS Clinician Coalition and Mayo Clinic Review.

The Harvard/Stanford TREATME Study

36% of individuals with Long COVID who tried guanfacine + NAC (n=25) reported “moderate to much better” symptom improvement. 28% of individuals with Long COVID who tried guanfacine alone (n=25) reported “moderate to much better” symptom improvement.

References

PMID: 38934345, 40261198, 40627388; PMCID: PMC9691274

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Medications

Trazodone

Especially Helpful For

Sleep dysfunction, insomnia

Notes

Start at 25-50mg 1hr before bed. Titrate up to 100-150mg as needed and tolerated.

Summary

ME/CFS experts report success with trazodone for sleep improvement, with the Mayo Clinic Review listing it among pharmacologic therapies that can help patients with ME/CFS and post-COVID conditions. In a patient-led survey, more than 50% respondents reported at least some improvement with trazodone, with 16.9% and 20% of people with ME/CFS and Long COVID, respectively, reporting moderate to significant improvement. Analyses combining data from over 40 randomized-controlled clinical trials found that trazodone was effective in maintaining and extending sleep duration, with patients on trazodone reporting better sleep quality than those receiving placebo. Long-term trazodone use has been associated with delayed cognitive decline, with users showing 2.6-fold slower cognitive decline compared to non-users over four years. Trazodone is also listed as a treatment option for the management of sleep in Long COVID and ME/CFS in the clinical care guidelines from the 2021 ME/CFS Clinician Coalition, AAPM&R, and Mayo Clinic Proceedings of ME/CFS.

The Harvard/Stanford TREATME Study

20% of individuals with Long COVID who tried trazodone or nefazodone (n=40) reported “moderate to much better” symptom improvement.

References

PMID: 34454716, 40627388, 39123094, 29680424, 30762713, 40261198

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Medications

GLP-1 Receptor Agonists (Tirzepatide, Semaglutide, etc.) [Emerging Therapy]

Especially Helpful For

Mast cell activation syndrome (MCAS), fatigue, cognitive impairment fog, edema reduction, pain, headaches, gastrointestinal symptoms, food intolerances, excessive hunger or cravings, mood, cardiopulmonary symptoms, autonomic symptoms, hypertension.

Notes

Lower doses than standard for weight loss may reduce side effects while still providing clinical benefit and can potentially be dosed more than once a week. Consider monitoring for muscle/strength loss over time, esp. in those with joint or spinal instability, hypermobility and/or Ehlers Danlos Syndrome. Because GLP-1 receptor agonists slow down gastric emptying and gastrointestinal motility, GI-associated side effects like nausea and constipation are common.

Summary

A 2025 case series found that GLP-1s used in patients with MCAS (a common comorbidity in Long COVID) for a mix of on-label and off-label indications improved symptoms for 89% (42/47) of patients. While a significant fraction experienced some side effects, many resolved on their own, and others were manageable with lower dosing, adjusting diet, magnesium supplementation, or extra doses of H1/H2 receptor blockers. Only 11% (5/47) stopped treatment: 3/5 due to toxicities, 2/5 due to cost. Brand and compounded GLP-1s were used. Another case study reports a patient with POTS improved significantly with semaglutide, but symptoms worsened after discontinuation of the drug. Preclinical studies demonstrate that GLP-1 can suppress microglial inflammation, which may be relevant to the pathophysiology of POTS. There is a clinical trial for tirzepatide for Long COVID that completed enrollment of 1,000 US participants in December 2025 and remains ongoing.

References

PMID: 22519295, 31881271, 41180125, 40525593; DOI: 10.1016/j.amjms.2025.07.006, 10.1007/s10286-026-01197-1; Trial ID: NCT07128082

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Supplements & Over the Counter (OTC) Medications

Supplements

Nattokinase and Lumbrokinase

Especially Helpful For

Fatigue, cognitive impairment, feeling of weakness, post-exertional malaise (PEM), dyspnea, chest pain, tachycardia and heart pounding

Notes

Nattokinase (NK) and lumbrokinase (LK) are derived from soybeans and earthworms respectively; patients with an allergy to one may try the other. Serrapeptase may be used in conjunction with either for more impact; however some patients may have adverse reactions to serrapeptase. Can start with NK or LK and then add serrapeptase once adjusted. The Boluoke brand of LK is most studied and it is usually dosed at 600,000 IU three times daily in studies. Surveys around the TREATME study have shown that most patients do better on NK doses from 4000 to 12,000 FU per day, with many landing on 4000 FU twice daily on an empty stomach. A retrospective analysis of 1,062 pts taking 10,800 FU of NK daily for a year did not report any safety issues at this dose. NK brands with enteric coating performed better in patient surveys.

Summary

NK and LK are both enzymes with fibrinolytic activity that have been used for their antihypertensive, anti-atherosclerotic, lipid-lowering, antiplatelet, neuroprotective effects, and in addressing blood clots in DVT, stroke, and Long COVID. A clinical trial on lumbrokinase for Long COVID is underway.

The Harvard/Stanford TREATME Study

29% of individuals with Long COVID who tried NK or LK (n=341) reported "moderate to much better" symptom improvement. 32.5% of people with Long COVID who tried LK and/or NK combined with serrapeptase (N=318) reported "moderate to much better" symptom improvement.

References

PMID: 36043493, 38947233, 40627388, 14565628, 24229674, 20473377, 36080170, 36072877; Trial ID: NCT06511050, NCT07229521

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Supplements & OTC Medications

H1 Blocking Antihistamines (Cetirizine, Fexofenadine, etc.)

Especially Helpful For

Mast cell activation, allergic symptoms, post-exertional malaise (PEM), cognitive impairment, gastrointestinal symptoms, insomnia, headaches, orthostatic intolerance

Notes

10mg QD to BID. May interact with psychiatric medications. Contraindicated for ESRD. Abrupt discontinuation can cause withdrawal symptoms.

Summary

Preliminary data suggests that blocking both histamine H1 and H2 receptors may significantly alleviate symptoms in Long COVID patients with manifestations linked to mast cell activation, with 29% of treated individuals experiencing complete resolution of their condition. A UK study found 72% of Long COVID patients treated with famotidine + loratadine had a reduction of symptoms, with 20% having complete symptom resolution, with one patient worsening. H1 receptor blockers are considered the cornerstone of Mast Cell Activation Syndrome (MCAS) treatment, with combinations of non-sedating antihistamines (cetirizine, fexofenadine, loratadine) and H2 antihistamines providing synergistic histamine receptor blockade to relieve symptoms. A large cluster RCT with an arm investigating famotidine + loratadine in LC is underway.

The Harvard/Stanford TREATME Study

25% of individuals with Long COVID who tried 2nd/3rd generation H1 blockers like cetirizine and fexofenadine (n=759) reported "moderate to much better" symptom improvement. 27% who tried 1st generation H1 blockers (n=114) reported "moderate to much better" symptom improvement; and 35% who tried a combo of H1 and H2 blocker (n=194) reported "moderate to much better" improvement.

References

PMID: 38526146, 37529714, 36791116, 34611034, 37389095, 40627388

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Supplements & OTC Medications

Famotidine

Especially Helpful For

Cognitive impairment, neuropsychiatric symptoms, mast cell activation, gastrointestinal symptoms

Notes

H2 blocking antihistamines (usually famotidine) are typically used in combination with an H1 blocking antihistamine in studies, but can be used on its own.

Summary

Famotidine may prevent SARS-CoV-2 spike protein entry into endothelial cells, and has also been shown to attenuate the cytokine storm and inflammation in acute COVID. Additionally, acid related disorders are among the most common Long COVID gastrointestinal conditions, which famotidine may mediate. Studies show using famotidine alone improved cognitive and neuropsychiatric scores after COVID. One study showed that combination treatment of famotidine + loratadine led to reduction of symptoms in 72% of patients, with 20% having complete symptom resolution. Additional data suggests that famotidine may significantly alleviate symptoms in Long COVID patients with manifestations linked to mast cell activation. A large cluster RCT with an arm investigating famotidine + loratadine in LC is underway.

The Harvard/Stanford TREATME Study

20% of individuals with Long COVID who tried H2 blocker famotidine (n=300) reported "moderate to much better" symptom improvement. Other H2 blockers, tried by 80 individuals with ME/CFS or Long COVID, were less effective, with 16% reporting "moderate to much better" symptom improvement.

References

PMID: 37529714, 37327698, 35144974, 36791116, 40627388, 36882400, 35548336; DOI: 10.1136/jim-2021-002051, 10.1186/s10020-022-00483-8

⚠ Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Supplements & OTC Medications

Oxaloacetate

Especially Helpful For

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), cognitive impairment, fatigue, post-exertional malaise (PEM)

Notes

Dose 500mg twice daily (morning and mid-day) with food to test tolerance for 2-3 days, then increase to 1000mg twice daily with food as tolerated (RCT studies used 1000mg twice daily). Taking it too late may disrupt sleep. Taking with food helps reduce stomach upset. Can take a few weeks to see improvements.

Summary

A 2025 randomized controlled trial on oxaloacetate in Long COVID missed primary endpoints of fatigue reduction, but did see significant fatigue reduction on a secondary endpoint questionnaire and significant improvement in cognitive testing scores. An open label study found oxaloacetate reduced fatigue by 33% in ME/CFS patients and 46.8% in Long COVID patients over six weeks, with dose-dependent effects in ME/CFS. A 2024 randomized control trial found oxaloacetate reduced fatigue by over 25% on average in ME/CFS patients, with 40% experiencing a 63% reduction as "super responders". Lower natural oxaloacetate levels in ME/CFS patients suggest supplementation may enhance mitochondrial energy production.

The Harvard/Stanford TREATME Study

29% of individuals with Long COVID who tried oxaloacetate (n=14) reported "moderate to much better" symptom improvement. 16% of individuals with ME/CFS who tried oxaloacetate (n=63) reported "moderate to much better" symptom improvement.

References

PMID: 40757370, 39664752, 35764955, 28059425, 41132887, 40627388

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Supplements & OTC Medications

Nicotine Patches

Especially Helpful For

Cognitive impairment, fatigue

Notes

Patients should start at as low a dose as possible - generally 3.5mg (half a 7mg patch), but even as low as 1.75 or .875. It is vital to communicate that some patches cannot be cut, as this will make all the nicotine release at once; some brands have two plastic sheets on the back to allow for a “half patch”, and additional plastic can be added to keep dose smaller. Nicotine can increase heart rate; patients with POTS and ME/CFS should be on medications that control tachycardia before starting. Caution advised in the two weeks after acute myocardial infarction, in unstable acute coronary artery disease, and during pregnancy and lactation. Addiction or dependence in non-smokers using transdermal nicotine was not specifically screened for, but no cases were reported among 608 non-smokers.
PMID: 15628577, 34153704

Summary

Transdermal nicotine has been shown to improve cognitive function, attention, and memory in mild cognitive impairment and in healthy adults. Nicotine also improves some inflammatory conditions, including ulcerative colitis, arthritis, sepsis, and endotoxemia. A survey involving 231 Long COVID patients taking low dose transdermal nicotine (LDTN) showed improvement in 73.5% of patients and reported remissions in a third of cases. A proposed hypothesis states Long COVID may be linked to impaired cholinergic neuromodulation caused by the SARS-CoV-2 virus attaching to nicotinic acetylcholine receptors (nAChRs), disrupting neuronal communication. A case study on transdermal nicotine for Long COVID showed symptom improvement as well as improved cholinergic function and increased the number of ligand binding sites in nAChRs.

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual’s tolerance.

Supplements & OTC Medications

Nicotine Patches (continued)

The Harvard/Stanford TREATME Study

43% of individuals with Long COVID who tried nicotine patches (n=7) reported "moderate to much better" symptom improvement. 17% of individuals with ME/CFS who tried nicotine patches (n=18) reported "moderate to much better" symptom improvement.

References

PMID: 40011942, 40627388, 36650574, 22232050, 33899218, 3525101, 27699443,

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Lifestyle

Lifestyle

Pacing

Especially Helpful For

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), post-exertional malaise (PEM)

Notes

#MEAction and Long COVID Physio have high quality guides for implementing pacing. (#MEAction, LC Physio)

Summary

Pacing is an activity management strategy to prevent and mitigate PEM by keeping activity levels within someone's energy limits, which may involve reducing and/or adapting activities and alternating them with periods of rest. Pacing is proven to reduce episodes of PEM and is adaptive since one's energy capacity limits may change over time. People with Long COVID who experience PEM may need assistance to implement pacing, such as caretaker support, help preparing meals and doing house chores, and work accommodations. Pacing is recommended for the management of PEM in the clinical guidelines from the Mayo Clinic Proceedings of ME/CFS, Bateman Horne Center, and the 2021 ME/CFS Clinician Coalition.

The Harvard/Stanford TREATME Study

37% of individuals with Long COVID who tried pacing (n=119) reported "moderate to much better" symptom improvement.

References

PMID: 36461167, 40627388, 34308300.

⚠ Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Lifestyle

Salt and Fluid Loading

Especially Helpful For

Postural orthostatic tachycardia syndrome (POTS), orthostatic hypotension, myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS)

Notes

A key component of POTS treatment is the consumption of fluids and salt, with clinical guidelines recommending 2-3 L of water and 10-12 g of salt daily. Increased salt intake may exacerbate symptoms with some presentations of hyperadrenergic POTS.

Summary

Studies show that a high-sodium diet significantly improved symptoms in POTS patients by increasing blood volume, lowering plasma norepinephrine levels, and reducing orthostatic tachycardia. These findings provide strong evidence supporting sodium intake as a beneficial treatment strategy for POTS management. Research demonstrates that short-term salt supplementation improves susceptibility to vasovagal syncope and associated symptoms, with responses most pronounced in those with baseline sodium excretion <170 mmol/day, and salt supplementation also improved symptoms, plasma volume, and orthostatic responses in patients with POTS. Salt and fluid loading is recommended for the management of orthostatic intolerance in the clinical care guidelines from the 2021 ME/CFS Clinician Coalition, Bateman Horne Center, 2015 Heart Rhythm Society, and the Mayo Clinic Proceedings of ME/CFS.

The Harvard/Stanford TREATME Study

33% of individuals with Long COVID who tried oral fluids and electrolytes (n=1,169) reported "moderate to much better" symptom improvement.

References

PMID: 35697326, 33926653, 34823150, 40627388

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Lifestyle

Compression Garments

Especially Helpful For

Postural orthostatic tachycardia syndrome (POTS), orthostatic hypotension (OH), myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

Notes

Ankle to high waist compression garments with at least 20mmHg at the ankle are generally preferred, however the exertion required to put on such compression garments may trigger post-exertional malaise (PEM). Consider compression garments with zippers or velcro to make it easier for patients to put them on and take them off. An abdominal binder alone is a good alternative for those who cannot tolerate or are excessively fatigued by full leg compression garments.

Summary

Studies show that abdominal and full lower body compression garments significantly reduced heart rate and improved symptoms in adults with POTS during head-up tilt testing. One study showed the median reduction in heart rate in the AM was –17 beats/min with medical/prescription style waist high compression (WHC) compared with –10 beats/min with sport/athletic-style WHC. Percentage change in heart rate was higher with medical/prescription WHC compared with sport/athletic-style WHC. Compression garments are recommended for the management of orthostatic intolerance in the clinical care guidelines from the Bateman Horne Center, 2015 Heart Rhythm Society, Mayo Clinic Proceedings of ME/CFS, and 2021 ME/CFS Clinician Coalition.

The Harvard/Stanford TREATME Study

26% of individuals with Long COVID who tried compression garments (n=430) reported "moderate to much better" symptom improvement.

References

PMID: 33478652, 32673524 DOI: 10.1016/j.cjca.2025.11.038, 10.1016/j.jacep.2024.09.033

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Lifestyle

Lymphatic Drainage Massage

Especially Helpful For

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), fatigue, cognitive impairment, insomnia

Notes

This can be learned to be done at home by the patient and is low cost. Perrin TechniqueTM is one type of lymphatic drainage massage, also known as manual lymphatic drainage (MLD) which aims to help with neurological symptoms by improving the flow of the cerebrospinal fluid. May trigger post-exertional malaise (PEM) from muscle tissue manipulation. The Perrin technique is a type of MLD used specifically in ME/CFS. In other MLD techniques, the effect of the intervention may vary.

Summary

MLD is a treatment for ME/CFS and may help glymphatic and lymphatic dysfunction that occurs in Long COVID. Case reports suggest that MLD may help improve Long COVID fatigue, breathlessness, cough, respiratory function, and symptom severity. One study of 20 Long COVID patients that were seen by a qualified Perrin TechniqueTM practitioner once a week for an average of nine treatment sessions (in addition to a daily home-based self-massage routine) reported a reduction in PFRS (profile of fatigue-related states) scores of 41.8% in men and 60.5% in women. The highest subscale scores on average were for fatigue, and all subscale scores showed, on average, a similar reduction of approximately 50% post-intervention.

The Harvard/Stanford TREATME Study

14% of individuals with Long COVID who tried MLD (n=14) reported "moderate to much better" symptom improvement. 25% of individuals with ME/CFS who tried MLD (n=83) reported "moderate to much better" symptom improvement.

References

PMID: 38155770, 40108491, 38063653, 35441129, 40627388

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Procedures

Procedures

Stellate Ganglion/Sympathetic Field Blocks

Especially Helpful For

Fatigue, cognitive impairment, tachycardia, paresthesia, dyspnea, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), joint pain, headache

Notes

May be more likely to help people who have been ill for a shorter duration. May need multiple blocks if longer illness duration. Blocks may be unilateral or bilateral.

Summary

Stellate ganglion blocks (SGBs) have been used for conditions affecting the sympathetic nervous system, including complex regional pain syndrome (CRPS), postherpetic neuralgia, refractory cardiac arrhythmias, anosmia, and PTSD. A study of 41 Long COVID patients ill between 3-29 months found 86% had symptom improvement, with some symptoms having higher rates of improvement than others. A trigeminal nerve block may help increase the likelihood of improving anosmia.

References

PMID: 38947233, 37711269, 38901177

Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Procedures

Hyperbaric Oxygen Therapy (HBOT)

Especially Helpful For

Cognitive impairment, fatigue, sleep, psychiatric, pain

Notes

Medical grade HBOT can be expensive in some areas, and time/energy consuming. Claustrophobia can make HBOT challenging. Can start with a shorter session at lower pressure and work up on pressure and time as tolerated in the beginning.

Summary

In a randomized, double-blind, placebo-controlled trial of 73 Long COVID patients, 40 sessions of HBOT led to significant improvements in attention, sleep quality, pain, and energy levels that persisted even one year after treatment. Echocardiogram assessment in the same cohort showed a meaningful reduction in global longitudinal cardiac strain. A separate 10-patient study reported statistically significant improvements in fatigue and cognitive function after 10 HBOT sessions over 12 days, though an interim safety analysis from an ongoing Karolinska Institute trial noted that nearly half of participants experienced cough or chest discomfort during treatment, though it remains unclear whether these effects were treatment-related or due to underlying Long COVID symptoms.

The Harvard/Stanford TREATME Study

38% of individuals with Long COVID who tried HBOT (n=13) reported "moderate to much better" symptom improvement. 25% of individuals with ME/CFS who tried HBOT (n=24) reported "moderate to much better" symptom improvement.

References

PMID: 38672710, 35821512, 38360929, 31953651, 34862223, 36670365, 40627388

⚠ Contraindications, drug-drug and drug-condition interactions, allergies, and potential side effects should always be reviewed with a qualified clinician before initiating treatment. Treatment sensitivities are common in Long COVID, so unless otherwise directed, consider starting new treatments at very low doses and tapering up slowly according to an individual's tolerance.

Glossary

Term	Definition
AN	Autonomic Neuropathy
CRPS	Complex Regional Pain Syndrome
GLP-1	Glucagon-Like Peptide-1 Receptor Agonist
HBOT	Hyperbaric Oxygen Therapy
IACCs	Infection-Associated Chronic Conditions
IST	Inappropriate Sinus Tachycardia
IVIG	Intravenous Immunoglobulin
LDN	Low Dose Naltrexone
MCAS	Mast Cell Activation Syndrome
ME/CFS	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
MLD	Manual Lymphatic Drainage
nAChRs	Nicotinic Acetylcholine Receptors
OH	Orthostatic Hypotension
PEM	Post-Exertional Malaise
PESE	Post-Exertional Symptom Exacerbation
POTS	Postural Orthostatic Tachycardia Syndrome
PrEP	Pre-Exposure Prophylaxis (HIV prevention)
Q4H	Every 4 hours
QAM	Every morning
SCIG	Subcutaneous Immunoglobulin
SFN	Small Fiber Neuropathy
SGB	Stellate Ganglion Block
TAF	Tenofovir Alafenamide
TDF	Tenofovir Disoproxil Fumarate
TRPM3	Transient Receptor Potential Cation Channel Subfamily M Member 3

About the Authors

PATIENT-LED RESEARCH COLLABORATIVE

The Patient-Led Research Collaborative (PLRC) is a research and data-driven organization run by people with Long COVID and associated conditions. Our mission is to improve the breadth, depth, and speed of global research into Long COVID and associated conditions, and to advocate for policies that improve the quality of life for Long COVID patients worldwide. We integrate our lived experience with our professional expertise, as well as deep knowledge of patient communities and their movements. Our work is grounded in the principles of disability justice, using evidence-based information from our own studies and others to advance research and improve healthcare access. We published the first report of Long COVID in May 2020 and have since authored over 40 papers, including two of the most-cited Long COVID papers ever published.

rthm

RTHM is a pioneering telehealth clinic and HIPAA-compliant intelligence platform dedicated to complex chronic illnesses like Long COVID, ME/CFS, POTS, and MCAS, offering personalized treatment suggestions, diagnostic paths, symptom tracking, and care team collaboration powered by the latest research. Cofounders Dr. Ryan Kellogg and Dr. Jennifer Curtin drew from their personal journeys through dismissed symptoms and scarce answers in a broken system. By blending their lived experiences and clinical expertise, they transformed a vision for accessible, science-driven care into a growing community and medical home for complex illnesses.