

Long COVID in Clinical Practice: A Practical Guide for Nurse Practitioners

Diagnosing, managing, and supporting patients with post-acute sequelae of COVID-19 (PASC)

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Featured Voices

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What You'll Learn

- How long COVID (PASC) is defined — and why more than 200 symptoms have been associated with it
- The most common presenting symptoms: post-exertional malaise, dyspnea, tachycardia, brain fog, and palpitations
- The key risk factors for developing long COVID — and who is most vulnerable
- How to take a history that distinguishes long COVID from other diagnoses — and what workup to order
- Which cardiac red flags require urgent evaluation and what monitoring tools to use
- The role of mast cell activation in long COVID — and a simple, accessible pharmacologic intervention
- How to manage autonomic symptoms including POTS using low-cost, evidence-informed strategies
- Why sleep is the most important target in long COVID recovery — and how to address it
- How to build a manageable, patient-centered treatment plan when no single cure exists
- When and how to refer to specialty — and how to build your own multidisciplinary team
- How to counsel patients on supplements, internet remedies, and unproven treatments
- What recovery looks like — and how to set realistic, honest expectations with patients

Key Takeaways

- **Name it to tame it — validation is the most impactful clinical intervention.**

More than 200 symptoms have been associated with long COVID (PASC). Patients often arrive having been dismissed or disbelieved. Giving them a diagnosis — or at minimum validating that their symptoms are real — has been shown in fibromyalgia literature to improve quality of life more than almost any other intervention. Believe them first.

- **Post-exertional malaise, dyspnea, tachycardia, and brain fog are the hallmark symptoms.**

Patients describe fatigue that is bone-wrenching and different from ordinary tiredness. They worsen with exertion — even minimal activity. Palpitations, POTS, and cognitive fog are common. A list of 25 symptoms at a single visit is itself a clinical signal that something systemic is happening.

- **Hospitalization, advanced age, and comorbidities are the strongest risk factors.**

70–80% of patients who were ventilated or hospitalized with COVID will develop long COVID. Female sex is also a risk factor. The more risk factors present, the longer and more complex the recovery. These patients need longitudinal, team-based care — not a single visit.

- **The history is your most powerful diagnostic tool — but rule out everything else first.**

There is no test for long COVID. A thorough history — including what changed and when — is how you get to 90% of your diagnoses. But do not let long COVID become a catch-all. Order a CBC, CMP, TSH, vitamin D, B12, ferritin, and an Epstein-Barr panel. COVID can reactivate latent viruses. Missing iron deficiency, thyroid disease, or cancer is a real risk.

- **Cardiac red flags require urgent evaluation — do not wait.**

COVID raises fibrinogen and D-dimer levels, increasing pulmonary embolism risk. Autopsy data from early COVID showed micro-clots throughout lung tissue and myocardial inflammation. Runs of SVT and new-onset AFib have been documented. Order an EKG, chest X-ray, and D-dimer/CTA when indicated. A 10-day cardiac monitor is appropriate for persistent palpitations.

- **Mast cell activation may explain brain fog, fatigue, and palpitations — and the fix is simple.**

A nurse practitioner-authored article in the Journal for Nurse Practitioners reported overnight improvement in fatigue, brain fog, and palpitations with antihistamines. A practical starting protocol: cetirizine 10–20 mg at bedtime, add famotidine (H2RA) if partial response, and consider montelukast for the leukotriene pathway. Explain the rationale — patients need to understand why an antihistamine is being prescribed when their nose is not running.

- **POTS and autonomic symptoms can often be managed with sodium tablets and hydration.**

A pulse increase of 10+ beats from lying to standing is a clinical indicator worth treating. Sodium capsules (OTC) taken 2–3 times daily, combined with good hydration, are a first-line intervention. Metoprolol extended-release is a second option. Tilt table testing is often inaccessible — treat based on orthostatic vitals including pulse.

- **Sleep is the most important target in long COVID recovery.**

Patients cannot heal without restorative sleep. Orexin receptor antagonists (now generic) are preferred over hypnotics — they turn off the wakefulness center without the risks associated with zolpidem or trazodone. Address depression and anxiety with SNRIs, which also help with pain and focus. Low-dose stimulants and clonidine have a role in select patients.

- **Movement matters — but start small and use physical therapy.**

Post-exertional malaise is real, but deconditioning compounds it. Encourage patients to start with 1–3 minutes of walking and build slowly. Refer to physical therapy for supervised, accountable progression — especially for patients who are deconditioned or fearful of cardiac symptoms. PT provides safety monitoring and structure that most patients cannot replicate alone.

- **Build your own multidisciplinary team — the long COVID clinics are largely gone.**

Most of the specialized multidisciplinary long COVID clinics that opened post-pandemic have closed due to underutilization and access barriers. Primary care providers must now assemble their own team: PT, physiatry, acupuncture, naturopathy (with appropriate guardrails), and mental health. You are the coordinator of this care.

- **Counsel patients on supplements with evidence and honesty — not dismissal.**

60% of supplements tested at major pharmacies contained only fillers. Advise patients to look for USP endorsement or the GMP (Good Manufacturing Practices) seal. Vitamin D (target 50–60 in long COVID), B12, folate, and ferritin replacement have the strongest rationale. Ivermectin has not shown benefit in controlled trials and carries real drug interaction risks. Do no harm — but do not spend \$1,000 a month on products that are not working.

- **Recovery is real — but it takes time and honest expectation-setting.**

Most patients improve significantly within 6–12 months. Not everyone recovers fully. Severity of initial illness, hospitalization, age, and sex all influence trajectory. The current Omicron-era variants are producing less long COVID than Delta and earlier strains. Repeated COVID infections increase long COVID risk — prevention still matters.

☑ Do This Next

- ☐ The next time a patient presents with a constellation of unexplained symptoms following a COVID illness, open with: "I believe you. Let's figure out what's going on together." Then take a full history before ordering anything.
- ☐ Add an Epstein-Barr panel and vitamin D level to your standard long COVID workup. If EBV IgG is elevated and the patient has profound fatigue, explain the connection — it validates their experience and guides management.
- ☐ For any long COVID patient with palpitations or racing heart, order an EKG at minimum. Consider a 10-day cardiac monitor if symptoms are persistent. Do not assume it is anxiety.
- ☐ Try the mast cell protocol in your next appropriate long COVID patient: cetirizine 10–20 mg at bedtime. If partial response, add famotidine. Explain the rationale. Document the response.
- ☐ For patients with dizziness or near-syncope on standing, check orthostatic vitals including pulse. If pulse rises 10+ beats from lying to standing, start sodium capsules OTC and increase hydration before escalating to medications.
- ☐ Refer your next deconditioned long COVID patient to physical therapy rather than simply advising them to exercise. Frame it as pulmonary or cardiac rehab — supervised, accountable, and safe.
- ☐ At your next long COVID visit, ask: "If you could pick one or two things that are most affecting your quality of life right now, what would they be?" Build the treatment plan around those answers.
- ☐ Screen every long COVID patient for depression and anxiety with a PHQ-9 and GAD-7. If positive, consider an SNRI — it addresses mood, pain, and focus simultaneously.
- ☐ Prioritize sleep in every long COVID visit. Ask about sleep quality, duration, and whether the patient wakes feeling rested. If sleep is disrupted, address it before adding other interventions.
- ☐ When a patient brings in a supplement list or asks about an internet remedy, ask: "Is it working? How do you know?" Help them evaluate it objectively. Advise USP or GMP-certified products only, and clear the deck if the current regimen is not producing results.
- ☐ Counsel patients on olfactory retraining if they have lost their sense of smell — essential oil kits used twice daily have shown benefit through neuroplasticity. It is low-cost, low-risk, and evidence-informed.
- ☐ Set a follow-up appointment before the patient leaves. Long COVID patients need to know you are in it with them for the long haul — not just for one visit.

? Long COVID Readiness: 3 Reflection Questions

Use these individually or to open a team conversation about your practice's approach to long COVID:

Diagnostic confidence: "When a patient presents with fatigue, brain fog, and palpitations after a COVID illness, what is my first instinct — to validate or to question? What would it look like to lead with belief and build the workup from there?"

Treatment approach: "Am I currently using symptom severity scores to track long COVID patients over time? If not, what would it take to add one objective measure to my long COVID visits?"

Team and resources: "Do I have a go-to PT, physiatrist, or mental health provider I can refer long COVID patients to? If not, what is one referral relationship I could build this month?"

▶ Red Flags & Cautions

- A patient with post-COVID palpitations, chest pain, or dyspnea is reassured without cardiac workup — pulmonary embolism, SVT, AFib, and myocardial inflammation are real and documented complications
- Long COVID becomes a catch-all diagnosis — and underlying iron deficiency, thyroid disease, B12 deficiency, or malignancy is missed because the workup was never done

- A patient is spending hundreds or thousands of dollars monthly on unregulated supplements with no objective evidence of benefit — and no one has asked whether they are actually working
- Post-exertional malaise is dismissed as deconditioning or lack of motivation — and the patient is pushed into exercise that worsens their symptoms and erodes trust
- A patient's long COVID symptoms are attributed to anxiety or depression without first ruling out organic causes — particularly cardiac and autonomic dysfunction
- No follow-up appointment is scheduled — leaving a complex, chronic patient without a care partner or longitudinal plan

Clinical Spotlight

★ The Mast Cell Activation Protocol:

Emerging evidence suggests that mast cell activation is a key driver of brain fog, fatigue, palpitations, and rashes in long COVID. A practical, low-cost protocol: cetirizine 10–20 mg at bedtime (preferred over diphenhydramine due to anticholinergic burden), add famotidine as an H2 receptor antagonist for partial responders, and consider montelukast (Singulair) for the leukotriene pathway. One patient reported complete resolution of PVCs overnight. Always explain the rationale — patients need to understand why an antihistamine is being prescribed.

★ The Metformin Study:

A randomized controlled trial found a 41% reduction in long COVID development in overweight or obese patients who were started on metformin (up to 1,500–2,000 mg) during their acute COVID illness for 10 days. This is not yet standard of care, but it is an emerging intervention worth watching — particularly for high-risk patients. The same trial included fluoxetine and ivermectin arms; ivermectin did not show benefit.

★ COVID Vaccination and Long COVID Recovery:

A randomized trial of COVID vaccination in patients who already had long COVID found that a meaningful percentage actually improved after vaccination. The hypothesis: some patients may carry a low-level viral reservoir (similar to varicella in dorsal nerve root ganglia), and vaccination-induced antibodies may suppress that viral load. This is not a recommendation for all long COVID patients — but it is a conversation worth having with those who are willing.

★ Olfactory Retraining:

For patients who lost their sense of smell — particularly those infected with Delta or earlier variants — olfactory retraining using essential oil kits (multiple scents, used twice daily) has shown benefit through neuroplasticity. The brain can retrain its olfactory pathways with consistent stimulation. Loss of smell also impairs taste, which affects nutrition and quality of life. This is a low-cost, low-risk, evidence-informed intervention that is easy to recommend.

★ Supplement Quality — What Patients Need to Know:

A study of over 200 supplement products sold at three major pharmacies found that 60% contained only fillers — no active ingredient. Supplements are regulated under the Food and Cosmetic Act, not the FDA drug approval process. Advise patients to look for USP (United States Pharmacopeia) endorsement or the GMP (Good Manufacturing Practices of America) seal. These certifications confirm that what is on the label is actually in the product.

Conversation Starter

"Think about the last patient you saw who said 'I just haven't felt like myself since COVID.' Did you have a framework for that visit — or did it feel overwhelming? What would it look like to go into that visit with a clear history structure, a targeted workup, and a treatment plan that starts with the two symptoms most affecting their quality of life? What would change for that patient — and for you?"

For Practice Teams: Consider a brief team huddle around: "Do we have a consistent approach to long COVID visits — history, workup, and follow-up? Are we screening for cardiac red flags? Do we have a PT or physiatry referral we trust?" Use the responses to identify gaps in your current workflow.

Resources & Links

Wright & Associates Family Healthcare:
wrightandfamilyhealthcare.com

Fitzgerald Health Education Associates:
fitzgeraldhealth.com

AANP (American Association of NPs): aanp.org

NIH RECOVER Initiative (Long COVID Research):
recovercovid.org

USP Supplement Verification: usp.org/verification-services

Elite Learning CE Podcasts: elitelearning.com/ce-podcasts

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Long COVID Symptom Severity Scores: Search: "Long COVID symptom severity score"

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