



In It for the Long Haul: Post-Acute Sequelae of Severe Acute Respiratory Syndrome Coronavirus 2

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Abstract

The COVID-19 pandemic has caused immeasurable clinical, economic, and societal challenges for the world since early 2020. Intense focus has been placed on determining evidence-based acute management of patients infected with the SARS-CoV-2 virus, as well as accelerating vaccination efforts for those eligible to receive it. As patients recover from infection, many are left with long-term symptoms, known as “Long COVID” or “Post-Acute Sequelae of COVID 19,” that challenges the ability to fully recover, return to baseline health status, and regain quality of life. As the most accessible healthcare professional, pharmacists can assist with the management of long COVID as a member of the multidisciplinary team. Pharmacists’ medication acumen is beneficial to the management of long COVID symptomatology as more research comes to the forefront of this deadly disease.

Keywords

COVID-19, syndrome coronavirus, long-haul COVID, pandemic

The World Health Organization (WHO) officially declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak as a pandemic in early March 2020, resulting in immense operational, financial, and clinical challenges for hospitals and health-systems worldwide. Unbeknownst to patients testing positive for coronavirus disease 2019 (COVID-19), this acute infection would not be their last experience with this novel virus. Many patients discover that they are left with lingering symptomatology weeks to months after initial infection, irrespective of care type (i.e., acute or outpatient). Reports of long-term symptoms after the acute infection quickly became evident, originating through countless patient discussions on social media and online forums. These post-infection symptoms have been coined “Post-Acute Sequelae of COVID19,” “Post-COVID-19 Syndrome,” “Long Haul COVID,” or “Long COVID.”¹ From this point forward, long COVID will be used in this paper to refer to lingering symptoms post-COVID-19 infection. While no universal definition exists, it is generally accepted that symptoms that persist for > 4 weeks after the initial infection are that of long COVID.² A Centers for Disease Control (CDC) survey of 292 adults demonstrated that patients with long COVID were more likely to be > 50 years old, have ≥ 3 chronic conditions, have a body mass index (BMI) ≥ 30 kg/m²,

and report a psychiatric condition. Race and/or ethnicity were not found to be predictors, though the sample size limited identification of such an association.³ Another study utilized the COVID Symptom Study app and found that patients with long COVID (N = 558) were more likely to be older and have a higher BMI. Younger long COVID patients were more likely to be female; however, in patients > 70 years old, sex distribution was equal. In patients > 70 years old, fever and anosmia were associated with presence of long COVID. Incomplete ethnicity data prevented this risk factor from being

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analyzed.⁴ An international online survey of 3762 patients with long COVID identified respondents as female (78.9%, $P < .001$), white (85.3%, $P < .001$), and between the ages of 30 and 60 years old.⁵ However, the reported demographics were heavily influenced by those who chose to respond to the survey—distributed via online COVID-19 support groups and social media—and may not represent the larger population affected by long COVID.

Clinical Features of Long COVID

The cause of long COVID is not yet known; however, it is thought to be due to a combination of factors, such as persistent viremia, inflammatory reaction, or post-traumatic stress.⁶ The most common long COVID symptoms described in existing literature to date include fatigue, cough, “brain fog,” and shortness of breath.^{3,7} While these are the most common, patients with long COVID may experience a variety of lingering symptoms across multiple organ systems (Table 1). These symptoms may not correlate with the severity of the acute infection experienced and does not forecast a consistent time to return to baseline. As such, the persistence of these symptoms greatly impacts a patient’s quality of life, management of comorbidities, and ability to resume activities at the same capacity as pre-COVID-19 infection. The ideal management of long COVID continues to be investigated; however, the general approach centers on improving quality of life and symptom management. Non-pharmacologic strategies are maximized for patients with mild symptomology, while those with more severe symptoms should engage the multidisciplinary team and specialists, especially if symptoms persist or worsen.⁶

The Pharmacist’s Role in Long COVID Management

Despite the continued lack of recognition of pharmacists as providers federally and the variable practice as providers across each state, pharmacists are well positioned to address the existing and emerging needs of those with long COVID. Those practicing within the emergency department (ED) and acute care settings can ensure a thorough history collection

when patients present with long COVID concerns. As part of a multidisciplinary team and a hospital collaborative practice agreement (CPA), pharmacists could also order and evaluate laboratory tests and contribute to the identification of undiagnosed long COVID sequelae. Pharmacists can also ensure successful transitions of care, an important call to action for both the discharging pharmacist (e.g., hospital pharmacist) and the receiving pharmacist (e.g., long-term care facility pharmacist and clinical ambulatory pharmacist) in an effort to reduce readmissions.^{8,9} Pharmacists should be strong advocates for discharging these individuals home with palliative care given the decreased risk of hospitalizations seen when palliative care is involved with general medicine patients.¹⁰ Home care, hospice, and palliative care pharmacists can play a key role in pain and symptom management as well. Those practicing in long-term and skilled care environments should be mindful of the atypical presentation of long COVID in older patients, including an increased risk for sarcopenia, malnutrition, depression, and delirium.¹¹ Pharmacists can deliver additional value by providing on-call services for nursing questions and provider consults, educating the multidisciplinary team, staying abreast of literature and guideline updates, and leading the development of algorithms for long COVID symptom management.

Pharmacists in the ED, community, and ambulatory care settings are well suited to screen patients for long COVID symptoms as part of a comprehensive medication review, especially when medications, including complementary and alternative medicines (CAM) and over the counter (OTCs), do not align with the diagnosis list. Pharmacists should assess the influence of pharmacotherapy on patients’ long COVID symptoms given the risk of adverse drug effects contributing to symptoms, as well as medications that may be contributing to or exacerbating symptoms of long COVID.¹² This is especially important in older adults where atypical presentation of long COVID is quite common. Pharmacists can lead optimization of medication regimens used for long COVID symptom relief, such as correct medication selection, dose titration, and/or mitigation of inappropriate opioid prescribing.^{13,14}

Table 1. Summary of Long COVID Symptoms by Organ System^{1,2,7}.

System	Signs and symptoms
Pulmonary	Dyspnea, cough, throat pain, decreased exercise capacity, hypoxia, ground-glass opacities, fibrotic changes
Neurocognitive	Brain fog; dizziness; headache; loss of attention; confusion; Guillain–Barre syndrome; nerve, nerve root, and plexus disorders; myoneural junction and muscle disease; Parkinson’s disease and Parkinsonism; encephalitis; dementia
Cardiovascular	Chest pain, palpitations, tachycardia, myocarditis, myocardial fibrosis
Gastrointestinal	Abdominal pain, diarrhea, vomiting
Psychiatric	Anxiety, depression, insomnia, post-traumatic stress disorder, mood disorders, substance use disorder
Musculoskeletal	Arthralgia, myalgia
Dermatologic	Hair loss
Other	Ageusia, anosmia, parosmia, skin rashes

Community and ambulatory care pharmacists have proven positive outcomes in the management of chronic diseases; therefore, the management of those with long COVID is a natural extension of the pharmacist's role.¹⁵ Both practice settings provide greater access to care for patients, helping offload work from the primary care provider, particularly in rural settings in which pharmacists are the only providers available to patients. Pharmacists can educate and monitor progress of non-pharmacologic strategies to help those with long COVID, such as tobacco smoking cessation and sleep hygiene training. Through a Collaborative Practice Agreement and where state practice allows, community and ambulatory care pharmacists may employ screening tools, order lab tests, and choose treatment for identified long COVID symptoms such as albuterol for persistent dyspnea. Community pharmacists are most likely to encounter individuals seeking relief with OTCs and can validate their symptoms, assist with product selection, and/or assess when further work-up or emergent evaluation is necessary. Attempting non-pharmacologic strategies first for long COVID can minimize the excessive and expensive tests that may result in significant medical bills.¹⁶ Given that symptoms of long COVID may cross multiple specialties, pharmacists can be the unifying provider for long COVID care. COVID-19 online forums reveal a population frustrated with their portrayal as hypochondriacs rather than a cohort with legitimate symptoms. Pharmacists would do well to approach these individuals with empathy and quickly align themselves as an integral part of the patient's care team. Utilization of a pharmacist can assist in optimizing specialist referrals, particularly to clinics that engage their clinical pharmacist for long COVID care, decreasing the overall cost of care. As long COVID clinics are created, pharmacists are an imperative addition and should serve as educators within community-based programs.¹²

Lastly, pharmacists are the most accessible healthcare professional, fully capable of providing vaccine education and guidance. This in turn helps to promote vaccine confidence, combat misinformation, and remove disinformation from the general knowledge of patients and providers alike. Instilling vaccine confidence is especially important given anecdotal evidence emerging for patients impacted by long COVID noting improvement or even complete resolution of symptoms, most notably "brain fog" and gastrointestinal (GI) symptoms, after vaccination. Pharmacy organizations at state and federal levels have successfully advocated for expanded scope of practice for pharmacists and technicians during the public health emergency, granting the ability to administer the COVID-19 vaccine to almost all age groups and providing prophylaxis and treatment of COVID-19 infection, thus decreasing the risk for developing long COVID.

Conclusion

The National Institutes of Health (NIH) has committed to investing \$1.15 billion over the next 4 years to better

understand prevention and treatment of long COVID.¹⁷ Pharmacist engagement in ongoing research efforts is key to best elucidate the medication management needs of patients with long COVID. Pharmacists should make it standard practice to screen all post-COVID-19 patients for long COVID symptomology upon presentation of any new symptom. Vaccination efforts have led to the protection of patients from mortality attributed to SARS-CoV-2 infection; however, there are still many unknowns related to the impact of vaccination on the risk for long COVID, as well as its role in resolution of symptoms. Studies examining long COVID are woefully limited in enrollment of patients of color, leaving a gap in our understanding of its impact on these communities. Outreach efforts that engage pharmacists may help improve access to care and ensure that the health equity chasm does not widen. Pharmacists must continue to advocate for legislation that provides the opportunity to care for patients as the medication experts on the team during the COVID-19 pandemic and beyond.

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