Post-COVID-19 Conditions Clinical Pathway

Diagnosis/Condition:	Long COVID Post-COVID-19 Conditions Post-acute Sequelae of SARS CoV-2 infection
ICD-10 Codes:	U09. 9
Origination Date:	2024
Reviewed/Revised Date:	04/2025
Next Review Date:	04/2027

Introduction

The COVID-19 Pandemic began in December 2019 when a novel coronavirus was first detected in China, later named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) with the term "COVID-19" used to name the infection.[1] By the end of January 2020, the World Health Organization (WHO) had declared a Public Health Emergency of International Concern (PHEIC), and then officially categorized the outbreak as a pandemic on March 11, 2020.[1] The PHEIC ended on May 5, 2023, per the recommendations of the WHO, but the COVID-19 pandemic continues.[1]

CHP Clinical Pathways are designed to support the evidence-based practice of integrative healthcare providers. Evidence-based practice incorporates the best research evidence, clinical expertise, and patient preferences to guide clinical decision making. The pathways have been developed from a combination of peer reviewed research evidence and clinical expertise, skills, and knowledge. Whenever possible, research literature is cited to support recommendations expressed in the pathways. Clinical expertise and knowledge from practitioners in the fields of chiropractic, naturopathic medicine, acupuncture, and massage therapy are also incorporated to produce an apprised and pragmatic document. The reader is encouraged to evaluate the evidence and recommendations presented in these pathways in the context of the unique characteristics, culture, and preferences of their patients and their own clinical knowledge.

While most individuals recover from COVID-19 within four weeks[2], not all make a complete recovery. It is estimated that 6% continue to suffer from chronic sequalae and may develop chronic symptoms despite testing negative or being unaware of a prior COVID-19 infection.[3,4]

The naming convention for these chronic symptoms is still evolving. The CDC reports the term "Long COVID" was originally created by patients and is the equivalent to the clinical term of "Post-COVID-19 Conditions" (PCC), while the term "Post-acute Sequelae of SARS CoV-2 infection" (PASC) is used by the research community.[5]

The National Academies' Interim Working Definition[6] states that;

"Long COVID is broadly defined as signs, symptoms, and conditions that continue or develop after initial COVID-19 or SARS-CoV-2 infection. The signs, symptoms, and conditions are present four weeks or more after the initial phase of infection; may be multisystemic; and may present with a relapsing–remitting pattern and progression or worsening over time, with the possibility of severe and life-threatening events even months or years after infection. Long COVID is not one condition. It represents many potentially overlapping entities, likely with different biological causes and different sets of risk factors and outcomes."

Research on the causes of Post-COVID-19 Conditions (PCC) continues, but the CDC offers the following etiological categories: organ damage resulting from acute phase infection, complications from a dysregulated inflammatory state, microvascular dysfunction, ongoing viral activity associated with an intra-host viral reservoir, autoimmunity, inadequate antibody response, and other potential causes.[2]

About 1.7% to 3.8% of the US adults were experiencing PCC that limited their activities on November 1, 2021, based on point prevalence modeling and adjustment for under-ascertainment of infection.[7] The prevalence of those who have ever experienced PCC averaged 6.9% of US adults in 2022, but this varied by location from a low of 1.9% in the US Virgin Islands, to 5.3% in Oregon and 5.2% in Washington, to greater than 9% in Alabama, Montana, North Dakota, and Oklahoma, and a maximum of 10.6% in West Virginia.[8]

Private insurance healthcare costs in the US with PCC for a 6-month period starting at 31 days after a COVID-19 diagnosis were on average $1,000 more for children and $1,500 more for adults under age 65 when compared with their peers who did not contract COVID-19 (an increase of 70% and 46% respectively).[9] These differences were greater for older adults and for those who had required hospitalization, peaking at about a 15 fold increase in healthcare costs in a 1-month period for those aged 50-64 who required hospitalization for acute COVID-19.[9]

Insights from an Integrated Health Lens

The manifestation of post-viral sequela occurring with COVID, is not unique, but rather quite common with many virus, e.g. SARS, polio and EBV.[10] Indeed, in Traditional East Asian Medicine (TEAM) there are long-standing traditions of recognizing the persistent nature of viral infections and this dates to the oldest medical text book, the *Huang Di Nei Jing (*~400 BCE - 260 CE*).* This historical text speaks directly to this concept, which is referred to as *Fú xié* ("Hidden/Lingering Pathogen/Evil *Qi*). *Fú xié* is often described as a pathogen (virus) that remains in the body after an illness and induces chronic or intermittent clinical symptoms and signs.[11]

History and Presentation*

Risk Factors:
- Anyone is at risk of developing PCC after a COVID-19 infection,[3,12] and each reinfection carries a risk of PCC.[3]

- Severe COVID-19 during the acute phase, such as requiring hospitalization or intensive care.[3]
- Development of multisystem inflammatory syndrome (MIS) during or after COVID-19 infection.[2]
- Underlying health condition before becoming infected with the SARS-CoV-2 virus.[3]
- "Health inequities may put some people from racial or ethnic minority groups and some people with disabilities at greater risk for developing Long COVID."[3]
- Adults appear to be more at risk than children.[3]
- Females ≥20yrs[4]
- Unvaccinated status.[3]
- The symptom of breathlessness.[12]

Associated/Co-Morbid Conditions:

- In children aged 0-17:[13]
  - acute pulmonary embolism
  - cardiomyopathy
  - venous thromboembolic event
  - acute and unspecified renal failure
  - type 1 diabetes
- In adults:
  - Myalgic encephalomyelitis/chronic fatigue syndrome[3]
  - Post-intensive care syndrome (PICS)[3]
  - Post-traumatic stress disorder (PTSD)[3]
  - Diabetes & Hypertension reported in 10% of cases (N=371)[14]

Symptom Location, Quality, and Severity:

The CDC reports the following common PCC symptoms:[2,3]

- General symptoms (Not a Comprehensive List)
  - Fatigue that interferes with daily life
  - Post-exertional malaise
  - Fever
- Respiratory and heart symptoms
  - Dyspnea or increased respiratory effort
  - Cough
  - Chest pain
  - Palpitations
  - Tachycardia
- Neurological symptoms
  - Cognitive impairment or "brain fog"
  - Headache
  - Insomnia and other sleep problems
  - Lightheadedness

- Paresthesia
- Change in smell or taste (anosmia or dysgeusia)
- Mood changes, depression or anxiety

- Digestive symptoms
  - Diarrhea
  - Abdominal pain
- Other symptoms
  - Arthralgia
  - Myalgia
  - Rash (e.g., urticaria)
  - Menstrual cycle irregularities
  - Erectile dysfunction

Symptom Onset/Timing, Frequency, Duration:

- The onset of symptoms is four weeks or more after infection.[5]
- Symptoms can worsen over time or have a relapsing-remitting pattern.[5]
- PCC can last weeks, months, or years.[3]
  - Largest data set (N=1.2million) suggests a mean symptom duration:[15]
    - Hospitalized individuals: 9 months
    - Non-hospitalized individuals: 4 months

Associated Symptoms:

- Any organ system symptoms[2]
- Often clustered as: 1) Physical; 2) Psychological; 3) Cognitive; and many patients experience symptoms in multiple categories[4]
- Physical symptoms (non-hospitalized patients)[16]
  - Fatigue: 34%
  - Dyspnea: 20%
  - Muscle pain/myalgias: 17%
  - Insomnia: 15%
  - Anosmia: 13%
- Psychological or cognitive symptoms: ~25%[4]
- Functional disability in ADL persisting >4mths: ~50%[4]

Traditional East Asian Medicine (TEAM) History:

Assess the 10 questions for pattern differentiation & disease level

1. Temperature (Hot, Cold and Fever, Chills)
2. Sweat (Location, nature & timing)
3. Head & Face (Headache, dizziness, eyes & ears)
4. Pain (Nature & location)
5. Urine, Stool (Nature & timing)
6. Thirst, Appetite, Taste (Altered tastes, e.g metallic, sour)
7. Sleep (including dreams)

8. Thorax, Abdomen (Pain, discomforts)
9. Gynecological (Menstrual cycle nature & timing)
10. History (Medical & family history, mental health status, medications & lifestyle foundation (e.g. diet/exercise)

Physical Exam Findings

Vital Signs:
- Usual/customary vitals should be assessed: (i.e., blood pressure, BMI, heart/respiratory rate, pulse-oximetry, body temperature)
- Additional measures include:
  - Patients with respiratory symptoms, fatigue/ malaise: Ambulatory pulse-oximetry.[2]
  - For patients with postural symptoms, dizziness, cognitive impairment, or fatigue/ malaise: Orthostatic vital signs.[2]

Observation:
- Posture, Gait & physical performance via:[17]
  - Timed Up and Go test (TUG)
  - Short Physical Performance Battery (SPPB)

Traditional East Asian Medicine (TEAM) Evaluation:

Four observations of TCM for pattern differentiation & disease level
1. Observation (body type, skin color variations, gait)
2. Listening/smelling (voice, respiration/cough, body odors)
3. Palpation (pulse, channels, abdomen)
4. Questions (covered above in History)

Segmental/Joint Evaluation:
- Assess for joint pain/stiffness; "Less common persistent physical symptoms" category

Palpation:
- Assess for symptoms and physical exam findings consistent with fibromyalgia. New or worsening symptoms, evidence of synovitis or other rheumatologic illness, refer to rheumatology[17]

Range of Motion:
- Assess for joint pain/stiffness; "Less common persistent physical symptoms" category

Neurological:
- Neurologic complications (e.g. stroke, seizures, neuromuscular weakness) or new neurologic symptoms, refer/perform complete neurologic history and examination; evaluate degree of impact on functional status.[17]

Psychiatric:
- Inquiry regarding symptoms of depression, anxiety, and posttraumatic stress disorder (PTSD).[17] Administer OATs as needed (See below)

Ears, Nose, Mouth, Throat:	• ~5% of patients report olfactory/gustatory symptoms lasting 6-12mths. If symptoms persist >3 months, refer to otolaryngologist[17]
Respiratory:	• SpO_2; Persistent, progressive, or new respiratory symptoms, refer for Pulmonary Function Testing[17]
Cardiovascular:	• Blood pressure & HR • Symptoms of orthostasis, presyncope, or syncope; assess postural blood pressure/pulse rate[17]
Gastrointestinal:	• Patients with swallowing dysfunction; consider Speech-language pathology evaluation.[17] • Persistent or new nausea and/or diarrhea symptoms, refer/consider antibiotic-associated diarrhea or *Clostridioides difficile* enterocolitis.[17]
Genitourinary:	• Assess for Covid-associated cystitis[18] (e.g. Overactive Bladder symptoms); abdominal & pelvic floor assessments as needed
Lymphatic:	• Assess lymph nodes; recommended in patients with cardiovascular symptoms (e.g. myocardial edema[19]).

Imaging Findings

The CDC reports that, "objective laboratory or imaging findings should not be used as the only measure or assessment of a patient's well-being; normal laboratory or imaging findings do not invalidate the existence, severity, or importance of a patient's Post-COVID Conditions."[2]

Ultrasound:	• Consider referral evaluation of lymphatics; recommended in patients with cardiovascular symptoms[19]
X-Ray/CT:	• Consider follow-up chest imaging for patients with pulmonary infiltrate (or other abnormalities) during the acute illness[17] • Consider with new or worsening respiratory symptoms or an abnormal cardiopulmonary physical examination[17]

Lab Work Findings

Currently, there is no laboratory test available to definitively diagnose Long COVID. The CDC suggests that, "…normal laboratory…findings do not invalidate the existence, severity, or importance of a patient's Post-COVID Conditions."[2] Laboratory testing is determined by symptom type and the severity/complications of acute COVID-19. If PCC is deemed mild with improving symptoms, laboratory testing is not recommended.[4]

Blood Work:

- For persistent symptoms, in moderate to severe illness consider:[4]
  - CBC
  - Blood chemistries: electrolytes, blood urea nitrogen, serum creatinine
  - Liver function (including serum albumin)

Assessment

Classification Systems:

- CDC & WHO suggests PCC is defined as:[2,12]
  - Persistent symptoms >12wks
  - Symptoms must have an impact on the patient's QOL
  - Not explained by an alternative diagnosis

Emerging research suggest several categorization models of PCC:

- Symptom Cluster: An analysis (N=34,605) suggests four sub-phenotypes:[20]
  - Cardiac/Renal
  - Respiratory/Sleep/Anxiety
  - Musculoskeletal/Nervous system
  - Digestive/Respiratory system
- Severity: A cohort (N=288) suggests three sub-categories:[21]
  - Mild: ~50% of cohort; less severe initial infection, fewer comorbidities, and few symptoms (mean of 3)
  - Moderate: Sleep & respiratory symptoms; mean of 11 symptoms
  - Severe: Vascular, urinary, and dermatological symptoms; >11 Symptoms total
- Duration: A commentary suggests four stages:[22]
  - ~4-5wks: Potentially infection related-symptoms
  - 5-12wks: Acute PCC symptoms
  - 12-24wks: long PCC symptoms
  - >24wks: persistent PCC symptoms

Outcome Assessment Tools (OATs)

- An international consensus conference recommends OATs to assess long-term cognition, mental health, and physical function:[23]
  - Cognition: Montreal Cognitive Assessment (MoCA)
  - Depression/Anxiety: Hospital Anxiety and Depression Scale (HADS)
  - PTSD: Impact of Event Scale (IES-R)
  - Physical function: EuroQol-5D-5L

Differential Diagnoses:

- PCC is a diagnosis of exclusion; symptoms/diagnoses should be "reasonably excluded," clinically and/or with additional testing.[4]
- Pre-COVID medical conditions, "physical and mental health consequences of illness with a long or complicated disease course, including depression and anxiety, as well as social, environmental, and economic stressors" may make it difficult to differentiate Long COVID symptoms.[2]
- COVID-19 reinfection.[2]
- Multisystem inflammatory syndrome (MIS)[2]
- Myalgic encephalomyelitis/chronic fatigue syndrome[3]
- Post-intensive care syndrome (PICS)[3]
- Post-traumatic stress disorder (PTSD)[3]
- Life threatening conditions such as pulmonary embolism, myocardial infarction, pericarditis with effusion, stroke, renal failure.[2]

Naturopathic Algorithms:

- Consider the mechanism or history of onset.

Bian Bing and *Bian Zheng* (TEAM):

- COVID belongs to the category: *Yi Li* (epidemic/pestilent diseases)[24] more specifically many classify it as *Wen Bing* (Warm Febrile Disease).
- Differentiate PCC symptoms based on *Bian Zheng* to determine depth and location. Common syndromes include *Qi* and *Yin Xu* of various organ levels/systems, e.g. Spleen & Lung *Qi Xu*[25,26]

Red Flags:

- Life threatening conditions such as pulmonary embolism, myocardial infarction, pericarditis with effusion, stroke, renal failure.[2]

Specialist Referral

When to Refer:

- Emergency referral for any suspected life threatening conditions such as pulmonary embolism, myocardial infarction, pericarditis with effusion, stroke, renal failure.[2]
- Further evaluation for patients with symptoms lasting more than 3 months.[2]

Specialty:

- Referral for outpatient COVID-19 recovery clinic or a subspecialty relevant to specific symptoms as needed (e.g, cardiology, neurology).[4]

World Health Organization:	WHO: Living Guidance for Clinical Management of COVID-19: Rehabilitation of adults with post COVID-19 condition; https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2023.2
Department of Veteran Affairs:	Whole Health System Approach to Long COVID (August 1, 2022) https://www.publichealth.va.gov/n-coronavirus/docs/Whole-Health-System-Approach-to-Long-COVID_080122_FINAL.pdf
National Institute of Health and Care (NICE) (United Kingdom):	COVID-19 rapid guideline: managing the long-term effects of COVID-19 (2020, last updated January 25, 2024) https://www.nice.org.uk/guidance/NG188
American Academy of Physical Medicine and Rehabilitation:	Multidisciplinary Quality Improvement Initiative[27] https://www.aapmr.org/members-publications/covid-19/multidisciplinary-quality-improvement-initiative Published works found on their above website (2022-2023): • Numerous Guidance statements are provided online per symptom cluster or population, e.g. Neurological, Pediatrics, Fatigue. o Neurological Symptoms Guidance Statement[28] o Pediatrics Guidance Statement[29] o Fatigue Guidance Statement[30]
American College of Cardiology (ACC):	ACC Expert Consensus Decision Pathway on Cardiovascular Sequelae of COVID-19 in Adults (2022)[31] https://www.jacc.org/doi/epdf/10.1016/j.jacc.2022.02.003
American Academy of Pediatrics:	Post-COVID-19 Conditions in Children and Adolescents (2022) https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/post-covid-19-conditions-in-children-and-adolescents/
American Family Physician:	Long COVID: A Primer for Family Physicians (2020) https://www.aafp.org/pubs/afp/issues/2020/1215/p716.html
European Respiratory Society	European Respiratory Society Statement on Long COVID-19 Follow-Up[32] https://erj.ersjournals.com/content/early/2022/02/03/13993003.02174-2021?ct

Treatment Modalities

High level scientific research, such as meta-analyses, systematic reviews, and clinical trials, have been prioritized for inclusion. Not all available data are incorporated in the summaries below.

Mind-Body Therapies:	These therapies include breathing techniques, meditation, Qi Gong, yoga, mindfulness, etc. Five RCTs have been published, each suggesting that breath-focused training programs may be beneficial to improve quality of life and long-COVID related symptoms.

RCT (2023) *Positive Impacts of a Four-Week Neuro-Meditation Program on Cognitive Function in Post-Acute Sequelae of COVID-19 Patients: A Randomized Controlled Trial.*[33]

- Funding: No external funding
- Participants: N=34; Adults diagnosed w/Long-COVID
  - Age: 48±10 years; 71% female; Location: France
- Interventions: 2 Groups: 1) Intervention group: Ten 30-min sessions of Rebalance® 2-3x/wk for 4wks (sound therapy & coach-guided meditation w/chromotherapy); 2) No treatment control
- Primary outcome: Performance on five computerized cognitive tasks at end of Tx (week 4)
- Results: Statistically significant difference of treatment reported for 3 of 5 outcomes
  - Choice reaction time ($p<0.001$); 2) Simon ($p<0.01$); 3) pattern comparison tasks ($p< 0.001$)
- Author's Conclusion: "The Rebalance® program hence constitutes a promising non-pharmacological intervention for the treatment of long-term psychological/cognitive outcomes of COVID-19."
- CHP Group Caveats: No funding listed, but seems authors were provided the treatment device and did not disclose this.

RCT (2022) *Inspiratory muscle training enhances recovery post-COVID-19: a randomised controlled trial*[34]

- Funding: Welsh Government
- Participants: N=281; Adults recovering from self-reported COVID (~9 months)
  - Age: 47±12 years; 88% female; Location: UK/Denmark (online)
- Interventions: 2 Groups: 1) 8-week Inspiratory muscle training (IMT) 3x/wk for 20 min w/a wireless handheld device; or 2) usual care waitlist control

- Primary outcome: Total score of King's Brief Interstitial Lung Disease (K-BILD) at end of Tx (week 8)
- Results: No difference between groups in K-BILD total score post-intervention (control: 59.5 ±12.4 vs. IMT: 58.2 ±12.3; $p<0.05$).
  - Clinically meaningful improvements noted for IMT in the K-BILD domains (breathlessness and chest symptoms).
- Author's Conclusion: "…despite the absence of an effect of IMT on K-BILD…IMT elicited clinically meaningful reductions…Our findings thus indicate IMT may be an efficacious home-based rehabilitation strategy during recovery from COVID-19."
- CHP Group Caveats: None to report

RCT (2022) *An online breathing and wellbeing programme (ENO Breathe) for people with persistent symptoms following COVID-19: a parallel-group, single-blind, randomised controlled trial*[35]

- Funding: Imperial College London
- Participants: N=150; Adults w/persistent breathlessness following COVID-19
  - Age: 49yrs ±12; Gender: 81% Female; Location: UK (online)
- Interventions: 2 Groups: 1) Online breath program 1hr/wk for 6-weeks (English National Opera (ENO Breathe program); 2) Continued usual care
- Primary outcome: Health related quality-of-life (HRQoL) via RAND 36-item instrument (mental health composite (MHC) and physical health composite (PHC) scores)
- Results: Compared with usual care, ENO Breathe program associated with an improvement in MHC score (2.42 [95% CI: 0.03 to 4.80]; p=0.05), but not PHC score (0.60 [-1.33 to 2.52]; p=0.54).
- Author's Conclusion: "…an online breathing and wellbeing programme can improve the mental component of HRQoL and elements of breathlessness in people with persisting symptoms after COVID-19."
- CHP Group Caveats: None to report

RCT (2022) *Evaluating the Efficiency of Breathing Exercises via Telemedicine in Post-Covid-19 Patients: Randomized Controlled Study*[36]

- Funding: No external funding
- Participants: N=52; Adults w/persistent dyspnea after Covid-19-related pneumonia
  - Age: ≥18yrs; Gender: 52% male (N=27); Location: Turkey (online)

- Interventions: 2 Groups: 1) Breathing exercise program (3x/d for 5 weeks; 1 session/wk via telemedicine); or 2)Control group (brochure explaining the exercises)
- Primary outcome: Two outcomes: 1) Spirometry (FVC, FEV1, FEV1/FVC Ratio, and MVV) and 2) six-minute walk test; both assessed at week 5 (end of the study)
- Results: Significant improvements in 6min walk test, FEV1, FVC, and MVV values in the intervention group compared to the control group ($p<0.001$).
- Author's Conclusion: "…breathing exercise training applied through telemedicine, improvements were observed in the pulmonary functions, quality of life, and exercise capacities of dyspneic post-Covid-19 individuals"
- CHP Group Caveats: Small sample size; Questionable statistics (2 primary outcomes)

RCT (2022) *Effect of a home-based inspiratory muscle training programme on functional capacity in postdischarged patients with long COVID: the InsCOVID trial*[37]

- Funding: Sociedad Española de Cardiología, Investigación Clínica en Cardiología
- Participants: N= 26; Adults >18 with long COVID and a previous admission due to SARS-CoV-2 pneumonia (>3mths ago)
  - Age: 50.4±12.2yrs; Gender: 42% Female; Location: Spain
- Interventions: 2 Groups: 1) 12-week home-based inspiratory muscle training (IMT; 2x/d with diaphragmatic breathing focus); 2) Continued usual care as needed.
- Primary outcome: Peak oxygen consumption (peakVO_2) at end of Tx (week 12)
- Results: IMT significantly improved peakVO_2 compared with usual care (MD 4.46 mL/kg/min; 95% CI: 3.10 to 5.81; $p<0.001$)
- Author's Conclusion: "Home-based IMT seems to be a suitable, feasible and effective alternative to supervised exercise training programmes for improving exercise capacity and quality of life in patients with long COVID and may offer an accessible physical therapy model, requiring minimal infrastructure resources."
- CHP Group Caveats: Small sample size

Diet:	This form of treatment includes named diets, TEAM-related dietary philosophies, etc. ***No research available that meets our inclusion criteria***

Herbal Medicine (Western):	This includes herbs, such as marshmallow, slippery elm, elderberry, echinacea, etc., used individually or in combination through a Western herbal medicine model that may focus on symptoms or constitutional factors. A single RCT was identified, suggesting a proprietary aromatherapy blend may improve energy levels among women recovering from COVID-19.

RCT (2022) *Aromatherapy blend of thyme, orange, clove bud, and frankincense boosts energy levels in post-COVID-19 female patients: A randomized, double-blinded, placebo controlled clinical trial*[38]

- Funding: Young Living Essential Oils
- Participants: N=40; Adults 19-49yrs old who were >5mths post-COVID infection and experiencing *"…fatigue at a level that was not present prior to COVID-19."*
  - Age: Not reported; Gender: 100% Female; Location: USA
- Interventions: 2 Groups: 1) Aromatherapy (proprietary essential oil blend: thyme, orange, clove bud, and frankincense) *vs.* 2) Placebo Aromatherapy (inert, odorless coconut oil).
  - Both groups inhaled BID for 2wks
- Primary outcome: Fatigue at the end of treatment (2wks); Multidimensional Fatigue Symptom Inventory (MFSI)
- Results: After adjusting for high variance, the authors report adjusted mean scores: 25.42 (SE 3.10) aromatherapy *vs.* 37.13 (SE 3.10) for placebo (F=1.39; p= 0.020, partial eta squared = 0.198).
- Author's Conclusion: "…a proprietary aromatherapy blend can significantly improve energy levels among women who are experiencing fatigue after recovering from COVID-19."
- CHP Group Caveats: Industry funded; Small sample size and high variation between groups; Data not provided for independent analysis.

Herbal Medicine (Traditional East Asian Medicine):	This includes the use of TEAM herbal formula (multiple herbs) or single herbs (e.g. ginger, licorice and ginseng) that are part of the Chinese herbal pharmacopeia. There is a paucity of research on the use of TEAM-based herbal medicine for Long-COVID symptoms. A 2022 scoping review identified a single case control & case study. Since then, a single RCT has been published suggesting benefit of herbal patent pills.

Scoping Review (2022)

A 2022 scoping review of assessed the literature for CAM interventions for treatment of long-COVID.[39] Two clinical publications (case control & case study) met the inclusion criteria (assessed through October 2021) and these suggest that *"Chinese herbal medications were effective in relieving symptoms of pulmonary dysfunction."* However, the authors aptly conclude, *"there is a lack of published studies about the effectiveness and safety of CAM interventions for long COVID."*

Project Overview (2021)

The three syndromes and six Chinese patent medicine study during the recovery phase of COVID-19[40]

- Article info: Research project Overview (2021)
- Funding: National Key R&D Program; State Administration of TCM; China
- Study Characteristics: 6 inter-related RCTs; 1,200 participants total
  - Age: 18-70; Gender distribution not reported; Adults with Long-COVID Sx
- Modalities Included: Six different Chinese patent medicines (1 per trial) to treat Patients with Long-COVID Sx affecting either cardiopulmonary function, sleep, or digestion.
- Author's Conclusion: *"Our research provides a guideline for treating COVID-19 sequelae in patients during the recovery period…"*
- CHP Group Concerns: Article is an overview of 6 inter-related RCTs. Limited info is provided, with no data or references to the clinical trials.

Homeopathy:	This includes naturally occurring substances in precisely prepared minute doses to work with the body's natural healing capacity. Official homeopathic drugs are monographed and accepted for inclusion in official registries (e.g. Homeopathic Pharmacopeia of the United States). ***No research available that meets our inclusion criteria***
Supplements and Nutrients:	This includes OTC products such as multi-vitamins, calcium, and fish oil that have a nutritional or supplementary purpose and are generally considered non-pharmaceutical. A scoping review concluded that preliminary evidence suggests nutritional interventions may be an important part of a rehabilitation program for long-COVID. This is supported by five RCTs, each assessing a different nutrient/supplement for differing symptoms (e.g. fatigue, anosmia). As a whole, the emerging evidence suggests these interventions may be useful, but more research is warranted.

Scoping Review (2023)

Nutritional Support During Long COVID: A Systematic Scoping Review[41]

- Funding: National Centre for Naturopathic Medicine; Southern Cross University
- Study Characteristics: N=5; 451 participants; Included case series, cohort, and RCTs through 1/31/2022
  - Participants 18+yrs, with long COVID and who underwent a nutritional intervention; Age ranged from 27-72; 62% female
- Modalities Included: Two broad supplement categories: 1) Stand-alone treatment or 2) incorporated as part of multidisciplinary rehabilitation program.
  - Most often reported supplements were: B-group vitamins, vitamin C, vitamin D, and acetyl-l-carnitine
- Results: Descriptive analysis was provided suggesting,"…preliminary evidence that nutritional interventions may be an important part of a rehabilitation program for people with severe long COVID symptomatology, including severe inflammation, malnutrition, and sarcopenia."
- Author's Conclusion: "Further clinical studies incorporating complex nutritional interventions are also warranted to strengthen the evidence base for using nutrition as a useful adjunctive treatment for people living with long COVID."
- CHP Group Caveats: Outcomes data & heterogeneous outcome measures; No pooling of data for meta-analysis.

Prospective Cohort Study (2022)

Coenzyme Q10 + alpha lipoic acid for chronic COVID syndrome[42]

- Funding: No external funding
- Participants: N=174; Adults 18–81 who contracted COVID-19 and who met the 2015 National Academy of Medicine diagnostic criteria for myalgic encephalomyelitis/chronic fatigue syndrome
  - Age: 51 ±13yrs; Gender: 49% female (N=85); Location: Italy
- Interventions: 2 Groups: 1) Coenzyme Q10 + alpha lipoic acid (Requpero®; N=116); 2) No additional treatment (N=58); both received usual care
- Primary outcome: Fatigue Severity Scale (FSS) at end of Tx (60d)
- Results: A complete response (>50% FSS change) was reached in 53.5% (N=62) of patients in treatment group vs. 3.5% (n=2) in control group.
  - A significant difference was also observed in non-responders (<20% change in FSS); 9.5% (N=11) in the treatment group vs. 25.9% in the control group (N=15) ($p < 0.0001$)
- Author's Conclusion: "…this is the first study that tests the efficacy of coenzyme Q10 and alpha lipoic acid in chronic Covid syndrome.

Primary and secondary outcomes were met. These results have to be confirmed through [RCTs]…"

- CHP Group Caveats: Non-Randomized Controlled Trial (nRCT); Exploratory trial

RCT (2022) *Molecular Hydrogen Positively Affects Physical and Respiratory Function in Acute Post-COVID-19 Patients: A New Perspective in Rehabilitation*[43]

- Funding: Palacký University Olomouc, Czech Republic
- Participants: N=54; Adults 18–65yrs with acute post-COVID-19 syndrome; 21-33 days after a positive COVID test
  - Age: 41 ±14 yrs; Gender: 43% female (N=23); Location: Czech Republic
- Interventions: 2 Groups: 1) Molecular hydrogen (H_2, ~300 mL/min); 2) Placebo inhalation. Both groups administered via nasal canula, (2x/d for 60min for 14 days).
- Primary outcome: 6-min walking test (6 MWT)
- Results: H_2 therapy significantly increased 6 MWT distance vs. placebo (64 ±39m *vs.* 9 ±29m ($p< 0.001$)
  - Secondary outcomes also favored H_2 therapy; FVC: 0.19 ±0.24L and FEV1: 0.11 ±0.28L ($p\leq0.025$)
- Author's Conclusion: "Our results suggest that 14 days of regular H2 inhalation may be considered as an efficient rehabilitation approach for improving both physical and respiratory function in acute post-COVID-19 patients."
- CHP Group Caveats: Small sample size; First published RCT on use of home-based H_2 therapy

RCT (2022) *Use of 1-MNA to Improve Exercise Tolerance and Fatigue in Patients after COVID-19*[44]

- Funding: No external funding
- Participants: N=50; Adults >18 with fatigue (>50% vs. pre-COVID levels) for at least four weeks post-COVID
  - Age: 49±10yrs; Gender: 68% female (N=34); Location: Poland
- Interventions: 2 Groups: 1) 1-Methylnicotinamide (1-MNA; 58mg qd); 2) Placebo
- Primary outcome: 6-minute walk test (6MWT) at end of Tx (1-month)
- Results: 1-MNA supplementation led to significant improvement in 6MWT of μ47m for 92% (N=23) vs. 60% (N=15%) of control ($p=0.0061$).
- Author's Conclusion: "The comprehensive action of 1-MNA, including anti-inflammatory and anticoagulant effects, may be beneficial for the recovery of patients with persistent symptoms of fatigue and low tolerance to exercise after COVID-19."

- CHP Group Caveats: Exploratory trial; Small sample size

Pilot RCT (2021) *Randomized clinical trial "olfactory dysfunction after COVID-19: olfactory rehabilitation therapy vs. intervention treatment with Palmitoylethanolamide and Luteolin": preliminary results*[45]

- Funding: Authors declare no conflicts of interest
- Participants: N=12; Adults 18-90yrs with post-COVID olfactory impairment (≥ 90 days)
  - Age: 42±14 yrs; Gender: 67% female (N=8); Location: Italy
- Interventions: 2 Groups: 1) Usual care: olfactory training (Sniffin' Sticks) 2x/day, 10min/session for 30 days; 2) Treatment group (TG): olfactory training plus Palmitoylethanolamide (PEA, 700mg) and Luteolin 70 mg (Glialia®).
- Primary outcome: Sniffin scores at end of Tx (30d)
- Results: TG patients had greater improvement in Sniffin score than usual care (MD: 2 for CG & 4 for TG; P=0.01)
- Author's Conclusion: "Treatment combining olfactory rehabilitation with oral supplementation with PEA and Luteolin was associated with improved recovery of olfactory function, most marked in those patients with longstanding olfactory dysfunction.
- CHP Group Caveats: : Exploratory trial; Small sample size

Pilot RCT (2022) *Preventive effects of Pycnogenol® on cardiovascular risk factors (including endothelial function) and microcirculation in subjects recovering from coronavirus disease 2019 (COVID-19)*[46]

- Funding: Unknown (Abstract only)
- Participants: N=60; symptom characteristics
  - Age: ± yrs; Gender: % female (N=); Location:
- Interventions: 2 Groups: Pycnogenol® (150 mg/d) + usual care vs. usual care alone for 3-months
- Primary outcome: None defined; pilot study
- Results: From abstract: *"Patients, supplemented with Pycnogenol® showed significantly better improvement compared to the control group patients. No side effects…were observed…"*
- Author's Conclusion: "Pycnogenol® may offer a significant option for managing some of the signs and symptoms associated with post-COVID-19 syndrome."
- CHP Group Caveats: Pilot study; Info retrieved from Abstract only

Pharmaceuticals (Over-the-Counter):	The scope of this Clinical Pathway does not include review of over-the-counter pharmaceuticals, though they are within the scope of practice of some providers on network. Quality evidence-based references already

	exist for these treatments; however, we have included some selected information.

Living Systematic Review (2022)

Interventions for the prevention of persistent post-COVID-19 olfactory dysfunction[47]

- Funding: National Institute for Health Research & Cochrane Programme Grant
- Study Characteristics: N=5; 691 participants; Included RCTs through 10/20/2021
  - Mean age & gender not reported; Adults ≥18yrs w/ COVID-19 related persistent olfactory disturbances (<4wks)
- Modalities Included:
  - 1) Intranasal corticosteroid sprays/drops (N=3)
    - Mometasone furoate 100mg; qd for 3-4wks
    - Triamcinolone acetonide 0.055%; bid for 4wks
  - 2) Intranasal hypertonic saline (N=1)
    - 10mL; bid for 4wks (tonicity was not reported)
  - 3) Zinc sulphate (N=1)
    - 220mg; bid until recovery (~7d)
- Results: Intranasal corticosteroid sprays/drops (N=3; 288 participants):
  - Descriptive analysis was provided, suggesting "The evidence is very uncertain…on both self-rated [measures]…and recovery of olfactory function using psychophysical tests at up to four weeks"
- Author's Conclusion: "There is very limited evidence available on the efficacy and harms of treatments for preventing persistent olfactory dysfunction following COVID-19 infection."
- CHP Group Caveats: Living systematic review; updated as new data becomes available.

Pharmaceuticals (Prescription):	The scope of this Clinical Pathway does not include review of prescription pharmaceuticals, though they are within the scope of practice of some providers on network. Quality evidence-based references already exist for these treatments; however, we have included some selected information

Scoping Review (2022)

A 2022 scoping review assessed literature (through November 2021) for any evidence on the use of any medications to specifically treat PASC/PCC.[48] Numerous study types were assessed (e.g. RCT, observational, case study) and 52 publications were included; of note 50% were trials in progress. The authors conclude that based on the limited literature available, *"Providers who opt to use pharmacologic therapy for PASC need to be vigilant in their knowledge of these evolving data."*

Telehealth	This includes the use of electronic information and telecommunication technologies to support long-distance clinical health care. Studies of intervention categories listed elsewhere in this table may be included here if they are provided via telemedicine. A Systematic review & RCT report on the effects of Aerobic/Strength & Respiratory/breathing exercises delivered remotely. Both of the articles summarized below are also included in sections: *Mind-Body Therapies & Movement/Exercise*

Systematic Review (2022)

Therapeutic Exercise Interventions through Telerehabilitation in Patients with Post COVID-19 Symptoms: A Systematic Review[49]

- Funding: No external funding
- Study Characteristics: N=3; 277 participants; Included clinical trials and observational studies through 9/30/2022
  - Age ~50; Gender not reported; Adults with persistent symptoms receiving tele-rehab
- Modalities Included: Aerobic/Strength & Respiratory exercise delivered via telerehabilitation
  - Protocols varied from 3-5x/wk (40–60min) for 4-7 weeks
- Results: Descriptive analysis was provided suggesting "very favorable results in all the cardiorespiratory measures and physical tests evaluated."
- Author's Conclusion: "Telerehabilitation through therapeutic exercise based on mixed protocols of aerobic, respiratory, and low-load strength exercises appears to be an effective and safe strategy for the recovery of short- and long-term post-COVID-19 sequelae."
- CHP Group Caveats: No pooling of data for meta-analysis; only 2/5 publications were RCTs

RCT (2022)

Evaluating the Efficiency of Breathing Exercises via Telemedicine in Post-Covid-19 Patients: Randomized Controlled Study[36]

- Funding: No external funding
- Participants: N=52; Adults w/persistent dyspnea after Covid-19-related pneumonia
  - Age: ≥18yrs; Gender: 52% male (N=27); Location: Turkey (online)
- Interventions: 2 Groups: 1) Breathing exercise program (3x/d for 5 weeks; 1 session/wk via telemedicine); or 2)Control group (brochure explaining the exercises)
- Primary outcome: Two outcomes: 1) Spirometry (FVC, FEV1, FEV1/FVC Ratio, and MVV) and 2) six-minute walk test; both assessed at week 5 (end of the study)

- Results: Significant improvements in 6min walk test, FEV1, FVC, and MVV values in the intervention group compared to the control group ($p<0.001$).
- Author's Conclusion: "…breathing exercise training applied through telemedicine, improvements were observed in the pulmonary functions, quality of life, and exercise capacities of dyspneic post-Covid-19 individuals"
- CHP Group Caveats: Small sample size; Questionable statistics (2 primary outcomes)

Immobilization, Bracing, Taping:	This includes techniques such as kinesio-taping, splinting (e.g. plantar fascia night boot), bracing (e.g. sacroilliac belt), etc. generally designed for joint immobilization and/or restriction of movement (e.g. for the treatment of strains, sprains, fractures, etc). ***No research available that meets our inclusion criteria***

Physical Modalities (Western):	This includes the application of heat, cold, ultrasound, electrical stimulation, laser, etc. Four small RCTs have been published, each using a different intervention (e.g. laser, E-stim), and each suggesting positive effects on varied symptoms of Long COVID (e.g. ageusia, brain fog, fatigue).

RCT (2023) *Non-invasive brain stimulation for fatigue in post-acute sequelae of SARS-CoV-2 (PASC).*[50]

- Funding: Government of Paraiba (Brazil)
- Participants: N=70; Adults with PASC-related fatigue
  - Age: 53±17 years; 64% female; Location: Brazil
- Interventions: 2 Groups, both received 10 sessions (2x/wk for 5wks) plus a rehabilitation program (consensus statement based): 1) High-Definition transcranial Direct Current Stimulation (HD-tDCS); or 2) Sham HD-tDCS
- Primary outcome: Fatigue using the Modified Fatigue Impact Scale (MFIS) at end of Tx (Wk 5)
- Results: Treatment group demonstrated a clinically and statistically significant effect compared to sham at end of treatment
  - MFIS (MD:14.03; 95% CI: 7.8-20.3; $P<0.001$)
    - Large effect size: 1.2
  - Secondary outcomes were mixed

- Author's Conclusion: "An intervention with M1 targeted HD-tDCS paired with a rehabilitation program was effective in reducing fatigue and anxiety, while improving quality of life in people with PASC."
- CHP Group Caveats: An author (MB), who was 1 of 3 involved in "formal analysis" declared a potential conflict of interest as a having "equity" in the company that manufactured the medical device used in this study (Soterix)

RCT (2023) *Diode laser in management of loss of taste sensation in patients with post-COVID syndrome: a randomized clinical trial.*[51]

- Funding: The Science, Technology & Innovation Funding Authority; Egyptian Knowledge Bank
- Participants: N=36; Adults with persistent (>4wks) loss of taste following COVID-19
  - Age: 42±15 years; 78% female; Location: Egypt
- Interventions: 2 Groups: 6 minutes of Tx on the tongue; 1) Diode Laser treatment (940nm); or 2) Sham laser (inactive)
- Primary outcome: Subjective taste sensation at end of Tx (4wks)
- Results: Significant effect was observed between groups at the end of Tx ($p = 0.041$). Laser treatment led to a higher percentage of:
  - Restoring taste after one week, 72% (n=13)
  - Complete restoration of taste 95% (n=17)
- Author's Conclusion: "The findings of this study indicate that low-level laser therapy is effective in restoring taste sensation in patients with post-COVID-19 dysfunction."
- CHP Group Caveats: Small sample size

RCT (2023) *Electrical stimulation to regain lower extremity muscle perfusion and endurance in patients with post-acute sequelae of SARS CoV-2: A randomized controlled trial.*[52]

- Funding: Avazzia Inc. [manufacturer of E-Stim device]
- Participants: N=18; Adults diagnosed with PASC; reporting persistent lower extremity musculoskeletal symptoms
  - Age: 52±9 years; 72% female; Location: USA
- Interventions: 2 Groups: Each group received daily sessions for 4wks (60min on both gastrocnemius muscles) of: 1) E-Stim: interactive high voltage pulsed alternative current (HVPAC; pulse duration 400-1400μs; 20-121 Hz); or 2) Sham E-Stim
- Primary outcome: 2 outcomes at end of Tx (4wks); 1) Plantar oxyhemoglobin (OxyHb); 2) Gastrocnemius muscle endurance (GNMe); None defined as primary
- Results: Compared to control, both outcomes improved ($P<0.004$)

- Significant association between ΔOxyHb and ΔGNMe (r = 0.628, p = 0.003) at 4wks.
- Author's Conclusion: "E-Stim can improve muscle perfusion and muscle endurance in individuals with PASC experiencing LE muscle deconditioning."
- CHP Group Caveats: Authors note that, "sponsor did not have any decision or contribution to the review, approval, and submission of this article."

Pilot RCT (2023) *Use of either transcranial or whole-body photobiomodulation treatments improves COVID-19 brain fog*[53]

- Funding: Shepherd University; Governor's office of West Virginia; Foundation for Photobiomodulation Research
- Participants: N=14; Adults with diagnosed COVID-19 and 5+mths of brain fog
  - Age: average of 56 years; 71% female; Location: USA
- Interventions: 2 active treatments of photobiomodulation (PBM); both received 12 sessions over 4wks
  - 1) Transcranial PBM (tPBM)
  - 2) Whole body PBM (wbPBM)
- Primary outcome: Several neuropsychological test outcomes pre-post; none defined as primary
  - Montreal Cognitive Assessment (MoCA); Digit symbol substitution test (DSST); Trail-making tests A and B (TRA/B); Physical reaction time (PRT); Quantitative electroencephalography system (WAVi)
- Results: Both interventions demonstrated pre-post treatment effects for 3/5 assessments
  - MoCA, DSST, WAVi ($P<0.05$)
- Author's Conclusion: "…PBM delivered by either whole body or transcranial…was effective in improving parameters of brain performance...The choice of wbPBM in an office setting versus at-home tPBM, which has shown efficacy with TBI and dementia, should be explored further."
- CHP Group Caveats: No CI's declared in paper; however the lead author is the President of the Foundation for Photobiomodulation Research (a funding source)

Ancillary TEAM Modalities:	This includes moxibustion, infrared heat lamp, diathermy, sonopuncture, laserpuncture, etc. (Gua sha and cupping are listed under "Soft Tissue Therapies" and pharmacopuncture is listed under "Injection Therapies".)

	No research available that meets our inclusion criteria
Movement and Exercise:	This includes walking, aerobic exercise, strengthening, stretching, Alexander Technique, Feldenkrais, etc. (Yoga and Qi Gong are found in "Mind-body Therapies".) To date, this category has the greatest number of publications. The most recent systematic review (SR) provides robust evidence that rehabilitation interventions (e.g. exercise therapy or physical therapy) are associated with improvements in function & QOL for patients with Long-COVID. This is supported by earlier reviews, RCTs, and quasi-experiment studies. Interestingly, a recent SR suggests similar effects when provided via telemedicine (compared to in-person); this is supported by a recent RCT.

Systematic Review and Meta-Analysis (2023)

Rehabilitation Interventions for Physical Capacity and Quality of Life in Adults With Post-COVID-19 Condition: A Systematic Review and Meta-Analysis.[54]

- Funding: Canadian Institutes of Health; Arthritis Society; Chevening Scholarship Program
- Study Characteristics: N=14; 1,244 participants; Included 14 RCTs through 2/28/23
  - Median Age: 50 [47-56]; 45% female; Adults diagnosed with long-COVID
- Modalities Included: Exercise therapy, rehabilitation, physical activity, and physical therapy
- Primary Outcome: Functional exercise capacity (6-min walk test), at the closest postintervention time point
- Results: Rehabilitation interventions were associated with improvements in functional exercise capacity compared with usual care (SMD: -0.56; 95% CrI: -0.87 to -0.22; N=7; 389 participants)
- Author's Conclusion: "The findings…suggest that rehabilitation interventions are associated with improvements in functional exercise capacity, dyspnea, and quality of life, with a high probability of improvement compared with the current standard care…"
- CHP Group Caveats: Most robust dataset; meta-analysis provided

Scoping Review (2022)

Rehabilitation Interventions for Post-Acute COVID-19 Syndrome: A Systematic Review[55]

- Funding: Italian Ministry of Health
- Study Characteristics: N=5; 512 participants; Included RCTs through 11/4/2021
  - Age 49–69; 45% female; Adults diagnosed with COVID-19 >4weeks; Dx w/PACS

- Modalities Included: Three exercise-based interventions (6–8 weeks; but heterogeneous re: other parameters)
  - 1) Aerobic/resistance training
  - 2) Pulmonary rehab
  - 3) Yoga-based breath exercises w/a hand-held spirometer
- Results: Descriptive analysis was provided suggesting, "Rehabilitation seemed to improve dyspnea, anxiety, and kinesiophobia…muscle strength, walking capacity, sit-to-stand performance, and quality of life"
- Author's Conclusion: "Results on pulmonary function were inconsistent…improvements were detected in muscle strength, walking capacity, sit-to-stand performance, and quality of life…these first findings seem to advocate for rehabilitation interventions to lessen disability due to PACS."
- CHP Group Caveats: Heterogeneous outcome measures; No pooling of data for meta-analysis.

Systematic Review (2022)

Therapeutic Exercise Interventions through Telerehabilitation in Patients with Post COVID-19 Symptoms: A Systematic Review[49]

- Funding: No external funding
- Study Characteristics: N=3; 277 participants; Included clinical trials and observational studies through 9/30/2022
  - Age ~50; Gender not reported; Adults with persistent symptoms receiving tele-rehab
- Modalities Included: Aerobic/Strength & Respiratory exercise delivered via telerehabilitation
  - Protocols varied from 3-5x/wk (40–60min) for 4-7 weeks
- Results: Descriptive analysis was provided suggesting "very favorable results in all the cardiorespiratory measures and physical tests evaluated."
- Author's Conclusion: "Telerehabilitation through therapeutic exercise based on mixed protocols of aerobic, respiratory, and low-load strength exercises appears to be an effective and safe strategy for the recovery of short- and long-term post-COVID-19 sequelae."
- CHP Group Caveats: No pooling of data for meta-analysis; only 2/5 publications were RCTs

RCT (2023)

Effectiveness of exercise training on the dyspnoea of individuals with long COVID: A randomised controlled multicentre trial[56]

- Funding: Groupe Hospitalier Paris Saint-Joseph

- Participants: N=60; Adults with dyspnoea, diagnosed with COVID-19-related acute respiratory distress syndrome (CARDS), discharged from ICU for >3mths
  - Age: 58±12 years; 38% female; Location: France
- Interventions: 2 Groups of physiotherapy led exercise programs, 20 session (2x/wk 10wks, 90days);
  - 1) Exercise Training Rehab (ETR): 60min sessions of individualized Cardio/endurance & strength training by physiotherapists with specialized, additional training and proper equipment.
  - 2) Standard Physiotherapy (SP): 30min sessions (usual and customary care: individualized cardio & strength training)
- Primary outcome: Multidimensional Dyspnoea Profile (MDP) at end of Tx (90 days)
- Results: Positive effect on dyspneoea for the ETR compared to SP group
  - MD -18.61 (95% CI -27.78 : -9.44; p<0.0001)
  - Mean MDP was 42% lower (26.15 vs. 44.76)
- Author's Conclusion: *"A 90-day exercise training rehabilitation course, improved dyspnoea in its 3 dimension amongst participants who had remained dyspnoeic after developing CARDS, compared to standard physiotherapy."*
- CHP Group Caveats: None to report

RCT (2023) *Inpatient post-COVID-19 rehabilitation program featuring virtual reality-Preliminary results of randomized controlled trial.*[57]

- Funding: Polish National Agency for Academic Exchange
- Participants: N=32; Adult inpatient pulmonary rehabilitation patients diagnosed with PASC
  - Age: 58±5 years; 69% female; Location: Poland
- Interventions: 2 Groups, both received a multi-disciplinary pulmonary rehabilitation program (15 Txs: 5x/wk for 3wks) via: 1) Virtual reality rehabilitation or; 2) Traditional in-person rehabilitation
- Primary outcome: Three outcomes: 1) Lung function; 2) Exercise performance; 3) Stress levels; none defined as primary.
- Results: Mixed effects at the end of Tx; non-inferiority of VR to usual care rehabilitation
  - Lung function: Normal at baseline; non-statistically significant improvements
  - Exercise performance and stress level demonstrated statistically significant improvements following the 6MWT
    - No difference between groups

- Author's Conclusion: "A comparison of the traditional form of rehabilitation to the novel form using VR, shows similar effectiveness in terms of exercise performance and stress levels."
- CHP Group Caveats: Small sample size

Quasi-experimental study (2023)

A safe and effective micro-choice based rehabilitation for patients with long COVID: results from a quasi-experimental study.[58]

- Funding: University of Bergen; Helse in Hardanger and Bergen Hospital Trust
- Participants: N=78; Adults
  - Age: 40±12 years; 82% female; Location: Norway
- Interventions: A 3-day micro-choice based rehabilitation program, then 3wks of implementation
  - 3-day Education: Shift in focus, from targeting and monitoring symptoms, to a focus on micro-choices to facilitate increased levels of physical activity/ function. Integrating changes into everyday living.
  - After 3wks, patients answered two questions once a day (0–100): 1) To what extent did you allow the symptoms to decide today? 2) To what extent did you make use of the principle of doing something else?
- Primary outcome: Five outcomes assessed at 1wk and 3mth follow-up; none defined as primary
  - 1) Fatigue; 2) functional levels; 3) sick leave; 4) dyspnea; 5) exercise capacity
- Results: Mixed results
  - Fatigue improved at both time points
  - Sick leave rates, dyspnea, exercise capacity and functional level increased improved at 3-month follow-up
- Author's Conclusion: "Rapid, sustained, and consistent improvements were observed for fatigue, dyspnea, sick leave, functional level, and exercise capacity…The findings are in agreement with results of the concentrated treatment format for other chronic conditions…."
- CHP Group Caveats: First publication of this intervention technique

Soft Tissue Therapies:	This includes Swedish massage therapy, trigger point therapy, myofascial release, TEAM-related massage (shiatsu, acupressure, tuina), instrument-assisted therapies (Astym, Graston, gua sha, cupping), etc. A single clinical trial has been published, suggesting that it is more beneficial to add a manual diaphragm release technique to an IMT program for patients with long-COVID symptoms.

RCT (2022) *Influence of Manual Diaphragm Release Technique Combined with Inspiratory Muscle Training on Selected Persistent Symptoms in Men with Post-Covid-19 Syndrome: A Randomized Controlled Trial*[59]

- Funding: No external funding
- Participants: N=60; Adults with post-COVID-19 syndrome, stage II HTN and low-moderate physical activity and lung fibrosis
  - Age: 40 ±3.5yrs; Gender: 100% Male; Location: Egypt
- Interventions: 2 Groups: 1) Diaphragm release (18 Tx's: 3x/wk for 6wks), plus inspiratory muscle training (IMT; 36 Tx's: 3x/wk for 6wks; 2x/d); 2) IMT only
- Primary outcome: Maximum static inspiratory pressure (PImax)
- Results: PImax increased significantly in the study group (48.2% $p<0.001$); no significant change in the control group (4.4%; $p=0.567$).
- Author's Conclusion: "…adding [diaphragm release] DR to the IMT programme improves long-term symptoms in hypertensive patients with post-COVID-19 syndrome, suggesting that DR should be considered for use with these patients."
- CHP Group Caveats: Exploratory trial; Small sample size; Questionable statistics (no between group comparisons presented)

Manual & Instrument-Assisted Adjustments/ Manipulation:	This includes techniques of joint manipulation to include chiropractic manipulative treatment, naturopathic and osteopathic manipulation, such as diversified, drop table, Activator or other tool-assisted techniques, etc. ***No research available that meets our inclusion criteria***
Acupuncture:	This includes acupuncture, auriculoacupuncture, electroacupuncture, named acupuncture techniques such as dry needling, ashi needling, etc. (Pharmacopuncture is found in "Injection Therapies" and acupressure is found in "Soft Tissue Therapies".) ***No research available that meets our inclusion criteria***
Injection Therapies:	This includes intradermal, subcutaneous, and intramuscular injections, pharmacopuncture, aquapuncture, PRP, prolotherapy, stem cell therapy, etc. One small RCT has been published, suggesting PRP may warrant further investigation for anosmia in patients with long-COVID.

RCT (2023) *Use of platelet-rich plasma for COVID-19-related olfactory loss: a randomized controlled tria*[60]

- Funding: American Rhinologic Society New Investigator Award; NIH/NIDCD
- Participants: N=30; Adults diagnosed w/COVID and olfactory dysfunction for 6-12mths (despite olfactory training and nasal steroid rinses)
  - Age: 44±14 years; 50% female; Location: USA
- Interventions: 2 Groups: 3 intranasal injections at 2wk intervals of either: 1) Treatment: platelet-rich plasma (PRP); or 2) Control: Sterile saline
- Primary outcome: Change in Sniffin' Sticks score (threshold, discrimination, and identification) at 3mths (8wk follow-up)
- Results: At 3mths the difference between groups was statistically & clinically significant for Sniffin' Sticks score
  - MD: 3.67 (95% CI: 0.05 : 7.29; P=0.047)
- Author's Conclusion: "PRP resulted in a greater improvement in measured olfactory function compared with placebo...Yet there was no subjective olfactory improvement...Given the paucity of definitive therapeutic options…PRP therapy may be a promising addition…"
- CHP Group Caveats: Small sample size

IV Therapies:	This includes therapies administered intravenously, such as chelation, hydration and nutrient therapies, etc. ***No research available that meets our inclusion criteria***

Resources for Clinicians*

- CDC: Clinical Overview of Long COVID; https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html
- NIH: Researching COVID to Enhance Recovery (RECOVER) initiative; https://recovercovid.org/
- VA: Whole Health System Approach to Long COVID; https://www.publichealth.va.gov/n-coronavirus/docs/Whole-Health-System-Approach-to-Long-COVID_080122_FINAL.pdf
- WHO: Living Guidance for Clinical Management of COVID-19: Rehabilitation of adults with post COVID-19 condition; https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2023.2

Resources for Patients*

- CDC: Long COVID Basics; https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/
- Nationally recognized condition-specific societal organizations, etc.

*Health Disparities/Inequities, Caveats to Race-Based Medicine, and Related Resources

- It is recognized that unequal distribution of resources (e.g. environmental, economic) and other social determinants of health (e.g. employment, housing) are root causes of health disparities and differences of health status in racial, ethnic, and other groups.[61,62] When a study attributes race to a difference in prevalence of a disease or clinical outcome or presentation, it should be understood that race is a social construct and genetic or biologic interpretations of race are not supported by science. Indeed, the Human Genome Project demonstrated that on average, humans are 99.9% identical at the DNA level; there is more genetic variation within 'races' than between them.[63]
- CDC: https://www.cdc.gov/healthequity/racism-disparities/index.html
- NIH: https://www.training.nih.gov/2020_inclusion_anti-racism_and_wellness_resources
- OHSU: https://www.ohsu.edu/center-for-diversity-inclusion/anti-racist-resources
- Seattle: https://providernews.seattlechildrens.org/anti-racism-resources-for-healthcare-professionals/

Clinical Pathway Feedback

CHP desires to keep our clinical pathways current. If you wish to provide additional input, please use the e-mail address listed below and identify which clinical pathway you are referencing. Thank you for taking the time to give us your comments.

Clinical Services Department: cs@chpgroup.com

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