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CLINICAL GUIDANCE

PM&R

Multidisciplinary collaborative consensus guidance statement on the assessment and treatment of neurologic sequelae in patients with post-acute sequelae of SARS-CoV-2 infection (PASC)

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INTRODUCTION

COVID-19 has been a transformative novel disease in modern health care. Unlike many other viral illnesses, COVID-19 not only causes multiorgan damage during the acute stage of the infection, but also has the potential to cause long-term sequelae, as part of post-acute sequelae of SARS-CoV-2 infection (PASC) or long-COVID syndrome. In a 2022 study released by the Centers for Disease Control and Prevention,[1] electronic health record (EHR) data were examined from the time period of March 2020–November 2021 for persons in the United States aged ≥18 years to assess the incidence of 26 conditions often attributable to post-COVID-19. Among all patients, 38% of individuals experienced an incident condition compared with 16% of controls; conditions affected multiple systems and included cardiovascular, pulmonary, hematologic, renal, endocrine, gastrointestinal, musculoskeletal, neurologic, and psychiatric signs and symptoms.[1]

Neurological symptoms occur in approximately 80% of hospitalized patients during the acute phase of COVID-19 infection.[2] The most prevalent PASC neurologic symptoms that remain after 3–4 weeks from the initial infection include "brain fog" (81%), headache (68%), numbness/tingling (60%), dysgeusia (59%), anosmia (55%), and myalgias (55%).[3] Importantly, studies of post-acute COVID-19 neurologic outcomes across the care-setting spectrum of the acute phase of the disease (nonhospitalized, hospitalized, and admitted to intensive care) continue to emerge. Addressing this knowledge gap is important in helping guide PASC care strategies and health care system capacity planning. The U.S. Department of Veterans Affairs national health care databases were used to build a cohort of 154,068 individuals with COVID-19, 5,638,795 contemporary controls and 5,859,621 historical controls to estimate risks and burdens of incident neurologic disorders at 12 months following acute COVID-19. The risks and burdens were elevated even in people who did not require hospitalization during acute COVID-19. Investigators found an increased risk of various neurologic sequelae including ischemic and hemorrhagic stroke, cognition and memory disorders, peripheral nervous system disorders, episodic disorders (eg, migraine and seizures), extrapyramidal and movement disorders, mental health disorders, musculoskeletal disorders, sensory disorders, Guillain–Barré syndrome (GBS), and encephalitis or encephalopathy.[4]

In an additional retrospective cohort study, researchers used data from EHRs of approximately 89 million patients from multiple countries, primarily in the United States but also in Australia, United Kingdom, Spain, Bulgaria, India, Malaysia, and Taiwan.[5] The data were derived from health system networks inclusive of hospitals, primary care, and specialist providers who contribute data from uninsured and insured patients. The analysis identified that post-COVID-19 neurological and psychiatric outcomes followed different risk trajectories:

- The risk of cognitive deficit, dementia, psychotic disorder, and epilepsy or seizures remained increased at 2 years after the COVID-19 diagnosis.
- The risks of other diagnoses (notably, mood and anxiety disorders) subsided early and showed no overall excess over the 2-year follow-up.

Importantly, up to 10% of critically ill COVID-19 patients have cranial nerve involvement.[6] Sleep patterns can also be disturbed by these neurological sequelae, and in turn, exacerbate other PASC symptoms.[7–10] Interestingly, the presence and severity of PASC symptoms do not fully correlate with initial COVID-19 symptoms.[11] Another study of U.S. health care claims data involving 78,252 patients demonstrated that 75.8% of patients with persistent PASC symptoms (coded as U09.9 post COVID-19 condition) including anosmia, headache, altered mental status, stroke, and seizure, which significantly affected activities of daily living, experienced initial asymptomatic or mild COVID-19 and did not require hospitalization.[12]

This guidance statement focuses on the neurologic sequelae of PASC, including headaches, neuropathies and neuropathic pain, muscular pain/weakness and tremors, and cranial nerve conditions. Fatigue, autonomic dysfunction, and cognitive function changes are reviewed in separate American Academy of Physical Medicine and Rehabilitation (AAPM&R) guidance statements.[8,10,13] In addition, an AAPM&R consensus document focused on mental health sequelae is currently in development.

PASC consensus guidance statement methods

Despite the prevalence of neurological sequelae of COVID-19 infection and emerging data on longevity of symptoms, limited guidance exists regarding the assessment and treatment of neurologic sequelae in patients with PASC. The AAPM&R Multi-Disciplinary PASC Collaborative (PASC Collaborative), consisting of experts in PM&R, neurology, internal medicine, family practice, pediatric specialties, cardiology, physical therapy, occupational therapy, social work among other disciplines, was convened to address the pressing need for guidance in the care of patients with PASC.

The PASC Collaborative is following an iterative, modified Delphi process to achieve consensus on assessment and treatment recommendations for a series of consensus guidance statements focused on the most prominent PASC symptoms. These recommendations and guidance are informed by experts from established PASC centers with experience in managing individuals across the spectrum of sequelae

experienced by patients with PASC.[8–10,13,14] There is an intentional focus on health equity as disparities in care and outcomes are critically important to address. Beyond patient care, the hope is that a broadened understanding of current patient care practices will help identify areas of future research. A full description of the methodology has been published previously.[15]

We acknowledge that the definition of PASC is evolving, and there are various factors that contribute to diagnosis and management. Literature available at the time of our consensus process suggested that PASC be defined as the persistence of symptoms beyond 4 weeks from the onset of acute infection.[16] Alternative definitions of PASC include symptoms lasting longer than 3 months.[17] The World Health Organization released a definition of "post-COVID condition," including describing the timing as "usually 3 months from the onset of COVID-19" and lasting "for at least 2 months."[18] Based on patient feedback during our consensus process, we agree that earlier evaluation, diagnosis, and management can improve access to beneficial interventions. For the purposes of this guidance statement, we recommend expanded assessment if symptoms are not improving 1 month after acute symptom onset.

At present, scientific evidence regarding effective assessment and treatment of PASC is limited, which prevents the creation of evidence-based clinical guidelines. This consensus guidance statement is intended to reflect current practice in patient assessment, testing, and treatments based on expert opinion from health care professionals who care for PASC patients regularly. It is intended as a resource and concise point of reference geared toward clinicians in different specialties caring for PASC patients. The recommendations should not preclude clinical judgment and must be applied in the context of the specific patient, with adjustments for patient preferences, comorbidities, and other factors.

TABLE 1 Initial evaluation of neurologic sequelae in patients with post-acute sequelae of SARS-CoV-2 infection (PASC).

	Neurologic sequelae initial evaluation recommendations
1	Clinicians should conduct a full patient history including a review of predisposing comorbidities, prior neurologic symptoms or disorders, relevant hospitalizations, time course and severity of COVID-19 infection(s), COVID-19 treatments, vaccines/boosters, pertinent family history, and social history. The patient history of present illness should address: • Most relevant symptoms that may be neurologic in nature: autonomic symptoms (eg, dizziness, lightheadedness, presyncope, syncope, orthostatic intolerance), headaches (including migraine), exercise intolerance, cognitive dysfunction (e.g., brain fog, processing rate, and memory skills), cognitive fatigue, changes in gait/walking, and pain. • Appropriate review of systems to identify contributions to neurologic symptoms. • The trajectory of neurologic sequelae over time (ie, improving, worsening, or unchanged) to triage need for further workup. • History and review of preexisting, comorbid chronic conditions (eg, pain, psychiatric, renal/endocrine, cardiovascular, neurological, respiratory, etc.) • Time course and severity of COVID-19 infection • Triggers of symptoms, including food, medication(s), activity, and positional changes
2	Clinicians should perform a thorough neurological examination to identify focal neurological deficits.
2a	For those patients identified with new or worsening focal neurologic deficits, an urgent/emergent referral to an emergency department for evaluation is warranted. (The section on Red Flags and corresponding table provides additional information). Determination of need for neuroimaging should be based on individual signs and symptoms. Consider consultation with a neurologist to guide imaging and further testing.
3	Evaluate for medication and supplement use that may impact signs, symptoms, or assessment parameters (i.e., medications with adverse side effects, such as dry mouth, visual changes, dizziness, and/or sleep/sedation). Include review of medications and supplement use and duration of use that have helped, worsened, or had little to no impact on symptoms. Of note, patients with PASC often present on antihistamine, anticholinergic, antidepressant/anxiolytic, and muscle relaxant medications that can contribute to neurologic symptoms.
4	The following basic lab workup should be considered in new patients or for those without a lab workup in the 3 months prior to the visit: complete blood count with differential; chemistries including renal and hepatic function tests, thyroid stimulating hormone, c-reactive protein, erythrocyte sedimentation rate, vitamins B1, B6, B12, and D, magnesium, and hemoglobin A1c (HbA1c). Other laboratory tests, including evaluation for new autoimmune syndromes, may be considered based on the patient history, physical exam, and/or concern for comorbid conditions as outlined in the relevant symptom tables that follow.
5	Assess for history of previous and/or current alcohol and substance use, current diet and exercise habits, physical and cognitive activity levels, and social determinants of health (eg, housing, employment, family, insurance, access to community resources, social stressors, etc.)
6	Assess for changes in basic and instrumental activities of daily living, including participation at work, school, community avocational (ie, hobbies) activities.
7	On initial evaluation, obtain standardized measures of activity performance to compare to normal control values and to guide the initial activity prescription. Repeat the standardized measures of activity performance at follow-up visits to quantify functional changes and guide progression of the activity prescription. Standardized measures may differ by neurologic symptom, refer to specific neurologic symptom assessment and treatment section for recommended standardized measures based on patient presentation.

ASSESSMENT AND TREATMENT OF NEUROLOGIC SEQUELAE IN PASC

This guidance statement is structured to first outline initial evaluation components (Table 1: Initial Evaluation of Neurologic Sequelae in Patients with PASC) and initial treatment recommendations (Table 2: Initial Treatment Options for Patients with Neurologic Sequelae) for the neurologic sequelae of patients with PASC. These initial evaluation recommendations review both how to consider a wide differential of possible conditions and aspects to help further guide the diagnostic workup. There is also a section dedicated to "Red Flag" presentations that should prompt emergent escalation of care specific to neurologic features of PASC. Subsequent narrative sections review a series of common neurologic sequelae and how to best guide care.

Initial evaluation of patients with neurologic sequelae from PASC

Neurologic red flags

As neurologic symptoms are common in PASC, patients may initially present to primary care or PASC specific clinics. These clinicians must undertake the task of identifying any ominous symptoms, particularly reports of progressive neurologic dysfunction, that warrant urgent referral to a neurologist, neurosurgeon, or emergency department as such findings may herald a severe, systemic neurologic disorder (Table 3: Red Flags). A thorough neurologic assessment includes gaining knowledge of a patient's sensory, motor, autonomic, and cognitive symptoms, with particular attention to symptoms that require prompt intervention for the safety of the patient. Identification of red flag symptoms that may be due to PASC versus another medical condition via history and physical examination is essential.

Progressive weakness

Any neurologic signs or symptoms that are new or progressive (especially if rapidly progressive) should be a red flag; progressive weakness, sensory changes or cranial nerve deficits may be indicative of a focal or diffuse neurologic condition such as stroke, spinal cord infarct, GBS, or an acute neuroimmune syndrome. These concerns should trigger a rapid referral and/or workup, which could potentially include magnetic resonance imaging (MRI) of the spinal cord or brain, additional blood work, cerebrospinal fluid (CSF) studies, and/or electrodiagnostic testing.

Unexplained upper motor neuron findings

The presence of upper motor neuron examination findings such as hyperreflexia, pathologic clonus reflexes, spasticity, impaired bowel or bladder continence, or evolving urinary retention or bowel impaction/obstruction may be signs of processes affecting the brain or spinal cord. If these signs and symptoms are present at evaluation, clinicians should consider the differential diagnosis of vascular (e.g., stroke, spinal cord infarct) and neuroinflammatory syndromes (e.g., transverse myelitis, Neuromyelitis Optica Spectrum Disorder, multiple sclerosis, GBS, etc.) Prompt diagnostic evaluation and treatment for patients with acute and progressive neurologic symptoms can often avert catastrophic and irreversible central and peripheral nervous system damage.[19–23]

TABLE 2 Initial treatment options for patients with neurologic sequelae of PASC.

#	Neurologic Sequelae Initial Treatment Recommendations
1	In collaboration with primary care or appropriate specialist treat underlying medical conditions, such as pain, psychiatric, renal/endocrine, cardiovascular, neurological, respiratory, etc., which may be contributing to neurologic symptoms.
2	In collaboration with primary care or appropriate specialist, consider polypharmacy reduction, weaning or deprescribing medications and supplements where medically feasible. Emphasis on medications and supplements with known impact on neurologic symptoms should be considered.
3	For patients who achieve a return to their daily activities, consider recommending regular physical activity as tolerated, which may be effective in improving many neurologic symptoms and also contribute to improved sleep patterns. Patients should be cautioned to avoid rapid escalation of physical and cognitive activities to avoid overuse syndrome triggered by exertion. This approach is recommended to ensure symptoms do not flare and activity is tolerated.
4	For patients with neurologic sequelae affecting gait, mobility, cognitive status or activities of daily living, consider referral to physical medicine and rehabilitation physician and/or allied health professionals (eg, physical therapy, occupational therapy, speech language pathology and social work) for patient-specific recommendations to increase function and independence. To optimize functional outcomes, allied health professionals should preferably be familiar with treating sensorimotor deficits, autonomic dysfunction, and post-exertional fatigue. Suggested approaches are offered in the discussion.
5	Provide counseling, referrals to community resources, and education for risk factor modification in the areas of: • Alcohol and substance use • Healthy dietary pattern and hydration • Return to activity, as tolerated • Medications and supplements • Sleep hygiene (see sleep section below) • Social determinants of health

TABLE 3 Neurologic red flags.

Neurologic signs/symptoms that may prompt more urgent neurologic assessment	Potential causes	Referral/action
Sudden or progressive weakness	Acute neurologic condition such as stroke, spinal cord infarct, GBS, myositis/myopathy, acute neuroimmune syndromes	Referral: consider emergency department (ED) versus neurology depending on time course/urgency. Action: Consider forced vital capacity assessment and neuroimaging as appropriate.
Sudden or progressive sensory changes	Acute neurologic condition such as stroke, spinal cord infarct, GBS, acute neuroimmune syndromes	Referral: consider ED versus neurology or neurosurgery depending on time course/urgency and associated neurologic signs and symptoms. Action: Consider forced vital capacity assessment and neuroimaging as appropriate.
Unexplained upper motor neuron signs (i.e., pathologic reflexes or spasticity) in the setting of weakness	Structural cause affecting the brain or spinal cord affecting the brain or spinal cord	Referral: neurology Action: neuroimaging, as appropriate.
Bladder incontinence or retention	Spinal cord dysfunction	Referral: consider ED versus neurology or neurosurgery depending on time course/urgency and associated neurologic signs and symptoms. Action: bladder scan, urinalysis, urodynamics, voiding diary, timed voiding
Bowel incontinence or retention		Action: bowel history, review medications, assess rectal sensation/tone
Syncopal episodes or transient loss of consciousness	Arrythmia, seizure, severe orthostatic hypotension, or vasovagal syncope	Referral to neurology or cardiology for consideration for EEG/arrhythmia monitoring. Action: Determine circumstances of recent events, timing following certain activities, if strenuous, any med changes or abnormalities in cardiac function—time to resolution.
Acute neuropsychiatric symptoms/psychosis	Reduced awareness, visual or auditory hallucinations, encephalopathy	Referral: ED versus neurology depending on time course/urgency. Action: Basic tests of pituitary and adrenal function, thyroid function, and inflammation, review and optimize medications, cognition assessment, evaluate safety.
Headaches—positional, worst headache of life, or associated with focal neurologic signs	Positional—increased intracranial pressure (or low CSF pressure) Worst headache of life (thunderclap headache)–subarachnoid hemorrhage Headache associated with structural cause affecting the brain or spinal cord	Referral: ED versus neurology depending on time course/urgency. Action: Refer to headache section in this statement.
Cranial nerve abnormalities on physical examination	Sudden onset cranial nerve deficits or pupillary changes potentially caused by stroke/intracranial bleeding	Referral: ED for urgent neurological evaluation

Abbreviations: CSF, cerebrospinal fluid; EEG, electroencephalogram, GBS, Guillain-Barré syndrome.

Diffuse peripheral nervous system syndromes

Acute inflammatory demyelinating polyneuropathy/GBS has been reported subsequent to COVID-19, both acutely and as part of PASC.[22,23] An evaluation of the peripheral nervous system and cranial nerves, detailed sensory and motor examination, muscle stretch reflexes, and postural reflexes should be performed. Screening for orthostatic hypotension is best accomplished by both direct questioning of the patient for such symptoms and by a clinical assessment of orthostatic blood pressures. If there is concern for coexistent autonomic dysfunction, especially if there is an orthostatic variation in symptoms, refer to the PASC Collaborative consensus guidance statement on autonomic dysfunction for assessment and treatment guidance.[13]

Other concerning symptoms

Neuropsychiatric symptoms such as hallucinations, headaches with focal neurologic signs, and rapid onset "thunderclap" headache should be identified and rapidly addressed. Episodes of unexplained loss of consciousness may also warrant a more rapid assessment and evaluation looking for an underlying arrhythmia or

TABLE 4 Signs, symptoms, and care guidance: cranial nerves.

Loss of smell or taste (cranial nerve: 1, 9, 10)

Signs
- Weight loss/gain
- Dry mucous membranes

Symptoms
- Loss of smell and/or taste
- Altered smell and/or taste
- Dry mouth
- Change in eating habits
- Stress from lack of pleasure in eating

Patient History and Evaluation:
- Assess for tobacco and alcohol use
- When appropriate, assess for other common comorbidities such as:
  - Neurodegenerative conditions
  - Head trauma

Additional Studies to Consider for Differential Diagnosis:
- Consider Sjögren's antibodies if concerned about potential autoimmune involvement.
- If associated with other cranial nerves, consider magnetic resonance imaging (MRI) brain with or without contrast and lumbar puncture (LP) for encephalitis workup.
- Given the increased clotting risk in post-acute sequelae of SARS-CoV-2 infection (PASC), neuroimaging should be considered prior to any LP to help rule out cerebral venous thrombosis or other central nervous system (CNS) lesion.

Initial Treatment Approach:
- Recommend avoidance of tobacco, alcohol, spicy foods, and foods with extreme temperature
- Consider educating on and recommending smell therapy (eg, Abscent)
- Recommend hydration of at least 64 ounces of fluids a day
- Consider recommending mouth moisturization products (eg, Biotene, Oasis)

Referral Options:
- Consider referral to ear, nose, throat physician (ENT) for abnormalities of smell lasting longer than 3 months,
- Consider referral to a dentist if associated with dry mouth for better dental hygiene.
- If suspicion of Sjögren's, consider referral to rheumatology for further evaluation.

Resources:
- Smell-Simple steps to recovering your sense of smell after COVID-19 and other viral infections: Abscent.org

Changes in vision (cranial nerves 3, 4, 6)

Signs
- Papilledema or pallor of optic nerve
- Abnormality in extraocular movements in any direction: out and up, out and down, in and up, in and down
- Inability to accommodate/cross eyes
- Changes to visual acuity
- Changes in color vision
- Changes in visual fields
- Droopy eyes/ptosis
- Nystagmus

Symptoms
- Blurry vision/loss of vision/change in color vision
- Painful eye movements
- Trouble focusing
- Double vision
- Headaches
- Head tilt
- Dry eyes

Patient History and Evaluation:
- Assess for changes in visual acuity, color vision and pupillary changes
- Assess for other common comorbid conditions as appropriate:
  - Diabetes
  - Uncontrolled hypertension
  - Preexisting autoimmune disorders
  - Other disorders with immune dysregulation
- Assess for medications that can worsen symptoms:
  - Oral contraceptives or hormone supplements increase risk of venous sinus thrombosis
  - Anticholinergics such as over-the-counter allergy medications can cause blurry vision or trouble focusing
  - Immunosuppressive treatments can predispose to post viral cranial neuropathies (varicella zoster virus [VZV]/herpes simplex virus [HSV]/Epstein–Barr virus [EBV] reactivation)

Additional Studies to Consider for Differential Diagnosis:
- Consider angiotensin-converting enzyme (ACE) level; serologies for VZV, HSV, EBV PCR (polymerase chain reaction); rapid plasma reagin (RPR); human immunodeficiency virus (HIV); and thyroglobulin and thyroid peroxidase antibodies (TPO and TG Ab).
  - Check vitamin A level if papilledema on exam
- If papilledema on exam consider an urgent referral for head imaging (ideally MRI or magnetic resonance venography, computed tomography is an option if unable to get MRI urgently) for venous sinus thrombosis.
- If optic pallor with painful eye movements and color/acuity changes, order MRI orbit/brain with or without contrast for optic neuritis

(Continues)

TABLE 4 (Continued)

Changes in vision (cranial nerves 3, 4, 6)

Initial Treatment Approach
- Recommend avoidance of medications (eg, anticholinergics or antihistamines) that can worsen symptoms
- If acute herpetic infection is identified, consider antiviral therapy and infectious disease evaluation
- Consider vision rehabilitation by occupational therapist.
- Consider prescription for steroids or immunotherapy if suggestive of autoimmune etiology
- Consider prescription for steroids or referral to emergency department for optic neuritis

Referral Options:
- Refer to the emergency department if worsening visual acuity, color vision or transient episodes of loss of vision or if weakness of extraocular muscles associated with or without changes in pupil reaction as may be an indication of cerebral aneurysm (red flag).
- Consider referral to neurology or neuro-ophthalmology:
  - If symptoms continue or worsen over time
  - If optic neuritis is identified
- Consider referral to neurology or ophthalmology if papilledema on exam.
- Consider referral to ophthalmology/optometry if there is evidence of visual loss or pupillary changes.
- Refer to optometry for fundoscopy to look for changes consistent with increased intracranial pressure from venous sinus thrombosis or optic neuritis

Resources:
- Eye exam-video by neuro-ophthalmologist: https://youtu.be/xW6B05a-LTw

Dizziness/vertigo/tinnitus/loss of hearing (cranial nerve 8)

Signs:
- Impaired midline orientation
- Falls
- Ataxia on finger to nose testing or knee heel testing or truncal ataxia
- Nystagmus

Symptoms
- Unsteady gait
- Poor balance
- Postural dizziness/instability
- Ear ringing
- Ear fullness
- Nausea/vomiting
- Hearing loss
- Being pulled to one side/leaning (impaired midline orientation)

Patient History and Evaluation:
- Evaluate for dysarthria, incoordination, and other sensorimotor deficits in arms or legs or face that may suggest vascular causes like brainstem/cerebellar stroke
- Determine if patient has had recent or persistent upper respiratory, ear infections, or known history of vestibular neuritis, labyrinthitis, benign paroxysmal positional vertigo, Meniere's disease, migraines, prior strokes, or history of multiple sclerosis
- Consider the following evaluation studies:
  - Bedside hearing test with tuning fork
  - Otoscopy to look for local changes
  - Finger to nose, heel to shin, tandem gait, Romberg test
- Conduct evaluation for nystagmus
- Evaluate for central vs. peripheral vertigo (maneuvers—see resources)
- Assess for other common comorbid conditions: diabetes and uncontrolled hypertension
- Assess for medications that may exacerbate symptoms:
  - Orthostatic dizziness related to medications – antihypertensives, medications for benign prostatic hypertrophy, antidepressants
  - Immunosuppressive treatments – can predispose to postviral cranial neuropathies (VZV/HSV/EBV reactivation)

Additional Studies to Consider for Differential Diagnosis:
- Consider ACE level, serologies for VZV, HSV, EBV PCR, RPR, HIV, TPO, and TG Ab
- Consider ordering MRI brain if physical exam findings suggest central etiology (eg, brainstem/cerebellar stroke)

Initial Treatment Approach
- Recommend adequate hydration of at least 64 ounces per day
- Recommend use of compression stockings (if postural)
- Consider vestibular rehabilitation with a neurological or vestibular trained physical therapist
- Consider trial of white noise for diagnosis of tinnitus or hearing loss
- Consider referral for hearing aids for diagnosis of tinnitus or hearing loss

Referral Options:
- Refer to ear, nose, throat and/or audiology if sensorineural hearing loss for hearing testing and possible imaging (MRI with/without and internal auditory canal protocol)
- Refer to neurology/autonomic specialist for autonomic evaluation if other symptoms (blood pressure fluctuations/heart rate variability, dryness/abnormal sweating/neuropathic pain). Refer to PASC Multi-Disciplinary collaborative consensus guidance statement on the assessment and treatment of autonomic dysfunction in patients with Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)[13]

(Continues)

TABLE 4 (Continued)

Dizziness/vertigo/tinnitus/loss of hearing (cranial nerve 8)

Resources:
- Dix-Hallpike maneuver: https://www.youtube.com/watch?v=8RYB2QIO1N4
- Epley maneuver: https://www.youtube.com/watch?v=ZqokxZRbJfw&NR=1
- Performing the Epley maneuver: home: https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/home-epley-maneuver
- HINTS exam: https://www.youtube.com/watch?v=1q-VTKPweuk
- Brandt-Daroff exercises: https://careguides-videos.med.umich.edu/media/brandt-daroff/1_cqhgjpik/44532291

Changes in facial expressions, chewing or swallowing (cranial nerves 5, 7, 9, 10, 12)

Signs
- Facial droop
- Inability to smile
- Inability to puff out cheeks
- Inability to stick out tongue
- Inability to elevate palate/absent gag reflex
- Hypophonia/dysphonia
- Weakness of face musculature
- Dysarthria

Symptoms
- Weight loss
- Hard to understand speech
- Coughing/choking while eating or drinking
- Dry mouth
- Nasal regurgitation of food

Patient History and Evaluation:
- Evaluate whether patients are experiencing peripheral (eg, Bell's Palsy) or central (eg, brainstem) cranial nerve damage to better guide management
- Evaluate for constitutional symptoms like fever, weight loss, night sweats for consideration infectious/paraneoplastic/neoplastic etiologies.
- Differentiate dysphagia with solids and/or liquids
- Assess for other common comorbid conditions:
  - Dry mouth
  - Uncontrolled hiccups

Additional Studies to Consider for Differential Diagnosis:
- Consider MRI brain with/without contrast for multiple lower cranial neuropathies or stroke or uncontrolled hiccups for possible CNS demyelinating disease like neuromyelitis optica.
- Consider evaluation for myasthenia gravis if signs or symptoms are worse with activity (fatigable) or if acetylcholine receptor antibodies are negative, proceed to nerve conduction study (NCS) or electromyography (EMG).
- Conduct a dysphagia evaluation via instrumental swallow assessment such as Video Swallow or Fiberoptic Endoscopic Evaluation of Swallowing

Initial Treatment Approach
- Recommend oral moisturizing or lubricating agents that contain carboxymethylcellulose, such as Biotene Oral Moisturizing gel or saliva substitutes with xylitol, such as Mouth Kote or Oasis mouth spray

Referral Options:
- Refer to ED for urgent evaluation if sudden onset or progressive symptoms and risk of aspiration are high.
- Refer to speech therapy for dysphagia evaluation and treatment, including Video Swallow or Fiberoptic Endoscopic Evaluation of Swallowing

Resources:
- Additional information on Bell's Palsy: https://www.aanem.org/Patients/Muscle-and-Nerve-Disorders/Bell-s-Palsy

seizure disorder. Cranial nerve abnormalities may require referral to neurology for specific workup depending on the affected nerve (refer to next section and Table 4). Symptoms of acute ischemic stroke as well as facial droop, aphasia, or unilateral weakness should be assessed. Assess for symptoms of lateral medullary infarction including vertigo, dizziness, nystagmus, ataxia, nausea and vomiting, dysphagia, and hiccups. Although cranial nerve abnormalities involving ptosis, ophthalmoplegia, or diplopia may result directly as part of PASC, more common visual conditions can also lead to blurred vision and must first be excluded. For example, ophthalmoplegia can also been seen in the Miller Fisher variant of GBS. In addition, signs of increased intracranial pressure (ICP) should be described (headache worse with supine position, nausea, vomiting, mental status changes, vision changes, focal signs, papilledema), as worrisome for cerebral venous thrombosis; clinicians should consider magnetic resonance venography or computed tomography (CT) venography. New onset visual difficulties of a central or peripheral visual nature must be addressed urgently to rule out a condition of increased intraocular pressure such as glaucoma.

COMMON NEUROLOGIC SEQUELAE AND HOW TO BEST GUIDE CARE

Based on the prevalence of neurologic symptoms in patients with PASC, coupled with multiorgan involvement, there is a need for multidisciplinary care.

The following sections focus on the most common neurologic sequelae encountered by clinics and clinicians serving patients with PASC and introduce the symptom or brain system area followed by approaches to obtaining histories, conducting a more detailed assessment beyond the initial evaluation, consideration of initial therapeutic approaches and when to refer to specialists or a broader multidisciplinary care team.

Cranial nerves

Multiple studies have demonstrated that COVID-19 infection commonly leads to cranial neuropathies that may linger as persistent symptoms of PASC.[7,24,25] One of the largest studies evaluating cranial neuropathies in a Turkish cohort of 356 patients hospitalized with COVID-19 found that 38% of patients developed cranial nerve abnormalities, with highest involvement of the facial (30%), olfactory (27%), glossopharyngeal (25%), and vestibulocochlear (17%) nerves, though many of the patients presented with multiple cranial neuropathies.[26] The hypoglossal nerve was the most resistant nerve to SARS-CoV-2, and olfactory nerve dysfunction was the most lingering (3–60 days) compared to other cranial neuropathies, such as loss of vision and hearing, vertigo, tinnitus, facial paresthesia, and trigeminal neuralgia. There was no significant difference in terms of age, gender, body mass index, comorbidities, or intensive care requirement in the group that developed cranial neuropathies compared to unaffected patients.[26]

Similarly, as presented in a systematic review of 56 patients across 36 studies, the most affected cranial nerves in patients with COVID-19 were facial (51%), abducens nerves (30%), and oculomotor (27%), manifesting as hypogeusia/ageusia, facial palsy, or ophthalmoparesis.[7] Cranial neuropathies, especially when bilateral, were often associated with GBS or Miller Fisher syndrome (MFS). This study also found that patients often displayed cranial nerve lesions (52%).[7]

Evaluation and workup for cranial neuropathies are summarized in Table 4. Notably, when patients develop multiple cranial neuropathies, lumbar puncture should be considered with evaluation of cytoalbuminologic dissociation toward a diagnosis of GBS/MFS. Although clinicians should have a high level of suspicion for cranial neuropathies and GBS/MFS in intubated patients, where these diagnoses may be more easily missed, cranial nerve issues can be present in PASC patients as well.

Isolated cranial neuropathies often respond favorably to steroids, and acyclovir/valacyclovir may be used to treat acute or reactivated latent neuronal herpes virus infection. Patients with GBS/MFS benefit further from intravenous immunoglobulin and plasma exchange.[7] Most patients with isolated cranial neuropathies have a favorable outcome with supportive care compared to patients with multiple cranial neuropathies with GBS, who may achieve partial recovery and experience longer symptom duration. The importance of proper diagnosis of GBS/MFS in acute COVID-19 is that these patients are at high risk for ongoing PASC symptoms if not properly treated in the acute period.

Headaches

Headache is a common post-COVID-19 symptom in both patients who were previously hospitalized with acute infection and in patients who did not require hospitalization.[27] A meta-analysis found the prevalence of post-COVID-19 headache ranged from 8% to 15% during the first 6 months after SARS-CoV-2 infection.[27]

Post-COVID-19 headaches have varied presentations that include those that may or may not have migraine features (estimated to be about 25%) with the rest having tension-type features and daily persistent and/or thunderclap presentations.[28] Viral infections have been known to trigger new daily persistent headache.[29] COVID-19 is also a risk factor for worsening previous headache disorders such as migraine. The cumulative lifetime incidence of migraine in the United States is 7.4% in males and 21% in females.[30] Three large population-based studies have demonstrated an inverse relationship between household income/education and migraine prevalence in the United States.[30]

Persistent headache can be seen even in those who did not experience headache in the acute COVID-19 phase.[31] Headache can be worsened or triggered by other commonly seen post-COVID-19 symptoms including sleep disturbances, mood disturbances, memory loss, dizziness, and fatigue.[31]

Headaches associated with PASC do not have a unique or specific clinical presentation. These require a standardized clinical approach to determine if the headache is primary or secondary.[32] The treatment of the primary headache should be determined by the headache's phenotype. Clinicians should be cognizant that patients with primary headache disorders may also develop secondary headache disorders. We recommend using the SNOOP4 tool: see Table 5: Warning Signals to Raise Suspicion of Secondary Causes of Headache Using the Mnemonic SNOOP4 to evaluate headaches for a primary versus secondary cause.[33]

A new daily persistent headache is a headache with a distinct and clearly remembered onset with pain becoming continuous and unremitting within 24 hours, present for over 3 months and not better accounted for by another International Classification of Headache Disorders-3 diagnosis.[34] New daily persistent headache is typically refractory to treatment. Table 6 describes additional evaluation considerations and initial treatment options for different types of headache phenotypes seen in patients with PASC.

TABLE 5 Warning signals to raise suspicion of secondary causes of headache using the mnemonic SNOOP4 (recreated with permission from Dr David Dodick).[33]

Letter	Warning Signal	Features	Differential diagnosis
S	Systemic symptoms	Fever, night sweats, chills, weight loss, jaw claudication	Metastases, giant cell arteritis, infection (central nervous system, systemic)
	Secondary diseases	Cancer, immunosuppression, chronic infection human immunodeficiency virus (HIV), tuberculosis	
N	Neurologic symptoms/ signs	Confusion, focal neurologic symptoms/signs, diplopia, transient visual obscurations, pulsatile tinnitus	Mass lesion, structural lesion, stroke, hydrocephalus
O	Onset	Thunderclap	RCVS, stroke, subarachnoid hemorrhage, cerebral venous sinus thrombosis, arterial dissection, pituitary apoplexy, idiopathic intracranial hypertension
O	Older (age > 50 years)	New onset, persistent/progressive headache	Mass lesion, giant cell arteritis
P1	Positional	Orthostatic, recumbent, or worsens with change in position	Low intracranial pressure (CSF leak), mass lesion, cerebral venous sinus thrombosis, sinus pathology
P2	Prior history	New onset or change to persistent/daily headache	Mass lesion, infection (central nervous system, systemic)
P3	Pregnancy/postpartum	New onset during pregnancy	Cerebral venous sinus thrombosis preeclampsia, RCVS, pituitary lesion, stroke
P4	Precipitated by Valsalva	Cough, sneeze, bending, straining	Intracranial/posterior fossa mass, Chiari malformation

Abbreviations: CSF, cerebrospinal fluid; RCVS, reversible cerebral vasoconstriction syndrome.

Medication overuse headache is a headache that occurs on 15 or more days a month and develops as a consequence of regular overuse of acute headache medications for more than 3 months. To avoid medication overuse headache, it is recommended that ergotamines, triptans, opioids, or combination analgesics not be taken more than 10 days a month for over 3 months and that simple analgesics (acetaminophen, aspirin, nonsteroidal anti-inflammatory drugs) not be taken more than 15 days per month for over 3 months.[34]

In addition to the evaluation and history review noted in Table 6, there are a number of considerations for imaging[33]:

- The presence of one or more warning signals detected from use of the SNOOP4 tool requires a thorough workup that may include brain imaging, intracerebral/extracerebral vascular imaging, labs, and/or lumbar puncture.
- For the majority of secondary causes of headache, an MRI of the brain is the imaging modality of choice if there are no contraindications; contrast may be helpful when suspecting parenchymal brain lesions or diseases associated with pachymeningeal abnormalities (CSF leaks, intracranial hypotension, granulomatous pathology, leptomeningeal abnormalities, tumors, infections, neuroimmune processes, or other mass lesions).
- CT of the head is useful in an emergent/urgent evaluation to rule out intracranial blood or to identify skull fractures.[33]
- CT angiogram of the head and neck may be considered if concern is high for vasculitis or other vascular central nervous system abnormality.

Sleep disturbances

Sleep is an important biological mechanism for maintaining internal homeostasis, tissue repair, immune regulation, memory processing/consolidation, and quality of life.[37] Optimal sleep has positive results on physical and mental health.[38] In research presented at Sleep 2022, a meeting of the Associated Professional Sleep Societies, investigators from the Cleveland Clinic found that 41.3% of patients reported at least moderate sleep disturbances and 8% indicated severe sleep issues. The study also indicates that Black patients were more than three times more likely to have moderate-to-severe sleep disturbances after recovering from COVID-19 and that anxiety was associated with a higher-than-average incidence of sleep disturbance.[39] In a recent meta-analysis of 31 studies evaluating 5153 patients with COVID-19, it was found that 34% of patients have sleep disturbances, which were associated with 45% and 57% prevalence of depression and

TABLE 6 Headaches.

Patient History and Evaluation:

- Assess for new, ongoing, and persistent symptoms including onset, duration, intensity, and location (does it move around or stay in one spot).
- Obtain detailed headache history including the features and co-occurring symptoms to determine if the headache is due to a primary headache disorder (like migraine or tension-type, etc.) or if it is due to a secondary cause (space-occupying lesions, infections, vascular disorders, structural abnormalities). Refer to Table 5: Warning Signals to Raise Suspicion of Secondary Causes or Headache Using the Mnemonic SNOOP4[33]
  - Obtain a family history of neurological conditions including migraines or other headache disorders.
  - Determine if history of trauma
  - Determine if patient able to recall date of onset of persistent headache
  - Determine if family history of aneurysm or brain cancer
- Complete a full medication review including vitamins and supplements to ascertain if they might be contributing to headaches. Assess if headache is nonresponsive to over-the-counter medications.
  - Also evaluate how prior trials of headache medications/doses affected the headache
- Obtain sleep and exercise history
- Obtain history of substance use, including caffeine, alcohol, and other drugs, to assess frequency and duration. Alcohol and drug use can interfere with sleep and response to treatment.
- Evaluate for contributing comorbidities:
  - sleep disturbances like insomnia or sleep apnea (refer to sleep section),
  - anxiety and depression,
  - postural orthostatic tachycardia syndrome (POTS)

Additional Studies to Consider for Differential Diagnosis:

- Human immunodeficiency virus (HIV) testing should be considered in patients with suspected infection or refractory chronic daily headache pattern. Lyme antibody testing may be important in endemic regions.
- Prolactin and cortisol should be obtained if concern for a pituitary lesion.
- A lumbar puncture may be indicated to evaluate opening pressure, rule out infections or subarachnoid hemorrhage, evaluate for granulomatous pathology, neuroimmune conditions or meningeal carcinomatosis.

Initial Treatment Approach

- Recommend lifestyle modifications; a useful strategy for the treatment of migraine and tension type headache using lifestyle modifications can be remembered using the mnemonic SEEDS (sleep, exercise, eat, diary, stress).[35]
- Recommend counseling on the negative effects of medication overuse (including acetaminophen and ibuprofen) (>3x/week) and how it can cause rebound headaches.
- Recommend counseling for alcohol and drug use effects
- Patients with PASC-related headache may benefit from a multidisciplinary approach to treatment that includes both pharmacologic and nonpharmacologic approaches.[32]
- Consider over-the-counter supplements for prophylaxis (eg, magnesium, melatonin, coenzyme Q10, riboflavin, feverfew) can be beneficial.
- Nonpharmacologic therapies (acupuncture, relaxation therapies with deep breathing exercises, biofeedback) may be beneficial for those patients with sensitivity, resistance, or inability to tolerate medication. Ideas for relaxation strategies include:
  - gentle stretching
  - ergonomics—positioning at work, headset,
  - trigger point injections
  - nerve blocks
  - neuromodulation devices

Consider the following treatment and referral approaches based on headache phenotype

Migraine	Moderate–severe headache	Tension type headache
• Headaches that meet the International Classification for Headache Disorders third edition (ICHD-3) diagnostic criteria for migraine can be treated acutely with acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), triptans, ergotamines, ditans, or gepants. • Consider preventative treatment of episodic migraine if indicated[32] • Consider referral for botulinum toxins for chronic migraine management	• Abortive regimens should not be overused. Avoid regular intake for greater than or equal to 10 days per month for more than 3 months of ergotamines, triptans, opioids, or combination-analgesic medications or greater than or equal to 15 days per month of NSAIDs or acetaminophen.[34]	• Headaches meeting the ICHD-3 criteria for tension type headache can be treated with acetaminophen, aspirin, or NSAIDs.

Referral Options:

- A neurology referral should be considered if the clinician is unsure of the diagnosis/etiology of the headache and/or if headaches are refractory to treatment or progressively worsening)

Resources:

- Advocacy for Migraine Relief: Strategic Planning to Eliminate the Burden[36]

anxiety.[40] Other studies have also noted that misalignment in sleep–wake cycle and circadian rhythms could negatively affect cognitive function, including attention, concentration, learning, and memory, which are some of the most prevalent concerns in patients with PASC.[41]

Management of insomnia requires a stepwise approach, beginning with attempts to eliminate or minimize contributing factors and comorbid illnesses, such as obstructive sleep apnea, that interfere with optimal sleep. Refer to Table 7 for evaluation and initial treatment considerations. Successful behavioral and pharmacologic approaches to insomnia can be devised only when all contributing factors are recognized and addressed. Most patients with PASC-associated insomnia have entered into the chronic phase of insomnia. The preferred first line therapy at this stage is cognitive behavioral therapy for insomnia (CBT-I), a multicomponent approach targeting cognitions and behavior associated with poor sleep. Behaviorally, the patient is encouraged to maintain a consistent routine by establishing a stable bed and wake time, try to lie on the bed only when sleeping, optimize the sleeping environment for comfort, avoid substances that interfere with sleep, and reduce time in bed (sleep restriction), and get out of bed when experiencing increased anxiety. CBT-I addresses anxious and catastrophic thoughts surrounding sleeplessness, sleep expectations, and insomnia, as well as promotes relaxation therapies such as progressive muscle relaxation, mindfulness, and meditation. Although CBT-I has been validated as a face-to-face therapy, remote applications (such as online or teletherapy) have shown promising results in small studies.[42]

CBT-I is not effective for all patients and is not accessible to many, either due to lack of therapists, limitations of insurance, or time. In such cases, a limited or short course of medications is an acceptable approach if the patient is thoroughly evaluated beforehand, is followed regularly during treatment, and continues to respond positively to the medication. A sleep diary can be a very helpful tool to gain more insight into sleep problems, or to monitor whether a treatment is successful. Sleep diaries are normally completed once or twice a day. A diary usually consists of several questions related to sleep and wake times, nap times, caffeine and alcohol use, and general mood or functioning.

The approach to patients with insomnia (less than 1 month) is to identify potential stressors and try to address the causes. However, if this fails or if insomnia is associated with substantial distress, short-term use of insomnia medication is warranted to help address immediate interference with daytime function and to control escalating anxiety about sleep. Interventions, including medications, should be tailored to individual patients and concerns such as polypharmacy in the elderly and medication use and dosing in pregnant or lactating women should be considered. Social determinants of health (SDOH) should also be considered regarding both diagnosis and treatment. For instance, someone who lives in a crowded multigenerational home and works the night shift may have difficulty with both quantity and quality of sleep. Refer to Table 8 for other examples of how SDOH may affect neurologic PASC sequelae (Table 8: Health Equity Considerations and Examples in PASC: Neurologic Sequelae).

Neuropathies and neuropathic pain

Patients with PASC may present with symptoms of peripheral neuropathy such as numbness, sensory changes, and neuropathic sensations (burning, tingling, hypersensitivity, phantom pain). In one study, 60% of patients seen in a neurologic COVID-19 clinic reported numbness/tingling.[3] In another study, 18.8% of patients reported numbness/tingling after 6 months.[75] Additional small studies have confirmed small fiber neuropathy in patients with PASC.[76,77] The presence of autonomic symptoms in patients with PASC should also raise suspicion of small fiber neuropathy. Identification of small fiber neuropathy could help facilitate treatment with immunotherapies, such as intravenous immunoglobulin, which has shown to be beneficial in early studies.[78,79] Focal neuropathies as well as critical illness neuropathy may be present in patients who were hospitalized with severe COVID-19.[80,81] In addition to weakness and sensory impairments patients may experience pain with movement that can cause limited mobility and affect daily activity. Refer to Table 9 for a comprehensive overview of signs, symptoms, and additional evaluation and treatment options for neuropathy and neuropathic pain. Pain can be a debilitating symptom for patients with neuropathies. Patients with PASC often describe pain as burning, tingling, sharp, stabbing, electrical sensation, vibration, itching, or heaviness. The symptoms are often worse at night. Examination can help differentiate large fiber neuropathies from small fiber neuropathies. Large fiber neuropathies are associated with loss of vibration and position sense with poor balance, abnormal Romberg test, and reduced deep tendon reflexes. Small fiber neuropathy can result only in loss of pin prick and pain or temperature evaluation but often the clinical examination can be normal.

Evaluation includes testing for other common causes of neuropathy such as thyroid stimulating hormone, B12/B6/B1 deficiency or excess, diabetes or prediabetes, infections like HIV/syphilis, or monoclonal gammopathies. In patients with persistent or progressive neuropathies, inflammatory and autoimmune markers, such as erythrocyte sedimentation rate, c-reactive protein, antinuclear antibodies (ANA), antimyelin oligodendrocyte, (myelin-associated glycoprotein

TABLE 7 Sleep disturbances.

Signs	Symptoms
• Restless legs • Observed apneic episodes • Hypertension • Arrhythmias • Impaired cognition • Metabolic dysfunction: glucose intolerance • Pain (muscle, headaches, nerve) • Sudden sleep/drop attacks • Insomnia regardless of attempts at behavioral approaches	• Poor sleep • Wakes frequently or wakes early • Non-restorative/unrefreshing sleep • 'Tired' on waking • Snoring • Frequent urination at night • Bad dreams/nightmares • Easily falls asleep during the day • Pain • Night sweats • Cognitive symptoms especially attention, processing speed, memory and executive function • Behavioral symptoms: irritability, anxiety, depression and mood lability • Headaches

Patient History and Evaluation:

- Obtain a sleep history to include review of:
  - Pre- and post-COVID quantity and quality of sleep, difficulty with sleep initiation, maintenance, or early wakening.
  - Presence of daytime naps and/or drowsiness.
  - Impact on cognition (attention, concentration, memory, decision making)
  - Severity: patients should be advised to monitor sleep patterns through the use of a sleep diary for at least 2 weeks and document specific sleep and wake habits over the specified a period of time.
- Review reports of sleep disruptions: nightmares (suggestive of post-traumatic stress disorder [PTSD]) sleep apnea, restless leg syndrome, presence of pain (muscle cramps; neuropathic pain). Abnormal parasomnias (sleep walking, talking), or drop attacks during day, both of which may suggest presence of autonomic or autoimmune disturbances
- Assess for other factors affecting sleep:
  - Routine exercise, or any physical activity limited by exertional fatigue
  - Presence of polypharmacy (>4 medications)
  - Excessive caffeine intake
  - Initiation of new supplements
  - Increased alcohol use
  - Anxiety
- Evaluate current sleep routine including use of sleep aids (apps, white noise machines), sleep medication, blue light, or behavioral strategies
- Actigraphy can be considered as an additional objective measurement tool.
- Review medications that may cause insomnia: alcohol, antidepressants, beta-blockers, caffeine, chemotherapy drugs, cold and allergy medications containing pseudoephedrine, diuretics, illicit drugs, such as cocaine and other stimulants, nicotine, stimulant laxatives
- Assess sleep characteristics. The following screening tools can be used: Epworth Sleepiness Scale (ESS), Stanford Sleepiness Scale, PROMIS Sleep, Sleep Scale Survey, Insomnia Severity Index
- Screen for Sleep Apnea: STOP-BANG questionnaire

Initial Treatment Approach

- The first line approach for insomnia should include cognitive behavioral therapy (CBT) for insomnia, whenever it is available.
- Manage underlying conditions that may impact sleep: asthma, heart failure, hyperthyroidism, acid reflux, anxiety
- Educate on behavioral strategies: Creating a sleep routine, avoiding stimulants, stopping electronic screens for at least an hour prior to bedtime, Journaling thoughts before bedtime, relaxation techniques
- Consider short-term use of over the counter medications and aids: melatonin, doxylamine succinate (Unisom SleepTabs), chamomile tea
- Consider pharmacology when over the counter medications and aids and behavioral strategies have not proven successful: Consider trazodone, zolpidem (Ambien), eszopiclone (Lunesta), zaleplon (Sonata), doxepin (Silenor), ramelteon (Rozerem), suvorexant (Belsomra), temazepam (Restoril). These medications must be used with caution in the older population and patients should be advised regarding potential for habituation to these medications over time.
- Clinician prescription of medication can be guided by the presence of other symptoms. The following medications often have side effects and should be used cautiously.
  - Headaches: gabapentin
  - Muscle aches or spasms: tizanidine or baclofen
  - Anorexia: mirtazapine
  - Pain: amitriptyline, gabapentin
  - Anxiety: gabapentin
  - Psychiatric disorders: quetiapine

Referral Options:

- Refer to pulmonology, sleep medicine for polysomnogram; closer follow-up or to adjust medications
- Refer to psychology, social work, or psychiatry for CBT, anxiety, or PTSD management

Resources:

- Veterans Affairs Insomnia Coach: https://mobile.va.gov/app/insomnia-coach
- American Academy of Sleep Medicine: http://www.sleepeducation.org/

(Continues)

TABLE 7 (Continued)

- American Sleep Apnea Association: http://www.sleepapnea.org/
- Circadian Sleep Disorders Network: http://www.circadiansleepdisorders.org/
- Narcolepsy Network: http://narcolepsynetwork.org/
- Restless Legs Syndrome Foundation: https://www.rls.org/
- Wake Up Narcolepsy: http://www.wakeupnarcolepsy.org/

[MAG]), and antibodies to gangliosides GM1, GD1b, and GQ1b, should also be considered as part of evaluation of post-infection inflammatory neuropathies. Nerve conduction studies can help evaluate for inflammatory demyelinating neuropathies like acute or chronic inflammatory demyelinating polyneuropathies and MAG neuropathy, which will need interventions such as immunoglobulin, plasmapheresis, or steroids. Imaging, for example MRI of the lumbar spine with contrast, can sometimes show nerve root enhancement suggesting inflammatory neuropathy. Skin biopsy to evaluate intraepidermal nerve fiber density or Quantitative Sudomotor Axon Reflex Test can be used to diagnose small fiber neuropathy. Both the neuroimmune clinical workup and skin biopsy evaluation can be helpful to diagnose inflammatory neuropathies that can be successfully treated with immune therapies, such as intravenous immunoglobulin.[84–87] We acknowledge these extensive clinical evaluations may not be practical or feasible in many primary care and PASC clinic settings. Patients with persistent neuropathy symptoms should be referred for subspecialty neuroimmunology or autoimmune neurology evaluations and considered for immunotherapies.

For patients with significant sensory loss, consider referral to a neurologist for definitive workup and diagnosis, especially in the setting of significant neuropathy, progressive weakness, or worsening gait instability. Consider referral to a physiatrist and the rehabilitation team for an individualized treatment plan to address neuropathic pain or peripheral neuropathy. Physical therapy may include strengthening, balance retraining, gait training, stretching (muscular and neural tension), and aquatic therapy. Occupational therapy may include desensitization, functional skills training including safety and compensatory strategies for sensory changes, and stretching (muscular and neural tension). Speech therapy can provide exercises and strategies for neuropathic pain that affects facial or cervical muscles, swallowing, or voice. An orthotist may be able to provide orthotics to help with foot/ankle joint stabilization to maintain gait function and prevent falls.

Although referral for ongoing outpatient physical and occupational therapy is beneficial, there remain significant gaps in health equity for certain populations. In a recent large national case–control study, African-American/Black individuals were significantly less likely to receive outpatient rehabilitation than their white counterparts (odds ratio = 0.89).[88] Specific to pain management, African-American persons continue to experience disparities in the prevalence, management, progression, and outcomes of chronic, nonmalignant pain-related conditions.[89]

Muscular pain/weakness/tremors

Muscle-related symptoms are common in patients with PASC. Several reviews have reported the frequency of muscular symptoms which include[90,91]:

- Muscle pain/myalgia: 2%–53.6%
- Myalgias–arthralgia: 5.9%–71%
- Muscle weakness: 31.4%–63%

Mobility problems are often included as muscle-related symptoms in the literature. These mobility issues are inclusive of problems related to personal care (1%–13%), usual activity (2%–67%), and decreased functional status (47.5%–64%).[90,91] In addition, studies have noted that muscular aches and pain may limit mobility and activity tolerance.[91] Critical illness myopathy has been seen in people with severe COVID-19 infection, with significant proximal greater than distal weakness, and can contribute to PASC symptoms of muscle weakness and mobility challenges for weeks to months post hospitalization.[16] In a study assessing the impact of SARS-CoV-2 infection on prevalence and severity of long-term neurological manifestations, 10.3% individuals reported abnormal movements 6 months after their COVID-19 diagnosis. Abnormal movements/tremor can affect self-care activities, feeding, and writing.[75]

Muscular pain associated with weakness can suggest inflammatory muscle disease or postviral myopathy (Table 10). Involvement of muscles of the face, speech, and swallowing may need an expedited workup given concern of pending intubation due to these symptoms, such as seen in patients with neuromuscular junction disorders.[92] Absence of abnormalities on sensory exam with myalgia and weakness can suggest primary muscle or neuromuscular junction disorder. Evaluation should include creatine kinase testing. If the result is high (greater than three times the upper limit of normal) at baseline or 7 days without significant exertion, the patient would need electromyography (EMG) and nerve conduction studies to evaluate for inflammatory myopathy. If EMG and nerve

TABLE 8 Health equity considerations and examples in post-acute sequelae of SARS-CoV-2 infection (PASC): neurologic sequelae.

Category	Comment	What is known	Clinical considerations
Racial/Ethnic Minority Groups *Example: People who identify as Black (including African-American), American-Indian/Alaska Native, Pacific Islander, Asian-American, and Mixed Race, and/or Latino/Hispanic (ethnicity)*	Individuals who identify with groups that have been historically, socially, or economically marginalized may be at higher risk for COVID-19 related morbidity and mortality.	Historically marginalized racial/ethnic minority groups have higher rates of COVID-19 infection and lower rates of access to health care services.[43] It is well documented that many of these disparities are affected by social determinants of health (SDOH).[44] In a study of provision of physical and occupational therapy services for those hospitalized with COVID-19 in the University of Colorado Health System, therapy sessions were significantly reduced for patients with Hispanic ethnicity.[45] The Household Pulse Survey from June 2022, showed nearly 9% of Hispanic adults having Long COVID, which was higher than non-Hispanic White (7.5%), Black (6.8%), and non-Hispanic Asian (3.7%) adults.[46]	Individuals from racial/ethnic minority groups have been reported to have lower referral rates to neurologic rehabilitation than people classified as White/Caucasian.[47,48] All individuals with neurologic impairment and symptomatology such as tremor, vestibular dysfunction, cognitive complaints, or paresis should be considered for specialized neurorehabilitation programs. Referrals should occur in a timely manner. Treating physicians should determine what type of rehabilitation interventions and/or programs will be most beneficial as well as considering other factors such as cost and accessibility. Every effort should be made to close gaps in health disparities and ensure optimal care for people who identify with racial/ethnic minority groups.
Biologic Sex *Example: Female adults*	Many studies have documented sex-related disparities affecting female adults with neurologic conditions. Knowledge of areas of potential bias are important for clinicians to recognize and intentionally counteract to provide equitable health care.	Biologically female adults have some differences in neurologic symptoms and diagnoses. For example, hormone levels (eg, estrogen) are related to both migraine and stroke in female adults. A meta-analysis showed that nonpregnant women were at a higher risk of having symptoms such as headache, myalgia, fever, diarrhea and anosmia as primary symptoms of COVID-19 compared to pregnant women.[49] The study also noted that pregnant women were more likely to be admitted to the intensive care unit and receive mechanical ventilation compared to non-pregnant women.[49] One report summarizing the COVID-19 literature to date stated, "Current evidence suggests that severity and mortality of COVID-19 is higher in men than in women, whereas women might be at increased risk of COVID-19 reinfection and development of long COVID."[50] Another study found that female adults were more symptomatic for both acute infection and PASC than male adults.[51] Further research is needed to better understand gender-related differences in PASC.	Sex-related disparities have been reported and female adults may be underdiagnosed and undertreated in neurologic conditions. For example, a systematic review concluded that women have worse stroke outcomes than men and this may be due to misdiagnosis and undertreatment.[52] Thus, it is important for clinicians to be aware of the potential for underdiagnosis, misdiagnosis, and undertreatment and ensure that people, including female adults, receive optimal care. Individuals with underlying and/or new PASC-related neurologic symptoms or diagnoses should be considered for multidisciplinary rehabilitation services and referred in a timely manner. Pregnant women with baseline neurologic conditions and/or PASC-related conditions should be treated by clinicians who have expertise in this population as there are often contraindications with testing and treatment interventions that must be adhered to in order to protect the mother and fetus. Primary care providers and other specialists (eg, neurologists, rehabilitation medicine physicians) should determine what type of rehabilitation interventions and/or programs will be most beneficial as well as considering other factors such as cost and availability.
Age *Example: Children compared to older individuals*	Age should be considered in PASC-related health conditions as this may affect clinical decision making.	Many clinical trials, including rehabilitation studies, have gaps in the inclusion of people across the age continuum, particularly children and older individuals. Thus, clinicians should be aware that while PASC-related care needs will outpace the research for everyone, studies to guide the care of children and older individuals may be particularly slow to evolve. A recent cross-sectional study with age-matched controls showed SARS-CoV-2-positive adolescent participants in the case group had greater odds of having at least one long COVID symptom lasting at least 2 months compared with the control group. In addition, the case group reported 16 or more sick	In older patients with type 2 diabetes mellitus, good control of blood sugar and other comorbidities, supervised physical activity and exercise, and optimal nutrition may be helpful in reducing and managing PASC symptoms.[54] Since older individuals may have low skeletal muscle mass with baseline sarcopenia, following infection they may become weaker than premorbidly. Clinicians should be vigilant about recognizing new or worsening neurologic or cardiovascular issues with activity and/or exercise. For older individuals who have an upcoming surgery, prehabilitation may help to

(Continues)

TABLE 8 (Continued)

Category	Comment	What is known	Clinical considerations
		days (18.2% vs. 11.6%; $p < .0001$) and 16 or more days of school absence (10.5% vs. 8.2%; $p < .0001$) compared to the control group.[53] A review in patients with type 2 diabetes mellitus and PASC highlighted issues related to older individuals.[54] The report explained that in diabetes, neuropathy and myopathy contribute to muscle atrophy and sarcopenia. In addition, acute COVID-19 infection, hospitalization, protein deficiency, and corticosteroid therapy often cause rapid onset of sarcopenia in severe COVID-19 infections. Acute COVID-19 infection may also contribute to new or worsening neurologic issues.	support optimal outcomes.[55] Virtual visits for telerehabilitation may enhance access to care for older individuals. Recognition of PASC-related conditions in skilled nursing facilities is a factor that should be considered for individuals from that specific living setting. Larger number of beds and location in an area with high COVID-19 prevalence were the strongest and most consistent predictors of facilities having more COVID-19 cases and deaths.[56] This multicenter cohort study showed that delirium was the sixth most common of all presenting symptoms and signs of acute COVID-19 infection, and factors associated with delirium were age older than 75 years, living in a nursing home or assisted living, vision impairment, hearing impairment, stroke, and Parkinson disease.[57] Though the studies in children are evolving, long COVID is recognized and should be considered at all ages. Expedited referrals to a multi-disciplinary PASC clinics should be considered for children when symptoms continue and to pediatric neurologists, pediatric rehabilitation medicine physicians, and other rehabilitation specialists when there are neurologic symptoms and sequelae.
Disability *Example: People with certain conditions that cause disability and neurologic dysfunction*	Individuals with baseline disability require special consideration in the workup and management of neurologic conditions in PASC. Further attention may be given for individuals with special needs and additional comorbidities.	People with disability due to spinal cord injury (SCI), stroke, multiple sclerosis (MS) and other common rehabilitation conditions have baseline neurologic dysfunction and may be at higher risk for COVID-19 acute infection and/or more severe disease. The incidence of PASC-related neurologic sequelae has yet to be fully explored in patient populations with pre-existing disability. However, clinicians should be aware of the overlapping issues of pre-morbid conditions associated with disability, risk of COVID-19 infection, severity of acute infection, and PASC sequelae. For example, patients with MS may be on disease modifying therapy (DMT), and both the MS and the DMT may put them at higher risk for COVID-19 acute infections as well as more severe course, though in a recent systematic review these were not consistent findings.[58] The review included more than 80 reports involving 2493 MS patients and 37 Neuromyelitis Optica Spectrum Disorder patients with COVID-19. Older age, higher expanded disability status scale (EDSS) scores, cardiac comorbidities, and obesity were independent risk factors for severe COVID-19. A systematic review of persons living with SCI showed similar clinical presentation, and low intensive care unit admission, but increased mortality for this population.[59]	The impact of PASC-related neurologic dysfunction should be considered in individuals with baseline comorbidities that involve disability. Neurologic assessments should be tailored to the individual. Treating clinicians such as primary care providers, neurologists, and rehabilitation physicians should determine what type of rehabilitation will be most helpful and accessible. People with disability may benefit from addressing issues related to social determinants of health such as travel-related access to care. They may require and benefit from telehealth visits or access to community or other available travel resources.[60,61] Consideration of the types of rehabilitation as well as the benefits, cost, and availability may vary, depending on a variety of factors. For safety purposes, patients may need to be cleared by a cardiologist prior to starting an exercise program. For those patients with SCI, a referral to a SCI-trained professional with experience in ventilation and pulmonary management of these patients may be indicated.[62] Safety precautions should be clearly documented and adhered to. Monitoring vital signs and pulse oximetry is important as is a patient's perceived exertion. Exercise and activity prescriptions, medications, injections, and other interventions aimed at supporting rehabilitation and enhanced function should be tailored to the individual and prescribed by clinicians who are experienced in caring for medically complex patients.

(Continues)

TABLE 8 (Continued)

Category	Comment	What is known	Clinical considerations
Obesity *Example: People who are diagnosed as overweight/obese*	Obesity may not only increase the incidence and mortality associated with acute COVID-19 infection, but also development of PASC-related symptoms.	Obesity is an important risk factor for the development of severe COVID-19 infection and mortality.[63] Moderate and severe obesity (body mass index [BMI] ≥ 35 kg/m^2) are associated with a greater risk of PASC.[63] Obesity has been thought to accelerate immunosenescence due to greater gene expression of inflammatory markers and oxidative stress.[64] In one study, PASC symptoms were characterized by fatigue, headache, dyspnea and anosmia and these were more likely with increasing age, increased BMI and female gender.[65] High BMI and previous pulmonary disease could be risk factors for development of PASC in exposed health care workers.[66]	Recognize that obesity as a comorbidity can increase a patient's risk for PASC and neurologic complications. Overweight individuals also face weight-related stigmatization. Furthermore, criteria for obesity using BMI may not be accurate for people with paralysis, who have lower ratios of fat to lean muscle mass. Addressing weight loss strategies can be done within patients' system of care and in consideration with their own SDOH. Exercise and physical activity should be appropriately prescribed and consider obesity as a comorbidity. Furthermore, avoiding stigmatization should be embraced to promote physical activity in this population.[67]
Insurance *Example: Individuals who are uninsured, underinsured, or cannot afford access to recommended health care services*	Insurance coverage, or lack thereof, should be considered when devising a treatment plan addressing health issues in PASC. Encouraging patient engagement and addressing psychosocial factors may improve adherence with treatment recommendations.	States with the highest rates of the uninsured will have widening disparities in health outcomes among racial/ethnic minority and low-income populations, worsening for those persons with PASC.[68] There may be lower participation in rehabilitation due to factors such as older age and reduced mobility or driving ability as well as social determinants of health such as being unemployed, having a low education level or lower income.[69] Access to telehealth services may be helpful for health care access to individuals with challenges with transportation, distance, and/or mobility.[70,71]	Clinicians should be aware of the cost of diagnostic and treatment interventions. Consider the value of diagnostic testing to rule in/out various conditions. Treatment interventions, such as physical therapy, may be limited by the cost of copayments and deductibles, even in patients who have medical insurance. Social services or community groups may assist persons with finding local support inclusive of free therapy services. While access to telehealth services may facilitate care for some people, technology poses significant challenges for others. For example, individuals may have difficulty downloading, installing, and using new technology software or applications, a limited number of available digital devices, insufficient internet speed and bandwidth to manage audio and visual data, and poor quality of the camera and/or microphone on the device thus affecting the quality and diagnostic accuracy.[72] Insurance coverage for telemedicine services, including telephone visits and virtual visits online, has expanded during the pandemic—leading to greater use of these services, though coverage for these services is changing. Telerehabilitation is often feasible, cost-effective, and may improve function in neurologic conditions as well as PASC.[73,74]

Note: This table is included to provide additional information for clinicians who are treating patients for PASC-related neurologic sequelae. This is not intended to be a comprehensive list, but rather to provide clinical examples as they relate to health equity, health disparities, and social determinants of health. The literature demonstrates that all marginalized groups face socioeconomic barriers and access to care barriers, though these may or may not be barriers for a specific individual patient. People with intersectional identities (eg, those who identify with more than one underrepresented or marginalized group), often face enhanced levels of bias and discrimination.

TABLE 9 Neuropathy/neuropathic pain.

Signs:
- Weakness
- Gait instability
- Sensory testing abnormalities
- Muscle atrophy
- Change in mobility

Symptoms:
- Numbness
- Sensory changes
- Nerve pain
- Burning
- Tingling
- Vibration
- Sharp shooting pain
- Hypersensitivity to touch
- Temperature instability with hot/cold feeling
- Phantom pain or sensations/itching
- Falls

Patient History and Evaluation:
- Assess for a personal history of diabetes, chemotherapy, alcohol use, autoimmune disorders, peripheral nerve injury or compression
- Assess for prolonged hospital stay, hospital stay including intensive care unit stay and/or prone positioning
- Manual muscle testing, with a focus on pattern of weakness (ie, proximal versus distal vs. focal vs. nerve distribution vs. dermatome)
- Sensory testing including light touch, pinprick vibration, proprioception, temperature
- Muscle stretch reflex testing
- Gait assessment, tandem gait
- Postural stability and alignment, dynamic balance (sitting or standing)

Additional Studies to Consider for Differential Diagnosis:
- Consider creatine phosphokinase, ferritin level, HIV and rapid plasma reagin, serum protein electrophoresis with immunofixation, methylmalonic acid may be considered in specific populations.
- Consider electromyography/nerve conduction studies (EMG/NCS) testing to identify and classify focal or diffuse neuropathy (motor/sensory, axonal/demyelinating)
- Consider small fiber neuropathy skin biopsy for intraepidermal nerve fiber density (may be done by neurology and trained internal medicine or dermatology clinicians)
- Magnetic resonance imaging imaging of spine can be considered in selected cases based on EMG/NCS or for presence of cord involvement (sensory level, bowel/bladder changes, increased reflexes) or look for root enhancement in polyradiculoneuropathy (chronic or acute inflammatory demyelinating polyneuropathy) (Refer to Table 3: Red Flags)

Initial Treatment Approach
- Consider use of pain management strategies for neuropathic pain (gabapentin, Lyrica, Cymbalta, Nortriptyline, topical capsaicin, dry needling, heat, ultrasound)[82]
- Consider use of "Evidence-based pain medicine for primary care physicians" as an evidence-based resource for pain management.[83]

Referral Options:
- Refer to neurology for significant neuropathy, progressive weakness, or worsening gait instability
- Refer to pain management for severe symptoms that do not respond to first-line medication therapy
- Refer to orthotist for joint protection or stabilization; compression garments
- Refer to physical therapy for strengthening, balance retraining, gait training, stretching (muscular and neural tension), Aquatic therapy and patient education on pain.
- Refer to occupational therapy for desensitization, functional skills training including safety and compensatory strategies for sensory changes, stretching (muscular and neural tension), and patient education on pain.
- Refer to speech language pathology/therapy for focal exercises for facial or cervical muscles, dysphagia therapy, voice.

conduction studies are unavailable, MRI of the muscle with fat suppressed images can help diagnose muscle inflammation. If EMG does not show spontaneous activity at rest, this is likely postviral myalgia/myopathy and the treatment would consist of physical therapy and rehabilitation. If EMG shows evidence of inflammation (spontaneous activity at rest or abnormal MRI suggesting myositis), evaluation by neurology or rheumatology with muscle biopsy may be necessary for diagnostic purposes.

Fatigable weakness with involvement of face or bulbar muscles can suggest a neuromuscular junction disorder like myasthenia gravis. These disorders are not usually associated with significant myalgias. Once myasthenia gravis is diagnosed in a patient with PASC, it will continue, and we would consider it to be part of ongoing symptoms of PASC.[93,94] Laboratory testing with acetylcholine receptor antibodies, voltage gated calcium channel antibodies and repetitive nerve conduction testing or single fiber EMG can help with diagnosis along with referral to neurology.

Tremor can be seen in weak muscles when activated. If the tremor is not associated with weakness and is present only with activity, consider essential tremor. If the tremor is at rest or associated with slowness of movements (bradykinesia) and postural instability, consider neurological evaluation for parkinsonian disorders. If the tremor is seen only on standing, consider orthostatic tremor.

For patients with muscular symptoms, such as pain, weakness, tremors, progressive weakness, or worsening gait instability, consider referral to a neurologist for definitive workup and diagnosis.

TABLE 10 Muscular pain, muscle weakness, tremor.

History and Physical Examination:
- Assess for prolonged hospital stay, hospital stay including intensive care unit stay; duration of hospitalization/bed rest
- Determine exposure to paralytics or steroid use
- Assess past medical history for previous neuromuscular pain/involvement or injury
- Perform range of motion assessments for all major joints; note contracture presence
- Conduct manual muscle testing, with a focus on pattern of weakness (ie, proximal versus distal; focal vs. diffuse nerve distribution; dermatome vs. myotome)
- Conduct sensory testing including light touch, pinprick vibration, proprioception, temperature
- Conduct muscles stretch reflex testing and a gait assessment (tandem gait)
- Assess for presence of fasciculations (muscle fiber twitching) or entire muscle contraction or tremors
- Conduct a tremor assessment (resting versus action versus postural; unilateral/bilateral)
- Assess for focal or generalized atrophy

Additional Studies to Consider for Differential Diagnosis:
- Consider creatine kinase (CK), ANA, lactate dehydrogenase, protein electrophoresis and immunofixation, aldolase, rheumatoid factor/anticitrullinated peptide antibodies and myasthenia gravis profile
- Consider myositis panel if CK is elevated or EMG demonstrates evidence of myositis
- Consider EMG/NCS testing: identify and classify myopathy
- Consider an order for magnetic resonance imaging (MRI) muscle to evaluate for myositis
- Consider MRI of the brain if abnormalities noted like resting tremor or involvement of muscles of the face/swallowing or speech (RED FLAGS)

Initial Treatment Options and Referrals:
- Refer to neurology for significant myopathy, progressive weakness, or worsening gait instability
- Refer to rheumatology for inflammatory myopathy or consideration for rheumatologic conditions
- Refer to orthotist for joint protection or stabilization, improved functional safety; night-time splinting and positioning (as needed)
- Refer to pain management for treatment strategies for myalgias
- Refer to physical therapy for strengthening, stretching (muscular and neural tension), balance retraining, gait training, aquatic therapy, adjunct therapies such as yoga or sports
- Refer to occupational therapy for strengthening, stretching (muscular and neural tension), pacing strategies, functional skills training including safety and compensatory strategies for pain, tremor and activities of daily living, myofascial pain techniques
- Refer to speech language pathology/therapy to perform focal exercises for facial or cervical muscles, dysphagia therapy, voice.

DISCUSSION AND FUTURE DIRECTIONS

Although initially thought to be primarily a respiratory illness, it has become clear that COVID-19 is a multisystemic condition. Importantly, the nervous system may be affected in patients with PASC,[95] manifesting as cranial neuropathies, headaches, sleep abnormalities, cognitive dysfunction/brain fog, peripheral neuropathies, muscular symptoms, and pain.

The etiology of neurological complications in PASC is not well understood. Whereas some reports suggest direct SARS-CoV-2 invasion of the nervous system,[96] other possible mechanisms include persistent inflammation and rise of autoimmunity,[97] neurotransmitter imbalance,[98] unmasking or exacerbation of prior neurological and neuropsychiatric conditions,[99] and gut–brain axis imbalance.[100] It is likely that there is not just one mechanism but rather different pathophysiological mechanisms that explain PASC in different patient populations.

Thus, further research is vital in randomized controlled trials to define the etiology of PASC and develop and test treatments and interventions that are patient and symptoms specific. Although not all the mechanistic answers about pathophysiology of PASC are known at this time, it is critical that clinicians continue to think broadly about etiology of new or worsening neurological symptoms in patients post COVID-19 infection and diagnose PASC when appropriate. Clinicians caring for patients with PASC who have neurological complications should pursue appropriate diagnostic workup, provide referrals to multidisciplinary clinical teams, and pursue treatment of new and/or exacerbated central and peripheral nervous system disorders.

AAPM&R HEALTH EQUITY STATEMENT

The AAPM&R recognizes the need to support equitable access to rehabilitation care for individuals with PASC. The AAPM&R states that equitable access to care includes (1) timely and local patient access to multidisciplinary care; (2) addressing inequities in the US health system that result in diminished access to sustained quality care because of structural racism or socioeconomic factors; and (3) strengthened safety-net care, including disability evaluation and benefits.[101]

Each of the AAPM&R's PASC guidance statements were produced by a diverse and multidisciplinary team of subject matter experts with patient input. Although an in-depth discussion of health equity issues is beyond the scope of the PASC guidance statements, each one highlights health equity concerns and refers readers to other publications and resources. The term "health equity" has many different definitions, and they generally focus on ensuring that every person is able to achieve the highest level of health and function. For example, the Centers for Disease Control and Prevention defines health equity as the opportunity for people to fulfill their full health potential and states that people should not be disadvantaged from achieving their potential because of social position or other socially determined circumstances.[102] The Centers for Medicare and Medicaid Services uses the definition established in Executive Order 13985, issued on January 25, 2021 that states equity is "the consistent and

systematic fair, just, and impartial treatment of all individuals, including individuals who belong to underserved communities who have been denied such treatment, such as Black, Latino, and Indigenous and Native American persons, Asian Americans and Pacific Islanders and other persons of color; members of religious minorities; lesbian, gay, bisexual, transgender, and queer (LGBTQ+) persons; persons with disabilities; persons who live in rural areas; and persons otherwise adversely affected by persistent poverty or inequality."[103] There are many root causes for health disparities, some of which fall under the categories within SDOH. Examples of SDOH include but are not limited to socioeconomic status, neighborhood, availability and access to healthy food, and access to a high-quality education.

In addition to advocating for equitable access to rehabilitation care for all persons with PASC, the AAPM&R supports four "Principles of Inclusion and Engagement" that include (1) valuing diverse group composition (a diverse group is more representative of AAPM&R's membership and volunteers may be selected as a member of a particular community to enhance diversity of thought and experiences); (2) mutual respect (cultivating a receptive space for differing opinions and viewpoints); (3) talent and skill-based selection for leadership opportunities (ensuring that broad criteria of diversity of experience, talent and knowledge are incorporated and removing barriers to involvement that support an equitable environment); and (4) comprehensive collaboration (building community among various member constituent and bringing together different perspectives).[104] Readers of the PASC guidance statements are encouraged to consider the recommendations through the lens of health equity in order to improve access to rehabilitation care for all individuals with PASC.

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