

TABLE 1: AAPM&R Multi-Disciplinary PASC Collaborative Consensus Methodology

<p>1) Given a goal of symptom-driven consensus guidance generation, PASC clinical cochairs conducted literature review and initial discussion of likely priorities based on existing PASC data informing the most prevalent and disabling symptoms.</p>
<p>2) At an initial meeting of the PASC collaborative, expert clinicians and patients experiencing PASC discussed and refined priority areas. These initial areas included fatigue, cognitive impairment, breathing discomfort, dysautonomia. In addition to symptoms, there was complete consensus that health equity would require a dedicated writing groups to address this critical topic in the context of PASC. The group also outlined future areas of focus to be addressed in subsequent guidance statements.</p>
<p>3) The PASC collaborative, consisting of 27 United States, geographically distributed centers, convened to discuss experience with assessment and treatment of PASC symptoms in 2-hour meetings for each symptom domain. These meetings began in April 2021, have convened once per month since then, and are ongoing as the collaborative works through each domain of interest.</p>
<p>4) Within the membership of the PASC collaborative, clinicians were identified with specific expertise in each area of focus and amongst them, a small writing group was formed to develop each consensus statement. These experts represent a broad array of specialties (e.g. brain injury specialists, speech language pathologists and cognitive neurologists for cognition; pulmonologists, cardiopulmonary rehabilitation physiatrists, and physical therapists for breathing discomfort).</p>
<p>5) The smaller writing group considered initial PASC collaborative discussion, reviewed existing literature, and generated an initial document of recommendations for assessment and treatment of the PASC symptom. The health equity writing group followed a similar process to consider equity in the context of PASC. The members of the writing group then conducted anonymous electronic voting (Alchemer) to designate areas they deemed important for inclusion as an assessment and treatment recommendations.</p>
<p>6) All recommendations were discussed, but those that did not meet an “importance” vote from the majority of writing group members did not progress as candidate recommendation statements. The writing group was directed to consider any of those recommendations that did not meet majority in the discussion section of the guidance statement. The remaining “important” recommendations are discussed further by the writing group to move them toward a 2nd round of voting by the full PASC collaborative.</p>
<p>7) Each individual Assessment and Treatment Recommendation statement, as proposed by the writing group, was presented within a survey to all PASC Collaborative members. Members are provided the opportunity to vote as “agree,” “agree with consideration,” “disagree” with initial recommendation statements. [Wiley Online Library - 024.015.004.250 - /doi/epdf/10.1002/pmjr.12670] at [03/08/2021].</p>
<p>8) Statements for which 80% consensus was achieved were retained, and statements with “agree with consideration” were then discussed among the full PASC collaborative and shared with the writing group for further refinement.</p>
<p>9) Statements for which >60 to <80% consensus was achieved were discussed among the full PASC collaborative and a determination was made if the recommended concept should be refined, excluded, or included in the discussion section of the Consensus Statement. For reference, prior groups examining clinical and research guidance regarding long-term sequelae of critical illness used a number of consensus thresholds varying from 60 to 80%. For example, in the “Society of Critical Care Medicine’s International Consensus Conference on Prediction and Identification of Long-Term Impairments After Critical Illness,” 80% agreement indicated a strong recommendation and 60% indicated a weak recommendation (9, 10). We felt that the absence of data and limited experience with this condition supported the need for more discussion of those statements not meeting an 80% agreement threshold.</p>
<p>10) The writing group finalized the Assessment and Treatment Recommendation Tables which were voted on as sets by the entire PASC Collaborative with options of “approve” or “do not approve.” Consensus of the set of Assessment and Treatment Recommendations were considered final with 80% approval by the full collaborative, consistent with earlier discussion of consensus threshold(9, 10). Collaborative participants are provided the opportunity to comment further, and additional discussion may be added to the full Consensus Statement document.</p>
<p>11) The writing group was responsible for final Consensus Statement approval and an author assigned for publication submission.</p>

TABLE 1: PASC Fatigue Assessment Recommendations

#	Statement
1	Patients should be assessed for fatigue patterns throughout their normal day to guide activity recommendations.
1a	Patients should be assessed for their responses to initiating and escalating activity on their fatigue.
1b	Patients should be evaluated for changes in daily functioning and activity levels.
1c	Patients' physical functioning and endurance should be assessed in order to inform activity and therapy recommendations. (Examples of tests that can be chosen based on an individual's activity tolerance: 30 second sit to stand (14); 2-minute step (seated or standing) (15); 6 minute walk test(16); 10 meter walk test(17)).
2	Clinicians should assess for changes in activities of daily living, independent activities of daily living, school, work, and avocational (i.e., hobbies)
3	A full patient history with review of pre-existing conditions should be conducted
4	Patients should be evaluated for conditions that may exacerbate fatigue symptoms and warrant further testing and potential subspecialty referral (see Table 2). Particular areas include: <ul style="list-style-type: none"> • Sleep • Mood, including anxiety, depression and PTSD. Note: Patients often report dissatisfaction with their care due to their persistent symptoms being attributed to psychological factors. It is important to note that mood disorders may be secondary to persistent medical issues or one of many factors leading to fatigue. • Cardiopulmonary • Autoimmune • Endocrine
5	A medication review should be conducted to investigate medications that may be contributing to fatigue. Of note, antihistamine, anticholinergic, and antidepressant/anxiolytic medications can contribute to fatigue in patients with PASC.
6	The following basic lab work-up should be considered in new patients or those without lab work-up in the 3 months prior to visit including complete blood count with differential, chemistries including renal and hepatic function tests, thyroid stimulating hormone, c-reactive protein or erythrocyte sedimentation rate, and creatinine kinase. Other laboratory tests may be considered based on the results of the above tests or if there is specific concern for co-morbid conditions as outlined in Table 2.

TABLE 2: Common PASC System Manifestations, Symptoms, Additional Testing/Studies and Referral Options

	Common Symptoms and Signs	Further Studies to Consider in addition to basic laboratory evaluation	Referral
▶ Cardiovascular	<p>Symptoms: Chest pains, palpitations, sweating, nausea, fatigue, leg swelling, shortness of breath – at rest / on exertion / lying flat / waking up at night, dizziness on standing, feeling faint / fainting</p> <p>Signs: Pallor, tachypnea, tachycardia, diaphoresis, pulmonary rales, lower extremity edema, hypotensive sitting / standing – orthostatic hypotension, pre-syncopal / syncopal, poor activity tolerance / endurance</p>	B-type natriuretic peptide (BNP), Troponins, D-dimer, chest-x-ray (CXR), electrocardiogram (EKG), echocardiogram (ECHO), exercise stress test/ cardiopulmonary exercise test (EST/CPET), Holter monitor, Cardiac Magnetic Resonance Imaging	Cardiology
▶ Pulmonary	<p>Symptoms: Shortness of breath – at rest / on exertion, cough, wheeze, fatigue, poor activity tolerance</p> <p>Signs: Tachypnea, tachycardia, cough, hypoxia / low pulse oximeter, pulmonary wheezes / rhonchi / ‘Velcro’ rales, poor activity tolerance / endurance</p>	D-dimer, pulmonary function tests (PFTs), CXR, computerized tomography (CT) chest (with contrast if concerned for a pulmonary embolism)	Pulmonology
▶ Endocrine	<p>Symptoms: palpitations, fatigue, dizziness, weight gain / loss, sense of chills / fever, irregular menstrual cycle, poor diabetic control, excessive thirst / urination</p> <p>Signs: tachycardia, poor activity tolerance, weight gain / loss, low / elevated temperature, elevated finger-stick / urine glucose, ketotic (fruity) breath</p>	Thyroid stimulating hormone (TSH)/Free T4 (thyroxine), cortisol levels, growth hormone, luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone (men), estradiol (women)	Endocrinology
▶ Autoimmune	<p>Symptoms: Rash, joint / muscle pain and stiffness, fever, mouth sores / ulcers, cold / pale / blue / red fingers, sharp chest pain, numbness / tingling / burning in fingers / toes, blurry / decreased vision</p> <p>Signs: Rash, arthropathy – swelling / warmth / decreased ROM, myopathy – tenderness / weakness, fever, Raynaud’s phenomena, pleuritic pain on deep breathing, altered sensation, decreased visual acuity</p>	Imaging of effected joints, antibody screen based on ongoing symptoms	Rheumatology
▶ Mood Disorders	<p>Symptoms: anxiety, irritability, chest tightness, low frustration tolerance, depression, fatigue, mood swings, palpitations, change in memory / recall</p> <p>Signs: flat affect / low mood, emotional lability i.e. crying / laughing inappropriately, limited impulse control, psychosis</p>	An anxiety and depression screen (for example, the Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI) fast screen; Patient Health Questionnaire (PHQ)-2/9, Geriatric Depression Scale (GDS)	Psychiatry
▶ Sleep Disorders	<p>Symptoms: Poor sleep – hard to fall asleep / wakes frequently / wakes early, non-restorative / refreshing sleep – ‘tired’ on waking, snoring, frequent urination at night, bad dreams / nightmares, falls asleep during the day, morning headaches</p> <p>Signs: Snoring, Restless legs, Observed apneic episodes, Hypertension, Arrhythmias, Narcolepsy, Congestive heart failure, Impaired neuro-cognition, poorly controlled mood disorder</p>	Sleep apnea screen (for example, the STOP-BANG questionnaire or Epworth Sleepiness Scale (ESS)) overnight sleep study for oximetry and sleep apnea	Sleep Medicine

**TABLE 3: National Academy of Sciences Proposed Diagnostic Criteria for ME/CFS.
(Reproduced with permission)**

Proposed Diagnostic Criteria for ME/CFS

Diagnosis requires that the patient has the following three symptoms:

1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, education, social, or personal activities that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest,
2. Post-exertional malaise, * and
3. Unrefreshing sleep*

At least one of the following manifestations is also required:

1. Cognitive impairment* or
2. Orthostatic intolerance

**Frequency and severity of symptoms should be assessed. The diagnosis of ME/CFS should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial or severe intensity.*



TABLE 4: PASC Fatigue Treatment Recommendations

#	Statement
1	Begin an individualized and structured, titrated return to activity program.
2	Discuss energy conservation strategies.
3	Encourage a healthy dietary pattern and hydration.
4	Treat, in collaboration with appropriate specialists, underlying medical conditions, such as pain, insomnia/sleep disorders (including poor sleep hygiene), and mood issues which may be contributing to fatigue.



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Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): FATIGUE



Category	Comment	What is Known	Clinical Considerations
<p>▶ Biologic sex</p> <p><i>Example: Pregnant women</i></p>	<p>Physiologic and biologic sex differences should be considered for both the diagnosis and treatment of PASC-related fatigue.</p>	<p>Pregnant women frequently have pregnancy-related fatigue, and they may be at higher risk for more severe COVID-19 infections and symptoms, particularly women who have certain comorbidities and other characteristics (e.g., older age, diabetes, kidney disease, obesity).^{HE-F-1}</p>	<p>Pregnant women who are status post COVID-19 infections may experience pregnancy-related fatigue in addition to PASC-related fatigue, and may need alternatives to diagnostic testing (e.g., radiation exposure) to avoid potential harm to the fetus. The risks and benefits of medications and other treatment interventions should be assessed for both mother and fetus. Exercise prescriptions may be impacted by symptoms such as excessive vomiting and weight loss in the first trimester and large girth, back pain, or pre-eclampsia in the third trimester.</p>
<p>▶ Gender</p> <p><i>Example: Transgender individuals</i></p>	<p>People across the gender spectrum may have unique health issues.</p>	<p>Gender affirming medical interventions such as hormonal therapy or surgery, may impact fatigue, strength, and endurance. Many individuals had challenges accessing gender-affirming care during the pandemic, and this may be related to an increase in sleep disorders and mental health symptoms^{HE-F-2} and/or delays in elective surgery.</p>	<p>In the context of rehabilitation for PASC-related fatigue, it is important to assess the current and planned future gender affirming care for transgender patients. Hormonal status, sleep, and mental health should be prioritized as they may all affect fatigue. If elective surgeries are planned in the future, prehabilitation may help to increase strength and endurance and decrease psychological stress.^{HE-F-3} Virtual visits may offer better access to care.^{HE-F-4, HE-F-5}</p>
<p>▶ Racial / Ethnic Minority Groups</p> <p><i>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)</i></p>	<p>BIPOC (Black, Indigenous and People of Color) communities have been especially impacted by the global pandemic. As result, these groups have worse outcomes after COVID-19 infection, including hospitalizations, morbidity and mortality.^{HE-F-6}</p>	<p>Social determinants of health, societal factors and structural racism have disproportionate effects on underinvested communities.^{HE-F-7, HE-F-8, HE-F-9} Statistical models that control for susceptibility, exposure, and healthcare access reveal no disparity or the degree of the disparity is decreased in multiple studies; thereby demonstrating that exposure-related factors are contributing more to disparities than biological susceptibility.^{HE-F-6}</p>	<p>PASC-related fatigue is multifactorial, with its effects compounded for individuals already under the burden of racial and ethnic disparities and injustice. Standardized treatment and management protocols may help decrease implicit bias from providers to patients from racial and ethnic minority groups.^{HE-F-10} In treating fatigue, anti-racist awareness of the above issues may require a multi-disciplinary approach to healthcare, including but not limited to addressing: low cost healthcare, food/housing insecurity, health literacy with access to low cost information, access to transportation, obtaining or maintaining employment. Where appropriate, consider providing documentation to support: food vouchers, housing assistance, transportation/vehicle parking pass, temporary workplace accommodations and neighborhood support network. Local and national advocacy is needed to address ongoing systemic inequities.</p>

Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): FATIGUE



Category	Comment	What is Known	Clinical Considerations
<p>▶ Justice Involved (Prisons/Detention Centers)</p> <p><i>Example: People who are incarcerated or detained in prisons, jails, youth detention centers, immigration detention centers, internment camps and other facilities</i></p>	<p>People who are involved in some manner with various aspects of the criminal justice system, particularly those who are incarcerated in correctional facilities and detention centers, have a unique vulnerability to healthcare inequity that is often overlooked.</p>	<p>There have been high rates of COVID-19 infection in United States (US) prisons, and this affects not only the health of incarcerated individuals but also the employees, and their families and communities.^{HE-F-11} The public health implications of these facilities should encourage clinicians and policymakers to consider the public health concerns posed by these facilities when developing pandemic-response policy. Incarcerated people have high levels of co-morbid conditions including other infectious diseases such as HIV/AIDS, Hepatitis C virus and Tuberculosis.^{HE-F-12, HE-F-13} They are also at risk for chronic diseases (e.g., hypertension, diabetes), and are risk for worse health outcomes. They have a disproportional burden of substance use disorders and mental health illnesses. <small>HE-F-12, HE-F-13</small></p>	<p>Public health measures should include modifications to general community recommendations that will adequately address the special needs of this population. Social distancing, quarantine upon exposure, and separate bathrooms may not be possible and/or may unintentionally cause physical or emotional distress, possibly worsened by PASC-related fatigue. Early and continual access to quality physical and mental healthcare may be optimized through telehealth, personalized fatigue management strategies, and outcomes accountability for the facility staff. Clinicians should be aware of the health disparities in the context of social determinants of health which lead to a disproportion of racial and ethnic minorities within the criminal justice system.^{HE-F-13}</p>

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Category	Comment	What is Known	Clinical Considerations
<p>► Disability</p> <p><i>Example: People who have impairments in physical/mobility, psychological/mental health, vision, hearing, emotional/social relationships, cognitive/learning, speech and communication, and other disabilities</i></p>	<p>Healthcare and society in general make assumptions, foster unconscious bias (that include stereotypes) towards people with disabilities; the consequences lead to devaluation and disparate treatment of people with disabilities.^{HE-F-14}</p>	<p>Prior to the COVID-19 pandemic, people with disabilities were marginalized, enduring reduced access to community resources, physical and emotional barriers to social services and decreased access to quality healthcare.^{HE-F-15} During the pandemic, community participation was further impaired by necessary public health mandates such as travel restrictions, social distancing, and wearing a face mask that did not allow lip reading.</p>	<p>As a group, many individuals with PASC-related fatigue advocate for treatment, funding, and research as a chronic disability.</p> <p>The federal government has several laws established to protect the rights of disabled persons.^{HE-F-16} Clinicians should familiarize themselves with the Americans with Disabilities Act (ADA), a civil right law that guarantees equal access and prevents discrimination in areas of social life (healthcare coverage, employment, transportation, state and local government services, telecommunication, school, etc.). The Rehabilitation Act of 1973 (Rehab Act) protects equal access for individuals with disabilities through the removal of architectural, employment, and transportation barriers for organizations that receive federal assistance.</p> <p>When appropriate, clinicians should advocate for patients with PASC-related fatigue to obtain disability insurance, a home health aide, durable medical equipment (e.g. hospital bed, mobility aids, communication devices) workplace/school modifications (e.g. classroom or workplace adaptations, accommodations for lectures, notes and test-taking, learning aides/special education resources, modified schedule), or an emotional support animal.</p> <p>Strategies for information dissemination should include options for those who are visual, hearing, communication and learning impaired. While telemedicine has augmented access for many who are mobility impaired, clinicians must consider telemedicine options such as telephone calls for those who do not have access to smart phones, consistent internet broadband access or the knowledge to operate video telecommunication.</p>
<p>► Immigration</p> <p><i>Example: People who have come from another country in order to live in the United States</i></p>	<p>Immigration-related issues may pose numerous barriers to health and health care for many individuals.</p>	<p>Many health inequity issues in immigrant communities in the United States during the COVID-19 pandemic are well documented (e.g., high rates of acute infections, more severe disease, worse outcomes).</p>	<p>Regarding PASC-related fatigue, both the diagnostic work up and treatment may take place in the context of patients being underinsured or uninsured, having physically demanding jobs, difficulty taking time off from work for financial reasons, and living in close quarters that may disrupt sleep. Some of the solutions to care that have been documented in the literature include engaging community leaders, providing virtual patient navigators, using language-appropriate educational materials, and offering free legal assistance to access resources.^{HE-F-17}</p>

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Category	Comment	What is Known	Clinical Considerations
<p>► Religion</p> <p><i>Example: People who identify with a shared belief in what is sacred, holy, divine, spiritual, or reverent</i></p>	<p>Religion based practices deserve special consideration during healthcare evaluation.</p>	<p>Physical and psychological factors that influence fatigue (e.g. disfavoring transfusion of whole blood product for severe anemia,^{HE-F-18} modesty^{HE-F-19} in communication about sensitive topics, or moral injury^{HE-F-20} during a global pandemic) can affect those committed to various religious practices.</p>	<p>For individuals with PASC-related fatigue, religious practices such as fasting may increase symptoms. Fasting might also reduce physical activity^{HE-F-21} and affect conditioning and/or ability to participate in rehabilitation therapies.</p> <p>Although certain nutritional supplements,^{HE-F-22} natural remedies^{HE-F-23} and faith-based practices may have varying potential for anti-inflammatory or antioxidant properties to treat fatigue, clinical decisions regarding their use for PASC-related fatigue should ideally be considered in conjunction with an experienced professional and if deemed safe should be used in a complementary manner with evidence-based therapies.</p>

Legend:

This table is included in the Appendix to provide additional information for clinicians who are treating patients for PASC-related fatigue. 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 (e.g., those who identify with more than one underrepresented or marginalized group), often face enhanced levels of bias and discrimination.

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Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): FATIGUE



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