Malone Laura A (Orcid ID: 0000-0002-9836-822X)
Fleming Talya Kianti (Orcid ID: 0000-0002-2034-8253)
Kokorelis Christina (Orcid ID: 0000-0001-6486-4391)
Ng Rowena (Orcid ID: 0000-0001-7193-4300)
Sampsel Sarah Lyn (Orcid ID: 0000-0002-7496-8482)
Verduzco-Gutierrez Monica (Orcid ID: 0000-0003-0964-5908)

Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) in Children and Adolescents

Short Running Title: Consensus Guidance Statement: PASC in Children and Adolescents

- Laura A. Malone MD PhD, Kennedy Krieger Institute, Department of Neurology, Johns Hopkins Medicine, Baltimore, MD, Department of Physical Medicine and Rehabilitation, Johns Hopkins Medicine, Baltimore, MD*
- Amanda Morrow, MD, Kennedy Krieger Institute, Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine, Baltimore, MD*
- Yuxi Chen, MD, Department of Rehabilitation Medicine, Montefiore Medical Center, Bronx, NY
- Donna Curtis, MD, MPH Department of Pediatric Infectious Diseases Children's Hospital Colorado and University of Colorado School of Medicine Aurora, CO
- Sarah D. de Ferranti, MD, MPH, Department of Pediatrics, Harvard Medical School, Boston MA Department of Cardiology, Boston Children's Hospital, Boston MA
- Monika Desai, MD, Department of Rehabilitation Medicine, Montefiore Medical Center/Albert Einstein School of Medicine, Bronx, NY.
- Talya K. Fleming, MD, Department of Physical Medicine and Rehabilitation, JFK Johnson Rehabilitation Institute at Hackensack Meridian Health, Edison, NJ
- Therese M Giglia MD, FAHA, Director of the Center on Cardiac Anticoagulation and Thrombosis and Director of the Infant Single Ventricle Monitoring Program, Children's Hospital of Philadelphia, Philadelphia, PA
- Trevor A. Hall, PsyD, ABPdN Department of Pediatrics Oregon Health & Science University Portland, Oregon
- Ellen Henning, PhD Department of Behavioral Psychology Kennedy Krieger Institute Baltimore, MD
- Sneha Jadhav, MD, Psychiatric Mental Health Program, Kennedy Krieger Institute, Baltimore MD.
- Alicia M Johnston, MD, Division of Infectious Diseases, Department of Pediatrics, Boston Children's Hospital, Boston, MA
- Dona Rani C Kathirithamby, MD, Department of Rehabilitation Medicine and Department of Pediatrics, Montefiore Medical Center, Albert Einstein college of Medicine, Bronx, NY10467
- Christina Kokorelis, MD, Department of Physical Medicine and Rehabilitation, Johns Hopkins University and Kennedy Krieger Institute, Baltimore, MD

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- Catherine Lachenauer, MD, Division of Infectious Diseases Boston Children's Hospital Harvard Medical School Boston, MA
- Lilun Li, MD, Department of Otolaryngology and Communication Enhancement Boston Children's Hospital Boston, MA
- Henry C Lin MD, Department of Pediatrics, Oregon Health & Science University, Portland OR
- Tran Locke, MD Department of Otolaryngology-Head and Neck Surgery Baylor College of Medicine Houston, TX
- Carol MacArthur, MD, Department of Otolaryngology, Head & Neck Surgery, Oregon Health & Science University, Portland, Oregon
- Michelle Mann, MD, Department of Pediatric Pulmonology, Baylor College of Medicine, Texas Children's Hospital, Houston, TX
- Sharon A. McGrath-Morrow, MD, Department of Pediatrics Division of Pediatric Pulmonary Children's Hospital of Philadelphia and the University of Pennsylvania
- Rowena Ng, PhD, Neuropsychology Department, Kennedy Krieger Institute; Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD
- Laurie Ohlms, MD, Department of Otolaryngology, Boston Children's Hospital, Harvard Medical School, Boston MA
- Sarah Risen, MD, Department of Pediatric Neurology and Developmental Neuroscience, Texas Children's Hospital and Baylor College of Medicine, Houston, TX
- S. Christy Sadreameli, MD, MHS, Eudowood Division of Pediatric Respiratory Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland
- Sarah Sampsel, MPH, SLSampsel Consulting, Albuquerque, NM
- S. Kristen Sexson Tejtel, MD, PhD, MPH, Associate Professor, Pediatric Cardiology, Texas Children's Hospital/Baylor College of Medicine, Houston, TX
- Julie K. Silver, MD, Department of Physical Medicine and Rehabilitation, Harvard Medical School, Spaulding Rehabilitation Hospital, Boston, MA
- Tregony Simoneau, MD, Division of Pulmonary Medicine, Department of Pediatrics, Boston Children's Hospital and Harvard Medical School, Boston, MA
- Rasha Srouji, DNP, Department of Neurology Boston Children's Hospital Boston, MA
- Sanjeev Swami, MD, Department of Pediatrics, Division of Infectious Diseases, Children's Hospital of Philadelphia, Philadelphia, PA
- Souraya Torbey MD Kennedy Krieger Institute Assistant Professor of Psychiatry Johns Hopkins School of Medicine Baltimore, MD
- Monica Verduzco, Gutierrez, MD, Department of Rehabilitation Medicine, Long School of Medicine at UT Health Science Center San Antonio, San Antonio, TX

- Cydni Nicole Williams, MD, MCR, Oregon Health & Science University, Department of Pediatrics, Division of Pediatric Critical Care; Pediatric Critical Care and Neurotrauma Recovery Program; Portland, OR
- Lori Allison Zimmerman, M.D., Pediatrics, Boston Children's Hospital, Boston, MA
- Louise Elaine Vaz, MD, MPH, Division of Pediatric Infectious Diseases, Department of Pediatrics, Oregon Health & Science University, Portland OR

***Co first authors**

Corresponding Author Contact Information

Sarah Sampsel, MPH

Email: Slsampsel@ssampselqlty.com

Phone: 505-977-0332

SLSampsel Consulting, LLC

5008 Noreen Dr. NE, Albuquerque NM 87111

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Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) in Children and Adolescents

Key Words: Long-COVID, COVID-19, Pediatrics, Children, Adolescents, PASC

Introduction

Children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are generally asymptomatic or have mild acute symptoms with low rates of hospitalization (<2%) and death (<0.03%). (1) After initial infection, some children, including those who

experienced mild or asymptomatic disease, develop other post-acute manifestations of COVID, including multisystem inflammatory syndrome in children (MIS-C, not discussed in this statement) or post-acute sequelae of SARS-CoV-2 infection (PASC). The latter post-COVID condition may be known as long COVID, long-haul COVID, post-acute COVID-19, long-term effects of COVID, or chronic COVID. (2) This guidance statement uses the terminology of post-acute sequelae of SARS-CoV-2 infection (PASC).

Data are limited on the epidemiology of and risk factors for PASC in children and adolescents. The prevalence of PASC symptoms in children varied considerably between studies from 4 to 66%. (1,3-5) There is also large variation in the reported frequency of persistent symptoms. Recent studies have suggested that possible risk factors for PASC in pediatric patients may be older age, female sex, and history of allergic disease. (6) In general, Hispanic or Latino (Hispanic) and non-Hispanic Black (Black) children had higher cumulative rates of COVID-19-associated hospitalizations (16.4 and 10.5 per 100,000, respectively) than did non-Hispanic White (White) children (2.1), although it is not currently known if hospitalization is a risk factor for PASC in children. (6) Studies have also investigated the effects of the pandemic itself on the care of children with developmental disabilities, (7-10) with a recent study finding that, other than age, intellectual disability was the strongest independent risk factor for COVID-19 mortality. (11) More studies in this area are needed.

Limited guidance exists regarding the assessment and treatment of manifestations of PASC in children and adolescents. Additional challenges in the diagnosis of PASC include the overlap of psychosocial effects (e.g., social isolation, loss of routine with school and activities, fear of illness, loss of family members or friends) of the pandemic on children. (12-14) While there may be overlap with adult presentations and intervention options, pediatric management and rehabilitation of PASC have unique considerations, and adult guidance cannot be systematically transcribed to pediatrics. First, the approach to the child may differ; developmentally, some young children or those with developmental disabilities may have difficulty describing their symptoms. Pediatric histories from vested parties (parents,

caregivers, coaches, teachers) are vital, and subsequently help guide diagnosis and management. Compared to adults, children have fewer pre-existing chronic health conditions, and some conditions which may increase risk of PASC, such as type 2 diabetes, are uncommon in pediatrics. (15) Therefore, children may not require the same laboratory or radiographic tests as adults. Finally, from a psychosocial perspective, children are often previously healthy; thus, the symptoms of PASC can represent a stark departure from baseline for individuals and their families, and present with increased stress or urgency to address. With this in mind, the American Academy of Physical Medicine and Rehabilitation (AAPM&R) Multi-Disciplinary PASC Collaborative (PASC Collaborative) convened a pediatric workgroup to address the urgent need for interim assessment and treatment guidance in the care of children and adolescents with PASC. The information below is meant to assist the primary care physician and initial specialty evaluations for children and adolescents with PASC.

PASC Consensus Guidance Statement Methods

The PASC Collaborative was created, in part, to develop expert recommendations and guidance from established PASC centers with extensive experience in managing patients with PASC. The PASC Collaborative is following an iterative modified Delphi approach to achieve consensus on assessment and treatment recommendations for a series of Consensus Guidance Statements focused on the most prominent PASC symptoms. (16-18) As with other PASC Collaborative guidance statements, a detailed literature review was performed prior to initiation of the modified Delphi approach, and the full description of our methodology has been published in detail previously. (19) As the assessment and treatment recommendations for each systemic section of this specific guidance statement were developed and refined, review of emerging studies and current literature was conducted on an ongoing basis. This monitoring of the literature occurred up until finalization of the manuscript and throughout the review process to ascertain that the best available and current evidence was used. In the expansion of the PASC Collaborative to include a Pediatric Workgroup the intent was to

recognize that assessment and treatment standards differ in younger populations requiring a pediatric specialization focus.

Achieving consensus on the assessment and treatment recommendations for children and adolescents with PASC followed the same published modified Delphi approach with one adjustment to reflect the specialized expertise of the Pediatric Workgroup. The 2nd wave of voting, to ensure the completeness and evidence base of recommendations was conducted at the Workgroup level as opposed to the full PASC Collaborative level. The Pediatric Workgroup then referred their consensus-based recommendations to the full PASC Collaborative for a final consensus vote prior to finalization. The PASC Collaborative Pediatric Workgroup is comprised of approximately 30 pediatric specialists representing 8 clinics or institutions from across the United States (U.S.) with engagement from patients or caregivers to gain the patient perspective in the care process.

The Pediatric Workgroup recognizes that patients with health manifestations due to PASC typically present with a cluster of symptoms that cross multiple body systems and may overlap. The recommendations and discussion presented in this report are intended to reflect common presenting symptoms and organ system manifestations seen by pediatric specialists and those that pediatricians, family medicine practitioners and pediatric subspecialists may encounter **(Table 1).** Importantly, the recommendations provided in the Guidance Statement 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. As with any treatment plan, clinicians treating patients with PASC are encouraged to discuss the unknowns of PASC treatments and prognosis, as well as the benefits and risks of any treatment approach.

Initial Evaluation of Children and Adolescents with PASC

The primary care system is often the first point of contact for patients with PASC and may provide the bulk of therapeutic management. For patients with complex medical needs, multidisciplinary and interdisciplinary approaches are often beneficial. (20-27) multi-disciplinary clinics to treat the population with PASC first opened in the spring of 2020, and as the pandemic continued, clinics focusing on the needs of the pediatric population emerged although may not be accessible to all, (28) in which case the primary care clinician will have a larger role in coordinating the specialty evaluation(s) and care. Pre-visit symptom checklists or screening tools may help facilitate information gathering and optimize the time providers have with patients and their caregivers at the initial evaluation. (21, 27, 29-30)

Goals of the initial visit are to 1) determine symptoms and their impact on patient function; 2) assess what additional detailed evaluations may be helpful; 3) identify "red flag" symptoms that warrant urgent further testing and/or referral to subspecialists; and 4) differentiate PASC from pre-existing or new conditions that require a different therapeutic approach.

PASC is a clinical diagnosis and can be supported by positive polymerase chain reaction (PCR), antigen and/or antibody testing for SARS-CoV-2; however, negative testing may not rule out PASC for multiple reasons. Some patients with PASC will not have a positive test for SARS-CoV-2 due to lack of testing, , waning antibody levels or false-negative testing. (31,32) As pediatric SARS-CoV-2 vaccination rates increase; the role of antibody testing may decrease unless providers specifically order anti-nucleocapsid antibodies. A strong epidemiological link (e.g., SARS-CoV-2 positive close contact) or distinctive clinical features of COVID-19 (anosmia/ageusia) without an alternative diagnosis

may also be considered evidence of prior infection. The evaluation should begin with a thorough history and review of systems, followed by a comprehensive physical examination and additional studies as warranted. Key areas to focus on in an initial evaluation are summarized in Table 2. This initial evaluation can guide the need for additional assessment considerations and treatment options based on findings (Tables 3 – 11).

Systemic/Constitutional Symptoms

Fatigue is a common symptom in children with PASC with a broad differential. (20,25-27,41) Physical activity / exercise intolerance is also reported which often overlaps with symptoms of fatigue. (3,20,42) Physical inactivity is a well-documented risk to both overall physical and mental health (43); thus, it is important to help mobilize those with physical activity intolerance in a timely fashion to minimize lasting effects of decreased activity or poor exercise tolerance.

Some patients with prolonged fatigue may meet criteria for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), which is a clinical diagnosis of exclusion. ME/CFS is characterized by profound fatigue occurring for at least 6 months with significant impairment in day-to-day functioning including physical functioning, school performance, and extracurricular activities. (44) Post-exertional malaise and unrefreshing sleep are hallmarks of the disorder, and cognitive impairment, and orthostatic intolerance are also commonly co-occurring conditions. (45) The relationship between ME/CFS and SARS-CoV-2 infection is unclear at this point, but ME/CFS has been noted after other viral illnesses, most prominently primary infection with Epstein-Barr virus. (37,46) If patients with PASC

report symptoms of post-exertional malaise or "crashing" after mild physical or cognitive activity, they should be educated on "pacing" and careful attention should be made to avoid post-exertional malaise and exacerbation of symptoms; patients may benefit from referral to pediatric rehabilitation medicine. (See Appendix 1 for a link to Centers for Disease Control and Prevention resources for ME/CFS)

Recommendations for physical activity programs should be tailored to each individual patient and take into account access to exercise opportunities and equipment (i.e., gym class, recess, safe neighborhood, bicycle). There have been some suggested protocols for return to play in pediatric and adult recreational athletes following mild-to-moderate COVID (43,47) utilizing a graduated exercise approach (48); however, these types of programs may cause symptom exacerbation in those with post-exertional malaise. A more gradual approach of slowly increasing physical activity through a sub-symptom threshold exercise program similar to protocols recommended for post-concussion syndrome may be better tolerated. (49) Oversight by a physical therapist or occupational therapist (in those with more significant symptoms limiting activities of daily living) may be helpful for more specific guidance. Recommendations for physical activity including any restrictions may need to be translated to school and other settings such as sports and extracurriculars (see: Pediatric Accommodations section below).

Sleep is critical for optimal function and development across multiple body systems. Insufficient sleep may be associated with mood changes, impaired attention and

concentration, and decreased immune response. Post-COVID sleep difficulties are often reported in children. (3,50-52) It is unclear whether sleep difficulties are a manifestation of having COVID-19, related to other psychological or medical conditions, a product of increased psychosocial distress, or some combination of factors. (53).

Mental Health and Psychiatric Symptoms

Mental health concerns for individuals with PASC can be influenced by biological (direct effects of infection) and psychosocial (disrupted quality of life, isolation, loss of loved ones and routine) factors. (54) This has resulted in an increase in the prevalence of anxiety, depression, irritability, boredom, inattention and new-onset psychological symptoms in youth during the COVID-19 pandemic. (55) Many children have undergone the trauma of losing a loved one to COVID-19 and may experience symptoms of grief, exacerbating psychological and physical symptoms of PASC. Additionally, the pandemic has exacerbated difficulty with access to mental health care for many populations such as racial and ethnic minority groups and gender/sexual minority individuals. (56) One study demonstrated that children, girls, those with Hispanic ethnicity, those with public versus private insurance, and those with more significant medical comorbidity were more likely to exhibit PASC neuropsychiatric symptoms (57), although these demographic and socioeconomic factors need to be studied further. With the increase in mental health problems since the start of the pandemic it is particularly important to screen for mental health symptoms in all youth with PASC, and in particular, screen for suicidal ideation especially if there are known past attempts, past

suicidal ideation, or changes in mood. Of note, emergency room visits for suicidal ideation and attempts started increasing in early 2020 for adolescents (ages 12-17 years) in the U.S., and have sustained at higher levels, especially for adolescent females. (58)

Anxiety: Anxiety is the most common mental health concern in adults with PASC symptoms (54) and studies have supported newly emerging anxiety symptoms in youth. (55) Children with primarily social anxiety may have a recurrence of symptoms upon return to in-person school after a prolonged absence (which may be prolonged due to PASC). Therefore, school avoidance should be monitored closely. Adolescents and young adults with disabilities may have differential impacts related to anxiety during the pandemic, especially if they identify with a minoritized racial/ethnic group and should be screened and monitored closely. (59)

Depression: Depression has been documented in adult PASC and to a lesser extent in some pediatric studies, both in patients with and without premorbid depression. (60,61) These symptoms are occasionally also associated with changes in behavior which may be uncharacteristic for the youth (e.g., increased irritability, social withdrawal).

Somatic Symptom and Related Disorders (SSRD): Clinical experience suggests there may be an increase in somatization and SSRDs in some pediatric cases of PASC; however, one should not assume PASC symptoms are all related to a SSRD and thorough medical investigation into any newly emerging physical symptom is always recommended. If considering a diagnosis of a somatic symptom disorder or functional neurological symptom

disorder, it is recommended to refer and collaborate with medical subspecialties (e.g., neurology, rheumatology, pediatric rehabilitation medicine, and gastroenterology) prior to diagnosis. When the diagnosis of functional neurologic symptoms disorder or other somatic disorder is made, patients should be referred to a specialized multi-disciplinary clinic or program and/or psychology when available. (62)

Post Traumatic Syndrome Disorder (PTSD): In adult studies, 25% of patients experiencing PASC had post traumatic symptoms up to 50 days post COVID-19 infection. (63) To date, rates of PTSD for youth with PASC have not been reported. PTSD symptoms may be elevated in children with history of hospitalization, prolonged period in intensive care, or history of multiple procedures. (64). In addition, one of the unfortunate outcomes of the pandemic has been the increase in prevalence of child maltreatment. (63,65) In a small study, the amassing of COVID-19 stressors was found to be a key risk factor implicated in higher parent-perceived stress, while anxiety and depression were associated with both higher parent-perceived stress and child abuse potential. (66) This consequently increases the odds of PTSD and is critical for physicians to be vigilant for signs of PTSD and potential underlying maltreatment both in patients with and without PASC.

When mental health concerns are identified and have a negative impact on functioning or are associated with significant distress, referral for evidence-based therapy (e.g., cognitive behavioral therapy) is warranted and in some cases consideration of medication and/or referral to psychiatry may be appropriate depending on severity and resources available. Treatment of

anxiety/depression symptoms can be initiated based on symptom severity, dysfunction, and comfort level of the primary care provider. From a psychotherapy perspective, families may benefit from assistance in identifying a provider who has experience working with individuals with chronic illness and cognitive behavioral interventions, such as for chronic pain, which may also be helpful to consider for this population. (67) Families may also benefit from parent training to promote comfort for their youth or learning behavioral management strategies for young children.

{Insert Table 5. Autonomic Dysfunction/ Postural Orthostatic Tachycardia Syndrome (POTS)}

Autonomic Dysfunction/ Postural Orthostatic Tachycardia Syndrome (POTS)

Symptoms

Postural Orthostatic Tachycardia Syndrome (POTS) is a chronic disorder of the autonomic nervous system characterized by symptoms (see table 5), which are orthostatic in nature. It is a condition primarily affecting females between the ages of 12–50 years, and is commonly triggered by infection, pregnancy, fever, surgery, or trauma. (70) Symptom burden can be significant, resulting in decreased quality of life and limited ability to participate in school and/or work.

According to the *2019 NIH Expert Consensus Meeting (70)*, current diagnostic criteria for POTS include:

1. A sustained heart rate (HR) increment of at least 30 beats/minute within 10 minutes of standing (65); for individuals between 12-19 years old, the required HR increment is at least 40 beats/minute.
2. An absence of orthostatic hypotension
3. Frequent orthostatic symptoms
4. Duration of symptoms for at least 3 months
5. Absence of other conditions explaining symptoms

In addition to POTS, there are other forms of autonomic dysfunction, such as orthostatic hypotension (OH), orthostatic tachycardia (OT), and vasovagal syncope. (70) First-line treatment for POTS consists of lifestyle management (see table 5) and focuses on reducing orthostatic symptoms and improving quality of life. Exercise training with increased water and salt intake has been shown to reduce orthostatic HR and improve quality of life in some patients with POTS. (68,72) Currently, there are no FDA-approved medications for POTS although medications that increase blood volume, decrease HR, and increase vasoconstriction are often trialed. In children with orthostatic symptoms who do not meet full criteria for POTS, lifestyle management should still be discussed, and medications can be considered to help with symptom management.

While there are several case reports documenting the onset of POTS following COVID-19 infection in adults (73,74), there is very limited literature available on pediatric patients. (75,76) Common presenting symptoms of PASC, including fatigue, brain fog, and nausea, overlap with symptoms of autonomic dysfunction and POTS. (77) In addition, it is important

to screen for mental health concerns as symptoms of POTS may present similarly to somatic symptoms of anxiety and depression for which referral to mental health services may be warranted. (78)

{Insert Table 6. Neurology}

Neurological Symptoms

Cognitive Symptoms: Case reports show patient and parent-reported concerns of fatigue and attention difficulties. (27) Objective neuropsychological data generally show increased attention deficits in these patients, with relatively preserved processing speed and executive functions and elevated mood/anxiety concerns. (27) Accordingly, those working with children with PASC should consider accommodations (see Table 6 and Accommodations Section) and intervention services (e.g., behavioral therapy) to ensure these cognitive and mood difficulties do not impede the child's ability to learn in school settings or engage in the community. Where available, neuropsychological testing is recommended to assist in determining the level and types of school supports these children may benefit from and to inform therapeutic approaches. A comprehensive neuropsychological evaluation is not always needed, unless a child had preexisting developmental disabilities or neurological conditions (e.g., seizure history, stroke). A brief, targeted neuropsychological evaluation could be completed (e.g., concussion model) for most patients. (80,81) Delaying a cognitive assessment until symptoms severely impair function increases the risk for additional comorbidities and prolongs recovery. (82-84)

Headaches: Headaches are common in children with PASC. (5,20,27,85,86) Recommendations for headache evaluation and management are in line with pediatric headache guidelines from the American Academy of Neurology and American Headache Society. (87) Abnormal neurological examination or a history concerning for central nervous system disease warrants prompt neuroimaging.

A primary headache type (e.g., migraine, tension) in patients with PASC has not yet been identified and some patients describe multiple "headache types." Orthostatic headaches are common in children with POTS (Table 5). The mainstay of treatment remains counseling and education for patients and families on behavioral and lifestyle factors that may influence headache frequency. (87,88) Clinicians should consider headaches as potentially multifactorial in children with PASC and may require a multifaceted approach beyond directly targeting headache treatment alone.

Providers may wish to consider treatment with a daily preventative medication to decrease headache frequency, severity, or headache related disability. Since many patients with PASC experience a constellation of symptoms (86), choice of treatment may be guided by comorbidity. Daily preventative treatments commonly used for headaches, might exacerbate other PASC symptoms. For example, a side effect of topiramate includes cognitive slowing which might worsen a patient's brain fog symptoms. Medications such as amitriptyline, which some providers use in treatment of post-concussive, tension headaches, and neuropathic pain (89,90), might worsen orthostatic intolerance in a child with PASC. However, in children with gastrointestinal or other body pain, amitriptyline can potentially treat both headaches and

other possible nerve related pain symptoms. Other preventive headache medications like propranolol for POTS, cyproheptadine for sleep disruption, abdominal pain, and appetite stimulation, or duloxetine for anxiety may be useful for headaches when these comorbid conditions are prominent. When starting a daily preventative medication for headaches it is important to start at low doses, be mindful of side effects, and individualize treatment based on comorbid symptoms.

{Insert Table 7. Respiratory/Pulmonary}

Respiratory/Pulmonary Symptoms

In children and adolescents with PASC, respiratory symptoms are commonly reported. (92,93) Pre-existing asthma has been found to be associated with a higher risk of PASC (92). Pulmonary evaluation of patients with PASC and persistent pulmonary symptoms should include, at minimum, pulse oximetry, chest x-ray (CXR) and spirometry, with a low threshold to refer to a pulmonologist where available. Some studies have indicated lung function tests are most often normal in children with PASC, (93) while others indicate more than 50% of children had mild imaging and spirometric abnormalities. (26). In patients with dyspnea, evaluation for exercise induced hypoxemia or intolerance (e.g., 6-minute walk test or one minute sit to stand test) is beneficial. (91) Additional tests may be indicated if symptoms persist, there are abnormal findings on lung exam, or an abnormal initial work-up.

Functional respiratory disorders should also be considered such as hyperventilation or sighing dyspnea, especially in the setting of anxiety. Inducible laryngeal obstruction (ILO), also

referred to as paradoxical vocal fold movement (PVFM), should also be considered when the history is specific for intermittent dyspnea, particularly symptoms of tightness in the throat and inability to get air in that does not respond to bronchodilators. Less common manifestations may include bronchiectasis/post-infectious scarring, pulmonary fibrosis (likely more common in patients who had a more severe initial illness), or in very rare instances, disorders such as post-infectious bronchiolitis obliterans (PIBO) that can also occur following other viruses. Immunosuppressed children (whether due to a primary immunodeficiency or secondary to medication) may be at higher risk for developing post-acute damage to their lungs.

Patients with hypoxemia should be treated with supplemental oxygen, but the majority of pediatric patients with PASC will have normal pulmonary imaging and pulmonary tests. Deep breathing exercises and humming to strengthen diaphragmic function have been recommended for adults with pulmonary symptoms post COVID and may be beneficial for children as well. (Refer to Appendix 1: Appendix 1: Additional Resources for the Assessment and Treatment of PASC in Children and Adolescents) Referral to a speech therapist with respiratory expertise to help with dyspnea has been recommended by some and is the recommended and effective treatment for ILO/PVFM (23). In general, the majority of patients without lung function or imaging abnormalities have resolution of symptoms over time.

{Insert Table 8. Cardiology}

Cardiac Symptoms

Cardiac symptoms reported in patients with PASC include chest pain, exercise intolerance, palpitations, and dizziness. (5,25-27,42,94-96) Cardiovascular disease, including myocarditis, pericarditis, heart failure and arrhythmias, may occur in children during and after COVID-19 infection, however, they are very uncommon in children with PASC. However, given the high stakes of missing a diagnosis, these diagnoses should be excluded in children with PASC. A consultation with a pediatric cardiologist may be warranted when chest pain, exercise intolerance, palpitations, and/or dizziness are judged to be of possible cardiac origin. Cardiac testing (i.e., EKG, Echocardiogram) should be interpreted by providers adept at pediatric interpretation and location of such testing will vary based on local availability.

Cardiac chest pain is rare in PASC and needs to be differentiated from chest pain from musculoskeletal and respiratory origins. Importantly, providers need to be sure that chest pain is not from complications of acute COVID-19 infection or a manifestation of MIS-C where there may be true cardiac pathology. Signs that raise concern include chest pain with exercise, radiation of the pain to the neck, jaw, or down the arms, and/or chest pain accompanied by dizziness and/or loss of consciousness. Musculoskeletal chest pain is diagnosed by reproducible tenderness on palpation, as in costochondritis. Respiratory chest pain is often accompanied or preceded by cough, wheezing and dyspnea.

Although palpitations are described as a symptom in children with PASC, documented arrhythmias are rare. (97) Sinus tachycardia associated with autonomic dysfunction (see Table 5), respiratory disease and acute illness should be differentiated from truly abnormal cardiac rhythms by EKG or other monitoring technology.

{Insert Table 9. Otolaryngology}

Otolaryngology Symptoms

COVID-19 infections can cause a range of smell and taste disturbances that last beyond the acute viral infection. Loss of smell (LOS) related to COVID-19 infections is generally not associated with concurrent nasal symptoms, such as congestion, obstruction, rhinorrhea or discharge. (98-100) Instead, COVID-19-related LOS is hypothesized to be a sensorineural deficit resulting from local damage by inflammatory mediators to the olfactory bulb. (101) Taste function is closely associated with smell; therefore, inflammation of chemoreceptors for smell can result in both LOS and loss of taste (LOT). (99) The presence of concurrent sinonasal symptoms should prompt further evaluation for other causes of smell disturbance.

Following history and physical examination, smell testing may be performed. Subjective smell testing involves patient-reported outcome measures (PROMs), like the Sinonasal Outcome Test (SNOT-22) or Questionnaire of Olfactory Disorders (QOD). However, objective testing is more sensitive for detection of smell disturbance than subjective testing and should be the test of choice if available. (102,103) Imaging is not typically performed for isolated loss of smell. (100) For patients with additional sinonasal symptoms and smell loss greater than 6 weeks, an MRI brain with contrast or maxillofacial CT without contrast may be performed. Maxillofacial CT should be the first study of choice if nasal endoscopy suggests chronic rhinosinusitis or a unilateral suspicious lesion. (100,104) An MRI brain with contrast should also be considered in all patients with loss of smell greater than 6 weeks with

additional neurologic symptoms. (100)

As most pediatric COVID-related loss of smell self-resolves, observation is a reasonable first strategy. (98,103) A recent study of 79 pediatric patients with COVID-related hyposmia found that on subjective smell testing, 71% recovered smell within 10 days after onset of symptoms, and 100% recovered within 6 months. (103) Despite the high rate of self-recovery, most authors still advocate for smell training to start 2 weeks after resolution of acute viral illness to improve the chances of recovery. (100) Olfactory training consists of smelling four scents (e.g., essential oils) for 20 seconds each twice daily, with introduction of new fragrances every 3 to 4 months. While unpleasant, the onset of parosmia and phantosmia may indicate the start of recovery of smell. (99) There is limited consensus on the medical treatment of COVID-related smell disturbance. The British Rhinological Society Consensus statement recommends intranasal steroids for loss of smell only if associated with nasal symptoms. A course of oral steroids may be considered for LOS after complete resolution of COVID-19 symptoms for isolated LOS>2 weeks. (100) There is insufficient literature to support the use of alpha-lipoic acid, vitamin A drops; Omega-3 supplements are optional. (100) Treatment of dysgeusia linked to LOS from COVID-19 is essentially the same as outlined for LOS. Patients may benefit from eating bland foods at room temperature, avoiding triggers such as eating fragrant or hot foods, opening refrigerator doors or trips to the market or from joining support groups for anosmia and dysgeusia.

{Insert Table 10. Musculoskeletal}

Musculoskeletal Symptoms

There is variable report of myalgias or arthralgias as a consequence of PASC in children and adolescents ranging from 1 to 61%. (3,5,25,26) All patients should have a motor and sensory exam performed with consideration of specialized joint testing if needed. Evidence of joint inflammation without inciting injury should prompt further rheumatologic workup. (106) Mechanisms for pain in PASC are unclear, but some data suggest consistencies with fibromyalgia. For example, a study of 616 adults surveyed three months after diagnosis of acute COVID-19, found that 30.7% met American College of Rheumatology Criteria for fibromyalgia. (107) Juvenile fibromyalgia is characterized by chronic widespread pain and associated symptoms of fatigue, nonrestorative sleep, cognitive symptoms, headaches, abdominal pain, and depressed mood. (108,109) The associated symptoms in fibromyalgia share several overlapping characteristics with ME/CFS as well.

Conservative approaches for pain management should be trialed first (e.g., topical analgesics for localized pain). Therapeutic exercise under the supervision of a physical therapist as well as cognitive behavioral therapy for pain coping and mindfulness skills are the mainstays of treatment. (105) If conservative measures fail and patients are interested in a trial of medications, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, anticonvulsants (gabapentin or pregabalin) and low dose tricyclic antidepressants, can be considered. (105) These medications may also help with mood disorders, sleep difficulties, and headaches and should be considered in those with comorbid symptoms. (105)

There are few studies evaluating weakness as a presenting symptom of PASC in children. (42) True weakness, as opposed to exercise intolerance or fatigue/malaise, must be determined via careful physical examination by the clinician. If patients present with focal weakness or proximal versus distal weakness, this may suggest an underlying neurologic or neuromuscular condition for which additional workup and referral to subspecialists are recommended. Otherwise, weakness may be managed as exercise intolerance, deconditioning or fatigue/malaise, utilizing rehabilitation approaches described above.

{Insert Table 11. Gastrointestinal}

Gastrointestinal Symptoms

The pathogenesis of gastrointestinal (GI) involvement in PASC is unknown but it is postulated in adults that immune activation leading to inflammatory cell recruitment in the intestinal epithelium. Commonly reported GI symptoms in PASC include abdominal pain, diarrhea, nausea, vomiting, and loss of appetite. GI manifestations, such as chronic diarrhea and nausea, have been reported to last for 2-3 months after recovering from the initial illness. In addition, the presence of abdominal pain, nausea, and vomiting do not seem to be associated with disease severity. (110,111) Management of GI symptoms is dependent on the symptoms and are detailed in the table above.

Return to Play or Activity in Children and Adolescents

Return to play guidance in the context of PASC follows the American Academy of Pediatrics (AAP) and American College of Cardiology (ACC) published guidelines for children post-COVID infection and are differentiated based on initial infection presentation and/or ongoing symptoms. (47, 112, 113) Children with PASC should increase activity slowly after being screened with a gradual return to play. Any difficulties with a child's a return to play require re-evaluation of triggers and symptoms with potential modification of the return to play plan. (47, 112, 113)

Accommodations for Schools and Activities

It is clear that significant long-term physical, cognitive, social and emotional limitations due to PASC in school aged children can disrupt child and family quality of life. Reasonable accommodations for children related to school, sports, and other extracurricular activities may need to be made in order to support a return to activity routine. Accommodations should be tailored to each child based on specific symptoms including physical fatigue, post-exertional malaise, cognitive symptoms/brain fog, and any other symptoms exacerbated by activity. School accommodations may be warranted with a goal of reducing support as symptoms improve (e.g., extra time to walk between classes, use of elevator instead of stairs, increased test taking time, limiting homework assignments, scheduled rest breaks, reduced after school activities). Evaluations by physical therapists or neuropsychology testing can provide input unique to each child's circumstance.

For many children and adolescents, early recognition and treatment of symptoms and supporting return to school and other activities is essential to overall recovery. Identification of family stressors (e.g., financial, housing, un/employment, safety, social isolation and/or other major concerns of living) and availability of support systems may be helpful to provide emotional and logistical support and tailor medical therapies.

Vaccinations in Children

Vaccination remains an important tool in preventing and mitigating acute COVID-19 infection, and a history of PASC is not a contraindication to future vaccination or boosters. (114, 115) PASC should not delay other routine childhood vaccinations unless individual circumstances warrant discussion with their provider.

Conclusions

PASC in children and adolescents is increasing in recognition. Some children may only have one or two symptoms of PASC, whereas others may have a constellation of symptoms. (86) Research is ongoing to better understand the pathogenesis behind PASC in both children and adults and optimal treatment approaches. Guidance regarding the evaluation and treatment of PASC in children and adolescents may change as further research is done to provide evidence-based recommendations, including the NIH Recover trial. (116, 117)

It is important to note that not all the symptoms regarding PASC may be attributed to SARS-CoV-2 alone as recent studies have reported a high prevalence of symptoms similar to PASC in children who serve as healthy negative controls. This speaks to the impact of the pandemic as a co-contributor to some symptoms. (3,4,118) Finally, given the demonstrated variability in

COVID-19 outcomes secondary to social inequalities in health, researchers and clinicians must remain vigilant and address pediatric PASC in the context of preserving health equity, noting that particular vulnerable groups and populations may be disproportionately affected by the effects of the pandemic and systemic barriers to optimal health. (119)

Health Equity Statement

The American Academy of Physical Medicine and Rehabilitation (AAPM&R) recognizes the need to support equitable access to rehabilitation care for individuals with Post-Acute Sequelae of SARS CoV-2 infection (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 United States 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. (120)

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 (CDC) 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. (121) The Centers for Medicare and Medicaid Services (CMS) 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." (122) There are many root causes for health disparities, some of which fall under the categories within social determinants of health (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" which 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). (123) 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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Tables

Table 1: Common PASC Symptoms in Children and Adolescents by System (3,20,21)

Systemic/Constitutional (Table 3)	Fatigue (generalized, exercise intolerance or post-exertional malaise) Sleep disturbances Fever
Mental Health and Psychiatric (Table 4)	Anxiety Depression / Low mood Increased somatic symptoms unexplained by systemic findings School avoidance Regression of academic or social milestones
Autonomic Dysfunction (Table 5)	Dizziness / Lightheadedness Orthostatic Intolerance Headache Nausea Syncope or pre-syncope
Neurological (Table 6)	Headache Tremulousness Paresthesias or numbness Dizziness and vertigo Difficulty with attention/concentration Difficulty with memory Cognitive fatigue or "brain fog"
Respiratory/Pulmonary (Table 7)	Shortness of breath or dyspnea Chest (thoracic) pain or tightness Cough Difficulty with activity/exercise intolerance
Cardiology (Table 8)	Palpitations or tachycardia Dizziness / Lightheadedness Syncope Chest pain Difficulty with activity/exercise intolerance
Otolaryngology (Table 9)	Abnormal (or no) smell or taste
Musculoskeletal (Table 10)	Weakness Muscle, bone, or joint pain
Gastrointestinal (Table 11)	Nausea/vomiting/reflux Abdominal pain Bowel irregularities (constipation / diarrhea) Weight loss Lack of appetite

Note: Additional organ systems may be involved; this paper covers the most predominant symptoms seen by PASC Clinics serving children and adolescents. The PASC Collaborative has published a number of Consensus Guidance Statements for the adult populations; please see Appendix 1for a list of available publications and links.

Malone Laura A (Orcid ID: 0000-0002-9836-822X)
Fleming Talya Kianti (Orcid ID: 0000-0002-2034-8253)
Kokorelis Christina (Orcid ID: 0000-0001-6486-4391)
Ng Rowena (Orcid ID: 0000-0001-7193-4300)
Sampsel Sarah Lyn (Orcid ID: 0000-0002-7496-8482)
Arduzco-Gutierrez Monica (Orcid ID: 0000-0003-0964-5908)

Table 2: Initial Assessment of PASC in Children and Adolescents

Part I: Review of history

I. *Post-acute sequelae of SARS-CoV-2 infection (PASC:)* refers to the sequelae of complications that occur after initial infection. There is no conclusive definition for PASC and varying opinions from experts and leading health organizations about the duration of symptoms to confirm diagnosis, which typically ranges from 4 to 12 weeks after the acute infection. Common symptoms include fatigue, headaches, palpitations, dizziness, and shortness of breath (**Table 1**). It is important to exclude other diagnoses that may present similar to PASC). (33)

II. *Description of the acute SARS-CoV-2 infection or "inciting event"*

- The majority of children with acute SARS CoV-2 infection are asymptomatic or present with mild symptoms. Other children may be hospitalized or develop MIS-C. (34-36) Understanding the initial illness may help to identify end organ damage contributing to persistent symptoms.

III. *Characterize pertinent PASC symptoms* (1,20,25,34)

- Presentation, duration, pattern, frequency, triggers and interventions or behaviors that lead to improvement or worsening should be noted for each symptom. Past treatments and responses should be detailed. (2)
- Factors that limit activity or result in fatigue should be noted, with attention to nutrition, sleep, exercise, and mental health. (2,27) Refer to Tables 3-11 for further guidance on assessment parameters.
    - Assess symptom patterns throughout the child's normal day to guide activity recommendations. Note: with post exertional malaise, symptoms may worsen 12-48 hours after activity. Evaluate for conditions that may exacerbate symptoms and warrant further testing and subspecialty referral.

IV. *Assess for level of functional activity limitations*

- Assess the current level of function compared to baseline, including the impact on physical activity and mobility, activities of daily living, school performance, work tolerance, sports, and avocations (i.e., hobbies and leisure activities).

V. *Past medical, surgical, family and social history*

- Review the *past medical history*. Specific attention should be placed on pre-existing conditions including mental and behavioral health, (2,35) surgeries or hospitalizations, and vaccination status including for SARS-CoV-2.

- Specific comorbidities that may be associated with PASC (36) include: attention issues, learning disabilities or difficulties, sleep disturbances, mood disorders, or prior pain syndromes.

- A *family medical history* should be obtained and should include identification of any other family members with PASC, autoimmune/inflammatory disorders, genetic conditions, attention issues, and anxiety/depression.

- A *social history* should include a review of school attendance and performance, extracurricular activities, family structure, and support networks. Identification of family stressors (e.g., financial, food and housing insecurity, un/employment, safety, social isolation and/or other major concerns of living) and availability of support systems may be helpful in order to provide emotional and logistical support and tailor medical therapies. (2)

VI. *A review of current medications, supplements and allergies* should be performed.

VII. *Vitals:* A basic set of vitals should be obtained, including temperature, blood pressure, oxygen saturation at rest, respiratory rate, heart rate, weight and height. If the patient endorses dizziness or lightheadedness, consider orthostatic vitals. (2)

VIII. *Physical examination:*

- A comprehensive physical should be performed. The findings may be normal.

- Additional components of the physical exam may be needed based on presenting symptoms (**Tables 3-11**).

VI. *Assessment:*

- Clinicians should incorporate history, prior laboratory or microbiological testing, and physical exam findings in making a diagnosis of PASC.

  - If there is diagnostic uncertainty because of lack of confirmed SARS-CoV-2 infection, or the patient's history and physical are consistent with another post-acute viral/infectious syndrome, these recommendations may still be helpful.

  - Based on presenting symptoms or duration, other clinical syndromes, such as myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) (37) or postural orthostatic tachycardia syndrome (POTS) may also be diagnosed. (38)

- Concerning symptoms and signs ("red flags") should be addressed and may require additional targeted evaluation prior to further therapies or management strategies related to PASC.

  - These include but are not limited to: prolonged fevers (100.4F or greater) for greater than 10 days; significant weight loss; vomiting or headaches at night or early morning; developmental regression, focal weakness or sensory changes; syncope; chronic cough.

  - Physical examination red flags include focal neurologic deficits, extra-cervical or enlarging lymphadenopathy (nodes > 2 cm), hepatosplenomegaly, joint swelling/redness, or cardiac murmurs.

- Labs/Radiology (2)

  - Laboratory values may be normal. Labs done within a reasonable time frame (e.g., 6 months), may not need to be repeated.

- Targeted testing may be considered if lab tests have not been performed. Please see **Tables 3-11** for specific guidance on testing based on symptom presentation.

VI. *Follow-up plan and referrals - Follow symptom-based treatment strategies as outlined in the specific sections that follow (Tables 3-11).*

- Structured care coordination by the primary care clinician or pediatric PASC clinic benefits many patients with PASC, especially those who experience barriers to navigating the healthcare system.
- Consider referral to subspecialists if patients do not respond to initial treatment or for complex or severe presentations. (16,23)
- Some patients may have significant or refractory symptoms that impact function necessitating inpatient evaluation or inpatient rehabilitation.
- Close clinical follow up to ensure continued and steady recovery as clinically indicated.

Table 3. Systemic/Constitutional

Fatigue and Physical Activity/Exercise Intolerance symptoms may include: tiredness, exhaustion, feeling worn out, subjective weakness, difficulty with physical activity, deconditioning

Patient History & Symptom Assessment:

- Screen for baseline physical activity level prior to initial COVID-19 infection
- Characterize fatigue pattern and sleep habits
- Evaluate for post-exertional malaise (worsened symptoms 12-48 hours after mild physical or cognitive exertion)
- Assess for degree of exercise intolerance (EI) with the modified pediatric Borg or the OMNI Rating of Perceived Exertion scales (39) (i.e., occurs while performing activity of daily living (ADLs), during minimal, moderate, or maximal physical exertion)
- Assess nutritional status including change in dietary habits or weight loss
- Review medication list including vitamins/supplements that could be contributing to fatigue
- Screen for substance use in age-appropriate populations
- Screen for other medical causes of fatigue and EI including autonomic dysfunction/postural orthostatic tachycardia syndrome (POTS), cardiology, respiratory/pulmonary, neurology, musculoskeletal pain, and mood concerns (see Tables 4-10 for further details)

Evaluation:

- Full physical exam including thorough neuromuscular exam and provocative musculoskeletal tests specific to any areas of pain
- Consider orthostatic vital signs/standing test if experiencing lightheadedness/ dizziness (See Autonomic Dysfunction/POTS section (Table 5) for more information)
- Consider formal testing of physical functioning and endurance (examples include 6-minute walk test (40), 30 second sit to stand test if feasible)
- Bloodwork: CBC, CMP, TSH/free T4, iron panel, ferritin, vitamin D
- Consider magnesium , Vitamin B12, ESR/C-Reactive Protein(CRP), celiac screening based on additional symptoms.
- If fatigue/exercise intolerance is associated with additional cardiopulmonary symptom (see Tables 7 & 8 for further details), consider B-type natriuretic peptide (BNP), Electrocardiogram (ECG), Echocardiogram, cardiopulmonary exercise stress test, pre/post exercise pulmonary function test, chest X-Ray (CXR)

Refer to Tables 4-10 for additional testing recommendations if concerned for co-morbid conditions contributing to fatigue or EI

Interventions/Considerations:

Medications:

- Treat any known medical causes of fatigue or EI based on screening results (e.g., iron supplementation for anemia, pain medication or modalities for musculoskeletal-related pain)

Lifestyle Modifications:

- Optimize nutrition, hydration, sleep

Physical activity:

- Recommend slowly advancing physical activity/exercise as tolerated with a focus on pacing and avoiding symptom exacerbation and post-exertional malaise.
- Activity and exercise programs should be individualized with a gradual return to baseline level of physical activity if possible. Oversight from a physical therapist is often beneficial.

Additional considerations:

- Multidisciplinary approach may be beneficial including rehabilitation
- Educational accommodations may be needed if symptoms interfere with school participation (e.g., rest breaks, reduced attendance/participating in non-essential classes)
- For more information regarding cognitive fatigue, see Table 6: Neurology: Cognitive Symptoms

When to Refer and to Whom:

- Pediatric Rehabilitation Medicine (PRM) for overall management and rehabilitation recommendations
  Physical therapy for oversight of individualized activity/exercise program with focus on pacing. Additional goals include improving range of motion, strengthening, endurance, mobility and safe ambulation. If tolerated, advance to higher levels of resistance training and aerobic exercise.
- Occupational therapy for those with EI with ADLs or minimal exertion to focus on an individualized plan for facilitating modified ADLS
  Complementary therapies such as acupuncture, yoga, Tai Chi, massage, meditation as adjunct to traditional treatments/therapies
- Mental health specialist for strategies to cope with physical symptoms and/or if any concerns for comorbid mood conditions
  Other subspecialists if concerns for cardiac, pulmonary, neuromuscular, or rheumatologic cause of fatigue or EI

Sleep difficulty symptoms may include: insomnia (difficulty falling asleep, sleep deprivation), difficulty with sleep maintenance, sleep events (e.g., restless leg syndrome, sleep apnea), hypersomnia (excessive daytime sleepiness)

Patient History & Symptom Assessment:

- Evaluate for any medications or other substances that may interfere with sleep
- Ask patients/caregivers to log sleep as part of a sleep diary for review

Evaluation:

- Consider thyroid studies, ferritin level (also part of fatigue panel above)
- Polysomnography (PSG) to evaluate for any evidence of sleep apnea if morning headaches, snoring, frequent nighttime awakenings or if concerned for sleep-related movement disorder
  Actigraphy if concerned about total sleep time and diary not able to be completed. If formal actigraphy is not readily available, consider utilizing a smart watch or wristband for activity tracking.

Interventions/Considerations:

Behavioral sleep interventions:

- Promote sleep hygiene and consistent sleep schedule (see Appendix 1 for additional resources)
- Limit screen time for 30-60 minutes prior to bedtime

Medications:

- If behavioral interventions fail, consider use of medications such as melatonin to reset circadian rhythm
- If treating comorbid conditions (i.e., headaches, mood disorders), consider agents that may also help with sleep

When to Refer and to Whom:

-Psychology or therapist for cognitive behavioral therapy for insomnia (CBTI) if behavioral interventions are not sufficient and/or to treat comorbid mental health concern (anxiety, depression).
-Sleep medicine specialist if abnormalities on PSG or concern for sleep disorder.

Table 4. Mental Health and Psychiatric Symptoms

Patient History & Symptom Assessment:

- Review of medical comorbidities, any prior mental health concerns/events/diagnoses, relevant hospitalization, treatment plans, and timeline of symptom evolution to include the following:
  - Pre-morbid or new mental health symptoms and the current status (e.g., stable, worsening);
  - New or worsening physical health symptoms impacting mental health;
  - Experience with past treatment/interventions including patient directed resolution attempts – what has been tried, what has helped, what has exacerbated physical or mental symptoms (e.g., food, supplements, environment, activity, external stressors);
  - Screening for medical conditions that may mimic mood disorders (e.g., palpitations associated with anxiety may be due to POTS or arrhythmia)
  - Family History to include mental and behavioral health diagnoses; and treatment (medications, psychotherapy);
  - Medication history – Evaluate for medications that may impact symptoms, signs, or assessment parameters (i.e., medications with anti-arrhythmic, diuretic, or cognitive impact); and,
  - Consideration of additional collateral history. This may include collection of information from patient's family and/or care team/primary care as available.

The following sections include examples of screening/assessment scales to consider for mental health diagnosis, initial treatment approaches and any special considerations for the most common mental health and neuropsychiatric symptoms in children with PASC. (Links to examples of screening/assessment scales are included in Appendix 1.) If a child psychiatry access program exists in the state, consultants can be contacted for more detailed treatment planning.

Anxiety	**Evaluation/Scales to consider:** o Generalized Anxiety Disorder Scale (GAD-7): (ages 12+ years): brief screening scale which indicates severity o PROMIS© Pediatric Item Bank v2.0 – Anxiety (ages 5-17 years): brief screening scale which can be converted to T-scores to indicate severity o Screen for Child Anxiety Related Emotional Disorders (SCARED): scale (ages 8-18 years): detailed screening scale which helps distinguish the type of anxiety symptoms
	Interventions/Considerations: • Consider referral to psychotherapy if significant dysfunction in daily life and supported by mild to moderate score on anxiety scales. • Consider trial of a selective serotonin reuptake inhibitor (SSRI) if significant dysfunction in daily life supported by moderate to severe score on anxiety scales. • Given the scarcity of FDA approved medications in youth, it is recommended to discuss FDA approval or lack thereof with guardians.
	When to Refer and to Whom: • Therapy referral for evidence-based therapies (e.g., cognitive behavioral therapy, exposure/response prevention if appropriate) • Child psychiatry referral if symptoms do not improve after 2 SSRI trials or if complicated with other psychiatric diagnoses.
Depression	**Evaluation/Scales to consider:** o Patient Health Questionnaire-9 (PHQ-9) scale* o PROMIS© Pediatric Item Bank v2.0 – Depressive Symptoms (ages 5-17 years): brief screening scale which can be converted to T-scores to indicate severity o Center for Epidemiological Studies Depression Scale for Children (CES-DC) scale *Note: the PHQ-9 contains a suicidality question; clinicians should be prepared with a plan if score is positive.

	Interventions/Considerations: • Significant dysfunction in daily life and supported by mild to moderate score on depression scales, consider therapy referral. • Significant dysfunction in daily life supported by moderate to severe score on depression scales, consider trial of SSRI • Given the scarcity of FDA approved medications in youth, it is recommended to discuss FDA approval or lack thereof with guardians.
	When to Refer and to Whom: • Therapy referral for evidence-based intervention [e.g., behavioral activation, cognitive behavioral therapy (CBT)]. • Consider referral to psychiatry if there is failure to improve after 2 SSRI trials or complicated with other diagnoses.
Suicidality	**Evaluation/Scales to consider:** o Patient Health Questionnaire-9 (PHQ-9) scale o Ask Suicide-Screening Questions (ASQ) questionnaire
	Interventions/Considerations: • Consult with mental health provider
	When to Refer and to Whom: • Urgent consultation with mental health (either within clinic through social worker or psychologist when available) • Refer to emergency room, crisis intervention services, or inpatient psychiatric unit for evaluation of acute suicidal ideation with imminent risk of harm to self. • Safety planning • Consider higher level of outpatient care (e.g., Outpatient Program/ Partial Hospital Program) based on acuity and risk level.
Post traumatic symptoms/ acute stress disorder	**Evaluation/Scales to consider:** o UCLA Posttraumatic stress disorder (PTSD) Assessment Tool o Clinician-Administered PTSD Scale for DSM-5 - Child/Adolescent Version (CAPS-CA-5)
	Interventions/Considerations: • Investigate for possible traumatic events including trauma symptoms following hospital admission or medical procedures. • Assess for child maltreatment (physical, emotional, or sexual abuse and neglect).
	When to Refer and to Whom: • Refer to evidence-based intervention - trauma-focused CBT (TF-CBT) • Consider referral to psychiatry if concerned if patient meets criteria for PTSD • Report any suspicion for abuse to child protective services.
School avoidance	**Evaluation/Scales to Consider:** o Vanderbilt attention deficit hyperactivity disorder (ADHD) Diagnostic Rating Scale (VADRS) can be used if ADHD is suspected o Assess level of support at school and presence of section 504/ individualized education program (IEP) plan o Assess for anxiety, depression, attention or learning issues o Obtain feedback from school (counselor, teachers, support staff, nurses).
	Interventions/Considerations:

	• Communicate with the school on establishing support for the child which may increase the likelihood of a successful school re-integration. Support accommodations at school in favor of ongoing attendance, even if initially partial attendance. Educational goals may need to be modified. • Consider inclusion of academic, social, and/or physical comfort measures as well as executive functioning and cognitive endurance measures in the plan
	When to Refer and to Whom: • Refer to therapy for additional assessment of school support measures and school avoidance behaviors • Neuropsychological testing may be helpful in assessing the level of cognitive/executive functioning deficit • Academic testing can be discussed with the school when there is a concern for learning difficulties and poor academic performance leading to avoidance. • Referral to child psychiatry if comorbid anxiety, depression, ADHD, somatic symptom disorder • Consider referral to a higher level of care such as a partial hospitalization program or inpatient admission if function is highly impacted.

Table 5. Autonomic Dysfunction/ Postural Orthostatic Tachycardia Syndrome (POTS)

Autonomic Dysfunction & Postural Orthostatic Tachycardia Syndrome symptoms may include: Fatigue, Lightheadedness/ dizziness in upright positions, Brain fog, Exercise intolerance, Post-exertional malaise, Headaches, Gastrointestinal symptoms, Heart racing, Palpitations, Heat intolerance, Hyperhydrosis

Patient History & Symptom Assessment:

- Assess whether symptoms were present prior to COVID-19 infection or are new
- Ask about family history of similar symptoms
- Screen for hypermobility as Ehlers Danlos Syndrome (EDS) is a common comorbidity
- Screen for sleep concerns (see systemic section for more details: Table 3)
- Screen for mood concerns (see mental health and psychiatric symptoms section for more details: Table 4)

Evaluation:

- Obtain vital signs including orthostatic vital signs (if unable to perform standing test in clinic or refer for tilt table testing). Consider assessing joint hypermobility with Beighton score
- Bloodwork: (CBC, CMP, ferritin, vitamin D, vitamin B12, ESR, CRP, TSH) to rule out other medical conditions
- Ten-minute passive standing test (68) can be performed in clinic or send for tilt table test to confirm diagnosis (see diagnostic criteria in discussion section) (See Appendix 1 for standing test resource)
- Echocardiogram if concern for EDS

Interventions/Considerations:

Lifestyle Modifications:

- Hydration (e.g., 2-3 liters of non-caffeinated fluid per day for a 40kg patient)
- Salt intake (4-6 grams per day)
- Physical activity with pacing (69)
  - Start with recumbent activity and progress to more upright positions as tolerated. Avoid exacerbating symptoms or triggering post-exertional malaise by slowly progressing time/intensity.
- Compression garments (20-30 mmHg)
- Elevate head of bed 4-6 inches
- Physical countermeasure maneuvers such as crossing legs, tensing muscles (See Appendix 1 for additional resources)

Medications:

- Consider the following first line medications if symptoms persist despite lifestyle modifications:
  - Beta blocker (such as atenolol or propranolol) to lower heart rate
  - Fludrocortisone to expand blood volume
  - Midodrine to increase vasoconstriction

Additional Considerations:

- Overlap with somatic symptoms in mental health (see discussion section)
- School accommodations related to physical activity or academics may be needed (i.e., extended time for tests and assignments, allowing hydration/salty snacks throughout the day, small breaks to reduce brain fog, avoiding prolonged sitting or standing)

When to Refer and to Whom:

- Physical therapy to supervise physical activity program
- Autonomic/POTS specialist if lifestyle interventions and first line medications are not enough
  Cardiology if palpitations/chest pain are the primary symptoms and cardiac workup has not already been completed
- Mental health specialist if needed (see additional guidance in mental health section)
- Genetics if concerned for EDS
  - joint hypermobility

  PLUS
  - abnormal echocardiogram
  - strong family history
  - skin involvement (bruising, poor wound healing, stretching)

Table 6. Neurology

Cognitive Symptoms in Children/Adolescents with PASC may include: attention difficulties, memory problems, word finding difficulties, trouble concentrating, "brain fog", declining school performance

Patient History & Symptom Assessment:

- Screen for and track cognitive function using validated tools when possible:
  - Changes to cognition (e.g., Patient-Reported Outcomes Measurement Information System (PROMIS) Parent Proxy Short forms. (77)
  - Increased academic difficulties or declining school grades
  - Observable changes in the home and community settings or functional decline (e.g., WHO Case Report Functional subsection)
  - ADHD symptoms (e.g., VADRS)

Anxiety and mood symptoms (e.g., PHQ-9, GAD-7, and pediatric symptom checklist). See mental health and psychiatry symptoms section for further details.

Evaluation:

- Conduct a full and thorough neurological examination
- Evaluate for conditions that may exacerbate cognitive symptoms and warrant further testing/referral. Particular areas include:
  - Sleep
  - Fatigue
  - Endocrine
  - Autoimmune
  - Mental health stressor/disorder
  - Psychosocial stressors (e.g., home, school, community)

  Obtain a comprehensive medication and supplement review
- Validate patient history through the collection of collateral history including pre-existing function and conditions, from care team/primary care, patient family or care partner, educators, or close contact as available

Additional Workup:

- Obtain a brain MRI if history or exam concerning for developmental regression or focal neurological deficits

Interventions/Considerations:

Treat, in collaboration with appropriate specialists, co-morbid medical conditions

- Examples include: pain, insomnia/sleep disorders (including poor sleep hygiene), mood disorders

- Complete medication polypharmacy reduction, weaning or discontinuing medications if medically feasible with emphasis on medications that may impact cognition.

Recommend important lifestyle modifications such as regular sleep, regular meals, good hydration, and stress management

- For patients who are able, regular exercise (at least 2-3 times/week of aerobic exercise) may be effective
- Frequently assess the impact of return to daily activities (including school, work, driving, social events) to ensure that symptoms do not flare and exercise is tolerated

School accommodations may be warranted with a goal of reducing support as symptoms improve (e.g., extra test taking time, notes in advance, decreased assignments, cognitive breaks during class time/school hours, reduced after school activities). These school accommodations may be tailored or modified following formal neuropsychological testing when needed.

When to Refer and to Whom:

- Brief/targeted neuropsychological evaluation if:
  - Significant change in cognitive status (e.g., increased or emergent concerns on screening inventories (e.g., PROMIS) based on clinical judgement)
    OR
  - Accommodations and/or compensatory strategies are still needed after 1-2 months of implementation
    OR
  - The child was in the intensive care unit (ICU) during the acute COVID infection or for MIS-C.

  Comprehensive neuropsychological evaluation if:

  - If premorbid medical or developmental concerns are present.

  OR

  - Accommodations and/or compensatory strategies are still needed after 6-12 months after brief/targeted neuropsychological evaluation.

- If available, referral to occupational therapy (OT) or a speech-language pathologist (SLP) for cognitive rehabilitation

- A referral to a specialty provider (Neurodevelopment, pediatric rehabilitation medicine, Development and Behavior Pediatrics, or psychology/psychiatry) might be warranted based on results from the neuropsychological evaluation.
- Refer to a Pediatric neurologist for developmental regression, or an abnormal neurological exam.

Headaches

Patient History & Symptom Assessment:

- Obtain detailed headache history:
  - Description
  - Pattern
  - Screen for "red flag symptoms" as well as signs of secondary headaches caused by an underlying condition.
    - These include: positional headache (worse when lying flat), headaches that wake the child from sleep, weakness of face, arm, or leg, worsens with strain (coughing, sneezing), recurrent vomiting without nausea, and worsening visual symptoms.
- Obtain a family history of neurological conditions including migraines or other headache disorders.
- Complete a full medication review including vitamins and supplements to ascertain if they might be contributing to headaches.

Evaluation:

Full neurological evaluation including fundoscopic examination for any patient with new or worsening headaches with visual changes.

- Consider vision examination for eye strain that might be contributing to headaches.

Additional Workup:

- "Red flag symptoms" are concerning for increased intracranial pressure. Obtain **urgent** neuroimaging (Head CT or, if readily available, Brain MRI and MRV) followed by referral to Pediatric Neurology and, if visual changes, Pediatric Ophthalmology.

Consider obtaining a sleep study to rule out obstructive sleep apnea in children with morning headaches, frequent nighttime awakenings, or history of snoring or pauses while breathing.

Interventions/Considerations:

- Recommend lifestyle modifications (e.g., regular sleep, regular meals, good hydration, regular exercise, and stress management).
- Recommend evaluation and targeted intervention for contributing comorbidities: sleep disturbances like insomnia or sleep apnea, anxiety, depression, postural orthostatic tachycardia syndrome (POTS).
- Recommend counseling on the negative effects of medication overuse (including acetaminophen or ibuprofen) (>3x/week) and how it can cause rebound headaches.
- Consider an abortive regimen for more severe headaches. Examples might be a headache cocktail (acetaminophen or ibuprofen with anti-nausea medicine and water or sports drink). Abortive regimens should not be overused (*>3x per week regularly)*.
- Consider a daily preventative medication if headaches are predominant symptoms and interfering with daily activities. (See Neurology discussion below for additional details).
- Vitamin supplementation (e.g., magnesium, melatonin, coenzyme Q10, riboflavin) can also be beneficial. Melatonin can be beneficial for sleep and headaches.
- Non-pharmacologic therapies (like yoga, acupuncture, relaxation therapies with deep breathing exercises) may be beneficial in particular for those patients with sensitivity, resistance, or inability to tolerate medication.

When to Refer and to Whom:

Referral to a Pediatric Neurologist or Headache specialist when available if the first or second trial of daily preventative medication is ineffective.

- Referral to Pediatric Ophthalmology if patient reports visual changes.

Table 7. Respiratory/Pulmonary

Respiratory/Pulmonary Symptoms may include: shortness of breath, cough, wheezing and chest pain

Patient History & Symptom Assessment:

Document current symptoms:

- *Cough:* dry or wet, tickle in the throat, severity, post-tussive emesis, interferes with sleep
- *Shortness of breath:* at rest, with activities, wakes you up at night, difficulty with inspiration or tightness to throat (suggestive of PVFM/ILO)
- *Wheezing:* at rest, with activities

- Assess frequency of symptoms:
  - Daytime, nighttime, both
  - Daily, weekly, monthly

- Assess Activity limitations:
  - Able or unable to participate in usual activities
  - Able to participate in mild, moderate or intense exercise, unable to participate in exercise

- Review Respiratory illnesses post-COVID
  - Yes or no,
  - If yes: how many, length of respiratory illness in days
  - symptoms with respiratory illnesses, severity

Review of symptoms should include:

- History of asthma, if yes, current, or previous, which medications prescribed
- History of other lung diseases or illness
- History of emergency department visits for respiratory illnesses, history of hospitalizations for respiratory illnesses
- Respiratory symptoms and treatment during acute COVID illness
- Weight loss or weight gain since COVID infection
- Previous history of syncope, anxiety, postural orthostatic tachycardia syndrome
- Sleep-related problems

Environmental history:

- History of smoking or e-cigarette use
- Exposure to secondhand smoke or e-cigarettes
- Exposure to cats, dogs, cockroaches, or rodent

Evaluation:

Focused exam: document presence of wheeze, crackles, decreased breath sounds, rhonchi, sternal wall tenderness, presence of scoliosis, digital clubbing, hypermobility

Recommended Testing (shortness of breath, cough, wheezing):

- Pulse oximetry
- Chest x-ray

Pre- and post-bronchodilator spirometry

- Consider extended pulse oximetry at rest and with walking
- If physical findings noted on lung exam, consider body plethysmography
- Consider diffusing capacity for carbon monoxide (DLCO) particularly if history of previous abnormal chest x-ray or requirement of supplemental oxygen during acute COVID illness

Recommended Testing (chest pain):

Pulse oximetry, spirometry

- Chest x-ray

Additional testing as noted above

Interventions/Considerations:

If history of asthma: optimize treatment with controller medications and bronchodilators per asthma guidelines

- Follow up to assess effectiveness of therapy

If no history of asthma:

- Presence of bronchodilator responsiveness on spirometry or suggestive history- consider bronchodilator therapy and consider inhaled corticosteroids per asthma guidelines
  - Follow up to assess effectiveness of therapy
- If any of the following: flattened inspiratory loop, history of throat tightness, inspiratory stridor would refer to ENT/speech for evaluation of paradoxical vocal fold movement (PVFM)/inducible laryngeal obstruction (ILO) and treatment with breathing exercises.

If presence of consolidation on chest x-ray after period of acute COVID-19 infection:

- Consider chest CT for further evaluation
- Consider short course of oral steroids
- Consider pulmonology referral for flexible lower airway bronchoscopy for evaluation of cell counts and to rule out infection

No history of asthma with normal physical exam and testing:

- Reassurance that most symptoms improve with time
- Consider education on breathing exercises to reduce breathlessness such as diaphragmatic breathing.
- Assess for mental health concerns

See cardiology section for further guidance (Table 8)

When to Refer and to Whom:

Referral to Pulmonology after optimization of current therapies, ongoing/persistent symptoms. Given the relatively common findings of diffusion abnormalities and tachycardia during the 6MWT [1], a trial of supplemental oxygen would be reasonable for patients with significant dyspnea or exercise intolerance, identified to have reliable measures of pulse oximetry levels below 93% at rest or with a decrease of 3% or more with exercise[2] but this should be done in conjunction with a Pulmonologist as further evaluation is likely necessary.

In conjunction with pulmonologist, consider systemic steroids if CT imaging suggestive of organizing pneumonia or bronchiolitis obliterans.

- Referral to Ear Nose and Throat (ENT) physician/SLP for respiratory training, particularly if ILO/PVFM suspected.
- Referral to cardiology if concerns for cardiac abnormalities on history, exam, or testing.

• Referral to Rehabilitation (e.g., physical therapy) for deconditioning treatment. • Referral to Pain Management if cardiorespiratory causes of chest/thoracic pain are ruled out and pain is still impeding function
Legend: 6MWT- 6 minute walk test (89); DLCO- diffusing capacity for carbon monoxide

Table 8. Cardiology

Chest Pain

Patient History & Symptom Assessment:

- Obtain complete history of symptomatology including associated symptoms and aggravated and alleviating symptoms.
- Signs that raise concern of cardiac etiology include chest pain with exercise, radiation of the pain to the neck, jaw, or down the arms, and/or chest pain accompanied by dizziness and/or loss of consciousness
- Respiratory chest pain is often accompanied or preceded by cough, wheezing and dyspnea.

Evaluation:

- Complete Cardiac and pulmonary physical examinations (PE) including examination for chest wall tenderness.

Additional workup: Testing will depend on the history and PE and may include:

- Troponin
- Chest Xray
- ECG
- Echocardiogram

Interventions/Considerations:

- Activity restriction if cardiac etiology is suspected
- Increase fluids
- Gradual return to activity

When to Refer and to Whom:

- **If concerns for acute ischemia, send to ER**
- **Pediatric cardiology referral if a cardiac etiology to the chest pain suspected (**e.g., chest pain with exercise, radiation of pain to the neck, jaw, or down the arms, and/or chest pain accompanied by dizziness and/or loss of consciousness**)**

Palpitations

Patient History & Symptom Assessment:

- Obtain complete history of symptomatology including associated symptoms and aggravated and alleviating symptoms
- Ask about the duration of palpitations and if exercise-induced
- Screen for syncope and association with palpitations
- Obtain family history of cardiac conditions, in particular sudden cardiac death or deafness, which raises concern for genetic conditions associated with palpitations (e.g., long QT syndrome)

Evaluation:

- Complete Cardiac Physical examination
- Orthostatic blood pressures and heart rates

Recommended Testing:

- Sinus tachycardia associated with autonomic dysfunction, respiratory disease and acute illness should be differentiated from truly abnormal cardiac rhythms by EKG or other monitoring technology
- Thyroid testing if concern for hyperthyroidism based on associated symptoms
- Other testing may include:
  - Holter monitor
  - Event Monitor
  - Echocardiogram if myocarditis or pericarditis is suspected

Interventions/Considerations:

- Increase fluids if autonomic dysfunction is suspected See Autonomic Dysfunction & POTS table for specifics
- Treat underlying rhythm problem with referral to or in consultation with pediatric cardiologist

When to Refer and to Whom:

- Pediatric cardiology referral if palpitations persist, myocarditis, pericarditis is suspected, or testing is abnormal.
- See Autonomic Dysfunction & POTS section autonomic dysfunction if suspected.

Dizziness

Patient History & Symptom Assessment:

- When developmentally appropriate, attempt to discern if reported symptoms are more consistent with lightheadedness or vertigo (i.e., sense of spinning)
- Obtain complete history of symptomatology including associated symptoms and aggravated and alleviating symptoms
  Screen for any additional cardiac symptoms with dizziness (e.g., palpitations, chest pain, etc.)
- Ask about provoking factors (e.g., standing up, rolling over in bed) and duration of symptoms
- Screen for any gait/balance instability or disequilibrium that may be associated with vestibular etiology to dizziness
- If dizziness is episodic and unprovoked by movement, ask about history of migraines or associated headache or other migraine features
  Obtain a comprehensive medication and supplement review

Evaluation:

- Complete cardiac physical examination including orthostatic blood pressures and heart rates
  If history is concerning for vertigo, perform a neurological examination

Recommended Testing if concerning for cardiac etiology:

- ECG
  Holter
- Event Monitor
- Echocardiogram if myocarditis is suspected

Interventions/Considerations:

- Increase fluids if autonomic dysfunction is suspected. See Autonomic Dysfunction & POTS table for specifics
- Treat underlying rhythm problem with referral to or in consultation with pediatric cardiologist
- Consider vestibular PT if vertigo is suspected on history and exam

When to Refer and to Whom:

- Pediatric cardiology referral if dizziness is assessed to be of cardiac origin (e.g., associated with palpitations, shortness of breath)

- Refer for vestibular testing if vertigo is suspected
- Pediatric neurology referral if neurological examination is abnormal or concern for vestibular migraines

Table 9. Otolaryngology

Anosmia/Hyposmia, Ageusia/Dysgeusia

Patient History & Symptom Assessment:

Obtain sinonasal history:
- Ask about timing, triggers, and duration of the nasal symptoms
  Ask about history of allergic rhinitis, chronic rhinosinusitis
- Ask about additional nasal symptoms (e.g., congestion, obstruction, rhinorrhea, +/- facial pain)

Evaluation:
Anterior rhinoscopy

Subjective smell testing (referral to ENT)
- Consider Sino-nasal Outcome Test (SNOT-22) or Questionnaire of Olfactory Disorders

Objective smell testing (referral to ENT)
- More reliable than subjective testing. Choose test based on patient age group/developmental stage[4]: Sniffin' sticks, pediatric smell wheel, University of Pennsylvania Smell Identification Test (UPSIT)

Nasal endoscopy indications (referral to ENT)
- Presence of associated nasal symptoms, to rule out nasal masses, polyps, mucopurulence, inflammation
- Isolated LOS/LOT >4 weeks without associated nasal symptoms

Imaging indications
- Maxillofacial CT without contrast: LOS/LOT >6 weeks associated with nasal symptoms OR any suspicious nasal endoscopy findings (ENT)
- MRI Brain with contrast: LOS/LOT with neurologic symptoms

Note: Imaging is NOT recommended for isolated LOS/LOT

Interventions/Considerations:
Observation
- Most pediatric anosmia/dysgeusia self-resolves in 3-6 months

Olfactory training

- Consider if LOS/LOT >2 weeks after resolution of other COVID-19 symptoms
- Examples of training programs or websites: 58bsent, Fifth Sense

Medical therapy

Intranasal steroids if LOS/LOT >2 weeks with associated nasal symptoms

- Oral steroids optional if isolated LOS/LOT >2 weeks, only after complete resolution of other COVID-19 symptom
- No evidence for the use of vitamin A drops, omega-3 supplements, or alpha-lipoic acid

When to Refer and to Whom:

Referral to otolaryngology

- Isolated LOS/LOT >3 months
- All patients with LOS/LOT >4-6 weeks with associated nasal symptoms

Referral to neurology

- All patients with LOS/LOT with associated neurologic symptoms

LOS: loss of smell, LOT: loss of taste, SNOT-22: sinonasal-outcome test, QOD: questionnaire of olfactory disorders, UPSIT: University of Pennsylvania Smell Identification Test

Table 10. Musculoskeletal

Pain: Muscular, Joint, Generalized

Patient History & Symptom Assessment:

- Characterize pain including quality, location, duration, frequency, severity, exacerbating and alleviating factors
- Assess for comorbid sleep and mood disturbances, fatigue, orthostatic symptoms and joint hypermobility that can be seen with fibromyalgia
- Assess for family history including pain disorders such as fibromyalgia and rheumatologic conditions
- Complete medication review in particular looking for causes of medication induced myopathy (e.g., rheumatologic agents, antifungal agents, statins, etc.)

Evaluation:

- Full neurological examination including reflexes, and somatosensory exam (pain, temperature, touch, proprioception).
- Musculoskeletal exam of involved joints and muscles including inspection, palpation, passive and active range of motion, and specialized joint specific testing as needed
- Evaluate for joint hypermobility with Beighton score

Additional Workup:

- Manual painful point survey if concerned for fibromyalgia (103)
- Joint aspiration if concerns for septic or reactive arthritis
- Consider initial imaging with ultrasound or x-ray if warmth, swelling, or erythema of joint
- ESR/CRP, CBC, serum chemistries if pain/swelling/stiffness of multiple joints are noted in a pattern concerning for autoimmune/ rheumatologic etiology
- Creatinine kinase and urinalysis if myalgias are associated with muscle weakness and/or changes in urine color to evaluate for rhabdomyolysis.

Interventions/Considerations:

Physical Activity/Exercise:

- Tailored approach to each patient based on location of pain and other symptoms with assistance of PT/OT
- Recommend gradual increase in physical conditioning with aerobic and muscular strengthening over time. Incorporate pacing strategies for any concerns for post-exertional malaise. See Systemic/Constitutional Section: Fatigue for further details.
- Consider physical modalities with therapies including ice/heat, myofascial release, transcutaneous electrical stimulation, desensitization, etc.

Lifestyle Modifications:

- Optimize nutrition and sleep
- Address any mental health concerns
- Establish good social support system

Medications:

- Topical anti-inflammatories (trolamine salicylate, diclofenac) or numbing agents (lidocaine) as needed for localized pain
- Over-the-counter pain medications (i.e., acetaminophen or ibuprofen) should be used sparingly to avoid iatrogenic side effects from overuse.
- If concerns for costochondritis, a short course of scheduled non-steroidal anti-inflammatory drugs (NSAIDs) may be helpful.
- In a rare situation of fibromyalgia that failed conservative measures, medication such as antiepileptics (gabapentin, pregabalin), SSRIs, (serotonin and norepinephrine reuptake inhibitors) SNRIs, or tricyclic antidepressants may be considered.

Additional Considerations:

- For patients with co-morbid fatigue/post-exertional malaise, please see Systemic Section for exercise recommendations
- School accommodations may be needed if pain interfering with mobility or participation in classes or physical education

When to Refer and to Whom:

- Psychology for cognitive behavioral therapy and pain coping strategies
- Neurology if concerns for myositis or neuropathic pain for additional evaluation.
- Rheumatology if concerns for autoimmune conditions including arthritis
- Physiatry or orthopedics to rule out non-rheumatologic musculoskeletal pain conditions including concerns for comorbid injuries, joint integrity or alignment, and for consideration of additional imaging
  - Physical therapy for back pain, lower extremity pain, and generalized pain including modalities. Strategies for joint protection if hypermobility.
  - Occupational therapy for upper extremity pain and generalized pain including modalitie
  - Complementary therapies for pain including acupuncture, yoga, massage, meditation, biofeedback, chiropractic etc. in age-appropriate groups
- Acute inpatient rehabilitation if conservative measures and outpatient therapies have failed for multidisciplinary approach with focus on improving function and independence

[redacted]

Weakness: Weakness may present as fatigue, refusal to move, motor impairment, irritability, and lethargy, especially in young children

Patient History & Symptom Assessment:

- Determine current levels of physical activity versus premorbid activity
- Assess whether weakness is localized or generalized and patterns such as proximal versus distal
- Assess nutritional status and sleep patterns
- Assess for family history of any neuromuscular disorders
- In addition to medication review above, prolonged use of steroids may cause painless steroid myopathy

Evaluation:

- Full musculoskeletal and neurological examination. In particular, complete manual muscle testing for strength if able to follow directions and > 5 yrs developmentally. Otherwise observe for asymmetries in use of arms/legs, ability to change position, stand, move, and the need for assistance.

Note: Fatigue and deconditioning may be mistaken for muscle weakness, so it is important to differentiate fatigue or malaise based "weakness" versus true neurological weakness.

Additional workup:

- CK and urinalysis as above to evaluate for rhabdomyolysis if weakness occurs with myalgias and/or urine color change.
- MRI brain/spine if central nervous system pathology suspected for weakness based on examination and history.

Interventions/Considerations:

- If suspect physical deconditioning and no true neurological weakness, please refer to Systemic/Constitutional Section for recommendations regarding increasing physical activity and exercise

- True neurological muscle weakness is a red flag that requires additional referral/subspecialty workup. Once workup has been completed and medically cleared for progression of activities, consider a program focusing on improving mobility and muscle strengthening under supervision of a physical therapist.

Emergent/urgent neurology referral is recommended for: neurological deficits with muscle weakness or sensory changes.

- Focal weakness with hyperreflexia is concerning for CNS pathology and requires emergent/urgent neuroimaging (MRI brain/spine with diffusion imaging)
- Weakness with diminished/absent reflexes in the setting of recent viral infection is concerning for diagnoses such as Guillain-Barré syndrome, acute flaccid myelitis, or other peripheral neuropathies and urgent treatment may be needed.

Table 11. Gastrointestinal

Abdominal Pain

Patient History & Symptom Assessment:

Obtain a medical history to identify red flags and triggers of pain (e.g., eating, stooling, stress)

Red flags: (weight loss, growth deceleration, focal abdominal pain vs periumbilical or nonspecific abdominal pain, hematochezia, family history of IBD or celiac, significant diarrhea)

Evaluation:

- Complete a full abdominal examination.
- If concerned for autoimmune or inflammatory diseases, complete a dermatologic exam to look for rashes that may be associated with particular diseases.

Additional workup:

- Bloodwork: CBC, Celiac serologies (total IgA, Tissue Transglutaminase IgA), ESR, CRP, liver function tests, fecal calprotectin
- Imaging: Ultrasound abdomen if pain is localized to right upper quadrant or if liver function tests are abnormal/ symptoms are concerning for liver pathology.

Interventions/Considerations:

- Consider treatment of constipation with osmotic laxative like polyethylene glycol
- Consider trial of acid blocker such as H2 blocker or proton pump inhibitor if dyspepsia is a concern
- Consider trial of probiotic if suspicion of irritable bowel syndrome or functional abdominal pain, provide positive symptom-based diagnosis, and identify triggers (e.g., food, microbiome, stress).

When to Refer and to Whom

- Refer to pediatric gastroenterology in patients with red flags by history, physical exam, or laboratory evaluation or if persistent abdominal pain
- Refer to psychology or social work if concern about psychosocial stressors that may be contributing to symptoms or in patients who are not functioning well (e.g., missing school activities) due to abdominal pain
- If there are other concerns for orthostatic intolerance or autonomic dysfunction, see Table 5 for additional recommendations.
- Consider dietician referral if there is a temporal relationship to food
- Refer to GI for evaluation and potential endoscopic evaluation or gastric emptying scan, when indicated

Nausea and/or vomiting

Patient History & Symptom Assessment:

Obtain history of nature of nausea and vomiting including temporal relationship to eating, specific triggers, relieving factors, time of day (e.g., morning vomiting), side effects of medications

- If vomiting, consider contents if bilious, coffee ground emesis, food consumed hours prior, projectile nature
- Screen for red flag symptoms such as weight loss, hematemesis, bilious emesis

Evaluation:

- Complete a full abdominal examination.

Additional Workup:

- Bloodwork: CBC, Electrolytes, liver function tests, amylase, lipase, urinalysis

- Imaging when indicated:
  - Upper GI if vomiting or significant regurgitation
- If concerns for gastroparesis, consult with pediatric gastroenterology for further work-up or consider trial with prokinetic or cyproheptadine
  Consideration of endoscopy in consultation with Pediatric Gastroenterology

Interventions/Considerations:

- Consider trial of acid blocker such as H2 blocker or proton pump inhibitor (PPI)
- If no response, consider diagnostic work-up in consultation with pediatric gastroenterologist

When to Refer and to Whom:

- Refer to pediatric gastroenterology for persistent nausea or vomiting or if nausea is associated with red flag symptoms such as weight loss, hematemesis, bilious emesis or other concerns
  Refer to psychology if concern about psychosocial stressors that may be contributing to symptoms

Chronic Diarrhea (≥ 2 weeks)

Patient History & Symptom Assessment:

- Take a thorough history about diarrhea including characteristics and frequency of stool, blood or mucus in stool, abdominal pain, or any weight loss

Evaluation:

Complete abdominal examination

Additional Workup:

CBC, Electrolytes, ESR, CRP, fecal calprotectin, occult blood, celiac serologies, infectious stool studies (if bloody sent culture for salmonella, shigella, campylobacter, Yersinia, E.coli and C. diff PCR or toxin; if non-bloody Giardia antigen)

Interventions/Considerations:

Start by checking infectious stool studies and also consider a fecal calprotectin

- If suspicion for infectious etiology, test for and treat the infection
- If fecal calprotectin elevated, refer to pediatric gastroenterology for consideration of colonoscopy
  Consider empiric trial of a probiotic, lactose free diet, or increasing fiber intake

When to Refer and to Whom:

- Refer to pediatric gastroenterology for consideration of colonoscopy if:
  - diarrhea is persistent or associated with blood in stool, weight loss, or other concerns and if inflammatory markers are positive.

  Refer to dietician for dietary counseling
- Refer to psychology if concern about psychosocial stressors that may be contributing to symptoms

Lack of Appetite

Patient History & Symptom Assessment:

Take a thorough history including characteristics and frequency of symptoms. Assess for associated symptoms such as nausea, vomiting, abdominal pain.

- Assess for loss/altered taste/smell.
- Screen for mental health conditions (e.g., depression, eating disorder)

Evaluation:

- Complete abdominal examination
- Complete head, eyes, ears, nose and throat (HEENT) and dermatologic examinations if concerned for conditions such as an eating disorder or Crohn's disease

Additional Workup:
- Electrolytes, CBC, ESR, CRP, celiac disease, thyroid function tests
- If concerns for gastroparesis, consult with pediatric gastroenterology for further work-up or consider trial with prokinetic or cyproheptadine

Interventions/Considerations:
- Can consider appetite stimulant such as cyproheptadine or an empiric trial of an acid blocker such as a proton pump inhibitor (PPI) (e.g., pantoprazole, omeprazole) or H2 blocker (e.g., famotidine)

When to Refer and to Whom:
- Refer to pediatric gastroenterology if weight loss or other associated symptoms such as vomiting, diarrhea, or abdominal pain
- Refer to psychology if concern about psychosocial stressors that may be contributing to symptoms

Reflux/Indigestion /Belching

Patient History & Symptom Assessment:
Take a thorough history including characteristics and frequency of symptoms, abdominal pain, or any weight loss

Evaluation
- Complete abdominal examination

Additional workup:
- Bloodwork: Electrolytes, CBC, Celiac serologies

Interventions/Considerations:
If medical history is consistent with gastroesophageal reflux, start with an empiric trial of an acid block such as a proton pump inhibitor (PPI) (e.g., pantoprazole, omeprazole) or H2 blocker (e.g., famotidine)
- Consider empiric trial of a probiotic

When to Refer and to Whom:
- Refer to gastroenterology for persistence of symptoms
- Consider referral to dietician to identify foods that may trigger symptoms
- Refer to psychology if concern about psychosocial stressors that may be contributing to symptoms