TABLE 1: Common PASC Symptoms in Children and Adolescents by System^{3,20,21}



Systemic/ constitutional (Table 3)	 Fatigue (generalized, exercise intolerance, or postexertional 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 presyncope
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)	WeaknessMuscle, 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 Postacute Sequelae of SARS-CoV-2 (PASC) Clinics serving children and adolescents. The PASC Collaborative has published a number of Consensus Guidance Statements for the adult populations; see Appendix 1 for a list of available publications and links.

TABLE 2: Initial Assessment of PASC in Children and Adolescents



- I. Postacute 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"
 - o The majority of children with acute SARS CoV-2 infection are asymptomatic or present with mild symptoms. Other children may be hospitalized or develop multisystem inflammatory syndrome in children. 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}
- o 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
- o 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 postexertional 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
- o 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 (ie, hobbies and leisure activities).
- V. Past medical, surgical, family, and social history
 - o Review the past medical history. Specific attention should be placed on preexisting 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 PASC³⁶ include attention issues, learning disabilities or difficulties, sleep disturbances, mood disorders, or prior pain syndromes.
 - o 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.
- o A social history should include a review of school attendance and performance, extracurricular activities, family structure, and support networks. Identification of family stressors (eg, 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:
- o A comprehensive physical should be performed. The findings may be normal.
- o Additional components of the physical exam may be needed based on presenting symptoms (Tables 3-11).

IX. Assessment:

- o 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 postacute 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
- o 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, extracervical or enlarging lymphadenopathy (nodes >2 cm), hepatosplenomegaly, joint swelling/redness, or cardiac murmurs.
- o 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. See Tables 3-11 for specific guidance on testing based on symptom presentation.
- X.Follow-up plan and referrals Follow symptom-based treatment strategies as outlined in the specific sections that follow (Tables 3-11).
- o 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 health care system.
- o Consider referral to subspecialists if patients do not respond to initial treatment or for complex or severe presentations.16,23
- o Some patients may have significant or refractory symptoms that affect function necessitating inpatient evaluation or inpatient rehabilitation.
- o 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 and symptom assessment:

- Screen for baseline physical activity level prior to initial COVID-19 infection
- · Characterize fatigue pattern and sleep habits
- Evaluate for postexertional 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 scales³⁹ (ie, 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 in 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: complete blood count, comprehensive metabolic panel, thyroid-stimulating hormone/ free T4, iron panel, ferritin, vitamin D
- Consider magnesium, vitamin B12, erythrocyte sedimentation rate/C-reactive protein, celiac screening based on additional symptoms.
- If fatigue/exercise intolerance is associated with additional cardiopulmonary symptom (see Tables 7
 and 8 for further details), consider B- type natriuretic peptide, electrocardiogram, echocardiogram,
 cardiopulmonary exercise stress test, pre/post exercise pulmonary function test, chest X-ray

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

Interventions/considerations:

Medications:

• Treat any known medical causes of fatigue or El based on screening results (eg, 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

- · Pediatric Rehabilitation Medicine for overall management and rehabilitation recommendations
- <u>Physical therapy</u> 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
- <u>Complementary therapies</u> 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 El

TABLE 3: Systemic/Constitutional

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

Patient history and 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)
- 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 using 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 (ie, 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 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 and 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:
- Premorbid or new mental health symptoms and the current status (eg, stable, worsening);
- New or worsening physical health symptoms affecting 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 (eg, food, supplements, environment, activity, external stressors);
- Screening for medical conditions that may mimic mood disorders (eg, palpitations associated with anxiety may be due to postural orthostatic tachycardia syndrome 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 (ie, medications with antiarrhythmic, 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 postacute sequelae of SARS CoV-2. (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:

- Generalized Anxiety Disorder Scale (GAD-7): (ages 12+ years): brief screening scale that indicates severity
- Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric Item Bank v2.0-Anxiety (ages 5- 17 years): brief screening scale that can be converted to T-scores to indicate severity79
- Screen for Child Anxiety Related Emotional Disorders (SCARED): scale (ages 8–18 years): detailed screening scale that 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 Food and Drug Administration (FDA)-approved medications in youth, it is recommended to discuss FDA approval or lack thereof with guardians.

- Therapy referral for evidence-based therapies (eg, 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.

TABLE 4: Mental Health and Psychiatric Symptoms



Depression

Evaluation/scales to consider:

- Patient Health Questionnaire-9 (PHQ-9) scale*
- Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric Item Bank v2.0-Depressive Symptoms (ages 5–17 years): brief screening scale that can be converted to T-scores to indicate severity
- 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 (eg, behavioral activation, cognitive behavioral therapy [CBT]).
- Consider referral to psychiatry if there is failure to improve after 2 SSRI

Suicidality

Evaluation/scales to consider:

- PHQ-9 scale
- · Ask Suicide-Screening Questions (ASQ) questionnaire

Interventions/considerations:

Consult with mental health provider

- 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 (eg, outpatient program/ partial hospital program) based on acuity and risk level.

TABLE 4: Mental Health and Psychiatric Symptoms



Posttraumatic symptoms/ acute stress disorder

Evaluation/scales to consider:

- UCLA Posttraumatic stress disorder (PTSD) Assessment Tool
- 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:

- · Vanderbilt attention deficit hyperactivity disorder (ADHD) Diagnostic Rating Scale (VADRS) can be used if ADHD is suspected
- · Assess level of support at school and presence of section 504/ individualized education program plan
- Assess for anxiety, depression, attention, or learning issues
- · 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 reintegration. 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

- · 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 affected.

TABLE 5: Autonomic Dysfunction/Postural Orthostatic Tachycardia Syndrome (POTS)



Autonomic dysfunction and postural orthostatic tachycardia syndrome symptoms may include fatigue, lightheadedness/dizziness in upright positions, brain fog, exercise intolerance, postexertional malaise, headaches, gastrointestinal symptoms, heart racing, palpitations, heat intolerance, hyperhydrosis

Patient history and 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: (complete blood count, comprehensive metabolic panel, ferritin, vitamin D, vitamin B12, erythrocyte sedimentation rate, C- reactive protein, thyroid-stimulating hormone) to rule out other medical conditions
- Ten-minute passive standing test68 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 (eg, 2–3 liters of noncaffeinated fluid per day for a 40 kg patient)
- Salt intake (4–6 grams per day)
- · Physical activity with pacing69
 - o Start with recumbent activity and progress to more upright positions as tolerated. Avoid exacerbating symptoms or triggering postexertional malaise by slowly progressing time/intensity.
- o Compression garments (20-30 mmHg)
- o Elevate head of bed 4-6 inches
- o 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 atendiol or proprandiol) 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 (ie, 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 postacute sequelae of SARS CoV-2 may include attention difficulties, memory problems, word finding difficulties, trouble concentrating, brain fog, declining school performance

Patient history and symptom assessment:

- Screen for and track cognitive function using validated tools when possible:
- Changes to cognition (eg, 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 (eg, World Health Organization Case Report Functional subsection)
- Attention deficit hyperactivity disorder (ADHD) symptoms (e.g., Vanderbilt ADHD Diagnostic Rating Scale)

Anxiety and mood symptoms (e.g., Patient Health Questionnaire-9, Generalized Anxiety Disorder Scale-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 (eg, home, school, community)
- Obtain a comprehensive medication and supplement review
- Validate patient history through the collection of collateral history including preexisting function and conditions, from care team/primary care, patient family or care partner, educators, or close contact as available

Additional workup:

 Obtain a brain magnetic resonance imaging (MRI) scan if history or exam concerning for developmental regression or focal neurological deficits

Interventions/considerations:

- Treat, in collaboration with appropriate specialists, comorbid 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 affect 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 (eg, 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 (eg, increased or emergent concerns on screening inventories [eg, PROMIS] based on clinical judgment)

OR

- Accommodations and/or compensatory strategies are still needed after 1–2 months of implementation OR
- The child was in the intensive care unit during the acute COVID infection or for multisystem inflammatory syndrome in children.
- Comprehensive neuropsychological evaluation 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.

TABLE 6: Neurology



- If available, referral to occupational therapy or a speech-language pathologist 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 and 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.
- o 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.
- o Obtain a family history of neurological conditions including migraines or other headache disorders.
- o 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 computed tomography or, if readily available, brain MRI and MR venography) 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 (eg, 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, 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 antinausea 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 for additional details).
- Vitamin supplementation (eg, magnesium, melatonin, coenzyme Q10, riboflavin) can also be beneficial. Melatonin can be beneficial for sleep and headaches.
- Nonpharmacologic 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.

- 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 and 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 paradoxical vocal fold movement [PVFM]/inducible laryngeal obstruction [ILO])
- · Wheezing: at rest, with activities
- Assess frequency of symptoms:
- o Daytime, nighttime, both
- o Daily, weekly, monthly
- · Assess activity limitations:
- o Able or unable to participate in usual activities
- o Able to participate in mild, moderate, or intense exercise; unable to participate in exercise
- Review respiratory illnesses post-COVID
- o Yes or no,
- o If yes: how many, length of respiratory illness in days
- o Symptoms with respiratory illnesses, severity

Review of symptoms should include:

- · History of asthma, if yes, current, or previous, which medications prescribed
- o History of other lung diseases or illness
- o 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 rodents

Evaluation:

<u>Focused exam:</u> 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 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 previously

Interventions/considerations:

- <u>If history of asthma</u>: optimize treatment with controller medications and bronchodilators per asthma guidelines
- o Follow up to assess effectiveness of therapy
- If no history of asthma:
- o 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
- o If any of the following: flattened inspiratory loop, history of throat tightness, inspiratory stridor would refer to ear, nose, and throat (ENT)/ speech for evaluation of PVFM/ILO and treatment with breathing exercises.

TABLE 7: Respiratory/Pulmonary

- If presence of consolidation on chest x-ray after period of acute COVID-19 infection:
- Consider chest computed tomography (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)

- Referral to pulmonology after optimization of current therapies, ongoing/persistent symptoms. Given the relatively common findings of diffusion abnormalities and tachycardia during the 6-minute walk test,89 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 exercise2 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 ENT physician/speech-language pathologist for respiratory training, particularly if ILO/ PVFM suspected.
- · Referral to cardiology if concerns for cardiac abnormalities on history, exam, or testing.
- Referral to rehabilitation (eg, 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



TABLE 8: Cardiology



Chest pain

Patient history and 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 x-ray
- Electrocardiogram (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 emergency department
- Pediatric cardiology referral if a cardiac etiology to the chest pain suspected (eg, 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 and 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 (eg, 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 ECG or other monitoring technology
- Thyroid testing if concern for hyperthyroidism based on associated symptoms
- Other testing may include:
 - o Holter monitor
 - o Event monitor
 - o Echocardiogram if myocarditis or pericarditis is suspected

Interventions/xonsiderations:

- Increase fluids if autonomic dysfunction is suspected See Autonomic Dysfunction and POTS in Table 5 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 and POTS section on autonomic dysfunction if suspected.

Dizziness

Patient history and symptom assessment:

- When developmentally appropriate, attempt to discern if reported symptoms are more consistent with lightheadedness or vertigo (ie, sense of spinning)
- Obtain complete history of symptomatology including associated symptoms and aggravated and alleviating symptoms
- Screen for any additional cardiac symptoms with dizziness (eg, palpitations, chest pain, etc.)

- Ask about provoking factors (eg, 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 and POTS in Table 5 for specifics
- Treat underlying rhythm problem with referral to or in consultation with pediatric cardiologist
- Consider vestibular physical therapy if vertigo is suspected on history and exam

- Pediatric cardiology referral if dizziness is assessed to be of cardiac origin (eg, 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 and 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 (eg, congestion, obstruction, rhinorrhea, +/- facial pain)

Evaluation:

Anterior rhinoscopy

Subjective smell testing (referral to ear, nose, and throat [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 stage4: 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 loss of smell/loss of taste (LOS/LOT) >4 weeks without associated nasal symptoms Imaging indications
- Maxillofacial computed tomography 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: AbScent (https://abscent.org), Fifth Sense (https://www.fifthsense.org.uk) 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

TABLE 10: Musculoskeletal



Pain: muscular, joint, generalized

Patient history and 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 (eg, 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 fibromyalgia103
- · Joint aspiration if concerns for septic or reactive arthritis
- Consider initial imaging with ultrasound or x-ray if warmth, swelling, or erythema of joint
- Erythrocyte sedimentation rate/C-reactive protein, complete blood count, 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 physical therapy/occupational therapy
- Recommend gradual increase in physical conditioning with aerobic and muscular strengthening over time. Incorporate pacing strategies for any concerns for postexertional 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 (ie, 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 may be helpful.
- In a rare situation of fibromyalgia that failed conservative measures, medication such as antiepileptics (gabapentin, pregabalin), selective serotonin and norepinephrine reuptake inhibitors, or tricyclic antidepressants may be considered.

Additional considerations:

- For patients with comorbid fatigue/postexertional malaise, plese see Systemic Section for exercise recommendations
- School accommodations may be needed if pain interfering with mobility or participation in classes or physical education

- 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 nonrheumatologic musculoskeletal pain conditions including concerns for comorbid injuries, joint integrity or alignment, and consideration of additional imaging
- o Physical therapy for back pain, lower extremity pain, and generalized pain including modalities. Strategies for joint protection if hypermobility.
- o Occupational therapy for upper extremity pain and generalized pain including modalities
- o 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

TABLE 10: Musculoskeletal



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

Patient history and 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, 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 years 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:

• Creatine kinase and urinalysis as described previously to evaluate for rhabdomyolysis if weakness occurs with myalgias and/or urine color change.

 Magnetic resonance imaging (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.

<u>Emergent/urgent neurology referral</u> 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 and symptom assessment:

• Obtain a medical history to identify red flags and triggers of pain (eg, eating, stooling, stress)
Red flags: (weight loss, growth deceleration, focal abdominal pain vs periumbilical or nonspecific abdominal pain, hematochezia, family history of inflammatory bowel disease 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: complete blood count, celiac serologies (total IgA, tissue transglutaminase IgA), erythrocyte sedimentation rate, C-reactive protein, 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 (eg, 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 (eg, 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 gastrointestinal for evaluation and potential endoscopic evaluation or gastric emptying scan, when indicated

Nausea and/or vomiting

Patient history and symptom assessment:

- Obtain history of nature of nausea and vomiting including temporal relationship to eating, specific triggers, relieving factors, time of day (eg, 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: complete blood count, electrolytes, liver function tests, amylase, lipase, urinalysis
- o Imaging when indicated:
- Upper GI if vomiting or significant regurgitation
- o If concerns for gastroparesis, consult with pediatric gastroenterology for further work-up or consider trial with prokinetic or cyproheptadine
- o Consideration of endoscopy in consultation with pediatric gastroenterology

Interventions/Considerations:

- Consider trial of acid blocker such as H2 blocker or proton pump inhibitor
- If no response, consider diagnostic workup 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 and 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:

Complete blood count, electrolytes, erythrocyte sedimentation rate, C-reactive protein, fecal calprotectin, occult blood, celiac serologies, infectious stool studies (if bloody sent culture for salmonella, shigella, campylobacter, Yersinia, E. coli, and C. diff polymerase chain reaction or toxin; if nonbloody Giardia antigen)

TABLE 11: Gastrointestinal



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 and 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., depression, eating disorder)

Evaluation:

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

Additional workup:

- Electrolytes, complete blood count, erythrocyte sedimentation rate, C-reactive protein, celiac disease, thyroid function tests
- If concerns for gastroparesis, consult with pediatric gastroenterology for further workup 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 (eg, pantoprazole, omeprazole) or H2 blocker (eg, 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 and 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, complete blood count, 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 (eg, pantoprazole, omeprazole) or H2 blocker (eg, famotidine)
- · Consider empiric trial of a probiotic

- 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