TABLE 1: Diagnostic criteria for common autonomic disorders.

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Autonomic disorder	Diagnostic criteria
POTS[20]	1. Sustained HR increase ≥30 bpm within 10 min for adults (≥40 bpm for adolescents 12–19 years of age) of standing or on TTT 2. Absence of OH 3. Symptoms of orthostatic intolerance for ≥6 months 4. Exclusion of other causes of postural tachycardia, such as dehydration, medication side effect, and other medical conditions
NCS[20]	1. Transient loss of consciousness typically preceded by prodromal symptoms and signs, such as pallor, diaphoresis, nausea, abdominal discomfort, yawning, sighing, and hyperventilation. That may occur up to 60 s prior to loss of consciousness. 2. A sudden fall in blood pressure, heart rate, and cerebral hypoperfusion on standing or on TTT
OH[21]	Sustained drop in blood pressure ≥20/10 mm Hg within 3 min of standing or on TTT
IST[22]	1. Average sinus HR exceeding 90 bpm over 24 hours or HR while awake and at rest ≥100 bpm 2. 2. Palpitations and other distressing symptoms associated with sinus tachycardia

Abbreviations: bpm, beats per minute; HR, heart rate; IST, inappropriate sinus tachycardia; NCS, neurocardiogenic syncope; OH, orthostatic hypotension; POTS, postural orthostatic tachycardia syndrome; TTT, tilt table test.

TABLE 2: Clinical features of autonomic disorders.

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Review of systems	Clinical features
Cardiovascular	• Orthostatic intolerance • Postural tachycardia • Orthostatic hypotension • Postprandial hypotension • Exercise intolerance • Syncope • Presyncope • Palpitations • Chest pain, pressure or discomfort
Neurologic	• Dizziness or lightheadedness • Cognitive dysfunction (a.k.a. “brain fog”) • Paresthesia • Generalized weakness • Neuropathic pain • Headache, including migraine
Respiratory	• Shortness of breath • Hyperventilation
Gastrointestinal	• Nausea • Dysphagia • Acid reflux • Early satiety • Abdominal fullness, distension or pain • Gastric and intestinal dysmotility • Diarrhea or constipation

Review of systems	Clinical features
Genitourinary	• Urinary frequency, urgency or hesitancy • Incomplete bladder emptying • Urinary retention • Overactive bladder • Polyuria • Nocturia • Interstitial cystitis • Erectile dysfunction • Vaginal dryness • Pelvic pain
Thermoregulatory	• Hypohydrosis • Hyperhidrosis • Anhidrosis • Gustatory sweating • Heat intolerance • Cold intolerance
Pupillomotor	• Blurred vision • Light sensitivity • Dilated pupils
Secretomotor	• Dry eyes • Dry mouth

Review of systems	Clinical features
Constitutional	• Fatigue • Sleep disturbance • Loss of appetite • Weight loss or gain • Pallor • Flushing • Diaphoresis • Myalgia

TABLE 3: Autonomic dysfunction in patients with PASC: assessment recommendations.

No.	Autonomic dysfunction assessment statement
1	Clinicians should conduct a full patient history including a review of predisposing comorbidities, prior autonomic symptoms or disorders, relevant hospitalizations, and timeline of symptom evolution The patient history should address: • Most disabling symptoms/signs that may be autonomic in nature: dizziness, lightheadedness, palpitations, presyncope, syncope, orthostatic intolerance, exercise intolerance, cognitive dysfunction, and fatigue (see Table 2) • Medication history: evaluate for medications that may impact symptoms, signs or assessment parameters (i.e., medications with side effects, such as orthostatic intolerance, orthostatic hypotension, or resting or postural tachycardia; these may include anti- hypertensive, anti-cholinergic, and stimulant medications) • Social history of previous and current substance use, current diet, fluid and salt intake, exercise routine, if any, employment status, and psychological stressors • Family history of autonomic, autoimmune and post-COVID complications
2	Clinicians should characterize symptoms including onset (new acute or chronic), frequency, intensity, aggravating and alleviating factors, and impact on function and activities
3	Clinicians should conduct a neurologic exam, including sensory exam to look for signs of small fiber neuropathy (particularly the loss of pinprick or temperature sensation) To evaluate for autonomic dysfunction, clinicians should perform a 10-min stand test recording heart rate and blood pressure while patients is supine and after standing 3, 5, 7 and 10 min. Consider obtaining a tilt table test in symptomatic individuals with a negative 10-min stand test
4	Recommended initial laboratory tests in individuals with suspected autonomic dysfunction including: CBC, CMP, TFT, vitamin B12, ferritin, morning cortisol, ANA, ESR, CRP • Consider obtaining a D-dimer to assess for pulmonary embolism in the appropriate clinical setting
5	Clinicians should consider obtaining a pulse oximetry at rest and with exertion/activity to rule out persistent hypoxemia, ECG, echocardiogram, and ambulatory cardiac monitoring with: • Holter monitor for palpitations and tachycardia occurring daily • Cardiac event monitor for recurrent palpitations, tachycardia, or syncope occurring less than daily Further cardiac evaluation may be warranted as per the PASC Collaborative Cardiovascular Complications Consensus Guidance Statement[18]
6	Where diagnosis is uncertain or symptoms are progressing, consider a referral to an autonomic specialist for more detailed assessment including autonomic function tests such as Valsalva maneuver, deep breathing test, quantitative sudomotor axon reflex test (QSART), and a skin biopsy for evaluation of small fiber neuropathy
7	On initial evaluation, obtain standardized measures of activity performance to compare to normal control values and to guide the initial activity prescription. Repeat the standardized measures of activity performance at follow-up visits to quantify functional changes and guide progression of the activity prescription

Abbreviation: ANA, antinuclear antibody; CBC, complete blood count; CMP, comprehensive metabolic profile; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; TFT, thyroid function tests.

TABLE 4: Health equity considerations and examples in post-acute sequelae of SARS-CoV-2 infection (PASC): Autonomic Dysfunction.

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Category	Comment	What is known	Clinical considerations
▸ **Disability** *Example: People with certain conditions that cause disability and autonomic dysfunction*	Individuals with pre-existing autonomic disorders require special consideration in the workup and management of autonomic dysfunction in PASC	The impact of PASC-related autonomic dysfunction should be considered early and often in individuals with possible baseline autonomic dysregulation. Autonomic dysfunction is known to occur in many different conditions that cause disability (e.g., Parkinson disease, multiple sclerosis, spinal cord injury [SCI], traumatic brain injury, and diabetes mellitus).[41] As an example, autonomic dysreflexia is a well- documented complication of SCI and can be a medical emergency warranting urgent attention. In SCI, autonomic dysfunction may be affected by the level and/or severity of the initial injury[42]	Depending on functional status, modifications may be required for a 10-min stand test in the office setting (e.g., some patients with SCI may be unable to perform supine to sitting to standing orthostatic maneuvers). Thus, modifications in usual testing protocols may be needed for this population The treatment of autonomic disorders in people with underlying SCI also requires careful consideration.[43,44] For example, increasing fluids may affect bladder protocols such as frequency of intermittent catheterization. Exercise and activity prescriptions should take into account paralysis, autonomic symptoms, and other considerations (e.g., underlying heterotopic ossification or rotator cuff dysfunction) People with SCI and other patients who have complicated medical conditions combined with autonomic dysfunction may require longer visits and more health care personnel (e.g., PM&R physicians, nurses, physical therapists, psychologists, social workers) to deliver optimal care[35]
▸ **Obesity** *Example: People diagnosed as overweight/obese*	Individuals who are overweight may have more severe COVID-19 acute infection and sequelae	Individuals who are overweight are at higher risk for COVID- 19 infections and associated morbidity and mortality.[45] Although research is still emerging, obesity may be a risk factor for PASC.[46] While the effect of excess weight on PASC-related autonomic function is not currently known, obesity does have documented effects on sympathetic nervous system activity[47,48]	Although it is unknown whether obesity is a risk factor for PASC-related autonomic dysfunction, it is important to recognize that individuals who are overweight and experiencing autonomic symptoms may need special consideration from a rehabilitation perspective. For example, addressing weight loss strategies can be done within their system of care and considering their own social determinants of health (SDOH). Identifying and treating sleep apnea, which is associated with obesity, is an important component of enhancing autonomic regulation and improving symptoms of fatigue.[48] Physical activity should be cautiously and appropriately prescribed to take into account obesity as a comorbidity

TABLE 4: Health equity considerations and examples in post-acute sequelae of SARS-CoV-2 infection (PASC): Autonomic Dysfunction.

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Category	Comment	What is known	Clinical considerations
▸ **Racial / Ethnic Minority Groups** *Example: People who identify as Black (including African- American), American-Indian/Alaska Native, Pacific Islander, Asian-American, and Mixed Race, and/or Latino/ Hispanic (ethnicity)*	Individuals who identify with historically, socially, or economically marginalized groups may be at higher risk for COVID-19 related morbidity and mortality	Throughout the pandemic, it has been documented that people who identify with racial/ethnic minority groups may be a higher risk for acute COVID-19 infection and more severe disease.[49] PASC- related sequelae have been reported to increase with more severe acute infection[5] and with more baseline comorbidities; race may also be a factor, though research is still emerging.[50] Race is among the factors that have been reported to affect heart rate variability, including with Postural Orthostatic Tachycardia Syndrome (POTS).[51] For example, while a majority of patients with POTS are young White/ Caucasian women, a diagnosis of POTS should not be missed in patients who identify with other races or in male patients[52]	While the incidence of autonomic dysregulation in various populations of PASC is still unknown, rehabilitation clinicians should be aware that patients who identify with historically, socially, or economically marginalized groups may experience disparities in diagnosis and treatment. The impact of SDOH should also factor into evaluation and management strategies to manage autonomic disorders. Vigilance about recognizing autonomic dysfunction is important. Educating clinicians and patients about how to access specialized care when needed is vital. The impact of PASC-related autonomic dysfunction should be considered in persons from all racial/ethnic minority groups and efforts to improve symptoms, function and participation should be a priority

TABLE 4: Health equity considerations and examples in post-acute sequelae of SARS-CoV-2 infection (PASC): Autonomic Dysfunction.

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Category	Comment	What is known	Clinical considerations
▸ **Biologic Sex** *Example: Pregnancy*	Sex differences should be considered for both the diagnosis and treatment of PASC-related autonomic disorders	Patients with POTS tend to present with a constellation of symptoms and the diagnosis is much more common in female adults (compared to male adults), typically occurring during childbearing years.[53] There is a paucity of literature on PASC-related autonomic dysfunction during pregnancy in individuals with pre-existing or new symptoms. However, it is known that both pregnancy and COVID-19 infection may affect autonomic regulation.[53,54] One survey study of patients with POTS showed challenges with diagnosis and multiple comorbidities.[55] In this study, female patients with POTS were impacted more regarding challenges with diagnosis, symptom burden, and quality of life. There was significant diagnostic delay of POTS, including 2 years longer in female than male patients	Among the medical community, there is limited awareness and recognition of autonomic conditions, inclusive of but not limited to POTS. POTS is a common autonomic disorder that is ideally managed by physicians and rehabilitation clinicians who recognize the heterogeneity of the syndrome and implement a tailored treatment approach.[56] Enhancing clinical education may reduce diagnostic delays as well as improve access to care and outcomes. Clinicians should be aware of implicit (unconscious) sex- related bias as this may add to the challenges for female patients with POTS or another autonomic related dysfunction; importantly, a misdiagnosis with psychiatric or psychological disorders is common[57] In pregnant individuals, rehabilitation interventions such as exercise prescriptions, should be carefully prescribed and based on an individual's ability to tolerate the exercise and the safety of the prescribed intervention for that person. Symptoms of POTS during pregnancy cannot be consistently predicted and may (perhaps counterintuitively) be worse in the first trimester whereas pregnancy related weight gain, pain, and balance problems (all of which may affect exercise prescriptions) may be more significant in the last trimester.[53] Diagnostic testing using radiation (e.g., chest x-ray or computed tomography) to rule out other conditions is usually contraindicated. Similarly, medications may be contraindicated during pregnancy (and in individuals who are breastfeeding) and therefore, caution is advised

TABLE 4: Health equity considerations and examples in post-acute sequelae of SARS-CoV-2 infection (PASC): Autonomic Dysfunction.

Category	Comment	What is known	Clinical considerations
▸ **Insurance** *Example: Individuals who are uninsured, underinsured, or cannot afford access to recommended healthcare services*	Insurance coverage, or lack thereof, should be considered when devising a treatment plan addressing autonomic-related issues in PASC. Encouraging patient engagement and addressing psychosocial factors may improve adherence with treatment recommendations	Autonomic disorders, including but not limited to POTS, are challenging to diagnose. This means that patients often undergo multiple evaluations and extensive medical testing.56 For patients who are uninsured or underinsured, the cost of securing a diagnosis and undergoing appropriate treatment may not be feasible. Financial hardships associated with COVID-19 acute infections and PASC- related sequelae are being increasingly documented57	Clinicians should be aware of the cost of diagnostic and treatment interventions. Consider the value of diagnostic testing to rule in/out various conditions. Treatment interventions, such as physical therapy, may be limited by the cost of copayments and deductibles, even in patients who have medical insurance. Individuals with post-COVID POTS and other autonomic disorders may need to be referred to an autonomic specialty clinic as guided by the assessment recommendation statements (Table 3).[5] Social services or community groups may assist persons with finding local support During the pandemic, there has been a broadening of insurance coverage for telemedicine services, including telephone visits and virtual visits online—leading to greater use of and access to these services. Telerehabilitation is evolving,[58] and patients have reported relatively high rates of satisfaction with physiatry[59] and therapy visits[60] Physicians should consider advocating on behalf of their patients who require immunotherapy to maintain their functional status by actively engaging in the appeal process when insurance deny coverage of this important therapy[61]

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

TABLE 5: Treatment recommendations for autonomic dysfunction in patients with PASC.

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No	Autonomic dysfunction in PASC treatment recommendations
1	For individuals diagnosed with autonomic dysfunction, provide education on etiology and management including identification of exacerbating and remitting factors
2	For individuals presenting with autonomic dysfunction and no evidence of post-COVID cardiovascular complications or other contraindications such as congestive heart failure, pericarditis, myocarditis, coronary artery disease or hypertension, start non- pharmacologic management including: • Increased fluid/salt intake: >3 L of fluid and >10 g of salt (4 mg of sodium) daily • Compression garments (waist-high stockings and/or abdominal binder) • Lifestyle management to include recognizing and avoiding symptom triggers and physical counterpressure maneuvers to mitigate orthostatic intolerance • Patient education, psychological support and coping skills • Consideration of discontinuation of medications or substances that may cause or exacerbate orthostatic intolerance, tachycardia or hypotension
3	For individuals with severe or persistent symptoms after a trial of non-pharmacologic measures, consider pharmacologic interventions • First-line medications: low-dose beta blockers (e.g. propranolol or atenolol); fludrocortisone; midodrine • Second-line medications: pyridostigmine; ivabradine; clonidine; methyldopa; modafinil, methylphenidate; selective serotonin reuptake inhibitors (SSRIs); serotonin and norepinephrine reuptake inhibitors (SNRIs); bupropion; droxidopa
4	Individuals with autonomic dysfunction may benefit from personalized autonomic rehabilitation program interventions to reduce fatigue and gradually improve exertional tolerance. This may start with activities in a supine or sitting position. The intensity of rehabilitation activities should be carefully titrated to avoid post- exertional symptomatic exacerbation. See: Multi- Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Fatigue in Post-Acute Sequelae of SARS-CoV-2 infection (PASC) Patients[17]
5	Consider referring individuals experiencing treatment- refractory or progressive symptoms to an autonomic specialist. https://americanautonomicsociety.org/ physician-directory/http://dysautonomiainternational.org/ page.php?ID=14

TABLE 6: Pharmacological treatment options for autonomic dysfunction.[84,85]

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Medication	Dose	Indications	Side effects/precautions
1st Line			
Propranolol Atenolol	5–10 mg BID to QID 12.5–25 mg QD to BID	POTS, IST, OH, NCS, episodic hypertension	Bradycardia, hypotension, fatigue, depression, asthma exacerbation
Fludrocortisone	0.05–0.2 mg QD	NCS, OH, POTS, hypotension	Hypokalemia, edema, headache
Midodrine	2.5–10 mg TID to QID	NCS, OH, POTS, hypotension	Scalp paresthesia, piloerection, supine hypertension
2nd Line			
Pyridostigmine	30–60 mg BID to TID	POTS, OH, AN, GI dysmotility with constipation	Diarrhea, muscle twitching
Ivabradine	2.5–7.5 mg BID	POTS, IST	Visual disturbance, headache, hypertension
Methylphenidate	5–10 mg BID to TID	NCS, OH, POTS, cognitive dysfunction, fatigue	Insomnia, headache, tachycardia
Modafinil	50–200 QD to BID	Cognitive dysfunction, hypersomnolence, fatigue	Tachycardia, insomnia
Clonidine	0.05–0.2 mg QD to TID or long- acting patch	POTS, episodic hypertension and/or tachycardia, anxiety	Hypotension, fatigue, brain fog
Methyldopa	125–250 mg BID	POTS, episodic hypertension and/or tachycardia, anxiety	Hypotension, fatigue, brain fog
Fluoxetine	10–40 mg QD	NCS, anxiety/depression	Anxiety, insomnia, nausea
Bupropion	75–150 mg QD to BID	POTS, NCS, fatigue, depression, hypersomnia	Nausea, anxiety, insomnia, decreased seizure threshold
Duloxetine	20–60 mg QD	NCS, OH, neuropathic pain, depression	Nausea, hypertension, Increased perspiration
Droxidopa	100–600 mg TID	FDA-approved for neurogenic OH; NCS and POTS in some cases	Headache, hypertension, tachycardia, nausea

TABLE 6: Pharmacological treatment options for autonomic dysfunction.[84,85]

Medication	Dose	Indications	Side effects/precautions
Other			
Desmopressin	0.1–0.2 mg QD prn	POTS, OH	Hyponatremia, edema
IV saline	1–2 L IV over 1–4 h prn	Decompensation of POTS, NCS, OH with dehydration, infection or GI dysmotility disorder	Avoid chronic frequent use that can lead to placement of central catheters, which can cause thrombosis and infection
IVIG	1–2 g/kg/month IV weekly to every 4 weeks	Severe, treatment-refractory POTS, SFN, and AN with positive autoimmune markers	Flu-like symptoms, headache, aseptic meningitis