# **TABLE 1:** Recommendations for the assessment of cardiovascular complications in patients with PASC



#	Cardiovascular complications assessment statement
1a	Patient History: A full patient history should be performed to include review of predisposing comorbidities, prior cardiovascular events, severity of the initial COVID-19 illness—mild, moderate, severe, including relevant hospitalization and care in the intensive care unit (ICU), need for ventilator, extra-corporeal membrane oxygenation (ECMO) etc., and timeline of symptom evolution.
	Additional components of the patient history should address:
	• Most common new or worsening cardiac symptoms: chest pain, palpitations, shortness of breath, near-or syncopal episodes, exercise intolerance, fatigue,
	• Studies conducted to date: labs, electrocardiogram, echocardiogram, chest imaging, other cardiac work-up if done (cardiac catheterization, cardiac magnetic resonance imaging, etc.),
	• Medication history—Evaluate for medications that may impact symptoms, signs or assessment parameters (ie, medications with antiarrhythmic, diuretic or vaso-active impact).
1b	Patient History: Symptoms should be characterized to understand contributing factors that limit activity including onset (new, acute or chronic), frequency, intensity, aggravating and alleviating factors, etc.
2a	Initial Evaluation: Clinicians should conduct a thorough examination of the cardiovascular system including routine vital signs (heart rate [HR], blood pressure [BP], pulse oximetry), auscultation of heart and lungs, peripheral pulses and bruits, and signs of volume overload.
2b	Initial Evaluation: For individuals reporting dizziness, lightheadedness, and syncope/presyncope clinicians should further characterize the perceived dizziness (lightheadedness vs. room spinning sensation) and differentiate between central or peripheral etiologies which warrant specialist referral.
2c	Initial Evaluation: To differentiate cardiovascular from autonomic dysfunction, check for orthostatic blood pressure and heart rate response in supine and standing position. If abnormal or symptoms are concerning for autonomic dysfunction, continue evaluation as per the autonomic dysfunction guideline including a 10-min active stand test. (Blitshteyn S, Abramoff B, Azola A, et al. Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Autonomic Dysfunction in Patients with Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): submitted to <i>PM&amp;R</i> , under review)
3	Order basic laboratory work-up in individuals with cardiac symptoms, or those without lab work-up in the 3 months prior to the visit. Consider: complete blood count, basic metabolic panel, troponin level (preferably high-sensitivity), brain natriuretic peptide or N-terminal pro b-type natriuretic peptide, D-dimer, C-reactive protein and erythrocyte sedimentation rate, lipid panel.
	Further laboratory work-up may be considered based on the results of the basic tests or if there is concern for specific cardiac conditions.
4	Clinicians should consider ordering electrocardiogram, echocardiogram, and/or ambulatory cardiac monitoring.
	Holter for symptoms occurring every day.
	• 14-day monitor (e.g., Ziopatch) for symptoms occurring every few days
	• Event monitor (looping or non-looping, mobile cardiac telemetry) for infrequent symptoms.
5	Where diagnosis is uncertain or symptoms are progressing or severe consider referral to a cardiologist for more detailed assessment (computed tomography of the chest, cardiac magnetic resonance imaging, cardiac stress testing, cardiopulmonary exercise testing).
6	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: PASC, postacute sequelae of SARS-CoV-2 infection.

## **TABLE 2:** Health Equity considerations and examples in post-acute sequelae of SARS-CoV-2 infection (PASC): Cardiovascular Complications



Category	Comment	What is known	Clinical considerations
Biologic Sex  Example: Female adults	Knowledge of areas of potential bias are important for clinicians to recognize and intentionally counteract in order to provide equitable healthcare.	Biologically female adults have some differences in cardiac risk factors as compared to male adults. For example, they go through menopause with ensuing physiologic changes (eg, hormonal, sarcopenia). Pregnancy has been reported to be a risk factor for more severe COVID-19 infection. <sup>54</sup>	Sex-related disparities have been reported and female adults may be underdiagnosed and undertreated for cardiac conditions, including referrals for cardiac rehabilitation. 55 Thus, it is important for clinicians to be aware of the potential for underdiagnosis or misdiagnosis and ensure that this group receives optimal care. Individuals with underlying and/or new PASC-related cardiac impairments should be considered for cardiac rehabilitation programs and referred in a timely manner. Pregnant individuals with baseline cardiac conditions and/or PASC-related cardiac conditions should be treated by clinicians who have expertise in this population as there are often contraindications with testing and treatment interventions that must be adhered to in order to protect the patient and fetus. Treating physicians should determine what type of rehabilitation interventions and/or programs will be most beneficial as well as considering other factors such as cost and availability.
Example: People with certain conditions that cause disability and cardiac dysfunction	Individuals with cardiovascular disease require special consideration in the workup and management of cardiac dysfunction in PASC. Further attention may be given for individuals with special needs and additional comorbidities.	People with disability due to spinal cord injury, stroke, and other common rehabilitation conditions are known to be at higher risk for cardiovascular disease. Many are also at higher risk for COVID-19 acute infection and/or more severe disease. The incidence of PASC-related cardiac sequelae has yet to be fully explored in patient populations with preexisting disability. However, clinicians should be aware of the overlapping issues of premorbid conditions associated with disability, risk of COVID-19 infection, severity of acute infection, and PASC sequelae. For example, patients with multiple sclerosis (MS) may be on disease modifying therapy (DMT), and both the MS and the DMT may put them at higher risk for COVID-19 acute infections as well as more severe course, though in a recent systematic review these were not consistent findings. The review included more than 80 reports involving 2493 patients with MS and 37 patients with "Neuromyelitis Optica Spectrum Disorder with COVID-19. Older age, higher expanded disability status scale (EDSS) scores, cardiac comorbidities, and obesity were independent risk factors for severe COVID-19.	The impact of PASC-related cardiac dysfunction should be considered in individuals with baseline comorbidities that involve disability. Cardiac assessments may need to be modified. For example, upper extremity aerobic exercise testing may replace lower extremity exercise testing in people with complete paralysis of the lower extremities 52; however, these tests may be challenging to interpret because of variability in cardiopulmonary responses. Treating physicians should determine whether the patient is referred for formal cardiac rehabilitation vs. other types of rehabilitation as the benefits, cost, and availability may vary, depending on a variety of factors. For safety purposes, patients may need to be cleared by a cardiologist prior to starting an exercise program. Safety precautions should be clearly documented and adhered to. Monitoring vital signs and pulse oximetry is important as is a patient's perceived exertion. Exercise and activity prescriptions, medications, injections, and other interventions aimed at supporting rehabilitation and enhanced function should be tailored to the individual and prescribed by clinicians who are experienced in caring for medically complex patients.

## **TABLE 2: Health Equity considerations and examples in post-acute sequelae of SARS- CoV-2 infection (PASC): Cardiovascular Complications** (continued)



Category	Comment	What is known	Clinical considerations
Racial / Ethnic Minority Groups  Example: People who identify as Black (including African- American), American-Indian/Alaska Native, Pacific Islander, Asian- American, and Mixed Race, and/or Latino/Hispanic (ethnicity)	Individuals who identify with groups that have been historically, socially, or economically marginalized may be at higher risk for COVID-19 related morbidity and mortality.	Historically marginalized racial/ ethnic minority groups have higher rates of COVID-19 infection and lower rates of access to health care services, <sup>57</sup> and these disparities are influenced by social determinants of health (SDOH). <sup>58</sup> The NACMI (North American COVID-19 and STEMI) registry demonstrated ST-segment elevation myocardial infarction (STEMI) in COVID positive patients disproportionately involving individuals from racial/ethnic minority groups (0%) with diabetes mellitus. <sup>59,60</sup>	Individuals from racial/ethnic minority groups have been reported to have lower referral rates to cardiac rehabilitation than people classified as White/Caucasian. All individuals with cardiac impairment and cardiovascular disease such as heart failure or myocardial infarction (MI) should be considered for cardiac rehabilitation programs and referred in a timely manner. Treating physicians should determine what type of rehabilitation interventions and/or programs will be most beneficial as well as considering other factors such as cost and availability. Every effort should be made to close gaps in health disparities and ensure optimal care for people who identify with racial/ethnic minority groups.
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 cardiovascular issues in PASC. Encouraging patient engagement and addressing psychosocial factors may improve adherence with treatment recommendations.	States with the highest rates of the uninsured will have widening disparities in health outcomes among minority and low-income populations, worsening for those persons with PASC. <sup>62</sup> Lower participation in cardiac rehabilitation has been documented in older participants, women, patients with comorbidities, unemployed and uncoupled persons, less educated people, and those with lower income. <sup>63</sup> A similar pattern was observed for cardiac rehabilitation adherence. Also, those potential participants who live farther from cardiac rehabilitation facilities, do not have transportation, or do not drive, attended fewer rehabilitation sessions. Access to telehealth services may be helpful for health care access to individuals with challenges transportation, distance, and/or mobility <sup>64,65</sup>	Clinicians should be aware of the cost of diagnostic and treatment interventions. Consider the value of diagnostic testing to rule in/out various conditions. Treatment interventions, such as physical therapy, may be limited by the cost of copayments and deductibles, even in patients who have medical insurance. Social services or community groups may assist persons with finding local support. Although access to telehealth services may facilitate care for some people, technology poses significant challenges for others. For example, individuals may have difficulty downloading, installing, and using new technology software or applications, a limited number of available digital devices, insufficient internet speed and bandwidth to manage audio and visual data, and poor quality of the camera and/or microphone on the device thus affecting the quality and diagnostic accuracy. <sup>66</sup> Insurance coverage for telemedicine services, including telephone visits and virtual visits online, has expanded during the pandemic—leading to greater use of these services. Telerehabilitation is often feasible <sup>65</sup> and patients have reported relatively high rates ofsatisfaction with physiatry <sup>67</sup> and therapy <sup>68</sup> .

## **TABLE 2: Health Equity considerations and examples in post-acute sequelae of SARS- CoV-2 infection (PASC): Cardiovascular Complications** (continued)



Category	Comment	What is known	Clinical considerations
Example: Younger and older individuals	Age should be considered in PASC-related cardiac conditions as this may affect clinical decision making.	Many clinical trials, including rehabilitation studies, have gaps in the inclusion of people across the age continuum, particularly children and older individuals. <sup>69</sup> Thus, clinicians should be aware that while PASC-related care needs will outpace the research for everyone, studies to guide the care of children and older individuals may be particularly slow to evolve. Nevertheless, studies are documenting issues such as multisystem inflammatory syndrome in children (MIS-C), also known as pediatric inflammatory multisystem syndrome, which is a potential complication in children recovering from COVID-19. <sup>70</sup> In a 1-year follow-up time period of a pediatric cohort, MIS-C associated cardiac manifestations included ventricular dysfunctions, pericarditis, coronaritis, and arrhythmias. <sup>71</sup> Fortunately, no subsequent cardiac anomalies were recorded on follow-up.  Myocarditis is a potential complication of viral syndromes, including for young athletes returning to sport, especially as this is an important cause of sudden cardiac death during exercise. <sup>72</sup> A review in patients with type 2 diabetes mellitus and PASC highlighted issues related to older individuals. <sup>73</sup> The report explained that in diabetes, neuropathy and myopathy contribute to muscle atrophy and sarcopenia and acute COVID-19 infection, hospitalization, protein deficiency, and corticosteroid therapy often cause rapid onset sarcopenia in severe COVID-19 infections. Acute COVID-19 infection may also contribute to new or worsening cardiovascular issues.	To prevent serious cardiac sequelae, including sudden death in younger athletes, cardiac return to play pathways have been developed. 72.74 Low-risk patients should rest for at least 10 days after being diagnosed with COVID-19. If asymptomatic for 7 days, they can begin a gradual return to physical activity.  Athletes with mild to moderate COVID-19 symptoms who fully recovered need a thorough assessment and history and physical examination. It is also recommended they have 12-lead electrocardiogram (EKG) and echocardiogram before return to play. If there are abnormalities, a cardiac magnetic resonance imaging (MRI) should be done to exclude myocarditis. Athletes with persistent COVID-19 symptoms who take longer than 14 days to recovery, are recommended to have a history and physical, 12-lead EKG, and cardiac MRI to check specifically for myocarditis. If the MRI is normal, then cardiopulmonary exercise testing and 23-h Holter EKG. These athletes cannot exercise maximally until initial investigations have been completed. Athletes with preexisting disabilities should ideally be followed by sports medicine specialists (eg, physiatrists, physical therapists).  If tests are abnormal in children and young athletes, a multidisciplinary team composed of specialists in cardiology, pulmonology, and sports medicine should collaborate to create a personalized exercise prescription for these patients.  In older patients with type 2 diabetes mellitus, strict control of blood sugar and other comorbidities, supervised physical activity and exercise, and optimal nutrition may be helpful in reducing and managing PASC symptoms. Because older individuals may have low skeletal muscle mass with baseline sarcopenia, following infection they may become weaker than premorbidly. Clinicians should be vigilant about recognizing new or worsening cardiovascular issues and cardiovascular stress with activity and/or exercise. For older individuals who have an upcoming surgery, prehabilitation may help to support optimal outcomes. For older ind

#### **TABLE 2:** Health Equity considerations and examples in post-acute sequelae of SARS- CoV-2 infection (PASC): Cardiovascular Complications (continued)



Category	Comment	What is known	Clinical considerations
• Obesity  Example: People who are diagnosed as overweight/obese	Obesity may not only increase the incidence and mortality associated with acute COVID- 19 infection but also development of PASC-related symptoms.	Obesity is an important risk factor for the development of severe COVID-19 infection and mortality. <sup>77</sup> Moderate and severe obesity (body mass index [BMI] ≥ 35 kg/m2) are associated with a greater risk of PASC.77 In one study, PASC symptoms were characterized by fatigue, headache, dyspnea, and anosmia and these were more likely with increasing age, increased BMI, and female sex. <sup>78</sup> High BMI and previous pulmonary disease could be risk factors for development of PASC in exposed health care workers. <sup>79</sup>	Recognize that obesity as a comorbidity can increase a patient's risk for PASC and cardiac complications. There may also be associations with sympathetic overactivity and hypertension. Addressing weight loss strategies can be done within the patients' system of care and in consideration with their own SDOH.  Obstructive sleep apnea is a common condition associated with obesity and should be addressed in order to optimize oxygenation and cardiac function as well as lessen fatigue.  Exercise and physical activity should be appropriately prescribed and consider obesity as a comorbidity.
Justice Involved (Prisons/Detention Centers)  Example: People who are incarcerated or detained in prisons, jails, youth detention centers, immigration detention centers, internment camps, and other facilities	People who are involved in some manner with various aspects of the criminal justice system, particularly those who are incarcerated in correctional facilities and detention centers, have a unique vulnerability to healthcare inequity that is often overlooked.	The proportion of COVID-19 cases is 5.5 times higher among people who are incarcerated. Literature describes the impact of COVID-19 on confined communities (including people who are immigrating, seeking asylum or incarcerated) and offers practical recommendations on physical activity recommendations to maintain their level of independence, physical health, mental health and wellbeing. Multiple factors contribute to a higher risk of cardiac disease in incarcerated women because of more cardiovascular health challenges.	Cardiovascular disease is a leading cause of death among individuals incarcerated in correctional facilities. <sup>82</sup> After accounting for differences in racial identity and socioeconomic status, persons recently released from correctional facilities have a higher risk of being hospitalized and dying of cardiovascular disease compared with the general population. <sup>82</sup> Appropriate testing and treatment for cardiac sequela of COVID-19 should be accessible for individuals under correctional supervision.

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

#### **TABLE 3:** Recommendations for the treatment of cardiovascular complications in patients with PASC



#	Cardiovascular complications treatment statement
1	Provide counseling and education for risk factor modification in individuals identified with risk factors for cardiovascular disease, including dyslipidemia, diabetes, hypertension, overweight/obesity, sedentary lifestyle, and depression. Education components can include:  • Lifestyle modifications • Diet/nutrition • Activity/exercise • Medications • Risk factors • Disease process • Reassurance
2	Evaluate and manage individuals diagnosed with new or worse complex arrhythmias in conjunction with a cardiologist.
3	Evaluate and manage individuals diagnosed with new or worse structural heart disease in conjunction with a cardiologist.
4	Evaluate and manage individuals diagnosed with new or worsened coronary heart disease in conjunction with a cardiologist.
5	Evaluate and manage individuals diagnosed with new or worse ventricular dysfunction in conjunction with a cardiologist.
6	Individuals with a recent history of cardiac events and diagnosis that qualifies them for cardiac rehabilitation—myocardial infarction, stable angina, coronary intervention (percutaneous coronary intervention including angioplasty or cardiac stenting), systolic heart failure with ejection fraction ≤ 35%, heart surgery such as coronary artery bypass surgery, heart valve repair or replacement, and heart or heart-lung transplant—should be referred for cardiac rehabilitation.
7	Individuals with prior history of athletic performance should be evaluated, counseled, and guided back to sports performance through a staged return to play approach

Abbreviation: PASC, postacute sequelae of SARS-CoV-2 infection.