

1 **Interim Guidance on the Preparticipation Physical Exam for Athletes**
2 **During the SARS-CoV-2 Pandemic**
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47 **Acknowledgments:**

48 The authors sincerely thank Jason Matuszak MD, for his encouragement and guidance of the
49 manuscript; Donald Kirkendall, ELS for his meticulous review of the references and manuscript;
50 Brian Williams, the Director for Advocacy of the American Medical Society for Sports
51 Medicine, for his expertise in this effort.

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54 **Conflicts of Interest and Source of Funding:**

55 Alex Diamond and Yvette Rooks are unpaid at-large members of the Sports Medicine Advisory
56 Committee of the National Federation of State High School Associations. The authors declare no
57 conflicts of interest and do not have any financial conflicts to disclose.

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ABSTRACT

The American Medical Society for Sports Medicine (AMSSM) convened a writing group to address the current evidence and knowledge gaps regarding preparticipation evaluation of athletes during the SARS-CoV2 pandemic. The writing group held a series of meetings beginning in April 2020. The task force reviewed the available literature and used an iterative process and expert consensus to finalize this Guidance Statement that is intended to provide clinicians with a clinical framework to return athletes of all levels to training and competition during the pandemic. The Statement is not intended to address treatment, infection control principles, or public health issues related to SARS-CoV2. The AMSSM task force acknowledges the clinical uncertainty, evolving public health objectives, and the limited data currently available to create this Guidance Statement.

[WORD COUNTS Abstract 125, Manuscript 3123 with 30 References and two supplementary tables]

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INTRODUCTION

As sports return to our landscape, an important step in “reopening the country” will be evaluating the health of each athlete and mitigating risk prior to participation. The number of confirmed severe acute respiratory syndrome corona virus 2 (SARS-CoV2) disease (COVID-19) cases and deaths continue to rise in the United States. While new information is published daily, much remains unknown about this virus and post infection risks to athletes. The potential effect of COVID-19 on an exposed or previously infected athlete is a major concern in sports medicine. There is, however, little data available on the young, fit, healthy, athletic population and much of these concerns are secondary to extrapolation of data from, hospitalized, older patients with comorbid conditions. This statement provides a framework and tools for evaluating athletes prior to sport participation in the setting of COVID-19 based on the best currently available evidence (as of July 2020) and expert opinion. The AMSSM Board of Directors appointed co-chairs (ABD, DMN) and task force members based on content expertise and the organization’s diverse membership demographics and practice settings. The co-chairs generated the outline and the writing group subsequently conducted an in-depth literature review. The writing group developed the manuscript based on exchanges from several virtual meetings, conference calls, and written communications.

THE ROLE AND OBJECTIVES OF THE PREPARTICIPATION PHYSICAL EXAM

The utility of preventive medicine visits in improving the health and outcomes of our patients is controversial among providers and national organizations. The preparticipation physical evaluation (PPE) is no different, especially when one considers the lack of standardization and

99 outcomes data related to the visits. The goals of the PPE are no different during the COVID-19
100 pandemic from those published in the 2019 Preparticipation Physical Evaluation Monograph 5th
101 edition (PPE5) ¹:

- 102 1. Determine the general physical and psychological health of the athlete.
- 103 2. Evaluate the athlete for conditions that may be life-threatening or disabling.
- 104 3. Evaluate for conditions that may predispose the athlete to injury or illness.
- 105 4. Serve as an entry point into the healthcare system for student athletes without an
106 established medical home.

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108 During the COVID-19 pandemic, an additional goal is to provide advice for student
109 athletes and parents regarding exercise volume and intensity, participation in sport, and
110 minimizing the risk of contracting the disease. In all patient encounters, healthcare providers
111 should emphasize the importance of exercise to both physical and mental health during a time
112 when we are supposed to be physical distancing.

113 Exercising outdoors with physical distancing is relatively safe, especially if there is no
114 sharing of athletic equipment (i.e., towels, clothing, shoes, balls, or sports specific equipment)
115 and there is no body contact. An important and challenging task within the PPE is to accurately
116 educate athletes about the increased risk of contracting the disease while participating in a team
117 sport, especially sports involving contact or collision. Sports organizations and professional
118 teams can control factors like disease testing, contact tracing, and quarantine of the athletes.
119 Teams at the high school level and most colleges will not have these resources available to help
120 decrease the risk of transmission. The potential risks need to be discussed in detail with the
121 patient and family at the time of the PPE. When determining medical eligibility and restarting

122 sport practice and competition, other factors should be considered, such as the disease burden in
123 the community, the overall health of the athlete, the living environment, each athlete's network
124 of friends and family members who may have comorbid conditions.

125 Finally, a currently infected or recovered athlete may have silent clinical pathology in any
126 organ, including the heart.² The cardiac complications may increase the risk of sudden death
127 associated with exercise. COVID-19 related damage to the kidney, lungs, and vascular system
128 have implications for fluid balance, coagulopathy, and heat stroke during exercise. The
129 healthcare provider needs to consider these implications for the recovering athlete and may need
130 additional diagnostic studies to determine medical eligibility.

131

132 General Considerations

- 133 • The PPE can be a part of the Health Supervision Visit (Well Child, Preventive, or
134 Wellness Exam) in the medical home but is not a substitute for the Health Supervision
135 Visit.
- 136 • A PPE determines medical eligibility for sports, but often does not address long-term
137 health concerns, immunizations, and healthy lifestyle when done outside the medical
138 home.
- 139 • If access to the medical home for a full PPE is not possible, at a minimum, the athlete and
140 parent should complete an interval history questionnaire that includes additional
141 questions about COVID-19 exposure, symptoms, or both. This will allow the PCP to
142 evaluate for recent COVID exposure or infection that may warrant further work-up or a
143 period of isolation before resuming sports.

- 144 • Health Supervision Visits are reimbursed by insurance and often require no copay while
145 Sports Physicals are typically an out of pocket expense. Billing for a health supervision
146 visit might preclude additional preventive visits for the calendar year.
- 147 • The ICD-10-CM code for sport related participation evaluation is Z02.5. Using the code
148 in the primary or secondary position may allow tracking of sports physicals within the
149 electronic medical record and also has the potential to allow research into the PPE visit
150 for short- and long-term outcomes.
- 151 • Integrating the return to sport across different ages and level of competition (e.g. youth,
152 secondary school, college, and professional) will vary and will be determined by
153 individual organizations and institutions according to local regulations and public health
154 considerations.

155

156 Timing, Setting, and Structure of the PPE

157 Timing

- 158 • PPE5 recommends a full evaluation every 2-3 years for athletes in grade school and high
159 school. The PPE should be performed at least six weeks before the start of practice with
160 annual updates of the history questionnaire and a limited exam for any problem areas
161 identified.
- 162 • Most states require a full PPE every 12-13 months, which is more frequent than
163 recommended.¹
 - 164 ○ The National Federation of State High School Associations (NFHS) released a
165 recommendation in April 2020 that recommends a one-year extension for PPEs
166 expiring during the 2020-21 academic year. This was recommended in the event

167 that limited access due to COVID-19 might result in significant delays in
168 obtaining an annual evaluation.³

169 ○ The American Academy of Pediatrics (AAP) recommends that there should be no
170 delay in either the PPE or well child checkups.¹ The AAP has guidance on
171 access to care during pandemic and on telehealth, recommending telehealth or in-
172 person as medically indicated.⁴

173 ● Providers must be aware of their state laws regarding the PPE. Sport association
174 requirements may have changed due to COVID-19. Sport associations continue to face
175 specific recommendations and providers need to keep abreast of policies that change
176 almost daily.

177

178 Setting and Structure

179 ● PPE5 recommends the evaluation be completed in the medical home with access to the
180 full medical record for all youth and high school athletes.¹

181 ● Group physicals are not recommended

182 ○ Group physicals may not even be possible due to physical distancing guidelines.

183 ● Providing PPEs in the medical home will improve continuity of care and confidentiality.¹

184 ● The authors recognize that performing PPEs in the medical home as well as
185 recommending no group PPEs may impose scheduling challenges for both health care
186 providers and families. We appreciate that these recommendations may limit access for
187 athletes who rely on mass physicals for their screening exam.

188 ● The athlete and accompanying parent or guardian should be screened for COVID-19
189 symptoms upon arrival to minimize risk of viral transmission during the PPE.

- 190 • An athlete who reports any recent symptoms should be evaluated and treated based on
191 clinical or laboratory diagnosis of COVID-19. The PPE should be postponed until the
192 athlete is well or symptom-free for at least two weeks. ⁵
- 193 • During the PPE, all parties (providers, patients, and family members) should wear masks
194 and stay six feet apart whenever possible.
- 195 • Virtual care visits may provide an alternative to in-person evaluation during the pandemic
196 ⁶⁻⁸ and can serve as an opportunity for athletes from underserved communities to access
197 care. ⁹ Health care providers will need to be flexible with patients that have internet,
198 language, or other barriers that might make virtual care difficult.
- 199 • Virtual care can potentially detect an athlete who is ill or was exposed to SARS-CoV2
200 and assist in directing timely care.
- 201 • Review the payment rules for the commercial plan(s) in which you participate,
- 202 ○ Virtual care visits for sports pre-participation evaluations are often not covered or
203 reimbursed
- 204 ○ Many commercial health insurance plans only allow virtual care encounters for
205 evaluation and management (E&M) codes.
- 206 • Given the potential health impacts of COVID-19 infection, affected athletes should be
207 evaluated in their medical home prior to resuming physical activity and organized sports.
208 ^{2,10}
- 209 ○ Athletes with sequelae related to COVID infection may require specialized
210 evaluation and care (cardiac, pulmonary, renal). ^{2,10-12}

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213 COVID-19 can have wide-ranging effects on the body both physically and mentally. Therefore,
214 the athlete will require individualized assessment of all body systems prior to resuming physical
215 activity and sports participation. Although COVID-19's effects have been found in most all
216 systems, the cardiovascular and pulmonary systems seem to be most concerning. The
217 supplemental questionnaire addressing medical issues specific to COVID-19 may be useful for
218 athlete screening (See Supplementary Table 1).^{2,10-12}

219

220 Cardiovascular

- 221 • Cardiac involvement is a recognized complication of COVID-19 with the potential for
222 myocarditis and rapid-onset heart failure.^{2,10-12}
- 223 • Myocarditis can lead to tissue scarring and fatal arrhythmias during and away from
224 exercise.^{10,12}
- 225 • The evaluation and management of athletes with prior infection regardless of
226 symptomatology is evolving (see Supplementary Table 2).^{13,14}

227

228 Pulmonary

- 229 • Lung tissue is directly affected by virus damage to the blood vessels.
- 230 • Athletes with pulmonary involvement may require additional testing during a potentially
231 long period of convalescence prior to returning to physical activity.

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234 Vulnerable Populations and Those with Preexisting Medical Conditions

235 As of July 2020, the CDC established that individuals of any age with the following underlying
236 medical conditions are at increased risk: chronic kidney disease, chronic obstructive pulmonary
237 disease, immunocompromised state (from solid organ transplant), obesity (BMI>30), serious
238 heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies), sickle cell
239 disease, type 2 diabetes mellitus. ¹⁵

240 While data is still fairly limited, the CDC has said people with the following
241 conditions might also be at an increased risk for severe illness from COVID-19: asthma
242 (moderate to severe), cerebrovascular disease, cystic fibrosis, hypertension,
243 immunocompromised state (from bone marrow transplant), immune deficiencies, HIV, use of
244 corticosteroids or use of other immune weakening medicines, neurologic conditions, liver
245 disease, pregnancy, pulmonary fibrosis, smoking, thalassemia, and type 1 diabetes mellitus. ¹⁵
246 Athletes with preexisting cardiac or pulmonary conditions should consult with their specialist
247 prior to athletic participation.

248 A few of these select issues are addressed further below:

249 The Pregnant Athlete

- 250 • Physical activity and exercise during pregnancy are associated with minimal risks and
251 have known benefits for most women. ¹⁵
- 252 • Pregnancy is on the list of conditions that may pose increased risk for severe COVID-19
253 illness. ¹⁶ Complications and adverse outcomes related to COVID-19 have been reported
254 among pregnant women. ¹⁶

- 255 • Pregnant athletes should take precautions to protect themselves against the virus and
256 immediately report any possible signs and symptoms to their primary obstetrics provider.

257 16

258 The Diabetic Athlete

- 259 • Diabetic athletes may present with abnormal blood glucose responses to otherwise
260 normal dietary intake and exercise instead of the usual initial symptoms associated with
261 the disease. 17,18

- 262 • Diabetic athletes should be instructed to watch for subtle manifestations of disease such
263 as elevated blood glucose, fatigue, polyuria, and polydipsia. 17,18

264 The Hypertensive Athlete

- 265 • Because of the interaction between SARS-COV-2 and ACE2 and the role of ACE2 in the
266 pathogenesis of hypertension, it has been speculated that hypertension may be involved in the
267 pathogenesis of COVID-19. 19 Early reports, however, have not revealed the extent of the
268 relationship between hypertension and disease severity. 20-22

- 269 • Hypertensive athletes with COVID-19 should continue ACE-I, angiotensin receptor blockers
270 (ARBs), or other medication unless they have hypotension or hypokalemia. 5,23

- 271 • Use of these medications by hypertensive patients is not associated with worse outcomes.

272 22,24

273 The Asthmatic Athlete

- 274 • Chronic pulmonary conditions and moderate-severe asthma are correlated with poor
275 COVID-19 outcomes. 15

- 276 • Athletes with asthma should use their usual medications, including inhaled steroids.

- 277 • Worsening asthma symptoms in a well-controlled athlete may be an early sign of COVID
278 infection. This should prompt daily use of a peak flow meter and COVID-19 antigen
279 testing.

280 Athletes with Severe Obesity

- 281 • Evidence suggests obese and excessively overweight weight people are at a higher risk of
282 death or serious outcome. Weight does not, however, appear to affect a person's chances
283 of contracting COVID-19.²⁵
- 284 • The CDC defines severe obesity as BMI ≥ 40 kg/m² and a potential risk for severe illness.
285 However, the literature associated with COVID-19 employs variable definitions of
286 obesity including BMI ≥ 25 kg/m².¹⁷
- 287 • Lifestyle modifications are generally recommended. The potential complications from
288 COVID-19 associated with obesity should be emphasized.^{17,18}
- 289 • Athletic participation should not be dependent exclusively on BMI. Participation should
290 take into account an athlete's overall risk-to-benefit ratio in engaging in physical activity.

291 Athletes with Sickle Cell Trait

- 292 • Although sickle cell disease is considered a higher risk condition for adverse outcomes
293 from COVID-19 infection by the CDC, sickle cell trait (SCT) is not.¹⁷
- 294 • No additional precautions are recommended for returning athletes with SCT; however, if
295 an athlete with SCT contracts COVID-19, team physicians should be vigilant for issues
296 related to hypercoagulability for several months into recovery.¹⁷

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During the COVID-19 Era or Pandemic

After the evaluation, the primary care provider’s decision about medical clearance remains consistent with PPE5 ¹:

- medically eligible for sports without restrictions
- medically eligible for sports without restriction, but further evaluation needed
- medically eligible for certain sports listed on the form
- not medically eligible for any sports, pending further evaluation
- not medically eligible for any sports

COVID-19 negative and asymptomatic athletes can participate based on their medical eligibility while following physical distancing guidelines and monitoring for symptom development on a daily basis. ¹² Individuals with comorbidities placing them at increased risk should be withheld from group training and competition with other athletes until participation is determined to be safe or a vaccine is available.

For athletes who have fully recovered from COVID-19, the medical eligibility criteria are rapidly evolving, and it will be essential for providers to stay abreast of the current recommendations.

- COVID-19 positive without symptoms should not exercise for a determined period of time and remain in self-quarantine while monitoring for symptoms. ^{12,13,26-28}
 - If the athlete is asymptomatic after a given period of time, exercise may be gradually resumed with medical supervision ^{12,13,26-28}
 - A 12-lead EKG should be considered in asymptomatic athletes.

- 322 • COVID-19 positive athletes with mild symptoms and no hospitalization should be
323 symptom-free for a determined period of time before beginning a gradual return to
324 activity and stop activity if symptoms return. ^{12,13,26-29}
- 325 ○ If symptoms return, an evaluation by a sports medicine physician or primary care
326 provider who is well versed in physical activity and COVID-19 is recommended.
327 ^{11,12}
- 328 ○ To determine medical eligibility for physical activity, an electrocardiogram
329 (ECG), echocardiogram (ECHO), and other evaluation may be required (See
330 Table 1). ^{12,13,26-28}
- 331 • COVID-19 positive athletes with symptoms that require hospitalization should have a
332 cardiac evaluation prior to discharge. ^{11,12}
- 333 ○ After discharge, the athlete will need to continue seeing the sports medicine
334 physician or primary care provider while they gradually return to sport. ¹²
- 335 • Various organizations provide recommendations regarding minimum resting period
336 without physical activity following exposure or infection. There is also similar debate on
337 the timing and processes regarding return to play. ^{12,26,27,29}
- 338 • Referral to a subspecialist may be necessary
- 339
- 340

341 ANTICIPATORY GUIDANCE

342 In the world of sport, the challenges of returning to training and competition must be met with
343 the reality that things have changed, and will continue to change, so our athletes will need to

344 adapt. The athlete must be an active participant in maintaining their own health and safety, and
345 the health and safety of others.

346

347 Expanding sport opportunities and returning to play will depend on many factors
348 including:

- 349 • Athlete health
- 350 • Athlete exposure to COVID-19
- 351 • Geographic location and local prevalence of COVID-19
- 352 • Local and state pandemic guidelines
- 353 • Type of sport
- 354 • Acceptance of risk by student-athletes and parents and willingness on the part of members of
355 the team to cooperatively participate in risk-reducing behaviors.

356

357 Epidemiologic and clinical data regarding return to play guidelines for athletes are
358 limited. All health care providers should use their best judgement along coupled with community
359 recommendations in their geographic location.¹²

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362 **ADVOCACY, LEGAL CONCERNS, AND FINANCIAL ISSUES**

363 The Health Insurance Portability and Accountability Act (HIPAA) and the Family Educational
364 Rights and Privacy Act (FERPA) continue during the pandemic, so private information in
365 updated medical histories and other materials should not be shared with school or athletic
366 administration.

367 PPE5 suggests rescinding medical eligibility, either temporarily or permanently, when
368 medical conditions are discovered after eligibility has been established and COVID-19 infection
369 is such a condition.

370 Who actually performs the PPE is determined by states and sport governing bodies. For
371 athletes with a prior COVID-19 infection, we recommend that a sports medicine physician or
372 primary care provider with expertise in the care of athletes should determine medical eligibility.

373 Performing out-of-state or international virtual care visits may have legal and malpractice
374 liability issues. Several states have granted temporary licensure or medical privileges to
375 providers in bordering states during the pandemic. Several state boards also issued a special
376 purpose license, telemedicine license or certificate, or a license to practice medicine across state
377 lines. Prior to providing out-of-state PPEs, it is essential for physicians to know the regulations
378 of both their home state as well as neighboring states that grant temporary privileges, which are
379 accessible at the Federation of State Medical Boards.³⁰

380 PPEs are often not covered or reimbursed for virtual care visits and coding. Commercial
381 health insurance plans vary in allowable codes for telemedicine encounters. We recommended
382 ongoing monitoring and reviewing payment rules for the commercial plan(s) in which you
383 participate.

384

385 **FUTURE DIRECTIONS**

386 Evidence-based data specifically addressing the athlete during the COVID-19 pandemic
387 continues to evolve and AMSSM supports research in this area to validate the evaluation and
388 activity recommendations provided in this statement. AMSSM is committed to developing a

389 longitudinal framework with all stakeholders for improving recommendations for medical
390 eligibility and return to sport for athletes at all levels during the pandemic.

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CONCLUSION

393 The PPE monograph 5th edition is the most comprehensive and appropriate guide for performing
394 the PPE. ¹ The purpose of this document is to address the unique issues associated with the
395 COVID-19 pandemic. Providers must remain alert for the ever-changing nature of this pandemic
396 and seek additional data to drive our medical decision making.

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LIST OF SUPPLEMENTARY TABLE CAPTIONS

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500

501 Table 1: Supplemental COVID-19 Questions

502

503 Table 2. Cardiac Evaluation in Athletes with Prior COVID-19 Infection

504

505 Table 1: Supplemental COVID-19 questions

506 1) Have you had any of the following symptoms in the past 14 days?

507 a) Fever or chills Y/N

508 b) Cough Y/N

509 c) Shortness of breath or difficulty breathing Y/N

510 d) Fatigue Y/N

511 e) Muscle or body aches Y/N

512 f) Headache Y/N

513 g) New loss of taste or smell Y/N

514 h) Sore throat Y/N

515 i) Congestion or runny nose Y/N

516 j) Nausea or vomiting Y/N

517 k) Diarrhea Y/N

518 l) date symptoms started _____

519 m) date symptoms resolved _____

520

521 2) Have you ever had a positive test for COVID-19? Y/N

522 a) If yes:

523 i) Date of test _____

524 ii) Were you tested because you had symptoms? Y/N

525 (1) If yes:

526 (a) Date symptoms started _____

527 (b) Date symptoms resolved _____

528 (c) Were you hospitalized? Y/N

529 iii) Were you tested because you were exposed to someone with COVID-19, but you did not have any
530 symptoms? Y/N

531

532 3) Have you ever had a positive test for COVID-19 antibodies Y/N

533 a) If yes: Date of test _____

534

535 4) Has anyone living in your household had any of the following symptoms or tested positive for COVID-19 in the
536 past 14 days? Y/N

537

538 i) If Yes, circle the applicable symptoms.

539 • Fever or chills

540 • Cough

541 • Shortness of breath or difficulty breathing

- 542 • Fatigue
- 543 • Muscle or body aches
- 544 • Headache
- 545 • New loss of taste or smell
- 546 • Sore throat
- 547 • Congestion or runny nose
- 548 • Nausea or vomiting
- 549 • Diarrhea

550

551 5) Have you been within 6 feet for more than 15 minutes of someone with COVID-19 in the past 14 days? Y/N

552 i) If yes: date(s) of exposure _____

553

554

555

556

Table 2. Cardiopulmonary Evaluation in Athletes with Prior COVID-19 Infection¹

Clinical Scenario	Recommended Assessment	Comments
Athletes with prior asymptomatic infection as confirmed antibody to SARS-Coronavirus-2	<p>Focused Medical History and Physical Examination to screen for findings newly emergent in the COVID-19 era.</p> <p>Consider 12-lead ECG²</p>	<ul style="list-style-type: none"> · Myopericarditis related to COVID-19 should be considered in patients with a history of new onset chest pain, pressure, or both (even in the absence of fever and respiratory symptoms), palpitations, or exercise intolerance. · Comprehensive clinical evaluation, regardless of ECG findings, is indicated in athletes with new onset cardiovascular symptoms or exercise intolerance. · If ECG is abnormal or shows new repolarization changes compared to a prior ECG, then additional evaluation with at minimum an echocardiogram and exercise test is warranted in conjunction with a sports cardiologist.
Athletes with a history of mild illness (non-hospitalized) related to confirmed or suspected COVID-19	<p>Focused Medical History and Physical Examination to screen for persistent or new post-infectious findings following COVID-19 infection.</p> <p>Perform 12-lead ECG²</p>	<ul style="list-style-type: none"> · ECG findings that may indicate viral-induced myocardial injury include pathological Q waves, ST segment depression, (new) diffuse ST segment elevation, and T-wave inversion. · Comprehensive clinical evaluation, regardless of ECG findings, is indicated in athletes with new onset cardiovascular symptoms or exercise intolerance. · If ECG is abnormal or shows new repolarization changes compared to a prior ECG, then additional individualized evaluation is warranted, including at minimum echocardiography and exercise testing, in conjunction with a cardiologist.

Athletes with a history of moderate to severe illness (**hospitalized**) related to confirmed or suspected COVID-19

Comprehensive evaluation prior to return to sport, in conjunction with a cardiologist, to include blood biomarker assessment (i.e. Tn, NP), 12-lead ECG, echocardiography, exercise testing, and ambulatory rhythm monitoring. Additional recommendations include chest radiograph, spirometry, pulmonary function testing, chest CT.

- Myocardial injury is more likely in patients with a more severe disease course, and normal cardiac function and exercise tolerance should be established prior to a return to exercise.
- Cardiac MRI may be considered based on clinical suspicion of myocardial injury.³

Athletes with a history of COVID-19 infection (regardless of severity) AND documented myocardial injury as indicated by one or more of the following: in-hospital ECG changes, HS-Tn or NP elevation, arrhythmia, or impaired cardiac function.

Comprehensive evaluation prior to return to sport, in conjunction with a sports cardiologist, to include blood biomarker assessment (i.e. Tn, NP), 12-lead ECG, echocardiography, exercise testing, ambulatory rhythm monitoring, and cardiac MRI.²

- Return to training should be gradual and under the supervision of a cardiologist.
- Longitudinal follow-up including serial cardiac imaging may be required in athletes with initially abnormal cardiac function.

Tn = cardiac troponin, NP = natriuretic peptide; ECG = electrocardiogram; MRI = magnetic resonance imaging

¹Table modified from Drezner, et al.²⁶

²ECG as a screening test to exclude myocarditis is limited. ECG in patients with myocarditis may be normal or show nonspecific abnormalities. Additional evaluation may be warranted based on clinical suspicion.

³Cardiac MRI should be performed with gadolinium to assess for myocardial scar and late gadolinium enhancement (LGE). The presence of LGE is associated with a higher risk of major adverse cardiovascular events.

