

**TITLE**

Recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people

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1 **Recent COVID-19 vaccination has minimal effects on the physiological responses**  
2 **to graded exercise in physically active healthy people**

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18  
19 **Running Title:** Exercise responses after COVID-19 vaccination

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## 40 Abstract

41 Athletes are advised to receive the COVID-19 vaccination to protect them from SARS CoV-2 infection  
42 during major competitions. Despite this, many athletes are reluctant to get the COVID-19 vaccine due to  
43 concerns that symptoms of vaccinosis may impair athletic performance. **OBJECTIVE:** To determine the  
44 effects of COVID-19 vaccination on the physiological responses to graded exercise. **METHODS:** Healthy  
45 physically active participants completed a 20-minute bout of graded cycling exercise at intensities  
46 corresponding to 50, 60, 70 and 80% of the pre-determined  $\dot{V}O_{2max}$  before and ~21 days after receiving  
47 the COVID-19 vaccine (2 dose Pfizer mRNA or 1 dose Johnson&Johnson). **RESULTS:** Vaccination had no  
48 effect on a large number of physiological responses to exercise measured in blood (e.g. lactate,  
49 epinephrine, cortisol) and by respiratory gas exchange (e.g. oxygen uptake,  $CO_2$  production, ventilation,  
50 respiratory exchange ratio, predicted  $\dot{V}O_{2max}$ , ventilatory threshold) ( $p>0.05$ ). We did, however, find  
51 significant elevations in heart rate (~5 bpm) and norepinephrine ( $p = 0.006$  and  $0.04$ , respectively) in  
52 response to vigorous (e.g. 70-80%  $\dot{V}O_{2max}$ ) intensity exercise after vaccination, particularly in those that  
53 received the two shot Pfizer mRNA vaccine regimen. These findings held true when compared to  
54 demographically matched controls who completed identical bouts of exercise several weeks apart  
55 without receiving a vaccine; delta values for heart rate ( $p=0.03$ ) and norepinephrine ( $p=0.01$ ) were  
56 elevated in the second trial for those that received the Pfizer mRNA vaccine compared to the controls at  
57 the 70% and 80%  $\dot{V}O_{2max}$  stages, respectively. **CONCLUSION:** Recent COVID-19 vaccination has minimal  
58 effects on the physiological responses to graded exercise in physically active healthy people. The small  
59 elevations in cardiovascular and neuroendocrine responses to exercise after the Pfizer mRNA vaccine  
60 regimen could have implications for athletes at the elite level and warrants investigation.

61 **Keywords:** SARS-CoV-2; athletes; metabolic response; Pfizer; Johnson & Johnson; physical activity

## 62 63 New and Noteworthy

- 64 • Recent COVID-19 vaccination does not affect a large number of physiological responses to  
65 graded exercise, indicating that vaccination is unlikely to impair exercise capacity in normal  
66 healthy people
- 67 • Small but significant elevations in heart rate and norepinephrine responses to exercise were  
68 found after the Pfizer mRNA vaccination but not controls
- 69 • The small elevations in cardiovascular and endocrine responses to exercise after recent COVID-  
70 19 vaccination could have implications for athletes performing at the elite level
- 71 • How COVID-19 vaccination affects metabolic responses to exercise and performance in elite  
72 athletes warrants investigation, particularly because booster shots or new vaccines may be  
73 required for continuous protection against SARS-CoV-2 and its evolving variants

## 74 75 Introduction

76 The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) - etiological agent of coronavirus  
77 disease 2019 (COVID- 19)- was first identified in December 2019 in Wuhan, China, before being declared  
78 a global pandemic in March 2020 (1). As of November 2021, more than 250 million people worldwide  
79 have been infected with SARS CoV-2, which has resulted in ~5.1 million deaths. The rapid production  
80 and distribution of mRNA (e.g. Pfizer and Moderna) and viral vector-based vaccines (e.g.  
81 Johnson&Johnson and AstraZeneca) was initiated in November 2020 and has greatly limited the spread  
82 of COVID-19 (2), with 40% of the world's population now fully vaccinated (3). Several clinical trials have

83 demonstrated the safety and efficacy of the current COVID-19 vaccines (4–6), with reported side-effects  
84 such as body aches, fever, arm soreness, malaise and flu-like symptoms usually mild and typically  
85 resolving within 48h (7). However, reports are emerging that COVID-19 vaccination in a minority of  
86 patients has been associated with more severe and longer lasting symptoms including myocarditis  
87 fatigue, shortness of breath, cough, joint and chest pain (8,9).

88 Athletes are recommended to receive all necessary vaccines prior to competition due to increased risks  
89 of viral exposure (10). A recent study in elite German athletes found that the quadrivalent inactivated  
90 influenza vaccine evoked a strong immune response with no reported side-effects or loss of training  
91 (11). However, due to emerging reports (albeit mostly anecdotal) of adverse symptoms associated with  
92 COVID-19 vaccines, there is a growing concern among the athletic community that vaccination might  
93 hinder athletic performance. This has resulted in many athletes refusing to get vaccinated prior to or  
94 during competition, leaving them susceptible to SARS-CoV-2 infections during major sporting events.  
95 Indeed, during current/recent sporting events such as the 2021 European Championship and Copa  
96 America international soccer tournaments, as well as the Tokyo Olympic Games, there were multiple  
97 incidences involving players/athletes having to miss games/competition due to contracting SARS-CoV-2,  
98 or having been in contact with infected individuals.

99 In order to alleviate or confirm concerns regarding the potential negative effects of COVID-19  
100 vaccination on athletic performance, there is a critical need to determine if recent COVID-19 vaccination  
101 affects physiological responses to various intensities of exercise. Here we investigated the effects of  
102 recent COVID-19 vaccination on metabolic and physiological responses to graded cycling exercise in  
103 physically active healthy individuals. We report that COVID-19 vaccination has minimal effects on the  
104 physiological responses to graded exercise in healthy people, although small increases in the  
105 cardiovascular and neuroendocrine response to vigorous exercise that were observed after vaccination  
106 could have implications for athletes at the elite level.

107

## 108 **Methods**

109

### 110 **Participants**

111 A total of eighteen (9 females, 9 males) healthy individuals between the ages of 24-43 years participated  
112 in this study. Baseline anthropometric and cardiovascular characteristics are shown in Table 1. Twelve  
113 participants received a COVID-19 vaccine during the study period [Pfizer mRNA vaccine (n=9),  
114 Johnson&Johnson viral vector-based vaccine (n=3)] while six participants, who were involved in a  
115 parallel non-vaccine related research study in our laboratory, served as controls. Prior to their  
116 enrollment, each subject completed an AHA-ACSM preparticipation screening questionnaire and  
117 medical history survey (12) to verify that they had not been previously diagnosed with any  
118 cardiovascular, metabolic, renal, liver, pulmonary, asthmatic, rheumatic, or other inflammatory  
119 disease/condition and were not currently under the administration of medication known to alter their  
120 inflammatory or metabolic profiles. All participants were additionally screened for physical activity  
121 participation to ensure the enrollment of active individuals – physical activity rating score > 4 (13).  
122 Moreover, research participants were non-users of tobacco products and consumed ten or less standard  
123 alcoholic beverages per week on average. Participants were asked to abstain from alcohol, caffeine, and  
124 physical activity 24h prior to exercise trials and complete an overnight (minimum 8h and maximum 12h)  
125 fast prior to each laboratory visit. Adherence to these pre-testing procedures were confirmed verbally  
126 with the participants upon their arrival to the laboratory. All participants provided written informed  
127 consent and all procedures were performed in accordance with the ethical guidelines provided by the

128 Belmont Report. The Institutional Review Board (IRB) of the University of Arizona granted ethical  
129 approval (#2102477676) and the trial was registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT05019456).

130

### 131 **Experimental Design**

132 The study required participants to visit the laboratory on three separate occasions. Visit 1 involved a  
133 pre-screening procedure to verify that participants were eligible for the study and healthy enough to  
134 perform vigorous intensity exercise and to provide written consent (ACSM/AHA questionnaire). Eligible  
135 participants then completed a submaximal graded exercise test on a cycling ergometer (Velotron, Quarq  
136 Technology, San Diego, CA) to determine predicted maximal oxygen consumption ( $\dot{V}O_{2max}$ ). Blood  
137 samples were also collected during this visit to confirm serological status against SARS-CoV-2 using a  
138 commercially available ELISA kit (SARS-CoV-2 Spike S1 Human IgG; Biolegend, San Diego, USA). Visit 2  
139 occurred 1-3 weeks after the first visit and required the participants to complete a continuous 20-  
140 minute graded cycling exercise with multiple blood collections from an intravenous catheter. Visit 3  
141 required participants to perform the exact same trial that was performed during Visit 2 at 1-3 weeks  
142 after receiving the final COVID-19 vaccine dose via their own health care provider. This corresponded to  
143 an elapsed time of 5-7 weeks between Visit 2 and Visit 3. Participants arrived at our laboratory at the  
144 exact same time of day across all trials, which were performed between 06:00-09:00 local time.

145

### 146 **Submaximal Exercise Testing Procedure (Visit 1)**

147 Upon arrival at the laboratory, participants were briefed regarding the nature of the testing protocol,  
148 and height, weight and resting blood pressure measurements were collected. Each participant was  
149 assessed for appropriate apparatus sizing (e.g., metabolic cart face mask) and cycling ergonomics (e.g.,  
150 saddle height, handlebar reach, etc.) and these were recorded so they could be replicated during  
151 subsequent visits. Prior to initiating the test, all participants performed 3-5 minutes of seated rest on the  
152 cycling ergometer) for the collection of resting heart rate and respiratory gas exchange data. This was  
153 followed by a 5-minute warm-up period of cycling at 50 watts (W). Thereafter resistance was increased  
154 by 15 watts every minute and participants were asked to maintain a consistent cycling cadence  
155 throughout the entire exercise bout ( $\geq 60$ rpm). Exercise continued until the participant reached 85% of  
156 age-predicted maximum heart rate ( $220 - \text{age}$ ). Estimated  $\dot{V}O_{2max}$  was determined using the built-in  
157 algorithm contained within the metabolic cart software (Quark CPET, COSMED, Pabona di Albona  
158 Laziale, Italy). Heart rate and rating of perceived exertion (RPE; Modified BORG 0-10 scale - (14)) were  
159 recorded during the final 15 seconds of each exercise stage. Individual linear regression equations were  
160 established for each participant and used to determine cycling power outputs corresponding to various  
161 percentages of the  $\dot{V}O_{2max}$  for the main exercise trials performed during Visit 2 and Visit 3.

162

### 163 **Main Exercise Trial (Visit 2 and 3)**

164 During Visit 2 and Visit 3, participants' weight was re-recorded, and an indwelling catheter (BD, Franklin  
165 Lakes, NJ, USA) was inserted to an antecubital vein so that serial blood draws could be collected before,  
166 during and after exercise. The catheter was flushed with isotonic saline after each blood draw and a 2mL  
167 volume was drawn and discarded prior to collecting the blood sample used for analysis. Blood was  
168 collected into a 6mL vacuum tube containing a serum separator gel (BD Vacutainer® blood collection  
169 tubes). Participants were then asked to complete a 5-minute warm up at 50W before cycling  
170 continuously for an additional 20-minutes at graded intensities. The 20-minute trial consisted of four  
171 incremental 5-minute stages with power outputs corresponding to 50%, 60%, 70%, and 80% of the  
172 individual predicted  $\dot{V}O_{2max}$ . Participants again were asked to maintain a consistent cycling cadence  
173 throughout the entire exercise session ( $\geq 60$ rpm) and heart rate and respiratory gas exchange were  
174 measured throughout with RPE being recorded during the final 15 seconds of each exercise stage. To  
175 reduce the influence of a respiratory lag phase at the beginning of each incremental stage of the

176 exercise protocol, the heart rate and breath-by-breath respiratory data obtained during the final 3-min  
177 of each stage was averaged and processed for analysis (15).

178  
179 Blood samples were collected at 4 separate time points during these visits: (i) at rest; (ii) during the 60%  
180  $\dot{V}O_{2max}$  stage; (iii) during the 80%  $\dot{V}O_{2max}$  stage; and (iv) at 1h after exercise cessation. An exception to this  
181 was the control participants who performed identical exercise protocols as part of a parallel but  
182 separate research study in our laboratory but had blood collected at rest and during the 80%  $\dot{V}O_{2max}$   
183 stage only. To maintain consistency, the absolute cycling power outputs for each individual were  
184 identical during Visit 2 and Visit 3. During Visit 3, the resting serum sample was also used to confirm that  
185 all vaccinated individuals had seroconverted and presented with a positive SARS-CoV-2 IgG titer. To  
186 exclude the possibility of including participants that had been infected naturally between laboratory  
187 visits, whole blood samples collected in two LH tubes was stimulated with overlapping peptide pools  
188 spanning the breadth of the spike, membrane and nucleocapsid antigens (10 $\mu$ g/mL; Miltenyi) prior to  
189 measuring IFN- $\gamma$  in plasma by ELISA (R&D Systems; Minneapolis, MN, USA) following methods we  
190 recently described (16). No responses to membrane or nucleocapsid antigen were found post-vaccine in  
191 the participants who had not been infected naturally (not shown)(17).

192  
193 **Assessment of Serum Biomarkers**  
194 Blood collected into vacutainers containing a serum gel separator were allowed to rest for 30 minutes  
195 and subsequently centrifuged at 1500 RCF for 10 minutes. Serum was then collected and stored at -80°C  
196 until future analysis of cortisol (EIAHCOR, INVITROGEN®, Frederick, MD, USA), lactate (MAK064, SIGMA-  
197 ALDRICH®, St Louis, MO, USA), and catecholamine release (BA E-6500R, LDN®, Nordhorn, Germany) by  
198 standard enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's instructions.

199  
200 **Statistical Analysis**

201 All data are presented as the mean  $\pm$  standard deviation (SD) unless otherwise stated. All statistical  
202 analyses were completed using GraphPad Prism 8.0. Linear mixed models (LMM) or repeated measures  
203 ANOVA were used to analyze all metabolic and blood data, with Sidak post hoc test to determine  
204 differences between trials and groups. The model included main effects for group (vaccinated vs  
205 control), time (exercise workload) and trial (Pre vs Post vaccine, or Trial 1 vs Trial 2 in the controls) and  
206 interaction (Group x Time x Trial) effects. Main effects for Time and Trial and interaction effects (Time x  
207 Trial) were also determined within each group. Paired sample T-tests were used to detect differences in  
208 predicted  $\dot{V}O_{2max}$  and time to ventilatory threshold between the trials performed during Visit 2 and Visit  
209 3. Significance was set at  $p < 0.05$

210 **Results**

211 *COVID-19 vaccination is associated with an elevated heart rate and norepinephrine response to graded*  
212 *cycling exercise in healthy individuals*

213 To determine if COVID-19 vaccination is associated with changes in the physiological responses to  
214 exercise, we first of all compared pre and post vaccine exercise responses in the entire vaccinated  
215 cohort (n=12) regardless of SARS CoV-2 exposure status or vaccine type (Figure 1). Overall, the  
216 physiological responses to exercise were similar between trials but we did find significant interaction  
217 (Time x Trial) effects for heart rate (HR) and serum norepinephrine levels, with were elevated during  
218 exercise after vaccination. Post-hoc analysis revealed that HR was elevated at the 60% and 70%  $\dot{V}O_{2max}$   
219 stage ( $p = 0.02$  and  $0.0005$  respectively) and norepinephrine levels were elevated at the 80%  $\dot{V}O_{2max}$   
220 stage ( $p=0.002$ ) compared to the pre-vaccine trial. The RPE tended to be lower post vaccine at the 50%

221  $\dot{V}O_{2\max}$  stage ( $p = 0.06$ ) but not at the other exercise intensities. We found no pre-to-post vaccine  
222 differences for ventilation (VE), oxygen uptake ( $\dot{V}O_2$ ),  $CO_2$  production ( $\dot{V}CO_2$ ), respiratory exchange ratio  
223 (RER), ventilatory equivalents of oxygen uptake ( $\dot{V}E/\dot{V}O_2$ ), carbon dioxide production ( $\dot{V}E/\dot{V}CO_2$ ), stroke  
224 volume (SV), cardiac output (Q), predicted  $\dot{V}O_{2\max}$ , time to ventilatory threshold (VT), rating of perceived  
225 exertion (RPE), serum lactate, serum epinephrine or serum cortisol ( $p>0.05$ ).

226 *Elevations in heart rate and norepinephrine responses to graded exercise were found in those receiving*  
227 *the Pfizer mRNA COVID-19 but not controls.*

228 As the majority of our vaccinated participants received the Pfizer mRNA vaccine (9/12), we decided to  
229 test if the increased heart rate and norepinephrine responses to exercise after vaccination were unique  
230 to this cohort. We found that the elevation in HR at the 70%  $\dot{V}O_{2\max}$  stage and norepinephrine response  
231 at the 80%  $\dot{V}O_{2\max}$  stage was still significant ( $p = 0.006$  and  $0.04$ , respectively) (Figure 2). As with the  
232 entire cohort, we did not find differences in any other physiological endpoint post vaccine. As this study  
233 was not randomized, we decided to include data collected from a parallel study being performed in our  
234 laboratory whereby two bouts of graded exercise were performed by healthy participants ~5-weeks  
235 apart (i.e., similar to the time elapsed between Visit 2 and Visit 3 for the vaccinated cohort) without  
236 receiving a vaccine. All participants in the control group were found to be seronegative for SARS-CoV-2  
237 at the time of testing (Visit 2 and Visit 3) and the exercise bouts performed by these control participants  
238 were identical to the vaccinated cohorts described here. When the control participants and the Pfizer  
239 mRNA vaccine cohort were included in the same LMM, we found no Group x Time x Trial interactions for  
240 HR or norepinephrine ( $p>0.05$ ). However, due to the preliminary nature of this study and the fact we  
241 had only 6 control participants to compared with 9 vaccinated participants, we were concerned that our  
242 small sample size and variability across groups could be causing a type II statistical error. To address this,  
243 we decided to compare delta values (Trial B – Trail A) between the vaccine and the control cohorts for  
244 heart rate and norepinephrine and analyzed these in the same LMM (Figure 3). In doing this, we found  
245 that both HR ( $p=0.03$ ) and norepinephrine ( $p=0.01$ ) was elevated in the second trial for those that  
246 received the Pfizer mRNA vaccine compared to the controls at the 70% and 80%  $\dot{V}O_{2\max}$  stages,  
247 respectively.

248

## 249 **Discussion**

250 Vaccination is strongly recommended to safeguard athletes from infection during training and  
251 competition (10). Several major sporting events (e.g., UEFA European and Copa America Soccer  
252 Championships, Tokyo Olympic Games) have been held during the COVID-19 pandemic, increasing the  
253 risk of SARS-CoV-2 infection for non-vaccinated athletes. While both vaccination (18) and natural  
254 immunity (e.g. from prior infection) (19) can protect against COVID-19 disease, non-vaccinated athletes  
255 are at an increased risk of contracting SARS-CoV-2 during training and competition. This could cause  
256 athletes to miss major sporting events and initiate isolation protocols for other athletes they were in  
257 close contact with. Despite this risk, anecdotal reports have emerged of athletes refusing the COVID-19  
258 vaccine due to perceived negative impacts it may have on both their health and performance.

259 This is the first study, to our knowledge, to report on physiological responses to exercise before and  
260 after COVID-19 vaccination. We found that recent COVID-19 vaccination in a group of physically active  
261 healthy individuals had no impact on a large number of physiological endpoints measured in blood and  
262 by respiratory gas exchange during graded cycling exercise. Principally, reliable markers of metabolism  
263 and aerobic capacity including blood lactate, oxygen uptake, carbon dioxide production, time to  
264 ventilatory threshold and predicted  $\dot{V}O_{2\max}$  were unaffected by recent COVID-19 vaccination. These

265 findings indicate that COVID-19 vaccination is unlikely to affect exercise capacity in normal healthy  
266 people and should alleviate concerns regarding potential negative effects of vaccination on the ability to  
267 carry out daily physically demanding tasks or in meeting recommended physical activity guidelines. We  
268 did, however, find significant elevations in heart rate (~5 bpm) and norepinephrine responses to  
269 vigorous (e.g. 70-80%  $\dot{V}O_{2max}$ ) intensity exercise after vaccination, particularly in those that received the  
270 two dose Pfizer mRNA vaccine regimen. Neither heart rate or norepinephrine changed in  
271 demographically matched control participants who completed identical bouts of exercise several weeks  
272 apart without receiving a vaccine. Although it is possible that these effects are due to reduced physical  
273 activity levels after vaccination (e.g., due to symptoms of vaccinosis), we deem a detraining effect  
274 unlikely as, despite reporting many of the common symptoms associated with COVID-19 vaccination,  
275 our participants did not report significant changes to their physical activity levels during the study  
276 period. The mechanisms by which recent COVID-19 vaccination might increase cardiovascular responses  
277 to graded exercise in healthy people are not known, although the elevated heart response after  
278 vaccination may have been driven by the concomitant elevation in the norepinephrine response to  
279 exercise (20). A more detailed examination of the cardiovascular and neuroendocrine responses to  
280 graded exercise after COVID-19 vaccination would be illuminating.

281 Despite finding that most physiological responses to exercise were unaffected by recent COVID-19  
282 vaccination in these physically active healthy people, it should be noted that the small increases in heart  
283 rate and norepinephrine response to exercise after vaccination could have implications for athletic  
284 performance at the elite level. Repeating this work in a group of elite athletes with an additional  
285 performance measure (e.g., cycling time trial or peak power test) is warranted. We also acknowledge  
286 that our study is not randomized, but it would have been unethical to administer a placebo or prevent  
287 eligible individuals from receiving a vaccine during a global pandemic. Our small sample size also  
288 restricted us from stratifying the exercise response by SARS CoV-2 infection history and vaccine type,  
289 and may have prevented us from detecting other physiological shifts during exercise after vaccination.  
290 We also do not know how long the increased heart rate and norepinephrine responses to exercise lasts  
291 beyond 2-3 weeks post vaccination. We purposefully tested our participants 2-3 weeks after vaccination  
292 as this is within the timeframe for neutralizing antibody production and SARS-CoV-2 T-cell detection  
293 (21), and because athletes are often vaccinated in close proximity to competition (10). Finally, we  
294 acknowledge that our  $\dot{V}O_{2max}$  assessments were made using submaximal as opposed to maximal tests,  
295 which may have affected the accuracy of the exercise intensity prescriptions. This was to alleviate  
296 concerns associated with maximal exercise testing in naturally infected and/or vaccinated individuals  
297 with undiagnosed myocarditis (22).

298 We conclude that recent COVID-19 vaccination has minimal effects on the physiological responses to  
299 graded exercise in physically active healthy people. However, small elevations in the cardiovascular and  
300 neuroendocrine responses to exercise observed after the Pfizer mRNA vaccine could have implications  
301 for athletes and more consideration should be given when it comes to administering vaccines in close  
302 proximity to major sporting events. Future studies are required to determine if these effects of COVID-  
303 19 vaccination will impact athletic performance at the elite level, particularly because booster shots or  
304 new vaccines may be required for continuous protection against SARS-CoV-2 and its evolving variants  
305 (23).

306

307 **Figure 1.** The physiological responses to graded exercise before (Pre) and after (Post) COVID-19  
308 vaccination (n=12). Endpoint measures include: (A)  $\dot{V}O_2$ , (B)  $\dot{V}CO_2$ , (C) RER, (D) Predicted  $\dot{V}O_{2max}$ , (E) VE,  
309 (F)  $\dot{V}E/\dot{V}O_2$ , (G)  $\dot{V}E/\dot{V}CO_2$ , (H) Time to VT, (I) HR, (J) SV, (K) Q, (L) RPE, (M) Lactate, (N) Cortisol, (O)



310 Epinephrine, and (P) Norepinephrine. Data are mean  $\pm$  SD. Significant difference from the Pre-trial  
 311 indicated by \*\*\* ( $p < 0.001$ ), \*\* ( $p < 0.01$ ) and \* ( $p < 0.05$ ).

312 **Figure 2.** The physiological responses to graded exercise before (Pre) and after (Post) vaccination in the  
 313 Pfizer mRNA vaccine cohort ( $n=9$ ) and non-vaccinated controls tested on two separate occasions ( $n=6$ ).  
 314 Endpoint measures include: (A)  $\dot{V}O_2$ , (B)  $\dot{V}CO_2$ , (C) RER, (D) Predicted  $\dot{V}O_{2max}$ , (E) VE, (F)  $\dot{V}E/\dot{V}O_2$ , (G)  
 315  $\dot{V}E/\dot{V}CO_2$ , (H) Time to VT, (I) HR, (J) SV, (K) Q, (L)RPE, (M) Lactate, (N) Cortisol, (O) Epinephrine, and (P)  
 316 Norepinephrine. Data are mean  $\pm$  SD. Significant difference from the Pre-trial indicated by \*\* ( $p < 0.01$ )  
 317 and \* ( $p < 0.05$ ).

318 **Figure 3.** Delta (Trial B – Trial A) HR and norepinephrine responses during exercise trial 1 (pre-vaccine)  
 319 compared to trial 2 (post-vaccine) for the Pfizer vaccine cohort ( $n=9$ ) vs non-vaccinated controls tested  
 320 on two separate occasions ( $n=6$ ). Data are mean  $\pm$  SD. Significant difference from controls indicated by \*  
 321 ( $p < 0.05$ ).

322 **Table 1.** Participant demographic data ( $n=18$ ). Vaccinated participants received either the two dose  
 323 Pfizer mRNA regimen ( $n=9$ ) or the single dose Johnson & Johnson vaccine ( $n=3$ ). The remaining  
 324 participants served as controls ( $n=6$ ). Median  $\pm$  SD

	Total ( $n=18$ )	Pfizer Cohort ( $n=9$ )	Controls ( $n=6$ )
Female	9/18	5/9	3/6
Age (yrs)	29 $\pm$ 5.4	29.1 $\pm$ 3.9	28 $\pm$ 8.4
Height (cm)	173.9 $\pm$ 11	170.1 $\pm$ 11	177.5 $\pm$ 11.7
Weight (kg)	67.4 $\pm$ 13.6	68.1 $\pm$ 10.9	70.2 $\pm$ 11.5
Resting HR (bpm)	70 $\pm$ 5.7	71.2 $\pm$ 5.6	70 $\pm$ 5.9
Resting Systolic Blood Pressure (mmHg)	115 $\pm$ 8.2	115.4 $\pm$ 6.4	119 $\pm$ 7.9
Resting Diastolic Blood Pressure (mmHg)	77 $\pm$ 6.7	75.7 $\pm$ 5.5	77 $\pm$ 4
Predicted $VO_{2max}$ (mL/kg/min)	40.7 $\pm$ 9.9	42.7 $\pm$ 7.2	44.1 $\pm$ 8.1
Time between main exercise trials (days)	52.5 $\pm$ 21.6	54.6 $\pm$ 15.7	26 $\pm$ 185.2
Time between final vaccine dose and last exercise trial (days)	14 $\pm$ 10.1	14.9 $\pm$ 6.5	N/A

325

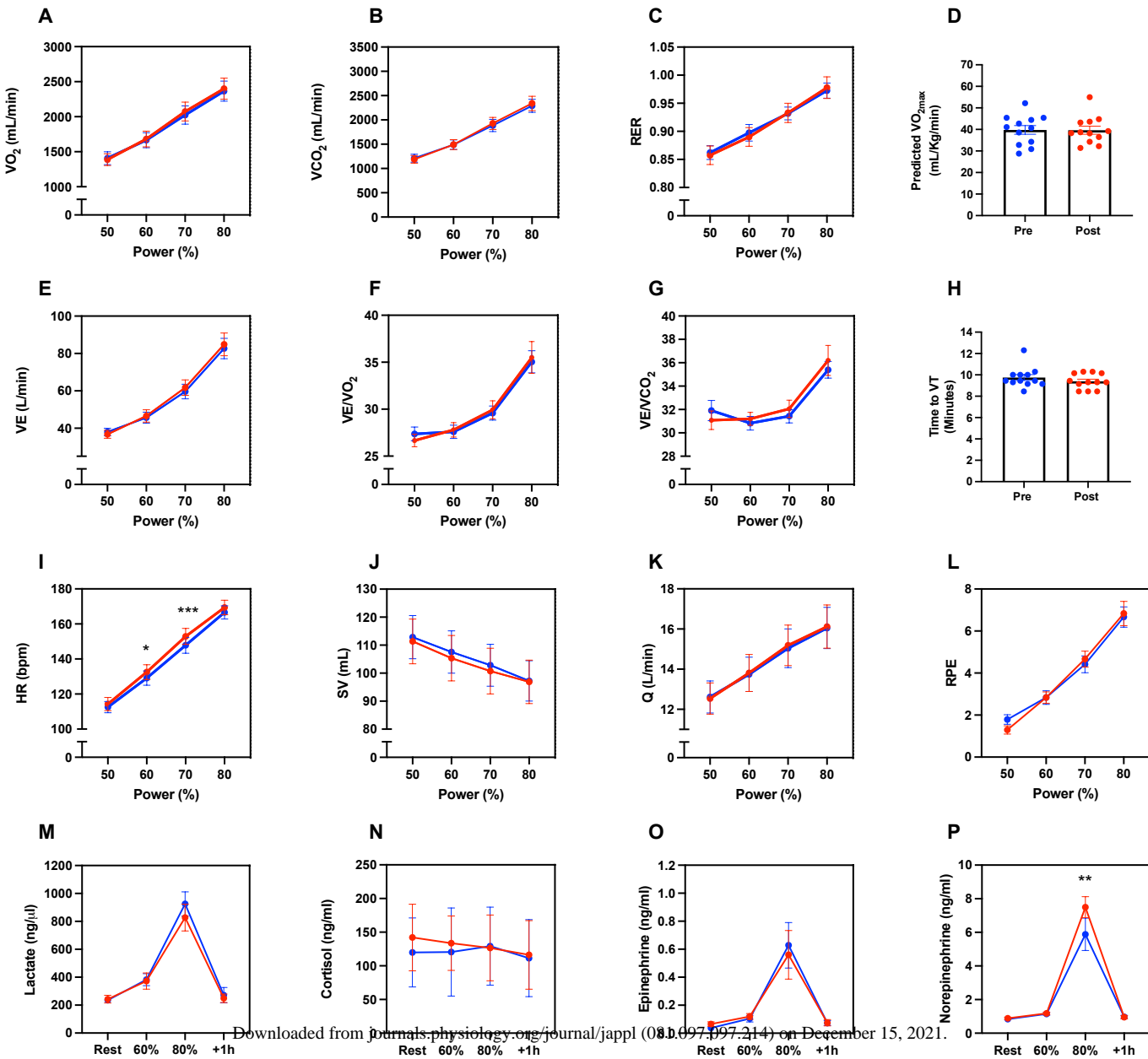
## 326 References

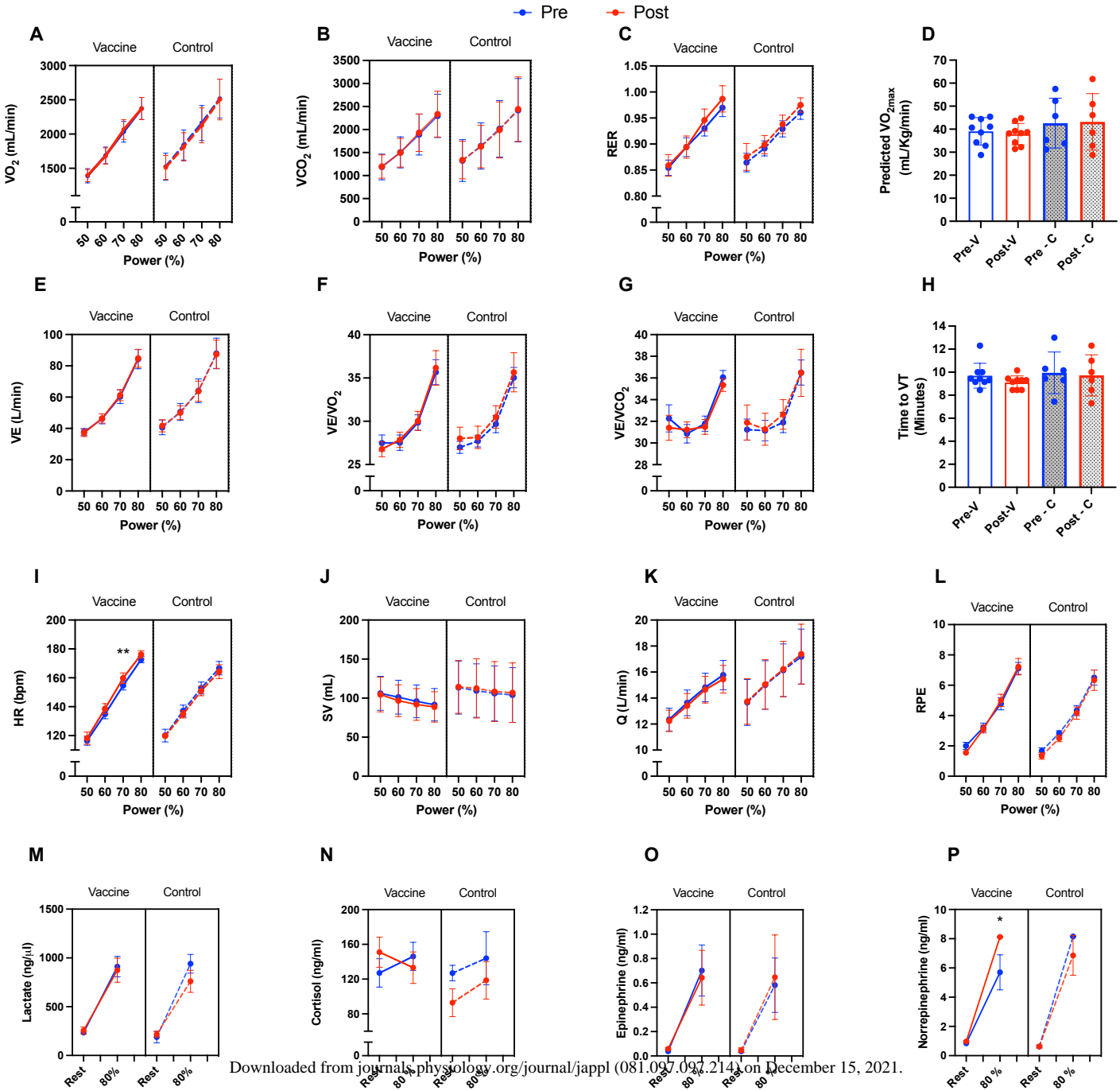
- 327 1. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2  
 328 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J  
 329 Antimicrob Agents. 2020 Mar;55(3):105924.
- 330 2. Srivastava N, Saxena SK. Prevention and Control Strategies for SARS-CoV-2 Infection. Coronavirus  
 331 Dis 2019 COVID-19. 2020 Apr 30;127–40.
- 332 3. Abdulla ZA, Al-Bashir SM, Al-Salih NS, Aldamen AA, Abdulazeez MZ. A Summary of the SARS-CoV-2  
 333 Vaccines and Technologies Available or under Development. Pathog Basel Switz. 2021 Jun  
 334 22;10(7):788.
- 335 4. Cheng H, Peng Z, Luo W, Si S, Mo M, Zhou H, et al. Efficacy and Safety of COVID-19 Vaccines in  
 336 Phase III Trials: A Meta-Analysis. Vaccines. 2021 Jun 1;9(6):582.

- 337 5. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the  
338 BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med*. 2020 Dec 31;383(27):2603–15.
- 339 6. Thomas SJ, Moreira ED, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of  
340 the BNT162b2 mRNA Covid-19 Vaccine through 6 Months. *N Engl J Med*. 2021 Nov  
341 4;385(19):1761–73.
- 342 7. Andrzejczak-Grządka S, Czudy Z, Donderska M. Side effects after COVID-19 vaccinations among  
343 residents of Poland. *Eur Rev Med Pharmacol Sci*. 2021 Jun;25(12):4418–21.
- 344 8. Singh B, Kaur P, Cedeno L, Brahimi T, Patel P, Virk H, et al. COVID-19 mRNA Vaccine and  
345 Myocarditis. *Eur J Case Rep Intern Med*. 2021;8(7):002681.
- 346 9. Larson KF, Ammirati E, Adler ED, Cooper LT, Hong KN, Saponara G, et al. Myocarditis After  
347 BNT162b2 and mRNA-1273 Vaccination. *Circulation*. 2021 Aug 10;144(6):506–8.
- 348 10. Gärtner BC, Meyer T. Vaccination in elite athletes. *Sports Med Auckl NZ*. 2014 Oct;44(10):1361–76.
- 349 11. Stenger T, Ledo A, Ziller C, Schub D, Schmidt T, Enders M, et al. Timing of Vaccination after  
350 Training: Immune Response and Side Effects in Athletes. *Med Sci Sports Exerc*. 2020  
351 Jul;52(7):1603–9.
- 352 12. Balady GJ, Chaitman B, Driscoll D, Foster C, Froelicher E, Gordon N, et al. Recommendations for  
353 cardiovascular screening, staffing, and emergency policies at health/fitness facilities. *Circulation*.  
354 1998 Jun 9;97(22):2283–93.
- 355 13. Jackson AS, Blair SN, Mahar MT, Wier LT, Ross RM, Stuteville JE. Prediction of functional aerobic  
356 capacity without exercise testing. *Med Sci Sports Exerc*. 1990 Dec;22(6):863–70.
- 357 14. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14(5):377–81.
- 358 15. Simpson RJ, Graham SM, Connaboy C, Clement R, Pollonini L, Florida-James GD. Blood lactate  
359 thresholds and walking/running economy are determinants of backpack-running performance in  
360 trained soldiers. *Appl Ergon*. 2017 Jan;58:566–72.
- 361 16. Baker FL, Smith KA, Zúñiga TM, Batatinha H, Niemi GM, Pedlar CR, et al. Acute exercise increases  
362 immune responses to SARS CoV-2 in a previously infected man. *Brain Behav Immun - Health*. 2021  
363 Dec;18:100343.
- 364 17. Zollner A, Watschinger C, Rössler A, Farcet MR, Penner A, Böhm V, et al. B and T cell response to  
365 SARS-CoV-2 vaccination in health care professionals with and without previous COVID-19.  
366 *EBioMedicine* [Internet]. 2021 Aug 1 [cited 2021 Nov 15];70. Available from:  
367 [https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00332-7/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00332-7/fulltext)
- 368 18. Sahin U, Muik A, Derhovanessian E, Vogler I, Kranz LM, Vormehr M, et al. COVID-19 vaccine  
369 BNT162b1 elicits human antibody and TH1 T cell responses. *Nature*. 2020 Oct;586(7830):594–9.

- 370 19. Shirin T, Bhuiyan TR, Charles RC, Amin S, Bhuiyan I, Kawser Z, et al. Antibody responses after  
371 COVID-19 infection in patients who are mildly symptomatic or asymptomatic in Bangladesh. *Int J*  
372 *Infect Dis IJID Off Publ Int Soc Infect Dis*. 2020 Dec;101:220–5.
- 373 20. Breuer HW, Skyschally A, Schulz R, Martin C, Wehr M, Heusch G. Heart rate variability and  
374 circulating catecholamine concentrations during steady state exercise in healthy volunteers. *Br*  
375 *Heart J*. 1993 Aug;70(2):144–9.
- 376 21. Akova M, Unal S. A randomized, double-blind, placebo-controlled phase III clinical trial to evaluate  
377 the efficacy and safety of SARS-CoV-2 vaccine (inactivated, Vero cell): a structured summary of a  
378 study protocol for a randomised controlled trial. *Trials*. 2021 Apr 13;22(1):276.
- 379 22. Halle M, Bloch W, Niess AM, Predel H-G, Reinsberger C, Scharhag J, et al. Exercise and sports after  
380 COVID-19-Guidance from a clinical perspective. *Transl Sports Med*. 2021 May;4(3):310–8.
- 381 23. Espi M, Charmetant X, Barba T, Pelletier C, Koppe L, Chalencon E, et al. Justification, safety, and  
382 efficacy of a third dose of mRNA vaccine in maintenance hemodialysis patients: a prospective  
383 observational study. *medRxiv*. 2021 Jul 6;2021.07.02.21259913.
- 384

Pre Post





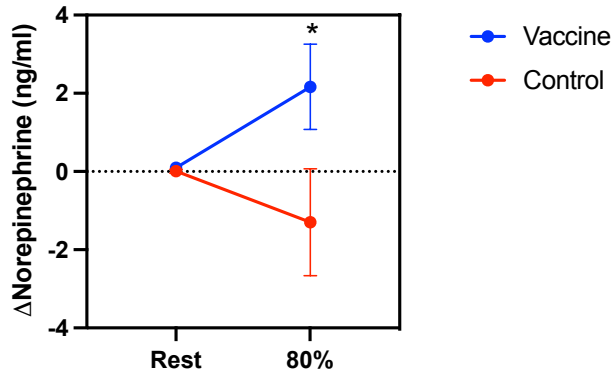
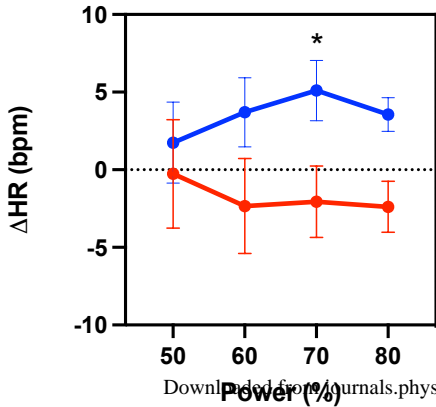
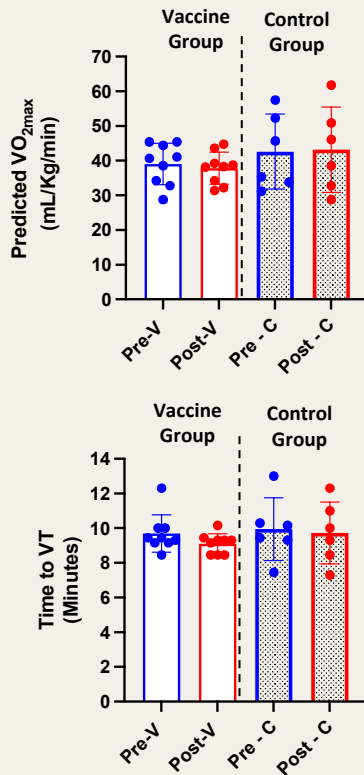


Table 1. Participant demographic data (n=18). Vaccinated participants received either the two dose Pfizer mRNA regimen (n=9) or the single dose Johnson & Johnson vaccine (n=3). The remaining participants served as controls (n=6). Median  $\pm$  SD

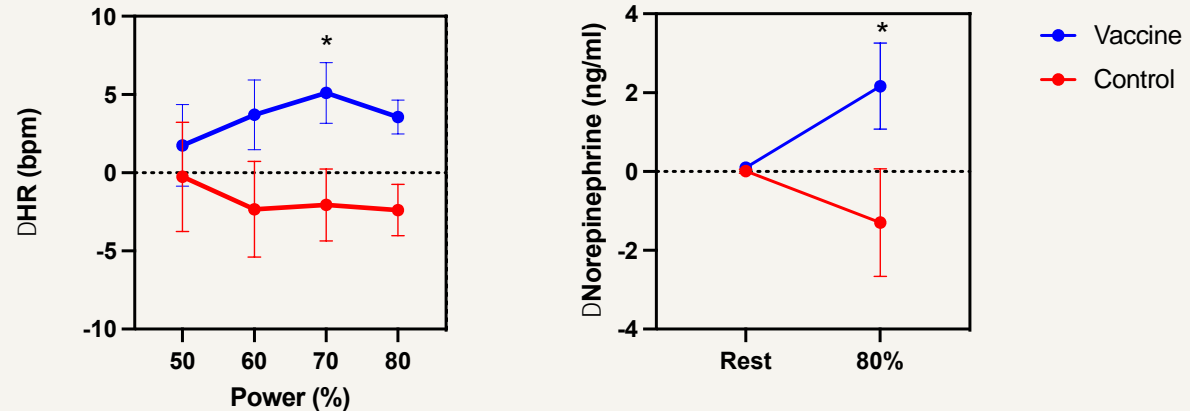
	<b>Total (n=18)</b>	<b>Pfizer Cohort (n=9)</b>	<b>Controls (n=6)</b>
<b>Female</b>	9/18	5/9	3/6
<b>Age (yrs)</b>	29 $\pm$ 5.4	29.1 $\pm$ 3.9	28 $\pm$ 8.4
<b>Height (cm)</b>	173.9 $\pm$ 11	170.1 $\pm$ 11	177.5 $\pm$ 11.7
<b>Weight (kg)</b>	67.4 $\pm$ 13.6	68.1 $\pm$ 10.9	70.2 $\pm$ 11.5
<b>Resting HR (bpm)</b>	70 $\pm$ 5.7	71.2 $\pm$ 5.6	70 $\pm$ 5.9
<b>Resting Systolic Blood Pressure (mmHg)</b>	115 $\pm$ 8.2	115.4 $\pm$ 6.4	119 $\pm$ 7.9
<b>Resting Diastolic Blood Pressure (mmHg)</b>	77 $\pm$ 6.7	75.7 $\pm$ 5.5	77 $\pm$ 4
<b>Predicted VO<sub>2max</sub> (mL/kg/min)</b>	40.7 $\pm$ 9.9	42.7 $\pm$ 7.2	44.1 $\pm$ 8.1
<b>Time between main exercise trials (days)</b>	52.5 $\pm$ 21.6	54.6 $\pm$ 15.7	26 $\pm$ 185.2
<b>Time between final vaccine dose and last exercise trial (days)</b>	14 $\pm$ 10.1	14.9 $\pm$ 6.5	N/A

# Recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people

## METHODS



## RESULTS



COVID-19 vaccination had no effect on a large number of physiological endpoints in response to graded cycling exercise at various percentages of the VO<sub>2max</sub>.

Small elevations in the heart rate (HR) and norepinephrine response to vigorous exercise (70-80% VO<sub>2max</sub>) were observed after vaccination (Pfizer mRNA) but not controls.

## CONCLUSION

Recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people. The small elevations in cardiovascular and neuroendocrine responses to exercise after the Pfizer mRNA vaccine regimen could have implications for athletes at the elite level.

Physiological Responses to graded cycling exercise were compared before and after COVID-19 vaccination and in controls.

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