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THE IMPACT OF COVID-19 ON ENDURANCE ATHLETES' RETURN TO PRE-ILLNESS LEVEL OF PARTICIPATION

Cheryl Anne Haley

A thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy.

Johannesburg, *June, 2025*

Declaration

I Cheryl Anne Haley declare that this thesis is my own, unaided work except to the extent indicated in the acknowledgements or contributions sections. It is being submitted for the degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg, South Africa. It has not been submitted before for any degree or examination at any other University.

Cheryl Anne Haley



_____

Signature of candidate

Date: 3 June 2025 in Johannesburg

Conference proceedings arising from the studies contained in this thesis

Findings from the studies found in this thesis were presented at the following academic conferences:

1. ‘”Every run is hard”: Endurance athletes’ experiences of return to sports participation after COVID-19. A mixed methods study’. Oral presentation at the Faculty of Health Sciences Research Day, University of the Witwatersrand, Johannesburg, South Africa, 5 September 2024.

2. ‘Protracted exercise tolerance post-coronavirus disease 2019 in endurance athletes: A survey’. Oral presentation at the World Physiotherapy Congress, Africa region, Cape Town, South Africa, 13 September 2024.

3. ‘”Every run is hard”: Endurance athletes’ experiences of return to sports participation after COVID-19. A mixed methods study’. Oral presentation at the World Physiotherapy Congress, Africa region, Cape Town, South Africa, 15 September 2024.

4. ‘Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes’. Poster presentation at the SASMA conference, Stellenbosch, South Africa.

Peer-reviewed publications arising from the studies contained in this thesis

The following studies included in this thesis were published in academic, peer-reviewed journals with full citations listed below:

1. Haley, C. A., van Aswegen, H., Libhaber, E. & Olivier, B. (2024). Protracted exercise tolerance post-coronavirus disease 2019 in endurance athletes: A survey. *South African Journal of Physiotherapy*, 80(1), 2063. https://doi.org/10.4102/sajp.v80i1.2063

2. Haley, C. A., van Aswegen, H. & Olivier, B. (2024). 'Every run is hard': Endurance athletes' experiences of return to sports participation after COVID-19 – A mixed methods study. *Translational Sports Medicine* (1), 1506534. https://doi.org/10.1155/2024/1506534

3. Haley, C. A., Torres, G., Olivier, B., & van Aswegen, H. (2024). Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes. *South African Journal of Sports Medicine*, 1(36), 1-8. https://doi.org/10.17159/2078-516X/2024/v36i1a18872

Abstract

The long-term impact of the highly infectious and pathological novel coronavirus disease of 2019 (COVID-19) on endurance athletes remains equivocal. For peak performance, the respiratory, cardiovascular and peripheral muscle systems must perform optimally. The respiratory system is fundamental for endurance athletes, who engage in extensive aerobic exercise and are thus expected to exceed the predicted thresholds for cardiorespiratory fitness. Participation in sport is an important determinant of quality of life for endurance athletes. Assessing both the psychosocial impact of COVID-19 and the physiological limitations to exercise capacity, will inform targeted interventions to assist endurance athletes' return to their pre-illness level of sport.

Paper 1 (Chapter 3) includes a cross-sectional study using a self-administered web-based questionnaire that was disseminated through running and cycling clubs' social media channels. The study aimed to assess acute and exertional COVID-19 symptoms experienced by the endurance athletes, their fatigue score and exercise performance. A comparison between those athletes who had returned to their pre-illness level of sport and those who had not, was made. This study found that one third of endurance athletes, mean age of 45 years, had not returned to their pre-illness level of sport participation after COVID-19. Persistent cardiopulmonary symptoms including dyspnoea and fatigue contributed to a protracted return to sport.

Paper 2 (Chapter 4) further explored the biopsychosocial impact of COVID-19 by conducting a mixed methods study. Quantitative data included symptom severity, management thereof, and barriers to resuming sports participation. Results showed that tachycardia, fatigue and dyspnoea were experienced on exertion, and the athletes had difficulty exercising at high intensities. Physical fatigue score significantly predicted return to sport. Qualitative data collected through open-ended questions were deductively grouped into three themes according to the biopsychosocial framework. Inductive coding revealed aspects of this novel disease that adversely affected quality of life including persistent cardiopulmonary symptoms, physical fatigue, emotional distress and social disengagement. Mixing the methods concluded that the quality of life of endurance athletes deteriorated due to protracted return to sport.

Paper 3 (Chapter 5) included a prospective observational cohort study that aimed to determine the influence of COVID-19 on cardiovascular, pulmonary, and skeletal muscle function. Athletes experiencing exercise intolerance were invited to comprehensively investigate their cardiorespiratory fitness and potential limitations to their aerobic capacity. This assessment included resting lung function, maximal inspiratory pressure measurement, and cardiopulmonary exercise testing. The tests were repeated after eight weeks of self-directed endurance training and compared to published reference values and a control group that was unaffected by COVID-19. Results showed that the fifty-seven athletes with exercise intolerance had poorer ventilatory threshold, workload, and respiratory exchange ratio than the control group. The group that was adversely affected by COVID-19 showed a positive response to endurance training with improved parameters at follow-up, highlighting the need for tailored rehabilitation of these athletes.

Study 4 (Chapter 6) includes a feasibility study of conducting a clinical trial of the effectiveness of inspiratory muscle training to enhance aerobic performance post-COVID-19. Given that respiratory function is crucial in endurance sports and inspiratory muscle training has been shown to improve dyspnoea in the general population, it is plausible that this intervention may be beneficial. The feasibility of a clinical trial was assessed in terms of practicality, acceptance and adherence, and implementation. The participants performed 30 breaths of inspiratory muscle training for six weeks, starting at 50% of the maximal inspiratory pressure and increasing progressively. Lung function, maximal inspiratory pressure and cardiopulmonary exercise tests were conducted before and after the intervention. Data were analysed per-protocol comparing the intervention and control group. Results showed that adherence and implementation were good, while acceptance and practicality could be amended in larger clinical trials. The intervention was effective in promoting recovery of respiratory muscle strength.

In conclusion, it is vital that medical professionals, coaches, and athletes understand the acute symptoms, impact on quality of life, and long-term consequences of COVID-19, as the imperative of a safe and successful return to sport cannot be overstated.

Keywords: COVID-19, exercise intolerance, quality of life, inspiratory muscle training

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I would like to express a huge thank-you to my supervisors Prof Heleen van Aswegen and Prof Benita Olivier, for their expert advice, support, and unending encouragement. Heleen, your calm demeanour helped me never get overly flustered by adverse events, while your professional approach gave me the guidance to produce my best possible work. Benita, thank you for continuing to supervise me from across the miles in the United Kingdom. You are a literal mastermind of research approaches, and your constant enthusiasm is massively appreciated and admired. It was a privilege to be supervised by both respiratory and sport physiotherapy experts. Together you allowed me to find the confidence within myself to tackle the recruitment of participants, the rollout of the studies, the tribulations of publication, and the joy in presenting my findings.

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List of Abbreviations

ACE2	angiotensin-converting enzyme 2
ACC	American College of Cardiology
AED	Automated external defibrillator
BMI	Body mass index
CI	Confidence interval
CO_2	Cardon dioxide
COVID-19	Coronavirus disease 2019
CPET	Cardiopulmonary exercise test
CRF	Cardiorespiratory fitness
ECG	Electrocardiogram
FAIR	Findable, Accessible, Interoperable and Re-usable
FRIEND registry	Fitness Registry and the Importance of Exercise National Database
FTP	Functional threshold power
HCO_3	Bicarbonate
HR	Heart rate
ICU	Intensive care unit
ICMJE	International Committee of Medical Journal Editors
IMT	Inspiratory muscle training
MDFI	Multidimensional Fatigue Inventory tool
MERS-CoV	Middle Eastern Respiratory Syndrome
MIP	Maximal inspiratory pressure
MRI	Magnetic resonance imaging
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health
NMCH	Nelson Mandela Children's Hospital
O_2	Oxygen
OR	Odds ratio
OUES	Oxygen uptake efficiency slope
PAH	Pulmonary artery hypertension
PCR	Polymerase chain reaction
POTS	Postural orthostatic tachycardia syndrome

QOL	Quality of life
REDCap	Research electronic data capture
RER	Respiratory exchange ratio
RCT	Randomised controlled trial
RMT	Respiratory muscle training
RPE	Rating of perceived exertion
RTS	Return to sport
S-Index	Strength Index
SARS-CoV-1	Severe acute respiratory syndrome coronavirus 1
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SpO2	Peripheral capillary oxygen saturation
VE	Minute ventilation
VCO_2	Volume of carbon dioxide expelled
VO_2	Volume of oxygen consumed
VO_{2peak}	Maximal oxygen consumption
V/Q	Ratio of ventilation to perfusion
VT	Ventilatory threshold
WHO	World Health Organisation

Definition of key terms

Alpha variant	First identified in the UK (Sept 2020) – Known for increased transmissibility and potentially more severe disease, leading to rapid spread globally.
Beta variant	First identified in South Africa (May 2020) – Noted for its immune escape potential, reducing vaccine and antibody effectiveness.
Delta variant	First identified in India (Oct 2020) **–** Highly transmissible with increased risk of hospitalization and severe disease.
Omicron variant	First identified in South Africa and Botswana (Nov 2021) – Characterized by extensive mutations, leading to significantly increased transmissibility and immune evasion but generally milder illness. Major subvariants include: BA.1 & BA.2 – Initial Omicron waves; BA.2 was more transmissible than BA.1. BA.4 & BA.5 – Led to reinfection waves due to further immune escape. XBB.1.5 ("Kraken") – Recombinant subvariant known for rapid spread and immune evasion. EG.5 ("Eris") – Subvariant of XBB.1.9 with slight growth advantage.

	JN.1 – Sub lineage of BA.2.86 with increasing prevalence in late 2023–early 2024.
	BA.2.86 ("Priola") – Marked by a high number of spike mutations, raising concerns about immune escape.
HR/VO_2 slope	The relationship between heart rate and oxygen uptake
Long-term effects of COVID-19	In this study, long-term effects pertain to the same description as “long-COVID”, which is used to describe new or persistent symptoms that appear after four weeks following the onset of illness, as defined by the National Institute for Health and Care Excellence.
MVV	Maximum voluntary ventilation: estimated by multiplying FEV_1 by 35.
RTS in running or cycling	The gradual process from the first testing run or cycle to a full return to pre-illness level of participation.
n-RTS	Those that had not returned to pre-illness level of sport
y-RTS	Those that had returned to pre-illness level of sport
S-Index	Dynamic inspiratory muscle strength during a fast inhale. The values strongly correlate with MIP

Preface and Description of Thesis Sections

Coronavirus disease 2019 (COVID-19) created a world-wide pandemic. A novel disease with multifaceted clinical presentations had manifestations like no other respiratory virus such as long-term dyspnoea and fatigue. These persistent symptoms may hinder endurance athletes as they return to a high volume of cardiovascular exercise. There remains a paucity of COVID-19 studies featuring endurance athletes, yet many of these athletes take part in events such as marathon running both in South Africa and internationally. Understanding the impact of COVID-19 on endurance athletes will aid management of these athletes to ensure a safe return to sport and the numerous health benefits thereof. The sections that follow describe how the studies included in this thesis contributed to answering to a pertinent research question.

Chapter 1 introduces the severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) that caused a global pandemic and disruption to life as we knew it. The definition of athletes is explained and the potential detrimental impact of the disease on endurance athletes particularly is introduced. The problem statement, aim of the research project, and significance of the studies incorporated in this thesis are detailed here.

Chapter 2 is a narrative review of the literature providing more detail about the subjects on which this research is based. It discusses the pathophysiology of COVID-19, exercise physiology, and the effect of COVID-19 on physiological athletic performance and quality of life. It concludes with the rationale for the studies included in this thesis based on the literature and the importance of the studies performed as part of this thesis.

Chapter 3 features a published paper namely, an observational study with a cross-sectional design. It compares a group of endurance athletes who had successfully returned to their pre-illness level of sport after COVID-19, to a group that had not. The study investigated acute and long-term symptoms of COVID-19 experienced by the athletes, the severity thereof, and exertional symptoms that were associated with protracted return to sport.

Chapter 4 comprises a published paper with a mixed-methods study design. This study expanded on the information incorporated in Study 1, by exploring the severity

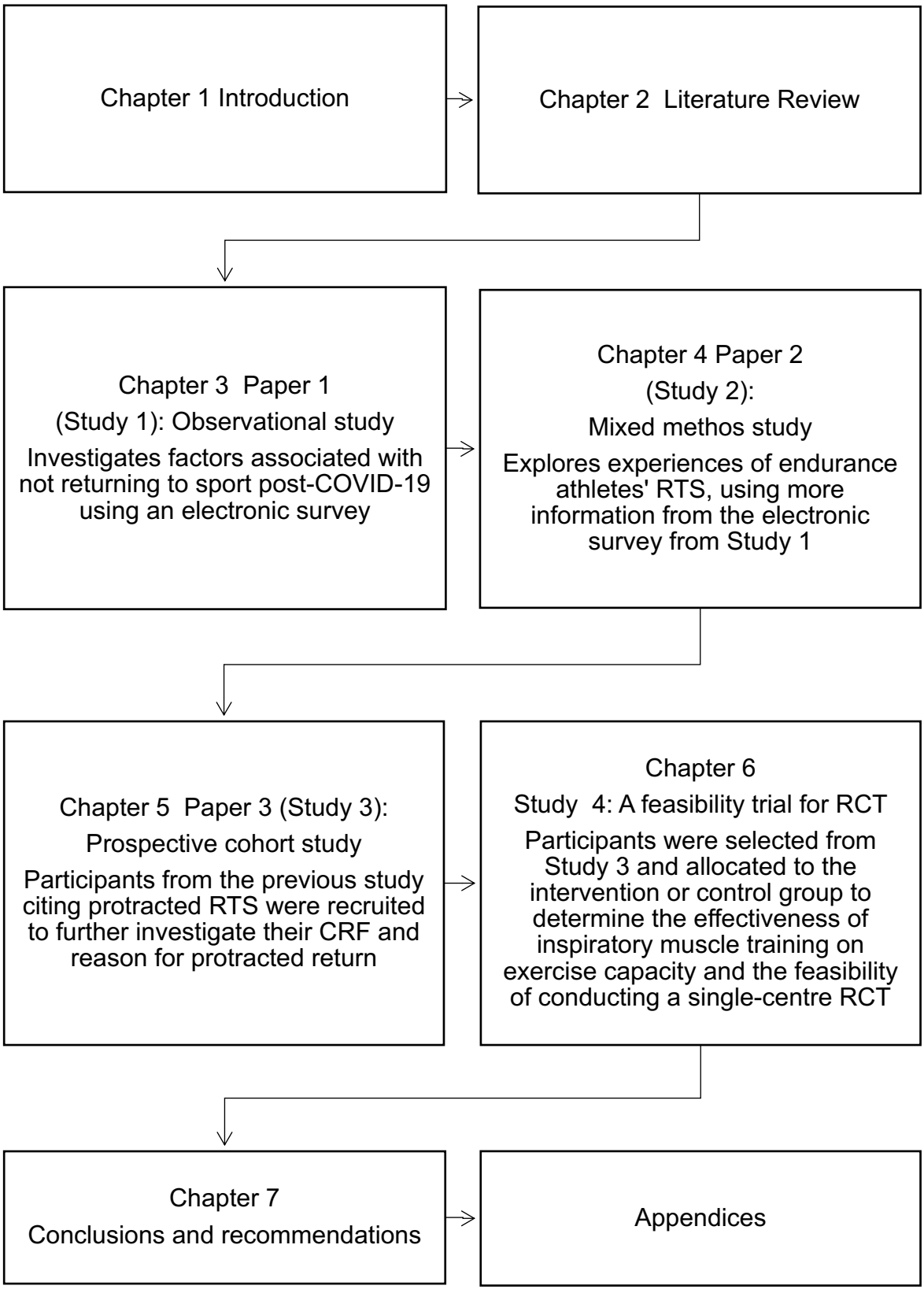
and management of COVID-19 symptoms, and the impact on their quality of life as the endurance athletes returned to their pre-illness level of sports participation. Studies 1 and 2 were derived from the same online survey using one electronic participant information and consent link.

Chapter 5 includes a published paper with a prospective cohort study design. Athletes who were experiencing exercise intolerance volunteered to undergo a lung function and cardiopulmonary exercise test that identified whether limitations to exercise capacity were of cardiovascular, pulmonary, or peripheral muscle system origin. These tests were repeated after eight weeks of endurance training that was self-directed by the participants according to their normal training programme. This allowed assessment of their response to endurance training.

Chapter 6 includes a feasibility study for a clinical trial in draft manuscript format, however is still to be submitted for review. This study investigates the effect of inspiratory muscle training on exercise capacity in masters age-group endurance athletes with low cardiorespiratory fitness or pulmonary limitations causing protracted exercise tolerance following COVID-19. It assesses the acceptability and adherence of the participants to the intervention, the implementation of the outcome measures, and the practicality of conducting a single-centre longitudinal clinical trial.

Chapter 7 summarises the results and discussions of the four studies included in the thesis. It collectively reflects on the limitations of the studies and considers future research questions that have arisen from the works in this thesis. This section concludes the research presented in the context of the rationale for the studies.

Graphic outline of the thesis



Contributions to the research

As part of the required declaration of this thesis, I acknowledge contributions by various individuals to this work as detailed below.

The study designs for all studies were devised by myself in conjunction with my supervisors, Prof Heleen van Aswegen and Prof Benita Olivier.

All data collection was performed by myself, with support from my supervisors, Prof Heleen van Aswegen and Prof Benita Olivier, as well as from Prof Georgia Torres.

All data analysis was performed by myself in conjunction with guidance from Prof Elena Libhaber (Study 1, 3 and 4), Prof Heleen van Aswegen and Prof Benita Olivier (Study 2), and Prof Georgia Torres (Study 3).

Drafting of written works was undertaken by myself with guidance from my supervisors.

All authors reviewed, contributed to the editing, and approved the drafts submitted for publication. The signed declaration of the student's contribution to articles and agreement of co-authors may be found in Appendix A.

Chapter 1 Introduction

1.1 Background

The highly infectious and pathological novel coronavirus disease of 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused a global health crisis. The virus was first detected in Wuhan, China, on 31 December 2019 and spread across international borders expeditiously. The World Health Organisation (WHO) declared a pandemic on 11 March 2020 (Edenfield, Dillon and Clugston, 2023). Previous coronavirus outbreaks include the severe acute respiratory syndrome caused by SARS-CoV-1 in 2003 and Middle Eastern Respiratory Syndrome caused by the MERS-CoV in 2012 (Barker-Davies et al., 2020). Coronaviruses are large enveloped, non-segmented positive sense ribonucleic acid viruses transmitted by respiratory droplets in humans and animals. Humans can host and spread the disease without experiencing any symptoms during the incubation period (Lopes et al., 2021). Since the SARS-CoV-2 virus was first discovered, it has mutated several times, resulting in genetically different variations. After the Wuhan strain, the beta strain was first identified in South Africa and exhibited a higher transmissibility and potentially greater severity as the immune system struggles to combat the virus. The delta strain, originating in India, has a large basic reproduction number, making it even more transmissible with efficient cell entry and possibly associated with a higher hospitalisation rate than the previous two strains. The omicron strain was identified in Botswana and has over 30 mutations of its spike protein. It is the most transmissible variant and can evade immunity from previous infections, causing breakthrough infections, however, causes milder disease (Stojmenovic et al., 2023).

The high number of mortalities and lack of imminent cure resulted in a grim global situation. Due to the nature of the spread of COVID-19 in the community, all sectors of the population, including athletes, were equally exposed (Ibarrola and Dávolos, 2020). Comorbid diseases predispose individuals to a more severe expression of COVID-19; therefore, most athletes were expected to experience an asymptomatic or mild form of the disease, with few being hospitalised and even fewer mechanically ventilated (Ibarrola and Dávolos, 2020). This multifaceted disease not only has a wide range of

symptoms affecting an athlete's return to sport, but the addition of external restrictions to limit the spread of the disease influenced their training ability and competition potential. The impact of COVID-19 on all athletes is important, from recreational athletes enjoying the benefits of improved quality of life, to professional athletes whose careers may be defined by the slightest increments of performance (Jorstad and van den Aardweg, 2020).

The American Heart Association defines an athlete as "one who participates in an organised team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training." (McKinney et al., 2018,532). Because athletes span a wide range of sports and competitive levels with varying degrees of technical and physical ability, athletes have been defined according to their physiological demands and thus classified according to their training volume and intent to compete as follows: 'Elite' athletes train more than 10 hours per week, 'competitive' athletes train more than six hours per week, 'recreational' athletes train more than four hours per week, and 'exercisers' engage in physical activity of at least two and a half hours per week (McKinney et al., 2018). Elite, competitive and recreational athletes intend to compete at events, and are included in the studies in this thesis. 'Exercisers' who exercise but have no intention of competing, were excluded. Endurance athletes satisfy the "athlete" criteria above through partaking in sports such as running, cycling, swimming and triathlon (Braga et al., 2023).

Running is a popular mass participation activity that has seen increasing involvement in recent years (Scheer et al., 2021; Poczta et al., 2022). Compared to other sports requiring high-end equipment, running is a relatively affordable sport (DeJong, Fish and Hertel, 2021). It is also very accessible to people with a vast range of athletic ability (DeJong, Fish and Hertel, 2021). An average of 50 000 athletes participate in any of the big city marathons such as Paris, Berlin, London and New York. In South Africa, 15 000 athletes entered for the iconic Comrades Marathon in 2019, the Cape Town Cycle Tour attracted 22 500, and 34 000 entered the Two Oceans Marathon (Scheer et al., 2021).

Prior to the COVID-19 pandemic, up to 25% of endurance athletes had some degree of airway obstruction (Wilson et al., 2020), and historically, acute respiratory tract

infections are the most common cause of non-injury related illness and time away from sport (Hull, Loosemore and Schwellnus, 2020). It was found that previous coronavirus infections (SARS-CoV-1 and MERS-CoV) sometimes caused reduced exercise capacity long after resolution of the illness (Hughes et al., 2020). Persistence of COVID-19 symptoms beyond the infectious period had been widely noted in the general population (Wilson et al., 2020; Carfì, Bernabei and Landi, 2020) which raised concerns of persistent symptoms hindering return to sports participation.

Cardiopulmonary complications as athletes return to sport after COVID-19 were by far the most threatening however, shortness of breath, general fatigue and body pain may be more common hinderances (Erickson et al., 2021). Evidence-based guidelines for safe return to sport (RTS) were published (Gluckman et al., 2022) (Appendix B), however at the time of study, reasons for athlete's not returning to pre-illness level of sport had not been elucidated (Schroeder et al., 2023). Underlying cardiac dysfunction may be one contributing factor (Topol, 2020), lung damage may be associated with exercise intolerance (Fraser, 2020), and deconditioning due to inactivity was also proposed (Komici et al., 2021). Additionally, psychological concerns such as anxiety, depression and poor concentration have been noted (Sivan et al., 2020).

Cardiorespiratory fitness (CRF) relates to functional capacity and performance and serves as an important predictor of all-cause mortality (Harber et al., 2017). The American Heart Association recommends routine CRF assessment as a clinical vital sign. Cardiorespiratory fitness can be measured in terms of VO_{2peak}, the highest oxygen uptake during dynamic exercise, and together with resting lung function and the S-Index are objective measures of cardiorespiratory capacity during high intensity physical activity (Mackala et al., 2020). The results of these tests can identify the limitations causing exercise intolerance. Once identified, management of endurance athletes with exercise intolerance will be more effective by tailoring rehabilitation to the specific limitations that they experience.

1.2 Problem Statement

The long-term impact of COVID-19 on endurance athletes had not been established at inception of the study in 2020 (Sivan et al., 2020). The higher number of athletes over 40 years of age and greater number of finishers in the 2022 Two Oceans

marathon compared to 2018 led Collins et al. (2022) to concluded that the pandemic had no impact on performance. In a more recent study, García-Arrabé et al. (2024) concluded that amateur runners had resumed pre-illness level of sport by 3 months post-COVID-19. However, these conclusions have been challenged by many other studies (Braga et al., 2023; Vollrath et al., 2022; Moulson et al., 2022). The athlete population investigated in the latter study would be described as 'exercisers' and not satisfying the 'athlete' criteria above, and all had mild illness with no long-term symptoms. The outcome of the former study was not the impact of the illness on athlete health. Therefore, more information regarding barriers to RTS will be useful in understanding and managing it better.

Competitive or elite athletes are likely to have access to sports medicine professionals who would disseminate the recommended RTS guidelines (Gluckman et al., 2022) and consider the increased risk of cardiac involvement in masters athletes (over the age of 35 years). However, it is unknown whether social endurance athletes are equally informed and updated as these protocols were revised repeatedly as variants of the virus and vaccine availability advanced (Steinacker et al., 2022). Despite following the published RTS guidelines after acute infections (Appendix B), reduced exercise capacity more than four weeks after the resolution of acute symptoms remained a problem (Vollrath et al., 2022). COVID-19 diagnosed during the pandemic was influenced by several factors affecting exercise tolerance, including deconditioning due to lockdowns, psychological stress and vaccine status (Scheer et al., 2021). These factors have become less relevant since the pandemic was officially declared over on 5 May 2023. Understanding the limitations to exercise capacity is vital considering the important benefits of regular exercise. Cardiorespiratory fitness and respiratory muscle strength declines with every decade of life (Kaminsky et al., 2018). Published norms for athletes in South Africa do not include athletes older than 35 years of age, nor indicate how these variables change over time with endurance training (Kroff and Terblanche, 2010). These normative values are essential to determine how COVID-19 has affected return to sport in masters age-group athletes, as older age is associated with pre-existing co-morbidities (Kaiser-Nielsen et al., 2017) and has been identified as a risk factor for persistent COVID-19 symptoms (Sudre et al., 2021). Globally, many studies have investigated the impact of COVID-19 on athletes' return to endurance training post COVID-19 (Scheer et al., 2021; Juhasz et al., 2022, Sliz et al., 2023 García-Arrabé et al., 2024) yet studies with longer follow-ups and matched control

groups are lacking (Schwendinger et al., 2024). Respiratory muscle training post-COVID-19 has been investigated (McNarry et al., 2022; Collet et al., 2023) however, most studies involve either young athletes (Mackała et al., 2020) or previously hospitalised patients (Palau et al., 2022). Thus, the effectiveness of IMT for the management of weak respiratory muscles in masters age-group endurance athletes was unknown.

1.3 Aim and Objectives

1.3.1 Aim of the thesis

To investigate the physiological and psychosocial impacts of COVID-19 on endurance athletes' return to sport, through assessing acute and chronic symptoms, biopsychosocial well-being, cardiorespiratory fitness response, and the potential role of inspiratory muscle training in optimising return to sport.

1.3.2 Objectives

- To compare acute and exertional symptoms, fatigue levels, and exercise performance by masters age-group endurance athletes who had returned to their previous level of sport to those who have not.
- To explore the impact of COVID-19 on the biopsychosocial well-being of masters age-group endurance athletes retuning to pre-illness level of participation.
- To determine the cardiorespiratory fitness response to endurance training of masters age-group athletes post-COVID-19 compared to unaffected athletes.
- To assess the feasibility of conducting a single-centre randomised controlled trial (RCT) of inspiratory muscle training on athletic performance in masters age-group athletes recovering from long-term COVID-19 exposure.

1.4 Significance

In South Africa, ultramarathon running is a widely popular sport. It is affordable, accessible, and inclusive, attracting participants from the country's diverse population. In 2021, Lopes et al. reported a need for more information on the impact of COVID-19 on different population groups, considering both socioeconomic and clinical factors

(Lopes et al., 2021). There was high research urgency in the beginning of the pandemic due to the novelty of this coronavirus. Therefore, it was worth assessing the factors associated with return to endurance sport including type, severity, and persistence of symptoms (Hull, 2022; Kaiser-Nielsen et al., 2017). One other study focusing on a South African population of runners and cyclists found that protracted RTS was associated with more severe illness (Emeran et al., 2022). Guidelines for RTS emerged according to severity of illness (Gluckman et al., 2022). As time progressed, the emergence of long-COVID, characterised by persistent symptoms or new symptoms after four weeks post-onset of the initial illness prompted further research (Hull, 2022). Dyspnoea and fatigue are the most common presentations of long-COVID (Hull, 2022). Endurance training requires the ability to resist fatigue (Barker-Davies et al., 2020). Fatigue not only affects performance capacity but also the perception of pain, motivation, and social well-being (Liška et al., 2022). A trajectory of research beyond the acute phase was required (Steinacker et al., 2022). Participation in sport is an important aspect of quality of life, thus the biopsychosocial impact of COVID-19 cannot be underestimated (Ussorowska-Krokosz et al., 2023).

Research to determine the limitations to exercise capacity after COVID-19 using cardiopulmonary exercise testing (CPET), with the inclusion of a control group was recommended (Lemes et al., 2022; Durstenfeld et al., 2022). Investigations combining inspiratory muscle strength (S-Index), resting lung function, and CPET had not been explored in other studies. This knowledge may assist healthcare professionals' understanding of the long-term effect on exercise capacity in endurance athletes who rely on efficient aerobic metabolism for sustained performance. Post-viral fatigue may exist regardless of the virus, and as increasing age is associated with long-COVID (Sudre et al., 2021), the impact on the growing masters age-group athlete population will remain a pertinent consideration after future viral illnesses. By 2025, the emergence of the milder Omicron variant, along with higher vaccination rates has led to less severe acute illness (Fairweather et al., 2023). However, while the threat of COVID-19 diminished, severe and long-term consequences such as myocarditis and pericarditis continue to be reported following Omicron infections (Fairweather et al., 2023). The health of masters age-group athletes will remain an important consideration (Kaiser-Nielsen et al., 2017). Lessons learned from research conducted during the COVID-19 pandemic will be valuable for the essential management of ubiquitous respiratory illnesses regardless of future COVID-19 outbreaks (Hull, 2022).

1.5 Ethical considerations for the entire thesis

Unconditional ethical clearance was provided by the University of the Witwatersrand's Human Research Ethics Committee (Medical) (Certificate no. M210657) (Appendix C). The study procedures adhered to the principles set forth in the Declaration of Helsinki, the South African Guidelines for Good Clinical Practice and the Medical Research Council. For Study 1 and Study 2, an information sheet (Appendix D) explaining the study purpose and data sharing was linked to the survey (Appendix E) and ensured confidentiality, anonymity and permission to withdraw from the study at any point. For Study 3 (Appendix F) and Study 4 (Appendix G), informed consent was signed by each participant before the first test and ensured confidentiality (including protection of personal information), anonymity, permission to withdraw from the study at any point and sharing of data. Study 4 was registered with the Pan-African Clinical Trials Registry no: PACTR202305590076796 (Appendix H).

1.6 References

1. Barker-Davies, R. M., O'Sullivan, O., Senaratne, K. P. P., Baker, P., Cranley, M., Dharm-Datta, S., ... & Bahadur, S. (2020). The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *British Journal of Sports Medicine*, 54(16), 949-959. https://doi.org/10.1136/bjsports-2020-102596
2. Braga, F., Domecg, F., Kalichsztein, M., Nobre, G., Kezen, J., Espinosa, G., Prado, C., Facio, M., Moraes, G., Gottlieb, I., Lima, R. L., Danielian, A., & Emery, M. S. (2023). Abnormal exercise adaptation after varying severities of COVID-19: A controlled cross-sectional analysis of 392 survivors. *European Journal of Sport Science*, 23(5), 829–839. https://doi.org/10.1080/17461391.2022.2054363
3. Carfì, A., Bernabei, R., & Landi, F. (2020). Persistent symptoms in patients after acute COVID-19. *Jama – Journal of the American Medical Association*, 324(6), 603-605. https://doi.org/10.1001/jama.2020.12603
4. Collins, M., & Bosch, A. N. (2023). Evaluating the impact of the COVID-19 pandemic on performance during the 2022 56 km Two Oceans ultra-marathon. *The Journal of Sports Medicine and Physical Fitness*, 63(6), 756-764. https://doi.org/10.23736/s0022-4707.22.14462-2

5. DeJong, A. F., Fish, P. N., & Hertel, J. (2021). Running behaviors, motivations, and injury risk during the COVID-19 pandemic: A survey of 1147 runners. *PloS ONE*, 16(2), e0246300. https://doi.org/10.1371/journal.pone.0246300
6. Durstenfeld, M. S., Sun, K., Tahir, P., Peluso, M. J., Deeks, S. G., Aras, M. A., ... & Hsue, P. Y. (2022). Use of cardiopulmonary exercise testing to evaluate long COVID-19 symptoms in adults: a systematic review and meta-analysis. *JAMA network open*, 5(10), e2236057-e2236057. https://doi.org/10.1001/jamanetworkopen.2022.36057
7. Edenfield, K. M., Dillon, M. C., & Clugston, J. R. (2023). COVID myocarditis in a collegiate athlete: Timeline and return to play. *American Heart Journal Plus: Cardiology Research and Practice*, 34, 100323. https://doi.org/10.1016/j.ahjo.2023.100323
8. Emeran, A., Lambert, E. V., Paruk, T., & Bosch, A. (2022). Changes in training activity post COVID-19 infection in recreational runners and cyclists. *South African Journal of Sports Medicine*, 34(1). https://doi.org/10.17159/2078-516X/2022/V34I1A13758
9. Erickson, J. L., Poterucha, J. T., Gende, A., McEleney, M., Wencl, C. M., Castaneda, M., ... & Jagim, A. R. (2021). Use of electrocardiographic screening to clear athletes for return to sports following COVID-19 infection. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes*, 5(2), 368-376. https://doi.org/10.1016/j.mayocpiqo.2021.01.007
10. Fairweather, D., Beetler, D.J., Di Florio, D.N., Musigk, N., Heidecker, B. & Cooper Jr, L.T. (2023). COVID-19, myocarditis and pericarditis. *Circulation research*, 132(10), 1302-1319. https://doi.org/10.1161/CIRCRESAHA.123.321878
11. Fraser, E. (2020). Long term respiratory complications of covid-19. *BMJ*, (3), 370. https://doi.org/10.1136/bmj.m3001
12. García-Arrabé, M., Giménez, M.J., Moriceau, J., Fevre, A., Roy, J.S., González-de-la-Flor, Á. & de la Plaza San Frutos, M., 2024. Assessing the Impact of COVID-19 on Amateur Runners' Performance: An Analysis through Monitoring Devices. *Sensors*, *24*(8), 2635. https://doi.org/10.3390/s24082635
13. Gluckman, T. J., Bhave, N. M., Allen, L. A., Chung, E. H., Spatz, E. S., ... & Verma, A. K. (2022). 2022 ACC expert consensus decision pathway on cardiovascular sequelae of COVID-19 in adults: myocarditis and other myocardial involvement, post-acute sequelae of SARS-CoV-2 infection, and return to play: a report of the American

College of Cardiology Solution Set Oversight Committee. *Journal of the American College of Cardiology*, 79(17), 1717-1756. https://doi.org/10.1016/j.jacc.2022.02.003

14. Harber, M. P., Kaminsky, L. A., Arena, R., Blair, S. N., Franklin, B. A., Myers, J., & Ross, R. (2017). Impact of cardiorespiratory fitness on all-cause and disease-specific mortality: advances since 2009. *Progress in Cardiovascular Diseases*, 60(1), 11-20. https://doi.org/10.1016/j.pcad.2017.03.001
15. Hughes, D., Saw, R., Perera, N. K. P., Mooney, M., Wallett, A., Cooke, J., ... & Broderick, C. (2020). The Australian Institute of Sport framework for rebooting sport in a COVID-19 environment. *Journal of Science and Medicine in Sport*, 23(7), 639-663. https://doi.org/10.1016/j.jsams.2020.05.004
16. Hull, J. H. (2022). Persistent symptoms in athletes following COVID-19: time to take a breath in the search for answers?. *British Journal of Sports Medicine*, 56(17), 952-953. https://doi.org/10.1136/bjsports-2022-105889
17. Hull, J. H., Loosemore, M., & Schwellnus, M. (2020). Respiratory health in athletes: facing the COVID-19 challenge. *The Lancet Respiratory Medicine*, 8(6), 557-558. https://doi.org/10.1016/S2213-2600(20)30175-2
18. Ibarrola, M., & Dávolos, I. (2020). Myocarditis in athletes after COVID-19 infection: The heart is not the only place to screen. *Sports Medicine and Health Science*, 2(3), 172-173. https://doi.org/10.1016/j.smhs.2020.09.002
19. Jorstad, H. T., & van den Aardweg, J. G. (2020). Balancing act: when is an elite athlete who has had COVID-19 safe to return to play? When does prudent investigation go offside into overmedicalising?. *British Journal of Sports Medicine*, 54(19), 1134-1135. https://doi.org/10.1136/bjsports-2020-103259
20. Juhász, V., Szabó, L., Pavlik, A., Tállay, A., Balla, D., Kiss, O. … & Országh, A. (2022). Short and mid-term characteristics of COVID-19 disease course in athletes: A high-volume, single-center study, *Scandinavian Journal of Medicine & Science in Sports* 33(3), 341–352. https://doi.org/10.1111/sms.14265
21. Kaiser-Nielsen, L. V., Tischer, S. G., Prescott, E. B., & Rasmusen, H. K. (2017). Symptoms, diagnoses, and sporting consequences among athletes referred to a Danish sports cardiology clinic. *Scandinavian Journal of Medicine & Science in Sports*, 27(1), 115-123. https://doi.org/10.1111/sms.12624
22. Kaminsky, L. A., Harber, M. P., Imboden, M. T., Arena, R., & Myers, J. (2018). Peak ventilation reference standards from exercise testing: From the FRIEND registry. *Medicine and Science in Sports and Exercise*, 50(12), 2603–2608. https://doi.org/10.1249/MSS.0000000000001740

23. Komici, K., Bianco, A., Perrotta, F., Dello Iacono, A., Bencivenga, L., D'Agnano, V., ... & Guerra, G. (2021). Clinical characteristics, exercise capacity and pulmonary function in post-COVID-19 competitive athletes. *Journal of Clinical Medicine*, 10(14), 3053. https://doi.org/10.3390/jcm10143053
24. Kroff, J., & Terblanche, E. (2010). The kinanthropometric and pulmonary determinants of global respiratory muscle strength and endurance indices in an athletic population. *European Journal of Applied Physiology*, 110, 49-55. https://doi.org/10.1007/s00421-010-1468-9
25. Lemes, I. R., Smaira, F. I., Ribeiro, W. J., Favero, N. K., Matos, L. D. N. J., de Sá Pinto, A. L., ... & Gualano, B. (2022). Acute and post-acute COVID-19 presentations in athletes: a systematic review and meta-analysis. *British Journal of Sports Medicine*, 56(16), 941-947. https://doi.org/10.1136/bjsports-2022-105583
26. Líška, D., Liptaková, E., Babičová, A., Batalik, L., Baňárová, P. S., & Dobrodenková, S. (2022). What is the quality of life in patients with long COVID compared to a healthy control group?. *Frontiers in Public Health*, 10, 975992. https://doi.org/10.3389/fpubh.2022.975992
27. Lopes, L., Miranda, V., Goes, R., Souza, G., Souza, G., Rocha, J., ... & Perini, J. (2021). Repercussions of the COVID-19 pandemic on athletes: a cross-sectional study. *Biology of Sport*, 38(4), 703-711. https://doi.org/10.5114/biolsport.2021.106147
28. Mackała, K., Kurzaj, M., Okrzymowska, P., Stodółka, J., Coh, M., & Rożek-Piechura, K. (2020). The effect of respiratory muscle training on the pulmonary function, lung ventilation, and endurance performance of young soccer players. *International Journal of Environmental Research and Public Health*, 17(1). https://doi.org/10.3390/ijerph17010234
29. McKinney, J., Velghe, J., Fee, J., Isserow, S., & Drezner, J. A. (2019). Defining athletes and exercisers. *The American Journal of Cardiology*, 123(3), 532-535. https://doi.org/10.1016/j.amjcard.2018.11.001
30. McNarry, M. A., Berg, R. M. G., Shelley, J., Hudson, J., Saynor, Z. L., Duckers, J., Lewis, K., Davies, G. A., & Mackintosh, K. A. (2022). Inspiratory muscle training enhances recovery post-COVID-19: a randomised controlled trial. *European Respiratory Journal*, 60(4). https://doi.org/10.1183/13993003.03101-2021
31. Moulson, N., Gustus, S. K., Scirica, C., Petek, B. J., Vanatta, C., Churchill, T. W., Guseh, J. S., Baggish, A., & Wasfy, M. M. (2022). Diagnostic evaluation and cardiopulmonary exercise test findings in young athletes with persistent symptoms

following COVID-19. *British Journal of Sports Medicine*, 56(16), 927–932. https://doi.org/10.1136/bjsports-2021-105157

32. Palau, P., Domínguez, E., Gonzalez, C., Bondía, E., Albiach, C., Sastre, C., ... & López, L. (2022). Effect of a home-based inspiratory muscle training programme on functional capacity in postdischarged patients with long COVID: the InsCOVID trial. *BMJ Open Respiratory Research*, 9(1), e001439. https://doi.org/10.1136/bmjresp-2022-001439
33. Poczta, J., Almeida, N., Paczyńska-Jędrycka, M., & Kruszyńska, E. (2022). The impact of COVID-19 incidence on motivation to participate in a triathlon. *International Journal of Environmental Research and Public Health*, 19(9), 5576. https://doi.org/10.3390/ijerph19095576
34. Scheer, V., Valero, D., Villiger, E., Rosemann, T., & Knechtle, B. (2021). The impact of the COVID-19 pandemic on endurance and ultra-endurance running. *Medicina*, 57(1), 52. https://doi.org/10.3390/medicina57010052
35. Schroeder, A. N., Getzin, A. R., Creswell, L. L., & Asplund, C. A. (2023). Recovery from COVID-19 in Adult Recreational Athletes: A Survey of American Triathletes. *Exercise, Sport, and Movement*, 1(2), e00005. https://doi.org/10.1249/esm.0000000000000005
36. Schwendinger, F., Infanger, D., Maurer, D. J., Radtke, T., Carrard, J., Kröpfl, J. M., … & Schmidt-Truckäss. A. (2024). Medium- to long-term health condition of patients post-COVID-19, exercise intolerance and potential mechanisms: A narrative review and perspective. *SAGE Open Medicine*, 12, 200503121241296701. https://doi.org/10.1177/20503121241296701
37. Śliż, D., Wiecha, S., Gąsior, J. S., Kasiak, P. S., Ulaszewska, K., Lewandowski, M., ... & Mamcarz, A. (2023). Impact of COVID-19 infection on cardiorespiratory fitness, sleep, and psychology of endurance athletes—CAESAR study. *Journal of Clinical Medicine*, 12(8), 3002. https://doi.org/10.3390/jcm12083002
38. Sivan, M., Halpin, S., Hollingworth, L., Snook, N., Hickman, K., & Clifton, I. J. (2020). Development of an integrated rehabilitation pathway for individuals recovering from COVID-19 in the community. *Journal of Rehabilitation Medicine*, 52(8), 1-5. https://doi.org/10.2340/16501977-2727
39. Steinacker, J. M., Kirsten, J., Schulz, S. V. W., Jerg, A., Kersten, J., Matits, L., & Schellenberg, J. (2022). Rehabilitation after COVID-19–the Challenge of Post-COVID Syndrome with Post-Exertional Malaise. *Dtsch Z Sportmed*, 73,163-166. https://doi.org/10.5960/dzsm.2022.539

40. Stojmenovic, D., Stojmenovic, T., Andjelkovic, M., Trunic, N., Dikic, N., Kilibarda, N., ... & Radovanovic, J. (2023). The Influence of Different SARS-CoV-2 Strains on Changes in Maximal Oxygen Consumption, Ventilatory Efficiency and Oxygen Pulse of Elite Athletes. *Diagnostics*, 13(9), 1574. https://doi.org/10.3390/diagnostics13091574
41. Sudre, C. H., Murray, B., Varsavsky, T., Graham, M. S., Penfold, R. S., Bowyer, R. C., … & Molteni, E. (2021). Attributes and predictors of long COVID. *Nature Medicine*, 274(4), 626-631. https://doi.org/10.1038/s41591-021-01292-y
42. Topol, E. J. (2020). COVID-19 can affect the heart. *Science*, 370(6515), 408-409. https://doi.org10.1126/science.abe2813
43. Ussorowska-Krokosz, A., Blecharz, J., Siekanska, M., & Grygorowicz, M. (2023). Coping with COVID-19: Can a Sense of Coherence and Social Support Play a Protective Role in the Perception of COVID-19 by Polish Women Football Players? A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*, 20(13), 6308. https://doi.org/10.3390/ijerph20136308
44. Vollrath, S., Bizjak, D. A., Zorn, J., Matits, L., Jerg, A., Munk, M., ... & Steinacker, J. M. (2022). Recovery of performance and persistent symptoms in athletes after COVID-19. *PLoS ONE*, 17(12), e0277984. https://doi.org/10.1371/journal.pone.0277984
45. Wilson, M. G., Hull, J. H., Rogers, J., Pollock, N., Dodd, M., Haines, J., ... & Sharma, S. (2020). Cardiorespiratory considerations for return-to-play in elite athletes after COVID-19 infection: a practical guide for sport and exercise medicine physicians. *British Journal of Sports Medicine*, 54(19), 1157-1161. https://doi.org/10.1136/bjsports-2020-102710

Chapter 2 Literature review

2.1 Search strategy

A narrative literature review was performed by searching the electronic databases PubMed and Google Scholar. The keywords COVID-19, athletes, prevalence, quality of life, fatigue, CPET, respiratory muscle training, and inspiratory muscle training were used in various combinations. Alerts were set on the databases to notify me by email about newly published literature fulfilling the search strategy. Reference lists and similar articles were checked. Relevant, published research from inception up to October 2024 were considered for inclusion.

2.2 Health benefits of regular exercise

Regular physical activity has numerous health benefits. High intensity exercise is documented to reduce the overall risk of cardiac disease (Guevarra et al., 2022). Regular moderate intensity exercise regulates blood sugar, reducing the risk of developing type II diabetes (Warburton, Nicol and Bredin, 2006). Weightbearing exercise is profoundly important in preventing the development of osteoporosis particularly in post-menopausal women (Warburton, Nicol and Bredin, 2006). Exercise enhances the immune response to help resist infection and is of particular importance during the COVID-19 pandemic (Kurowski et al., 2022). There is inconclusive and minimal evidence on the immune benefits of regular repeated exercise reducing the risk of chronic disease, versus an isolated short, intense exercise session that spikes immune cell activity (Shukla et al., 2023). Physical activity has been shown to improve not only physical health but mental health as well (Oswald et al., 2020). Running for an indeterminate amount of time and intensity is beneficial for improving mood and mental health (Shukla et al., 2023). Running triggers endorphin and serotonin release, lowers cortisol levels, improves sleep, and provides a sense of achievement (Shukla et al., 2023; Oswald et al., 2020). It has been found that poor mental health, depression and anxiety is less common in runners than inactive individuals (Oswald et al., 2020). Physical activity is an important modulator of the psychological consequences of COVID-19 (Shukla et al., 2023).

2.2.1 Special considerations for endurance athletes

Recreational endurance athletes have intense training programs and often compete at a high level into advanced age (Kaiser-Nielsen et al., 2017). These athletes are fit with low to normal body mass index (BMI) and normal blood pressure, which does not predispose cardiovascular disease (Kaiser-Nielsen et al., 2017). Ultra-endurance exercise puts a huge load on the left and right ventricles due to increased cardiac output requirements. Therefore, enlarged ventricle(s) may be a benign finding due to long-term training adaptations (Jorstad and van den Aardweg, 2020; Teske et al., 2009). Psychophysical stress, heart rate fluctuations, exercise intolerance, myalgia, and fatigue in these athletes may be attributed to their high training loads and should not be confused with abnormal cardiac consequences (Gervasi et al., 2021; Halle et al., 2021).

Prior to the COVID-19 pandemic, myocardial injury has been reported in marathon runners after completion of events (Burtscher et al., 2022). These athletes may physiologically be more prone to blood clotting for various reasons, including dehydration after prolonged aerobic exercise, increased systemic inflammation after intense training, and physiological hormone production in response to exercise, which can all increase thrombophilic potential (Scudiero et al., 2021). As more endurance athletes compete at a masters age, the risk of cardiac symptoms may be more prevalent than in young elite athletes (Kaiser-Nielsen et al., 2017). Physical exercise may provoke symptoms of any infection that are not present at rest, as the increased physical exertion can exacerbate underlying or mild symptoms that remained unnoticed during inactivity (Fletcher et al., 2001). The aim of management in the athlete population is focused on human performance (Barker-Davies et al., 2020). Small delays in recovery can be the determining factor in a professional athlete's career (Jorstad and van den Aardweg, 2020). Yet similar small impairments can mean the cessation of sport in recreational athletes (Jorstad and van den Aardweg, 2020).

2.3 Exercise physiology and cardiopulmonary exercise testing

2.3.1 Exercise physiology

As physical exercise begins, heart rate, cardiac output, blood pressure and pulmonary ventilation increase (Fletcher et al., 2001). To achieve peak exercise performance, it

is essential for oxygen (O_2) to be delivered efficiently to the working muscles, while carbon dioxide (CO_2), a biproduct of metabolism, must be removed (Toma et al., 2010). Consequently, the lungs, heart, pulmonary and peripheral circulation, and skeletal muscles must function optimally (Toma et al., 2010). The process of gas exchange during physical activity is depicted in Figure 2.1 (Milani et al., 2006). Lactate concentration rises minimally during incremental exercise load, then increases sharply at the anaerobic threshold (Wasserman, 1997). This marks the point where glycolysis accelerates, leading to muscle lactic acidosis, known as the ventilatory or lactate threshold. Here, CO_2 output increases relative to O_2 uptake as the body produces additional CO_2 through the bicarbonate (HCO_3) buffering of lactic acid. Once the respiratory exchange ratio (RER) of O_2 to CO_2 exceeds 1.0, anaerobic metabolism is dominant and often accompanied by hyperventilation (Mezzani, 2017). At higher intensities of exercise, the sympathetic nervous system stimulates vasoconstriction in all systems except skeletal muscle, heart and brain (Fletcher et al., 2001). At termination of exercise, the vagus nerve reactivates the parasympathetic nervous system, facilitating the return of haemodynamic functions to a normal resting state.

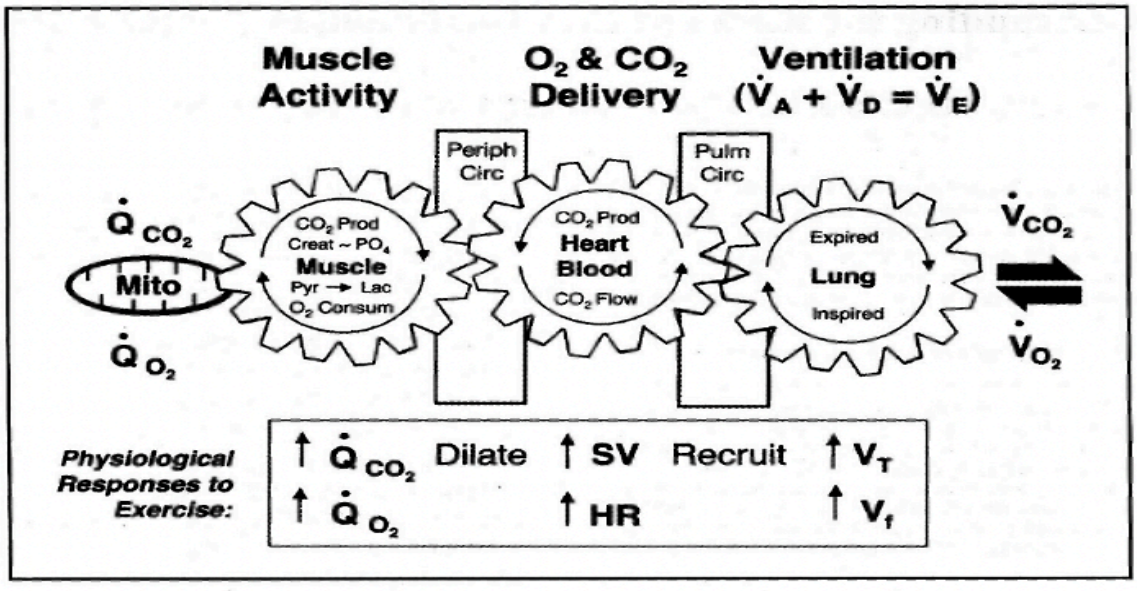


Figure 2.1 Gas transport mechanisms coupling cellular respiration to pulmonary respiration (Reproduced from Milani et al., 2006)

Circ = circulation, Consum = consumption, Creat = creatine, Lac = lactate, HR = heart rate, Mito = mitochondria, PO_4 = phosphate, Periph = peripheral, Prod = production, Pulm = pulmonary, Pyr = pyruvate, QCO_2 = carbon dioxide production, QO_2 = oxygen utilisation, SV = stroke volume, V_A = minute alveolar ventilation, V_D = minute dead space ventilation, V_E = minute ventilation, V_f = breathing frequency, V_T = tidal volume, VCO_2 = carbon dioxide output, VO_2 = oxygen uptake.

2.3.2 Cardiopulmonary exercise testing

Cardiopulmonary exercise testing provides a quantifiable measure of CRF. It is a non-invasive assessment of the integrated response of the respiratory, cardiovascular and peripheral muscle systems during incremental physical work (Wasserman, 1997; Winkert and Kirsten, 2022). Additionally, the test aids identification of the limitations to exercise tolerance that may arise from respiratory, cardiac, or musculoskeletal metabolic pathways (Andonian et al., 2021). It can also be used to evaluate the effectiveness of interventions aiming to enhance physical performance (Andonian et al., 2021). Indirect tests to estimate peak oxygen uptake (VO_{2peak}) exist however, it can vary by 20%-25% from the actual measured capacity using CPET (Schmidt-Trucksäss, 2022; Wells and Norris, 2009). Cardiopulmonary exercise test results are displayed using Wasserman's "nine-panel plot" (Figure 2.2), which organises the data into scatter plots and is described according to the three "gears" that are pulmonary, cardiac, and peripheral muscle systems (Figure 2.1) (Milani et al., 2006; Wasserman, 1997). In Figure 2.2 the top row: first panel, the minute ventilation increases with workload suggesting a normal response; second panel, the HR increases but the plateau in O_2-pulse suggests a cardiovascular limitation; third panel, VO_2 increases then plateaus at VO_{2peak}. In the middle row: first panel, ventilatory efficiency (VE/VCO_2) is determined by a slope < 34, and is normal in this case; second panel, VT can be assessed; third panel, the ventilatory equivalent where metabolism switches from aerobic to anaerobic. In the bottom row: first panel indicates the tidal volume reaching capacity and starting to downturn indicating a ventilatory limitation, second panel, confirms a maximal test (RER >1.1) and shows reduced breathing reserve; third panel, demonstrates VT at the point where the O_2 and CO_2 curves diverge. The parameters measured during CPET are described in Table 2.1.

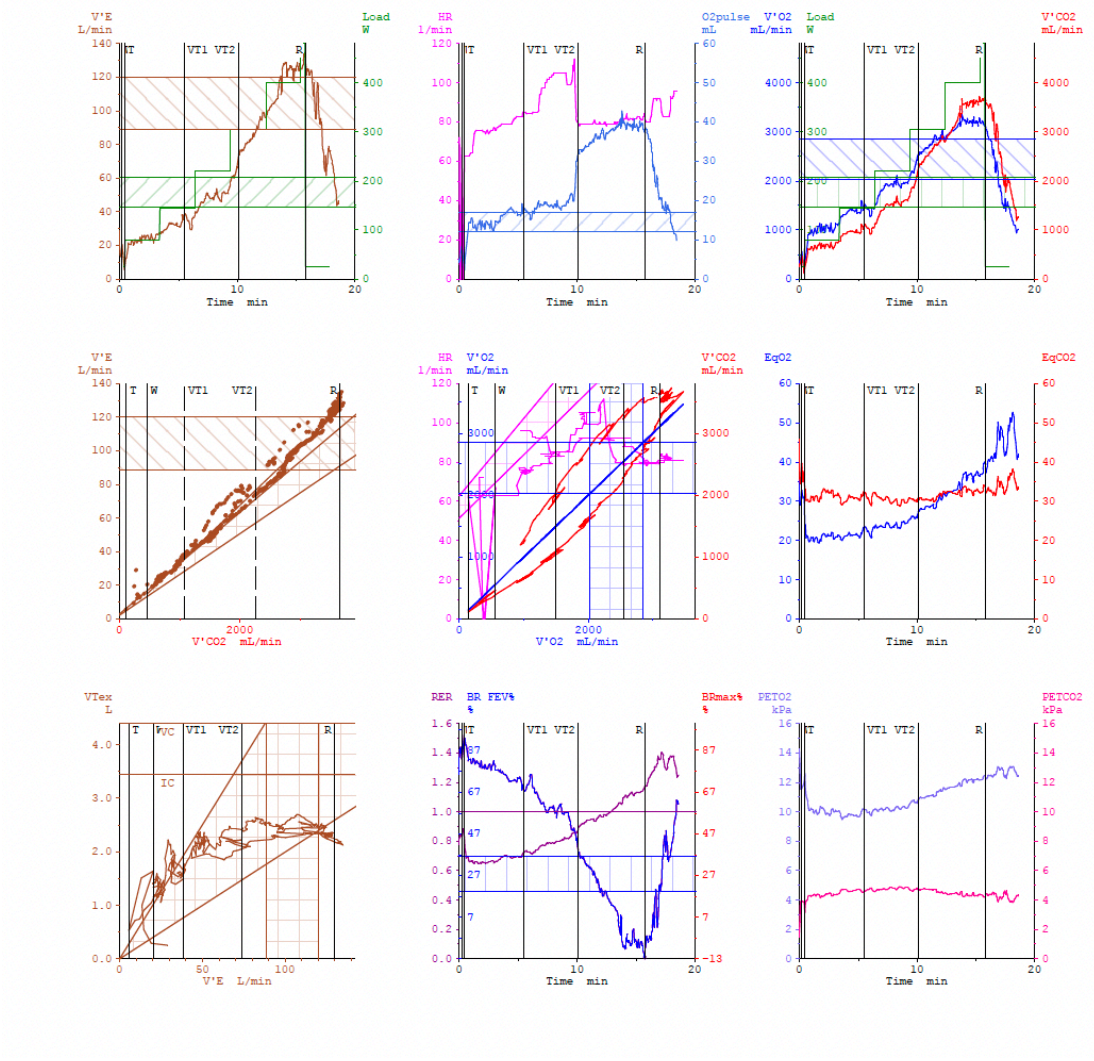


Figure 2.2 Example of a nine-panel plot of one of the participants in Study 3, generated by the General Electric Healthcare CASE^{TM} exercise testing system

2.3.3 Parameters measured with cardiopulmonary exercise testing

Cardiopulmonary exercise testing is usually preceded by a resting lung function test using spirometry. The parameters measured during these tests are described in Table 2.1.

Table 2.1 Description of the physiological parameters measured with spirometry and CPET

Measurement	**Description**
Lung function	

FVC (l)	Forced vital capacity is the volume of air forcefully expired from total lung capacity to residual volume
FEV_1 (l)	The volume of air forcefully expired in one second
PEF ($l.min^{-1}$)	Peak expiratory flow is the maximum volume of air forcefully expired per minute, indicate the speed of exhaled air flow.
CPET	
VO_{2peak} ($ml.kg^{-1}.min^{-1}$)	Peak volume of oxygen in millilitres consumed per minute per kilogram of body weight
VE ($l.min^{-1}$)	Minute Ventilation: The number of litres per minute that is inspired and expired
VE/VCO_2 slope	The volume of CO_2 expelled per litre of air ventilated. Indicative of ventilatory efficiency. An increase in slope indicates increased dead space ventilation in the lung, pulmonary vascular disease or pulmonary limiting disease.
Y-intercept on VE/VCO_2 slope ($l.min^{-1}$)	A negative y-intercept is indicative of cardiac limitation
RER	Respiratory exchange ratio is the rate of CO_2 produces per O_2 consumed. It starts at 0.8 and progresses to 1.05 to 1.1 at maximal effort.
VT ($ml.min^{-1}$)	Ventilatory threshold = The point at which VCO_2 deviated from the linear relationship with VO_2. Indicative that oxygen-independent energy systems are starting to contribute relatively more to energy production with a slight increase in blood lactate levels above resting levels.
HR (bpm)	Heart rate
SpO_2 (%)	Peripheral capillary oxygen saturation. Drops by 5% in healthy adults and 10% in athletes during maximum exercise
Relative workload ($W.kg^{-1}$)	Power (W) divided by body weight
VE/MVV (%)	Dyspnoea index: the ratio of peak minute ventilation to maximum voluntary ventilation. Indicates respiratory limitation if it approximates 100%.
BR	Breathing reserve = 1-VE/MVV
Peak O_2-pulse	

	Oxygen pulse calculated by VO_{2peak}/HR_{max}. It is a surrogate measure of left ventricular stroke volume.

Milani et al. (2006), Andonian et al. (2021), Myers et al. (2017), Kaminsky et al. (2018)

2.3.3.1 VO_{2peak}

Cardiorespiratory fitness is best measured in terms of VO_{2peak} (Milani et al., 2006), an indicator of oxidative capacity and the overall cardiopulmonary response (Andonian et al., 2021). Oxygen uptake (VO_2) increases linearly until its maximal uptake is reached (Wasserman, 1997). At this point, VO_2 plateaus, despite continued or increased workload (Wasserman, 1997). VO_{2max} is defined as the average oxygen uptake during a 20–30 second plateau in VO_2, and it differs from VO_{2peak}, which refers to the highest oxygen uptake value recorded during progressive exercise (Toma et al., 2010; Andonian et al., 2021). Oxygen uptake (VO_2) is expressed as an absolute value ($ml.min^{-1}$) or a relative value ($ml.kg^{-1}.min^{-1}$) (Andonian et al., 2021).

Peak oxygen uptake is determined by the cardiac output, the haemoglobin content of the blood, peripheral muscle blood flow including capillary density, oxygen extraction by skeletal muscle mitochondria, and the ventilation and oxygen perfusion capacity of the lungs (Joyner and Coyle, 2008). Peak oxygen uptake decreases by 10% per decade after the age of 30**,** partly due to a decline in maximum heart rate (HR) (Myers et al., 2017). Higher values are seen in males due to a higher stroke volume and haemoglobin concentration (Mezzani, 2017), with greater muscle versus lower body fat percentage than females (Joyner and Coyle, 2008). There are also genetic differences (Fletcher et al., 2001). According to the European Society of Cardiology, normal healthy individuals have adequate cardiopulmonary responses (Wernhart et al., 2023). For athletes, VO_{2peak} should be more than 100% of the predicted value, and for sedentary adults 80-85% of the predicted value, using the percentage of predicted VO_{2peak} accounts for age and sex differences (Wernhart et al., 2023). Peak oxygen uptake is attained at maximum exertion at RER of 1.3 (age 20-39 years), at RER of 1.1 (40-59 years), and at RER of 1.06 (60-69 years), with a maximal HR of 210 minus age (Schmidt-Trucksäss, 2022).

For patients unable to perform a maximal test to determine VO_{2peak}, a submaximal test can be used to estimate CRF using the oxygen uptake efficiency slope (OUES), which correlates oxygen uptake with total ventilation (Hollenberg and Tager, 2000). It is

dependent on body surface area, age, and sex, and affected by deconditioning, early onset of lactic acidosis, physiological dead space ventilation, and the partial pressure of arterial CO_2.

2.3.3.2 The respiratory response

The respiratory system is the key component in delivering oxygen to muscles during activity (Milani et al., 2006; Wasserman, 1997). Resting spirometry may be of little predictive value in cases of low aerobic fitness, however, should be assessed if persistent respiratory symptoms are hindering exercise tolerance (Schwendinger et al., 2023). Maximal inspiratory pressure is a surrogate measure of inspiratory muscle strength and may be a valuable adjunct to resting lung function testing (HajGhanbari et al., 2013). When analysed in conjunction with resting lung function, CPET indicates potential pulmonary limitations to exercise capacity. This is particularly useful in assessing persistent dyspnoea or bronchial hyperreactivity (Halle et al., 2021). Ventilatory or pulmonary vascular limitations are identified by reduced breathing reserve at peak exercise, abnormal ventilatory response, ventilatory inefficiency, or ventilation/perfusion (V/Q) mismatch (Schwendinger et al., 2023).

An abnormal dyspnoea index (VE/MVV greater than 85%) with adequate cardiovascular reserve, suggests respiratory limitations to exercise capacity (Guenette et al., 2013). Breathing reserve (1-VE/MVV) indicates the oxygen demand versus available oxygen capacity, however, does not allow a conclusion to be made about the cause of the pulmonary limitation (Guenette et al., 2013). A low breathing reserve is characteristic of patients with primary lung disease therefore, if the breathing reserve is high, exercise performance may be limited by cardiovascular or other causes (Toma et al., 2010). Patients with restrictive lung disease have low VO_{2peak} and low VT (Toma et al., 2010). Oxygen desaturation during exercise of more than 5% in the general population and more than 10% in athletes suggests pulmonary limitations to exercise capacity (Andonian et al., 2021). Figure 2.3 shows some of the potential contributors to exertional dyspnoea (Milani et al., 2006).

Dynamic hyperinflation occurs when there is an abnormal increase in lung volume during exercise (Guenette et al., 2013). This higher volume strains the elastic and threshold capacity of inspiratory muscles leading to inspiratory muscle fatigue,

increased work of breathing, reduced tidal volume and ultimately a ventilatory limitation to exercise capacity with CO_2 retention, and dyspnoea (Guenette et al., 2013). If CPET variables are within normal ranges, hyperventilation and dyspnoea may be caused by a breathing pattern disorder, exercise-induced laryngeal obstruction, or anxiety (Toma et al., 2010, Carlsen et al., 2024).

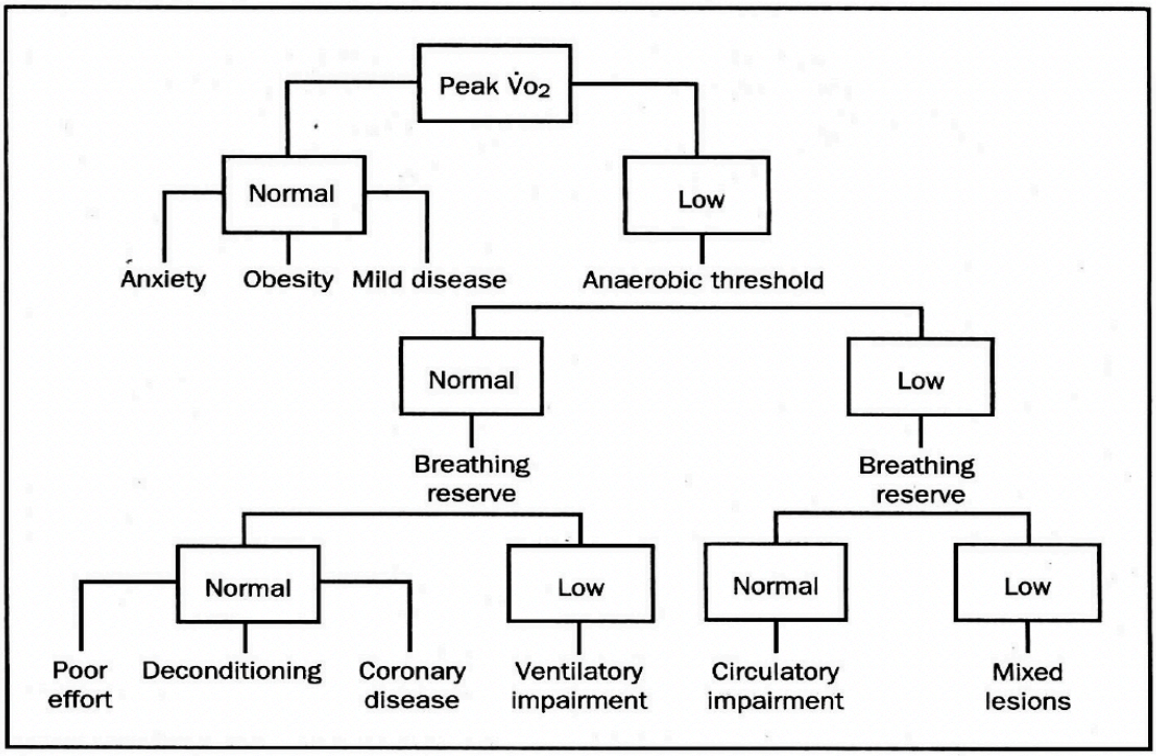


Figure 2.3 The differential diagnosis of exertional dyspnoea
(Reproduced from Milani et al., 2006)

2.3.3.3 The cardiovascular response

The cardiovascular system supplies oxygenated haemoglobin to the skeletal muscles during exercise (Milani et al., 2006; Wasserman, 1997; Schwendinger et al., 2023). Limitations in this system are indicated by a low O_2-pulse, low HR_{max}, low VT, or abnormal HR/VO_2 slope (Schwendinger et al., 2023). Chronotropic incompetence (HR_{max} less than 85% of predicted maximum) directly hinders the supply of O_2 to the muscle and is predictive of cardiovascular disease and all-cause mortality (Schwendinger et al., 2023). Persistent autonomic dysfunction can lead to reduced cardiac output and low VO_{2peak}. Anaemia causes poorer blood oxygen-carrying capacity, resulting in a decreased ventilatory threshold (VT), with normal breathing

reserve (Toma et al., 2010). Higher cardiac output and heart rate are required to compensate for the decreased oxygen supply.

Increased minute ventilation (VE) may be due to increased dead space ventilation and, together with increased VCO_2, is a valuable indicator of early cardiovascular disease (Schwendinger et al., 2023) and may be predictive of heart failure (Toma et al., 2010). The relationship between ventilation and perfusion (VE/VCO_2) should normally be less than 30, where heart rate increases linearly with VO_2. A higher than normal slope may indicate a mismatch (Mezzani, 2017). Raised VE/VCO_2 may be due to hyperventilation, a normal physiological response used by athletes to achieve peak performance (Alba et al., 2021). However, a VE/VCO_2 slope over 40 is abnormal and may indicate cardiac failure or pulmonary artery hypertension (Andonian et al., 2021).

If cardiac limitations to exercise capacity exist, there is less blood being ejected from the left ventricle. The VO_2 starts reducing while the heart rate increases in an attempt to supply the required oxygen (Andonian et al., 2021). On the nine-panel plot (Fig. 2.2), the O_2-pulse curve will be down turning. According to Fick's equation, cardiac output = stroke volume x heart rate. At maximal exertion, peak oxygen uptake is reached and because it is largely unchanging, the O_2-pulse can estimate stroke volume (Milani et al., 2006; Wernhart et al., 2023). Reduced O_2-pulse thus suggests dysfunction of the left ventricle or heart valves (Milani et al., 2006).

2.3.3.4 The metabolic response in peripheral muscles

Limitations to exercise capacity by the peripheral muscular system and mitochondria are indicated by abnormal RER, reduced VT, and a shallow increase of VO_2 to work rate (Milani et al., 2006; Wasserman, 1997; Schwendinger et al., 2023). In the absence of oxygen supply limitations, the ability of the mitochondria to use the oxygen may be the reason VO_{2peak} is reduced. The ventilatory threshold is the highest VO_2 that can be sustained without an increase in blood lactate (Wasserman, 1997). It can be determined by a steeper increase in VCO_2 slope than the VO_2 slope. The VT is highly reproducible and accurately measured with CPET (Wasserman, 1997). A low VT may be due to deconditioning, decreased cardiac output, or impaired mitochondrial function (Andonian et al., 2021). It is related to skeletal muscle capacity and, therefore, a better predictor of endurance capacity in endurance athletes (Andonian et al., 2021; Ladlow

et al., 2022). Once muscles begin to rely on anaerobic glycolysis, the ventilatory threshold and lactate threshold are closely related (Andonian et al., 2021). In untrained individuals, blood lactate concentration increases sharply at about 60% of VO_{2peak}. In athletes, it rises at 75-90% of VO_{2peak}.

2.4 Coronavirus disease 2019 information

2.4.1 Pathophysiology

The virus primarily targets epithelial and immune cells, binding to the ubiquitous angiotensin-converting enzyme 2 (ACE2) on cell membranes (Córdova-Martínez et al., 2022). The permeation of the cells can lead to complications across several systems, including respiratory, cardiac, central nervous system, skeletal muscle, and gastrointestinal systems (Córdova-Martínez et al., 2022). Moreover, due to the high density of ACE2 receptors in the heart, lungs, and muscle tissue, direct binding of the virus to these tissues has deleterious effects (Goergen et al., 2021). An overstimulation of the immune system triggers a surge of pro-inflammatory cytokines, also known as the cytokine storm (Goergen et al., 2021), inducing widespread endothelial tissue inflammation (Halle et al., 2021). The coronavirus can penetrate the nervous system by breaking through the blood-brain barrier in the cytokine storm, or via the transnasal route through the olfactory nerve, leading to varying degrees of neural dysfunction (Córdova-Martínez et al., 2022). Testing for the presence of the disease is performed using a polymerase chain reaction (PCR) test, the accuracy of which depends on the viral load (Luoto et al., 2023). Lopes et al. (2021) found 1% that tested positive were asymptomatic, and 26% who tested negative had more than three symptoms. In South Africa, many athletes had limited access to and affordability for PCR testing due to great economic heterogeneity.

COVID-19 can manifest clinically from asymptomatic to severe and even fatal respiratory distress syndrome (Chen et al., 2020). Acute COVID-19 symptoms are categorised as asymptomatic, mild, moderate, severe and critical illness according to the National Institutes of Health (NIH) (COVID-19 treatment guidelines, 2023). Mild illness symptoms include malaise/fatigue, headache, myalgia, ageusia/anosmia, cough, fever, and diarrhoea/vomiting. Symptoms associated with moderate illness include dyspnoea and clinical evidence of lower respiratory disease on imaging with

normal oxygen saturation (≥94% on room air). Individuals with severe illness present with respiratory distress, dyspnoea and oxygen saturation of <94%, and critical illness include respiratory failure, septic shock and multiorgan failure.

COVID-19 is a multifaceted disease with manifestations like no other respiratory virus (Schwellnus et al., 2021). Symptoms that are uncommon in other respiratory illnesses have been described following COVID-19 including abdominal pain, skin rash on fingers and toes, ground-glass opacity on radiological imaging of the lungs, altered liver function, lymphadenopathy, kidney dysfunction, neurological impairment and venous and arterial hypercoagulation, necrosis and thrombosis (Siddiq et al., 2021). COVID-19 infection suppresses the neuroendocrine-immune system (Mehrsafar et al., 2020). In the acute phase of the disease, disturbance of the nervous system may manifest as fatigue, palpitations, dysautonomia, headaches, anosmia (lack of sense of smell), ageusia (lack of taste), and cognitive impairments causing poor concentration and memory loss, also described as “brain fog” (Chilazi et al., 2021).

2.4.2 Effect on the respiratory system

COVID-19 is primarily a respiratory illness. The coronavirus penetrates the respiratory epithelium via the widespread ACE2 receptor resulting in direct inflammation and cellular damage. The common signs and symptoms of all upper respiratory tract infections are prevalent in COVID-19. These include a dry cough, rhinorrhoea, sore throat, dyspnoea and chest tightness (COVID-19 treatment guidelines, 2023). Pulmonary complications of COVID-19 include pneumonia, pulmonary embolism, impaired diffusion capacity, pulmonary fibrosis, new or worsening asthma, bronchial hyperreactivity, and pulmonary vascular inflammation (Gluckman et al., 2022). Chest pain may be pulmonary in origin with vascular impairment causing pleuritic chest pain.

Should any respiratory symptoms persist, it is likely to adversely affect RTS (Lemes et al., 2022). The reduction in physical activity coupled with persistent symptoms such as chest pain, cough and fatigue places additional strain on the respiratory system, leading to a difficult RTS (Williams and Hull, 2022). The pulmonary impact is especially relevant in aerobic exercise, where a continuous supply of O_2 to the skeletal muscles and removal of CO_2 is required, suggesting that endurance athletes may experience greater challenges than sprint or power-sport athletes (Parker et al., 2021).

2.4.3 Effect on the cardiac system

The coronavirus, SARS-CoV-2, affects the cardiovascular system by directly affecting the ACE-2 enzyme, hypercoagulability that predisposes thrombosis, cytokine release whereby immune response is exaggerated, or hypoxia of cardiac muscle cells due to pneumonia or respiratory distress syndrome (Monosilio et al., 2023). Cardiac symptoms include chest pain, syncope (particularly concerning is exertional syncope), dyspnoea, palpitations, and exercise intolerance (Kaiser-Nielsen et al., 2017). Cardiac symptoms have a high specificity for detecting cardiac disease. Cardiac consequences may present as arrhythmias, myocarditis, thromboembolism, or heart failure (Monosilio et al., 2023). Injury and scarring of the heart, enlarged left ventricle and atrial fibrillation are all potential sequalae of COVID-19 in athletes (Kaiser-Nielsen et al., 2017). Atrial fibrillations are the most common diagnosis as a higher risk of atrial fibrillations exists in middle-aged athletes who have been doing vigorous exercise for many years (Kaiser-Nielsen et al., 2017).

Historically, myocarditis due to viral infection is a common cause of sudden cardiac death in young athletes (Goergen et al., 2021). COVID-19-induced myocarditis occurs more frequently than myocarditis induced by other viruses and became an enormous concern for athletes and sports medicine clinicians at the beginning of the pandemic (Goergen et al., 2021; Patel and Thompson, 2022). Sudden death usually has a structurally normal heart, thus the association of viral myocarditis in sudden death is unclear (Ruuskanen et al., 2024). The period for which this risk may be present is uncertain as cardiac inflammation has been detected on cardiac magnetic resonance imaging (MRI) more than three months post-infection (Edenfield, Dillon and Clugston, 2023). Most studies reported that cardiovascular involvement resolved over time, with one study that reported persistent late gadolinium enhancement on MRI indicating unresolved myocardial injury. However, these studies mostly involve young elite athletes, and a paucity of studies reported on the long-term follow-up of these cases (Goergen et al., 2021; Monosilio et al., 2021). As research has emerged, a 0.5% to 3% incidence of cardiac consequences after COVID-19 has been reported (Monosilio et al., 2021; Edenfield, Dillon and Clugston, 2023). This is higher than the pre-COVID-19 incidence of post-viral adverse cardiac events which was 0.01% to 0.1% (Golpour et al., 2017; Fairweather et al., 2023).

2.4.4 Effect on the peripheral muscle system

Muscle tissue has a high density of ACE2 receptors, thus a target for SARS-CoV-2. Myopathy commonly results from COVID-19 as muscle fibres are affected in various ways. Direct inflammation results when the virus binds to muscle cells (Hejbøl et al., 2022). Virus replication occurs in the cells causing muscle injury and death (Silva et al., 2022). Damaged fibres and immobility during recovery leads to a reduced number of oxidative fibres and therefore, muscle atrophy (Córdova-Martínez et al., 2022; Hejbøl et al., 2022). In the mitochondria, there may be abnormal changes to the sub-sarcolemma, cristae, and cytochrome C oxidase activity (Hejbøl et al., 2022). The finding of microthrombi indicate that capillaries in muscles are affected by the virus (Hejbøl et al., 2022). This abnormal histology indicates that muscle cells targeted by SARS-CoV-2 causes myalgia and muscle fatigue for up to 14 months post-illness (Hejbøl et al., 2022), which would adversely affect endurance athletes' ability to train at high volumes.

After intense or sustained exercise, muscle proteins and enzymes such as troponin are released due to muscle damage and inflammation (Córdova-Martínez et al., 2022). A similar process occurs with the SARS-CoV-2 infection thus blood test results can be confounding (Córdova-Martínez et al., 2022). Therefore, it is hypothesized that patients with COVID-19 may feel the same fatigue as if they had run a marathon (Córdova-Martínez et al., 2022). After sustained exercise or intense loading under normal circumstances, positive adaptations occur to hypertrophy muscles, whereas in COVID-19, myalgia and fatigue coupled with forced inactivity result in loss of strength and functional capacity (Córdova-Martínez et al., 2022).

At the advent of the pandemic, little was understood about the impact of COVID-19 on the musculoskeletal system other than deterioration due to bed rest (Barker-Davies et al., 2020). Musculoskeletal symptoms include myalgia, muscle weakness, fatigue, and reduced physical performance (Silva et al., 2022). Myalgia can be exacerbated by arthralgia, nervous system dysfunction, hospitalisation, and use of corticosteroids and immunotherapies (Disser et al., 2020). Hypoxaemia due to lung damage leads to reduced oxygen delivery to the muscle tissue, which affects mitochondria. In the mitochondria, reduced oxygen causes decreased adenosine triphosphate production,

which is necessary for muscle contraction, therefore impairs muscle energy generation (Silva et al., 2022). Anaerobic cell metabolism ensues and may perpetuate the inflammation of muscle cells by the increased lactate produced. Inflammatory cytokines cause muscle tissue damage in the acute phase but may be present months after infection (Silva et al., 2022). Muscle damage can be detected by biomarkers of muscle injury in the blood.

2.5 Impact of COVID-19 on CPET

Even after mild to moderate illness, tissue damage of the lungs, heart, nervous system, renal system, and peripheral muscle will affect exercise capacity for an indeterminant length of time (Halle et al., 2021). The European Respiratory Society/ American Thoracic Society task force guidelines for COVID-19 follow-up suggest that CPET should be used to determine exercise capacity (Rinaldo et al., 2021). It is used to determine prognosis and assess safety for exercise prescription therefore an important part of clinical assessments of patients returning to sport after COVID-19. Research exploring the long-term effects of the disease should employ CPET because the cause of long-COVID is yet to be elucidated and may be multifactorial (Mihalick et al., 2021). It is recommended that CPET is performed after training has resumed. This will minimise the effects of detraining during the acute and subacute recovery phase. Athletes whose results then show normal aerobic capacity can be reassured that they were not negatively affected by any long-term consequences of COVID-19 (Williams and Hull, 2022).

Cardiopulmonary exercise testing used to assess aerobic capacity of athletes after COVID-19 has revealed equivocal results. A review by Williams & Hull (2022), showed that many studies involving young elite athletes found no limitations, while others found a decline in VO_{2peak}, VE, O_2-pulse, breathing reserve, and peak power. Studies showing a decline in VO_{2peak} within 60 days of infection, highlighted the need for longer-term investigations (Ladlow et al., 2022; Crameri et al., 2020). In a systematic review by Durstenfeld et al. (2022), symptomatic adults had on average a 4.9 $ml.kg^{-1}.min^{-1}$ lower exercise capacity compared to asymptomatic adults, over three months post-COVID-19. There was wide variability in clinical presentation and methodology regarding type of testing (cycle or treadmill) and protocols used. Age, sex, BMI, and

CRF level prior to infection were found to be associated with VO_{2peak}, which may partly explain the diversity of results across studies. Few studies performed longitudinal follow-up investigations (Durstenfeld et al., 2022). It has been demonstrated that VO_{2peak} declines rapidly in masters-age athletes without illness if exercise is stopped, likely due to reduced cardiac output and mitochondrial dysfunction (Burtscher et al., 2022). However, VO_{2peak} should recover quickly upon resumption of training, with older athletes recovering particularly well (on average VO_{2peak} recovers by 0.5 $ml.min^{-1}.kg^{-1}$ after 12 weeks) (Bacon et al., 2013). There is a paucity of literature focusing on CPET in masters-age athletes and in a diversity of races and cultures (Williams and Hull, 2022). Pulmonary investigations may be less frequently performed in low-income populations or under-resourced geographical areas, of which there are many in South Africa (Parker et al., 2021).

Resting spirometry has rarely detected abnormalities post-COVID-19 in athletes, with only one study (mean age 34 years) showing decreased FVC and FEV_1 in those who were struggling with dyspnoea (Schmucker et al., 2022). The author suggested alveolar membrane damage or lung impairment was responsible, however CPET was not performed. Impaired pulmonary diffusion capacity is slow to resolve and may contribute to protracted exercise tolerance after COVID-19 (Vignesh, Preetha and Devi, 2018). Additionally, physical deconditioning of respiratory muscles can lead to a low maximum voluntary ventilation (MVV) (Jimeno-Almazán et al., 2023). In a review by Durstenveld et al. (2022) ventilatory limitations were due to hyperventilation, dysfunctional breathing, or ventilatory inefficiency with isolated cases of pulmonary vascular limitation or reduced mechanical efficiency. Even well trained, asymptomatic individuals may have abnormal ventilatory responses, potentially due to dysautonomia (Brito et al., 2023). Less commonly, pulmonary artery hypertension (PAH) can be caused by damage to the pulmonary vascular bed, thromboembolism, reduced ejection fraction and hypoxia-induced vasoconstriction. Athletes with PAH can exercise safely without overloading the right ventricle (Halle et al., 2021).

Athletes with post-exertional malaise and an inadequate cardiopulmonary response to exercise (plateau of O_2-pulse and VE/VCO_2 >30) may be at increased risk of long-COVID (Wernhart et al., 2023). In a systematic review, cardiac limitations after COVID-19 were uncommon with a few studies reporting chronotropic incompetence and reduced stroke volume (Durstenfeld et al., 2022). Brito et al. (2023) found that

symptomatic athletes had higher VE/VCO_2 with an average of 30.6 compared to asymptomatic highly trained athletes. Impairment of the vascular system is a short-term sequela of COVID-19 due to endothelium and blood cell damage that can lead to reduced oxygen supply and hypoxemia (Mezzani, 2017).

Mitochondrial damage interferes with clearing of lactic acid and fatty acid oxidisation (San-Millán, 2023). COVID-19 affects metabolic adaptation during physical activity. Many studies reported deconditioning or impaired oxygen utilisation in the muscles but distinguishing between deconditioning and altered O_2 delivery or mitochondrial dysfunction is unreliable without comparing results before and after COVID-19 or performing an invasive CPET (Durstenfeld et al., 2022). Sliz et al. (2023) compared pre-COVID-19 CPET results to post-COVID-19 in 40-year-old endurance athletes and showed a significant drop in VO_{2peak}, however the average time between the tests was 592 days. Here, blood tests for biomarkers of inflammation and muscle protein degradation could be useful as elevated creatinine kinase and lactate dehydrogenase levels have been noted after COVID-19 (Schwendinger et al., 2023). Some studies found normal breathing reserves and an absence of desaturation in all their participants, leading to the conclusion that deconditioning was responsible for low exercise capacity (Rinaldo et al., 2021; Brito et al., 2023; Komici et al., 2021). Only the latter two authors, however, assessed an athletic population. Musculoskeletal impairments potentially accelerate the transition to anaerobic metabolism (as evident by a decreased in VT) (Vonbank et al., 2021). This higher concentration of CO_2 lowers the pH and causes chemosensitivity that stimulates the metaboergoreflex and is thought to be responsible for hyperventilation resulting in an elevated VE/VCO_2, rather than increased dead space (Baratto et al., 2021).

Absolute and relative contraindications, and the description of the CPET procedure and protocol used in the study for this thesis is described in the linking notes between Study 2 and 3.

2.6 Impact of COVID-19 on quality of life

Quality of life is inclusive of an individual's physical health, mental health, social interactions and emotional well-being (WHO Quality of Life, 2012). It is influenced by both the resources available and conditions in the community, as well as the

individual's functional status (Líška et al., 2022). Pandemics fall into a similar context as major disasters and traumatic events, particularly given the life-threatening nature of COVID-19, causing high stress levels in the global population, and an increase in physical and mental illness (Barker-Davies et al., 2020; Córdova-Martínez et al., 2022).

Persistent symptoms have been labelled with various terms, but in this study, the term "long-COVID" is used to describe new or persistent symptoms that appear after four weeks following the onset of illness, as defined by the National Institute for Health and Care Excellence (NICE Covid19 Rapid Guideline, 2021). Long-COVID has the potential to diminish quality of life in all sectors of the population, including athletes (Jurecka, Skucińska and Gądek et al., 2021). It has manifestations such as chronic fatigue, shortness of breath, musculoskeletal pain, tachycardia, headaches, depression, anxiety, cognitive impairment, exercise intolerance, and poor sleep quality among a constellation of other symptoms (Líška et al., 2022; Jurecka, Skucińska and Gądek et al., 2021). Female sex, increased age, the presence of comorbidities, and experiencing five or more acute symptoms are associated with higher risk of long-COVID (Líška et al., 2022). It is estimated that 10% of the population will develop long-COVID after being infected with SARS-CoV-2 (Steinacker et al., 2022). Overstimulation of the sympathetic nervous system increases heart rate and blood pressure (Córdova-Martínez et al., 2022) while postural orthostatic tachycardia syndrome (POTS) can affect safety during sport (Halle, 2021). The lack of diagnostic tests makes it challenging to diagnose, and the absence of a definitive diagnosis often leads to the condition being misunderstood or trivialised by others. This increases the individual's anxiety about their condition (Líška et al., 2022). During sports participation, athletes require an optimal cognitive and psychological state for motivation, tactics, skills and performance (Córdova-Martínez et al., 2022).

The virus can cause neuroendocrine impairment leading to a poorer ability to cope with stress, anxiety or depression (Mehrsafar et al., 2020). Under normal circumstances, athletes use physical activity to cope with stress through adaptation and increased resilience (Ussorowska-Krokosz et al., 2023). To capitalise on this stress-response strategy, they require optimal performance (Córdova-Martínez et al., 2022). Uncertainties about how long the virus will remain prevalent and its impact on the resumption of sporting events is stressful for athletes (Córdova-Martínez et al., 2022). Prolonged stress can weaken the immune system and is a large contributor to the

development of psychosocial problems (Córdova-Martínez et al., 2022; Poczta et al., 2022). Urbanski defined coping as “cognitive and behavioural efforts to master, reduce, or tolerate the internal and/or external demands that are created by the stressful transaction” (Urbanski et al., 2023:512). While student athletes must balance academic and sporting demands, there is little research describing the mental impact of COVID-19 on recreational athletes who juggle both occupational and sporting responsibilities (Conde et al., 2021). Poor mental health increases the risk of morbidity and thus places a burden on healthcare worldwide (Oswald et al., 2020).

Athletes may experience a wide range of emotional responses to the pandemic, being positive, negative or neutral reactions (Conde et al., 2021). Uncertainties create fear, stigma and discrimination (Kumar and Nayar, 2020). Some people were advised to consider every individual as potentially carrying COVID-19 and every surface as if it might be contaminated (Kumar and Nayar, 2020). Conformist behaviour is common when feeling threatened by a disease (Poczta et al., 2022). Fear of contagion or spreading the virus, the stigma associated with being infected, and information overload increases psychological stress (Burtscher et al., 2022), which in turn can lower immunity (Luoto et al., 2023).

Lockdown measures and lack of competition reduced the motivation to exercise in athletes (Washif et al., 2022). There was poorer communication between coaches and athletes during these stages (Urbański et al., 2023). The health crisis led to changes in routine, self-identity, occupational and cultural realms (Conde et al., 2021). No competition meant a less than normal training load and so deconditioning ensued (Conde et al., 2021). Females, and athletes competing at higher levels were more affected by lockdowns (Conde et al., 2021). On the positive side, it created a good opportunity to recover from injuries and work on weaknesses in their performance (Conde et al., 2021). Because physical activity is an important modulator of stress, and even more so when exercising outdoors or in groups, an important coping mechanism was removed by the imposed lockdowns (Luoto et al., 2023). Home-based exercise routines such as following online exercise programs was encouraged. Once restrictions were lifted and competition resumed, no supporters in stadiums and along the roadside were permitted. Social connections and supporting of teammates are integral to an athlete’s identity (Conde et al., 2021). The support from fans is a great

motivation for athletes and aids in promoting performance excellence (Córdova-Martínez et al., 2022).

2.7 Respiratory muscle training

During endurance training, cardiovascular and skeletal muscle adaptations are dominant (McKenzie, 2012). Therefore, limitations to performance by the respiratory system mainly results from respiratory muscle fatigue (McKenzie, 2012). Those with poorer respiratory muscle strength may have a delayed recovery post COVID-19, and it is speculated that commencing respiratory muscle training will improve outcomes post-COVID-19 (Severin et al., 2020). Persistent fatigue, dyspnoea, and exercise intolerance following COVID-19 may be attributed to diaphragm fatigue, which has been shown to improve with IMT (Del Corral et al., 2022). For athletes, effective management of respiratory conditions will improve physical performance capacity (HajGhanbari et al., 2013). Mackala et al. (2019) found that eight weeks of threshold inspiratory muscle training (IMT) improved inspiratory muscle strength and indirect VO_{2peak} estimated by the Cooper's test. Similarly, a four-week intervention of IMT at 50%S-Index improved the S-Index however suggested that the improvement in VO_{2peak} was likely due to exercise training (Ogawa et al., 2020). Notter et al. (2023) reported improved S-Index without improved athletic performance after four weeks of IMT. It was proposed that respiratory muscle training allows higher intensity exercise without dyspnoea, thereby increasing exercise tolerance (Holm, Sattler and Fregosi, 2004). However, all these studies included a sample of young competitive athletes.

A six-week post-COVID-19 rehabilitation programme for sedentary adults, implemented by Daynes et al. (2021) consisted of two sessions per week of supervised walking, muscle strengthening of upper and lower limbs and education. The programme was progressed according to their tolerance and considering their symptoms to avoid an exacerbation of post-viral fatigue. They showed improved respiratory symptoms, fatigue, exercise capacity, and cognition. Because inspiratory muscle training has been shown to improve respiratory muscle strength, exercise capacity and dyspnoea, it is recommended as an adjunct to strength training and aerobic exercise in patients with long-COVID (Silva et al., 2022). The efficacy of an eight-week IMT intervention was investigated in non-athletes with long-COVID and found that inspiratory muscle strength and endurance and lower limb strength

improved, however there was no change in exercise tolerance (del Corral et al., 2023). Conversely, a 12-week home-based IMT programme improved VO_{2peak} significantly in a sample of non-athletes, average age 50 years (Palau et al., 2022).

Inspiratory muscle strength training enhances cardiovascular function, can be performed independently without supervision, is time-efficient to support adherence, and uses compact, handheld devices (Craighead et al., 2022). Moderate intensity aerobic exercise requires an inspiratory resistance of less than 20mmHg. Inspiratory muscle training is performed at a much higher pressure (more than 45mmHg). Initiation of exercise post-COVID-19 is vital and should commence within 30 days of onset, considering comorbidities and post-COVID sequalae (Halle et al., 2021; Barker-Davies et al., 2020). The positive effects of IMT on athletic performance and its use in post-COVID-19 rehabilitation raised the question of whether IMT can enhance athletic performance after COVID-19.

2.8 Rationale for this thesis based on the literature

Regular physical activity is vital as it reduces the overall risk of cardiovascular disease (Guevarra et al., 2022). Physical activity, particularly running, has been shown to improve not only physical health but mental health as well (Oswald et al., 2020). Endurance athletes have high weekly training loads that far exceed the minimum physical activity volume for good general health (Joyner and Coyle, 2008). These athletes often compete at high levels into advanced age, and as the prevalence of co-morbidities increases with age, the risks of cardiopulmonary consequences are likely to be higher than that of young elite athletes (Kaiser-Nielsen et al., 2017). During exercise the lungs, heart, pulmonary and peripheral circulation, and skeletal muscles must function co-operatively to deliver oxygen to working muscles (Toma et al., 2010). Endurance athletes with comorbidities or persistent symptoms may suffer with exercise intolerance. This may result in reduced participation in sport. Physical activity is an essential coping mechanism used by athletes against stress (Ussorowska-Krokosz et al., 2023). The impact of COVID-19 on mental health of elite athletes has been explored (Jurecka, Skucińska, and Gądek, 2021) and the importance of social support investigated in only one study at the time of writing (Ussorowska-Krokosz et al., 2023). In South Africa, group training is very popular among recreational and competitive endurance and creates a beneficial social support system (Conde et al., 2021). Thus,

this multifaceted nature of long-COVID has the potential to severely compromise the biopsychosocial well-being of these athletes. Despite this, no studies to date have investigated this specific impact within the endurance athlete population.

The coronavirus SARS-CoV-2 binds to the ACE2 enzyme found prolifically in lung, heart and skeletal muscle tissue. The direct damage to these tissues will impair exercise capacity. Indirectly, systemic inflammation caused by the cytokine storm, small vessel hypercoagulation and neuroendocrine impairment, together with deconditioning further limits exercise capacity. Quantifying cardiorespiratory fitness using resting lung function, S-Index, and CPET tests is important because athletes should exceed 100% of the predicted thresholds for sedentary adults (Wernhart et al., 2023). Values below this threshold may indicate cardiorespiratory impairments. Assessing the integrated response of the respiratory, cardiovascular and peripheral muscle systems will aid identification of limitations to exercise capacity (Wasserman, 1997). The impact on the respiratory system is especially pertinent for endurance athletes doing many hours of aerobic exercise (Parker et al., 2021). Few studies investigating cardiorespiratory fitness in masters age-group endurance athletes exist and to my knowledge, no studies have been performed with longitudinal follow-up investigations (Durstenfeld et al., 2022). In 2025, management of respiratory conditions is shifting from the acute pandemic response to optimising athletic participation and performance. Athletes experiencing exercise intolerance due to long-COVID may benefit from an intervention such as inspiratory muscle training to assist their RTS. As the global burden of chronic disease continues to rise, the resumption of sport and the vital health benefits thereof cannot be overstated (Guevarra et al., 2022).

2.9 Theoretical framework

The theoretical framework embedded in this thesis is the Biopsychosocial model, first described by Engel (1977) as a more complete framework to guide clinicians in their patient management. This model links physical health with mental health and social engagement. Health is not solely a biomedical concern as psychological well-being can play an important part in the manifestation of disease (Engel, 1977). Patient care should include the performance of activities of daily living and integration into social roles. Their intellectual capability and emotional state should be considered, particularly in chronic conditions (Fava and Sonino, 2007). This is important because

preventable behaviour such as physical inactivity still largely leads to chronic disease and health care system burdens (Fava and Sonino, 2007). Approaching research using this model allows a more comprehensive understanding of the impact of this multifaceted disease.

2.10 Importance of the studies presented in this thesis

The pandemic has increased focus on the benefits of health, wellness, and healthcare with physical activity an important component (Poczta et al., 2022). Endurance sports including long-distance cycling, running, swimming, triathlon and canoeing are growing into mass participation events worldwide (Braga et al., 2023). Knowledge on the nature and severity of acute and long-term COVID-19 symptoms and the management thereof may assist healthcare professionals' understanding of the expression of this disease in athletes who place a high demand on their cardiovascular system. In South Africa ultramarathon running is a very popular sport primarily attracting masters age-group individuals from all sectors of the population (Scheer et al., 2021). For medical professionals, coaches and athletes alike it is important to understand the acute clinical conditions, long-term cardiopulmonary consequences, the impact on quality of life and safe RTS (Schroeder et al., 2023).

Assessing the physiological and psychosocial impacts of COVID-19 on endurance athletes' exercise capacity and potential measures to improve their return to sport was the impetus for the studies presented in this thesis. It has been found that subjective measures were superior to objective measures in detecting changes in the well-being of athletes as training load increased (Saw, Main and Gastin, 2023). Thus, living data on COVID-19 convalescent athletes is important for their optimal mental and physical health. To my knowledge to date, no other studies have been published exploring the impact of COVID-19 on endurance athletes' quality of life.

The high burden of quality-of-life impairments due to persistent symptoms necessitates CPET, spirometry, and electrocardiogram (ECG) assessments (Jimeno-Almazán ET AL., 2023). Objectively measuring the influence of COVID-19 on the CRF of endurance athletes and identifying whether limitations to exercise capacity originate from the respiratory, cardiac or skeletal muscle systems will greatly assist rehabilitation and RTS. Determining normal values of cardiorespiratory fitness and respiratory muscle

strength in South African endurance athletes will assist both this study in illustrating the difference in CRF of athletes recovering from COVID-19 to the norms, and future studies requiring the same data. Inspiratory muscle strength training improves diaphragm thickness, respiratory muscle strength and endurance, exercise capacity, and reduces dyspnoea (Severin et al., 2020) and is an important consideration for future research (Craighead et al., 2022). If an intervention to assist athletes' recovery from long-COVID symptoms is beneficial, it will contribute to a safer return to sport and somewhat reduce the devastating impact this coronavirus disease has had.

2.11 Conclusion

Endurance athletes engage in high volumes of cardiovascular exercise and are generally at low risk for chronic diseases. However, the physiological effects of endurance training may create unique predispositions to negative consequences of COVID-19, potentially hindering their return to sports participation. After the acute COVID-19 infection has subsided, persistent symptoms such as dyspnoea and fatigue may cause exercise intolerance. Given that protracted resumption of sport may be associated with reduced quality of life, a comprehensive investigation of the biopsychosocial impacts of COVID-19 on endurance athletes' RTS is needed.

Exercise intolerance can be investigated using CPET to identify limitations in the respiratory, cardiac or peripheral muscle systems. Abnormal respiratory responses to exercise after COVID-19 have been documented and are primarily due to dysfunctional breathing, ventilatory inefficiency, bronchial hyper-reactivity, and pulmonary vascular impairment. COVID-19 is primarily a respiratory illness. Inspiratory muscle training has been shown to improve respiratory muscle strength in healthy athletes and increases exercise tolerance in the general population after COVID-19. It is essential that endurance athletes resume sports participation for the important physical and mental health benefits thereof.

2.12 References

1. Alba, G. A., Ziehr, D. R., Rouvina, J. N., Hariri, L. P., Knipe, R. S., Medoff, B. D., ... & Hardin, C. C. (2021). Exercise performance in patients with post-acute sequelae of SARS-CoV-2 infection compared to patients with unexplained dyspnea. *EClinicalMedicine*, 39. https://doi.org/10.1016/j.eclinm.2021.101066
2. Andonian, B. J., Hardy, N., Bendelac, A., Polys, N., & Kraus, W. E. (2021). Making cardiopulmonary exercise testing interpretable for clinicians. *Current Sports Medicine reports*, 20(10), 545-552. https://doi.org/10.1249/JSR.0000000000000895
3. Bacon, A. P., Carter, R. E., Ogle, E. A., & Joyner, M. J. (2013). VO2max trainability and high intensity interval training in humans: a meta-analysis. *PloS ONE*, 8(9),e73182. https://doi.org/10.1371/journal.pone.0073182
4. Baratto, C., Caravita, S., Faini, A., Perego, G. B., Senni, M., Badano, L. P., & Parati, G. (2021). Impact of COVID-19 on exercise pathophysiology: a combined cardiopulmonary and echocardiographic exercise study. *Journal of Applied Physiology*, 130(5), 1470-1478. https://doi.org/10.1152/japplphysiol.00710.2020
5. Barker-Davies, R. M., O'Sullivan, O., Senaratne, K. P. P., Baker, P., Cranley, M., Dharm-Datta, S., ... & Bahadur, S. (2020). The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *British Journal of Sports Medicine*, 54(16), 949-959. https://doi.org/10.1136/bjsports-2020-102596
6. Brito, G. M., Prado, D. M. L. D., Rezende, D. A., de Matos, L. D. N. J., Loturco, I., Vieira, M. L. C., ... & Coalition SPORT-COVID-19. (2023). The utility of cardiopulmonary exercise testing in athletes and physically active individuals with or without persistent symptoms after COVID-19. *Frontiers in Medicine*, 10, 1128414. https://doi.org/10.3389/fmed.2023.1128414
7. Burtscher, J., Strasser, B., Burtscher, M., & Millet, G. P. (2022). The impact of training on the loss of cardiorespiratory fitness in aging masters endurance athletes. *International Journal of Environmental Research and Public Health*, 19(17), 11050. https://doi.org/10.3390/ijerph191711050
8. Carlsen, P. H., Muralitharan, P., Fenne, H., Hammer, I. J., Engan, M., Vollsaeter, M., …& Clemm, H. H. (2024). Laryngeal response to high-intensity exercise in healthy athletes. *British Medical Journal open Sport & Exercise Medicine*, 10, e001850. https://doi.org/10.1136/bmjsem-2023-001850

9. Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., ... & Zhang, L. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*, 395(10223), 507-513. https://doi.org/10.1016/S0140-6736(20)30211-7
10. Chilazi, M., Duffy, E. Y., Thakkar, A., & Michos, E. D. (2021). COVID and cardiovascular disease: what we know in 2021. *Current Atherosclerosis Reports*, 23(7), 37. https://doi.org/10.1007/s11883-021-00935-2
11. Conde, E., Martínez-Aranda, L. M., Sanz, G., López de Subijana, C., Sánchez-Pato, A., Díaz-Aroca, Á., ... & Torregrossa, M. (2021). Effects of the COVID-19 health crisis on sports practice, life quality, and emotional status in Spanish high-performance athletes. *Frontiers in Psychology*, 12, 736499. https://doi.org/10.3389/fpsyg.2021.736499
12. Córdova-Martínez, A., Caballero-García, A., Roche, E., Pérez-Valdecantos, D., & Noriega, D. C. (2022). Effects and causes of detraining in athletes due to COVID-19: A review. *International Journal of Environmental Research and Public Health*, 19(9), 5400. https://doi.org/10.3390/ijerph19095400
13. COVID-19 Treatment Guidelines. (2023). *NIH: Clinical spectrum of SARS-CoV-2 infection*. https://www.covid19treatmentguidelines.nih.gov/. Accessed 13 February 2013.
14. Craighead, D. H., Freeberg, K. A., Maurer, G. S., Myers, V. H., & Seals, D. R. (2022). Translational potential of high-resistance inspiratory muscle strength training. *Exercise and Sport Sciences Reviews*, 50(3), 107-117. https://doi.org/10.1249/JES.0000000000000293
15. Crameri, G. A. G., Bielecki, M., Züst, R., Buehrer, T. W., Stanga, Z., & Deuel, J. W. (2020). Reduced maximal aerobic capacity after COVID-19 in young adult recruits, Switzerland, May 2020. *Eurosurveillance*, 25(36), 2001542. https://doi.org/10.2807/1560-7917.ES.2020.25.36.2001542
16. Daynes, E., Gerlis, C., Chaplin, E., Gardiner, N., & Singh, S. J. (2021). Early experiences of rehabilitation for individuals post-COVID to improve fatigue, breathlessness exercise capacity and cognition–A cohort study. *Chronic Respiratory Disease*, 18, 14799731211015691. https://doi.org/10.1177/14799731211015691
17. Del Corral, T., Fabero-Garrido, R., Plaza-Manzano, G., Fernández-de-Las-Peñas, C., Navarro-Santana, M., & López-de-Uralde-Villanueva, I. (2023). Home-based respiratory muscle training on quality of life and exercise tolerance in long-term post-

COVID-19: Randomized controlled trial. *Annals of Physical and Rehabilitation Medicine*, 66(1), 101709. https://doi.org/10.1016/j.rehab.2022.101709

18. Disser, N. P., De Micheli, A. J., Schonk, M. M., Konnaris, M. A., Piacentini, A. N., Edon, D. L., ... & Mendias, C. L. (2020). Musculoskeletal consequences of COVID-19. *Journal of Bone and Joint Surgery*, 102(14), 1197-1204. https://doi.org/10.2106/JBJS.20.00847
19. Durstenfeld, M. S., Sun, K., Tahir, P., Peluso, M. J., Deeks, S. G., Aras, M. A., ... & Hsue, P. Y. (2022). Use of cardiopulmonary exercise testing to evaluate long COVID-19 symptoms in adults: a systematic review and meta-analysis. *JAMA network open*, 5(10), e2236057-e2236057. https://doi.org/10.1001/jamanetworkopen.2022.36057
20. Edenfield, K. M., Dillon, M. C., & Clugston, J. R. (2023). COVID myocarditis in a collegiate athlete: Timeline and return to play. *American Heart Journal Plus: Cardiology Research and Practice*, 34, 100323. https://doi.org/10.1016/j.ahjo.2023.100323
21. Engel, G. L. (1977). The need for a new medical model: a challenge for biomedicine. *Science*, 196(4286), 129-136. https://doi.org/10.1126/science.847460
22. Fava, G. A., & Sonino, N. (2007). The biopsychosocial model thirty years later. *Psychotherapy and Psychosomatics*, 77(1), 1-2. https://doi.org/10.1159/000110052
23. Fairweather, D., Beetler, D.J., Di Florio, D.N., Musigk, N., Heidecker, B. & Cooper Jr, L.T. (2023). COVID-19, myocarditis and pericarditis. *Circulation research*, 132(10), 1302-1319. https://doi.org/10.1161/circresaha.123.321878
24. Fletcher, G. F., Balady, G. J., Amsterdam, E. A., Chaitman, B., Eckel, R., Fleg, J., Froelicher, V. F., Leon, A. S., Piña, I. L., Rodney, R., Simons-Morton, D. G., Williams, M. A., & Bazzarre, T. (2001). Exercise Standards for Testing and Training A Statement for Healthcare Professionals From the American Heart Association. *Circulation*, 104(14), 1694-1740. https://doi.org/10.1161/hc3901.095960
25. Gervasi, S. F., Pengue, L., Damato, L., Monti, R., Pradella, S., Pirronti, T., ... & Palmieri, V. (2021). Is extensive cardiopulmonary screening useful in athletes with previous asymptomatic or mild SARS-CoV-2 infection?. *British Journal of Sports Medicine*, 55(1), 54-61. https://doi.org/10.1136/bjsports-2020-102789
26. Gluckman, T. J., Bhave, N. M., Allen, L. A., Chung, E. H., Spatz, E. S., ... & Verma, A. K. (2022). 2022 ACC expert consensus decision pathway on cardiovascular sequelae of COVID-19 in adults: myocarditis and other myocardial involvement, post-

acute sequelae of SARS-CoV-2 infection, and return to play: a report of the American College of Cardiology Solution Set Oversight Committee. *Journal of the American College of Cardiology*, 79(17), 1717-1756. https://doi.org/10.1016/j.jacc.2022.02.003

27. Goergen, J., Bavishi, A., Eimer, M., & Zielinski, A. R. (2021). COVID-19: the risk to athletes. *Current Treatment Options in Cardiovascular Medicine*, 23, 1-14. https://doi.org/10.1007/s11936-021-00941-2
28. Golpour, A., Patriki, D., Hanson, P.J., McManus, B., & Heidecker, B. (2021). Epidemiological Impact of Myocarditis. *Journal of Clinical Medicine*, 10, 603. https://doi.org/10.3390/jcm10040603
29. Guenette, J. A., Chin, R. C., Cory, J. M., Webb, K. A., & O′ Donnell, D. E. (2013). Inspiratory capacity during exercise: measurement, analysis, and interpretation. *Pulmonary Medicine*, 1, 956081. https://doi.org/10.1155/2013/956081
30. Guevarra, C. C., Murray, N., Cipriani, D., Mailland, K., Char, A., Coffman, K., ... & Gaal, W. (2022). Cardiovascular involvement among collegiate athletes following COVID-19 infection. *Journal of Clinical and Translational Research*, 8(1), 1. https://doi.org/10.18053/jctres.08.202201.004
31. HajGhanbari, B., Yamabayashi, C., Buna, T. R., Coelho, J. D., Freedman, K. D., Morton, T. A., ... & Reid, W. D. (2013). Effects of respiratory muscle training on performance in athletes: a systematic review with meta-analyses. *The Journal of Strength & Conditioning Research*, 27(6), 1643-1663. https://:doi.org/10.1519/jsc.0b013e318269f73f
32. Halle, M., Binzenhöfer, L., Mahrholdt, H., Johannes Schindler, M., Esefeld, K., & Tschöpe, C. (2021). Myocarditis in athletes: A clinical perspective. In *European Journal of Preventive Cardiology,* 28(10), 1050–1057. https://doi.org/10.1177/2047487320909670
33. Hejbøl, E. K., Harbo, T., Agergaard, J., Madsen, L. B., Pedersen, T. H., Østergaard, L. J., ... & Tankisi, H. (2022). Myopathy as a cause of fatigue in long-term post-COVID-19 symptoms: Evidence of skeletal muscle histopathology. *European Journal of Neurology*, 29(9), 2832-2841. https://doi.org/10.1111/ene.15435
34. Hollenberg, M., & Tager, I. B. (2000). Oxygen uptake efficiency slope: an index of exercise performance and cardiopulmonary reserve requiring only submaximal exercise. *Journal of the American College of Cardiology*, 36(1), 194-201. https://doi.org/10.1016/S0735-1097(00)00691-4

35. Holm, P., Sattler, A., & Fregosi, R. F. (2004). Endurance training of respiratory muscles improves cycling performance in fit young cyclists. *BMC Physiology*, 4, 1-14. https://doi.org/10.1186/1472-6793-4-9
36. Jimeno-Almazán, A., Buendía-Romero, Á., Martínez-Cava, A., Franco-López, F., Sánchez-Alcaraz, B. J., Courel-Ibáñez, J., & Pallarés, J. G. (2023). Effects of a concurrent training, respiratory muscle exercise, and selfmanagement recommendations on recovery from post-COVID-19 conditions: the RECOVE trial. *Journal of Applied Physiology*, 134(1), 95–104. https://doi.org/10.1152/japplphysiol.00489.2022
37. Jorstad, H. T., & van den Aardweg, J. G. (2020). Balancing act: when is an elite athlete who has had COVID-19 safe to return to play? When does prudent investigation go offside into overmedicalising?. *British Journal of Sports Medicine*, 54(19), 1134-1135. https://doi.org/10.1136/bjsports-2020-103259
38. Joyner, M. J., & Coyle, E. F. (2008). Endurance exercise performance: the physiology of champions. *The Journal of physiology*, 586(1), 35-44. https://doi.org/10.1113/jphysiol. 2007.143834
39. Jurecka, A., Skucińska, P., & Gądek, A. (2021). Impact of the SARS-CoV-2 coronavirus pandemic on physical activity, mental health and quality of life in professional athletes—a systematic review. *International Journal of Environmental Research and Public Health*, 18(17), 9423. https://doi.org/10.3390/ijerph18179423
40. Kaiser-Nielsen, L. V., Tischer, S. G., Prescott, E. B., & Rasmusen, H. K. (2017). Symptoms, diagnoses, and sporting consequences among athletes referred to a Danish sports cardiology clinic. *Scandinavian Journal of Medicine & Science in Sports*, 27(1), 115-123. https://doi.org/10.1111/sms.12624
41. Kaminsky, L. A., Harber, M. P., Imboden, M. T., Arena, R., & Myers, J. (2018). Peak ventilation reference standards from exercise testing: From the FRIEND registry. *Medicine and Science in Sports and Exercise*, 50(12), 2603–2608. https://doi.org/10.1249/MSS.0000000000001740
42. Komici, K., Bianco, A., Perrotta, F., Dello Iacono, A., Bencivenga, L., D'Agnano, V., ... & Guerra, G. (2021). Clinical characteristics, exercise capacity and pulmonary function in post-COVID-19 competitive athletes. *Journal of Clinical Medicine*, 10(14), 3053. https://doi.org/10.3390/jcm10143053
43. Kumar, A., & Nayar, K. R. (2020). COVID-19: Stigma, discrimination, and the blame game. *International Journal of Mental Health*, 49(4), 382-384. https://doi.org/10.1080/00207411.2020.1809935

44. Kurowski, M., Seys, S., Bonini, M., Del Giacco, S., Delgado, L., Diamant, Z., ... & Couto, M. (2022). Physical exercise, immune response, and susceptibility to infections—current knowledge and growing research areas. *Allergy*, 77(9), 2653-2664. https://doi.org/10.1111/all.15328
45. Ladlow, P., O'Sullivan, O., Bennett, A. N., Barker-Davies, R., Houston, A., Chamley, R., ... & Holdsworth, D. A. (2022). The effect of medium-term recovery status after COVID-19 illness on cardiopulmonary exercise capacity in a physically active adult population. *Journal of Applied Physiology*, 132(6), 1525-1535. https://doi.org/10.1152/japplphysiol.00138.2022
46. Lemes, I. R., Smaira, F. I., Ribeiro, W. J., Favero, N. K., Matos, L. D. N. J., de Sá Pinto, A. L., ... & Gualano, B. (2022). Acute and post-acute COVID-19 presentations in athletes: a systematic review and meta-analysis. *British Journal of Sports Medicine*, 56(16), 941-947. https://doi.org/10.1136/bjsports-2022-105583
47. Líška, D., Liptaková, E., Babičová, A., Batalik, L., Baňárová, P. S., & Dobrodenková, S. (2022). What is the quality of life in patients with long COVID compared to a healthy control group?. *Frontiers in Public Health*, 10, 975992. https://doi.org/10.3389/fpubh.2022.975992
48. Lopes, L., Miranda, V., Goes, R., Souza, G., Souza, G., Rocha, J., ... & Perini, J. (2021). Repercussions of the COVID-19 pandemic on athletes: a cross-sectional study. *Biology of Sport*, 38(4), 703-711. https://doi.org/10.5114/biolsport.2021.106147
49. Luoto, R., Waris, M., Valtonen, M., & Ruuskanen, O. (2023). Respiratory viral infections-impact on sport and exercise medicine. *Exercise Immunology Review*, 29, 7-21. PMID: 37358372
50. Mackała, K., Kurzaj, M., Okrzymowska, P., Stodółka, J., Coh, M., & Rożek-Piechura, K. (2020). The effect of respiratory muscle training on the pulmonary function, lung ventilation, and endurance performance of young soccer players. *International Journal of Environmental Research and Public Health*, 17(1). https://doi.org/10.3390/ijerph17010234
51. McKenzie, D. C. (2012). Respiratory physiology: adaptations to high-level exercise. *British Journal of Sports Medicine*, 46(6), 381-384. https://doi.org/10.1136/bjsports-2011-090824
52. Mehrsafar, A. H., Gazerani, P., Zadeh, A. M., & Sánchez, J. C. J. (2020). Addressing potential impact of COVID-19 pandemic on physical and mental health of elite athletes. *Brain, Behavior, and Immunity*, 87, 147. https://doi.org/10.1016/j.bbi.2020.05.011

53. Mezzani, A. (2017). Cardiopulmonary exercise testing: Basics of methodology and measurements. *Annals of the American Thoracic Society*, *14*, S3–S11. https://doi.org/10.1513/AnnalsATS.201612-997FR
54. Mihalick, V. L., Canada, J. M., Arena, R., Abbate, A., & Kirkman, D. L. (2021). Cardiopulmonary exercise testing during the COVID-19 pandemic. *Progress in Cardiovascular Diseases*, 67, 35-39. https://doi.org/10.1016/j.pcad.2021.04.005
55. Milani, R. V., Lavie, C. J., Mehra, M. R., & Ventura, H. O. (2006). Understanding the Basics of Cardiopulmonary Exercise Testing. In *Mayo Clinic Proceedings,* 81(12), 1603-1611. https://doi.org/10.4065/81.12.1603
56. Monosilio, S., Prosperi, S., Squeo, M. R., Spataro, S., Spataro, A., & Maestrini, V. (2023). Short and long-term cardiovascular sequelae after SARS-CoV-2 infection: a narrative review focusing on athletes. *Viruses*, 15(2), 493. https://doi.org/10.3390/v15020493
57. Myers, J., Kaminsky, L. A., Lima, R., Christle, J. W., Ashley, E., & Arena, R. (2017). A reference equation for normal standards for VO2 max: analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND Registry). *Progress in Cardiovascular Diseases*, 60(1), 21-29. https://doi.org/10.1016/j.pcad.2017.03.002
58. NICE. (2021). *Covid19 Rapid Guideline: Managing the long-term Effects of Covid19*. National Institute for Health and Care Excellence (NICE) SIGN (SIGN) and CR of GP (RCGP). https://www.nice.org.uk/guidance/ng188. Accessed 8 February 2023.
59. Notter, D. A., Verges, S., Renggli, A. S., Beltrami, F. G., & Spengler, C. M. (2023). Similar effects on exercise performance following different respiratory muscle training programs in healthy young men. *Scientific Reports*, 13(1), 16135. https://doi.org/10.1038/s41598-023-41580-w
60. Ogawa, T., Nagao, M., Fujii, N., & Nishiyasu, T. (2020). Effect of inspiratory muscle-loaded exercise training on peak oxygen uptake and ventilatory response during incremental exercise under normoxia and hypoxia. *BMC Sports Science, Medicine and Rehabilitation*, 12, 1-10. https://doi.org/10.1186/s13102-020-00172-1
61. Oswald, F., Campbell, J., Williamson, C., Richards, J., & Kelly, P. (2020). A scoping review of the relationship between running and mental health. *International Journal of Environmental Research and Public Health*, 17(21), 8059. https://doi.org/10.3390/ijerph17218059
62. Palau, P., Domínguez, E., Gonzalez, C., Bondía, E., Albiach, C., Sastre, C., ... & López, L. (2022). Effect of a home-based inspiratory muscle training programme on

functional capacity in postdischarged patients with long COVID: the InsCOVID trial. *BMJ Open Respiratory Research*, 9(1), e001439. https://doi.org/10.1136/bmjresp-2022-001439

63. Parker, A. M., Brigham, E., Connolly, B., McPeake, J., Agranovich, A. V., Kenes, M. T., ... & Turnbull, A. E. (2021). Addressing the post-acute sequelae of SARS-CoV-2 infection: a multidisciplinary model of care. *The Lancet Respiratory Medicine*, 9(11), 1328-1341. https://doi.org/10.1016/S2213-2600(21)00385-4
64. Patel, P., & Thompson, P. D. (2022). Diagnosing COVID-19 myocarditis in athletes using cMRI. *Trends in Cardiovascular Medicine*, 32(3), 146-150. https://doi.org/10.1016/j.tcm.2021.12.009
65. Poczta, J., Almeida, N., Paczyńska-Jędrycka, M., & Kruszyńska, E. (2022). The impact of COVID-19 incidence on motivation to participate in a triathlon. *International Journal of Environmental Research and Public Health*, 19(9), 5576. https://doi.org/10.3390/ijerph19095576
66. Rinaldo, R. F., Mondoni, M., Parazzini, E. M., Pitari, F., Brambilla, E., Luraschi, S., ... & Centanni, S. (2021). Deconditioning as main mechanism of impaired exercise response in COVID-19 survivors. *European Respiratory Journal*, 58(2). https://doi.org/10.1183/13993003.00870-2021
67. Ruuskanen, O., Valtonen, M., Waris, M., Luoto, R., & Heinonen, O. J. (2023). Sport and exercise during viral acute respiratory illness-Time to revisit: Exercise during acute respiratory viral illness. *Journal of Sport and Health Science*, S2095-2546. https://doi.org/10.1016/j.jshs.2023.12.002
68. San-Millán, I. (2023). The key role of mitochondrial function in health and disease. *Antioxidants*, 12(4), 782. https://doi.org/10.3390/antiox12040782
69. Saw, A. E., Main, L. C., & Gastin, P. B. (2016). Monitoring the athlete training response: subjective self-reported measures trump commonly used objective measures: a systematic review. *British Journal of Sports Medicine*, 50(5), 281-291. https://doi.org/10.1136/bjsports-2015-094758
70. Scheer, V., Valero, D., Villiger, E., Rosemann, T., & Knechtle, B. (2021). The impact of the COVID-19 pandemic on endurance and ultra-endurance running. *Medicina*, 57(1), 52. https://doi.org/10.3390/medicina57010052
71. Schmidt-Trucksäss, A. (2022). Cardiorespiratory Fitness–Properly Measured, Interpreted and Applied?. *Dtsch Z Sportmed*, 73(6), 199-202. https://doi.org/10.5960/dzsm.2022.543

72. Schmucker, A., Jerg, A., Schulz, S. V. W., Zorn, J., Vollrath, S. & Steinacker, J. M. (2022). Changes in Lung Diffusion Capacity after SARS-CoV-2 Infections in Highly Trained Athletes. *Dtsch Z Sportmed*, 73(5), 189-196. https://doi.org/10.5960/dzsm.2022.540
73. Schroeder, A. N., Getzin, A. R., Creswell, L. L., & Asplund, C. A. (2023). Recovery from COVID-19 in Adult Recreational Athletes: A Survey of American Triathletes. *Exercise, Sport, and Movement*, 1(2), e00005. https://doi.org/10.1249/esm.0000000000000005
74. Schwellnus, M., Sewry, N., Snyders, C., Kaulback, K., Wood, P. S., Seocharan, I., ... & Jordaan, E. (2021). Symptom cluster is associated with prolonged return-to-play in symptomatic athletes with acute respiratory illness (including COVID-19): a cross-sectional study—AWARE study I. *British Journal of Sports Medicine*, 55(20), 1144-1152. https://doi.org/10.1136/bjsports-2020-103782
75. Schwendinger, F., Knaier, R., Radtke, T., & Schmidt-Trucksäss, A. (2023). Low cardiorespiratory fitness post-COVID-19: a narrative review. *Sports Medicine*, 53(1), 51-74. https://doi.org/10.1007/s40279-022-01751-7
76. Scudiero, O., Lombardo, B., Brancaccio, M., Mennitti, C., Cesaro, A., Fimiani, F., ... & Frisso, G. (2021). Exercise, immune system, nutrition, respiratory and cardiovascular diseases during COVID-19: a complex combination. *International Journal of Environmental Research and Public Health*, 18(3), 904. https://doi.org/10.3390/ijerph18030904
77. Severin, R., Arena, R., Lavie, C. J., Bond, S., & Phillips, S. A. (2020). Respiratory Muscle Performance Screening for Infectious Disease Management Following COVID-19: A Highly Pressurized Situation. *American Journal of Medicine*, 133(9), 1025–1032. https://doi.org/10.1016/j.amjmed.2020.04.003
78. Shukla, A., Dogra, D. K., Bhattacharya, D., Gulia, S., & Sharma, R. (2023). Impact of COVID-19 outbreak on the mental health in sports: a review. *Sport Sciences for Health*, 19(4), 1043-1057. https://doi.org10.1007/s11332-023-01063-x
79. Siddiq, M. A. B., Rathore, F. A., Clegg, D., & Rasker, J. J. (2020). Pulmonary Rehabilitation in COVID-19 patients: A scoping review of current practice and its application during the pandemic. *Turkish Journal of Physical Medicine and Rehabilitation*, 66(4), 480. https://doi.org/10.5606/TFTRD.2020.6889
80. Silva, C. C., Bichara, C. N. C., Carneiro, F. R. O., Palacios, V. R. D. C. M., Berg, A. V. S. V. D., Quaresma, J. A. S., & Magno Falcao, L. F. (2022). Muscle dysfunction in

the long coronavirus disease 2019 syndrome: Pathogenesis and clinical approach. *Reviews in Medical Virology,* 32(6), e2355. https:doi.org/10.1002/rmv.2355

81. Śliż, D., Wiecha, S., Gąsior, J. S., Kasiak, P. S., Ulaszewska, K., Lewandowski, M., ... & Mamcarz, A. (2023). Impact of COVID-19 infection on cardiorespiratory fitness, sleep, and psychology of endurance athletes—CAESAR study. *Journal of Clinical Medicine*, 12(8), 3002. https://doi.org/10.3390/jcm12083002
82. Steinacker, J. M., Kirsten, J., Schulz, S. V. W., Jerg, A., Kersten, J., Matits, L., & Schellenberg, J. (2022). Rehabilitation after COVID-19–the Challenge of Post-COVID Syndrome with Post-Exertional Malaise. *Dtsch Z Sportmed*, 73,163-166. https://doi.org/10.5960/dzsm.2022.539
83. Teske, A. J., Prakken, N. H., De Boeck, B. W., Velthuis, B. K., Martens, E. P., Doevendans, P. A., & Cramer, M. J. (2009). Echocardiographic tissue deformation imaging of right ventricular systolic function in endurance athletes. *European HeartJjournal*, 30(8), 969-977. https://doi.org/10.1093/eurheartj/ehp040
84. Toma, N., Bicescu, G., Enache, R., Dragoi, R., & Cinteza, M. (2010). Cardiopulmonary exercise testing in differential diagnosis of dyspnea. *Maedica*, 5(3), 214-218. PMID:21977155
85. Urbański, P. K., Rogoza, R., Brewer, B., & Tasiemski, T. (2023). Coping with the COVID-19 pandemic by Paralympic athletes preparing for elite sport events: A longitudinal study. *Scandinavian Journal of Medicine & Science in Sports*, 33(4), 512-520. https://doi.org/10.1111/sms.14270
86. Ussorowska-Krokosz, A., Blecharz, J., Siekanska, M., & Grygorowicz, M. (2023). Coping with COVID-19: Can a Sense of Coherence and Social Support Play a Protective Role in the Perception of COVID-19 by Polish Women Football Players? A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*, 20(13), 6308. https://doi.org/10.3390/ijerph20136308
87. Vignesh, P., Preetha, S., & Gayatri Devi, R. (2018). Assessment of pulmonary function test in athletes. *Drug Invention Today*, 10(12).
88. Vonbank, K., Lehmann, A., Bernitzky, D., Gysan, M. R., Simon, S., Schrott, A., ... & Gompelmann, D. (2021). Predictors of prolonged cardiopulmonary exercise impairment after COVID-19 infection: a prospective observational study. *Frontiers in Medicine*, 8, 773788. https://doi.org/10.3389/fmed.2021.773788
89. Warburton, D. E., Nicol, C. W., & Bredin, S. S. (2006). Health benefits of physical activity: the evidence. *CMAJ : Canadian Medical Association Journal*, 174(6), 801–809. https://doi.org/10.1503/cmaj.051351

90. Washif, J. A., Farooq, A., Krug, I., Pyne, D. B., Verhagen, E., Taylor, L., ... & Chamari, K. (2022). Training during the COVID-19 lockdown: knowledge, beliefs, and practices of 12,526 athletes from 142 countries and six continents. *Sports Medicine*, 52(4), 933-948. https://doi.org/10.1007/s40279-021-01573-z
91. Wasserman, K. (1997). Diagnosing Cardiovascular and Lung Pathophysiology From Exercise Gas Exchange. *Chest*, 112(4), 1091–1101. https://doi.org/10.1378/chest.112.4.1091
92. Wells, G. D., & Norris, S. R. (2009). Assessment of physiological capacities of elite athletes & respiratory limitations to exercise performance. *Paediatric Respiratory Reviews*, 10(3), 91-98. https://doi.org/10.1016/j.prrv.2009.04.002
93. Wernhart, S., Weihe, E., Totzeck, M., Balcer, B., Rassaf, T., & Luedike, P. (2023). Cardiopulmonary Profiling of Athletes with Post-Exertional Malaise after COVID-19 Infection—A Single-Centre Experience. *Journal of Clinical Medicine*, 12(13), 4348. https://doi.org/10.3390/jcm12134348
94. WHO Quality of Life (2012). *WHO.* https://who.int./tool/whoqol. Accessed October 28 2023.
95. Williams, Z., & Hull, J. H. (2024). Respiratory complications following COVID-19 in athletic populations: A narrative review. *Scandinavian Journal of Medicine & Science in Sports*, 34(1), e14275. https://doi.org/10.1111/sms.14275
96. Winkert, K., & Kirsten, J. (2022). Cardiopulmonary Exercise Testing—Methodological Aspects. *Dtsch. Z. Sportmed*, 73, 184-188. https://doi.org/10.5960/dzsm.2022.538

Chapter 3 Paper 1

This chapter includes the full text publication of Paper 1, original research.

3.1 Title: Protracted exercise tolerance post-coronavirus disease 2019 in endurance athletes: A survey

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3.1.2 Journal

South African Journal of Physiotherapy

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Protracted exercise tolerance post-coronavirus disease 2019 in endurance athletes: A survey

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Background: The global coronavirus disease 2019 (COVID-19) pandemic irrevocably influenced our lives, yet research in a diversity of countries is lacking. Cardiorespiratory fitness may be impaired for up to a year post-COVID-19 infection.

Objectives: Our study aimed to compare acute and exertional symptoms, fatigue, and exercise performance in masters-age endurance athletes according to their return-to-sport status.

Method: A cross-sectional survey-based observational study of long-distance runners and cyclists was conducted. Data were stratified into two groups: those who returned to their pre-illness level of sport and those who did not and were compared statistically.

Results: A total of 308 survey responses were included in the analysis. The mean age of the athletes was 44.9 + 10.2 years, with 55.2% being male. The group that did not return to their pre-illness level of sport (31.5%) had more post-COVID sequelae, worse illness severity, with a higher frequency of resting and exertional symptoms, notably fatigue and dyspnoea. Decreased exercise capacity was correlated with increased physical fatigue scores.

Conclusion: Almost one-third of endurance athletes suffered protracted exercise tolerance post-COVID-19. Long-term symptoms may be more consequential in this athlete population.

Clinical Implications: Symptoms that may indicate cardiopulmonary consequences in recreational athletes should be investigated in order to facilitate return to sport and the important mental and physical benefits thereof. This will augment outcomes after respiratory tract infections and management of return to sport and expectations of endurance athletes.

Keywords: COVID-19; endurance athletes; return to sport; exercise capacity; fatigue.

Introduction

The global coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has irrevocably influenced our lives. Extensive research has explored this disease and its devastating consequences on the world's population and concurrently enhanced global knowledge of respiratory illnesses (Burgstahler et al. 2023). Comorbid diseases and a lack of regular physical activity predispose individuals to a more severe expression of COVID-19 (Chen et al. 2020; Snyders et al. 2022). However, high-intensity exercise may lower immune function and increase susceptibility to upper respiratory tract infections (Agha-Alinejad et al. 2022). Cardiorespiratory fitness is now classed as a vital sign (Mihalick et al. 2021), thus lagging athlete health and the hinderance of persistent symptoms in resuming pre-illness level of sport is worth assessing (Schroeder et al. 2023).

Coronavirus disease 2019 is a multifaceted disease with manifestations like no other virus, such as blood clotting and long-standing fatigue and dyspnoea (Schwellnus et al. 2021). The cardiovascular consequences of COVID-19 are by far the most threatening and range from peri-myocarditis, arrhythmias, thromboembolism, myocardial infarction, to sudden death (Monosilio et al. 2023). However, according to the American College of Cardiology (ACC) 2022 expert consensus statement, there is fortunately a low prevalence (Gluckman et al. 2022). Long-term respiratory sequelae are more likely post-COVID-19 (Durstenfeld et al. 2022). Pulmonary limitations have been found to be responsible for low exercise tolerance up to 1-year post-COVID-19 infection (Braga et al. 2023), even after mild illness (Vollrath et al. 2022).

Acute COVID-19 symptoms are categorised as asymptomatic, mild, moderate, severe, and critical illness according to the National Institute of Health (COVID-19 Treatment Guidelines 2023). Mild illness symptoms include malaise and/or fatigue, headache, myalgia, ageusia and/or anosmia,

cough, fever, and diarrhoea and/or vomiting. Symptoms associated with moderate illness include dyspnoea and clinical evidence of lower respiratory disease on imaging with normal oxygen saturation (≥ 94% on room air). Individuals with severe illness present with respiratory distress and dyspnoea with oxygen saturation of < 94%, and critical illness includes respiratory failure, septic shock and multiorgan failure. In our study, the term long-COVID is used for new or persistent symptoms after 4 weeks post onset of illness as defined by the National Institute for Health and Care Excellence (NICE 2021). Fatigue is a multidimensional and subjective symptom that may or may not relate to other physiological factors (Smets et al. 1995).

During the early phase of the pandemic, most studies explored symptom severity and duration in collegiate elite athletes. There remains a paucity of literature concerning the masters athlete (over the age of 35 years) (Juhász et al. 2022). Endurance athletes require the ability to resist fatigue; typically training high volumes and placing a huge demand on their cardiorespiratory system (Joyner & Coyle 2008). To define and classify athletes, it has been proposed that competitive athletes exercise for 6 h or more per week and recreational athletes for at least 3 h; although endurance runners and cyclists often train equal volumes to professional athletes (pelliccia et al. 2021). Running is a highly accessible and affordable sport attracting long-distance adult athletes predominantly at a recreational level (DeJong, Fish & Hertel 2021). Unlike elite athletes, they may lack access to sports medicine professionals who disseminate return to sport (RTS) guidelines and screen for the risk of cardiac involvement (Elliott et al. 2020). Published RTS criteria are primarily based on the presence and severity of symptoms (Steinacker et al. 2022). This leads to concerns about adult recreational athletes exercising while potentially still feeling unwell (Ruuskanen et al. 2022). There is a need for prolonged observation and follow-up of athletes who had COVID-19, particularly with cardiovascular sequelae (Monosilio et al. 2023).

Our study aims to compare acute and exertional symptoms, fatigue, and exercise performance experienced by masters age group endurance athletes who had returned to their previous level of sport to those who had not. The results of our study may provide valuable insights for healthcare professionals, coaches, and athletes alike to understand variables associated with protracted RTS after COVID-19. This will facilitate better outcomes after respiratory tract infections and more effective management of RTS and expectations of competitive and recreational endurance athletes after respiratory tract infections.

Research methods and design

Study design

Our study is a cross-sectional survey-based observational to determine the difference in demographic and sport-specific characteristics, disease severity, duration, and symptoms, self-reported approach to RTS and exercise capacity, and fatigue score between athletes who had returned to their pre-illness level of sport and those who had not. The impetus for our study was the threat of COVID-19 consequences in athletes over the age of 35 years, doing a high volume of cardiovascular exercise. Participants were recruited by snowball sampling from athletic clubs in South Africa between December 2021 and July 2022. Emailers were sent to 64 athletic clubs containing the invitation to participate in the online survey and a request to forward it on to their members. The invitation was also disseminated via social media to 18 WhatsApp groups and 25 Facebook pages. Athletic clubs approved the post on their social media pages and chats. Invitations could then be forwarded by the recipients in a snowball fashion to fellow athletes.

Study population and sampling strategy

Eligible participants were adult (age 18+) endurance athletes of both sexes who ran for three or more hours per week or cycled for three or more hours per week (McKinney et al. 2019). Those who participated in additional sports over and above were also included and described as multisport athletes. The athletes had either been diagnosed with COVID-19 through a positive polymerase chain reaction (PCR) test or exhibited the known symptoms of COVID-19. Athletes who were admitted to the intensive care unit (ICU) were excluded as ICU-acquired weakness occurs from 15–29 days, and necessitates prolonged rehabilitation to return to normal function (Van Aerde et al. 2020). Other exclusion criteria for athletes were not being proficient in the English language, residing outside of South Africa, and a lack of informed consent. The sample size estimation equalled 178. This was based on the change in aerobic capacity of the athletic population infected with COVID-19 compared to a control group (10.0% vs. 3.5%) (Crameri et al. 2020), with an effect size of 0.63, a confidence interval (CI) of 0.05, power of 0.9, and adding 10% for each confounding variable that is age, sex, sport, stage of disease. To achieve this sample size, we assumed a 30% response rate and 50 members per athletics club. At the time, the prevalence of COVID-19 infections in the city was 5.4%, thus, the questionnaire needed to be accessed by 3200 athletes at 64 clubs.

Data collection

A self-administered web-based questionnaire was developed by the research team using the Research Electronic Data Capture (REDCap) platform and was based on current literature. Sociodemographic data including sex, age, and sport-specific data constituted the first 10 questions, followed by 10 questions on COVID-19 status, prevalence of comorbidities, and post-COVID sequelae. The third section included questions regarding the management of their acute illness based on the World Health Organization (WHO) Severity Scale (Marshall et al. 2020) and symptoms classified according to the National Institutes of Health (NIH) clinical

spectrum (COVID-19 Treatment Guidelines, 2023). Symptom duration and time to return to their pre-illness level of sport were categorised to align with the NICE definitions (NICE 2021). The change in exercise tolerance was based on self-reported pace and power values.

Fatigue was scored using the standardised Multidimensional Fatigue Inventory (MDFI) tool (Smets et al. 1995). The MDFI consists of 20 questions that assess five categories of fatigue, namely: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. The scales used are freely available, thus no permissions were required. The MDFI has good internal consistency (Cronbach's alpha = 0.84), and construct and convergent validity are reported (Smets et al. 1995). A professional panel in the field of sports medicine and respiratory health validated our study questionnaire. Construct validity of the questionnaire as a research tool was performed by sending a test questionnaire to 10 COVID-19 convalescent athletes, 4 of whom were medical professionals. Test-retest reliability was performed 2 weeks apart to avoid a learning effect. The null hypothesis of this study was that there was no difference in the effect of COVID-19 on the group that had returned to their pre-illness level of sports participation (y-RTS) versus those that had not (n-RTS). The primary outcome was a return to the pre-illness level of sport. Therefore, in the statistical analysis, we abbreviated the subgroup of athletes who selected the option 'still not returned to pre-illness level of sport' in the questionnaire as the n-RTS group. All others were combined into the y-RTS group.

Data analysis

A lack of consent, answering 'No' to contracting COVID-19, or incomplete symptom data resulted in exclusion from data analysis. There was minimal missing data as radio button questions were marked *required. Data were extracted from REDCap into Microsoft Excel and imported into SPSS Statistics for Mac 28.0.1.1.(14) (IBM, Chicago, IL, United States [US]), which was used for all analyses. Descriptive characteristics were calculated using means and standard deviations for continuous variables, and percentages and frequencies for categorical variables for the total sample (All), the group that had returned to pre-illness level of sport (y-RTS), and the group that had not (n-RTS). The normality of distribution of continuous variables was assessed with the Shapiro–Wilk test. Independent t-tests were used to compare normally distributed variables and Mann–Whitney U test for parametric continuous data. Chi-square or Fisher's exact tests were used to compare categorical data, with Cochran trend for 'symptom duration'. Univariate and multivariate logistic regression was performed to evaluate the risk of not returning to pre-illness level of sport associated with the following variables: sex, age, general fatigue, physical fatigue, reduced activity, mental fatigue, reduced motivation, and exertional dyspnoea. Because of a strong association of general fatigue, physical fatigue and dyspnoea, only physical fatigue was included in the multivariate model. Model assumptions including goodness of fit, removal of residuals and collinearity were met.

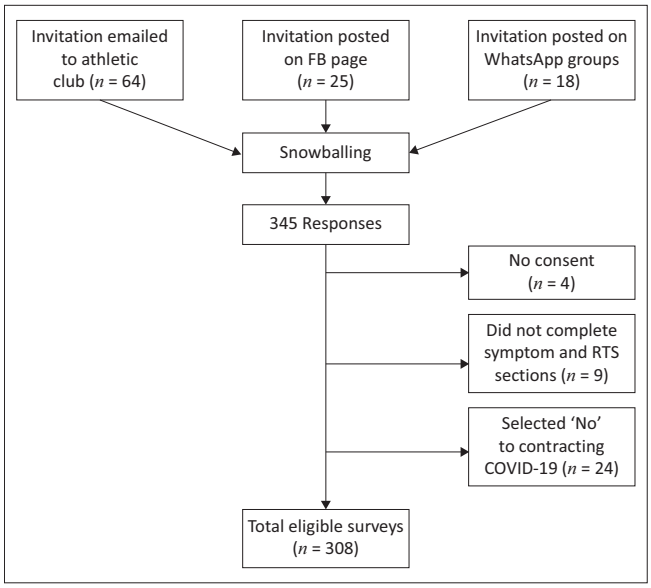
Ethical considerations

Unconditional ethical approval was provided by the University of the Witwatersrand's Human Research Ethics Committee (Medical) (Certificate no. M210657). Our study procedures adhered to the principles set forth in the Declaration of Helsinki and the South African Guidelines for Good Clinical Practice and the Medical Research Council. An information sheet explaining our study purpose and data sharing according to the FAIR principles (GO FAIR, FAIR principles 2016) was linked to the survey and ensured confidentiality and anonymity and permission to withdraw from our study at any point. The participants were asked if they consented to the anonymised data being used for research purposes. After electronic consent was obtained, the full questionnaire opened. The completion of the questions implied that consent was given throughout. Only the research team had access to the REDCap platform on which the information sheet and survey was developed and data were stored. The exported data were stored one password-protected computer and backed up to Apple iCloud Drive.

Results

Demographic, sport-specific, and return to pre-illness level of sport characteristics of our study population

After the surveys were assessed for eligibility, 308 participants were included in data analysis (Figure 1). Table 1 summarises our study population characteristics in three groups: all 308 participants, 211 (68.5%) who returned to pre-illness level of sport (y-RTS), and 97 (31.5%) who had not yet returned (n-RTS). The mean age was 44.9 $\pm$ 10.2 years, and 170 (55.2%) were male. There is no significant



COVID-19, coronavirus disease 2019; FB, Facebook; RTS, return to sport.

FIGURE 1: Study sample selection process.

TABLE 1: Demographic, sport-specific and coronavirus disease 2019 characteristics of our study population.

Variable	All (N = 308)		y-RTS (n = 211)		n-RTS (n = 97)		p
	n	%	*n*	%	*n*	%	
Sex	-	-	-	-	-	-	0.531
Male	170	55.2	119	56.4	51	52.6	-
Female	138	44.8	92	43.6	46	47.4	-
Age groups (years)	-	-	-	-	-	-	0.417
18–29	22	7.1	18	8.5	4	4.1	-
30–39	70	22.7	43	20.4	27	27.8	-
40–49	115	37.4	82	38.9	33	34.0	-
50–59	80	26.0	54	25.6	26	26.8	-
60–71	21	6.8	14	6.6	7	7.2	-
Type of sport†	-	-	-	-	-	-	0.598
Running	122	39.6	85	40.3	37	38.1	-
Cycling	55	17.9	40	19.0	15	15.5	-
Multisport	124	40.3	81	38.4	43	44.3	-
Level of participation	-	-	-	-	-	-	0.506
Elite	16	5.2	13	6.2	3	3.1	-
Competitive	99	32.1	66	31.3	33	34.0	-
Recreational	193	62.7	132	62.6	61	62.9	-
Pre-COVID training volume (hours per week)	-	-	-	-	-	-	0.503
< 6	84	30.3	63	29.8	21	21.7	-
≥ 6	224	72.7	148	70.1	76	78.4	-
Comorbidities	-	-	-	-	-	-	0.672
Yes	55	17.9	39	18.5	16	16.5	-
No	253	82.1	172	81.5	81	83.5	-
Deteriorated pre-existing co-morbidities	-	-	-	-	-	-	0.189
Yes	14	4.5	8	3.8	6	6.2	-
No	41	13.3	31	14.7	10	10.3	-
Time from the onset of COVID-19 to study‡	-	-	-	-	-	-	0.151
$\leq$ 3weeks	36	11.7	25	11.8	11	11.3	-
4–8 weeks	54	17.5	30	14.2	24	24.7	-
3–6 months	87	28.2	61	28.9	26	26.8	-
> 7 months	131	42.5	95	45.0	36	37.1	-
Treatment WHO severity§	-	-	-	-	-	-	0.032
0–2	158	51.3	117	55.5	41	42.3	-
3	150	48.7	94	44.5	56	57.7	-

COVID-19, coronavirus disease 2019; n-RTS, not returned to pre-illness level of sport; WHO, World Health Organization; y-RTS, returned to pre-illness level of sport.

†, type of sport was divided into 'running' = running only, 'cycling' = cycling only, and 'multisport' = additional sports including running or cycling.

‡, we assume variant based on the elapsed time since onset of illness: omicron < 8 weeks, beta 3–6 months, delta > 7 months.

§, World Health Organization COVID-19 Severity Scale: 0–2 = No treatment or did not consult a healthcare professional, 3 = Consulted a healthcare professional or admitted to hospital.

difference in the demographic and sport-specific characteristics of y-RTS versus n-RTS.

Most athletes did not have coexisting comorbidities (n = 253, 82.1%). However, comorbidities that were reported include asthma (n = 18, 5.8%), hypertension (n = 12, 3.8%), and cardiac disease (n = 4, 1.3%). The majority (94%) of athletes (n = 289) experienced one or more of the known COVID-19 symptoms. The only significant difference in COVID-19 characteristics of the y-RTS group compared to the n-RTS was the severity of the disease according to the WHO COVID-19 Severity Scale, indicating that more athletes consulted healthcare professionals and/or were admitted to hospital in the n-RTS group (p = 0.032).

Acute and subacute symptoms

Table 2 summarises symptoms at the time of illness. There was no significant difference in asymptomatic disease experienced by the y-RTS versus n-RTS groups. A total of 21 participants (6.8%) tested negative, but their symptom presentation implied false negative tests. Fatigue was the only mild symptom more prevalent in the n-RTS group (p = 0.044). We found a higher proportion of moderate disease in n-RTS group (p = 0.006). There were eight athletes in total with severe illness requiring supplemental oxygen, with no significant difference between the groups (p = 0.710). No participants cited critical illness. Post-COVID-19 sequelae included cardiac (n = 15, 4.9%) and pulmonary (n = 12, 3.9%) consequences, and were more prevalent in the n-RTS group (p = 0.031).

Factors associated with return to pre-illness level of sport

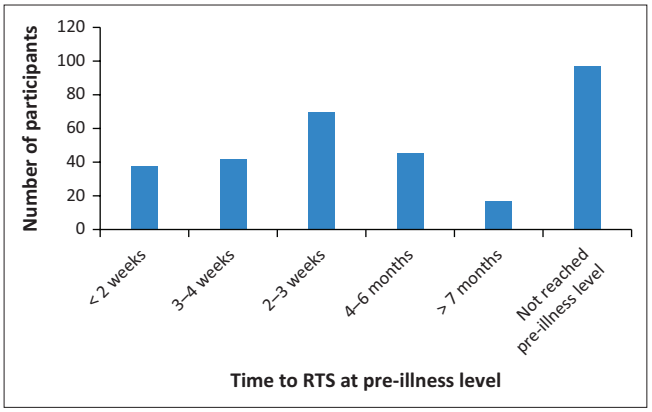
The time frame in which athletes in the whole group returned to pre-illness level of sport is displayed in Figure 2, with n = 97 (31.5%) not yet at their previous level and constituted the n-RTS group. Table 3 displays the presence and severity of symptoms while exercising and other self-reported factors limiting their RTS. The athletes approached their resumption of training with similar consideration of most factors, with only pace being monitored more closely in the n-RTS group

TABLE 2: Coronavirus disease 2019 symptoms experienced at the time of illness.

Variable	All (N = 308)		y-RTS (n = 211, 68.5%)		n-RTS (n = 97, 31.5%)		p
	n	%	n	%	n	%	
COVID-19	-	-	-	-	-	-	0.201
symptoms	289	93.8	195	92.4	94	96.9	-
asymptomatic	19	6.2	16	7.6	3	3.1	-
Acute symptoms†							
Mild:							
Malaise or Fatigue	184	59.7	118	55.9	66	68.0	0.044
Headache	139	45.1	92	43.6	47	48.5	0.427
Myalgia	133	43.2	85	40.3	48	49.5	0.130
Ageusia or anosmia	84	27.3	56	26.5	41	42.3	0.670
Cough	83	26.9	51	24.2	32	33.0	0.105
Fever	63	20.5	42	19.9	21	21.6	0.724
Diarrhoea	21	21.6	9	4.3	3	3.1	0.445
Moderate:							
Dyspnoea SpO2 ≥ 94	97	31.5	56	26.5	41	42.3	0.006
Severe:							
Dyspnoea SpO2 ≤ 94	8	2.6	5	2.4	3	3.1	0.710
Symptom duration (weeks)	-	-	-	-	-	-	0.009
< 1	83	26.9	68	32.2	15	15.5	-
1–2	118	38.3	83	39.3	35	36.1	-
3–4	51	16.6	7	12.8	24	24.7	-
5–8	28	9.1	15	7.1	13	13.4	-
> 8	28	9.1	18	8.5	10	10.3	-
Post-COVID-19 sequalae	44	14.3	24	11.4	20	20.6	0.031

COVID-19, coronavirus disease 2019; n-RTS, not returned to pre-illness level of sport; WHO, World Health Organization; y-RTS, returned to pre-illness level of sport.

†, Multiple responses were allowed in the survey, resulting in cumulative percentages exceeding 100%. Symptoms are classified as mild, moderate, or severe illness according to the National Institute of Health (COVID-19 Treatment Guidelines).



RTS, return to sport.

FIGURE 2: Time to return to pre-illness sport for our study population (n = 308).

(p = 0.035). There was a distinctly higher proportion (n = 27, 27.8%) of athletes still experiencing symptoms at rest in the n-RTS group. The most frequently reported exertional symptoms by the whole group were fatigue (n = 216, 70.1%), and elevated heart rate (n = 216, 70.1%), followed by dyspnoea (n = 174, 56.5%). All symptoms except musculoskeletal pain occurred significantly more frequently in the n-RTS group. All self-reported limitations to exercise capacity were more common in the n-RTS group (p < 0.001). Training volume (p < 0.001), running pace (p < 0.001), and cycling threshold power (p = 0.024) were lower in the n-RTS group compared to the y-RTS group.

Fatigue and the endurance athlete

The MDFI (Table 4) assesses five categories of fatigue (general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue). Athletes who had not yet returned to pre-illness level scored higher in all fatigue categories, indicating considerably worse overall fatigue compared to the y-RTS group (p < 0.001). The results of the univariate regression analysis in Table 5 suggest all variables excluding age and sex are associated with RTS. The multivariate regression analysis adjusted for dyspnoea and general fatigue, showed that an increase in physical fatigue is associated with decreased odds of return to sport (OR 0.673, p < 0.001). An increase in mental fatigue is associated with increased odds of return to sport (OR 1.0361, p = 0.047).

Discussion

Our study provides insight into acute and exertional symptoms associated with protracted exercise tolerance in a masters-age athlete population that does a high volume of cardiovascular exercise yet has had little investigation. Following several studies earlier in the pandemic that focussed on elite team sport athletes (Petek et al. 2021), our study included a large sample of endurance athletes, closely matching the demographics of marathon runners worldwide. Because of a global shortage of polymerase chain reaction (PCR) tests in 2020, and the questionable reliability thereof (Burgstahler et al. 2023), many diagnoses were based on symptom presentation or positive contact. Therefore, studies such as ours included symptomatic individuals who may not have been tested or had either a positive or negative PCR test result. Our findings suggest that acute fatigue, longer symptom duration, post-COVID-19 sequelae, exertional symptoms especially

TABLE 3: The athlete's approach to return to sport, the presence of exertional symptoms, challenges, and exercise capacity.

Variable	All (N = 308)				y-RTS (n = 211, 68.5%)				n-RTS (n = 97, 31.5%)				p
	n	%	Median	95% CI	n	%	Median	95% CI	n	%	Median	95% CI	
Received RTS guidelines	-	-	-	-	-	-	-	-	-	-	-	-	0.853
Yes	121	39.3	-	-	83	39.3	-	-	38	39.2	-	-	-
No	187	60.7	-	-	128	60.7	-	-	59	60.8	-	-	-
Symptoms at rest	-	-	-	-	-	-	-	-	-	-	-	-	0.005
Yes	56	18.2	-	-	29	13.7	-	-	27	27.8	-	-	-
No	252	81.8	-	-	182	86.3	-	-	70	72.2	-	-	-
Monitoring during RTS													
Resting, average, and maximal heart rate	215	69.8	-	-	143	67.8	-	-	72	74.2	-	-	0.252
Pace or speed	186	60.4	-	-	119	56.4	-	-	67	69.1	-	-	0.035
Rate of perceived exertion	100	32.5	-	-	71	33.6	-	-	29	29.9	-	-	0.514
Sleep quality	103	33.4	-	-	68	32.2	-	-	35	36.1	-	-	0.505
Stress	52	16.9	-	-	38	18.0	-	-	14	14.4	-	-	0.539
Fatigue	121	39.3	-	-	78	37.0	-	-	43	44.3	-	-	0.219
Myalgia	103	33.4	-	-	70	33.2	-	-	33	34.0	-	-	0.884
Presence of symptoms while exercising†													
Fatigue	216	70.1	-	-	134	63.4	-	-	82	84.6	-	-	< 0.001
Post-exertional malaise	183	59.4	-	-	105	49.8	-	-	78	80.4	-	-	< 0.001
Headache	105	34.2	-	-	61	29.0	-	-	44	45.4	-	-	0.005
Musculoskeletal pain	189	61.4	-	-	126	59.7	-	-	63	64.9	-	-	0.381
Autonomic disturbance including POTS‡	132	42.9	-	-	74	35.0	-	-	58	59.7	-	-	< 0.001
Elevated heart rate	216	70.0	-	-	131	62.1	-	-	85	87.6	-	-	< 0.001
Dyspnoea	174	56.5	-	-	104	49.3	-	-	70	72.2	-	-	< 0.001
Chest pain	64	20.7	-	-	30	14.2	-	-	34	35.0	-	-	< 0.001
Self-reported factors limiting exercise tolerance													
Poor endurance	199	64.6	-	-	108	51.2	-	-	91	93.8	-	-	< 0.001
Poor peak power	223	72.4	-	-	129	61.1	-	-	94	96.8	-	-	< 0.001
Difficulty hill climbing	220	71.4	-	-	133	63.0	-	-	87	89.7	-	-	< 0.001
Long-COVID-19 concerns	184	59.8	-	-	104	49.3	-	-	80	82.5	-	-	< 0.001
Anxiety or depression	147	47.7	-	-	82	38.9	-	-	65	67.0	-	-	< 0.001
Training volume pre-post§ (hours per week)	308	-	0.5	0.97–1.69	211	-	0.0	0.24–1.07	97	-	3.0	2.19–3.40	< 0.001
Running pace pre-post (min.km^{-1})	244	-	0.0	0.54–0.80	164	-	0.0	0.19–0.46	80	-	1.0	1.18–1.66	< 0.001
FTP pre-post (W.kg^{-1})	60	-	17.0	7.55–29.06	46	-	8.0	-4.62–22.68	14	-	30.0	17.53–61.87	0.024

CI, confidence interval; COVID-19, coronavirus disease 2019; FTP, Functional threshold power; n-RTS, not returned to pre-illness level of sport; RTS, return to sport; POTS, postural orthostatic tachycardia syndrome; y-RTS, returned to pre-illness level of sport.

†, Multiple responses were allowed in the survey, resulting in cumulative percentages exceeding 100%. Symptoms are classified as mild, moderate, or severe illness according to the National Institute of Health (COVID-19 Treatment Guidelines).

‡, Data can fall in more than one category.

§, Pre-post: Pre-COVID-19 minus post-COVID-19.

TABLE 4: Multidimensional fatigue inventory scores.

Variable	All (N = 308) Mean ± s.d.	y-RTS (n = 211) Mean ± s.d.	n-RTS (n = 97) Mean ± s.d.	p
General fatigue	11.04 ± 3.99	9.70 ± 3.57	13.89 ± 3.28	< 0.001
Physical fatigue	9.48 ± 4.12	7.93 ± 3.49	12.79 ± 3.33	< 0.001
Reduced activity	8.36 ± 3.41	7.29 ± 2.86	10.63 ± 3.38	< 0.001
Reduced motivation	8.48 ± 3.45	7.58 ± 3.12	10.40 ± 3.34	< 0.001
Mental fatigue	10.11 ± 4.06	9.51 ± 4.06	11.37 ± 3.77	< 0.001
MDFI Total	47.44 ± 16.33	41.99 ± 14.40	59.08 ± 13.98	< 0.001

MDFI, multidimensional fatigue inventory; n-RTS, not returned to pre-illness level of sport; y-RTS, returned to pre-illness level of sport.

dyspnoea, and chronic physical fatigue are associated with protracted RTS in endurance athletes.

Nearly one third of the athletes had not yet returned to pre-illness levels at the time of data collection. Many (27.8%) were still experiencing symptoms at rest, potentially explaining the less than 6-h per week training volume typical of recreational endurance athletes (McKinney et al. 2019). The most frequently reported acute symptoms in our study (fatigue, headache, and myalgia) were consistent with the findings of other studies (Lopes et al. 2021; Magnusson et al. 2022; Sewry et al. 2022), yet only fatigue was associated with protracted RTS in our study. Athletes have missed training more often because of fatigue after COVID-19 than any other viral illnesses or symptoms (Schwellnus et al. 2021).

The presence of exertional symptoms is widely documented, suggesting that athletes begin training while feeling unwell (Schroeder et al. 2023). Our study confirmed this, as 70% of the entire group experienced fatigue or elevated heart rate while exercising, 57% experienced dyspnoea, and 21% experienced chest pain. Hughes et al. (2022) proposed no exercise resumption until symptoms had abated or diminished. Whether the 35% of the n-RTS group who experienced chest pain followed RTS guidelines and thereby

TABLE 5: Univariate and multivariate logistic regression analysis to determine the likelihood of variables explaining the variation in return to sport.

Variable	Univariate logistic regression			Multivariate logistic regression†		
	OR	95% CI	*p*	OR	95% CI	*p*
Age	0.995	0.971–1.019	0.672	1.019	0.988–1.052	0.222
Sex	0.857	0.529–1.389	0.531	1.311	0.696–2.470	0.402
General fatigue	0.781	0.659–0.783	< 0.001	-	-	-
Physical fatigue	0.702	0.645–0.764	< 0.001	0.673	0.592–0.766	< 0.001
Reduced activity	0.724	0.662–0.791	< 0.001	0.884	0.756–1.034	0.123
Mental fatigue	0.891	0.837–0.948	< 0.001	1.036	1.001–1.223	0.047
Reduced motivation	0.777	0.781–0.841	< 0.001	1.107	0.898–1.194	0.632
Dyspnoea	0.375	0.223–0.630	< 0.001	-	-	-

OR, odds ratio; CI, confidence interval.

†, Hosmer and Lemershow goodness-of-fit test $p = 0.495$.

reduced their training is unknown, as 14% of the y-RTS group also reported chest pain. Although the reasons why the athletes did not return to pre-illness level was not specifically investigated, the results suggest that persistent symptoms interfered with full athletic performance.

In our study, athletes with post-COVID-19 sequelae were less likely to return to their previous performance levels, consistent with Schroeder et al. (2023). Our study found a higher prevalence of cardiovascular sequelae (8.8%) compared to those reviewed by Monosilio et al. (2023), probably because of this study's higher average age. Herein lies an important finding. Myocarditis, arrythmias and other cardiopulmonary post-COVID-19 sequelae presented in our study, are a concern and may be underreported in masters age-group athletes. Ventricular arrhythmias were found to occur in asymptomatic or mild disease (Casasco et al. 2022), and these athletes, constituting the bulk of the field in marathons events, may not have undergone routine cardiac screening. Our findings imply that older athletes and those with post-COVID-19 sequelae require better management. These athletes should monitor resting and exertional heart rate, sleep quality, cardiopulmonary symptoms, and fatigue after resuming exercise (Steinacker et al. 2022). While the athletes in our study were adept at monitoring heart rate and pace facilitated by popular wearable devices, it is recommended that athletes be more aware of the symptoms they experience and the implications thereof on RTS.

A novel finding in our study was the significantly decreased odds of RTS in those with physical fatigue, while mental fatigue is strongly associated with increased odds of RTS. This may seem counterintuitive as fatigue and impaired neurocognitive ability can lead to protracted exercise tolerance (Steinacker et al. 2022). Mental fatigue often occurs because of a prolonged period of demanding cognitive tasks yet may also develop from the frustration of trying harder to resume fitness compared to other respiratory illnesses (Marcora et al. 2009). In a scoping review by Oswald et al. (2020), running has been unequivocally positively associated with improving mood, sense of well-being, self-efficacy, and decreased depression. Regular runners who were prevented from running for 2 weeks had increased anxiety and depression compared to the runners who continued (Oswald et al. 2020). Hence, an unexpected finding becomes expected. This relationship may further explain the tendency for endurance athletes to resume training before recovering sufficiently.

Our study is one of the first to compare individuals who successfully rebuilt their pre-illness fitness level to those who were still struggling. Our results suggest that the n-RTS group intentionally reduced the intensity of their training during recovery. Post-COVID-19 performance capacity as determined by training volume, running speed, and cycling threshold power was lower in the n-RTS group when compared to pre-COVID-19 levels. In contrast, Emeran et al. (2022) found no difference in running speed or training volume. A large proportion of athletes did not return to sport after having moderate illness, likely because of the symptom severity directly precluding RTS, or recommendations from healthcare providers (Schroeder et al. 2023), as more consultations were attended by athletes in the n-RTS group. Longer symptom duration, and especially persistent fatigue was more prevalent in the n-RTS group, which can negatively affect quality of life (Vollrath et al. 2022). As research investigating long-term consequences of COVID-19 on cardiorespiratory fitness and sports participation emerges, the knowledge gained needs to be disseminated to athletes, coaches, and medical professionals.

Strengths and limitations

The main strength of this study is the sample size and statistical power. Athletes were recruited throughout South Africa, which enhances generalisability to the South African athletic population, although generalisation may not be translated to other countries. The focus of our study was endurance athletes and therefore mostly older than 35 years of age, fulfilling a gap in the literature. Quantifying subjective descriptions of fatigue by using the MDFI is a strength of our study as to our knowledge, it has not been used in other studies on athletic populations. Future studies using the MDFI in athletes is recommended. This is one of few studies that has associated exertional symptoms with RTS status.

As is customary for surveys, certain limitations exist. Snowball sampling will not allow a response rate to be calculated and recorded, thus reducing the power of our study. The participant's responses rely on retrospective recall

(recall bias) and the period from illness to the time of our study will vary between participants. The inclusion criteria did not specify the presence of COVID-19 symptoms, thus selection bias caused underrepresentation of the number of asymptomatic cases. Vaccine status was unknown; however, by deducing from the time of illness, most athletes would not have had the opportunity to be vaccinated. Athletes in our study would have been infected by a mix of viral strains. We did not ask whether home oxygen was used, which may have placed some participants not admitted to the hospital in the 'severe illness' category. These limitations were unavoidable with the current knowledge at the time of our study. No direct cause-effect relationship can be determined from our observational study.

Interpretation

These findings may provide valuable insights into the acute and long-term manifestations of this disease in a masters-age athlete population. Symptoms that may indicate cardiopulmonary consequences in an athlete population that does a high volume of cardiovascular exercise should be investigated. An interdisciplinary approach to management is vital to facilitate return to sport and the important mental and physical benefits thereof. This will augment outcomes after respiratory tract infections in endurance athletes.

Conclusion

Our findings suggest that acute fatigue, longer symptom duration, post-COVID sequelae, the presence of exertional symptoms particularly dyspnoea, and chronic physical fatigue are associated with protracted RTS in endurance athletes. These symptoms still abound albeit less frequently after infection by the current Omicron variant. Such symptoms should continue to be flagged and managed to prevent protracted RTS, with further investigations if cardiopulmonary consequences are suspected. Consideration of the mental gains of physical activity ought to be given high regard while building the endurance athlete's training load to return to their pre-illness level.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

C.A.H., H.v.A., B.O. contributed to the study design. C.A.H. collected the data. C.A.H. and E.L. performed the statistical analysis. C.A.H. wrote the original draft of the article. C.A.H., H.v.A., B.O. and E.L. contributed to the editing and revision of the article.

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Data availability

Data will be made available upon request and after considering the intentions of use, ethical clearance, and appropriateness of available data. The corresponding author, C.H., may be contacted in this regard.

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References

Agha-Alinejad, H., Ahmadi Hekmatikar, AH., Ruhee, R.T., Shamsi, M.M., Rahmati, M., Khoramipour, K. et al., 2022, 'A guide to different intensities of exercise, vaccination, and sports nutrition in the course of preparing elite athletes for the management of upper respiratory infections during the COVID-19 pandemic: A narrative review', *International Journal of Environmental Research and Public Health* 19(3), 1888. https://doi.org/10.3390/ijerph19031888

Braga, F., Domecg, F., Kalichsztein, M., Nobre, G., Kezen, J., Espinosa, G. et al., 2023, 'Abnormal exercise adaptation after varying severities of COVID-19: A controlled cross-sectional analysis of 392 survivors', *European Journal of Sport Science* 23(5), 829–839. https://doi.org/10.1080/17461391.2022.2054363

Burgstahler, C., Plank, C., Niess, A.M., Schobersberger, W., Niebauer, J. & Scharhag, J., 2023, 'Effects of the corona pandemic on competitive sports – An online survey amongst 2981 German and Austrian elite athletes', *German Journal of Sports Medicine/Deutsche Zeitschrift fur Sportmedizin* 74(1), 7–12. https://doi.org/10.5960/dzsm.2022.552

Casasco, M., Iellamo, F., Scorcu, M., Parisi, A., Tavcar, I., Brugin, E. et al., 2022, 'Return to play after SARS-CoV-2 infection in competitive athletes of distinct sport disciplines in Italy: A FMSI (Italian Federation of Sports Medicine) study', *Journal of Cardiovascular Development and Disease* 9(2), 59. https://doi.org/10.3390/jcdd9020059

Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y. et al., 2020, 'Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study', *The Lancet* 395(2), 507–513. https://doi.org/10.1016/S0140-6736(20)30211-7

COVID-19 Treatment Guidelines 2023, *NIH: Clinical spectrum of SARS-CoV-2 infection*, viewed 13 February 2023, from http://www.covid19treatmentguidelines.nih.gov/overwiew/clinical-spectrum.

Crameri, G.A.G., Bielecki, M., Zust, R., Buehrer, T.W., Stanga Z. & Deuel, J.W., 2020, 'Reduced maximal aerobic capacity after COVID-19 in young adult recruits, Switzerland, May 2020', *Eurosurveillance. European Centre for Disease Prevention and Control (EDC)* 25(36), 2001542. https://doi.org/10.2807/1560-7917.ES.2020.25.36.2001542

DeJong, A.F., Fish, P.N. & Hertel, J., 2021, 'Running behaviors, motivations, and injury risk during the COVID-19 pandemic: A survey of 1147 runners', *PloS One* 16(2), e0246300. https://doi.org/10.1371/journal.pone.0246300

Durstenfeld, M.S., Sun, K., Tahir, P., Peluso, M.J., Deeks, S.G., Aras, M.A. et al. 2022, 'Use of cardiopulmonary exercise testing to evaluate long COVID-19 symptoms in adults: A systematic review and meta-analysis', *JAMA Network Open* 5(10), e2236057–e2236057. https://doi.org/10.1001/jamanetworkopen.2022.36057

Elliott, N., Martin, R., Heron, N., Elliott, J., Grimstead, D. & Biswas, A., 2020, 'Infographic. Graduated return to play guidance following COVID-19 infection', *British Journal of Sports Medicine* 54(19), 1174–1175. https://doi.org/10.1136/bjsports-2020-102637

Emeran, A., Lambert, E.V., Paruk, T. & Bosch, A., 2022, 'Changes in training activity post COVID-19 infection in recreational runners and cyclists', *South African Journal of Sports Medicine* 34(1), 1–7. https://doi.org/10.17159/2078-516X/2022/v34i1a13758

Gluckman, T.J., Bhave, N.M., Allen, L.A., Chung, E.H., Spatz, E.S., Ammirati, E. et al., 2022, '2022 ACC expert consensus decision pathway on cardiovascular sequelae of COVID-19 in adults: Myocarditis and other myocardial involvement, post-acute sequelae of SARS-CoV-2 infection, and return to play: A report of the American College of Cardiology Solution Set Oversight Committee', *Journal of the American College of Cardiology* 79(17), 1717–1756. https://doi.org/10.1016/j.jacc.2022.02.003

GO FAIR, FAIR principles, 2016, *GO FAIR*, viewed 13 May 2023, from https://www.go-fair.org/fair-principles/.

Hughes, D.C., Orchard, J.W., Partridge, E.M., La Gerche, A. & Broderick, C., 2022, 'Return to exercise post-COVID-19 infection: A pragmatic approach in mid-2022', *Journal of Science and Medicine in Sport* 25(7), 544–547. https://doi.org/10.1016/j.jsams.2022.06.001

Joyner, M.J. & Coyle, E.F., 2008, 'Endurance exercise performance: The physiology of champions', *The Journal of Physiology* 586(1), 35–44. https://doi.org/10.1113/jphysiol.2007.143834

Juhász, V., Szabó, L., Pavlik, A., Tállay, A., Balla, D., Kiss, O. et al., 2022, 'Short and mid-term characteristics of COVID-19 disease course in athletes: A high-volume, single-center study', *Scandinavian Journal of Medicine & Science in Sports* 33(3), 341–352. https://doi.org/10.1111/sms.14265

Lopes, L.R., Miranda, V.A., Goes, R.A., Souza, G.G., Souza, G.R., Rocha, J.C. et al., 2021, 'Repercussions of the COVID-19 pandemic on athletes: A cross-sectional study', *Biology of Sport* 38(4), 703–711. https://doi.org/10.5114/biolsport.2021.106147

Magnusson, K., Kristoffersen, D.T., Dell'Isola, A., Kiadaliri, A., Turkiewicz, A., Runhaar, J. et al., 2022, 'Post-covid medical complaints following infection with SARS-CoV-2 Omicron vs Delta variants', *Nature Communications* 13(1), 7363. https://doi.org/10.1038/s41467-022-35240-2

Marcora, S.M., Staiano, W. & Manning, V., 2009, 'Mental fatigue impairs physical performance in humans', *Journal of Applied Physiology* 106(3), 857–864. https://doi.org/10.1152/japplphysiol.91324.2008

Marshall, J.C., Murthy, S., Diaz, J., Adhikari, N.K., Angus, D.C., Arabi, Y.M. et al., 2020, 'A minimal common outcome measure set for COVID-19 clinical research', *The Lancet Infectious Diseases* 20(8), e192–e197. https://doi.org/10.1016/S1473-3099(20)30483-7

McKinney, J., Velghe, J., Fee, J., Isserow, S. & Drezner, J.A., 2019, 'Defining athletes and exercisers', *The American Journal of Cardiology* 123(3), 532–535. https://doi.org/10.1016/j.amjcard.2018.11.001

Mihalick, V.L., Canada, J.M., Arena, R., Abbate, A. & Kirkman, D.L., 2021, 'Cardiopulmonary exercise testing during the COVID-19 pandemic', *Progress in Cardiovascular Diseases* 67, 35–39. https://doi.org/10.1016/j.pcad.2021.04.005

Monosilio, S., Prosperi, S., Squeo, M.R., Spataro, S., Spataro, A. & Maestrini, V., 2023, 'Short and long-term cardiovascular sequelae after SARS-CoV-2 infection: A narrative review focusing on athletes', *Viruses* 15(2), 493. https://doi.org/10.3390/v15020493

National Institute for Health and Care Excellence (NICE) SIGN (SIGN) and RC of GP (RCGP), 2021, *COVID-19 rapid guideline: Managing the long-term effects of COVID-19*, Updated November 2021, viewed 08 February 2023, from https://www.nice.org.uk/guidance/ng188.

Oswald, F., Campbell, J., Williamson, C., Richards, J. & Kelly, P., 2020, 'A scoping review of the relationship between running and mental health', *International Journal of Environmental Research and Public Health* 17(21), 8059. https://doi.org/10.3390/ijerph17218059

Pelliccia, A., Sharma, S., Gati, S., Bäck, M., Börjesson, M., Caselli, S. et al., 2021, '2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease: The task force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC)', *European Heart Journal* 42(1), 17–96. https://doi.org/10.1093/eurheartj/ehaa605

Petek, B.J., Moulson, N., Baggish, A.L., Kliethermes, S.A., Patel, M.R., Churchill, T.W. et al., 2022, 'Prevalence and clinical implications of persistent or exertional cardiopulmonary symptoms following SARS-CoV-2 infection in 3597 collegiate athletes: A study from the Outcomes Registry for Cardiac Conditions in Athletes (ORCCA)', *British Journal of Sports Medicine* 56(16), 913–918. https://doi.org/10.1136/bjsports-2021-104644

Ruuskanen, O., Luoto, R., Valtonen, M., Heinonen, O.J. & Waris, M., 2022, 'Respiratory viral infections in athletes: Many unanswered questions', *Sports Medicine* 52(9), 2013–2021. https://doi.org/10.1007/s40279-022-01660-9

Schroeder, A.N., Getzin, A.R., Creswell, L.L. & Asplund, C.A., 2023, 'Recovery from COVID-19 in adult recreational athletes: A survey of American triathletes', *Exercise, Sport, and Movement* 1(2), e00005. https://doi.org/10.1249/ESM.0000000000000005

Schwellnus, M., Sewry, N., Snyders, C., Kaulback, K., Wood, P.S., Seocharan, I. et al., 2021, 'Symptom cluster is associated with prolonged return-to-play in symptomatic athletes with acute respiratory illness (including COVID-19): A cross-sectional study-AWARE study I', *British Journal of Sports Medicine* 55(20), 1144–1152. https://doi.org/10.1136/bjsports-2020-103782

Sewry, N., Schwellnus, M., Readhead, C., Swanevelder, S. & Jordaan, E., 2022, 'The incidence and transmission of SARS-CoV-2 infection in South African professional rugby players-AWARE II', *Journal of Science and Medicine in Sport* 25(8), 639–643. https://doi.org/10.1016/j.jsams.2022.06.004

Smets, E.M.A., Garssen, B., Bonke, B.D. & De Haes, J.C.J.M., 1995, 'The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue', *Journal of Psychosomatic Research* 39(3), 315–325. https://doi.org/10.1016/0022-3999(94)00125-O

Snyders, C., Schwellnus, M., Sewry, N., Kaulback, K., Wood, P., Seocharan, I. et al., 2023, 'Symptom number and reduced preinfection training predict prolonged return to training after SARS-CoV-2 in athletes: AWARE IV', *Medicine and Science in Sports and Exercise* 55(1), 1–8. https://doi.org/10.1249/MSS.0000000000003027

Steinacker, J.M., Schellenberg, J., Bloch, W., Deibert, P., Friedmann-Bette, B., Grim, C. et al., 2022, 'Recommendations for return-to-sport after COVID-19: Expert consensus', *German Journal of Sports Medicine/Deutsche Zeitschrift fur Sportmedizin* 73(4), 127–136. https://doi.org/10.5960/dzsm.2022.532

Van Aerde, N., Van den Berghe, G., Wilmer, A., Gosselink, R. & Hermans, G., 2020, 'Intensive care unit acquired muscle weakness in COVID-19 patients', *Intensive Care Medicine* 46, 2083–2085. https://doi.org/10.1007/s00134-020-06244-7

Vollrath, S., Bizjak, D.A., Zorn, J., Matits, L., Jerg, A., Munk, M. et al., 2022, 'Recovery of performance and persistent symptoms in athletes after COVID-19', *PloS One* 17(12), e0277984. https://doi.org/10.1371/journal.pone.0277984

Chapter 4 Paper 2

This chapter includes the full text publication of Paper 2, research article.

4.1 Title: “Every run is hard”: Endurance athletes’ experiences of return to sports participation after COVID-19- A mixed methods study

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Research Article

'Every Run Is Hard': Endurance Athletes' Experiences of Return to Sports Participation After COVID-19—A Mixed Methods Study

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Protracted return to sport (RTS) following COVID-19 is common due to long-term cardiopulmonary symptoms and persistent fatigue. In athletes, low exercise tolerance may result in emotional distress. The aim of this study is to assess the symptom severity, the management thereof and the impact on quality of life (QOL) as endurance athletes return to their preillness level of sports participation. A cross-sectional survey-based mixed methods study of long-distance athletes was performed. Quantitative data included sport and disease characteristics, fatigue score and management of persistent symptoms. A total of 295 survey responses were included. The mean age was 45.1 (10.2) years and 54.7% were male. Barriers to exercise included tachycardia (72%), fatigue (72%), dyspnoea (58%) and inability to exercise at high intensities (75%). High physical and mental fatigue scores were found, the former significantly predicting return to sport. Qualitative data were collected through open-ended questions exploring challenges faced when returning to sport post-COVID-19 convalescence and the impact on their QOL. Biopsychosocial well-being constituted three themes: Physical, Psychological and Social. Categories with high code frequencies included persistent cardiopulmonary symptoms, physical fatigue, emotional distress and social disengagement. Mixing the methods revealed that the athletes' QOL deteriorated due to protracted RTS after COVID-19. A multidisciplinary approach to management may be required by endurance athletes.

Keywords: cardiopulmonary; COVID-19; fatigue; quality of life; return to sport

1. Introduction

The coronavirus disease (COVID-19) has affected billions of people, including athletes who, despite the protective effect of regular exercise, may have been as frequently infected [1]. The novelty of the crisis evoked uncertainty, unpredictability and uncontrollability in the world we live in [2]. Moreover, being incapable of controlling or predicting the course of disease within one's own body may be severely psychologically taxing, especially for athletes [3]. Running is a highly accessible and affordable sport attracting long-distance adult athletes predominantly at a recreational level [4]. Cardiopulmonary fitness is so prognostic of all-cause mortality, and it is now classed as a vital sign [5]. Therefore, the impact of COVID-19 on all athletes is important, from recreational athletes enjoying the benefits of improved quality of life (QOL) to professional athletes whose careers may be defined by the slightest increments of performance [3].

Symptom severity of COVID-19 in athletic populations has been well documented [6, 7]. This multifaceted disease commonly causes mild to moderate cardiovascular symptoms, with a low prevalence of critical cardiac consequences [8]. Pulmonary limitations have been found responsible for low exercise tolerance long after COVID-19 infection, even following mild illness [7, 9]. In this study, the term long-COVID is used for new or persistent symptoms four weeks post-onset of illness as defined by the National Institute for

Health and Care Excellence [10]. Long-COVID symptoms are heterogeneous, with fatigue most commonly reported, followed by dyspnoea and chest pain [11]. Endurance athletes require the ability to resist fatigue, placing a huge demand on their cardiopulmonary system [7, 12]. This symptom burden results in a protracted return to sport (RTS) and decreased general well-being [6, 13].

The virus primarily affects physical health; however, mental health consequences such as anxiety, depression and poor concentration in athletes are reported [14]. The mental health of professional athletes has gained a lot of research of late [13]. QOL is a multidimensional concept that encompasses domains related to physical, mental, social and emotional functioning [15]. It is defined by the World Health Organization (WHO) as 'An individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns' [16]. There is a paucity of literature describing the post-COVID-19 biopsychosocial state of elite and recreational endurance athletes, encompassing their physical, psychological and social well-being [13].

Both quantitative and qualitative studies exist exploring the effect of the pandemic on athletes [2, 14, 17, 18]. To mitigate the spread of the virus, several major competitions were cancelled or postponed, and training facilities closed [1, 19], resulting in immediate reduction or cessation of exercise and, with it, an important mechanism for coping with stressors used by athletes [2]. Numerous studies reported the negative impacts of these measures on finances, physical activity and mental health of young elite athletes [17, 20]. However, more literature regarding the complexities of recovering from the disease itself, particularly in an endurance athlete population, is required [6, 13].

Pelliccia et al. [21] defined competitive athletes as those who exercise for six hours or more per week and recreational athletes for at least three hours, although the training load of endurance runners and cyclists is typically equal to professional athletes. Understanding the challenges faced by these athletes as they return to a high volume of cardiovascular exercise was the impetus for the study, as the results may suggest treatment strategies for athletes facing physical and mental health challenges in the future [11]. Thus, the aim of this mixed methods study is to assess the severity of COVID-19 symptoms and their management in endurance athletes and to explore the impact of the disease on their QOL as they return to preillness level of participation and performance in sport.

2. Methods

The researchers' positions can be described as follows: Two of the researchers are long-distance runners, and thus an insider perspective in interpreting the sport-specific data exists. None of the researchers contracted COVID-19, and thus an outsider perspective in interpreting the illness-specific data exists. All three authors are healthcare providers who understand the seriousness of the symptoms. Reflexivity exists as the researchers were aware of their own reactions that may influence their interpretation of the qualitative data [22].

2.1. Study Design, Setting and Participants. This is a mixed methods study with convergent design using a cross-sectional survey [23]. The quantitative data include demographic characteristics, symptom severity, management of illness, fatigue score and their approach to RTS. Understanding context was important, and thus the study elaborated on the participants' responses by collecting qualitative data through open-ended questions. The quantitative data and qualitative data were collected at the same time and given equal priority. The responses were triangulated and compared to further contextualise our understanding [23]. The Good Reporting of a Mixed Methods Study (GRAMMS) guidelines and the COREQ checklist were followed [24, 25].

Adult endurance runners and cyclists of both sexes were eligible if they partook in cardiovascular exercise for three or more hours per week and were at any time diagnosed with COVID-19 by a positive polymerase chain reaction (PCR) test or experienced the known COVID-19 symptoms [7]. Athletes who were admitted to the intensive care unit (ICU) were excluded as ICU-acquired weakness occurs from 15 to 29 days and necessitates prolonged rehabilitation to return to normal function [26]. Further exclusions were not being proficient in the English language and residing outside of South Africa. Due to the nature of the study, no a priori sample size could be calculated. The recruitment of participants is illustrated in Figure 1.

Unconditional ethical clearance was provided by the University's (*information removed to allow for anonymous peer review*) Human Research Ethics Committee (Medical) (Certificate no. M21065). The study is designed according to ethical considerations in accordance with the Declaration of Helsinki, the South African Guidelines for Good Clinical Practice and the Medical Research Council. An information sheet explaining the study purpose and data sharing according to the FAIR principles [27] was linked to the survey and ensured confidentiality, anonymity and permission to withdraw from the study at any point. Due to potential COVID-19 adversary, participants were asked if they had, or would like to receive counselling.

2.2. Outcome Measures and Data Collection. A self-administered web-based questionnaire using the Research Electronic Data Capture (REDCap) platform was developed by the research team and based on current literature [7]. This platform was accessed through the University (*information removed to allow for anonymous peer review*). Sociodemographic data, including sex, age and sport-specific data, constituted the first ten questions, followed by eight questions on COVID-19 status, symptoms according to the NIH classification [28] and prevalence of comorbidities. The third section included questions regarding the management of their acute illness based on the WHO Severity Scale [29].

Fatigue was scored using the standardised Multidimensional Fatigue Inventory (MDFI) tool, imbedded into the questionnaire [30]. The MDFI consists of 20 questions that assess five categories of fatigue, namely, general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. Psychometric tests conducted on

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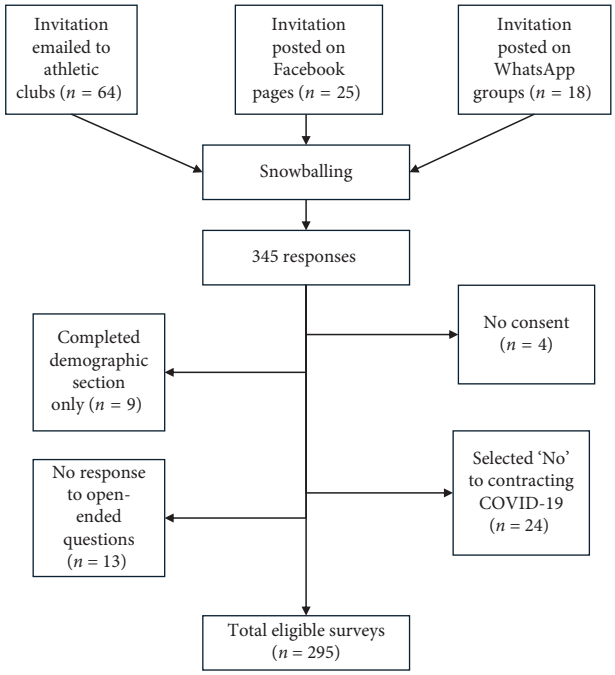

Figure 1: Recruitment of participants.

development of the MDFI showed good internal consistency (Cronbach's alpha = 0.84), construct validity established by comparing between and within groups and convergent validity analysed by correlating the MDFI score with a visual analogue scale measuring fatigue ($0.22 < r < 0.78$) [30]. In subsequent research, the scale structure of the MDFI tool was assessed using seven samples and yielded an acceptable Cronbach's alpha for most of the scales with a total score of 0.89 [31]. Although the confirmatory factor analysis could not confirm the scale structure in this study, it was advised that the MDFI structure should be maintained [31]. Our own instrument was developed by a professional panel in the field of sports medicine and respiratory health and pilot tested to identify weaknesses in the instrument. To assess content validity, three experts in the field commented on the clarity of some of the short questions and on the MDFI, a legal expert ensured anonymity and protection of personal information, two academics commented on the format of the survey and four athletes commented on the sport-specific data. The content in our study-specific questions was modified accordingly while the MDFI is a validated instrument and has not been modified for the purposes of this study. We piloted the tool among five participants who completed the survey twice, two weeks apart to avoid a learning effect. The outcome of this showed inconsistencies in the ratings of symptom severity in three surveys, so it was restructured according to the NIH symptom severity scale. One inconsistency in the impact of QOL question was found, so it remained unchanged.

The participants were given information about the objectives of the fourth section of the questionnaire, i.e., four questions exploring their RTS management, challenges faced and the psychosocial impact of this disease, followed by four open-ended questions as follows:

1. What is the main concern or challenge that you have experienced while returning to training?
2. Were you stressed about recovering fully and quickly from COVID-19?
3. Many athletes partake in sport for enjoyment, physical health, taking on a challenge and/or improved QOL. Can you comment on how COVID-19 has affected these in your life?
4. Is there any further information you can share about how COVID-19 affected you?

The primary researcher structured the questions as simply as possible to encourage a good response rate while eliciting relevant information from the athletes to answer the research question.

2.3. Procedures. Participants were recruited by snowball sampling from athletic clubs in South Africa between December 2021 and July 2022 [7]. Invitations to complete the online survey were disseminated using social media: 18 WhatsApp groups and 25 Facebook pages, and emailed to 64 athletic clubs. Athletic clubs approved the post on their social media pages and chats. Invitations could then be forwarded to fellow athletes by the recipients in a snowball fashion. The invitations to participate contained a link to the participant information sheet on REDCap. The survey became accessible after providing consent to participate.

2.4. Data Analysis. Answering 'No' to contracting COVID-19 and absent responses to all open-ended questions resulted in exclusion from data analysis.

Quantitative data were extracted from REDCap into Microsoft Excel, cleaned and imported into IBM SPSS Statistics for Mac 28.0.1.1 (4), which was used for all analyses. Descriptive characteristics were summarised using means and standard deviations for continuous variables and percentages and frequencies for categorical variables. Regression analyses were performed using ANCOVA and multivariate logistic regression.

The qualitative data were analysed using content analysis within the deductive framework of the biopsychosocial model. The established themes included physical, psychological and social. An inductive approach to content analysis was then used where the initial codes were derived from the data itself in an exploratory analysis to allow new information to present itself about this novel disease [32]. Coded data counts indicate patterns in the data where the more commonly described codes versus less commonly described codes lie [23, 32]. This enhances the context; however, it does not attach meaning to the code [32]. Thereafter, similar codes were grouped into categories and were allocated to one of the three overarching themes. No identifiable data were extracted. Two of the authors (one athlete and one non-athlete) independently coded the responses. This was followed by a discussion to gain consensus on the codes and categories. The third author verified that the codes were allocated to the correct themes and the data

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sufficiently supported the themes, thereby triangulating the data and credibility of the analysis. All three authors discussed their perspective on the understanding of the data.

Mixing of data was accomplished by merging of data [23]. This integration was achieved by presenting the quantitative and qualitative results simultaneously, primarily in the discussion section. Data integration is evident in Table 1, where quantitative and qualitative data are listed side by side [23]. Additionally, Table 2 displays the content analysis revealing the frequency of citations for the codes [32].

Since the survey questions used required radio buttons, respondents had to provide an answer for each item, resulting in minimal missing data. A blank response to an open-ended question was not recorded as 'no impact', as one cannot assume this. Participants may have felt they already noted their concerns in the first question and/or may have not thought about a particular point at the time of answering.

3. Results

3.1. Quantitative Data Analysis. Table 3 summarises the study population characteristics. The mean age was 45.1 (10.2) years, with 54.7% ($n = 158$) male respondents and 95% ($n = 274$) recreational athletes. Of those with pre-existing comorbidities ($n = 54$), 14 reported a deterioration of their condition. Based on the timeframe from onset of illness to answering the questionnaire, it can be assumed that the majority were infected with the COVID-19 beta- or delta-variant. Approximately half the athletes consulted outpatient medical professionals or were admitted to hospital.

The survey questions that focused on exercise intolerance and the management of RTS included response options suggested by the tool. These results are presented in Table 1, in the column labelled 'Variable'. Additional information provided by the respondents in the open-ended questions that related to exercise intolerance and their RTS was coded based on content. These codes are presented in the adjacent column labelled 'Codes related to the quantitative parameter'. The qualitative data build on the quantitative data and in this way provide more information about athletic performance post-COVID-19 [23]. Almost one-third of the athletes had not yet returned to their preillness level of sport at the time of the survey. Results of the MDFI indicate higher general fatigue and mental fatigue scores, indicating worse fatigue in these categories. The self-reported limitations to exercise indicated that athletes aimed to resume training but experienced difficulties at high loads with elevated HR and fatigue. The number of athletes who pushed through their RTS challenges closely matched those who chose to rest.

Athletes were stressed about recovering fully and quickly from COVID-19 (63.4%), and 18% felt stigmatised due to their positive COVID-19 status. The biopsychosocial impact of their illness is illustrated in Figure 2, where the percentages of athletes citing improved, neutral or worsened qualities are displayed. Most selected a neutral response but many indicated a worsened QOL after contracting COVID-19.

In the regression analyses (Table 4), sex and severity of illness are shown to be significant determinants of fatigue; however, the low R-squared indicates that the variables in this model explain only a minor variance in the MDFI score. Severity of illness and physical fatigue were shown to be significant predictors of returning to sport in the regression model with a strong goodness of fit.

3.2. Qualitative Data Analysis. All responses to the open-ended questions were included in the qualitative content analysis. This generated rich data on their experiences and perceptions during their recovery from COVID-19. We identified 42 codes and 10 categories in the three key themes (physical, psychological and social) from 295 respondents (Table 2). The response rate to the open-ended questions was as follows: Question 1 was unanswered by $n = 1$; Question 2 was unanswered by $n = 228$; Question 3 was unanswered by $n = 2$; Question 4 was unanswered by $n = 158$.

3.3. Physical. There was a perpetual reporting of persistent cardiopulmonary symptoms well after recovering from the viral illness. The study's participants expressed concern about serious cardiac consequences following their COVID-19 convalescence. On exertion, participants emphasised a markedly elevated HR compared to pre-COVID-19 HR together with irregular HR, chest pain and longer time to return to a normal resting HR. Quantitative results showed that exercise tolerance was limited by elevated HR (72%) and dyspnoea (72%), and the severity of the initial viral illness (2%) indicating the significant fear of exercise-induced respiratory distress and having a heart attack. Only 1% of the athletes had pre-existing cardiac comorbidities, and 2.7% suffered severe illness, yet 72.2% closely monitored their HR during training while gradually increasing training time. This has negatively affected their ability to maintain a consistent pace and their confidence to train at their optimum level. Some participants required further investigations including electrocardiograms (ECGs) and blood troponin levels or medication to manage sequelae such as thrombosis, asthma and tachycardia.

> *'It's been over a year and I am still battling with breathing' [205].*

Fatigue emerged as a formidable challenge in reaching their previous fitness levels for several weeks to months after recovering from COVID-19. At the time of study, 33% of athletes had not yet reached their preillness participation level with reduced exercise tolerance the most frequently cited reason. Many participants reported low energy availability and rapid fatigue during and after physical activity. The high MDFI scores for general and mental fatigue are consistent with the burden of fatigue qualitatively described as needing to reduce exercise intensity or duration. Some individuals portrayed feeling weak, taking longer to recover from exercise and struggling with stamina and endurance. Common adaptations cited by the participants included longer complete rest compared to non-COVID-19

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Table 1: Athletic performance-related factors ($n = 295$).

Parameter	Variable	*n* (%)	Codes related to the quantitative parameter
Received RTS guidelines	Yes	120 (40.7%)	Followed RTS guidelines from doctor
	No	175 (59.3%)	
Returned to preillness level of sport	Yes	199 (67.5%)	Exercise intolerance
	No	96 (32.5%)	
Self-reported factors limiting exercise tolerance[a]	Unable to sustain intensity	221 (74.9%)	Exercise intolerance Weakness Low energy availability/fatigue Recurrent injury Tachycardia Chest pain Dyspnoea Anxiety about having a heart attack Sympathetic nervous system dysregulation Feeling anxious
	Difficulty hill climbing	218 (73.9%)	
	Elevated heart rate	213 (72.2%)	
	Fatigue while training	213 (72.2%)	
	Poor endurance	198 (67.1%)	
	Musculoskeletal pain	186 (63.1%)	
	Long-COVID concerns	183 (62%)	
	Dyspnoea	172 (58.3%)	
	Anxiety/depression	145 (49.2%)	
	Autonomic dysfunction	130 (44.1%)	
	Chest pain	64 (21.7%)	
Monitor during RTS[a]	Resting, average and maximal heart rate	213 (72.2%)	Tachycardia Recurrent injury Low energy availability/fatigue Feeling anxious Work-related stress Feeling vulnerable Sleep disturbances
	Pace/speed	184 (62.4%)	
	Musculoskeletal pain	128 (43.4%)	
	Fatigue	118 (40%)	
	Sleep quality	102 (34.6%)	
	Rate of perceived exertion	99 (33.6%)	
	Stress	52 (17.6%)	
Management of concerns and challenges[a]	Reduced exercise intensity	144 (48.8%)	RTS adaptations by pacing and increasing recovery RTS guidelines Positive influence Health awareness
	Reduced exercise duration	126 (42.7%)	
	Followed RTS guidelines	117 (39.7%)	
	Resting	117 (39.7%)	
	Pushing through the challenges	113 (38.3%)	
	Cleared for exercise by a medical professional	49 (16.6%)	
	ECG	30 (10.2%)	
	Required medication	19 (6.4%)	
	Spirometry	14 (4.7%)	
	Chest X-ray/CT scan	2 (0.7%)	
	Physiotherapy	2 (0.7%)	
Parameter	**Variable**	**Median (95% CI)**	**Corresponding Code**
Multidimensional Fatigue Inventory (MDFI) score	General fatigue	11.0 (10.7–11.6)	RTS adaptations by pacing and increasing recovery demotivation Frustration depression disappointment brain fog
	Physical fatigue	9.0 (9.1–10.1)	
	Reduced activity	8.0 (8.1–8.8)	
	Reduced motivation	8.0 (8.2–9)	
	Mental fatigue	10.0 (9.7–10.7)	
	MDFI total	47.0 (46.1–49.8)	

Note: Data can fall into more than one category.
[a]The participants could choose more than one response.

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Table 2: Results of the content analysis of the responses to the open-ended questions.

Themes	Categories	Codes	*n* = (%)	Quotation (participant number)
Physical	Persistent cardiopulmonary symptoms	Anxiety about having a heart attack	60 (20.3%)	"*I worry about the sustainability of my high heart rate during hard training. What long-tern damage am I doing due to COVID?*" *[226]*
		Tachycardia	52 (17.6%)	
		Shortness of breath	44 (15%)	
		Chest pain	14 (4.8%)	
		Followed RTS guidelines from doctor	7 (2.4%)	
		Severe illness	5 (1.7%)	
		Interventions	2 (0.7%)	
		Thrombosis	2 (0.7%)	
	Physical fatigue	Exercise intolerance	95 (32.2%)	"*It's been a long road, difficult to get back to a normal level of training. Long recovery time*" *[187]*
		Low energy availability/fatigue	45 (15.3%)	
		Protracted RTS	44 (14.9%)	
		RTS adaptations by pacing and increasing recovery	42 (14.2%)	
		Weakness	23 (7.8%)	
	Neuromusculoskeletal concerns	Sympathetic nervous system dysregulation	19 (6.4%)	*"I also get dizzy spells one year after having COVID" [206]*
		Recurrent injury	17 (5.8%)	
		Body weight fluctuations	15 (5.1%)	
		Persistent symptoms, e.g., headache	11 (3.7%)	

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Table 2: Continued.

Themes	Categories	Codes	n = (%)	Quotation (participant number)
Psychological	Emotional distress	Disappointment	48 (16.3%)	*"I used to run and enjoy it. Now I have to force myself to do it knowing that I will only be disappointed with my effort" [31]*
		Demotivation	42 (14.2%)	
		Depression	28 (9.5%)	
		Frustration	16 (5.4%)	
		Bereavement	4 (1.4%)	
	Anxiety and fear	Feeling anxious	24 (8.1%)	*"It's frustrating because I feel it's all I talk about in relation to exercise. Running now adds to my anxiety rather than helps me with it" [164]*
		Uncertainty	19 (6.4%)	
		Rapid loss of fitness	19 (6.4%)	
		Worried about future infections	8 (6.1%)	
		Work-related stress	13 (4.4%)	
		Feeling vulnerable	6 (2%)	
		Sleep disturbances	2 (0.7%)	
	Positivity	No negative impact	60 (20.3%)	*"The pandemic has made me aware of how blessed I am to be able to do the things I do on a daily basis" [122]*
		Positive influence	22 (7.5)	
		Health awareness	16 (5.4%)	
	Cognitive concerns	Concentration	7 (2.4%)	*"I found that I had to really pull back on my physical training while writing up my thesis otherwise I could not get anything done. Terrible concentration and attention span" [285]*
		Memory	5 (1.7%)	
Social	Societal restrictions	Lack of competition	27 (9.2%)	*"Having an entire race season cancelled was very difficult as racing is one of my main motivations" [40]*
		Disrupted routine	12 (4.1%)	
		Training facilities closed	7 (2.4%)	
		Financial gains of competition	2 (0.7%)	
	Social disengagement	Missed their friends and social connections	40 (13.6%)	*"I really missed the social connections. Social interactions contribute to my motivation to get out there" [236]*
		Challenging training alone as group training is prohibited	25 (8.5%)	
	Prejudice	Stigmatise	11 (3.7%)	*"People in my running group seem nervous around me. Like I can still give them COVID-19" [65]*
		Guilt	3 (1%)	

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Table 3: Summary of the study population characteristics ($n = 295$).

Characteristic	Variable	*n* (%)
Sex	Male	158 (54.7%)
	Female	131 (45.3%)
Age groups	18–29	22 (7.5%)
	30–39	68 (23.1%)
	40–49	109 (36.9%)
	50–59	77 (26.1%)
	60–71	19 (6.4%)
Type of sport[a]	Running	116 (39.3%)
	Cycling	52 (17.6%)
	Multisport	127 (43.1%)
Level of participation	Recreational	184 (62.4%)
	Competitive	96 (32.5%)
	Elite	15 (5.1%)
Comorbidities	Yes	
	• Asthma	17 (5.8%)
	• Hypertension	12 (4.1%)
	• Anxiety/depression	4 (1.4%)
	• Cardiac disease	3 (1%)
	• Diabetes	3 (1%)
	• Hyperthyroidism	2 (0.7%)
	• Hyperlipidaemia	1 (0.3%)
	• Other	12 (4.1%)
	None	241 (81.7%)
Time from onset of COVID-19 disease[b]	≤ 3 weeks	36 (12.2%)
	4–8 weeks	51 (17.3%)
	3–6 months	81 (27.5%)
	> 7 months	127 (43%)
Severity of COVID-19 illness[c]	Mild	196 (66.4%)
	Moderate (dyspnoea SpO2 ≥ 94%)	91 (30.9%)
	Severe (dyspnoea SpO2 < 94%)	8 (2.7%)
Treatment	WHO severity[d] = 0–2: no treatment or did not consult a healthcare professional	148 (50.2%)
	WHO severity = 3: consulted a healthcare professional or admitted to hospital	147 (49.8%)

[a]'Running' = running only, 'cycling' = cycling only and 'multisport' = running and/or cycling and other sports.
[b]We assume variant based on the elapsed time since onset of illness: omicron < 8 weeks, beta 3–6 months and delta > 7 months.
[c]NIH symptom classification: mild: fatigue; malaise; headache; myalgia; ageusia/anosmia; cough; fever; diarrhoea; moderate: dyspnoea with SpO2 ≥ 94; severe: dyspnoea with SpO2 < 94.
[d]World Health Organization COVID-19 severity scale.

illnesses, listening to their bodies, adjusting their training based on physical symptoms and beginning with alternative aerobic exercise such as cycling, which is consistent with the quantitative data. The results of the multivariate analysis support these findings, with the physical fatigue scores significantly predicting the likelihood of RTS.

'I have had to be really patient, and accept that progress will be slow' [33].

Ongoing postural orthostatic tachycardia syndrome (POTS) and paraesthesia are symptoms of neurodynamic dysregulation and were barriers to regaining preillness fitness. While more than half the participants monitored musculoskeletal pain in the quantitative results, only 6% cited recurrent injuries in the qualitative component. Weight gain was cited as a challenge in RTS; however, nutrition remained constant according to results in Figure 2. Altered taste and smell were deemed a nuisance and may have affected diet and nutritional intake.

'Fluctuating heart rate, pins and needles in my hands and body pains, especially in both Achilles tendons' [161]

3.4. Psychological. In our study, the number of athletes reporting worse mood and emotional states was eight times as many as those with improved states after COVID-19. Double the number complained that they felt demotivated. Disappointment resulted as many witnessed the decline in their fitness levels. Our athletes felt a sense of purposelessness, consistent with the lost sense of normalcy and accomplishment. Many were forced to forfeit competition due to prolonged RTS, and the fear of never being able to return to their preillness level ensued. The ongoing fatigue was frustrating and athletes were not enjoying running anymore. Some cited

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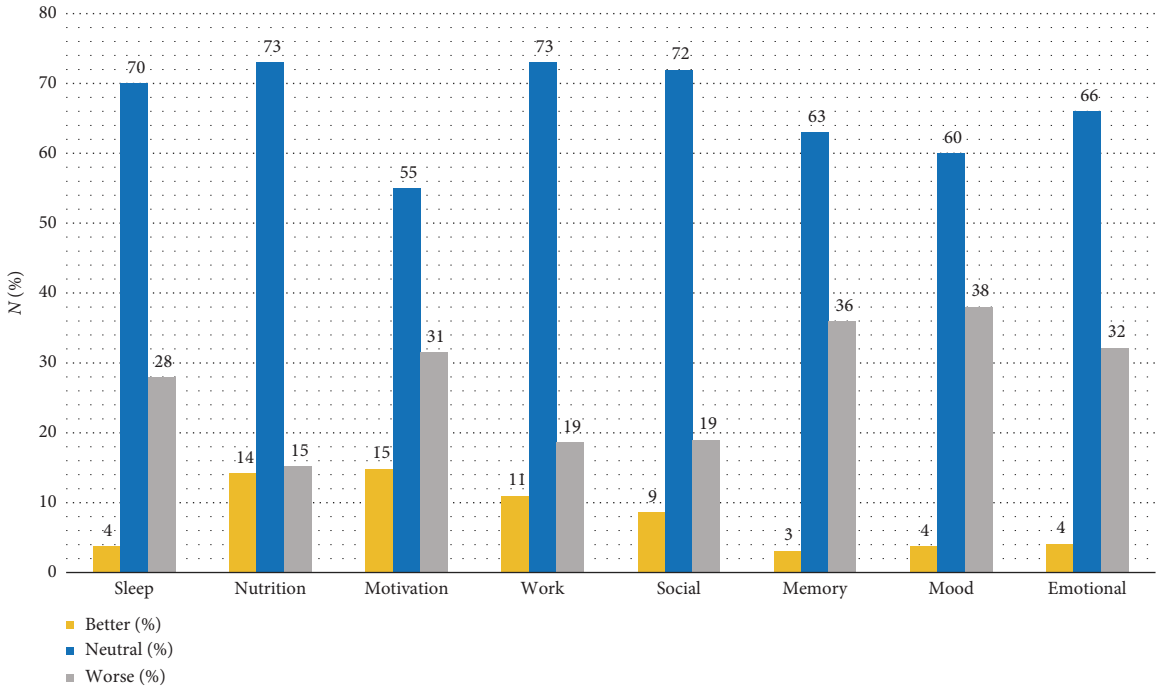

Figure 2: The impact of COVID-19 illness on endurance athletes' quality of life ($n = 295$).

Table 4: Regression analyses.

The relationship of variables with the total Multidimensional Fatigue Inventory score (R-square = 0.088, lack of fit test $p = 0.742$)			
Correlations	***B***	**95% CI**	***p* value**
Sex	7.439	3.763–11.116	< 0.001*
Age	0.092	−0.089–0.273	0.317
Level	1.204	−1.852–4.260	0.439
Severity of illness	6.296	2.476–10.115	0.001*
Stage of disease	−0.343	−1.577–0.891	0.585
Multivariate logistic regression analysis to determine the likelihood of variables explaining RTS (Hosmer and Lemeshow goodness of fit test $p = 0.713$)			
	OR	**95% CI**	***p* value**
Age	1.015	0.985–1.047	0.329
Sex	1.501	0.795–2.833	0.211
Severe illness	7.195	1.184–43.724	0.032*
Physical fatigue	0.688	0.606–0.782	< 0.001*
Reduced activity	0.891	0.765–1.039	0.141
Mental fatigue	1.091	0.990–1.203	0.079
Reduced motivation	1.029	0.893–1.186	0.690

*significance level is $p < 0.05$.

depression and poor mental health states. These statements echo the quantitative results for motivation, mood and emotional state (Figure 2). The reduced motivation score on the MDFI supports these results. Some participants experienced devastating bereavement, grieving the death of fellow athletes, and for one, their spouse.

> *'My world has fallen apart. We use to travel the world running marathons. Now I have lost interest' [190].*

Feelings of apprehension and anxiety about their body's response and future performance capacity emanated from the lack of information about this novel virus. Anxiety or depression was pre-existing in 1.4% of the study population, yet 49.2% stated that this had become a limitation to exercise tolerance and was elucidated in the qualitative responses. According to the narrative, participants felt vulnerable and stressed about their COVID-19 positive diagnosis, fearing the unpredictable seriousness of the consequences they might suffer. The threat of critical illness propagated anxiety and prompted behavioural changes such as excessive mask-wearing, avoidance of gatherings and sanitising frequently. Considering that 70% of the participants were enrolled in the study more than three months after contracting COVID-19, the concerns of the athletes regarding persistent symptoms and protracted RTS are substantiated. The feeling that illness

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dominated every aspect of their lives provoked ongoing stress in their home and work lives. Evidently, exercise plays a crucial role in their resilience to occupational stress.

'Being unable to train and even reducing my workload post-COVID had a negative effect on my mental health and my mood in general' [125].

Despite the severe hardships that athletes faced post-COVID-19, many athletes were not negatively impacted and few even gave positive acclamations. They were determined to resume their normal occupation, exercise routines and athletic pursuits. Positive expressions from participants included enjoying the outdoors, an increased appreciation for life, resilience in the face of adversary and reprioritised health as highly important. These findings align with the quantitative results in Figure 2, with the small percentage of participants reporting improved QOL after COVID-19. Those who experienced mild symptoms and recovered quickly expressed gratitude. Participants highlighted the role of physical activity in improving their general well-being and instilling a sense of normalcy during the pandemic.

'Shows that we can adapt and cope with anything that comes our way' [276].

Mental fatigue, short-term memory deterioration and poor concentration were noted by the participants. These cognitive concerns became more pronounced when trying to balance athletic training with work or academic commitments and were exacerbated by increased anxiety. Although many did not make note of this in the open-ended questions, the quantitative component indicated that 36% experienced worsening memory after COVID-19 (Figure 2).

'My memory has worsened. And does not seem to be getting better either' [292].

3.5. Social. Participants faced lockdowns aimed at curbing the spread of the virus including the cancellation of races, the closure of public training facilities and the ban on group training. They expressed difficulty in adapting to new exercise routines. Additionally, exercising alone outdoors could pose safety risks. Some participants claimed the external factors of the lockdown measures had a greater impact on their lives than the illness caused by the virus. Furthermore, the restrictions had a negative impact on finances and income generated from competition. With no support from relief funds, stress in their homes and families was intensified.

'The lockdowns had a big impact on the social part of my running' [341].

Many athletes cited that reduced social contact with others had a major impact on their motivation to run. Meeting friends or club mates encouraged commitment and adherence to their training. Some athletes missed the competitive element where their abilities could be tested against each other within their team or running group. Once group training was permitted, many athletes suffered from exercise intolerance and were unable to maintain the pace required to run with their team or club. Similarly, they could not participate in races as the intensity was too strenuous. Thus, the resumption of competition did not imply an immediate return to normality.

'I am not seeing friends I used to train with which was a huge part of my social life. Now I am having to decline because I cannot keep up with them' [135].

Once restrictions were lifted, would gathering to regain social connection be deemed irresponsible behaviour, potentially spreading the virus, or risk contracting COVID-19 again? Society's views on appropriate behaviour during the pandemic were evident with 18.3% of athletes participating in this study feeling stigmatised. There was mention of a social stigma associated with contracting the virus, as well as the guilt of infecting others. Additionally, the COVID-19 vaccine elicited feelings of discrimination if participants chose not to be vaccinated or were precluded from vaccination due to pre-existing comorbidities. Fears of the unknown long-term consequences of the vaccination were conflicted by the benefits of vaccination in preventing critical illness and allowing attendance at sporting events.

'Difficult to train in groups because of the many strong disagreements people have around COVID-19/vaccines/lockdown. Less camaraderie' [87].

4. Discussion

The testament of COVID-19 convalescent recreational endurance athletes has been given. Immense emphasis was placed on cardiopulmonary health after even mild or moderate illness. Most athletes were in the masters-age group and experienced increased HR and chest pain during exercise, leading to major concerns about their hearts. Prior to the COVID-19 pandemic, Kaiser-Nielsen et al. [33] suggested that due to the increasing number of recreational athletes in the masters-age group participating in high-level events, cardiac conditions may be more prevalent than in younger, elite athlete populations. Thus, the presence of serious consequences in this population should not be overlooked [7]. Our results are consistent with Juhász et al. [6], who showed that although the rate of myocardial involvement was low, nearly one-third of athletes were hindered in their RTS by persistent symptoms. The athletes adapted their RTS by pacing themselves and monitoring their fatigue. Subjective fatigue affects performance capacity, pain, emotions (reduced motivation) and social well-being [15]. Clearly, recovering from COVID-19 and returning to preillness fitness levels can be a slow and challenging process. Due to their protracted RTS, the activity they previously enjoyed was now tiresome and unappealing.

In our study, participants expressed a range of emotional and psychological difficulties in response to their inability to

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train and compete, which are a source of motivation for their athletic pursuits. Early in the pandemic, the paucity of information about COVID-19 made it difficult to manage individual expectations. The prolonged recovery propagates self-doubt in one's abilities, and loss of self-worth and athletic identity.2, 10 Prior to the pandemic, a review of elite athletes found alarming rates of depression, stress and anxiety despite the well-documented benefits of physical activity [13]. Exercise has positive effects on mental health by stimulating the production of endorphins in the brain, helping this study's participants cope with the stress and anxiety caused by the pandemic [20]. Although the amount of exercise required to improve mood is uncertain, increased physical activity is associated with reduced depression, anxiety and fear, regardless of age [30]. However, many had not returned to their preillness level of participation and may not have been protected from depression by their preillness resilience [35]. The participants in this study valued the enjoyment sport brings and the opportunity to achieve ambitious goals. Concerns about long-term consequences can be interpreted as an athlete's desire to be proactive in their recovery, trusting their healthcare providers. One published account of athletes' resilience to hardships focused on secondary gains such as more time for relationships and education, during imposed lockdowns [14].

Many athletes felt the absence of the social connections made through sport. The friendships made during training together were a great source of social support, which the participants longed for during the periods of lockdown. Athletes enjoyed many other benefits of training in a group such as the commitment, structure, motivation, encouragement, advice shared and general conversation. Athletes who receive social support from coaches and fellow athletes tend to have better coping mechanisms [14]. Group training in South Africa is not only attractive for the social aspect but also a profound safety measure. In the quantitative section of the survey, social factors were limited to participants' rating of their work and social life, along with the percentage reporting feeling stigmatised. The qualitative data further explored this theme. At the advent of the pandemic, avoidance of PCR tests or admitting their infection status was common due to guilty feelings and fear of social stigma [32]. There is a further stigma associated with mental health treatment due to a culture of toughness inherent in sport, and thus athletes may not acknowledge their emotional distress [36]. These sentiments imply social pressure and judgements that affect athletes. Hence, some athletes pushed themselves to train through the challenges they were experiencing. Vaccine prejudice became prominent when mass participation events resumed, and proof of vaccination was compulsory. These findings provide valuable insight into the experiences related to COVID-19 illness and the diversity of challenges that endurance athletes face in RTS.

4.1. Strengths and Limitations of the Study. Limitations of this study include recall bias as many of the participants' responses rely on retrospective recall and based on the participants' perceptions of threats and concerns. No response rate could be determined, reducing the power of the study. The period from illness to the time of the study varied between participants. Athletes taking part in this study would have been in various stages of the disease and infected by the range of viral strains from the more severe beta and delta to milder omicron variants. Therein lies a strength of the study; narratives from a range of temporal points and variants are included regarding this novel virus. The sample size is large. It has been found that subjective measures were superior to objective measures in detecting changes in the well-being of athletes as the training load increased [37]. Employing a mixed methods study design increases the external validity of the findings. The categories and codes were analysed by inductive coding, allowing multiple viewpoints about the impact of this novel virus. However, the validity of our own instrument is a limitation. Further investigations such as interviews and focus groups would have provided additional qualitative data to increase meaning and thereby our understanding of the real-life impact of COVID-19 on this population. The themes were deduced by the aim of the study; however, the social factors were underrecognised in the quantitative questions. This is a potential weakness of this study and further studies including quantitative analysis of social factors in this athlete population are recommended. Because the impact on RTS was interpreted from an insider perspective, personal experiences or assumptions potentially led to bias by overemphasizing certain themes.

5. Conclusion

This mixed methods study aimed to assess the severity and management of COVID-19 symptoms and QOL as endurance athletes returned to their preillness level of sports participation. The quantitative results found that one-third of the athletes had not returned to their preillness level of sport and complained of high HR, dyspnoea, fatigue and poor exercise tolerance. Physical fatigue scores were high and likely to explain the poor RTS rate. The qualitative results revealed testimonies of cardiopulmonary consequences, severe illness, persistent exertional symptoms, emotional distress, societal pressures and individual resilience influencing their QOL. The integration of the data found that QOL of endurance athletes deteriorated post-COVID-19 due to protracted resumption of preillness level of sport. It can be concluded that recognition of the biopsychosocial well-being of convalescent athletes is essential. A multidisciplinary approach may be required to ensure resumption of physical activity and the mental gains thereof. Lest we forget the devastating effects of the COVID-19 pandemic, future research should employ the biopsychosocial perspective to enhance athlete recovery after future illnesses.

5.1. Perspective. Lessons learnt from this study can be applied to future situations that result in a long-term sport hiatus, whether due to illness or injury, pandemics or political situations. A review by Williams and Hull [38] on respiratory complications post-COVID-19 suggested a need

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for research involving more diverse age and racial groups, which is somewhat fulfilled by this study of South African endurance athletes. This study suggests that cardiopulmonary consequences of COVID-19 should not be overlooked in the masters-age group. Both short and long-term interdisciplinary interventions are required to manage biopsychosocial well-being post-COVID-19 as the importance of resuming sport exceeds the recreational value. Pandemic-specific coping strategies and training programs should be established [39] that consider the severity of the initial illness, sex, fatigue and endurance-type sport as suggested by our results. Symptoms hindering RTS still abound after the milder omicron variant infection [7]. Athletes who received guidelines and trusted doctors were more positive, highlighting the importance of communication between athletes, coaches and primary healthcare providers. Through this understanding of perceived biopsychosocial challenges, increased confidence has been achieved leading to better outcomes in athlete rehabilitation during future health challenges.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

Unconditional ethical clearance was provided by the University's (*information removed to allow for anonymous peer review*) Human Research Ethics Committee (Medical) (Certificate no. M21065). The study is designed according to ethical considerations in accordance with the Declaration of Helsinki, the South African Guidelines for Good Clinical Practice and the Medical Research Council.

Consent

An information sheet explaining the study purpose and data sharing according to the FAIR principles was linked to the survey and ensured confidentiality and anonymity and permission to withdraw from the study at any point.

Disclosure

This is an observational study design employing an anonymous online survey and therefore does not satisfy the definition of a clinical trial according to the ICMJE. Because the participants were not enrolled by the researcher, no intervention was performed and the exposure was not dictated by the researcher, we did not register the research as the ICMJE guidelines recommend, but do not require it.

Conflicts of Interest

The authors declare no conflicts of interest.

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References

[1] L. R. Lopes, V. A. R. Miranda, R. A. Goes, et al., "Repercussions of the COVID-19 Pandemic on Athletes: A Cross-Sectional Study," *Biology of Sport* 38, no. 4 (2021): 703–711, https://doi.org/10.5114/biolsport.2021.106147.

[2] S. Gupta and P. J. McCarthy, "Sporting Resilience During COVID-19: What is the Nature of This Adversity and How are Competitive Elite Athletes Adapting?" *Frontiers in Psychology* 12 (2021): https://doi.org/10.3389/fpsyg.2021.611261.

[3] H. T. Jorstad and J. G. Van Den Aardweg, "Balancing Act: When is an Elite Athlete Who has had COVID-19 Safe to Return to Play? When Does Prudent Investigation Go Offside Into Overmedicalising?" *British Journal of Sports Medicine* 54, no. 19 (2020): 1134–1135, https://doi.org/10.1136/bjsports-2020-103259.

[4] A. F. DeJong, P. N. Fish, and J. Hertel, "Running Behaviors, Motivations, and Injury Risk During the COVID-19 Pandemic: A Survey of 1147 Runners," *PLoS One* 16, no. 2 (2021): e0246300, https://doi.org/10.1371/journal.pone.0246300.

[5] V. L. Mihalick, J. M. Canada, R. Arena, A. Abbate, and D. L. Kirkman, "Cardiopulmonary Exercise Testing During the COVID-19 Pandemic," *Progress in Cardiovascular Diseases* 67 (2021): 35–39, https://doi.org/10.1016/j.pcad.2021.04.005.

[6] V. Juhász, L. Szabó, A. Pavlik, et al., "Short and Mid-Term Characteristics of COVID-19 Disease Course in Athletes: A High-Volume, Single-Center Study," *Scandinavian Journal of Medicine & Science in Sports* 33, no. 3 (2023): 341–352, https://doi.org/10.1111/sms.14265.

[7] C. A. Haley, H. van Aswegen, E. Libhaber, and B. Olivier, "Protracted Exercise Tolerance Post-Coronavirus Disease 2019 in Endurance Athletes: A Survey," *South African Journal of Physiotherapy* 80, no. 1 (2024): 2063, https://doi.org/10.4102/sajp.v80i1.2063.

[8] T. J. Gluckman, N. M. Bhave, L. A. Allen, et al., "2022 ACC Expert Consensus Decision Pathway on Cardiovascular Sequelae of COVID-19 in Adults: Myocarditis and Other Myocardial Involvement, Post-Acute Sequelae of SARS-CoV-2 Infection, and Return to Play," *Journal of the American College of Cardiology* 79, no. 17 (2022): 1717–1756, https://doi.org/10.1016/j.jacc.2022.02.003.

[9] S. Vollrath, D. A. Bizjak, J. Zorn, et al., "Recovery of Performance and Persistent Symptoms in Athletes After COVID-19," *PLoS One* 17, no. 12 (2022): e0277984, https://doi.org/10.1371/journal.pone.0277984.

[10] National Institute for Health and Care Excellence, "Covid19 Rapid Guideline: Managing the Long-Tern Effects of COVID-19," (2021), https://www.nice.org.uk/guidance/ng188.

[11] C. Callan, E. Ladds, L. Husain, K. Pattinson, and T. Greenhalgh, "I Can't Cope With Multiple Inputs': A Qualitative Study of the Lived Experience of Brain Fog' After COVID-19," *BMJ Open* 12, no. 2 (2022): e056366, https://doi.org/10.1136/bmjopen-2021-056366.

[12] M. J. Joyner and E. F. Coyle, "Endurance Exercise Performance: The Physiology of Champions," *The Journal of Physiology* 586, no. 1 (2008): 35–44, https://doi.org/10.1113/jphysiol.2007.143834.

[13] V. F. Corona, M. R. Gualano, M. F. Rossi, et al., "Psychological and Mental Sequelae in Elite Athletes With Previous SARS-CoV-2 Infection: A Systematic Review," *International Journal of Environmental Research and Public Health* 19, no. 24 (2022): 16377, https://doi.org/10.3390/ijerph192416377.

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[14] A. Ussorowska-Krokosz, J. Blecharz, M. Siekanska, and M. Grygorowicz, "Coping With COVID-19: Can a Sense of Coherence and Social Support Play a Protective Role in the Perception of COVID-19 by Polish Women Football Players? A Cross-Sectional Study," *International Journal of Environmental Research and Public Health* 20, no. 13 (2023): 6308, https://doi.org/10.3390/ijerph20136308.

[15] D. Líška, E. Liptaková, A. Babičová, L. Batalik, P. S. Baňárová, and S. Dobrodenková, "What is the Quality of Life in Patients With Long COVID Compared to a Healthy Control Group?" *Frontiers in Public Health* 10, no. 1 (2022): https://doi.org/10.3389/fpubh.2022.975992.

[16] WHO, "Quality of Life," (2012), https://who.int./tool/whoqol.

[17] L. Pillay, D. C. C. Janse van Rensburg, A. Jansen van Rensburg, et al., "Nowhere to Hide: The Significant Impact of Coronavirus Disease 2019 (COVID-19) Measures on Elite and Semi-Elite South African Athletes," *Journal of Science and Medicine in Sport* 23, no. 7 (2020): 670–679, https://doi.org/10.1016/j.jsams.2020.05.016.

[18] E. Conde, L. M. Martínez-Aranda, G. Sanz, et al., "Effects of the COVID-19 Health Crisis on Sports Practice, Life Quality, and Emotional Status in Spanish High-Performance Athletes," *Frontiers in Psychology* 12 (2021): https://doi.org/10.3389/fpsyg.2021.736499.

[19] V. Juhász, E. Csulak, L. Szabó, et al., "Retrospective Study of COVID-19 Experiences in Elite Multinational Aquatic Athletes," *Scientific Reports* 13, no. 1 (2023): https://doi.org/10.1038/s41598-023-40821-2.

[20] A. Jurecka, P. Skucińska, and A. Gądek, "Impact of the SARS-CoV-2 Coronavirus Pandemic on Physical Activity, Mental Health and Quality of Life in Professional Athletes-A Systematic Review," *International Journal of Environmental Research and Public Health* 18, no. 17 (2021): 9423, https://doi.org/10.3390/ijerph18179423.

[21] A. Pelliccia, S. Sharma, S. Gati, et al., "2020 ESC Guidelines on Sports Cardiology and Exercise in Patients With Cardiovascular Disease," *European Heart Journal* 42, no. 1 (2021): 17–96, https://doi.org/10.1093/eurheartj/ehaa605.

[22] L. H. Mabuza, I. Govender, G. A. Ogunbanjo, and B. Mash, "African Primary Care Research: Qualitative Data Analysis and Writing Results," *African Journal of Primary Health Care & Family Medicine* 6, no. 1 (2014): E1–E5, https://doi.org/10.4102/phcfm.v6i1.640.

[23] J. W. Creswell, A. C. Klassen, V. L. Plano Clark, and K. C. Smith, *Best Practices for Mixed Methods Research in the Health Sciences* (Bethesda, MD: National Institutes of Health, 2011).

[24] A. O'Cathain, E. Murphy, and J. Nicholl, "The Quality of Mixed Methods Studies in Health Services Research," *Journal of Health Services Research & Policy* 13, no. 2 (April 2008): 92–98, https://doi.org/10.1258/jhsrp.2007.007074.

[25] A. Tong, P. Sainsbury, and J. Craig, "Consolidated Criteria for Reporting Qualitative Research (COREQ): A 32-Item Checklist for Interviews and Focus Groups," *International Journal for Quality in Health Care* 19, no. 6 (December 2007): 349–357, https://doi.org/10.1093/intqhc/mzm042.

[26] N. Van Aerde, G. Van den Berghe, A. Wilmer, et al., "Intensive Care Unit Acquired Muscle Weakness in COVID-19 Patients," *Intensive Care Medicine* 46, no. 11 (2020): 2083–2085, https://doi.org/10.1007/s00134-020-06244-7.

[27] FAIR, "FAIR Principles," (2016), https://www.go-fair.org/fair-principles/.

[28] NCBI, "COVID-19 Treatment Guidelines 2023. NIH: Clinical Spectrum of SARS-CoV-2 Infection," https://www.ncbi.nlm.nih.gov/books/NBK570371/pdf/Bookshelf_NBK570371.pdf.

[29] J. C. Marshall, S. Murthy, J. Diaz, et al., "A Minimal Common Outcome Measure Set for COVID-19 Clinical Research," *The Lancet Infectious Diseases* 20, no. 8 (2020): e192–e197, https://doi.org/10.1016/S1473-3099(20)30483-7.

[30] E. M. A. Smets, B. Garssen, B. Bonke, and J. C. J. M. De Haes, "The Multidimensional Fatigue Inventory (MFI) Psychometric Qualities of an Instrument to Assess Fatigue," *Journal of Psychosomatic Research* 39, no. 3 (1995): 315–325, https://doi.org/10.1016/0022-3999(94)00125-O.

[31] A. Hinz, C. Benzing, E. Brahler, et al., "Psychometric Properties of the Multidimensional Fatigue Inventory (MFI-20), Derived From Seven Samples," *Journal of Pain and Symptom Management* 59, no. 3 (2020): 717–723, https://doi.org/10.1016/j.jpainsymman.2019.12.005.

[32] H.-F. Hsieh and S. E. Shannon, "Three Approaches to Qualitative Content Analysis," *Qualitative Health Research* 15, no. 9 (2005): 1277–1288, https://doi.org/10.1177/1049732305276687.

[33] L. V. Kaiser-Nielsen, S. G. Tischer, E. B. Prescott, and H. K. Rasmusen, "Symptoms, Diagnoses, and Sporting Consequences Among Athletes Referred to a Danish Sports Cardiology Clinic," *Scandinavian Journal of Medicine & Science in Sports* 27, no. 1 (2017): 115–123, https://doi.org/10.1111/sms.12624.

[34] M. Roche, K. Sainani, D. Noordsy, and M. Fredericson, "The Impacts of COVID-19 on Mental Health and Training in US Professional Endurance Athletes," *Clinical Journal of Sport Medicine* 32, no. 3 (2022): 290–296, https://doi.org/10.1097/JSM.0000000000000983.

[35] A. H. Mehrsafar, P. Gazerani, A. Moghadam Zadeh, and J. C. Jaenes Sánchez, "Addressing Potential Impact of COVID-19 Pandemic on Physical and Mental Health of Elite Athletes," *Brain, Behavior, and Immunity* 87 (2020): 147–148, https://doi.org/10.1016/j.bbi.2020.05.011.

[36] A. Kumar and K. R. Nayar, "COVID-19: Stigma, Discrimination, and the Blame Game," *International Journal of Mental Health* 49, no. 4 (2020): 382–384, https://doi.org/10.1080/00207411.2020.1809935.

[37] A. E. Saw, L. C. Main, and P. B. Gastin, "Monitoring the Athlete Training Response: Subjective Self-Reported Measures Trump Commonly Used Objective Measures: A Systematic Review," *British Journal of Sports Medicine* 50, no. 5 (2016): 281–291, https://doi.org/10.1136/bjsports-2015-094758.

[38] Z. Williams and J. H. Hull, "Respiratory Complications Following COVID-19 in Athletic Populations: A Narrative Review," *Scandinavian Journal of Medicine & Science in Sports* 34, no. 1 (2024): e14275, https://doi.org/10.1111/sms.14275.

[39] P. K. Urbański, R. Rogoza, B. Brewer, and T. Tasiemski, "Coping With the COVID-19 Pandemic by Paralympic Athletes Preparing for Elite Sport Events: A Longitudinal Study," *Scandinavian Journal of Medicine and Science in Sports* 33, no. 4 (2023): 512–520, https://doi.org/10.1111/sms.14270.

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Chapter 5 Paper 3

This chapter includes the full text publication of Paper 3, original research and the supplementary file, and further methodological information that was not included in the publication.

5.1 Title: Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes

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5.1.2 Journal

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Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes

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Background: Endurance sports primarily attract recreational athletes over 35 years, who impose an exceptionally rigorous and sustained demand on their cardiorespiratory systems.
Objectives: This study aimed to determine the influence of COVID-19 on the cardiovascular, pulmonary, and skeletal muscle function of endurance athletes with exercise intolerance. Secondly, it aimed to compare the exercise response of endurance athletes post-COVID-19 to those unaffected using cardiopulmonary exercise test-related variables.
Methods: This is a prospective observational cohort study of endurance athletes. An exposure group with protracted exercise tolerance underwent a resting lung function test and maximal cardiopulmonary exercise test. These were repeated after eight weeks of endurance training and compared to the published reference values and a control group of athletes unaffected by COVID-19.
Results: The post-COVID-19 exposure group (n=57), mean age 44.5±8.1years showed a poorer ventilatory threshold (p=0.004), and workload (p=0.05), with higher respiratory exchange ratio (p=0.05) than the control group (n=34), mean age 41.8±7.7 years. Maximal inspiratory pressure improved at follow-up in the COVID-19 group compared to the controls (p=0.03). Increased odds of pulmonary and skeletal muscle limitation to aerobic capacity were found in the COVID-19 group. The COVID-19 group responded positively to endurance training with improved VO_2peak (p=0.005), maximal inspiratory pressure (p=0.04), oxygen-pulse (p=0.02), and maximal workload (p<0.001).
Conclusion: COVID-19 has led to pulmonary and extrapulmonary limitations to exercise capacity. Tailored intensity and duration of physical activity are vital after COVID-19 to restore skeletal muscle health. This multidisciplinary rehabilitation approach will optimise the resumption of participation in long-distance events.
Keywords: cardiopulmonary exercise test, coronavirus, exercise intolerance

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The highly infectious novel coronavirus disease of 2019 (COVID-19) caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2) caused a worldwide pandemic. The expression of this disease ranged from completely asymptomatic, through a wide variety of symptoms classed as mild, moderate, or severe illness, to death.[1] The pathophysiology of COVID-19 can lead to persistent symptoms, predominantly dyspnoea and fatigue[2], which are associated with poor exercise tolerance.[3] Scheer et al.[4] have shown that average marathon times declined worldwide during the pandemic. However, the impact of COVID-19 on athletic ability remains equivocal as some studies found a decrease in cardiorespiratory fitness (CRF),[5] while others found no difference.[6] Physical activity has numerous benefits, including enhanced immune response, which mitigates the risk of post-COVID cardiopulmonary events.[7] Additionally, exercise fosters mental resilience, muscular endurance, and emotional well-being.[8] Therefore, the resumption of sport and competition is paramount for athlete health.

Endurance sport typically involves physical activity for a prolonged duration, such as marathon running and long-distance cycling.[4,9] Endurance athletes impose an exceptionally rigorous and sustained demand on their cardiorespiratory system throughout training and competitive events.[7] Respiratory muscles fatigue over time during endurance exercise. Therefore, pulmonary limitations will have a greater impact than in power sport athletes.[10] The work of breathing, measured by maximal inspiratory pressure (MIP), relates to respiratory muscle strength and elasticity of the lung and chest wall,[10] both of which are adversely affected by COVID-19. This sport primarily attracts recreational athletes over the age of 35, who often participate at a competitive level.[11] For COVID-19 convalescent athletes, regaining adequate levels of CRF is crucial as a small decrease in performance capacity can have a marked effect on an athlete's goals.

Cardiopulmonary exercise testing (CPET) is the gold standard measurement of CRF[3] and objectively detects limitations to exercise capacity by the pulmonary, cardiovascular, or skeletal muscle systems.[5,12] It is especially beneficial for assessing athletes with a protracted return to the sport due to persistent exertional symptoms without direct viral organ damage.[13] The cardiopulmonary exercise test measures the maximum oxygen uptake during dynamic exercise (VO_2peak), directly evaluating an individual's CRF.[6] Endurance athletes are expected to exceed the published thresholds for CPET parameters applicable to healthy adults.[14] Failing which, concerns regarding possible impairments arise.[15] Limited research exists on long-term limitations to exercise capacity in endurance athletes[5] and the cardiorespiratory response as these athletes resume endurance

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training. Insight into the mechanisms impacting athletic performance after recovering from the acute phase of the disease will assist clinicians in preparing athletes for the successful resumption of competition.[10] This study aimed to determine the influence of COVID-19 on the cardiovascular, pulmonary, and skeletal muscle function of endurance athletes using CPET-related variables. Secondly, it aimed to compare the exercise adaptation of endurance athletes post-COVID-19 to a control group of athletes unaffected by COVID-19. In this post-pandemic era, the imperative of regular physical activity cannot be overstated; thus, identifying persistent limitations to exercise capacity is vital.

Methods

Study design

This is a prospective observational cohort study. The STROBE Statement is a checklist of items that should be included in cohort studies reports, which was followed accordingly.[16] The study occurred in Johannesburg, the most populous city in South Africa (1450 m above sea level). Participants were recruited between 15 December 2021 and 1 October 2022. The initial testing and simultaneous data collection commenced on 8 March 2022, and eight-week follow-up testing terminated on 28 October 2022.

Participants

Social media advertisements were approved by athletic clubs and posted on their Facebook pages (n=25) and WhatsApp groups (n=18). They included a clickable link to more information about the study according to ethical principles. Long-distance runners and cyclists who responded to the advertisements were eligible for participation. It is assumed that participants responded to the advertisement randomly, reducing potential selection bias and confounding variables such as comorbidities. The process of recruitment of participants is displayed in Figure 1.

The inclusion criteria for both study groups were adult endurance athletes (marathon minimum age is 18 years), who were eligible if they engaged in cardiovascular exercise for three or more hours per week.[11] COVID-19 convalescent athletes who had persistent symptoms affecting their exercise capacity were allocated to the exposure group (COVID-19), and COVID-negative or those who were unaffected by the infection and had successfully returned to their pre-illness fitness levels were allocated to the control group (N-COVID-19). A minimum time since infection of 18 days and the ability to run for 30 min was required. Those with comorbidities or severe disease needed to consult a sports physician before participating.

Exclusion criteria were: athletes with ICU-acquired weakness, lack of signed informed consent, not being proficient in English, residing outside of Gauteng, and published contraindications to CPET.[17]

Testing procedure

The research team developed self-administered web-based questionnaires for the exposure and control group using the Research Electronic Data Capture (REDCap) platform. These were disseminated via email or WhatsApp to potential participants and were completed before testing to establish the subjective examination. They included demographic and sport-specific data; physical activity level determined by the number of hours per week the athlete exercised; and questions regarding the severity of symptoms directed to the exposure group and classified according to the NIH clinical spectrum.[1]

Eligible participants were sent a link to an online calendar to book their CPET. At each visit, all participants were assessed to determine their medical history and management, and the presence of known contra-indications to CPET. The time interval from infection to first test and between tests was recorded. Age, sex, weight, height, BMI, and blood pressure were collected before the lung function test and CPET were performed. Data collection was standardised by using consistent measurement tools in the same setting.

Lung function

The primary researcher assessed resting lung function in standing using spirometry. The Vyaire Medical CPET BxB Sentry Suite™ V2.21 software was used to record data during the test. Measurements are described in Table 1. Maximal inspiratory pressure was assessed in standing using the POWERBreath K3 device. The best of three attempts with a less

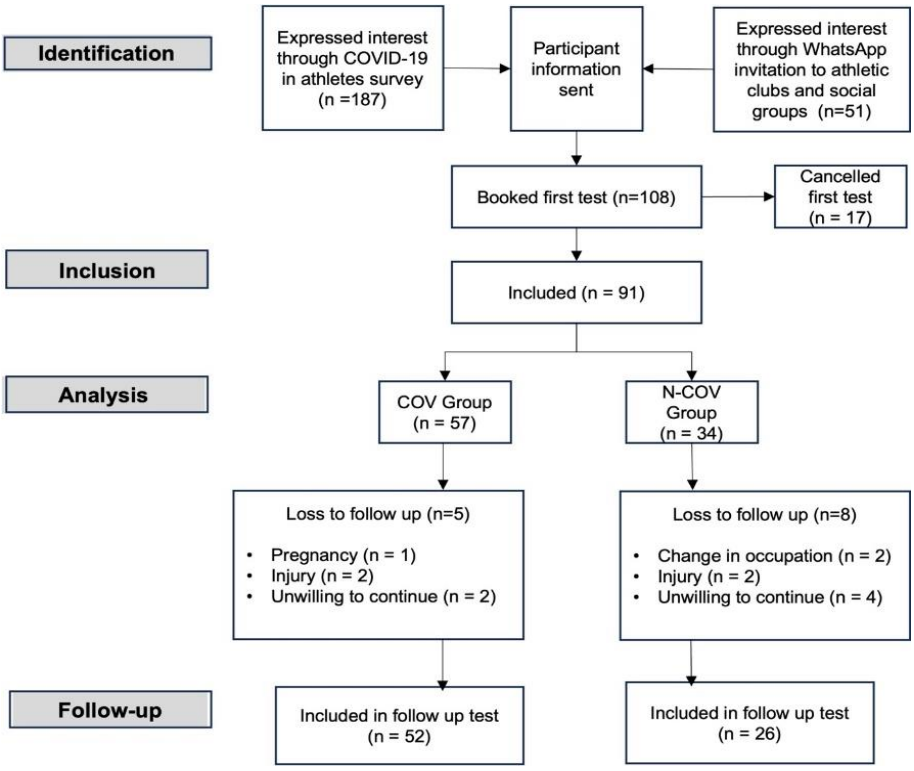

Fig. 1. Process of participant recruitment

than 5% difference was recorded according to the American Thoracic Society protocol.

Cardiopulmonary exercise testing (CPET)

CPET was conducted using a treadmill test rather than a cycle ergometer as it gives higher peak oxygen uptake results to athletes.[18] A General Electric Healthcare CASE™ exercise testing system, version 6.7, Milwaukee, USA, was programmed according to the Bruce protocol suitable for athletes. [18] Throughout the test, continuous monitoring of heart rate was done using a 12-lead ECG, and oxygen saturation (SpO_2) using a pulse oximeter. Participants were blinded to test data while performing the treadmill test. Rating of perceived exertion (RPE) on the 20-point Borg scale was collected at each stage[19] and the reason for termination was noted. The Vyaire Medical CPET BxB Sentry Suite™ V2.21 software was used to record data during the test. A gas analyser allowed the analysis of inspired and expired gases every five seconds.[17] The participants were verbally encouraged to give their best effort and keep going until volitional termination due to exhaustion or provocation of symptoms, with the participant rating above 18 on the RPE scale. Respiratory exchange ratio (RER) >1.1 is defined as a maximal test. The results were displayed in the Wasserman "nine-panel plot" format.[12] Physiological parameters that were calculated by the software are described in Table 1.

Statistical analysis

The sample size calculation was based on the difference in VO_2peak in the COVID-19 vs N-COVID-19 groups from the study by Ladlow et al.[5] with a confidence interval of 0.05 and a statistical power of 0.8 selected. We added 10% for each confounding factor: age, sex, stage of disease, and loss to follow-up. Therefore, a sample size n=50 was required. We aimed for a 2:1 ratio of symptomatic to control/recovered.

Data were collected and managed using MS Excel and imported into the Statistical Package for the Social Sciences software, IBM SPSS Statistics for Mac, Version: 28.0.2.0 (142), which was used for all analyses. Descriptive characteristics were used to summarise the data. The normality of the distribution of continuous variables was assessed with the Shapiro-Wilk test. Continuous variables are expressed as means and standard deviations for normally distributed data, medians and interquartile range for skewed data. Categorical variables are expressed as percentages and frequencies. Normative values have been categorised by sex and age groups in decades, according to the FRIEND Registry.[15] Independent t-tests and paired t-tests were used to compare normally distributed parametric variables, and the Mann-Witney U test and Wilcoxon Signed Rank for skewed, nonparametric continuous data. Chi-square or Fisher's exact tests were used to compare categorical data. Odds ratios determined the likelihood of limitations to exercise capacity after having COVID-19. A p-value of <0.05 determined statistical significance. Missing data of loss-to-follow-up participants was only excluded in comparing the CRF response to endurance training between the COVID-19 and N-COVID-19 groups. No imputation was used for the missing data.

Data availability

Data will be made available upon request and after considering the intentions of use, ethical clearance, and appropriateness of

Table 1. Description of the physiological parameters measured during lung function and CPET

Measurement	Description
Lung function	
FVC (l)	Forced vital capacity
FEV_1 (l)	Forced expiratory volume in one second
PEF ($l \cdot min^{-1}$)	Peak expiratory flow
MVV ($l \cdot min^{-1}$)	Maximum voluntary ventilation: estimated by multiplying FEV_1 by 35[18]
Cardiopulmonary exercise testing (CPET)	
VO_2peak ($ml \cdot kg \cdot min^{-1}$)	Maximum volume of oxygen in millilitres consumed per minute per kilogram of body weight
VE ($l \cdot min^{-1}$)	Minute Ventilation: The litres per minute that is inspired and expired
VE/VCO_2 slope	The volume of CO_2 expelled per litre of air ventilated. Indicative of ventilatory efficiency. An increase in slope indicates increased dead space ventilation in the lung, pulmonary vascular disease or pulmonary limiting disease.
Y-intercept on VE/VCO_2 slope ($l \cdot min^{-1}$)	A negative y-intercept is indicative of cardiac limitation
VT ($ml \cdot min^{-1}$)	Ventilatory threshold = The point at which VCO_2 deviated from the linear relationship with VO_2. Indicative that oxygen-independent energy systems are starting to contribute relatively more to energy production with a slight increase in blood lactate levels above resting levels.
HR (bmp)	Heart rate (beats per minute)
SpO_2 (%)	Peripheral capillary oxygen saturation. Drops by 5% in healthy adults and 10% in athletes during maximum exercise.
Relative workload ($W \cdot kg^{-1}$)	Power (W) divided by body weight
VE/MVV (%)	Dyspnoea index: the ratio of peak minute ventilation to maximum voluntary ventilation. Indicates respiratory limitation if it approximates 100%. Breathing reserve = 1-VE/MV
Peak O_2-pulse ($ml \cdot bpm^{-1}$)	Oxygen pulse calculated by VO_2peak/HRmax. It is a surrogate measure of left ventricular stroke volume.[17]

available data. The corresponding author may be contacted in this regard.

Ethical considerations

Unconditional ethical clearance was provided by the University of the Witwatersrand (25 October 2021). The study procedures adhered to the principles outlined in the Declaration of Helsinki, the South African Guidelines for Good Clinical Practice, and the Medical Research Council. Each participant signed informed consent before the first test. It ensured confidentiality (including protection of personal information), anonymity, permission to withdraw from the study at any point, and data sharing.

Results

The first assessment was attended by: the COVID-19 group (n=57), mean age 44.5±8.1 years, and the N-COVID-19 control group (n=34), mean age 41.8±7.7 years.

No significant differences in population demographics between COVID-19 and N-COVID-19 groups existed (Table 2).

During the pre-test assessment, the researcher found that two participants had been diagnosed with myocarditis post-COVID-19. One was prescribed beta-blockers and cleared for exercise, while the other confirmed that the condition had resolved. All participants reached a maximal heart rate of at least 85% maximum, predicted at the termination of both tests. In the first test, systolic blood pressure >250mmHg was the reason for termination in n=1 (1.8%) in the COVID-19 group and was referred for further investigation. Hypotension was found in one participant, and paraesthesia was found in two participants. Dyspnoea terminated the test in n=24 (42%), three of whom had been suffering from anxiety. Volitional

Table 2. Descriptive characteristics of participants: COVID-19 vs N-COVID-19 groups

Parameter	COVID-19 (n=57)	N-COVID-19 (n=34)	p-value	95% CI	Effect size
Male sex n (%)	36 (63%)	25 (74%)	0.25		
Age groups (years) n (%)					
21-29	2 (3.5%)	1 (2.9%)	1.00		
30-39	12 (21%)	13 (38%)	0.08		
40-49	30 (53%)	15 (44%)	0.43		
50-59	11 (19%)	4 (12%)	0.40		
60-65	2 (3.5%)	0	0.53		
Weight (kg)	73.4±13.2	74.8±12.9	0.62		
Height (cm)	174.2±9.2	175.9±10.1	0.40		
BMI (kg/m²)	24.1±2.9	24.0±2.3	0.84		
Level n (%)					
Recreational	22 (39%)	14 (41%)	0.81		
Competitive	26 (46%)	18 (53%)	0.50		
Elite	9 (16%)	2 (5.9%)	0.20		
Weeks between tests	8 (7; 10)	8 (7; 8)	0.13		
Comorbidities n (%)					
Asthma	8 (14%)	2 (5.9%)	0.31		
Hypertension	4 (7.0%)	3 (8.8%)	1.00		
Hyperthyroidism	3 (5.3%)	1 (2.9%)	1.00		
Cardiac disease	3 (5.3%)	2 (5.9%)	1.00		
Hyperlipidaemia	1 (1.8%)	2 (5.9%)	0.55		
Anxiety/depression	4 (7.0%)	1 (2.9%)	0.65		
Months from illness to test	6.6 ± 3.8	n/a			
Severity of illness n (%)					
Mild	15 (26%)	n/a			
Moderate	36 (63%)	n/a			
Severe	6 (11%)	n/a			
Lung Function					
FVC (l)	4.8±1.0	5.0±1.0	0.20	-0.7–0.2	-0.28
FEV_1 (l)	3.9±0.8	4.1±0.8	0.22	-0.5–0.1	-0.25
FEV_1/FVC (%)	81.6±5.3	81.0±5.3	0.55	-1.6–3.0	0.13
PEF ($l \cdot min^{-1}$)	8.6±2.5	9.1±2.1	0.28	-1.6–0.5	-0.24
MVV ($l \cdot min^{-1}$)	135.2±27.8	142.21±27.0	0.24	-19.8–4.9	-0.25
MIP (cmH_2O)	102.0±25.9	107.88±21.8	0.24	-16.7–4.3	-0.26
Cardiopulmonary exercise testing (CPET)					
VO_2peak ($ml \cdot kg \cdot min^{-1}$)	39.1±8.6	42.0±7.6	0.12	-6.4–0.7	-0.34
VO_2peak% ref	126.6±33.7	128.1±26.3	0.82	-15.0–11.9	-0.05
VE/VCO_2 slope	32.0±3.1	31.4±2.4	0.30	-0.6–1.9	0.23
y-intercept ($l \cdot min^{-1}$)	1.1±3.5	1.0±2.7	0.89	-1.3–1.5	0.03
VO_2 at VT ($ml \cdot min^{-1}$)	65.7±10.6	72.6±10.6	0.004	-11.4– -2.3	-0.65
RER at max	1.2±0.6	1.1±0.04	0.05	0–0.05	0.43
VE max ($l \cdot min^{-1}$)	108.1±25.5	115.4±26.6	0.20	-18.4–3.8	-0.28
VE/MVV	80.3±12.6	81.5±14.0	0.67	-6.9–4.4	-0.09
HR max (bpm)	172.8±10.3	174.1±9.7	0.57	-5.6–3.1	-0.12
Max O_2-pulse ($ml \cdot bpm^{-1}$)	16.4±3.9	18.1±4.6	0.07	-3.5–0.1	-0.40
Drop in SpO_2 %	7.5 (5;11)	6 (5;8)	0.17	-2–0	0.39
RPE	19 (18;20)	19 (18;20)	0.29	0–1	0
Max Workload ($W \cdot kg^{-1}$)	4.6 (3.9;5.2)	5.21 (5.2;6.2)	0.05	0–1	0.71

95% Confidence Interval and Effect size as applicable. We assume variants based on the elapsed time since onset of illness: omicron <8 weeks, beta 3-6 months, delta >7 months. NIH Symptom classification: Mild: fatigue; malaise; headache; myalgia; ageusia/anosmia; cough; fever; diarrhoea; Moderate: dyspnoea with SpO_2 ≥94%; Severe: dyspnoea with SpO_2 <94%. Data expressed as mean±SD, or median (interquartile range) as applicable. BMI, body mass index; SD, standard deviation; FVC (1), forced vital capacity; FEV_1 (l), forced expiratory volume in one second; PEF, peak expiratory flow; MVV, maximum voluntary ventilation; VO2peak, maximum volume of oxygen in millilitres consumed, VE, minute ventilation, HR, heart rate; MIP, maximal inspiratory pressure; RER, respiratory exchange ratio; RPE, rating of perceived exertion; VT, ventilatory threshold

exhaustion terminated all the tests in the N-COVID-19 group, with two participants complaining of dizziness at maximal exertion. No adverse events occurred during the maximal exercise tests.

Baseline CPET found a higher respiratory exchange ratio at maximal exercise (p=0.05, CI=0-0.05, d=0.43), and strong evidence of a lower ventilatory threshold (p=0.004, CI=-11.42– -2.29, d=-0.65) and lower maximal workload (p=0.05, CI=0-1.10, d=0.71) in the COVID-19 group. No differences in lung function measures were noted when comparing the two groups.

On follow-up, dyspnoea terminated the test in n=17 (33%) in the COVID-19 group. When comparing the exercise response to endurance training (Table 3) there is strong evidence of a process of recovery shown by improved MIP in the COVID-19 group versus a decline in the N-COVID-19 group (p=0.03, CI=0.94-16.22, d=0.54). The difference in maxRER in the COVID-19 group declined, whereas it increased in the N-COVID-19 group (p=0.05, CI=0.03-0.05, d=0.58).

Table 3. The difference between COVID-19 and N-COVID-19 groups: lung function and CPET from baseline test (1) to follow-up (2)

Parameter	COVID-19 (2)-(1) (n=52)	N-COVID-19 (2)-(1) (n=26)	p-value	95% CI	Effect size
Lung Function					
FVC (l)	0.06 (-0.04; 0.22)	0.01±0.18	0.60	-0.11–0.7	0.27
FEV_1 (l)	-0.01±0.24	-0.06±0.17	0.41	-0.06–0.15	0.20
FEV_1/FVC (%)	-0.89±4.69	-1.01 (-2.75; 0.91)	0.68	-1.65–1.16	0.02
PEF ($l \cdot min^{-1}$)	0.41±1.85	0.25±1.34	0.70	-0.66–0.97	0.09
MVV ($l \cdot min^{-1}$)	-0.40± 8.5	-2±6.07	0.41	5.23–4.9	0.20
MIP (cmH_2O)	5.12±17.19	-3.46±13.15	0.03	0.94–16.22	0.54
Cardiopulmonary exercise testing (CPET)					
VO_2peak ($ml \cdot kg \cdot min^{-1}$)	1.75±4.31	0.05±3.77	0.09	-0.27–3.69	0.41
VO_2peak% ref	5.8±14.7	2.8 (-6.09; 6.30)	0.33	-8.9–2.27	0.23
VE/VCO_2 slope	-0.17±2.39	0.13±1.98	0.58	-1.39–0.78	-0.13
y-intercept ($l \cdot min^{-1}$)	0.5±2.79	0.23±1.66	0.65	-0.91–1.46	-0.11
VO_2 at VT ($ml \cdot min^{-1}$)	-0.01 (-0.04; 0.03)	0.02 (-0.01; 0.06)	0.05	0.03–0.05	0.58
RER at max	2.50±13.11	-3.08±14.26	0.09	-0.88–12.29	0.41
VEmax ($l \cdot min^{-1}$)	3.35±16.19	1.65±14.16	0.65	-5.75–9.13	0.11
VE/MVV	2.76±10.64	2.57±9.28	0.94	-4.69–5.08	0.02
HRmax (bpm)	-0.06±9.29	0.04±5.30	0.96	-4.02–3.82	-0.01
MaxO_2-pulse ($ml \cdot bpm^{-1}$)	0.70±2.26	-0.04±1.79	0.14	-0.26–1.76	0.12
Drop in SpO_2%	-1.0 (-4.3; 0)	0 (-2; 2)	0.31	-1.0–3.0	-0.32
RPE	0 (-1.0; 1.0)	0 (-0.6; 1.0)	0.61	0–1	0
Max Workload ($W \cdot kg^{-1}$)	0 (0; 1.25)	0 (0; 0.2)	0.27	-0.06–0	0

Data expressed as mean±SD, or median (interquartile range) as applicable. FVC (1), forced vital capacity; FEV_1 (l), forced expiratory volume in one second; PEF, peak expiratory flow; MVV, maximum voluntary ventilation; VO2peak, maximum volume of oxygen in millilitres consumed, VE, minute ventilation, HR, heart rate; MIP, maximal inspiratory pressure; RER, respiratory exchange ratio; RPE, rating of perceived exertion; VT, ventilatory threshold

When comparing the exercise response in the COVID-19 group (baseline versus follow-up tests), there is strong evidence of a process of recovery over time shown by improved VO_2peak (p=0.005, d=0.-41) and maximal workload (p<0.001, d=0.5), moderate improvement in MIP (p=0.04, d=-0.38), and weak evidence of improved O_2-pulse (p=0.03, d=-0.31), (Supplementary Table 1). No meaningful differences were found in the N-COVID-19 group (Supplementary Table 2).

There is considerable heterogeneity in the range of aerobic capacity of the sample (Supplementary Figure 1). Table 4 displays the odds of pulmonary and extrapulmonary limitations to exercise capacity following COVID-19. There are higher odds of exercise-induced hypoxia post-COVID-19 (p=0.05, OR=7.02, CI=0.86–57.53). The odds ratio of abnormal MIP post-COVID-19 is high, although not showing statistical significance (p=0.07, OR=3.19, CI=1.15–12.2). Similarly, there are higher odds of pulmonary limitations after COVID-19 implied by combining MIP with VE/MVV (p=0.07, OR=4.27, CI=0.89–20.39).

These results may have clinical relevance. Baseline testing of VT suggested skeletal muscle oxygen extraction limitations in the COVID-19 group up to nine months post-illness (p=0.03, OR=5.21, CI=1.11–24.56).

Discussion

This study provides insight into protracted exercise intolerance following COVID-19 in an athlete population with a high volume of cardiovascular exercise, predominantly of masters-age. VO_2peak of less than 85% of the predicted value indicates functional cardiorespiratory limitation to exercise capacity in the general population,[5] and in athletes, less than 100% warrants further clinical investigation.[15] Our findings suggest that the athletes had poorer maxRER, VO_2 at VT, and maximal workload during CPET testing for an average of six months post-COVID-19, when compared to matched athletes. The minimal differences in lung function between groups suggest this cohort's limitations are not primarily pulmonary.

In our study there is strong evidence of skeletal muscle oxygen extraction limitations in the COVID-19 group, as indicated by the low VT. For endurance athletes, VT is a better predictor of endurance capacity as it relates to skeletal muscle capacity,[5,15] and should typically reach 70–80% of VO_2peak.[18] The mean time from acute illness to the first test in this study was six months, indicating a prolonged adverse effect on the skeletal muscle system. Fatigue and muscle weakness are common after the onset of COVID-19, potentially accelerating the transition to anaerobic metabolism (as evidenced by a decrease in VT).[13] This stimulates the metaboergoreflex causing an increased VE/VCO_2 slope.[3] Decreased cardiac output may be the cause; however, it is more likely in our study to be due to impaired mitochondrial function.[8] Physical

Table 4. Pulmonary and extra-pulmonary limitations to exercise capacity in COVID-19 and N-COVID-19 groups at baseline test

Parameter indicating limitation	Condition	COVID-19 n=57	N-COVID-19 n=34	p-value	OR	95% CI
VO_2peak <100% ref applicable to athletes[19]	No limitation	43 (75%)	28 (82%)	0.44	1.5	0.52-4.42
	With limitation	14 (25%)	6 (18%)			
FEV_1/FVC <80%[26]	No limitation	36 (63%)	22 (65%)	0.88	1.1	0.44-2.58
	With limitation	21 (37%)	12 (35%)			
VE/MVV 70-80%[19]	No limitation	16 (28%)	9 (27%)	0.87	0.9	0.36-2.4
	With limitation	41 (72%)	25 (74%)			
Drop in SpO_2 >10% in athletes[14]	No limitation	47 (83%)	33 (97%)	0.05	7.0	0.86-57.53
	With limitation	10 (18%)	1 (3%)			
VE/VCO_2 slope >34[19]	No limitation	44 (77%)	28 (82%)	0.56	1.4	0.47-4.05
	With limitation	13 (23%)	6 (17%)			
MIP <85% ref	No limitation	40 (70%)	30 (88%)	0.07	3.2	1.15-12.2
	With limitation	17 (30%)	4 (12%)			
MIP <85% ref and abnormal breathing reserve	No limitation	45 (79%)	32 (94%)	0.07	4.3	0.89-20.39
	With limitation	12 (21%)	2 (6%)			
Abnormal breathing reserve and abnormal resting lung function with normal VO_2peak (80%-120%) = true pulmonary limitation[30]	No limitation	53 (93%)	30 (88%)	0.47	0.6	0.13-2.43
	With limitation	4 (7%)	4 (12%)			
Abnormal breathing reserve with normal resting spirometry and supranormal VO_2peak (>120%) = physiological limitation[30]	No limitation	42 (74%)	23 (67.6%)	0.54	0.8	0.3-1.89
	With limitation	15 (26%)	11 (32.4%)			
Max O_2-pulse[17]	No limitation	46 (80.7%)	28 (82.4%)	0.85	1.1	0.37-3.35
	With limitation	11 (19.3%)	6 (17.6%)			
VT <60%VO_2peak	No limitation	43 (75.4%)	32 (94.1%)	0.03	5.2	1.11-24.56
	With limitation	14 (24.6%)	2 (5.9%)			

ref, reference value; OR, odds ratio; FVC (1), forced vital capacity; FEV_1 (l), forced expiratory volume in one second; PEF, MVV, maximum voluntary ventilation; VO_2peak, maximum volume of oxygen in millilitres consumed, VE, minute ventilation; MIP, maximal inspiratory pressure; VT, ventilatory threshold

activity at low intensity restores mitochondrial health,[8] and athlete training programs must consider the prolonged healing time required to achieve this.

In a study investigating patients with exercise intolerance post-COVID-19, a maximum invasive CPET was performed and found that impaired peripheral oxygen extraction and hyperventilation limited exercise capacity more than cardiac abnormalities.[13] Heterogeneity exists in the published literature regarding the primary limitation to aerobic capacity, with reduced O_2-pulse cited as a potential mechanism.[2] In our study, O_2-pulse improved at follow-up in the COVID-19 group, consistent with another study,[20] however, athletes with persistently low O_2-pulse should not be overlooked. There were 23% of the athletes in the COVID-19 group that had elevated VE/VCO_2 slopes, as opposed to the 18% in the N-COVID-19 group. Considering the positive y-intercept of the VE/VCO_2 slope in the COVID-19 group, this may be clinically relevant and indicate pulmonary rather than cardiac involvement.

Pulmonary limitations cause impaired perfusion, effectively detected by CPET.[5] Our study results agree with Moulson et al. [20], who found that among individuals with low breathing reserve, 50% had a true pulmonary limitation. In comparison, 38% had normal resting lung function and supranormal fitness (VO_2peak>120%), indicating a normal physiological response in well-trained athletes. Further studies assessing aerobic capacity should consider low MIP with abnormal breathing reserve as an indicator of pulmonary limitation. The respiratory system can limit exercise capacity by four mechanisms: increased work of breathing, exercise-induced hypoxemia, respiratory muscle fatigue, or dyspnoea.[10] When comparing the exercise response of endurance athletes, this study found minimal improvement in the resting lung capacity of the N-COVID-19 group. In contrast, the COVID-19 group showed marked improvement in MIP, indicating recovery of respiratory muscle strength.[21] This implies the immediate need for respiratory rehabilitation from the acute phase of the illness, as these results indicate persistent pulmonary limitations more than six months post-COVID-19. Respiratory muscle training may be valuable in this population.

Limitations

Convenience sampling can lead to selection bias in the control group. However, one assumes that responses to advertisements were random. Participants would have required access to social media. Although pre-illness lung function and CPET data were unavailable, comparison with controls indicated that the difference was likely due to COVID-19 infection. The control group was also exposed to the environmental and psychological impact of the pandemic and related restrictions. These global effects were unavoidable and potentially reduced exercise capacity in the control group; therefore, they may have created a negative bias of the results of the control group.[4] Illness dates are subject to recall bias. The athletes in this study

may have been infected with a mixture of different virus strains. The results of this study are generalisable to endurance athletes in a predominantly masters-age group. The broad variance in results reduced statistical significance, and a larger sample size may be required in further studies. These results could be valuable when combined in a systematic review and meta-analysis. The strengths of the study include the demographic characteristics closely matching that of marathon runners worldwide, which fills a gap in the literature. Both exposure and control groups had follow-up tests to account for retraining. This is one of the first studies to describe pulmonary limitations to exercise capacity based on abnormal MIP with low breathing reserve. Future studies investigating pulmonary rehabilitation, including respiratory muscle training is recommended. Physical activity aiming to restore mitochondrial health warrants further research in athletes with post-viral fatigue. Further research is recommended to determine whether targeted interventions will facilitate the return to pre-illness CRF. The long-term effects of COVID-19 to date warrant investigation.

Conclusion

This study aimed to determine the influence of COVID-19 on the cardiovascular, pulmonary, and skeletal muscle function of endurance athletes with exercise intolerance and compare their exercise response to a control group. Our findings suggest impaired oxygen extraction by the skeletal muscle reduces aerobic capacity in endurance athletes after COVID-19. Pulmonary limitations were present in the post-COVID group, including weakened respiratory muscle strength. Resisting fatigue is imperative when exercising for a prolonged duration. Thus, both pulmonary and extrapulmonary limitations need to be managed. This underscores the need for rehabilitation tailored to recovering pulmonary or skeletal muscles in athletes after respiratory diseases. A multidisciplinary approach is recommended to restore athlete health and their ability to achieve their athletic goals.

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Author contributions: CH: conceptualisation; methodology; formal analysis; investigation; data curation; writing – original draft, writing review and editing; funding acquisition, approval of final version to be published. GT: conceptualisation; methodology; validation; investigation; resources; editing; supervision; project administration; approval of final version to be published. BO: conceptualisation; methodology; editing; supervision; approval of final version to be published. HvA: conceptualisation; methodology; validation; resources; editing; supervision; approval of final version to be published.

References

1. Clinical Spectrum of SARS-CoV-2 Infection. Available:. https://www.ncbi.nlm.nih.gov/books/NBK570371/pdf/Bookshelf_NBK570371.pdf. (Accessed, 13 February 2023).
2. Evers G, Schulze AB, Osiaevi I, Harmening K, Vollenberg R, Wiewrodt R, Pistulli R, Boentert M, Tepasse PR, Sindermann JR, Yilmaz A. Sustained impairment in cardiopulmonary exercise capacity testing in patients after COVID-19: A single center experience. Can Respir J. 2022;2022(1):2466789. [doi: 10.1155/2022/2466789] [PMID: 35242250].
3. Braga F, Domecg F, Kalichsztein M, Nobre G, Kezen J, Espinosa G, Prado C, Facio M, Moraes G, Gottlieb I, Lima RL. Abnormal exercise adaptation after varying severities of COVID-19: A controlled cross-sectional analysis of 392 survivors. Eur J Sport Sci. 2023 May;23(5):829-39. [doi: 10.1080/17461391.2022.2054363] [PMID: 35306969].
4. Scheer V, Valero D, Villiger E, Rosemann T, Knechtle B. The impact of the COVID-19 pandemic on endurance and ultra-endurance running. Medicina. 2021 Jan 9;57(1):52. [doi: 10.3390/medicina57010052] [PMID: 33435292].
5. Ladlow P, O'Sullivan O, Bennett AN, Barker-Davies R, Houston A, Chamley R, May S, Mills D, Dewson D, Rogers-Smith K, Ward C. The effect of medium-term recovery status after COVID-19 illness on cardiopulmonary exercise capacity in a physically active adult population. J Appl Physiol. 2022 Jun 1;132(6):1525-35. [doi: 10.1152/japplphysiol.00138.2022] [PMID: 35608204].
6. Larkin Chuatrakoon B, Konghakote S, Sa-Nguanmoo P, Nantakool S. Long-term impact of SARS-CoV-2 infection on cardiorespiratory fitness: a meta-analysis. Front Public Health. 2023 Oct 18;11:1215486. [doi: 10.3389/fpubh.2023.1215486] [PMID: 37920575].
7. Harber MP, Kaminsky LA, Arena R, Blair SN, Franklin BA, Myers J, Ross R. Impact of cardiorespiratory fitness on all-cause and disease-specific mortality: advances since 2009. Prog Cardiovasc Dis. 2017 Jul 1;60(1):11-20. [doi: 10.1016/j.pcad.2017.03.001] [PMID: 28286137].
8. Deng S, Deng J, Yin M, Li Y, Chen Z, Nassis GP, Zhu S, Hu S, Zhang B, Li Y. Short-term effects of SARS-CoV-2 infection and return to sport on neuromuscular performance, body composition, and mental health—A case series of well-trained young kayakers. J Exerc Sci Fit. 2023 Oct 1;21(4):345-53. [doi: 10.1016/j.jesf.2023.08.002] [PMID: 37701125].
9. Joyner MJ, Coyle EF. Endurance exercise performance: the physiology of champions. J Physiol. 2008 Jan 1;586(1):35-44. [doi: 10.1113/jphysiol.2007.143834] [PMID: 17901124].
10. Wells GD, Norris SR. Assessment of physiological capacities of elite athletes & respiratory limitations to exercise performance.

Paediatr Respir Rev. 2009 Sep 1;10(3):91-8.
[doi: 10.1016/j.prrv.2009.04.002] [PMID: 19651378].

11. McKinney J, Velghe J, Fee J, Isserow S, Drezner JA. Defining athletes and exercisers. Am J Cardiol. 2019 Feb 1;123(3):532-5. [doi: 10.1016/j.amjcard.2018.11.001] [PMID: 30503799].
12. Wasserman K. Diagnosing cardiovascular and lung pathophysiology from exercise gas exchange. Chest. 1997 Oct 1; 112(4):1091-101.
[doi: 10.1378/chest.112.4.1091] [PMID: 9377922].
13. Singh I, Joseph P, Heerdt PM, Cullinan M, Lutchmansingh DD, Gulati M, Possick JD, Systrom DM, Waxman AB. Persistent exertional intolerance after COVID-19: insights from invasive cardiopulmonary exercise testing. Chest. 2022 Jan 1;161(1):54-63. [doi: 10.1016/j.chest.2021.08.010] [PMID: 34389297].
14. Myers J, Kaminsky LA, Lima R, Christle JW, Ashley E, Arena R. A Reference Equation for Normal Standards for VO2 Max: Analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND Registry). Prog Cardiovasc Dis. 2017;60(1):21-29.
[doi: 10.1016/j.pcad.2017.03.002] [PMID: 28377168].
15. Andonian BJ, Hardy N, Bendelac A, Polys N, Kraus WE. Making cardiopulmonary exercise testing interpretable for clinicians. Curr Sports Med Rep. 2021 Oct 1;20(10):545-52.
[doi: 10.1249/JSR.0000000000000895] [PMID: 34622820].
16. STROBE Statement-Checklist of Items That Should Be Included Available: https://www.strobe-statement.org (Accessed, 23 November 2023).
17. Datta D, Normandin E, ZuWallack R. Cardiopulmonary Ann Thorac Med. 2015 Apr 1;10.
[doi: 10.4103/1817-1737.151438] [PMID: 25829957].
18. Smart Mezzani A. Cardiopulmonary exercise testing: basics of methodology and measurements. Ann Am Thorac Soc. 2017 Jul;14(Supplement 1):S3-11.
[doi: 10.1513/AnnalsATS.201612-997FR] [PMID: 28510504].
19. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982 Jan 1;14(5):377-81. [PMID: 7154893].
20. Moulson N, Gustus SK, Scirica C, Petek BJ, Vanatta C, Churchill TW, Guseh JS, Baggish A, Wasfy MM. Diagnostic evaluation and cardiopulmonary exercise test findings in young athletes with persistent symptoms following COVID-19. Br J Sports Med. 2022 Aug 1;56(16):927-32.
[doi: 10.1136/bjsports-2021-105157] [PMID: 35584886].
21. Vonbank K, Lehmann A, Bernitzky D, Gysan MR, Simon S, Schrott A, Burtscher M, Idzko M, Gompelmann D. Predictors of prolonged cardiopulmonary exercise impairment after COVID-19 infection: a prospective observational study. Front Med. 2021 Dec 24;8:773788.
[doi: 10.3389/fmed.2021.773788] [PMID: 35004742].

5.2 Supplementary file

Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes

Supplementary Table 1. Comparison of lung function and CPET between the first test (1) and follow up test (2) in the COVID-19 group.

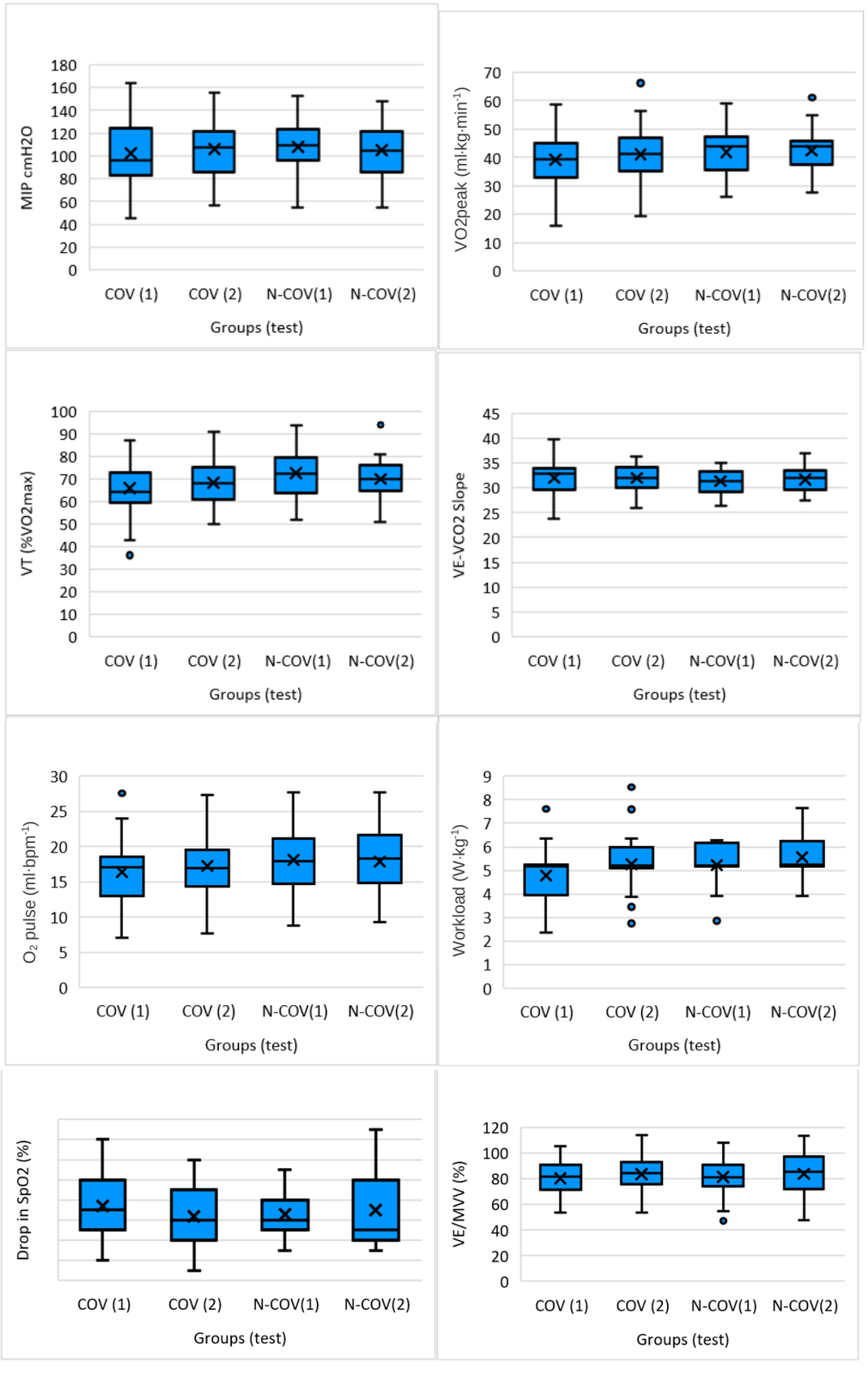
Parameter	COVID-19 (1) (n=57)	COVID-19 (2) (n=52)	*p*-value	Effect size
Lung function				
FVC (l)	4.8 ± 1.0	4.4 (3.9; 5.7)	0.60	0.29
FEV_1 (l)	3.9 ± 0.8	3.9 ± 0.9	0.73	0.05
FEV1/FVC	81.6 ± 5.3	80.7 ± 4.8	0.18	0.19
PEF ($l \cdot min^{-1}$)	8.6 ± 2.5	9.0 ± 2.7	0.11	-0.22
MVV ($l \cdot min^{-1}$)	135.2 ± 27.8	133.4 ± 34.4	0.98	0.22
MIP (cmH2O)	102.0 ± 25.9	105.5 ± 24.0	0.04	-0.38
Cardiopulmonary exercise testing (CPET)				
VO_2peak ($ml \cdot kg \cdot min^{-1}$)	39.1 ± 8.6	41.2 ± 8.5	0.005	-0.41
VO_2peak % ref ($ml \cdot kg \cdot min^{-1}$)	126.6 ± 33.7	134.0 ± 31.0	0.006	-0.40
VE/VCO_2 slope	32.0 ± 3.1	32.0 ± 2.7	0.61	0.07
y-intercept ($l \cdot min^{-1}$)	1.09 ± 3.5	1.4 ± 2.7	0.15	0.27
RER at max	1.2 ± 0.6	1.2 (1.1; 1.2)	0.42	0.02
VO_2 at VT ($ml \cdot min^{-1}$)	65.7 ± 10.6	68.3 ± 9.3	0.18	-0.19
VE max ($l \cdot min^{-1}$)	108.1 ± 25.5	112.8 ± 28.7	0.14	-0.21
VE/MVV	80.3 ± 12.6	83.9 ± 13.2	0.075	-0.26
HR max (bpm)	172.8 ± 10.3	172.9 ± 7.8	0.96	0.00
O_2-pulse ($ml \cdot bpm^{-1}$)	16.4 ± 3.9	17.2 ± 4.0	0.029	-0.31
Drop in SpO_2 %	7.3 ± 3.2	5 (4.0; 8.3)	0.07	0.73
RPE	18.8 ± 1.0	19 (19; 19	0.66	-0.93
Workload ($W \cdot kg^{-1}$)	4.8 ± 1.1	5.2 (5.1; 6.0)	<0.001	-0.50

Data expressed as mean ± standard deviation or (median; interquartile range) as applicable and determined using the T-test for paired samples or Wilcoxon signed rank test. RPE: Rate of perceived; FVC (1), forced vital capacity; FEV_1 (l), forced expiratory volume in one second; PEF, peak expiratory flow; MVV, maximum voluntary ventilation; VO_2peak, maximum volume of oxygen in millilitres consumed, VE, minute ventilation, HR, heart rate; MIP, maximal inspiratory pressure; RER, respiratory exchange ratio; VT, ventilatory threshold

Supplementary Table 2. Comparison of lung function between the first test (1) and follow-up test (2) in the N-COVID-19 group.

Parameter	N-COVID-19 (1) (n=34)	N-COVID-19 (2) (n=26)	*p*-value	Effect size
Lung function				
FVC (l)	5.0 ± 1.0	5.0 ± 1.0	0.75	-0.06
FEV_1 (l)	4.1 ± 0.8	4.0 ± 0.8	0.11	0.32
FEV_1/FVC	81.0 ± 5.3	81.0 (68.2; 78.3)	0.06	-0.009
PEF ($l \cdot min^{-1}$)	9.1 ± 2.1	9.6 ± 2.1	0.33	-0.19
MVV ($l \cdot min^{-1}$)	142.2 ± 27.0	139.7 ± 26.6	0.11	0.32
MIP (cmH_2O)	107.9 ± 21.8	104.7 ± 23.7	0.19	0.26
CPET				
VO_2peak ($ml \cdot kg \cdot min^{-1}$)	42.0 ± 7.6	42.4 ± 7.6	0.95	-0.012
VO_2peak % ref ($ml \cdot kg \cdot min^{-1}$)	128.1 ± 26.3	124.8 (112.3; 132.2)	0.74	0.15
VE/VCO_2 slope – measured	31.4 ± 2.4	31.6 ± 2.6	0.75	-0.06
y-intercept ($l \cdot min^{-1}$)	0.99 ± 2.7	1.3 ± 2.3	0.51	0.21
RER at max	1.1 ± 0.04	1.2 (1.1; 1.2)	0.00	-0.49
VO_2 at VT ($ml \cdot min^{-1}$)	72.6 ± 10.6	70.0 ± 9.1	0.28	0.22
VE max ($l \cdot min^{-1}$)	115.4 ± 26.6	116.2 ± 30.1	0.56	-0.12
VE/MVV	81.5 ± 14.0	83.8 ± 17.8	0.72	-0.28
HR max (bpm)	174.1 ± 9.7	174.3 ± 9.1	0.97	-0.007
O_2-pulse ($ml \cdot bpm^{-1}$)	18.1 ± 4.6	17.9 ± 4.6	0.89	0.025
Drop in SpO_2 %	6 (5;8)	5 (4;10)	0.92	0.32
RPE	19 (18;20)	19 (19;20)	0.33	0
Workload ($W \cdot kg^{-1}$)	5.2 (5.2;6.1)	5.2 (5.2;6.3)	0.23	-0.034

Data expressed as mean ± standard deviation or (median; interquartile range) as applicable and determined using the T-test for paired samples or Wilcoxon signed rank test. RPE: Rate of perceived; FVC (1), forced vital capacity; FEV_1 (l), forced expiratory volume in one second; PEF, peak expiratory flow; MVV, maximum voluntary ventilation; VO_2peak, maximum volume of oxygen in millilitres consumed, VE, minute ventilation, HR, heart rate; MIP, maximal inspiratory pressure; RER, respiratory exchange ratio; VT, ventilatory threshold



Supplementary Figure 1. *Distribution of physiological parameters across the four tests: baseline (1), follow-up (2), COVID-19 group (COV), N-COVID-19 group (N-COV)*

5.3 Further methodological information

The following section describes the procedure for Study 3 in more detail. This was partly extracted from the publication due to the word count limit of the journal.

5.3.1 Recruitment of participants

In the survey used for Study 1 and 2, participants citing that they had still not returned to their pre-illness level of sport were invited to participate in the observational cohort study (Study 3), and leave their email address if interested. This study investigated whether the limitations to their exercise capacity are of pulmonary or extrapulmonary origin and compared the results to a control group. Participants in this study booked an appointment using an online calendar, which sent a confirmation to the participant, myself as the principal investigator and the staff at the outpatient cardiac unit at the Nelson Mandela Children's Hospital (NMCH).

5.3.2 Preparation of the equipment

The principal investigator Cheryl Haley, co-author Georgia Torres, research assistant Daphne Nevhufumva, and the staff of the cardiac outpatient unit at the Nelson Mandela Children's Hospital (NMCH) attended a tutorial with the representative from General Electric, the company supplying the CPET system (Figure 5.1). The protocol, the methods, equipment principles, calibration, verification and maintenance checks were discussed. The testing room was equipped with a resuscitation station including an automated external defibrillator (AED). All researchers and staff involved underwent training in the use of the resuscitation equipment in case of emergency during CPET. On the General Electric Healthcare CASE^{TM} exercise testing system, version 6.7, Milwaukee, USA, we selected the breath-by breath analyser, recording values every 5 seconds. We used the modified Bruce protocol to determine maximal oxygen consumption (Mezzani, 2017). Three-minute stages were used with the following treadmill speeds and gradients:

Stage 1: 2.7 km.h^{-1}; 10%

Stage 2: 4 km.h^{-1}; 12%

Stage 3: 5.5 km.h^{-1}; 14%

Stage 4: 6.8 km.h^{-1}; 16%

Stage 5: 8 km.h^{-1}; 18%

Stage 6: 8.9 km.h^{-1}; 20%

Stage 7: 9.7 km.h^{-1}; 22%

A 3-minute cool down after termination of the maximal test allowed assessment of the return to resting heart rate and blood pressure. The treadmill ergometer is more applicable for athletes as it requires activation of more muscle mass and higher fitness levels, therefore we could obtain a higher VO_{2peak} (Mezzani, 2017).



Figure 5.1 The CPET set up including General Electric Healthcare CASE^{TM} exercise testing system, ECG monitoring system, and treadmill

The principal investigator arrived early to prepare. The testing equipment needed to be turned on and warmed up for 15 minutes. The gas analyser had to be calibrated for quality control. During calibration, the machine needed to be clear of people standing nearby to accurately calibrate the room air. The ECG leads were checked and the electrodes that were donated by the sports science department for this study were attached.

5.3.3 Absolute and relative contraindications to CPET

Absolute contraindications to CPET include unstable angina, acute myocardial infarction, acute myocarditis, pericarditis or endocarditis, acute pulmonary embolism, decompensated symptomatic heart failure, severe aortic stenosis, acute infection, renal failure, physical injury or disability that precludes optimal performance, and lastly the lack of informed consent (Fletcher et al., 2001).

Relative contraindications include left coronary artery stenosis, moderate valvular heart disease, tachycardia, atrial fibrillation, mental impairment, a high degree of AV block, and hypertrophic cardiomyopathy (Fletcher et al., 2001).

We added adherence to the COVID-19 protocols because lung function and CPET is an aerosol generating activity.

1. All participants were required to sanitise their hands, have their body temperature taken, and filled in the visitor book at the entrance to the NMCH.
2. Participants wore their masks continuously until they performed the tests. The testing staff wore masks throughout the assessment.
3. The plastic masks used for gas analysis during CPET were immersed in Milton after use as per protocol for test procedures.
4. Each participant received their own filters for the spirometry and S-Index assessments.
5. The spirograph was rinsed in Milton after use and air dried as per protocol.
6. Large siding doors were opened to the outside ensuring a well-ventilated room.
7. Collection and cleaning of masks were done by the investigator using gloves.

5.3.4 The lung function and CPET procedure

A brief medical history was taken from each participant, which included questions about their symptoms, their current running volume and pace, and challenges experienced. Also, past medical history included the timeframe since they were infected with COVID-19 and how many times they had it. Medication use was important, particularly the use of beta-blockers that may prevent the participant from reaching maximal heart rate (Fletcher et al., 2001).

The lung function and S-Index test procedure (Fig 5.2) was explained to the participant by the principal investigator, Cheryl Haley. A nose peg was used to optimise O_2 and CO_2 capture by the spirograph. They performed three rounds of testing to allow the results to reflect their best effort.



Figure 5.2 Lung function (Left) and S-Index (Right) testing in progress

Participants with hairy chests were asked if we may shave a spot to apply the electrode. The area was cleaned with alcohol rub and ECG stickers attached. The blood pressure cuff and waist belt were sanitised before and after every use. Standardised temperature was achieved by setting the room air conditioning as well as opening the large doors. Correct fitting of the mask is important. There were two sizes available. When the participant exhaled forcefully, no air should have escaped into their eyes. On the treadmill we checked that all wires from the ECG leads, pulse oximeter, and gas analyser were well secured to allow unhindered running. The treadmill had front and side rails, but the participants were requested not to hold onto the rails as it decreases the workload reading. Due to their peripheral vision being limited by the mask, they were instructed to focus on a point in front of them. The participant was given clear instruction of the test procedure by the principal investigator. A poster of the Borg scale of perceived exertion was shown to the participant. It was explained that they would be asked to rate their RPE periodically throughout the test and they needed to respond by shouting out or pointing at the appropriate number (Fig 5.3) (Borg, 1982). The researchers ensured that participants did not run too close to the back of the treadmill.

6	**No exertion**
7	
8	
9	
10	
11	**Light**
12	
13	**Somewhat hard**
14	
15	**Hard (heavy)**
16	
17	**Very hard**
18	
19	
20	**Maximal exertion**

Figure 5.3 Rating of perceived exertion (Borg, 1982)

During CPET (Fig 5.4), the principal investigator asked the participant about symptoms, watched them for apical breathing and took note of audible wheezing (without the use of a stethoscope). They needed to indicate when they had reached volitional exhaustion, or provocation of their exertional symptoms at which point the test was stopped. Termination of a maximal test occurs at maximal RER (1.05-1.15), HR of 85% predicted maximum, >18 on Borg scale of perceived exertion (Borg 6-20 scale in Figure 5.3), or provocation of exertional symptoms (Mezzani, 2017; Andonian et al., 2021). In this study, not all participants reached a 20-30 second plateau at maximal power (VO_{2max}), therefore VO_{2peak} was used in all tests. A bottle of water or an electrolyte drink was provided after each test. The participants were told what their VO_{2peak} value was and that a full report would be compiled for them after the follow-up test. Any further questions were encouraged.

There are other factors that may cause exercise intolerance. These include motivational and sociological factors, which have a large influence on performance beyond physiological parameters. These may be the cause of perceived exercise

intolerance when CRF parameters are normal on CPET (Joyner and Coyle, 2008). Altitude and ambient temperature can also influence performance (Joyner and Coyle, 2008). The temperature in the room was controlled by using an air conditioner. Peak VO_2 values will be lower when tested at an altitude of 1450m (in Johannesburg) than if the group was tested at sea level. Sleep quality, mental health, training intensity, and nutrition can impact performance and confound CPET results, therefore participants were encouraged to sleep well and eat two hours before both tests (Śliż et al., 2023). Autonomic nervous system imbalances such as hypotension may be exacerbated by deconditioning and therefore exertional dizziness may be due to limitations in the skeletal muscle system (Messinger-Rapport and Grubb, 2023).

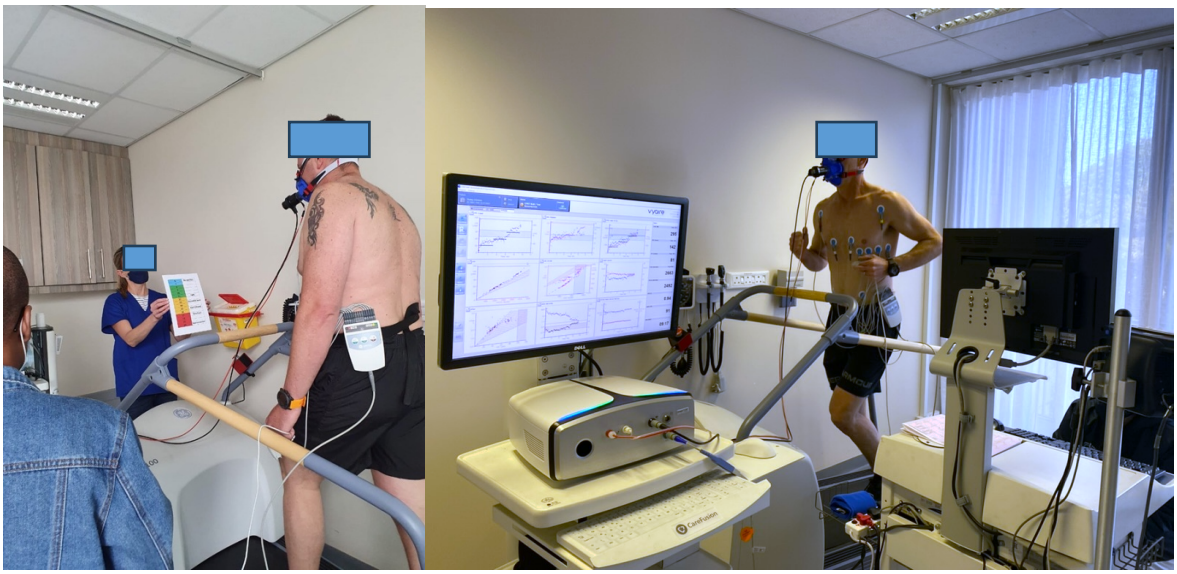


Figure 5.4 The participant rating their perceived exertion (left) and the researcher's perspective of the CPET in progress, observing the parameters on the General Electric Healthcare CASE™ exercise testing system display (right)

5.3.5 Reference tables

The norms of the parameters used in this study are displayed in the tables below (Tables 5.1 - 5.4). The 50th percentile was used as the reference value (FRIEND Registry protocol) (Myers et al., 2017; Arena et al., 2021; Arena et al., 2020).

Table 5.1 Maximal inspiratory pressure (MIP) for men and women in different age groups derived from the random-effects model used in the meta-analysis, published by HajGhanbari et al. (2013). These values approximate the S-Index

Age group	Men MIP(cmH_2O), mean (95% CI)	Women MIP(cmH_2O), mean (95% CI)
18-29	128.0 (116.3–139.5)	97.0 (88.6–105.4)
30-39	128.5 (118.3–138.7)	89.0 (84.5–93.5)
40-49	117.1 (104.9–129.2)	92.9 (78.4–107.4)
50-59	108.1 (98.7–117.6)	79.7 (74.9–84.9)
60-69	92.7 (84.6–100.8)	75.1 (67.3–82.9)
70-83	76.2 (66.1–86.4)	65.3 (57.8–72.7)

Table 5.2 CRF Percentiles for the FRIEND cohort by age group for treadmill with directly measured VO_2peak (ml $O_2.kg^{-1}.min^{-1}$), published by Myers et al. (2017)

Age group, years														
	Male							Female						
Percentile	20-29	30-39	40-49	50-59	60-69	70-79	80-89	20-29	30-39	40-49	50-59	60-69	70-79	80-89
90th	58.6	55.5	50.8	43.4	37.1	29.4	22.8	49.0	42.1	37.8	32.4	27.3	22.8	20.8
80th	54.5	50.0	45.2	38.3	32.0	25.9	21.4	44.8	37.0	33.0	28.4	24.3	20.8	18.4
70th	51.9	46.4	40.9	34.3	28.7	23.8	20.0	41.8	33.6	30.0	26.3	22.4	19.6	17.3
60th	49.0	43.4	37.9	31.8	26.5	22.2	18.4	39.0	31.0	27.7	24.6	20.9	18.3	16.0
50th	46.5	39.7	35.3	29.2	24.6	20.6	17.6	36.6	28.3	25.7	22.9	19.6	17.2	15.4
40th	43.6	37.0	32.4	26.9	22.8	19.1	16.6	34.0	26.4	23.9	21.5	18.3	16.2	14.7
30th	40.0	33.5	29.7	24.5	20.7	17.3	16.1	30.8	24.2	21.8	20.1	17.0	15.2	13.7
20th	35.2	29.8	26.7	22.2	18.5	15.9	14.8	27.2	21.9	19.7	18.5	15.4	14.0	12.6
10th	28.6	24.9	22.1	18.6	15.8	13.6	12.9	22.5	18.6	17.2	16.5	13.4	12.3	11.4

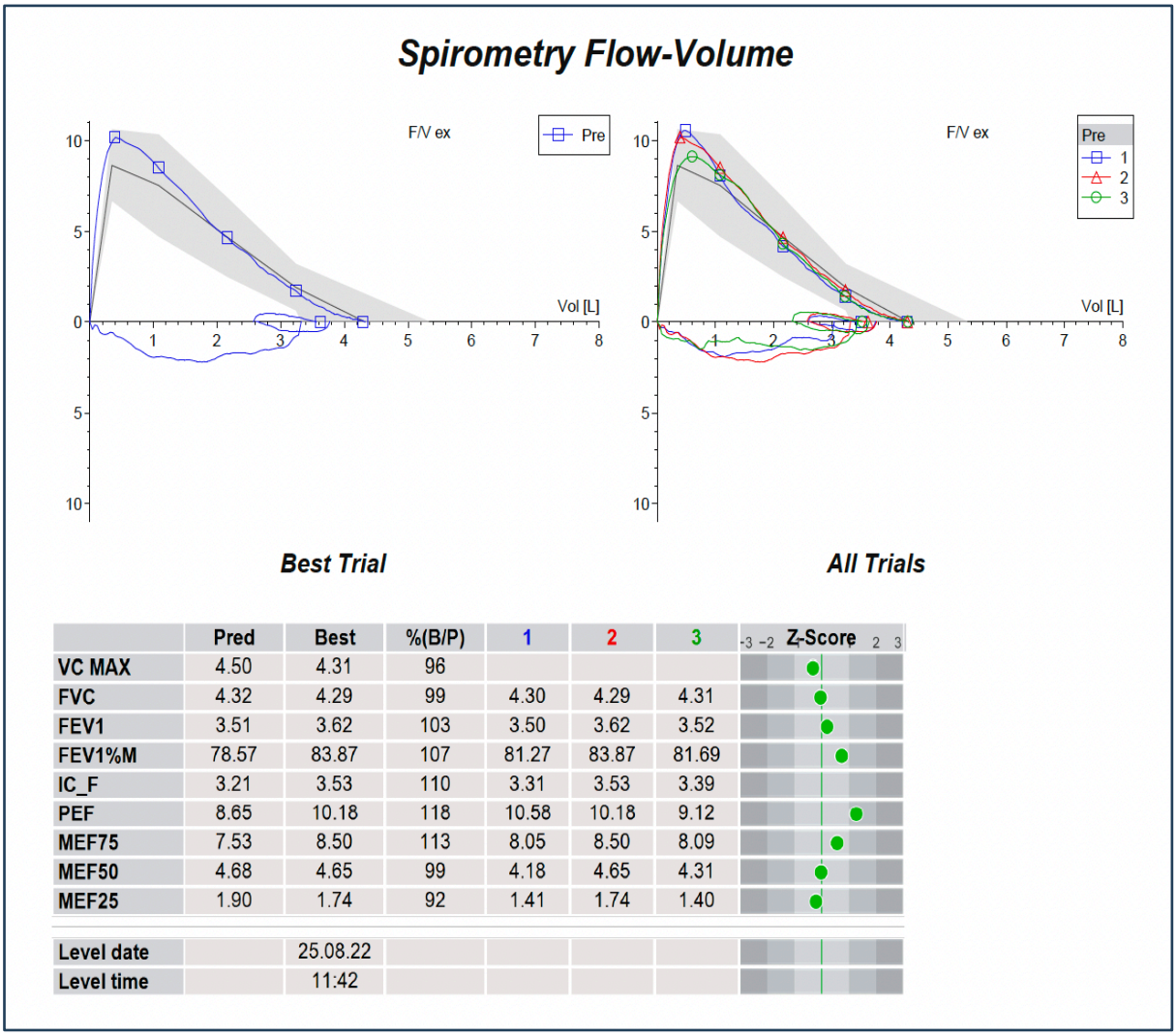
Table 5.3 VE/VCO_2 slope according to percentiles and decades, published by Arena et al. (2021)

Age group, years														
	Male							Female						
Percentile	20-29	30-39	40-49	50-59	60-69	70-79	80-89	20-29	30-39	40-49	50-59	60-69	70-79	80-89
90th	33.0	31.6	32.7	32.5	36.5	37.2	41.2	33.8	32.9	34.4	32.6	36.8	39.1	44.5
80th	31.1	29.5	30.4	30.8	35.0	34.9	37.8	31.9	31.1	31.9	30.9	34.1	36.0	38.9
70th	29.3	28.3	28.9	29.3	33.0	32.9	36.6	31.0	30.0	30.3	30.2	32.4	34.3	36.4
60th	28.1	27.5	27.3	28.2	31.5	31.2	34.4	29.6	28.9	29.0	29.0	31.3	32.8	34.7
50th	27.1	26.7	25.8	27.3	29.4	30.7	33.9	28.5	27.6	27.9	27.7	29.9	32.0	33.7
40th	26.3	25.7	24.7	26.5	27.8	29.7	33.2	27.5	26.7	26.5	26.8	28.7	31.0	33.0
30th	25.4	24.6	24.1	25.5	27.0	28..7	31.9	26.8	25.4	25.4	25.8	27.7	29.7	32.6
20th	24.4	23.4	23.3	24.6	26.2	27.3	30.9	25.5	24.5	24.0	24.3	26.0	28.0	30.3
10th	22.5	21.9	21.9	23.0	24.9	24.5	29.6	23.5	22.3	21.9	22.8	24.7	26.3	29.2

Table 5.4 Maximal oxygen pulse according to percentile and decades, published by Arena et al. (2020)

Age group, years														
	Male							Female						
Percentile	20-29	30-39	40-49	50-59	60-69	70-79	80-89	20-29	30-39	40-49	50-59	60-69	70-79	80-89
90th	26.4	25.6	25.3	23.8	22.3	20.2	17.6	17.6	16.9	16.6	15.7	14.9	13.8	10.4
80th	24.3	23.6	23.3	21.9	20.4	18.7	16.3	16.0	15.4	15.3	14.4	13.7	12.7	9.9
70th	23.0	22.5	21.9	20.7	19.3	17.7	14.0	15.1	14.4	14.3	13.5	12.8	11.8	8.9
60th	21.9	21.2	20.7	19.6	18.4	16.7	11.9	14.4	13.5	13.4	12.8	12.2	11.3	8.1
50th	20.8	20.3	19.6	18.6	17.4	15.9	11.2	13.6	12.8	12.6	12.1	11.4	10.8	7.9
40th	19.7	19.2	18.5	17.5	16.5	15.2	10.3	12.8	11.9	11.8	11.4	10.8	10.2	7.6
30th	18.7	18.2	17.4	16.5	15.6	14.4	9.8	12.1	11.2	11.1	10.8	10.1	9.6	6.9
20th	17.4	16.7	16.2	15.4	14.5	13.4	9.1	11.2	10.4	10.3	10.0	9.4	8.9	6.5
10th	15.8	15.2	14.6	13.8	12.9	12.4	8.4	10.3	9.4	9.3	9.0	8.4	8.2	5.6

After each test was terminated, the results were viewed on the General Electric Healthcare CASE^{TM} exercise testing system as displayed in Fig 5.5 and Fig 5.6. Some of the parameters were not displayed and required calculation. These included breathing reserve, oxygen pulse, VE/VCO_2 slope and y-intercept.



	Pred	Best	%(B/P)	1	2	3	Z-Score
VC MAX	4.50	4.31	96				
FVC	4.32	4.29	99	4.30	4.29	4.31	
FEV1	3.51	3.62	103	3.50	3.62	3.52	
FEV1%M	78.57	83.87	107	81.27	83.87	81.69	
IC_F	3.21	3.53	110	3.31	3.53	3.39	
PEF	8.65	10.18	118	10.58	10.18	9.12	
MEF75	7.53	8.50	113	8.05	8.50	8.09	
MEF50	4.68	4.65	99	4.18	4.65	4.31	
MEF25	1.90	1.74	92	1.41	1.74	1.40	
Level date		25.08.22					
Level time		11:42					

Figure 5.5 The lung function results produced by the General Electric Healthcare CASE^{TM} exercise testing system



Last Name:	Langenhoven	Date of Birth:	11/08/1956	Age:	66 Years
First Name:	Godfried	Height:	176 cm	Weight:	70.0 kg
Identification:	038	Gender:	male	BSA:	1.86 m²
Pred. Module:	Standard EU	Operator:		Physician:	
Diagnosis:					
18.08.2022					
Cheryl phD					

Exercise Results

Summary		Rest (R)	Warm (R)	MAX (R)	Reco (R)	MAX (R) Pred	MAX (R) % PredMax
Time	[min]	00:06	00:00	14:50	15:54	-	-
Load	[W]	-	0	365	20	134	272
V'E	[L/min]	17	0	94	70	91	104
V'O2	[mL/min]	627	0	2094	1398	1941	108
V'O2/kg	[(mL/min)/kg]	9.0	0.0	29.9	20.0	27.7	108
V'CO2	[mL/min]	443	0	2514	1897	-	-

Cardiovascular-Results

Summary		Rest (R)	Warm (R)	Peak (R)	Reco (R)	Peak (R) [Pred]	Peak (R) [%PredMax]
HR	[1/min]	57	0	173	140	154	112
O2pulse	[mL]	11.0	0.0	12.1	10.0	12.6	96
Psys	[mmHg]	-	0	-	-	-	-
Pdia	[mmHg]	-	0	-	-	-	-
HRR (B)	[1/min]	97	0	-19	14	-	-
SpO2	[%]	98	0	88	89	-	-
PaO2	[kPa]	-	-	-	-	-	-
PaCO2	[kPa]	-	-	-	-	-	-
AaDO2	[kPa]	-	-	-	-	-	-
V'Eslo		-	0	-	-	-	-

Physiological thresholds

Summary		VT1 [Manuell]	VT2 [Manuell]	VT3 [Manuell]
Time	[min]	04:00	09:30	11:50
Load	[W]	130	275	275
V'E	[L/min]	26	59	70
V'O2	[mL/min]	800	1531	2103
RER		0.75	0.93	0.99
HR	[1/min]	76	110	157

18.08.2022 HOSPITAL NAME 1 5

Figure 5.6 The CPET results produced by the General Electric Healthcare CASE™ exercise testing system

The participants were sent a report compiled by the principal investigator. This included the results of their baseline and follow-up tests with an explanation of what the lung function and CPET parameters mean. If no limitations to their exercise capacity were found, the participant was reassured that they had fully recovered from COVID-19 and their exercise response is normal. If skeletal muscle system limitations were found, the participants were advised to include strength training in their endurance training program. Those presenting with cardiac limitations were referred to their physician or cardiologist. Participants with pulmonary limitations to their exercise capacity were invited to participate in the subsequent study investigating the feasibility of an RCT

investigating the efficacy of inspiratory muscle training to improve exercise capacity (Study 4).

5.3.6 References

1. Andonian, B. J., Hardy, N., Bendelac, A., Polys, N., & Kraus, W. E. (2021). Making cardiopulmonary exercise testing interpretable for clinicians. *Current sports medicine reports*, 20(10), 545-552. https://doi.org/10.1249/JSR.0000000000000895
2. Arena, R., Myers, J., Harber, M., Wisloff, U., Stensvold, D., & Kaminsky, L. A. (2020). Peak oxygen pulse responses during maximal cardiopulmonary exercise testing: Reference standards from FRIEND (Fitness Registry and the Importance of Exercise: an International Database). *International journal of cardiology*, 301, 180-182. https://doi.org/10.1016/j.ijcard.2019.11.106
3. Borg GA. (1982). Psychophysical bases of perceived exertion. *Medicine and Science in Sport and Exercise*, 14(5), 377–381. PMID: 7154893
4. Fletcher, G. F., Balady, G. J., Amsterdam, E. A., Chaitman, B., Eckel, R., Fleg, J., Froelicher, V. F., Leon, A. S., Piña, I. L., Rodney, R., Simons-Morton, D. G., Williams, M. A., & Bazzarre, T. (2001). Exercise Standards for Testing and Training A Statement for Healthcare Professionals From the American Heart Association. *Circulation*, 104(14), 1694-1740. https://doi.org/10.1161/hc3901.095960
5. HajGhanbari, B., Yamabayashi, C., Buna, T. R., Coelho, J. D., Freedman, K. D., Morton, T. A., ... & Reid, W. D. (2013). Effects of respiratory muscle training on performance in athletes: a systematic review with meta-analyses. *The Journal of Strength & Conditioning Research*, 27(6), 1643-1663. https://doi.org/10.1519/jsc.0b013e318269f73f
6. Joyner, M. J., & Coyle, E. F. (2008). Endurance exercise performance: the physiology of champions. *The Journal of physiology*, 586(1), 35-44. https://doi.org/10.1113/jphysiol. 2007.143834
7. Messinger-Rapport, B., & Grubb, B. (2023). Patient-centered paradigm for managing autonomic long COVID symptoms during sports and exercise. *Clinical Journal of Sport Medicine*, *33*(2), e14-e15. https://doi.org/10.1097/JSM.0000000000001093
8. Mezzani, A. (2017). Cardiopulmonary exercise testing: Basics of methodology and measurements. *Annals of the American Thoracic Society*, *14*, S3–S11. https://doi.org/10.1513/AnnalsATS.201612-997FR

9. Myers, J., Kaminsky, L. A., Lima, R., Christle, J. W., Ashley, E., & Arena, R. (2017). A reference equation for normal standards for VO2 max: analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND Registry). *Progress in Cardiovascular Diseases*, 60(1), 21-29. https://doi.org/10.1016/j.pcad.2017.03.002
10. Śliż, D., Wiecha, S., Gąsior, J. S., Kasiak, P. S., Ulaszewska, K., Lewandowski, M., ... & Mamcarz, A. (2023). Impact of COVID-19 infection on cardiorespiratory fitness, sleep, and psychology of endurance athletes—CAESAR study. *Journal of Clinical Medicine*, 12(8), 3002. https://doi.org/10.3390/jcm12083002

Chapter 6 Study 4: Efficacy of inspiratory muscle training to improve exercise capacity in athletes post-COVID-19: A feasibility study for a single centre parallel-group randomised controlled trial

6.1 Abstract

Background: Long-term respiratory limitations after COVID-19 may cause low exercise tolerance in athletes. Inspiratory muscle training has been shown to improve dyspnoea in the general population.

Aim: To assess the feasibility of conducting a single-centre randomised controlled trial of inspiratory muscle training on athletic performance in athletes recovering from COVID-19.

Methods: Endurance athletes in Johannesburg, South Africa, over the age of 35 years were recruited from a previous observational study investigating the effect of COVID-19 on their cardiorespiratory fitness. The primary objective was to assess the feasibility in terms of practicality, acceptance and adherence, and implementation of conducting a single-centre longitudinal clinical trial to determine the effect of inspiratory muscle training on exercise capacity in masters age-group athletes. Lung function, S-Index and CPET were conducted at baseline and after six weeks in both groups. The participants were randomly allocated into the intervention or control groups according to an auto-generated number sequence and were blinded to their allocation. The intervention group performed 30 breaths through a spring-loaded inspiratory muscle training (IMT) device, five days a week for six weeks starting at 50% of the S-Index and increased progressively, while the control group had no intervention. Data were analysed per-protocol comparing participants in the parallel groups. Paired t-tests or Wilcoxon Signed-Rank tests were used to compare the repeated measures of the two groups. Cohen's d coefficient was used to determine the effect size of continuous data.

Results: From the eighteen athletes screened, six were allocated to the intervention group (mean age 50 ± 4.5 years) and seven to the control group (mean age 50 ±3.1 years). Acceptance and adherence were good but an adaptation for aerobic capacity testing could be made. Implementation was good as CPET and POWERBreathe tools

show good reliability and validity. The S-Index improved in the intervention group (p=0.031). No adverse events occurred during the trial.
Conclusion: With adaptations to the methodology, it may be feasible to conduct a single-center RCT investigating the effects of IMT on athletic performance in masters age-group athletes recovering from COVID-19.
Trial registration: Pan-African Clinical Trials Registry no. PACTR202305590076796
Funding: Respiratory Care Africa (Pty) Ltd, University of the Witwatersrand Faculty of Health Sciences Individual Research Grant.

Key words: Inspiratory muscle training, COVID-19, athletes, exercise capacity

6.2 Introduction

The high prevalence of COVID-19 worldwide calls for comprehensive research to understand and effectively manage its long-term impacts (Shelley et al., 2022). Acute symptoms generally resolve within four weeks (NICE, 2021), however, low exercise tolerance due to pulmonary limitations may persist for up to one-year post-infection (Braga et al., 2023). Recent studies are shedding light on the enduring sequelae of post-COVID-19 complications (McNarry et al., 2022). Physical activity is vital in mitigating the long-COVID effects and is a key component of pulmonary rehabilitation (Jimeno-Almazán et al., 2023). Therefore, the resolution of respiratory impairments is essential in order to regain the pre-illness level of performance in endurance sports (Halle et al., 2021).

Persistent dyspnoea may be associated with diminished breathing reserve, poor respiratory muscle strength, reduced lung tissue compliance, and underlying anxiety, although the exact aetiology is unknown (McNarry et al., 2022). In healthy lungs, an opening pressure of 40cmH_2O is required to fully inflate the alveoli, whereas diseased lungs may require 55cmH_2O (Severin et al., 2020). Maximal inspiratory pressure (MIP) measurements, which are approximated by the S-Index, prove valuable when reasons for limitations to exercise capacity or ongoing exertional dyspnoea remain unclear (Halle et al., 2021).

Pulmonary rehabilitation aims to alleviate symptoms, enhance physical functional ability, and improve quality of life (McNarry et al., 2022). It is a commonly used

rehabilitation tool in hospitalised patients, young asthmatic athletes, or older patients with chronic obstructive pulmonary disease. Respiratory muscle training (RMT) has demonstrated benefits in increasing respiratory muscle strength and endurance, diaphragm thickness, exercise capacity, and reducing dyspnoea (Severin et al., 2020). Inspiratory muscle training (IMT) utilises a handheld device in which a pre-determined pressure is required to initiate inspiration. This home-based intervention may be beneficial for those without the time or financial resources to travel to therapy (Collet et al., 2023). In a paucity of research involving the general population, RMT has been shown to improve long-COVID symptoms, particularly dyspnoea (McNarry et al., 2022; Collet et al., 2023) and combined with physical exercise to improve cardiorespiratory fitness (Jimeno-Almazán et al., 2023). Inspiratory muscle training was perceived to improve the quality of life in adults with long-COVIID (Shelley et al., 2022).

Endurance sport places a large and sustained demand on the cardiorespiratory system. Hence, respiratory muscle fatigue occurs even among otherwise healthy athletes (HajGhanbari et al., 2013). The impact of RMT on the performance of healthy athletes has yielded equivocal results, with many studies featuring small samples of elite athletes, typically under 35 years of age (HajGhanbari et al., 2013; Mackała et al., 2020). Endurance sport, particularly marathon distance running, attracts thousands of recreational athletes from a diversity of socioeconomic backgrounds, predominantly in the masters age-group (over the age of 35). Although results of studies investigating the effect of RMT on healthy athletes have been equivocal (HajGhanbari et al., 2013), the largely positive outcomes on respiratory and athletic performance suggest that a beneficial outcome for athletes struggling with persistent exercise intolerance long after COVID-19 is plausible.

The importance of implementing evidence-based interventions underscores the necessity of conducting feasibility studies prior to initiating resource-intensive trials, which assess whether testing an intervention is advisable and to identify potential barriers and facilitators (Bowen et al., 2009). Pilot studies increase the efficiency and internal validity of the proposed trial by investigating logistics, recruitment, intervention acceptance and adherence, and implementation (Avery et al., 2017). To our knowledge, there are globally no studies investigating the effect of IMT on the exercise tolerance of endurance athletes suffering from long-term post-COVID consequences. There is a need for research assessing the feasibility of IMT as an intervention to assist

pulmonary rehabilitation. This feasibility study was, therefore, conducted to assess the potential implementation of a single-centre randomised controlled trial (RCT) to determine the effect of IMT on exercise capacity in masters age-group endurance athletes. These findings will provide valuable insight for physiotherapists and sports medicine clinicians in assisting the full recovery of athletes following future COVID-19 variant infections and other respiratory diseases.

6.2.1 Aim of the study

This study assessed the feasibility of conducting a single-centre randomised controlled trial of inspiratory muscle training on athletic performance in athletes recovering from long-term COVID-19 exposure.

6.2.2 Objectives

- To assess the acceptability of the intervention, including the response of participants to the intervention and adherence to the intervention.
- To assess the implementation of the intervention, including the approach and extent to which the intervention can be studied by using reliable and valid outcome measures.
- To assess the practicality of conducting a single-centre longitudinal randomised controlled trial.
- To report on the estimated effects of respiratory muscle training on exercise capacity, specifically cardiorespiratory fitness, in athletes who are recovering from long-COVID.

6.3 Materials and Methods

6.3.1 Trial design and setting

A single-blind, parallel-group feasibility pilot study was done to test the study objectives. The study was drafted according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines: extension to randomised pilot and feasibility trials (Eldridge et al., 2016) and reported according to the stop/amend/go progression criteria (Avery et al., 2017). Participants were adult endurance athletes recruited from the community and took part in the study at an academic hospital associated with the

University of the Witwatersrand in Johannesburg, South Africa. Johannesburg (1450m above sea level) is the largest and most populous city in South Africa with the highest rate of COVID-19 infection (NICD, 2021).

6.3.2 Participants

The inclusion criteria for both groups were endurance athletes of both sexes over the age of 35 years who responded to an advertisement to participate in a previous observational study (Study 3 of this thesis) investigating limitations to exercise capacity post-COVID-19 (n=52). Those presenting with cardiopulmonary limitations to aerobic capacity were eligible for inclusion in the intervention trial.

The exclusion criteria were athletes in quarantine or isolating due to a positive COVID-19 test result, new onset of COVID-19 symptoms or a positive exposure within 10 days of commencing the study. Athletes who are already using RMT as part of their training programme post-COVID-19 were excluded. Further exclusions were not being proficient in English, residing outside of Gauteng, and published contraindications to CPET (Fletcher et al., 2001; Datta, Normandin and Zuwallack, 2015).

6.3.3 Outcome measures

The questions on REDCap included sociodemographic and sport-specific data, COVID-19 symptom classification (COVID-19 Treatment Guidelines, 2023), fatigue score using the standardised Multidimensional Fatigue Inventory (MDFI) tool (Smets et al., 1995), and their return to sport challenges. The time interval from infection to first test was recorded. At the first assessment and 6-week follow-up, the primary investigator performed a subjective assessment, which included current and past medical history and management thereof, and the presence of any of the known contra-indications to CPET, including resting blood pressure. Current participation in physical activity, competition goals, and persistent symptoms were noted. Objective measures including age, sex, weight, height, and BMI were collected before beginning each test.

6.3.3.1 Progression criteria

The prespecified criteria (acceptability, implementation and practicality) to determine the feasibility of an RCT were classified according to a red/amber/green traffic light system as suggested by Avery et al. (2017). A “red light” indicates that the criteria had major issues that cannot be rectified and may threaten the success of a trial. An “amber light” suggests that the criteria could be amended. A “green light” signals that the criteria had no concerns and can be implemented into a larger trial.

6.3.3.2 Lung function

Resting lung function was assessed in standing prior to the CPET. The Vyaire Medical CPET BxB Sentry Suite™ V2.21 software was used to record data during the test. Measurements included forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and peak expiratory flow (PEF). Maximum voluntary ventilation (MVV) was estimated by multiplying FEV_1 by 35 (Kaminsky et al., 2018). The S-Index was assessed in standing using the POWERBreathe K3 device. The best of three attempts of less than 5% difference was recorded according to the American Thoracic Society protocol (2002).

6.3.3.3 Cardiopulmonary exercise test

Cardiopulmonary exercise tests were conducted using a treadmill test rather than a cycle ergometer as it gives higher peak oxygen uptake results applicable to athletes (Mezzani, 2017). A General Electric Healthcare CASE™ exercise testing system, version 6.7, Milwaukee, USA was programmed according to the Bruce protocol, suitable for athletes (Fletcher et al., 2001) and continuously monitored heart rate using a 12-lead ECG. Oxygen saturation (SpO_2) was monitored using a pulse oximeter. Rating of perceived exertion (RPE) on the 20-point Borg scale was collected at each stage (Borg, 1982). The reason for termination (dyspnoea, leg fatigue or other symptoms) was noted. The Vyaire Medical CPET BxB Sentry Suite™ V2.21 software was used to record data during the test. The use of a pneumotachograph allowed analysis of inspired and expired gases every 5 seconds (Datta, Normandin and Zuwallack, 2015). The participants were verbally encouraged to give their best effort and keep going until volitional termination due to exhaustion or provocation of symptoms, with the participant rating above 18 on the RPE scale. Respiratory exchange ratio (RER) >1.1 defined a maximal test. The results are displayed in the Wasserman “nine-panel plot” format (Wasserman, 1997).

Physiological parameters that were calculated by the software include the maximum amount of oxygen in millilitres consumed per minute per kilogram of body weight (VO_{2peak}), minute ventilation (VE) and the volume of CO_2 expelled per litre of air ventilated (VE/VCO_2 slope). An increase in slope indicates increased dead space ventilation in the lung, pulmonary vascular disease or pulmonary limiting disease. A negative y-intercept on the VE/VCO_2 slope is indicative of cardiac limitation. Ventilatory threshold (VT) is the point at which VCO_2 deviates from the linear relationship with VO_2. This is indicative that oxygen-independent energy systems are starting to contribute relatively more to energy production with a slight increase in blood lactate levels above resting levels. Heart rate, peripheral capillary oxygen saturation (SpO_2), and relative workload ($W.kg^{-1}$) are also measured. The dyspnoea index (VE/MVV) indicates a respiratory limitation if it approximates 100%. At peak effort, oxygen-pulse is a surrogate measure of left ventricular stroke volume. The breathing reserve is the ratio between ventilatory efficiency and maximum voluntary ventilation, calculated by 1-VE/MVV. Oxygen-pulse indicates left ventricular function, calculated by VO_{2peak}/HR_{max}. Because oxygen uptake is maximal at peak exercise, O_2-pulse is a good measure of stroke volume and used in our study (Milani et al., 2006).

6.3.4 Procedures

The potential participants were sent a link to the REDCap platform (Harris et al., 2009) containing information explaining the study, their involvement and tasks required, and the potential benefits and disadvantages of participation. A self-administered web-based questionnaire using REDCap was developed by the research team and based on literature at the time of the study. This platform was accessed through the University of the Witwatersrand. The participants names were replaced by a unique ID. Participants performed the baseline testing (as part of a previous study), and those who satisfied the inclusion criteria were eligible to participate in this intervention study. Generation of the randomisation sequence was performed. Participants were consecutively allocated to one of two groups (experimental and control groups). There was one change after the trial commenced. The participants who declined the intervention were reallocated to the control group. This was decided because there was a shortage of IMT devices at the time, and waiting would have confounded results as the time variation between tests would have been too great in the intervention group.

6.3.5 Randomisation

6.3.5.1 Sequence generation

The participants were stratified according to age and allocated to the intervention or control group with equal randomisation [1:1] by using a computer-generated list of random numbers (Randomizer, 2021).

6.3.5.2 Concealment

The participants were not informed of their allocation to the intervention group or control group. Once a potential participant was identified, the sequence was checked, and intervention was assigned accordingly.

6.3.5.3 Implementation

A separate assistant with no clinical involvement generated the random sequence. The primary researcher assessed eligibility for inclusion, enrolled the participants, assigned them according to the sequence, and administered the intervention.

6.3.6 Interventions

Participants in the intervention group were given their own Phillips Respironics Threshold IMT device and accompanying written instructions regarding the correct manner to perform the IMT. These included exhaling completely before the next inspiratory breath to avoid an increase in intrathoracic pressure, the frequency of the exercises, and a training log. Threshold training requires a specific predetermined threshold pressure to be achieved in order to open the valve and allow an inflow of air (HajGhanbari et al., 2013). A 50% to 80% target pressure resulted in significant improvements in MIP according to previous studies (HajGhanbari et al., 2013; Lorca-Santiago et al., 2020), therefore the IMT device in this study provided a consistent specific pressure starting at 50% of each participant's predetermined S-Index. A nose peg was used to prevent the initiation of the sniff reflex. The participant then continued the home-based IMT of 30 breaths once a day, five days a week, for six weeks, and kept a training diary to increase compliance. Every 10 days the participant increased the pressure on the IMT devices by increments of 10% to 60%, then 70%, and finally 80%S-Index during the 6-week study period. In two systematic reviews by HajGhanbari et al. (2013) and Lorca-Santiago et al. (2020), IMT commenced at

between 30% and 80% MIP. Progressive increases in dose were reported in some studies and not in others, all demonstrating an increase in performance post IMT. Shei (2020) suggested that IMT should load respiratory muscles in healthy athletes to illicit strengthening, thus the progression of IMT training intensity from 50% to 80% S-Index was chosen for this study (Shei, 2020). A follow-up to find out if they managed the increased pressure was done verbally or by text message. If they were unable to manage 30 breaths at the increased pressure, they were instructed to remain on the lower setting. The control group was given a report explaining their test results and advised that respiratory training may be beneficial. The athletes in the intervention group and the control group were encouraged to continue their normal athletic training and log it on the Strava Application linked to their wearable devices. After six weeks, the participants from both groups were required to repeat the lung function, S-Index test and CPET.

6.3.7 Blinding

After the participants were allocated to the groups, the researcher delivered the intervention and was no longer blinded to group allocation; however, the researcher was blinded to the execution of the intervention, which the participants performed at home. The researcher performing the outcomes assessments was blinded during the measurement but not in the interpretation of the results, therefore creating bias. Participants were blinded to their group allocation and their results while performing the tests. Data collection was standardised by consistently using measurement tools in the same setting thus avoiding measurement bias. All objective data was included, therefore minimising the impact of unblinded data analysts on the group allocation.

6.3.8 Statistical analysis

Data were analysed per-protocol, as intention-to-treat analysis would not be a valid estimate of the treatment effect when there is incomplete adherence in a study that involves only a single intervention (Hernán and Robins, 2017). Data were collected and managed using MS Excel and imported into the Statistical Package for the Social Sciences software, IBM SPSS Statistics for Mac, Version: 29.0.2.0 (20), which was used for all analyses.

The normality of data distribution was determined using the Shapiro-Wilk test. Descriptive characteristics were calculated using means and standard deviations for continuous variables and percentages and frequencies for categorical variables. Independent t-tests and paired t-tests were used to compare normally distributed parametric variables and the Mann-Witney U test and Wilcoxon Signed Rank for skewed, nonparametric continuous data. Cohen's d coefficient was used to determine the effect size. Fisher's exact tests were used to compare categorical data. Missing data for loss-to-follow up participants was excluded. No imputation was used for the missing data.

The criteria classified according to the traffic light system described by Avery et al. (2017) were used to determine feasibility. A "red light" alerts a stop to proceeding with a larger trial unless a modification to the criteria is possible. An "amber light" advises that the trial can proceed with caution. A "green light" implies that it is feasible to proceed with a larger trial (Avery et al., 2017). The classification of the criteria is described in Table 6.2.

6.3.9 Ethical considerations

Unconditional ethical clearance was provided by the University of the Witwatersrand (Certificate no. M210657). The study procedures adhered to the principles set forth in the Declaration of Helsinki, the South African Guidelines for Good Clinical Practice and the Medical Research Council. Informed consent was signed by each participant before the first test and ensured confidentiality (including protection of personal information), anonymity, permission to withdraw from the study at any point and sharing of data according to the FAIR principles (Principles, F.A.I.R., 2023). This trial was registered with the Pan-African Clinical Trials Registry no: PACTR202305590076796 (Appendix H).

6.4 Results

6.4.1 Demographic characteristics of the study sample

Eighteen endurance athletes were assessed for eligibility for the IMT study after presenting with pulmonary limitations to aerobic capacity in a previous observational

study (Figure 6.1). The intervention group (n=6) had a mean age of 49.83 ± 4.45 years, and the control group (n=7) had a mean age of 50.17 ± 3.06 years.

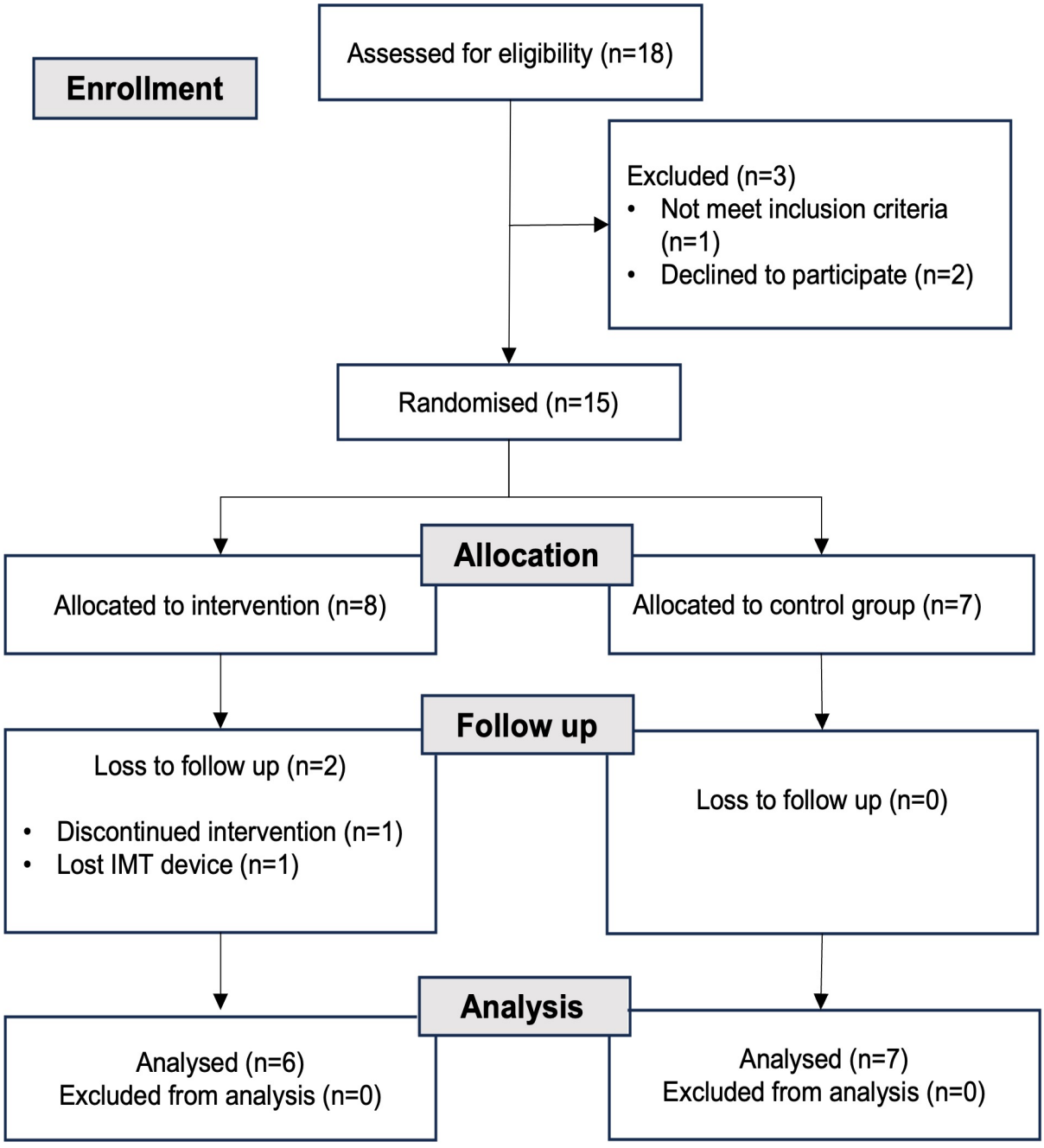


Figure 6.1 Recruitment of participants

The recruitment of participants commenced on 30 May 2022, and follow-up testing terminated on 30 April 2023. Testing commenced at a mean of 9.5 ± 3.8 months post-illness. Eight IMT devices were available at the time, therefore after eight participants had been allocated to the intervention group, the feasibility trial ended. No significant

differences in demographic and clinical characteristics between the intervention and control groups were found other than height (Table 6.1).

Table 6.1 Baseline demographic and clinical characteristics of the study sample

	Intervention group (n=6)	**Control group (n=7)**	***p*-value**
Male sex n(%)	3 (50%)	3 (42.9%)	1.000
Weight (kg)	70 ± 8.74	68.67 ± 16.05	0.602
Height (cm)	173.83 ± 5.32	166.5 ± 6.29	0.029
BMI ($kg.m^{-2}$)	24.35 (20.63; 24.49)	24.7 ± 5.09	1.000
Weeks between tests	8 (7; 9)	9 (7.75; 9)	0.836
Physical activity level (h:min)	6:04 (4:10-6:58)	5:54 (2:44; 7:01)	0.731
Months from illness to baseline test	9.5 ± 4.68	9.67 ± 3.61	0.975
Severity of illness[a]			
Mild	3 (50%)	4 (57.1%)	1.000
Moderate	3 (50%)	3 (42.9%)	1.000
Severe	0	0	
Comorbidities:			
- Anxiety	1 (16.6%)	0	0.462
- Cardiac disease	0	1 (14.3%)	0.538
- Hyper-cholesterolaemia	0	1 (14.3%)	0.538
- Hypo-thyroidism	1 (16.6%)	0	0.462

MDFI score			
- General fatigue	10.57 (6.57; 14)	10.67 ± 3.33	0.628
- Physical fatigue	8.83 ± 3.66	11 ± 2.83	0.253
- Reduced activity	7.33 ± 2.81	8.71 ± 2.93	0.406
- Reduced motivation	7.17 ± 1.6	8.29 ± 4	0.535
- Mental fatigue	10.17 ± 3.82	8.71 ± 2.98	0.457
- MDFI total	44.67 ± 13.4	47.14 ± 13.8	0.750
Symptoms at rest	1 (16.6%)	2 (28.6%)	1.000
Exertional symptoms			
- High HR	4 (66.7%)	6 (85.7%)	0.559
- Chest pain	2 (33.3%)	1 (14.3%)	0.559
- Dyspnoea	3 (50%)	3 (42.9%)	1.000
- Fatigue	5 (83.3%)	7 (100%)	0.462
- Autonomic dysregulation	2 (33.3)	1 (14.3%)	0.559

BMI: body mass index; Physical activity level based on weekly training volume (hours:minutes). [a]NIH Symptom classification: Mild: fatigue; malaise; headache; myalgia; ageusia/anosmia; cough; fever; diarrhoea; Moderate: dyspnoea with SpO_2 $\geq$94%; Severe: dyspnoea with SpO_2 <94%. Data expressed as mean ± SD, or median (interquartile range) as applicable.

6.4.2 Acceptability and adherence to the intervention

Acceptability in feasibility research assesses the response of participants to an intervention (Bowen et al., 2009). The participants, who had previously committed to a study recruiting athletes with protracted RTS post-COVID-19, were interested in a further study as they desired to improve their performance. Fifteen of the 17 eligible participants (88%) agreed to participate in the study suggesting a high acceptability rate. The nature of a pandemic implies a large number of affected patients at a particular time, thus, recruitment of athletes after future COVID-19 infections and respiratory illnesses may take longer than extrapolated from this study. Some of these participants were severely affected by COVID-19 and therefore willing to undergo comprehensive testing and interventions which may assist them feeling better while running and ultimately returning to pre-illness level of sport. The two athletes who

declined participation did so because the maximal CPET is unpleasant. Although the athletes are still required to run at maximal effort, it is more pleasant than wearing the pneumotachograph mask together with uphill running during CPET. The acceptance of the intervention gets a “green light” for the good adherence rate, however, the acceptance of the outcome measure is “amber” as adaptations may be appropriate for a RCT (Table 6.2).

Adherence was 75%; two participants dropped out of the intervention despite attempts made by the researcher to contact them via text message and telephone calls. One did not have the time they anticipated to have for the exercises, and one misplaced the device while travelling for work. This drop-out rate is similar to other studies (Collet et al., 2023; McNarry et al., 2022). The appropriateness of the intervention is good as it improved perceived dyspnoea. In summary, the satisfaction, intention to continue use and appropriateness of the intervention get a “green light” (Table 6.2). No adverse, “red light” effects were encountered during the study (Avery et al., 2017).

6.4.3 Implementation of the intervention

Outcome measures of the CPET, lung function, and S-Index tests have excellent validity and reliability (Gluckman et al., 2022; HajGhanbari et al., 2013). The Bruce Protocol has been validated by Kaminsky and Whaley (1998). The BORG CR10 scale has been validated by Scherr J *et al*. (2013). The use of cardiopulmonary exercise testing to identify respiratory impairments would be more beneficial in recruiting a sample for an IMT clinical trial than indirect performance testing. The use of the portable POWERBreathe K-device to measure S-Index is recommended for future studies. Therefore, the execution of the study was successful, and the study can be reproduced in any clinical context or community using similar tools. The data were analysed per protocol, including only the participants who were interested in the intervention and completed it without major deviations to the training protocol. This analysis allows assessment of the efficacy of the intervention under ideal conditions, which is important when planning a RCT. The results of this study may be used to estimate effect size, power, and sample size for a full RCT. The disadvantage of adapting the outcome measure would be the compromised validity and reliability of Cooper’s test compared to the CPET. In summary, the implementation of the feasibility trial received a “green light” for data analysis (Table 6.2) (Avery et al., 2017).

6.4.4 Practicality of the intervention

Practicality explores the constraints of resources, time, and commitment in conducting the study. Logistics around the lung function and CPET assessments are a potential barrier as using a single centre study design required participants to travel a distance to the site, compounded by the inconvenience of the facility only being available during office hours. This is particularly pertinent in low-income countries. Funding for the IMT devices would need to be considered, and importantly, the availability of stock of devices from the supplier. In our study, importing of the devices by the supplier ceased, and the study was terminated due to lack of stock, which was an unforeseen circumstance. The timeframe of new stock delivery was uncertain and thus became a limitation of the study. Each participant required their own filter for the CPET and for the POWERBreathe K-device. The latter is portable and could be taken to multiple sites to measure the S-Index, however, for a multisite study, purchase of an additional POWERBreathe K-device is recommended. The CPET available for use in our study was not portable. At least one qualified, responsible researcher is needed to manage these expensive machines. Participants are required to set aside some time during their day to perform their breathing exercises. All but one managed, thus, the commitment required to carry out the intervention is reasonable. In summary, practicality received an “amber light” for a full trial to go ahead, but with prior consideration of the above-mentioned barriers (Table 6.2) (Avery et al., 2017).

Table 6.2 Progression of feasibility criteria according to the traffic light system

Criteria		**Red light = STOP trial**	**Amber light = proceed with caution**	**Green light = Proceed to RCT**
Acceptability	Description	Poor recruitment rate and no rectification is possible.	88% agreed to participate and an adjustment could be made to the testing procedure in future trials	All the participants agreed to participate
	Interpretation	No	Yes	No

Adherence	Description	<75% adhered to the intervention and no rectification is possible	<75% adhered to the intervention and a modification to increase adherence could be made	> 75% adhered to the intervention similar to other studies[8]
	Interpretation	No	No	Yes
Implementation	Definition	Reliability and validity of outcome measures not reported	Amendments to outcome measures can be made to improve reliability and validity	Excellent reliability and validity of outcome measures
	Interpretation	No	No	Yes
Practicality	Definition	Time, commitment and resources constrained the success of the feasibility study and cannot be amended	Time, commitment and resources partially constrained the feasibility study but can be amended by confirming funding and stock availability	Time, commitment and resources posed no constraints on the feasibility study
	Interpretation	No	Yes	No

6.4.5 Estimated effects of IMT on cardiorespiratory fitness

During the pre-test assessment, the researcher found that one patient had been diagnosed with myocarditis and prescribed beta-blockers, and one participant had raised blood troponin levels after training. Both were cleared for exercise by their consulting physicians. All participants reached a maximum heart rate of at least 85%

maximum predicted at the termination of both tests. Dyspnoea terminated the test in n=7 (53.8%) and leg fatigue in n=6 (46.2%), with one participant complaining of dizziness and paraesthesia at maximal exertion. No adverse events occurred during the maximal exercise tests. No difference in baseline lung function or CPET between groups was found (Table 6.3). Both groups showed lung diffusion impairment as oxygen saturation fell below a mean of 6% (Halle et al., 2021), and had low breathing reserves.

Table 6.3 Baseline lung function and CPET findings

	Intervention group (n=6) Mean ± SD or median (IQR)	**Control group (n=7) Mean ± SD or median (IQR)**	***p*-value**	**Effect Size**	**95% CI of ES**
Lung function					
FVC (l)	4.11 ± 0.61	4.11 ± 0.8	0.994	0.004	-1.087 – 1.094
FEV_1 (l)	3.25 ± 0.5	3.18 ± 0.71	0.840	0.115	-0.979 - 1.204
FEV_1/FVC	79.15 ± 3.27	77.35 ± 5.53	0.501	0.387	-0.724 – 1.48
PEF ($l.min^{-1}$)	8.76 (6.4; 9.3)	8.76 (6.4; 9.3)	0.836	0	-2.65 – 2.74
MVV ($l.min^{-1}$)	113.87 ± 17.45	111.35 ± 24.97	0.840	0.115	-0.979 – 1.2-4
S-Index (cmH_2O)	88.5 ± 14.07	89.71 ± 22.93	0.912	-0.063	-1.152-1.03
CPET					
VO_{2peak} ($ml.kg.min^{-1}$)	34.37 ± 8.69	39.26 ± 8.6	0.331	-0.566	-1.669 – 0.561
VO_{2peak} % ref ($ml.kg.min^{-1}$)	125.58 ± 30.29	145.93 ± 33.36	0.277	-0.636	-1.744 – 0.499
VE/VCO_2 slope	32.98 ± 3.01	32.47 ± 2.34	0.736	0.192	-0.905 – 1.281
y-intercept ($l.min^{-1}$)	0.15 ± 3.53	0.39 ± 3.19	0.902	-0.07	-1.16 – 1.022
VE/VO_2 slope	2.57 ± 0.78	2.69 ± 0.6	0.761	-0.173	-1.262 – 0.924
RER_{max}	1.17 ± 0.05	1.15 ± 0.03	0.620	0.284	-0.819 – 1.375

VO_2 at VT ($\%VO_{2peak}$) ($ml.min^{-1}$)	67.5 ± 13.66	68.43 ± 4.54	0.868	-0.095	-1.184 – 0.999
VE_{max} ($l.min^{-1}$)	94 ± 27.62	101 ± 27.01	0.654	-0.257	-1.346 – 0.845
VE/MVV	82.61 ± 20.39	95.7 ± 27.03	0.353	-0.54	-1.641 – 0.585
HR_{max} (bpm)	173.83 ± 4.45	170.57 ± 9.24	0.448	0.438	-0.677 – 1.534
O_2-pulse $_{max}$ ($ml.bpm^{-1}$)	13.79 ± 4.31	14.88 ± 3.66	0.633	-0.273	-1.363 – 0.829
Drop in SpO_2 %	6.67 ± 2.88	6 ± 4.04	0.743	0.187	-0.91 – 1.276
RPE	19 (19; 19)	18.79 ± 0.99	0.836	0.287	-1 - 1
Workload ($W.kg^{-1}$)	4.94 ± 1.36	5 (4; 5.27)	0.731	-0.045	-1.188 – 1.229

SD: Standard deviation, IQR: interquartile range, FVC: forced vital capacity, FEV_1: forced expiratory volume in one second, PEF: peak expiratory flow, MVV: maximum voluntary ventilation, VO_2peak: maximum volume of oxygen in millilitres consumed, VE: minute ventilation, HR: heart rate, S-Index: inspiratory muscle strength index, RER: respiratory exchange ratio, RPE: rating of perceived exertion, VT: ventilatory threshold

On follow-up at six weeks, dyspnoea terminated the test in n=6 (46.2%) and leg fatigue in n=7 (53.8%). In the intervention group, one participant had been diagnosed with anaemia and four of the participants reported that they felt stronger during physical exercise and will continue the inspiratory muscle training. In the control group, one had mild dizziness at the termination of the test, and one continued to have a productive cough after exercise. When comparing the exercise adaptation of endurance athletes (Table 6.4) there is strong evidence of a process of recovery shown by improved the S-Index in the intervention group versus a decline in the control group (p=0.031, d=1.38, CI=0.124 – 2.583). The difference in RER_{max} in the intervention group declined whereas it increased in the control group, yet did not reach statistical significance (p=0.057, d=1.183, CI=-0.034 – 2.355).

Table 6.4 The difference between the intervention and control groups: change in lung function and CPET parameters from baseline to follow-up

	Change in parameters: intervention group (n=6)	Change in parameters: control group (n=7)	*p*-value	Effect size	95% CI of ES
Lung function					
FVC (l)	4.11 ± 0.61	4.11 ± 0.8	0.994	0.004	-1.087 - 1.094
FEV_1 (l)	-0.07 (-0.1; -0.03)	-0.6 ± 0.13	0.731	5.187	-0.16 – 0.11
FEV_1/FVC	0.25 (-1.17; 1.48)	0.49 (-0.47; 5.8)	0.534	0.065	-2.36 – 6.978
PEF ($l.min^{-1}$)	-0.17 (-0.39; 0.02)	-0.34 ± 0.75	0.628	0.288	-1.75 – 0.37
MVV ($l.min^{-1}$)	-2.28 (-3.5; -1.05)	-2.05 ± 4.55	0.731	0.064	-5.6 – 3.85
S-Index (cmH_2O)	18.67 ± 24.09	-7.14 ± 12.64	0.031	1.38	0.124 – 2.583
CPET					
VO_{2peak} ($ml.kg.min^{-1}$)	2.68 ± 9.37	2.64 ± 4.44	0.992	0.006	-1.085 – 1.096
VO_{2peak} % ref ($ml.kg.min^{-1}$)	7.82 ± 28.02	10 ± 17	0.868	-0.095	-1.184 – 0.998
VE/VCO_2 slope	1.27 ± 1.99	1.4 (0.75; 3.5)	0.366	-0.064	-1.3 – 5.1
y-intercept ($l.min^{-1}$)	1.05 (-0.3; 1.1)	0 ± 3.04	0.628	0.447	-5.9 -1.6
VE/VO_2 slope	0.28 ± 0.48	0.1 (0.1; 0.2)	0.628	0.548	-0.5 – 0.5
RER $_{max}$	0.02 ± 0.04	-0.03 ± 0.05	0.057	1.183	-0.034 – 2.355
VO_2 at VT ($ml.min^{-1}$)	-7 ± 17.07	-3.57 ± 13.18	0.690	-0.228	-1.317 – 0.872
VE $_{max}$ ($l.min^{-1}$)	10 ± 20.15	8 ± 13.52	0.835	0.119	-0.976 – 1.208
VE/MVV	8.82 ± 16.55	4.02 ± 20	0.650	0.26	-0.842 – 1.35

HR_{max} (bpm)	-4.5 ± 7.23	-5 (-6.5; 0)	0.945	-0.083	-12 – 9
O_2-pulse $_{max}$ ($ml.bpm^{-1}$)	1.52 ± 3.74	1.42 (0.4; 2.29)	0.628	0.037	-2.439 – 4.605
Drop in SpO_2 %	0.17 ± 3.66	0.14 ± 3.76	0.991	0.006	-1.084 – 1.097
RPE	0.5 (0; 1)	0.357 ± 1.49	0.731	0.118	-1 – 1
Workload ($W.kg^{-1}$)	0.43 ± 0.92	0 (0; 0.63)	1	0.606	-1.189 – 1.039

Data expressed as mean ± SD, or median (interquartile range) as applicable.

SD: Standard deviation, IQR: interquartile range, FVC: forced vital capacity, FEV_1: forced expiratory volume in one second, PEF: peak expiratory flow, MVV: maximum voluntary ventilation, VO_2peak: maximum volume of oxygen in millilitres consumed, VE: minute ventilation, HR: heart rate, S-Index: inspiratory muscle strength index, RER: respiratory exchange ratio, RPE: rating of perceived exertion, VT: ventilatory threshold

6.5 Discussion

This feasibility study demonstrated the acceptability, implementation, and practicality of conducting a single centre RCT implementing IMT in endurance athletes with persistent exercise intolerance following COVID-19 infection. The high recruitment rate (88%) reflects strong acceptability of the intervention among endurance athletes experiencing persistent post-COVID-19 symptoms. This supports previous findings that individuals feel proactive in addressing their recovery with perceived benefits of improved exercise capacity and reduced dyspnoea (Shelley et al., 2022). However, the discomfort associated with maximal CPET may be a barrier for some, suggesting that future studies might consider using less invasive yet still reliable testing protocols to maximise participant uptake. Adherence was moderate (75%), with dropouts attributed to practical barriers such as time constraints and logistical issues. These dropout rates align with previous IMT studies (Collet et al., 2023; McNarry et al., 2022).

Adaptation focuses on changing the procedures to be more appropriate for the study population. In this study, the change in VO_{2peak} and ventilatory efficiency did not reach statistical significance, and it was proposed that a type 2 error occurred due to the small sample size. Another explanation is that an incremental, maximal test does not offer the time to adjust to the workload and reaches a metabolically unsustainable

point. Romer et al. (2002) conducted a double-blind RCT of 16 cyclists and found that inspiratory muscle strength and time trial test improved significantly in the intervention group with no difference in maximal exercise performance. Thus, differences at maximal exertion are likely to be small and similarly a lack of statistical power can create a type 2 error. Direct measure of aerobic capacity such as the maximal CPET have excellent internal validity, however, may lack the external validity of a sustained submaximal test, such as the timed Cooper's or Shuttle test relevant for long-distance athletes (Wells and Norris, 2009). Additionally, this could be expanded to a multicentre RCT to reduce researchers and participants need to travel to a single testing site. The need for single-site testing limited accessibility, particularly where travel and scheduling flexibility were restricted. This challenge is especially pronounced in resource-constrained settings or low-income countries. Device availability also proved problematic, with cessation of imports resulting in study termination, highlighting the need for secured supply chains and contingency planning in future trials.

The intervention was safe and well tolerated, with all participants achieving at least 85% of their age-predicted maximal heart rate, indicative of adequate exertion. While no between-group differences were observed in baseline lung function or CPET variables, improved S-Index in the intervention group provides preliminary evidence of physiological benefit from IMT. This implies that the intervention effectively improved recovery of respiratory muscle strength, concurring with results in recent post-COVID studies on non-athletes (Shelley et al., 2022; McNarry, et al., 2022; Collet et al., 2023). In the meta-analysis by HajGhanbari et al. (2013) it was found that MIP improved after RMT with greater improvement in endurance sport athletes. In athletes, VO_{2peak} is expected to be greater than 100% of the reference for healthy adults, and was true for all athletes except one in the intervention group. HajGhanbari et al. (2013) found no significant difference in VO_{2peak} after RMT, in agreement with our study. The same study found that swimmers showed the least change in performance after RMT, possibly due to inherent respiratory muscle training against water pressure, suggesting that there will be responders and non-responders to an intervention and sports performance should be highly individualised. Both groups continued physical exercise, a mandatory component of a study on an athletic sample and do not confound results because athletes will ordinarily face respiratory muscle fatigue with increased demand on the musculoskeletal system. Our sample had a broad range of

baseline VO_{2peak} and S-Index values, and where the IMT prescription was based on the baseline S-Index, baseline VO_{2peak} was not considered.

The VE/VCO_2 slope was raised in both groups. Values greater than 34 may indicate pulmonary vascular disease or cardiac or mitochondrial dysfunction creating hyperventilation. These values continued to rise in both groups at follow-up. Most results had a positive y-intercept of the slope, indicating pulmonary rather than cardiac involvement. Ventilatory thresholds fell just below the normal range for athletes (70-80%) at baseline and further declined in both groups. This is evident in impaired skeletal muscle oxygen extraction, indicating mitochondrial dysfunction in skeletal muscle. Arterial CO_2 becomes raised, lowering the pH, and through this chemosensitivity stimulates the metaboreflex responsible for hyperventilation and the increase in VE/VCO_2 slope (HajGhanbari et al., 2013). The dyspnoea index is high in both groups (>80%), indicating pulmonary limitations to aerobic capacity, more so in the control group at 96%. The dyspnoea index continued to increase in both groups, which together with normal resting lung function and supranormal VO_{2peak}, is indicative of a normal physiological response to high-intensity exercise by well-trained athletes (Moulson et al., 2022). The feasibility study supports the implementation of the intervention and while the effect size of preliminary data is compromised by the small sample, progression to an RCT is feasible.

6.5.1 Limitations

The information provided noted that exercises would follow the baseline test, therefore the participants could determine which group they had been allocated to. The implementation of the intervention has certain limitations. As the % S-Index increases, breathing patterns and quality of inspiratory manoeuvre can be compromised. The IMT was carried out at home therefore the technique was not observed to ensure full inspiratory manoeuvres from residual volume to total lung capacity. Missing data for two participants occurred due to non-adherence to the IMT intervention. Although travel to the study site was required, assistance with transport costs was offered to avoid the exclusion of participants due to socioeconomic constraints. Limitations of per protocol analysis include selection bias in that a particular kind of participant may have agreed to participate in the intervention group, potentially overestimating the treatment effect. Training load will confound results as athletes training at higher loads are likely

to show better performance results. Other confounding factors such motivational factors, nutrition, sleep, and environmental factors exists. The use of Cooper's test to estimate VO_{2peak} at a single site such as a running club could be much simpler to implement and time effective for a large group. Some values may not have reached statistical significance due to the small sample size, thus, a full trial testing the same parameters is recommended with a sample of at least 50 participants in each group. This sample size calculation was based on VO_{2peak} (ml.kg.min^{-1}) outcome measure (Intervention group 34.37ml.kg.min^{-1} ± 8.69; Control group 39.26 ± 8.6 ml.kg.min^{-1}) with an alpha of 0.05, a power of 80% and an enrolment ratio of 1, however, results other outcome measures will reveal different sample size requirements.

6.5.2 Strengths

Performing a per-protocol analysis eliminates selection bias by excluding participants from the intervention group who did not fully adhere to the intervention, which is critical for estimating treatment effectiveness in ideal conditions (Hernan and Robins, 2017). This approach enhances study generalisability to real-world scenarios as opposed to the intention-to-treat analysis, which reflects the effectiveness in ideal practice. By reallocating non-adherent participants to the control group for baseline and follow-up testing, confounding of results was minimised. Although no pre-illness data are available, a strength of this study is that the sample consisted of previously healthy athletes who continue to experience protracted exercise tolerance following COVID-19.

6.5.3 Generalisability

Due to the small sample size, the study results can only be generalised to a similar population of masters age-group endurance athletes in a similar area and performing the same intervention at the same dose.

6.6 Conclusions

Restoring respiratory function and exercise capacity is crucial to achieving pre-COVID-19 levels of performance in endurance sports. This feasibility study has identified facilitators as green lights and potential barriers as amber lights to guide important

evidence-based trials in the future. The intervention was effective in improving the S-Index in masters age-group athletes who had previously experienced COVID-19. The intervention was moderately acceptable to endurance athletes, as a larger number consenting to participate would have been preferable, and modifications to the testing procedure could be considered for future trials. Implementation using the single-centre outcome measures was excellent, as they demonstrated good consistency and reliability. Practicality requires moderate adaptation of outcome measures that are more time efficient and reflect endurance performance more accurately than the maximal CPET. Both acceptability and practicality could be increased by using a portable CPET machine or conducting a Cooper's test to estimate VO_{2peak}. Before trials with a larger sample size take place in the future, consideration of funding and stock availability of IMT devices and filters is important.

6.7 Interpretation and recommendations

Inspiratory muscle training improved respiratory muscle strength in this group of master-age endurance athletes. Commencing IMT immediately after recovery from acute COVID-19 may prevent long-term limitations to aerobic capacity after respiratory illnesses. Future trials should consider funding and stock availability of IMT devices and filters, and travel costs of researchers and participants. CPET assessments at a single location are both timeous sacrifices for the researcher and participant. A single or multicentre study using a portable CPET machine or conducting a Cooper's test to estimate VO_{2peak} will be more practical and acceptable for a large sample size.

6.8 Registration

This trial is registered with the Pan-African Clinical Trials Registry no: PACTR202305590076796.

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6.9 References

1. ATS/ERS Statement on Respiratory Muscle Testing. (2002). *American Journal of Respiratory and Critical Care Medicine*, 166(4), 518–624. https://doi.org/10.1164/rccm.166.4.518
2. Avery, K. N. L., Williamson, P. R., Gamble, C., Francischetto, E. O. C., Metcalfe, C., Davidson, P., Williams, H., Blazeby, J. M., Blencowe, N., Bugge, C., Campbell, M., Collinson, M., Cooper, C., Darbyshire, J., Dimairo, M., Doré, C., Eldridge, S., Farrin, A., Foster, N., … Treweek, S. (2017). Informing efficient randomised controlled trials: Exploration of challenges in developing progression criteria for internal pilot studies. *BMJ Open*, 7(2). https://doi.org/10.1136/bmjopen-2016-013537
3. Borg GA. (1982). Psychophysical bases of perceived exertion. *Medicine and Science in Sport and Exercise*, 14(5), 377–381. PMID: 7154893
4. Bowen, D. J., Kreuter, M., Spring, B., Cofta-Woerpel, L., Linnan, L., Weiner, D., Bakken, S., Kaplan, C. P., Squiers, L., Fabrizio, C., & Fernandez, M. (2009). How We Design Feasibility Studies. *American Journal of Preventive Medicine,* 36(5), 452–457. https://doi.org/10.1016/j.amepre.2009.02.002
5. Braga, F., Domecg, F., Kalichsztein, M., Nobre, G., Kezen, J., Espinosa, G., Prado, C., Facio, M., Moraes, G., Gottlieb, I., Lima, R. L., Danielian, A., & Emery, M. S. (2023). Abnormal exercise adaptation after varying severities of COVID-19: A controlled cross-sectional analysis of 392 survivors. *European Journal of Sport Science*, 23(5), 829–839. https://doi.org/10.1080/17461391.2022.2054363
6. Collet, R., Van Egmond, M., Van der Schaaf, M., & Major, M. (2023). Feasibility of inspiratory muscle training for patients with persistent dyspnoea after COVID-19 infection: A pilot study. *Journal of Rehabilitation Medicine-Clinical Communications*, 6. https://doi.org/10.2340/jrmcc.v6.6507

7. COVID-19 Treatment Guidelines. (2023). *NIH: Clinical spectrum of SARS-CoV-2 infection*. Accessed 13 February 2013. https://www.covid19treatmentguidelines.nih.gov/
8. Datta, D., Normandin, E., & Zuwallack, R. (2015). Cardiopulmonary exercise testing in the assessment of exertional dyspnea. *Annals of Thoracic Medicine,* 10(2), 77–86. https://doi.org/10.4103/1817-1737.151438
9. Eldridge, S. M., Chan, C. L., Campbell, M. J., Bond, C. M., Hopewell, S., Thabane, L., Lancaster, G. A., Altman, D., Bretz, F., Campbell, M., Cobo, E., Craig, P., Davidson, P., Groves, T., Gumedze, F., Hewison, J., Hirst, A., Hoddinott, P., Lamb, S. E., … Tugwell, P. (2016). CONSORT 2010 statement: Extension to randomised pilot and feasibility trials. *The BMJ*, 355. https://doi.org/10.1136/bmj.i5239
10. Fletcher, G. F., Balady, G. J., Amsterdam, E. A., Chaitman, B., Eckel, R., Fleg, J., Froelicher, V. F., Leon, A. S., Piña, I. L., Rodney, R., Simons-Morton, D. G., Williams, M. A., & Bazzarre, T. (2001). Exercise Standards for Testing and Training A Statement for Healthcare Professionals From the American Heart Association. *Circulation*, 104(14), 1694-1740. https://doi.org/10.1161/hc3901.095960
11. HajGhanbari, B., Yamabayashi, C., Buna, T. R., Coelho, J. D., Freedman, K. D., Morton, T. A., ... & Reid, W. D. (2013). Effects of respiratory muscle training on performance in athletes: a systematic review with meta-analyses. *The Journal of Strength & Conditioning Research*, 27(6), 1643-1663. https://doi.org/10.1519/jsc.0b013e318269f73f
12. Halle, M., Binzenhöfer, L., Mahrholdt, H., Johannes Schindler, M., Esefeld, K., & Tschöpe, C. (2021). Myocarditis in athletes: A clinical perspective. In *European Journal of Preventive Cardiology,* 28(10), 1050–1057. https://doi.org/10.1177/2047487320909670
13. Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, *42*(2), 377–381. https://doi.org/10.1016/j.jbi.2008.08.010
14. Hernán, M. A., & Robins, J. M. (2017). Per-Protocol Analyses of Pragmatic Trials. In *New England Journal of Medicine,* 377(14), 1391-1398.
15. Jimeno-Almazán, A., Buendía-Romero, Á., Martínez-Cava, A., Franco-López, F., Sánchez-Alcaraz, B. J., Courel-Ibáñez, J., & Pallarés, J. G. (2023). Effects of a concurrent training, respiratory muscle exercise, and selfmanagement recommendations on recovery from post-COVID-19 conditions: the RECOVE trial.

Journal of Applied Physiology, 134(1), 95–104. https://doi.org/10.1152/japplphysiol.00489.2022

16. Kaminsky, L. A., Harber, M. P., Imboden, M. T., Arena, R., & Myers, J. (2018). Peak ventilation reference standards from exercise testing: From the FRIEND registry. *Medicine and Science in Sports and Exercise*, 50(12), 2603–2608. https://doi.org/10.1249/MSS.0000000000001740
17. Kaminsky, L.A. and Whaley, M.H., 1998. Evaluation of a new standardized ramp protocol: the BSU/Bruce Ramp protocol. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *18*(6), 438-444. https://doi.org/10.1097/00008483-199811000-00006.
18. Lorca-Santiago, J., Jimenez, S. L., Pareja-Galeano, H., & Lorenzo, A. (2020). Inspiratory muscle training in intermittent sports modalities: A systematic review. *International Journal of Environmental Research and Public Health,* 17(4448). https://doi.org/10.3390/ijerph17124448
19. Mackała, K., Kurzaj, M., Okrzymowska, P., Stodółka, J., Coh, M., & Rożek-Piechura, K. (2020). The effect of respiratory muscle training on the pulmonary function, lung ventilation, and endurance performance of young soccer players. *International Journal of Environmental Research and Public Health*, 17(1). https://doi.org/10.3390/ijerph17010234
20. McConnell AK, R. L. (2003). Respiratory muscle training in healthy humans: Resolving the controversy. *International Journal of Sports Medicine*, 25(04), 284-293. https://doi.org/10.1055/s-2004-815827
21. McNarry, M. A., Berg, R. M. G., Shelley, J., Hudson, J., Saynor, Z. L., Duckers, J., Lewis, K., Davies, G. A., & Mackintosh, K. A. (2022). Inspiratory muscle training enhances recovery post-COVID-19: a randomised controlled trial. *European Respiratory Journal*, 60(4). https://doi.org/10.1183/13993003.03101-2021
22. Mezzani, A. (2017). Cardiopulmonary exercise testing: Basics of methodology and measurements. *Annals of the American Thoracic Society*, 14, S3–S11. https://doi.org/10.1513/AnnalsATS.201612-997FR
23. Milani, R. V., Lavie, C. J., Mehra, M. R., & Ventura, H. O. (2006). Understanding the Basics of Cardiopulmonary Exercise Testing. In *Mayo Clinic Proceedings,* 81(12), 1603-1611. https://doi.org/10.4065/81.12.1603
24. Moulson, N., Gustus, S. K., Scirica, C., Petek, B. J., Vanatta, C., Churchill, T. W., Guseh, J. S., Baggish, A., & Wasfy, M. M. (2022). Diagnostic evaluation and cardiopulmonary exercise test findings in young athletes with persistent symptoms

following COVID-19. *British Journal of Sports Medicine*, 56(16), 927–932. https://doi.org/10.1136/bjsports-2021-105157

25. National Institute for Communicable Diseases. (2021). *NICD*. National Institute for Communicable Diseases. https://nicd.ac.za. Accessed 3 November 2021
26. NICE. (2021). *Covid19 Rapid Guideline: Managing the long-term Effects of Covid19*. National Institute for Health and Care Excellence (NICE) SIGN (SIGN) and CR of GP (RCGP). https://www.nice.org.uk/guidance/ng188. Accessed 8 February 2023.
27. Principles, F.A.I.R., *GO FAIR*, https://www.go-fair.org/fairprinciples/. Accessed 13 May 2023
28. Randomizer. (2021). *Randomizer*. https://www.randomizer.org. Accessed 3 April 2021.
29. Romer, L. M., McConnell, A. K., & Jones, D. A. (2002). Inspiratory muscle fatigue in trained cyclists: effects of inspiratory muscle training. *Medicine and Science in Sports and Exercise*. (34), 785-792. https://doi.org/10.1097/00005768-200205000-00010
30. Scherr, J., Wolfarth, B., Christle, J.W., Pressler, A., Wagenpfeil, S. & Halle, M., 2013. Associations between Borg's rating of perceived exertion and physiological measures of exercise intensity. *European Journal of Applied Physiology*, 113, 147-155. https://doi.org/10.1007/s00421-012-2421-x
31. Severin, R., Arena, R., Lavie, C. J., Bond, S., & Phillips, S. A. (2020). Respiratory Muscle Performance Screening for Infectious Disease Management Following COVID-19: A Highly Pressurized Situation. *American Journal of Medicine*, 133(9), 1025–1032. https://doi.org/10.1016/j.amjmed.2020.04.003
32. Shei, R. (2020). Training load influences the response to inspiratory muscle training. *Journal of Science and Medicine in Sport,* 19, 772-773. PMID: 33239952
33. Shelley, J., Hudson, J., Mackintosh, K. A., Saynor, Z. L., Duckers, J., Lewis, K., Davies, G. A., Berg, R. M. G., & McNarry, M. A. (2022). Perceptions of inspiratory muscle training in adults recovering from COVID-19. *PLoS ONE*, *17* (11 November). https://doi.org/10.1371/journal.pone.0270620
34. Smets, E. M. A., Garssen, B., Bonke, B.D., & De Haes, J. C. J. M. (1995). The multidimensional fatigue inventory (mfi) psychometric qualities of an instrument to assess fatigue. In *Journal of Psychosomatic Research,* 39(5), 315-325. https://doi.org/10.1016/0022-3999(94)00125-O
35. Wasserman, K. (1997). Diagnosing Cardiovascular and Lung Pathophysiology From Exercise Gas Exchange. *Chest*, 112(4), 1091–1101. https://doi.org/10.1378/chest.112.4.1091

36. Wells, G. D., & Norris, S. R. (2009). Assessment of physiological capacities of elite athletes & respiratory limitations to exercise performance. *Paediatric Respiratory Reviews*, 10(3), 91-98. https://doi.org/10.1016/j.prrv.2009.04.002

6.10 Change to the outcomes explained further

There was a change to the outcomes after trial commenced: The control group was going to be given the opportunity to receive RMT after the study, however due to a shortage of devices (Figure 5.2) and some of those participants unwilling to perform the RMT, that option was not given to the control group. The participants had been blinded to the group allocation, thus was not disadvantaged by this decision. All the participants (exposure and control groups) from both Study 3 and Study 4 were given a report containing their lung function, S-Index and CPET results and an explanation of what the parameters mean. If limitations to their exercise capacity were identified, advice regarding exercises or further investigations was given.



Figure 6.2 The Threshold IMT device used for the intervention

Chapter 7 Conclusion and Recommendations

7.1 Conclusion

The primary objective of this research was to investigate the overall physiological and psychological impact of COVID-19 on endurance athletes' return to pre-illness level of participation utilizing the biopsychosocial theoretical framework. The study commenced by examining the severity and symptoms of the initial illness. It was expanded to consider athletes' RTS by exploring exertional symptoms experienced, the challenges faced in returning to sport, and how they managed their return. The impact of COVID-19 on the endurance athletes' quality of life could thus be reported within the biopsychosocial framework. To further investigate exercise intolerance, cardiorespiratory fitness was tested using CPET related variables, which allowed identification of limitations to their exercise capacity. A control group was enrolled because no pre-COVID-19 data, nor published norms for South African endurance athletes over the age of 35 years existed. The lung function and CPET tests revealed that some athletes suffered from low aerobic capacity and respiratory limitations. A sample of athletes was invited to partake in an intervention trial to determine the feasibility of conducting a RCT investigating the effectiveness of IMT in improving exercise tolerance.

Almost one-third of the endurance athletes in this study had not returned to their pre-illness level of sport, the reason for which was predominantly biological. The athletes with protracted RTS had worse illness severity, fatigue and cardiovascular sequalae than those who has RTS, and that described in many other studies. This could possibly be due to this study's higher average age of 45 years. The observation that older recreational athletes displayed persistent impairments in VO_{2peak}, the S-Index, and oxygen saturation during exertion supports the growing evidence that age is a significant factor in post-COVID-19 recovery. As aerobic capacity and respiratory muscle strength naturally decline with age, these athletes may be less resilient to viral-induced physiological stress. This suggests a need for age-tailored rehabilitation protocols, particularly for master athletes who often compete at high levels despite age-related changes.

The athletes with protracted RTS exhibited poorer exercise performance as they trained fewer hours and had reduced their running pace and cycling power. They cited more symptoms at rest, and elevated heart rate, chest pain, fatigue, and dyspnoea when resuming training. The likelihood of returning to sport decreased with higher physical fatigue scores, which is unsurprising given that physical fatigue naturally impairs physical exertion. These findings suggest incomplete recovery even in previously healthy and active individuals. Some limitations that may not be detected through resting assessments alone but become apparent under stress, such as during CPET. This highlights the importance of exercise-based diagnostics.

The presence of exertional symptoms implies that many athletes had resumed training while still feeling unwell. According to the published RTS criteria, athletes should be symptom free before resuming sport after COVID-19, and their clinical assessments should be clear (Gluckman et al., 2022). This hopefully explains why athletes that were still experiencing symptoms at rest, had not returned to their pre-illness level of sport. Either the unpleasantness of the symptoms discouraged the athlete from exercising, or they were advised against it by healthcare professionals. However, those citing exertional symptoms are a concern, indicating that cardiopulmonary consequences may be under reported in endurance athletes. These findings suggest that some athletes continue to experience persistent physiological impairments that warrant further investigation. Encouraging routine follow-up for those with lingering symptoms could help prevent complications and ensure a safe RTS.

The results of the third study that assessed 57 endurance athletes with exercise intolerance found reduced VO_{2peak} and S-Index. This may be the result of both viral injury and deconditioning due to prolonged inactivity during illness and recovery. After eight weeks of endurance training, improvements were observed in the COVID-19 group's respiratory function on CPET, including increases in VO_{2peak} and S-Index, compared to the control group. Older athletes may take longer to regain pre-illness performance levels, suggesting that structured reconditioning programs are needed. Endurance sports commonly attract recreational athletes over 35 years of age, a population that often performs at a competitive level despite age-related declines in muscle strength and mass. Ventilatory threshold and workload remained low at follow-up, which may reflect ongoing limitations in oxygen extraction by the skeletal muscle system. This could potentially contribute to delayed RTS observed in this cohort.

Including inspiratory muscle training (IMT) together with their progressive endurance training programs may help mitigate this decline as restoring respiratory function is crucial to achieving pre-illness levels exercise capacity in endurance sports. The fourth study assessed the feasibility of conducting a single-centre parallel-group RCT to determine the effect of IMT on exercise capacity in masters age-group endurance athletes. Feasibility was crucial when designing interventions for older, competitive athletes who may juggle training, work, and family commitments. The intervention was well-tolerated by endurance athletes and a significant increase in inspiratory muscle strength was observed in the intervention group. Although the intervention showed promise, and the implementation of outcome measures demonstrated good consistency and reliability, the need for maximal exertion in the CPET protocol may have limited participant enrolment. This highlights the importance of adaptable protocols in future large-scale trials. Incorporating remote assessment tools**,** multi-centre collaboration**,** and inclusion criteria determined by comorbidities or level of sports participation could enhance generalisability and the clinical relevance.

The experience of endurance athletes recovering from COVID-19 highlights the complex and ways in which physical and mental health factors intersect. Physical health is complicated by psychological issues such as depression and anxiety causing management to be more difficult (Córdova-Martínez et al., 2022). While the qualitative data were analysed within the deductive framework of the biopsychosocial model, inductive coding of the responses was appropriate to discover new aspects of this novel disease. The qualitative results revealed testimonies of cardiopulmonary consequences, emotional distress, anxiety, reduced motivation, and lack of social engagement. Because running improves mood and is an important coping skill, these athletes were starting to suffer from anxiety and depression. The participants in this study lacked motivation, felt disappointed in themselves and were frustrated with long-term fatigue. This severely suppressed their enjoyment of sport and, subsequently, their quality of life. Musculoskeletal injury and fear of failure once competition resumes are concerns that all athletes face after time away from sport due to injury or illness (Salles et al., 2023). For endurance athletes whose goals are often months away and whose training is largely self-directed, these fears may be intensified compared to team sport athletes who participate in regular matches. Introducing a mental health outcome into physical rehabilitation programs may be beneficial.

One of the most intriguing and unexpected findings is the positive association between higher mental fatigue and RTS**.** While fatigue typically hinders performance, this outcome suggests that mental exhaustion may have acted as a motivator. The mental health benefits of exercise, and particularly running, is well documented (Oswald et al., 2020). Endurance athletes, who are generally self-motivated and goal-oriented, may be more likely to turn to exercise as a coping mechanism to improve mood, reduce anxiety and increase emotional resilience, especially in the absence of other support structures during the pandemic. This reveals the concept of exercise as therapy, where initiation of exercise post-COVID-19 is vital particularly for individuals whose identity and routine are closely tied to their athletic pursuits.

Athletes in this study longed for the social community of running that provided a source of encouragement and emotional support. The training community forms an important part of their training structure which increases the adherence to training. Participation was not only affected by long-COVID, but by lock-down measures which place additional restrictions on all gatherings and events. The social engagement of group training increases motivation to attend training sessions and optimal performance during the session. Athletic community networks such as WhatsApp groups offer platforms for peer interaction that fosters both camaraderie and motivation. Important interpersonal relationships develop through shared experiences, and valuable friendships and support structures grow. However, the social dynamics of group training can also create pressure to exercise while still symptomatic, which should be cautioned against. For many endurance athletes, athletic performance may be tied to self-worth and identity, therefore being unable to participate at their previous level of sport may further supress their enjoyment of sport and self-esteem.

Safety while training for endurance sports, particularly running and cycling are important concerns for South Africans. As a result, training in groups and often at the group's pace, and duration may be the only viable option, as training alone may be unsafe. This further delays the resumption of sport and amplifies anxiety and frustration associated with protracted RTS. The profound psychological and social impact of COVID-19 experienced by athletes were a novel finding of this research. The integration of the quantitative and qualitative data concluded that the quality of life of

endurance athletes deteriorated after having COVID-19 due to the protracted resumption of sport.

7.2 Clinical/Practical Recommendations

The results of this study suggest that coaches and sports medicine professionals should consider comorbidities and post-COVID sequalae while building an athlete's training load. While the use of wearable devices has certain limitations such as recording inaccuracies and variation between brands, they may be helpful to inform training load increases. Athletes are already using technology to track athletic activities therefore, the same system can ensure that pacing, intensity, duration and frequency is controlled (Pillay et al., 2020). The ability to monitor HR will increase awareness in athletes for safe RTS, but persistent cardiopulmonary symptoms should always be investigated. It remains essential to thoroughly investigate the reason for any endurance athlete experiencing cardiopulmonary exertional symptoms and exercise intolerance following respiratory illnesses, particularly using exertional tests such as CPET. In Study 3, some comparisons failed to reach statistical significance, however, the clinical significance of cardiopulmonary impairments in an athlete population is notable. A multidisciplinary team including the primary care physician, specialists (e.g. pulmonologist, cardiologist, neurologist, rheumatologist), social worker, psychologist, and physiotherapists may be required to tackle the multifactorial presentations (Gluckman et al., 2022).

Physical activity at low intensity is the only known way to restore mitochondrial health, so athlete training programs should consider this together with the prolonged healing time that may be required. Endurance exercise of at least five hours per week has been shown to double the mitochondrial enzymes in 12 weeks (San-Millán, 2023). This suggests a need for age-tailored rehabilitation protocols, particularly for master athletes who often compete at high levels despite age-related changes. Resumption of physical activity is recommended even in those diagnosed with cardiac consequences, rather than abstaining from exercise (Kaiser-Nielsen et al., 20217). Thus, both pulmonary and extrapulmonary limitations need to be managed. Including inspiratory muscle training (IMT) together with their progressive endurance training programs may help mitigate this decline as restoring respiratory function is crucial to achieving pre-illness levels exercise capacity in endurance sports. If IMT was

introduced shortly after recovery from acute COVID-19, the benefits may be more remarkable. Inspiratory muscle training can be performed by sub-speciality therapists if athletes come from under-resourced, low-income populations (Parker et al., 2021).

Depending on the geographical region, political situation and infection rates, access to healthcare facilities may be difficult. Tele-rehabilitation can include remote consultations with clinicians, and psychological counselling, which may work particularly well in some populations and areas in South Africa. It allows therapy to be delivered remotely, reducing the need for direct patient contact and travel between regions, and is generally more cost-effective than in-person consultations (Pillay et al., 2020). Social media platforms can be used to teach respiratory rehabilitation, physical exercises, and conduct mental health assessments. These platforms can be used constructively to improve social engagement and motivation. Introducing a mental health outcome into physical rehabilitation programs may be beneficial.

7.3 Recommendation for Future Research

The quantification of subjective descriptions of fatigue, and the differentiation between types of fatigue using the MDFI were a strength of this study. It is recommended for future athletic research investigating illness, training load or psychological stress, especially when athletes report subjective fatigue or low exercise tolerance despite normal objective measures of performance (Smets et al., 1995). The MDFI is quick to complete and non-invasive, and therefore well suited for longitudinal monitoring. Because the results of this study found significant anxiety and depression post-COVID-19, future studies investigating similar outcomes after respiratory illnesses in athletes could implement a psychometrically tested, validated instrument to measure mental health, especially an anxiety or depression scale. There was minimal quantitative data compared to the volume of qualitative data retrieved concerning the social impact of COVID-19, suggesting that this is an important factor in informing RTS in an endurance athlete population and, therefore, obtaining more quantitative data is recommended in further research. With 308 participants responding to four open-ended questions, there was a considerable amount of information gained, and a myriad of concerns raised. Future studies could employ focus groups to further explore the challenges. Including inspiratory muscle training (IMT) together with their progressive endurance training

programs may help mitigate this decline as restoring respiratory function is crucial to achieving pre-illness levels exercise capacity in endurance sports.

The results of the cohort study could be combined in a systematic review where analysing combined data could prove more statistically significant. This study found pulmonary and extra-pulmonary limitations to exercise capacity remained after endurance training had resumed, suggesting that the reason for the limitations is not the detraining effect of resting during the acute illness phase. Further research is recommended to determine whether interventions targeted to either the pulmonary or extra-pulmonary limitation will facilitate the return to pre-illness level of sport. To explore the option of pulmonary rehabilitation, a feasibility trial of inspiratory muscle training followed the cohort study and proposed alterations that could be employed for future research design of a single-centre or multi-centre randomised controlled trial with a larger sample size. The use of a portable CPET machine or conducting a Cooper's test to estimate VO_{2peak} will be more practical and acceptable for a larger sample size. Before trials take place in the future, consideration of funding and stock availability of IMT devices and filters is important.

7.4 Limitations of the study

As is customary for research, certain limitations exist. Limitations of the survey used in Study 1 and 2 include snowball sampling that did not allow a response rate to be calculated and reduced the power of the study. The participant's responses relied on retrospective recall (recall bias) which may have resulted in inaccurate reporting or exaggerating severe symptoms versus underreporting mild symptoms. The period from illness to the time of the study varied between participants, potentially introducing responses that were based on current health or social situations. This inconsistency may have reduced reliability of the results. Some athletes may have been in the acute or subacute stage of the disease, while many took part in the study months afterwards. Similarly, participants would have been infected by a range of viral strains. The validity of the survey, which was my own instrument and had not been psychometrically tested is a limitation of these two studies. Because post-viral fatigue occurred in previous viral strains, it was an expected barrier to RTS (Hughes et al., 2021). Therefore, a validated fatigue scale (the MDFI) was included in the survey. The prevalence of anxiety and depression and the hindrance it played to RTS was a finding brought to light by the

research results. Had this been anticipated, a psychometrically tested instrument to assess anxiety and depression could have been included and increased the generalisability of the psychological impact of COVID-19 on endurance athletes. These limitations were unavoidable with the current knowledge at the time of the study.

A limitation of the prospective cohort study is that comparisons could not be made to pre-illness lung function and CPET, as that data did not exist. Comparisons to the control group suggest that the observed differences were likely attributed to COVID-19 infection, however, the control group also experienced the stress of the pandemic and lockdown restrictions that may have affected their exercise capacity and potentially led to a negative bias in their results. Several comparisons did not reach statistical significance, which was likely due to the small sample size and the wide range of cardiorespiratory fitness of the athletes included in the sample. From Study 3, the sample for Study 4 was recruited. The potential for selection bias exists, as certain types of participants may have been more likely to agree to participate in the intervention group, potentially overestimating the treatment effect. This became a limitation of the per-protocol analysis that was performed. Due to the limited availability of IMT devices at the time, only eight participants were assigned to the intervention group thus concluding the recruitment into the feasibility trial at that point.

7.5 Strengths of the study

The studies in this thesis investigated the RTS after COVID-19 in an athlete population that constitutes the bulk of the field in mass participation events such a marathon running yet has had little investigation. These athletes are primarily in the masters age-group (>35 years), and the prevalence of pre-existing comorbidities is greater than young elite athletes. In South Africa, long-distance running attracts athletes from all socioeconomic groups, and this study disseminated by snowball sampling allowed participation from all who had internet access. Endurance athletes train at high volumes and increasingly more athletes are competing at high levels in their age-group. They require the ability to resist fatigue therefore, the study included a psychometrically tested fatigue score. Fatigue, participation, and general well-being are all associated with quality of life. While some became anxious and depressed through lack of participation, others pushed themselves to exercise while feeling

unwell. The findings of these studies provided insight into the diversity of challenges that endurance athletes face in RTS.

COVID-19 still abounds as the current Omicron variant continues to mutate (Tracking SARS-CoV-2 variants, 2025). Knowledge gained about the management of respiratory illnesses is highly valuable as these remain the leading cause of time away from sport. Determining the limitations to exercise capacity gives a comprehensive assessment of the athlete's condition and allows structured and targeted rehabilitation. Because the impact on the respiratory system is especially pertinent for endurance athletes doing many hours of aerobic exercise, IMT is a likely option for rehabilitation. The studies in this thesis may improve outcomes after future respiratory illnesses and can be applied to future situations that result in a long-term sport hiatus. Lest we forget the devastating effects of the COVID-19 pandemic, it is imperative that we communicate the vast knowledge that we have gained to athletes, coaches and sports practitioners both nationally and internationally.

7.6 References

1. Barker-Davies, R. M., O'Sullivan, O., Senaratne, K. P. P., Baker, P., Cranley, M., Dharm-Datta, S., ... & Bahadur, S. (2020). The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *British Journal of Sports Medicine*, 54(16), 949-959. https://doi.org/10.1136/bjsports-2020-102596
2. Córdova-Martínez, A., Caballero-García, A., Roche, E., Pérez-Valdecantos, D., & Noriega, D. C. (2022). Effects and causes of detraining in athletes due to COVID-19: A review. *International Journal of Environmental Research and Public Health*, 19(9), 5400. https://doi.org/10.3390/ijerph19095400
3. Gluckman, T. J., Bhave, N. M., Allen, L. A., Chung, E. H., Spatz, E. S., ... & Verma, A. K. (2022). 2022 ACC expert consensus decision pathway on cardiovascular sequelae of COVID-19 in adults: myocarditis and other myocardial involvement, post-acute sequelae of SARS-CoV-2 infection, and return to play: a report of the American College of Cardiology Solution Set Oversight Committee. *Journal of the American College of Cardiology*, 79(17), 1717-1756. https://doi.org/10.1016/j.jacc.2022.02.003

4. Hughes, D. C., Orchard, J. W., Partridge, E. M., La Gerche, A., & Broderick, C. (2022). Return to exercise post-COVID-19 infection: A pragmatic approach in mid-2022. *Journal of Science and Medicine in Sport*, 25(7), 544-547. https://doi.org/10.1016/j.jsams.2022.06.00
5. Joyner, M. J., & Coyle, E. F. (2008). Endurance exercise performance: the physiology of champions. *The Journal of Physiology*, 586(1), 35-44. https://doi.org/10.1113/jphysiol. 2007.143834
6. Kaiser-Nielsen, L. V., Tischer, S. G., Prescott, E. B., & Rasmusen, H. K. (2017). Symptoms, diagnoses, and sporting consequences among athletes referred to a Danish sports cardiology clinic. *Scandinavian Journal of Medicine & Science in Sports*, 27(1), 115-123. https://doi.org/10.1111/sms.12624
7. Myers, J., Kaminsky, L. A., Lima, R., Christle, J. W., Ashley, E., & Arena, R. (2017). A reference equation for normal standards for VO2 max: analysis from the Fitness Registry and the Importance of Exercise National Database (FRIEND Registry). *Progress in Cardiovascular Diseases*, 60(1), 21-29. https://doi.org/10.1016/j.pcad.2017.03.002
8. Oswald, F., Campbell, J., Williamson, C., Richards, J., & Kelly, P. (2020). A scoping review of the relationship between running and mental health. *International Journal of Environmental Research and Public Health*, 17(21), 8059. https://doi.org/10.3390/ijerph17218059
9. Parker, A. M., Brigham, E., Connolly, B., McPeake, J., Agranovich, A. V., Kenes, M. T., ... & Turnbull, A. E. (2021). Addressing the post-acute sequelae of SARS-CoV-2 infection: a multidisciplinary model of care. *The Lancet Respiratory Medicine*, 9(11), 1328-1341. https://doi.org/10.1016/S2213-2600(21)00385-4
10. Pillay, L., van Rensburg, D. C. C. J., van Rensburg, A. J., Ramagole, D. A., Holtzhausen, L., Dijkstra, H. P., & Cronje, T. (2020). Nowhere to hide: The significant impact of coronavirus disease 2019 (COVID-19) measures on elite and semi-elite South African athletes. *Journal of Science and Medicine in Sport*, 23(7), 670-679. https:doi.org/10.1016/j.jsams.2020.05.016
11. Salles, J. I., Silva, C., Wolff, A., Orwert, L., Ribeiro, P., Velasques, B., & Morrissey, D. (2023). Anxiety, insomnia, and depression during COVID-19 lockdown in elite individual and team sport athletes. *Psicologia: Reflexão e Crítica*, 35, 33. https://doi.org/10.1186/s41155-022-00233-z
12. San-Millán, I. (2023). The key role of mitochondrial function in health and disease. *Antioxidants*, 12(4), 782. https://doi.org/10.3390/antiox12040782

13. Scheer, V., Valero, D., Villiger, E., Rosemann, T., & Knechtle, B. (2021). The impact of the COVID-19 pandemic on endurance and ultra-endurance running. *Medicina*, 57(1), 52. https://doi.org/10.3390/medicina57010052
14. Shukla, A., Dogra, D. K., Bhattacharya, D., Gulia, S., & Sharma, R. (2023). Impact of COVID-19 outbreak on the mental health in sports: a review. *Sport Sciences for Health*, 19(4), 1043-1057. https://doi.org10.1007/s11332-023-01063-x
15. Tracking SARS-CoV-2 variants. *WHO*. https://www.who.int/activities/tracking-SARS-CoV-2-variants. Accessed 18 January

Appendix

Appendix A: Declaration by co-authors

Declaration: Student's contribution to articles and agreement of co-authors

I, Cheryl Anne Haley, student number 9703995n, declare that this Thesis is my own work and that I contributed adequately towards research findings published in the article(s) stated below which are included in my thesis.

Signature of Student

Date 5 November 2024

Name of Primary Supervisor: Heleen van Aswegen

Signature of Primary Supervisor …

Date: 22/11/2024

Agreement by co-authors: By signing this declaration, the co-authors listed below agree to the use of the article(s) by the student as part of her thesis. In cases where the student is not the 1st author of a published article, the primary supervisor must explain (under comments) why the student is entitled to use the paper for his/her degree purposes.

Article 1: Title: Protracted exercise tolerance post-coronavirus disease 2019 in endurance athletes: A survey

Journal name, year, volume and page numbers: South African Journal of Physiotherapy, 2024, 80, a2063.

Authors	Name	Signature	Date
1st author	Cheryl A Haley		5/11/2024
2nd author	Heleen van Aswegen		22/11/2024
3rd author	Elena Libhaber		6.11.2024
4th author	Benita Olivier		20-11-2024

Comments by primary supervisor: Not applicable

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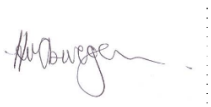
Article 2: Title: “Every run is hard”: Endurance athletes’ experiences of return to sports participation after COVID-19- A mixed method study

1. **Journal name, year, volume and page numbers:** Translational Sports Medicine. 2024(1):1506534.

Authors	Name	Signature	Date
1st author	Cheryl Haley		5/11/2024
2nd author	Heleen van Aswegen		22/11/2024
3rd author	Benita Olivier		20-11-2024

Comments by primary supervisor: Not applicable

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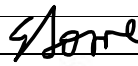
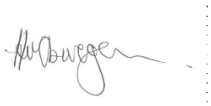
Article 3: Title: Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes

Journal name, year, volume and page numbers: South African Journal of Sports Medicine, 2024, 36, 1-8.

Authors	Name	Signature	Date
1st author	Cheryl Haley		5/11/2024
2nd author	Georgia Torres		12.11.2024
3rd author	Benita Olivier		20-11-2024
4th author	Heleen van Aswegen		22/11/2024

Comments by primary supervisor: Not applicable

……

……

Appendix B: Post-COVID-19 RTS criteria

Return to sport criteria is based on expert opinion and symptom burden, mostly targeted towards elite, young athletes (Hughes et al. 2022). Early in the pandemic, before exercising the athlete should have their body temperature taken, undergo PCR or rapid antigen tests, and disclose any COVID-19 related symptoms, exposure to COVID-19 positive persons, and recent travel (Toresdahl & Asif 2020). There have many published RTS guidelines that have emerged as the pandemic progressed. A decision pathway according to the ACC, is displayed in figure A.1 (Gluckman et al. 2022).

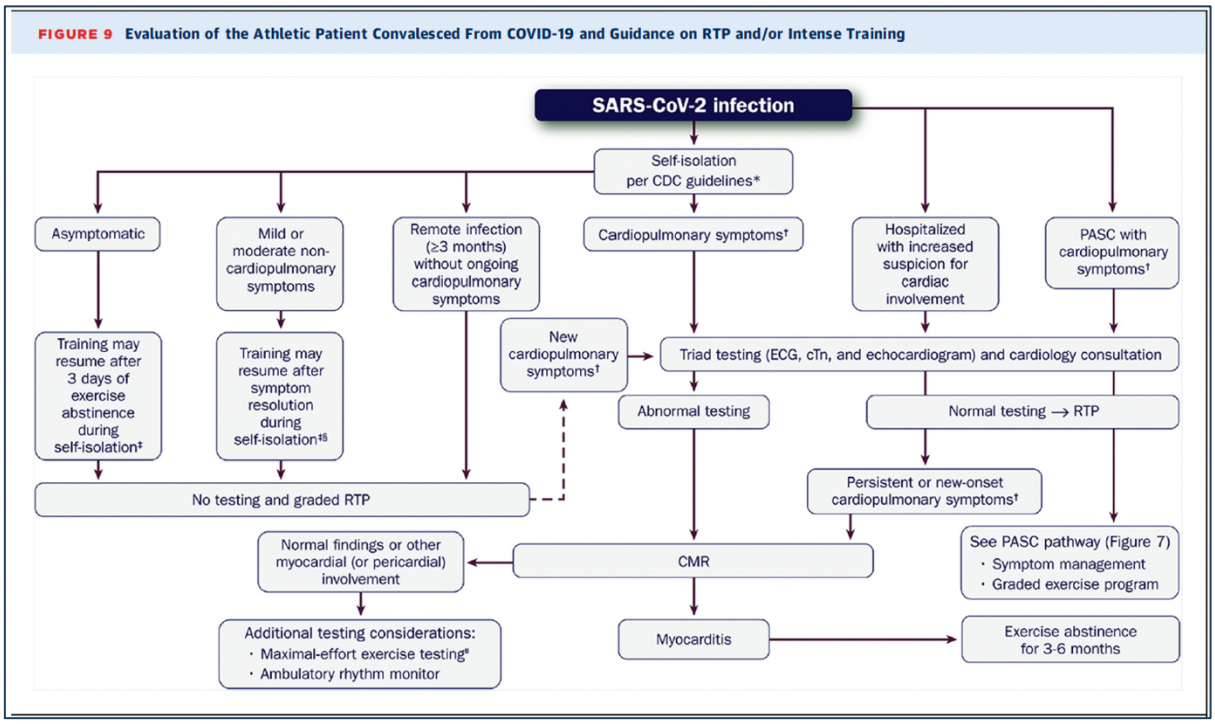
Asymptomatic illness requires no restriction (Barker-Davis et al. 2020), or 3 symptom free days after exposure or isolation. Exercise may then resume and slowly increase the duration and intensity on an individual basis, monitoring symptoms and exercise response (Steinacker et al. 2022). The athlete should be informed of the possibility of symptoms on exertion once they RTS (Monosilio et al. 2023).

Mild illness requires light exercise for one week (Barker-Davis et al. 2020). When beginning their RTS, athletes should monitor their subjective load capacity, sleep quality, fatigue and any feelings of being unwell. If resting or exertional symptoms are experienced, exercise should be discontinued, and a medical consultation is necessary if cardiovascular or pulmonary symptoms were present.

Moderate illness requires three symptom free days and medical diagnostics (such as a doctor consultation with physical examination) need to clear before resuming exercise. They will then proceed as described above for mild disease. If they have not been cleared or following a severe course of the disease, individualised diagnostics are required (Steinacker et al. 2022). Should there be no structural damage and cleared diagnosis, athletes may start with two to three days of graded RTS per day lost due to illness (Goergen et al. 2021). First increase frequency, then duration and lastly intensity (Goergen et al. 2021). Fortunately, athletes can easily manage their heart rate and even oxygen saturation through wearable devices (Goergen et al. 2021). Córdova-Martinez et al. (2022) recommends resuming exercise at 50% intensity and a gradual 10-30% per week to allow the organs time to adapt. If RTS is too rapid, insufficient neuromuscular control and strength can lead to injury.

In the case of severe disease or cardiac symptoms, a resting and stress ECG, blood protein testing for NT-Pro-BNP and troponin, echocardiography, CPET, 24-hour holter

monitoring is recommended (Monosilio et al. 2023, Steinacker et al. 2022). In the case of any abnormal findings, a cardiac magnetic resonance imaging may be required (Steinacker et al. 2022). Once the investigations have been cleared, sport should continue to be avoided for 3-6 months in the case of myocarditis (Goergen et al. 2021). If pulmonary symptoms are present, a lung function test and CPET is recommended, possibly with blood gas analysis. Return to competition is allowed after ten symptom free days and after regaining fitness (Steinacker et al. 2022). There needs to be awareness of decreased performance due to bed rest (Ruuskanen et al. 2024). Most importantly, safety is paramount.



†Cardiopulmonary symptoms include chest pain/tightness, dyspnoea, palpitations, and light-headedness/syncope; this also includes symptoms occurring <1 week following COVID-19 mRNA vaccination. ‡Strategies to minimise transmission of SARS-CoV-2 to other athletes 3-10 days following a positive COVID-19 test include 1) training in isolation, 2) participating in socially-distant outdoor training, 3) training with a face mask in a well-ventilated facility with appropriate social distancing, and 4) participating in group training after a single negative NAAT (eg, RT-PCR test) or 2 negative rapid antigen tests 24-48 hours apart. § Excludes prolonged, isolated anosmia/ageusia, which should not delay return to training. ||Maximal effort exercise testing to be deferred until myocarditis has been excluded. CDC = Centres for Disease Control and Prevention; CMR = Cardiac Magnetic Resonance Imaging; COVID-19 = novel coronavirus disease 2019; cTn = cardiac troponin; ECG = electrocardiogram; NAAT = nucleic acid amplification test; PASC = post-acute sequalae of SARS-CoV-2 infection; RTP = return to play; RT-PCR = reverse transcription polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. (Reproduced from Gluckman et al. 2022)

Figure A: COVID-19 Quarantine and isolation

Appendix C: Ethical clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Mrs Cheryl Haley

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M210657

NAME: (**Principal Investigator**)	Mrs Cheryl Haley
DEPARTMENT:	Physiotherapy CESSEM, Wits Education Campus
PROJECT TITLE:	The Impact of COVID-19 on Endurance Athletes' Return to Pre-illness Level of Participation
DATE CONSIDERED:	25/06/2021
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof B Olivier and Prof H van Aswegen
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	25/10/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I **agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **June** and will therefore be due in the month of **June** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

25 October 2021

Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix D: Participant information leaflet and consent for Study 1 and 2

Title of the research project: The Impact of COVID-19 on Endurance Athletes' performance when returning to sport

Principal researcher: Cheryl Haley

Department of Physiotherapy

University of the Witwatersrand

Johannesburg

Contact number: 0823355649, email: cheryl@ourphysio.co.za

Study supervisors: Prof Benita Olivier, Prof Heleen van Aswegen.

Dear Athlete,

Thank you for your interest in participating in this study. I, Cheryl Haley, am doing research on the impact of COVID-19 on endurance athletes. Your input will be extremely valuable and will broaden scientific knowledge of how the disease has impacted athletes, and to enable us to manage return to training optimally.

Please take some time to read the information presented here, which will explain the details of this project. You are welcome to ask any questions about any part of the project. It is very important that you are fully satisfied and clearly understand what the research entails and how you could be involved. Your participation is entirely voluntary, and you are free to decline at any time without any negative consequences to you whatsoever. I would be most grateful if you would allow for your data, which includes

your responses to the questionnaires to be used as part of this study and to contribute to the body of knowledge around ongoing research.

Who is eligible to take part in this study?

Male or female endurance athletes over the age of 18. You may be affiliated to a club or coach or participate at an amateur or elite level prior to the COVID-19 pandemic.

What is this study about?

Endurance athletes are generally considered to be individuals who place a high premium on training, competition, and sports achievement. As an endurance athlete, you have been invited to complete this questionnaire that takes about 15 minutes to complete. The questionnaire aims to determine the severity and duration of symptoms you experienced. I would like to explore the impact of this on your quality of life and athletic performance.

What will your responsibilities be?

Should you agree to participate in the study, you will be asked to fill out the tick box questionnaire by March 2022. After reading the information, your consent to participate needs to be given.

Will you benefit from taking part in this research?

The most important benefit is furthering scientific knowledge to improve the management of this and future pandemics where endurance athletes are concerned.

Are there any risks involved in taking part in the study?

There are no risks involved in this study.

Who will have access to the information you provide?

All information will be anonymous, and confidentiality will be protected at all times. The email address you may enter for continued questions, will be stored separately from the survey responses. These details will be deleted after completion of the study.

Information related to the use of the data in future research projects:

I would like to get permission to deposit your responses into a research database that may be used for future research by bona fida researchers. At this stage we don't know what research question will emerge going forward, but if there are any topics you would prefer the data not to be used for, you can specify this. Your data will not be sold for profit or used for commercial projects.

Will access to my data be controlled?

Anonymous information from the survey, will be kept in an access-controlled database which is only accessible by the data manager, access control committee and research group director. If you would like to review the accuracy of your data, feel free to contact the data manager (via Benita Olivier, benita.olivier@wits.ac.za) who will set up a meeting for you to verify information.

Where will my data be stored?

Your data will be stored on a secure platform called REDCap (Research Electronic Data Capture) which is hosted by the University of the Witwatersrand. This platform is access-controlled, secured on two different servers and only a data manager, data access committee and the research group director will have access to the data.

How will researchers gain access to my data?

Researchers who would like to use your data in future research projects will apply for ethical clearance, which is reviewed in light of your original consent. Once the future research project is completed, the new datasheet will be uploaded on the REDCap system and the researcher will remove the copies from his/her computer, whereafter the researcher's access to REDCap will be terminated.

This data set will not contain any identifying factors such as names or contact details, however should you like to withdraw your consent for re-use of your data in future research projects you are free to do so by sending an email to me, the principal investigator, Cheryl Haley.

Ethical clearance has been applied for from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand. For more information on, or for the reporting of ethical concerns, you may contact the chair of the Human Research Ethics Committee (Medical) of the University of the Witwatersrand: Dr Clement Penny (Clement.Penny@wits.ac.za); Ms Zanele Ndlovu (Zanele.Ndlovu@wits.ac.za) / Mr Rhulani Mkansi (Rhulani.Mkansi@wits.ac.za); Administrative Officers 011 717 2700/2656/1234/1252.

You may download or print this information document for your records. Any pertinent information will be shared on request after the results are available. For further information please contact me or my study supervisor on the contact details given above.

By agreeing to participate in this study, you declare that:

1. I have read the participant information leaflet explaining the study in a language I fully understand.

2. I have had the opportunity to ask any questions and the answers are satisfactory.

3. I fully understand why the study is being conducted and what the outcomes are.

4. I agree for my data to be used as part of the research project described in the information sheet and titled: “The impact of COVID-19 on Endurance Athletes”.

5. I am aware that I can withdraw from the study at any time and/or request for my data to be withdrawn from this particular research study, without suffering any repercussions.

6. I understand that there are no immediate benefit to me and no monetary rewards for allowing my data to be used as part of this research study and that participation is voluntary and I am not in any way obliged to take part.

7. I agree for my data, after my name, surname and contact details have been removed, be re-used in future research projects without my additional informed consent (tick all that apply).

☐ Yes, my data can be stored and re-used for an unlimited period of time.

☐ Yes, my data can be stored and re-used for a limited period of time with an end date specified here: _____(DD/MM/YYYY).

☐ Yes, my data cannot be re-used for topics such as: _____(leave blank if not applicable).

☐ No, I do not agree for my data to be used in future research projects.

If you are willing to participate, please continue to the questionnaire.

Yours sincerely,

Cheryl Haley (M Physio)

Principal researcher

Physiotherapy Department, University of the Witwatersrand



Figure B: The advertisement that was disseminated through social media and email, and contained the link to the survey and participant information leaflet

Appendix E: Study 1 and 2 survey

The Impact of COVID-19 on Endurance Athletes

Please complete this important survey below.

Thank you!

If you are willing to participate, please continue to the questionnaire by clicking "yes" to consent	◯ Yes
What is your sex?	◯ Male ◯ Female ◯ Prefer not to say
Date of birth	_____ (YYYY-MM-DD)
Which of the following sports do you participate in?	☐ Running ☐ Cycling ☐ Triathlon ☐ None of the above
What was the highest level that you were competing at prior to the COVID-19 pandemic?	◯ International e.g. world cup/world champs ◯ National representation ◯ Competitive in age group ◯ Social/ recreational
What was the minimum number of hours per week that you were training prior to the COVID-19 pandemic?	◯ 1-2 ◯ 3-5 ◯ 6-9 ◯ 10-12 ◯ 13-15 ◯ 16+
The next section is about COVID-19 Have you had COVID-19?	☐ Yes ☐ No ☐ I am unsure
Please select all the option(s) from the list below that are true	◯ I tested positive for COVID-19 and had COVID-19 symptoms ◯ I tested positive for COVID-19 but was asymptomatic ◯ I tested negative for COVID-19 and had no symptoms ◯ I tested negative for COVID-19 but did have COVID-19 symptoms ◯ I did not test but did have COVID-19 symptoms ◯ I tested positive for COVID-19 antibodies
How long ago did you have COVID-19?	◯ 1 month ago ◯ 2 months ago ◯ 3 - 6 months ago ◯ More than 7 months ago

How were you treated for your symptoms?

- ◯ No treatment necessary
- ◯ Self-medicated and recovered at home
- ◯ Consulted a healthcare professional and wasn't admitted to hospital
- ◯ Admitted to hospital on oxygen in a general ward
- ◯ Admitted to hospital - High care or ICU, no mechanical ventilation
- ◯ Admitted to hospital - ICU and mechanically ventilated

Did you have any pre-existing medical conditions or co-morbidities e.g. asthma, hypertension, diabetes?

- ◯ Yes
- ◯ No

Have any of your pre-existing medical conditions worsened since contracting COVID-19?

- ◯ Yes
- ◯ No

Have you been diagnosed with any new medical conditions since having COVID-19?

- ◯ No
- ◯ Yes _____ (Please specify)

Which of the following was your worst symptom at the time of illness?

- ◯ Body ache
- ◯ Cough
- ◯ Diarrhoea
- ◯ Fatigue
- ◯ Fever
- ◯ Headache
- ◯ Loss of smell and/or taste
- ◯ Shortness of breath
- ◯ I had no symptoms

	Mild	Moderate	Severe
In the first 2 weeks of being ill, how would you describe your worst symptom?	◯	◯	◯

How long did your symptoms persist for?

- ◯ Less than 1 week
- ◯ 1 - 2 weeks
- ◯ 3 - 4 weeks
- ◯ 5 - 8 weeks
- ◯ More than 8 weeks

	No symptoms	Mild	Moderate	Severe
After 1 month how would you describe your worst symptom	◯	◯	◯	◯

How many hours per week are you currently training?

- ◯ 1-2
- ◯ 3-5
- ◯ 6-9
- ◯ 10-12
- ◯ 13+

How long did it take you to get back to pre-COVID performance levels?

- ◯ 2 weeks
- ◯ 1 month
- ◯ 2-3 months
- ◯ 4-6 months
- ◯ more than 7 months
- ◯ I'm still not at my pre-COVID performance level
- ◯ I do not intend returning to training

This section is about persistent symptoms

◯ Yes
◯ No

Do you still experience any COVID-19 symptoms at rest?

By means of the following statements we would like to get an idea of how you have been feeling lately.

"I FEEL RELAXED"
If you think that this is entirely true, that indeed you have been feeling relaxed lately, please, choose the response in the extreme left box; like this:
yes, that is true ●1 ○2 ○3 ○4 ○5 no, that is not true

The more you disagree with the statement, the more you can choose a response in the direction of "no, that is not true". Please do not miss out a statement and choose only one response for each statement.

	yes, that is true1	2	3	4	no, that is not true5
I feel fit.	◯	◯	◯	◯	◯
I feel able to only do a little physical activity.	◯	◯	◯	◯	◯
I feel very active.	◯	◯	◯	◯	◯
I feel like doing all sorts of nice things.	◯	◯	◯	◯	◯
I feel tired.	◯	◯	◯	◯	◯
I think I do a lot in a day.	◯	◯	◯	◯	◯
When I am doing something, I can keep my thoughts on it.	◯	◯	◯	◯	◯
I can take on a lot of physical activity.	◯	◯	◯	◯	◯

	yes, that is true1	2	3	4	no, that is not true5
I dread having to do things.	◯	◯	◯	◯	◯
I think I do very little in a day.	◯	◯	◯	◯	◯
I can concentrate well.	◯	◯	◯	◯	◯
I am rested.	◯	◯	◯	◯	◯
It takes a lot of effort to concentrate on things.	◯	◯	◯	◯	◯
Physically I feel I am in a bad condition.	◯	◯	◯	◯	◯
I have a lot of plans.	◯	◯	◯	◯	◯
I tire easily.	◯	◯	◯	◯	◯
I get little done.	◯	◯	◯	◯	◯
I don't feel like doing anything.	◯	◯	◯	◯	◯
My thought easily wander.	◯	◯	◯	◯	◯
Physically I feel I am in an excellent condition.	◯	◯	◯	◯	◯

Are you are experiencing any of the following WHILE TRAINING? Please rate the severity

	None	Mild	Moderate	Severe
High heart rate	◯	◯	◯	◯
Shortness of breath	◯	◯	◯	◯
Poorer endurance / need to reduce training time	◯	◯	◯	◯

Reduced power / unable to sustain the intensity	◯	◯	◯	◯
Difficulty hill climbing	◯	◯	◯	◯
Muscle soreness or joint pain	◯	◯	◯	◯
Headache	◯	◯	◯	◯
Fatigue / excessive tiredness	◯	◯	◯	◯
Slower recovery	◯	◯	◯	◯
Aggravation of asthma	◯	◯	◯	◯
Chest pain	◯	◯	◯	◯
Other sports injuries	◯	◯	◯	◯
Concerns about consequences of COVID-19 such as stress on your heart	◯	◯	◯	◯
Anxiety / depression	◯	◯	◯	◯

What is the main concern or challenge that you have experienced while returning to training?

_____

How have you managed it?

☐ Pushing yourself though the challenges
☐ Resting until you feel better
☐ Having an ECG
☐ Having a lung function test
☐ Consulting a medical doctor to clear you for exercise
☐ Using a structured program to build up again
☐ Medication
☐ Reduced mileage
☐ Reduced intensity
☐ Other _____
(Please select all that are true)

Have you received any guidelines for training after illness?

◯ Yes
◯ No
(e.g. recommendations from a coach / doctor / internet)

Please select which of the following you monitor or consider with every training session

☐ Resting and maximal heart rate
☐ Rate of Perceived Exertion
☐ Sleep quality
☐ Stress
☐ Fatigue
☐ Muscle soreness
☐ Injury

Have you done respiratory muscle training since being ill?

◯ Yes ◯ No

If you have had COVID-19 and have not yet returned to your pre-COVID performance level, or are currently struggling with persistent COVID-19 symptoms inhibiting your athletic performance, please consider the opportunity to take part in the study which aims to investigate the impact of COVID-19 on VO2max and physiotherapy measures to improve athletic performance.

Please leave your email address for more information

_____
(This information will be stored separately, so the survey will remain anonymous)

The next section is about the impact of COVID-19 on your life.

Were you stressed about recovering fully and quickly from COVID-19?

◯ No
◯ Yes _____
(Please give more information)

Did you feel stigmatised because you had contracted COVID-19?

◯ Yes
◯ No

How have the following have been affected since you contracted COVID-19?

	Better	Neutral	Worse
Sleep quantity and quality	◯	◯	◯
Nutrition	◯	◯	◯
Motivation	◯	◯	◯
Work life	◯	◯	◯
Social life	◯	◯	◯
Memory or concentration	◯	◯	◯
Mood and energy	◯	◯	◯
Emotional state	◯	◯	◯

Many athletes partake in sport for enjoyment, stress relief, improving general physical health, mental health, the social aspect and/or taking on a physical challenge such as a race. Can you comment on how COVID-19 has affected these in your life?

_____

Is there any further information you can share about how COVID-19 affected you?

_____

Have you received counselling for the stressful effects of COVID-19?

◯ Yes
◯ No

Would you like to receive counselling?

◯ Yes
◯ No

Please type your email address to forward a counselling contact. This information will be stored separately to maintain anonymity of the survey,

_____

Appendix F: Participant information leaflet and consent for Study 3

Title of the research project: Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes

Principal researcher: Cheryl Haley
Department of Physiotherapy
University of the Witwatersrand
Johannesburg

Contact number: 0823355649, email: cheryl@ourphysio.co.za

Study supervisors: Prof Benita Olivier, Prof Heleen van Aswegen.

Dear Athlete,

My name is Cheryl Haley, and I am a physiotherapist and PhD student at the University of the Witwatersrand. You are invited to participate in m|\
y research project that aims to determine how fitness changes in response to endurance training post-COVID-19 infection compared to unaffected athletes of the same sex and age group, in South Africa.

Please take some time to read the information presented here, which will explain the details of this project. You are welcome to ask any questions about any part of the project. It is very important that you are fully satisfied and clearly understand what the research entails and how you could be involved. Your participation is entirely voluntary, and you are free to decline at any time without any negative consequences to you whatsoever. All personal details and results will be kept completely anonymous. I would be most grateful if you would allow for your data (names and contact details excluded) and the results from the physical tests performed, to be used for this research project and to contribute to the body of knowledge around ongoing research.

Who is eligible to take part in this study?
Male or female endurance athletes over the age of 18 who have either not had COVID-19, recovered completely and you are at your pre-illness level of fitness, or experienced COVID-19 and have persistent symptoms affecting your athletic performance. Your

input will be extremely valuable and will broaden scientific knowledge of how the disease has impacted athletes, and to enable us to manage return to training optimally. You may not participate if you have been newly diagnosed with COVID-19 and are still in the infectious stage or have had any contact with a COVID-19 positive patient in the last 10 days.

What is this study about?

As an endurance athlete, you have been invited to participate in this study which aims to determine how your fitness changes in terms of VO_2max and respiratory (breathing) muscle strength.

What will your responsibilities be?

You will be required to undergo a VO_2max test and measure your maximum inspiratory pressure (MIP), which measures the strength of your muscles that do inhalation. You will perform a run test of approximately 25 minutes during which your heart rate, time, distance will be recorded. Please record your Rate of Perceived Exertion (RPE). You will then continue your normal training and log it on Strava or a separate file to send me. After six weeks you will be required to perform the same tests again. To optimise similar conditions, it will be helpful if the repeat test is done at the same time of day with similar nutrition and sleep the day before. It is advised not to eat just before the test and avoid an extremely tough session the day before. Data from these sessions will be analysed and all data will remain anonymous.

Will you benefit from taking part in this research?

The most important benefit is furthering scientific knowledge as the change in VO_2max and MIP with training has not been published worldwide, and no data on South African athletes over the age of 35 has been published.

Are there any risks involved in taking part in the study?

You will not be exposed to any additional risks other than the risks that you are normally exposed to when you are running. All COVID-19 protocols will be strictly adhered to.

Will access to information be controlled?

Names will be replaced by numbers to maintain anonymity of data collected from you and together with contact details will be stored separately. Confidentiality of all results

will be protected. The principal researcher, research assistant and supervisors will have access to data provided. This signed consent will be kept separate from the study data. You can request for your data to be withdrawn from this study by emailing Cheryl Haley, without any repercussions.

Information related to the use of the data in future research projects:
I would like to get permission to deposit your responses into a research database that may be used for future research by bonafida researchers. At this stage we don't know what research question will emerge going forward, but if there are any topics you would prefer the data not to be used for, you can specify this. Your data will not be sold for profit, and you can indicate in the consent form if you prefer for your data not to be used in commercial projects (e.g. device development).

Will access to my data be controlled?
Identifying information, such as your name, surname, and contact details, will be removed from your data and a study number will be allocated to your data. The link between the study number and the identifying information will be kept in an access-controlled database which is only accessible by the data manager, access control committee and research group director. If you would like to review the accuracy of your data, feel free to contact the data manager (via Benita Olivier, benita.olivier@wits.ac.za) who will set up a meeting for you to verify information.

Where will my data be stored?
Your data will be stored on a secure platform called REDCap (Research Electronic Data Capture) which is hosted by the University of the Witwatersrand. This platform is access-controlled, secured on two different servers and only a data manager, data access committee and the research group director will have access to the data.

How will researchers gain access to my data?
Researchers who would like to use your data in future research projects will apply for ethical clearance, which is reviewed in light of your original consent. In addition, these applications will be reviewed by a data access control committee in the light of the intension of your original consent. If the committee is satisfied with the intentions of use, access will be granted to your data. Once the future research project is completed, the new datasheet will be uploaded on the REDCap system and remove the copies

from his/her computer, whereafter the researcher's access to REDCap will be terminated.

This data set will not contain any identifying factors such as names or contact details, however should you like to withdraw your consent for re-use of your data in future research projects you are free to do so by sending an email to me, the principal investigator, Cheryl Haley.

Ethical clearance has been applied for from the Human Research Ethics Committee of the University of the Witwatersrand. For more information on, or for the reporting of ethical concerns, you may contact the chair of the Human Research Ethics Committee of the University of the Witwatersrand: Dr Clement Penny (Clement.Penny@wits.ac.za); Ms Zanele Ndlovu (Zanele.Ndlovu@wits.ac.za) / Mr Rhulani Mkansi (Rhulani.Mkansi@wits.ac.za); Administrative Officers 011 717 2700/2656/1234/1252.
You will be given any pertinent information on this study while you're involved and after the results are available. You may have a copy of this document for your records. For further information please contact me or my study supervisor on the contact details given above.

Yours sincerely,

Cheryl Haley
M Physio
Principal researcher
Physiotherapy Department, University of the Witwatersrand

If you are willing to participate, please sign the consent below:

INFORMED CONSENT FORM: ATHLETE
Study title: Cardiorespiratory fitness response to endurance training in athletes post-COVID-19 compared to unaffected athletes
By agreeing to participate in this study, you declare that:

1. I have read the participant information leaflet explaining the study in a language I fully understand.

2. I have had the opportunity to ask any questions and the answers are satisfactory.

3. I fully understand why the study is being conducted and what the outcomes are.

I_____(e-mail address: _____ and cell phone number:_____) hereby agree to for my data to be used as stipulated below:

I agree for my data to be used as part of the research project described in the information sheet and titled: “Changes in cardiorespiratory fitness due to endurance training in athletes post-COVID-19 compared to unaffected athletes in South Africa”.

☐ Yes

☐ No

I am aware that I can withdraw from the study at any time and/or request for my data to be withdrawn from this particular research study, without suffering any repercussions.

☐ Yes

☐ No

I understand that there are no monetary rewards for allowing my data to be used as part of this research study and that participation is voluntary and I am not in any way obliged to take part.

☐ Yes

☐ No

I agree for my data, after my name, surname and contact details have been removed, be re-used in future research projects without my additional informed consent (tick all that apply).

☐ Yes, my data can be stored and re-used for an unlimited period of time.

☐ Yes, my data can be stored and re-used for a limited period of time with an end date specified here: _____(DD/MM/YYYY).

☐ Yes, my data can be used as part of any project that has been approved by the data access committee except for topics such as: _____(leave blank if not applicable).

☐ Yes, my data can be used in commercial or device development projects.

☐ No, I do not agree for my data to be used in future research projects.

I _____ (print name) hereby sign consent to participate in the study detailed above.

Signed by participant: _____

Date (Month and Year): _____

Place: _____

Signed by researcher: _____

Study number (Official use):_____

Appendix G: Participant information leaflet and consent for Study 4

Title of the research project: Efficacy of Inspiratory Muscle Training to Improve Exercise Capacity in Athletes post-COVID-19

Principal researcher: Cheryl Haley
Department of Physiotherapy
University of the Witwatersrand
Johannesburg

Contact number: 0823355649, email: cheryl@ourphysio.co.za

Study supervisors: Prof Benita Olivier, Prof Heleen van Aswegen.

Dear Athlete,

My name is Cheryl Haley and I am a physiotherapist and PhD student at the University of the Witwatersrand. You are invited to participate in my research project that aims to investigate whether physiotherapy interventions will improve exercise tolerance in endurance athletes after having COVID-19.

Please take some time to read the information presented here, which will explain the details of this project. You are welcome to ask any questions about any part of the project. It is very important that you are fully satisfied and clearly understand what the research entails and how you could be involved. Your participation is entirely voluntary, and you are free to decline at any time without any negative consequences to you whatsoever. All personal details and results will be kept completely anonymous. I would be most grateful if you would allow for your data (names and contact details excluded) and the results from the physical tests performed, to be used for this research project and to contribute to the body of knowledge around ongoing research.

Who is eligible to take part in this study?
Male or female endurance athletes over the age of 18 who have experienced COVID-19 and have persistent symptoms affecting your return to training. Your input will be extremely valuable and will broaden scientific knowledge of how the disease has

impacted athletes, and to enable us to manage return to training optimally. You may not participate if you have been newly diagnosed with COVID-19 and are still in the infectious stage or have had any contact with a COVID-19 positive patient in the last 10 days.

What is this study about?

As an endurance athlete, you have been invited to participate in this study which aims to investigate whether physiotherapy interventions will improve athletic performance.

What will your responsibilities be?

You will be required to attend a physiotherapy consultation in Johannesburg and perform baseline tests to determine the strength of your respiratory (breathing) muscles and a VO_2max test performed by a research assistant. You will perform a run test that takes approximately 25-minute during which your heart rate, time and distance will be recorded. Please record your Rate of Perceived Exertion (RPE). You might then be required to implement the prescribed exercises five days a week for six weeks. These exercises will take approximately 10 minutes, and together with your normal training need to be recorded; either manually logged into the log provided or onto Strava or Training Peaks and allow me to follow you for the duration of the study. Every ten days you will increase the difficulty of the exercises. This increase is dependent on the results from your tests at the consultation, so I will guide you through it. I will also follow up to hear how it is going. After six weeks you will be required to perform the same tests again. To optimise similar conditions, it will be helpful if the repeat test is done at the same time of day with similar nutrition and sleep the day before. Data from these sessions will be analysed and all data will remain anonymous.

Will you benefit from taking part in this research?

The most important benefit is furthering scientific knowledge to improve the management of this and future pandemics where endurance athletes are concerned. We hope that you will benefit from the physiotherapy intervention if you are fully compliant with the treatment regime given to you.

Are there any risks involved in taking part in the study?

You will not be exposed to any additional risks other than the risks that you are normally exposed to when you are running. During the physiotherapy intervention session, all COVID-19 protocols will be strictly adhered to. Your transport costs to the consultations where the VO2max testing will be done will be reimbursed at a flat rate of R50.00 per trip.

Will access to information be controlled?
Names will be replaced by numbers to maintain anonymity of data collected from you and together with contact details will be stored separately. Only the principal researcher, Cheryl Haley, will have access to this file, which will be deleted after completion of the study. All results will be anonymous, and confidentiality will always be protected. The principal researcher, research assistant and supervisors will have access to data provided. This signed consent will be kept separate from the study data. You can request for your data to be withdrawn from this study by emailing Cheryl Haley, without any repercussions.

Information related to the use of the data in future research projects:
I would like to get permission to deposit your responses into a research database that may be used for future research by bona fida researchers. At this stage we don't know what research question will emerge going forward, but if there are any topics you would prefer the data not to be used for, you can specify this. Your data will not be sold for profit, and you can indicate in the consent form if you prefer for your data not to be used in commercial projects (e.g. device development).

Will access to my data be controlled?
Identifying information, such as your name, surname, and contact details, will be removed from your data and a study number will be allocated to your data. The link between the study number and the identifying information will be kept in an access-controlled database which is only accessible by the data manager, access control committee and research group director. If you would like to review the accuracy of your data, feel free to contact the data manager (via Benita Olivier, benita.olivier@wits.ac.za) who will set up a meeting for you to verify information.

Where will my data be stored?

Your data will be stored on a secure platform called REDCap (Research Electronic Data Capture) which is hosted by the University of the Witwatersrand. This platform is access-controlled, secured on two different servers and only a data manager, data access committee and the research group director will have access to the data.

How will researchers gain access to my data?
Researchers who would like to use your data in future research projects will apply for ethical clearance, which is reviewed in light of your original consent. In addition, these applications will be reviewed by a data access control committee in the light of the intension of your original consent. If the committee is satisfied with the intentions of use, access will be granted to your data. Once the future research project is completed, the new datasheet will be uploaded on the REDCap system and remove the copies from his/her computer, whereafter the researcher's access to REDCap will be terminated.

This data set will not contain any identifying factors such as names or contact details, however should you like to withdraw your consent for re-use of your data in future research projects you are free to do so by sending an email to me, the principal investigator, Cheryl Haley.

Ethical clearance has been applied for from the Human Research Ethics Committee of the University of the Witwatersrand. For more information on, or for the reporting of ethical concerns, you may contact the chair of the Human Research Ethics Committee of the University of the Witwatersrand: Dr Clement Penny (Clement.Penny@wits.ac.za); Ms Zanele Ndlovu (Zanele.Ndlovu@wits.ac.za) / Mr Rhulani Mkansi (Rhulani.Mkansi@wits.ac.za); Administrative Officers 011 717 2700/2656/1234/1252.

You will be given any pertinent information on this study while you're involved and after the results are available. You may have a copy of this document for your records. For further information please contact me or my study supervisor on the contact details given above.

Yours sincerely,

Cheryl Haley
M Physio
Principal researcher
Physiotherapy Department, University of the Witwatersrand

If you are willing to participate, please sign the consent below:

INFORMED CONSENT FORM: ATHLETE

Study title: Do Physiotherapy Interventions Assist Return to Sport Participation after COVID-19 in Endurance Athletes?

By agreeing to participate in this study, you declare that:

1. I have read the participant information leaflet explaining the study in a language I fully understand.

2. I have had the opportunity to ask any questions and the answers are satisfactory.

3. I fully understand why the study is being conducted and what the outcomes are.

I_____(e-mail address: _____ and cell phone number:_____) hereby agree to for my data to be used as stipulated below:

I agree for my data to be used as part of the research project described in the information sheet and titled: “Do Physiotherapy Interventions Assist Return to Sport Participation after COVID-19 in Endurance Athletes?”

☐ Yes

☐ No

I am aware that I can withdraw from the study at any time and/or request for my data to be withdrawn from this particular research study, without suffering any repercussions.

☐ Yes

☐ No

I understand that there are no monetary rewards for allowing my data to be used as part of this research study and that participation is voluntary and I am not in any way obliged to take part.

☐ Yes

☐ No

I agree for my data, after my name, surname and contact details have been removed, be re-used in future research projects without my additional informed consent (tick all that apply).

☐ Yes, my data can be stored and re-used for an unlimited period of time.

☐ Yes, my data can be stored and re-used for a limited period of time with an end date specified here: _____(DD/MM/YYYY).

☐ Yes, my data can be used as part of any project that has been approved by the data access committee except for topics such as: _____(leave blank if not applicable).

☐ Yes, my data can be used in commercial or device development projects.

☐ No, I do not agree for my data to be used in future research projects.

I _____ (print name) hereby sign consent to participate in the study detailed above.

Signed by participant: _____

Date (Month and Year): _____

Place: _____

Signed by researcher: _____

Study number (Official use):_____

Appendix H: Registration of Study 4 with the Pan African Clinical Trial Registry

02 May 2023

To Whom It May Concern:

RE: Respiratory Muscle Training for Athletes post COVID-19: A Pilot Study for a Randomised Controlled Trial to determine Efficacy in Improving Cardiorespiratory Fitness

As project manager for the Pan African Clinical Trial Registry (www.pactr.org) database, it is my pleasure to inform you that your application to our registry has been accepted. Your unique identification number for the registry is **PACTR202305590076796**.

Please be advised that your trial is registered under an initiative within our system that allow us to capture data of trials that are already in progress or completed. As such, your trial registration may not adhere to the mandates set forth by the International Committee of Medical Journal Editors for registration requirements, and it is your duty to be transparent to any journal that may ask about the retrospective status of your registration.

Please note you are responsible for updating your trial, or for informing us of changes to your trial. Additionally, please provide us with copies of your ethical clearance letters as we must have these on file (via email or post or by uploading online) at your earliest convenience if you have not already done so.

Please do not hesitate to contact us at +27 21 938 0835 or email epienaar@mrc.ac.za should you have any questions.

Yours faithfully,

Elizabeth D Pienaar
www.pactr.orgProject Manager
+27 021 938 0835

Appendix I: Turnitin report

CH Thesis written text

ORIGINALITY REPORT

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