COVID-19 – does exercise prescription and maximal oxygen uptake (VO_2 max) have a role in risk-stratifying patients?

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As the UK shields 'high risk' patients and enforces social distancing measures, patients will be at risk of significantly reducing physical activity levels. We explore the evidence base for COVID-19-specific recommendations and exercise interventions to 'precondition' patients prior to infection and appraise the role of maximal oxygen uptake (VO₂ max) as a risk-stratifying triage tool. We conclude that structured exercise programmes can be used to maintain physical activity levels and prevent deconditioning and that VO₂ max has the potential to be used as a clinically relevant triage tool during the COVID-19 outbreak.

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'Exercise is medicine'

The current (COVID-19) pandemic has generated discussion about the impact of public health measures designed to protect critical care capacity across the NHS. We explore how aerobic testing can be adapted to 'triage' patients and help to allocate resources appropriately. With the crisis likely to continue for some time, we evaluate the role structured exercise programmes have in maintaining patients' physical activity (PA) levels and explore the theory that exercise can be used to 'precondition' patients prior to infection.

How will public health measures impact patients' physical activity levels?

The World Health Organization (WHO) has urged governments across the world to take immediate action and urgently 'suppress transmission' of the virus.¹ While the UK undertakes practical measures to implement these recommendations and shield 1.5 million² high risk patients at risk of severe illness and hospitalisation,² the NHS will inevitably need to evaluate and minimise any potential negative impact this may have on patients' health.

One smart watch company has estimated that 'social distancing' measures have led to a 9% reduction in weekly PA levels across the UK as of 22 March, 2020.³ Patients who are self-isolating may be disproportionately affected by these measures, as PA has been shown to reduce the risk of disease-specific and all-cause mortality.⁴ In addition, exercise has been shown to be an effective treatment option in the control of long term conditions (LTCs) such as hypertension, diabetes and cardiovascular disease.⁵

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A study from the Hong Kong flu epidemic of 1997 demonstrated that patients who regularly performed 'low/moderate exercise' had a significantly lower risk of mortality than patients who 'never/seldom' exercised (odds ratio 0.62).⁶ Furthermore, murine studies indicate that moderate PA reduces susceptibility to respiratory infections and improved antiviral lymphocyte function.⁷ Based on this evidence, maintaining moderate PA will have an overall benefit to patients' general physical health and may reduce the risk of contracting a respiratory infection.

What do we know about COVID-19 and high-risk patients?

Early data from the outbreak suggest that 80% of patients develop mild symptoms, 15% severe symptoms and 5% become critically ill.8 A case series of 138 hospitalised patients from Wuhan (China) has identified hypertension, diabetes and previous cardiovascular disease (CVD) as risk factors for intensive care admission.9 The median age of hospitalised patients was 51, compared to 66 for those admitted to intensive care.9

These case series suggest that discrete 'high risk' (age >65 and/ or with pre-existing health conditions)⁹ COVID-19 populations exist, which are associated with a poorer prognosis and may have a disproportionate requirement for intensive care resources.⁹ Given the high rates of mechanical ventilation and subsequent high mortality,⁹ it may be more appropriate to consider early community intervention and avoidance of hospital admission in this group. Previous community-based models in cardiovascular disease have proven to be cost-effective,¹⁰ reduce mortality and reduce unplanned hospital admissions.¹⁰ They also allow patients to maintain autonomy and be involved in active therapies that respect their preferred place of care.

Could exercise capacity help to triage patients and fairly allocate resources during the COVID-19 outbreak?

The current epidemiological models predict that the NHS is likely to face extended periods where demand for intensive care and ventilators will far exceed capacity. ¹¹ The NHS will therefore need to find ways to rapidly 'triage' a large volume of patients, to ensure the greatest benefit for the largest number of patients. In a scenario where the NHS approaches peak capacity the decision to offer one patient a critical care bed may deny another patient that same opportunity.

If it is available, maximal oxygen uptake (VO_2 max, measured in mL/kg/min) could be added to existing 'triage' criteria such as age and clinical background. While this idea is novel, and untested at scale, the current COVID-19 outbreak is challenging us to think of new ways to ensure just and equitable admission criteria. It would allow clinicians to make objective decisions on a case-by-case basis that takes into account patients' biological age and premorbid condition

What can we learn from perioperative care?

Cardiopulmonary exercise testing (CPET) for VO_2 max is a routine part of preoperative assessment for some 'high-risk' surgical patients in the NHS. Previous studies have shown that disease-specific peak VO_2 cut-offs (such as <18.3mL/kg/min for colorectal surgery) can be used to predict increased risk of 90-day mortality and risk of postoperative admission to high-dependency care.¹²

Given the high prevalence of post-intensive-care syndrome (PICS), 13 it is important to consider the baseline physical status of the patients prior to intervention. 13 Certain risk factors — mechanical ventilation, age >65, admission >7 days and deconditioning — are associated with significant long-term disability and poor quality of life. 13 Up to 25% of patients need help with activities of daily living one year after discharge and these patients are at increased risk of readmission to hospital. 13

At this early stage of the outbreak there are no studies to support the routine testing of VO_2 max prior to infection with COVID-19, but it is likely to provide a global assessment of patients baseline physiological reserves. A low VO_2 max could be used to identify patients who are unlikely to tolerate the physical demands of an intensive care admission and post-admission rehabilitation.

Can we physically precondition patients prior to infection?

The Centre of Perioperative Care has already issued expert guidance advocating for 'brisk exercise', smoking cessation, alcohol-free days and good nutrition as preventative measures in this outbreak.¹⁴ It is hoped that these simple measures will reduce the risk of patients requiring hospital admission, and potentially precondition 'high risk' patients prior to infection with COVID-19. We propose that even a small increase in baseline maximal oxygen uptake (VO $_2$ max) across the population may have the effect of shifting a significant proportion of high-risk patients into a lower risk category.

Cardiac, ¹⁰ pulmonary ¹⁵ and preoperative ¹⁶ home-based exercise programmes have been shown to be cost effective and significantly increase aerobic capacity in patients in a 4–6-week timeframe. ¹⁶ The addition of strength-based programmes that incorporate balance and flexibility have also been shown to improve function and reduce the risk

of falls in elderly patients. 17 A balanced exercise programme will help to avoid deconditioning, improve the control of LTCs and help 'high risk' patients to maintain their independence.

There are currently no studies that evaluate the impact of preconditioning exercise interventions on COVID-19-specific mortality and morbidity. Given that 5% of patients become critically ill, it seems reasonable to assume that any baseline improvement in VO_2 max is likely to confer benefit. We will however need further data to confirm this.

How could we practically test exercise capacity on a large scale?

There are a number of validated tests including the 6-minute walk test, 18 activity monitors 19 and the resting heart rate method 20 that can be used to give an estimate of a patient's $\rm VO_2$ max. All three methods can be performed remotely, be self administered $^{19.20}$ or in the case of resting heart rate be extracted from existing data in healthcare records. This would allow clinicians to remotely assess patients' exercise capacity at home, without any additional burden in clinic time.

As we embrace new ways of working during the COVID-19 outbreak, the use of an app-based or streamed exercise programme may be a feasible and cost-effective way to deliver exercise interventions. The use of ${\rm VO}_2$ max has many advantages as it is easy to collect and can be recorded in a patient's summary care record, in a similar way to a list of past medical conditions. It may also be used to initiate advanced care plans for 'high risk' patients that take in account their wishes and outline appropriate levels of medical intervention.

Formulating an exercise prescription

In order to safely prescribe exercise, clinicians can use the 'frequency, intensity, time, type, volume and progression' (FIIT-VP) principle²¹ (Table 1). Patients are advised to avoid extremes of temperature and include rest days. Expert opinion advises that patients displaying COVID-19 symptoms should rest for: '≥10 days from onset of symptoms plus 7 days from symptom resolution'.²² Adhering to a graduated exercise programme and not over-training (limiting training to 90 minutes per day) will reduce the risk of injury or compromising immunity.²³

Table 1. Example of FIIT-VP exercise recommendation for patients regularly taking part in exe	rcise with
well-controlled hypertension. ²¹	

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	Aerobic training	Strength training	Flexibility/balance training	
Frequency	5–7 days/week	2–3 days/week (aim for non- consecutive days)	2–3 days/week (aim for non- consecutive days)	
Intensity	Moderate (40–59% of VO ₂ max) This intensity will cause noticeable increases in heart rate and breathing but patient would still be able to maintain a conversation whilst exercising	Progress to start in keeping with patient's baseline capacity Seated or bodyweight exercises can be used to start	Stretch to the point of feeling tightness or slight discomfort Seated exercises can be used to start	
Туре	Prolonged activities using large muscle groups (eg walking, cycling, cross-trainer or rowing)	Body weight, free weight or machine exercises	Can be static, or dynamic stretching (eg pilates, yoga)	
Time	Aim for >30 minutes a day. This can be accumulated continuously or in shorter 10-minute blocks	2–4 sets of 8–12 repetitions	Hold static stretch for 10–30s, 2–4 repetitions for each exercise	
Volume	Aim for 150 mins/week	To include all major muscle groups	To include all major muscle groups	
Progression	Patient can aim to start in 5–10-minute blocks with a 10% increase in weekly volume	Gradual increase in load from body weight to 40–50% of 1RM and then 60–70% of 1RM	Gradual increase in range of motions and difficulty	

^{*}Adapted using recommendations from American College of Sports Medicine Guidelines for Exercise testing and prescription.²¹ 1RM = one repetition maximum, the maximum amount of weight that patient can possibly lift for one repetition.

Conclusion

Maintaining physical activity levels during the COVID-19 outbreak will have significant physical health benefits to all patients. Further data will be needed to evaluate the role of exercise in 'preconditioning' patients prior to infection.

Maximal oxygen uptake (VO₂ max), where available, has the potential to be used as part of existing 'triage' criteria to help risk stratify patients. ■

Key points

Physical activity will help provide general health benefits to all patients.

Maximal oxygen uptake $({\rm VO}_2\,{\rm max})$ may prove to be a clinically relevant 'triage' tool in addition to age and clinical criteria.

The role of exercise in preconditioning patients prior to COVID-19 infection is currently based on expert opinion. ■

References

- 1 World Health Organization. WHO director-general's opening remarks at the media briefing on COVID-19 – 11 March 2020. WHO, 2020. Available from: www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020 [Accessed 1 April 2020].
- 2 Philpotts E. GPs asked to review 1.5 million patients most at risk from coronavirus [Internet]. *Pulse Today*, 23 March 2020. Available from: www.pulsetoday.co.uk/news/gps-asked-to-review-15-million-patients-most-at-risk-from-coronavirus/20040414.article [Accessed 12 April 2020].
- 3 FitBit. The impact of coronavirus on global activity. Available from https://blog.fitbit.com/covid-19-global-activity/ [Accessed 12 April 2020].
- 4 Ekelund U, Tarp J, Steene-Johannessen J et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis BMJ 2019;366:14570.
- 5 Kujala U. Evidence on the effects of exercise therapy in the treatment of chronic disease. *Br J Sports Med* 2009;43:550–5.
- 6 Wong C-M, Lai H-K, Ou C-Q et al. Is exercise protective against influenza-associated mortality? PLoS One 2008;3:e2108.
- 7 Davis JM, Kohut ML, Colbert LH et al. Exercise, alveolar macrophage function, and susceptibility to respiratory infection. J Appl Physiol 1997;83:1461–6.
- 8 Razai M, Doerholt K, Ladhani S, Oakeshott P. Coronavirus disease 2019 (COVID-19): a quide for UK GPs. *BMJ* 2020;368:m800.
- 9 Wang D, Hu B, Hu C et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus—infected pneumonia in Wuhan, China. JAMA 2020, in press (DOI: 10.1001/jama.2020.1585).

- 10 Downing J, Rose T, Saini P *et al.* Impact of a community-based cardiovascular disease service intervention in a highly deprived area. *Heart* 2019;106:374–9.
- 11 WHO Collaborating Centre for Infectious Disease Modelling; MRC Centre for Global Infectious Disease Analysis; Abdul Latif Jameel Institute for Disease and Emergency Analytics; Imperial College London. Report 9 Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. Imperial College, 2020. Available from www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-9-impact-of-npis-on-covid-19/
- 12 West M, Asher R, Browning M et al. Validation of preoperative cardiopulmonary exercise testing-derived variables to predict in-hospital morbidity after major colorectal surgery. Br J Surgery 2016;103:744–52.
- 13 Colbenson G, Johnson A, Wilson M. Post-intensive care syndrome: impact, prevention, and management. *Breathe* 2019;15:98–101.
- 14 O'Connor M. Stay fit to fight coronavirus, say medics. *BBC News*, 28 March 2020. Available from www.bbc.co.uk/news/uk-52076856 [accessed 1 April 2020].
- 15 Boxall A, Barclay L, Sayers A, Caplan G. Managing chronic obstructive pulmonary disease in the community. *J Cardiopulm Rehabil* 2005;25:378–85.
- 16 Huang G, Ismail H, Murnane A, Kim P, Riedel B. Structured exercise program prior to major cancer surgery improves cardiopulmonary fitness: a retrospective cohort study. Support Care Cancer 2015;24:2277–85.
- 17 Davies SC, Atherton F, McBride M and Calderwood C. UK chief medical officers' physical activity guidelines. UK Government, 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/832868/uk-chief-medical-officers-physical-activity-quidelines.pdf.
- 18 Jones S. Assessment of exercise capacity and oxygen consumption using a 6 min stepper test in older adults. *Front Physiol* 2017;8:408.
- 19 Kwon S, Ahn J, Lee S *et al.* Estimating maximal oxygen uptake from daily activity data measured by a watch-type fitness tracker: cross-sectional study. *JMIR mHealth and uHealth* 2019;7:e13327.
- 20 Uth N, Sorensen H, Overgaard K, Pedersen PK. Estimation of VO₂max from the ratio between HRmax and HRrest the heart rate ratio method. Eur J Appl Physiol 2004;91:111–5.
- 21 American College of Sports Medicine. *ACSM's guidelines for exercise testing and prescription*. *10th ed*. Philadelphia; Wolters Kluwer: 2018.
- 22 Hull J, Loosemore M, Schwellnus M. Respiratory health in athletes: facing the COVID-19 challenge. *Lancet Resp Med* 2020, in press (doi: 10.1016/S2213-2600(20)30175-2).
- 23 Campbell JP and Turner JE. Debunking the myth of exerciseinduced immune suppression: redefining the impact of exercise on immunological health across the lifespan. Front Immunol 2018;9:648.

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