

The positive impact of physical activity and exercise on immune function; *The critical prevention and recovery tool to fight a second wave of COVID-19*

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The world is experiencing an extraordinary, life-altering challenge due to the COVID-19 pandemic (WHO, 2020). Its epidemiology highlights that age and inequalities in health, wellbeing and economic status makes people more vulnerable. The disease can be particularly severe for those that are older, obese with comorbidities and people of ethnic minority backgrounds.

The conditions created by the pandemic has raised the *importance of physical activity and wellbeing for society. Now is the time to translate this elevated profile into tangible social, behavioural and environmental change.*

Research centres (including the Advanced Wellbeing Research Centre¹), comprising teams of highly skilled individuals across Universities, the private and public sector as well as experts across the world, have developed high quality studies to understand how the virus affects the body and to mitigate spread. Significant investment has also been made seeking an effective COVID-19 vaccine to reduce further impact.

Whilst more than 39,200 research papers have been published in 2020 (PubMed database references including the term “COVID-19”²), less than 1% of them (n= 383) relate to the potential role and/or impact that physical activity might have on addressing the pandemic and importantly here, preventing a second wave (PubMed database references including the terms “COVID-19 and exercise”³).

This is somewhat surprising given the extant evidence linking an active lifestyle (involving informal physical activity, regular exercise and/or sports participation) and reinforced immune function across the lifespan, including viral defense (Neiman, Wentz, 2019).

1 <https://www.shu.ac.uk/research/specialisms/advanced-wellbeing-research-centre/ricovr>

2 <https://pubmed.ncbi.nlm.nih.gov/?term=covid+19&size=200>

3 <https://pubmed.ncbi.nlm.nih.gov/?term=covid+19+and+exercise&size=200>



Our role as a proactive and responsible industry⁴ is to communicate these facts effectively, and to create the conditions that make activity easy, attractive, social and safe. This so that individuals can engage in and benefit from the protective effects of regular physical activity from communicable and non-communicable disease.

The potential risk of exercising at training facilities during the COVID-19 pandemic (providing good hygiene and distancing measures) is very low compared to the negative health impact of physical inactivity...

Regular physical activity supports both physical and mental health in adults, teens, and children. Physical activity is especially important amid the COVID-19 pandemic given its role in helping to strengthen and improve immune functioning and lower risk of viral illness (Nieman, Wentz 2019). Physical activity plays a central role in the prevention and management of cardiovascular and metabolic health conditions as well as some cancers (WHO GAPP, 2018⁵), which can increase risk of severe adverse COVID-19 outcomes. Additionally, as many people have been at home and isolated for long periods, the mental health (Chekroud et al., 2018) and social benefits of community physical activity cannot be ignored.

⁴ Jimenez, A., Mayo, X., Copeland, R.J. "The Economic and Social Impact of promoting active living after the COVID-19 crisis. The role, value and impact of a proactive and responsible health and fitness industry"
https://www.europeactive.eu/sites/europeactive.eu/files/covid19/Economic-Social-Impact_050620.pdf

⁵ Global Action Plan on Physical Activity (GAPPA): <https://www.who.int/ncds/prevention/physicalactivity/global-action-plan-2018-2030/en/>

A recent randomized control trial, involving 3,764 participants, developed by the University of Oslo (Helsingen et al., 2020⁶), showed no virus transmission or increase in COVID-19 disease related to opening of training facilities *providing good hygiene and distancing measures were observed*. This initial trial highlights that facility-based activity can be undertaken safely, with limited risk. Moreover, that it is unnecessary to close training facilities and instead mitigation can be provided to enable people to continue to be active prevent societal downsides of the pandemic and limit its negative effect on health and wellbeing.

Last May, EuropeActive, alongside IHRSA and WFSGI, developed guidance on the *key considerations on the health safety aspects of the operation of sports, fitness, aquatics, thermal facilities/clubs in the context of COVID-19*⁷. This document, together with an accompanying COVID-19 Risk Assessment Tool and Mitigation Checklist, was developed to support club/facility operators to make an evidence-based decision on the risks associated with reopening facilities.

Furthermore, to help them identify and address the specific and additional risks pertaining to exercising in a leisure facility during the pandemic.

Fully committed with the implementation of solid and evidence-based safety and protection measures for the public, EuropeActive has developed a *practical guide to re-opening and operating a fitness facility*. This is delivered as an online learning programme covering best practice to help guide fitness club owners and operational staff on procedures for re-opening. The guidance covers running health & fitness clubs with consideration of COVID-19 pandemic restrictions and limitations⁸ and represents an industry standard.

The impact of inactivity for an ageing and obese society in Europe is negatively related to immune capacity...

In a provocative recent review paper, Professor Nieman (2020) highlighted that the world is experiencing a major demographic shift toward an older more obese population⁹, which *both impair host viral defense*. Indeed, by 2050, the world's population aged 60 years and older is expected to total 2 billion, an increase from 900 million in 2015 (GBD, 2018). Global estimates (WHO, 2020¹⁰) also suggest that more than 1.9 billion adults, are currently overweight and of these over 650 million are obese. If recent trends continue, nearly 60% of all adults worldwide will be overweight and obese, by 2030 (Kelly et al., 2008; Ward et al., 2019).

6 The TRAIIn Study Group. Randomized Re-Opening of Training Facilities during the COVID-19 pandemic. <https://www.medrxiv.org/content/10.1101/2020.06.24.20138768v2.full.pdf>

7 IHRSA, EuropeActive, WFSGI, et al. (2020) Key considerations for sports, fitness, aquatics, thermal facilities/clubs in the context of COVID-19.

https://cdn2.hubspot.net/hubfs/167081/Advocacy/Letter%20PDFs/Key%20Considerations%20for%20Sports%20Fitness%20Aquatics%20Ancillary%20Facilities%20Clubs%20in%20the%20Context%20of%20COVID-19_May_2020.pdf

8 EuropeActive (2020). A practical guide to re-opening and operating a fitness facility (e-learning programme). <https://www.europeactive.eu/covid19-guidance>

9 Nieman DC. Coronavirus disease-2019: A tocsin to our aging, unfit, corpulent, and immunodeficient society. *J Sport Health Sci*, 2020; 9:293-301.

10 <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>

According to Nieman's review (2020), the rationale behind the **role of ageing** impairing host viral defense could be summarized as follows:

- *"Aging in and of itself leads to negative changes in innate and adaptive immunity, a process termed immunosenescence (Duggal et al., 2019).*
- *The function of nearly every type of immune cell is negatively affected with increase in age, resulting in increased susceptibility to infectious diseases, reduced antibody responses to vaccinations, systemic inflammation, and decreased immune surveillance against cancer (Duggal et al., 2019; Van Beek et al., 2019; Simpson et al., 2012).*
- *Influenza and COVID-19 infections are associated with high rates of complicated illness, including pneumonia, among the elderly (Zhou et al., 2020; Grasselli et al., 2020; Garg et al., 2020; Richardson et al., 2020; Simonnet et al., 2020; Wu et al., 2020; Jordan et al., 2020; McElhaney, 2011)."*

If we look at the main reasons making **obesity a critical risk factor** for viral infections (including COVID-19), Nieman (2020) identify the following factors within his review paper:

- *"Obesity causes systemic inflammation and adversely impacts immune function and host defense in a way that patterns immunosenescence (Milner, Beck, 2012; Green, Beck, 2017).*
- *Obese patients have higher rates of nosocomial infections following surgery and experience altered pharmacokinetics of antimicrobial drugs (Milner, Beck, 2012; Green, Beck, 2017; Honce, Schultz-Cherry, 2019; Huttunen, Karppelin, Syrjänen, 2013; Hainer et al., 2015).*
- *Obesity emerged as an important risk factor for increased hospitalization and infection severity during both the 2009 influenza A virus H1N1 and COVID-19 pandemics (Simonnet et al., 2020; Luzi, Radaelli, 2020; Morgan et al., 2010; Sun et al., 2016; Van Kerkhove et al., 2011; Carter, Baranauskas, Fly, 2020; Lighter et al., 2020).*
- *The antibody response to the seasonal influenza vaccine is impaired in obese individuals, and virus shedding is prolonged during influenza illness (Maier et al., 2018).*
- *Compared to vaccinated normal-weight adults, vaccinated obese adults have twice the risk of influenza or influenza-like illness (Green, Beck, 2017).*
- *Animal-based studies suggest that obesity increases the severity and duration of viral infections, increasing the potential for the evolution of pathogenic viral variants (Honce et al., 2020)".*

For some, particularly those with long-term conditions, COVID-19 and the conditions it has created, present a perfect storm where inactivity and sedentary behaviors are exacerbated. This potentially worsens the impact of future pandemics (Hall et al., 2020). Indeed, individuals infected with COVID-19 are much more likely to be hospitalized and have poorer health outcomes if underlying medical conditions are present (Chow et al., 2020).



All projections indicate that the world's population will be older, more obese, and therefore increasingly more immunodeficient in the approaching decades (Nieman, 2020). According to Nieman, *"this shift is likely to increase the odds that infectious disease pandemics spawned by novel pathogens will continue to inflict widespread morbidity and mortality"* (Nieman, 2020; see Figure 1).

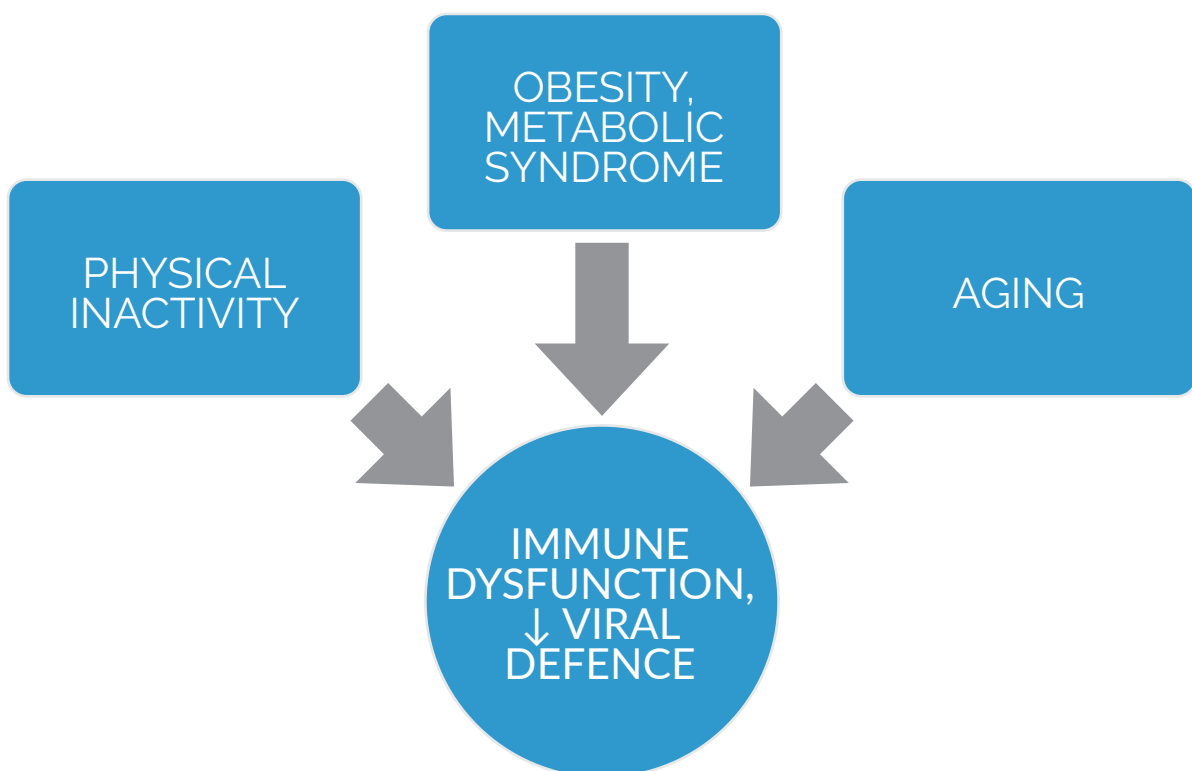


Figure 1: Linkage between physical inactivity, aging, and obesity and the metabolic syndrome with immune dysfunction and diminished viral defense (Nieman, 2020).

Summarizing the positive impact of regular physical activity and exercise on immune function.

Individuals with obesity/overweight, insulin resistance and type 2 diabetes typically have chronic low-grade inflammation. This is characterized by increased pro-inflammatory cytokines and inflammasomes, which predisposes these individuals to greater risk of infection along with more adverse health outcomes. This is certainly the case regarding COVID-19 with individuals with underlying medical conditions being much more likely to be hospitalized if they contract COVID-19 compared to healthy counterparts (Chow et al, 2020).

One of the mechanisms through which physical activity is thought to prevent chronic disease is by reducing cell inflammation (Booth et al., 2012). This could have important implications for the prevention of communicable as well as non-communicable disease. Indeed, in a recent review, Zbinden-Foncea and colleagues (2020) suggested that high cardiorespiratory fitness could confer innate immune protection against Covid-19. The mechanism proposed by Zbinden-Foncea and colleagues was that the protective effect might occur by attenuating the “cytokine storm syndrome”, often experienced by “at risk” individuals. It is important to highlight that this mechanism requires further research attention. Indeed, we are aware of reports that individuals who were previously very active continue to suffer Covid-related symptoms – particularly fatigue –for months after first diagnosis¹¹.

11 <https://blogs.bmj.com/bmj/2020/05/19/paul-garner-covid-19-and-fatigue-a-game-of-snakes-and-ladders/>



High cardiorespiratory fitness could potentially attenuate the pro-inflammatory state induced by COVID-19 and prevent a severe response to the disease. More broadly, *having elevated cardiorespiratory fitness and exercising at moderate to vigorous intensity on a regular basis can improve immune responses to vaccination, reduce chronic low-grade inflammation (Simpson & Katsanis, 2020) and improve various immune markers in several disease states including cancer, HIV, cardiovascular disease, diabetes, cognitive impairment and obesity (Duggal et al., 2019; Walsh et al., 2011).*

The positive impact of physical activity on immune function has been highlighted in another recent review. Redefining the potential impact of exercise immunological health function across the lifespan, the authors (Campbell, Turner, 2018) identified that regular physical activity and frequent exercise augment aspects of immune competency across the lifespan. In fact, just a single acute bout of exercise appears to enhance immune responses to vaccination in both younger and older individuals.

The beneficial effects of physical activity on immune function are likely to be greatest for older adults exhibiting the age-associated deterioration of immune competency, also referred to as immunosenescence (Aw et al., 2007). Moreover, preliminary evidence suggests that physical activity and regular structured exercise might even limit or delay immunological aging (Campbell, Turner, 2018; Nieman, 2020).

Epidemiological data also indicate that physically active people are less likely to report symptoms of upper respiratory illness and there is evidence that exercise can protect the host from many types viral infection including influenza, rhinovirus (another cause of the common cold) and the reactivation of latent herpesviruses such as Epstein-Barr (EBV), varicella-zoster (VZV) and herpes-simplex-virus-1 (HSV-1) (Duggal et al., 2019). A study by Martin and colleagues (2009) also showed that moderate intensity exercise training during an active influenza infection protected mice from death and promoted favorable immune cell composition and cytokine shifts in the lungs associated with improved survival (Martin et al., 2009).

Physically active individuals have shown better control over latent viral infections, even during periods of isolation and confinement. For instance, recent work from Simpson & Katsanis demonstrated that astronauts with increased cardiorespiratory fitness and skeletal muscle endurance were ~40% less likely to reactivate a latent herpesvirus during a 6-month mission to the International Space Station (ISS). Particularly if they were able to maintain their fitness on the ISS (Agha et al., 2020). Even in astronauts who did reactivate a virus, copies of viral DNA were fewer in the fitter astronauts indicating that they were less contagious than their less-fit counterparts. Latent viral reactivation is a hallmark of compromised immunity, which, in this context, we deem to be due to the stressors associated with isolation and inactivity as a result of confinement on the ISS (Simpson and Katsanis, 2020). Finally, research also has shown how periods of isolation and confinement elevate glucocorticoids (e.g. cortisol) that can inhibit many critical functions of our immune system (Simpson and Katsanis, 2020). These include the ability of our lymphocytes to multiply in response infectious agents and the effector functions of NK-cells and CD8+ T-cells, all of which are essential in the recognition and elimination of cancerous or virally infected cells (Duggal et al., 2019).

Taken collectively, these studies support the view that regular physical activity and maintenance of a healthy weight improve immune health while reducing the risk for several types of respiratory illnesses (Nieman, Wentz, 2019). As discussed previously, “these primary prevention strategies against respiratory illnesses are particularly important in aging societies with a high prevalence of obesity and related comorbidities and are essential adjuvants to mitigation practices” (Nieman, 2020). Figure 2 summarizes, the six key areas of positive impact of regular physical activity on improving and reinforcing immune function.

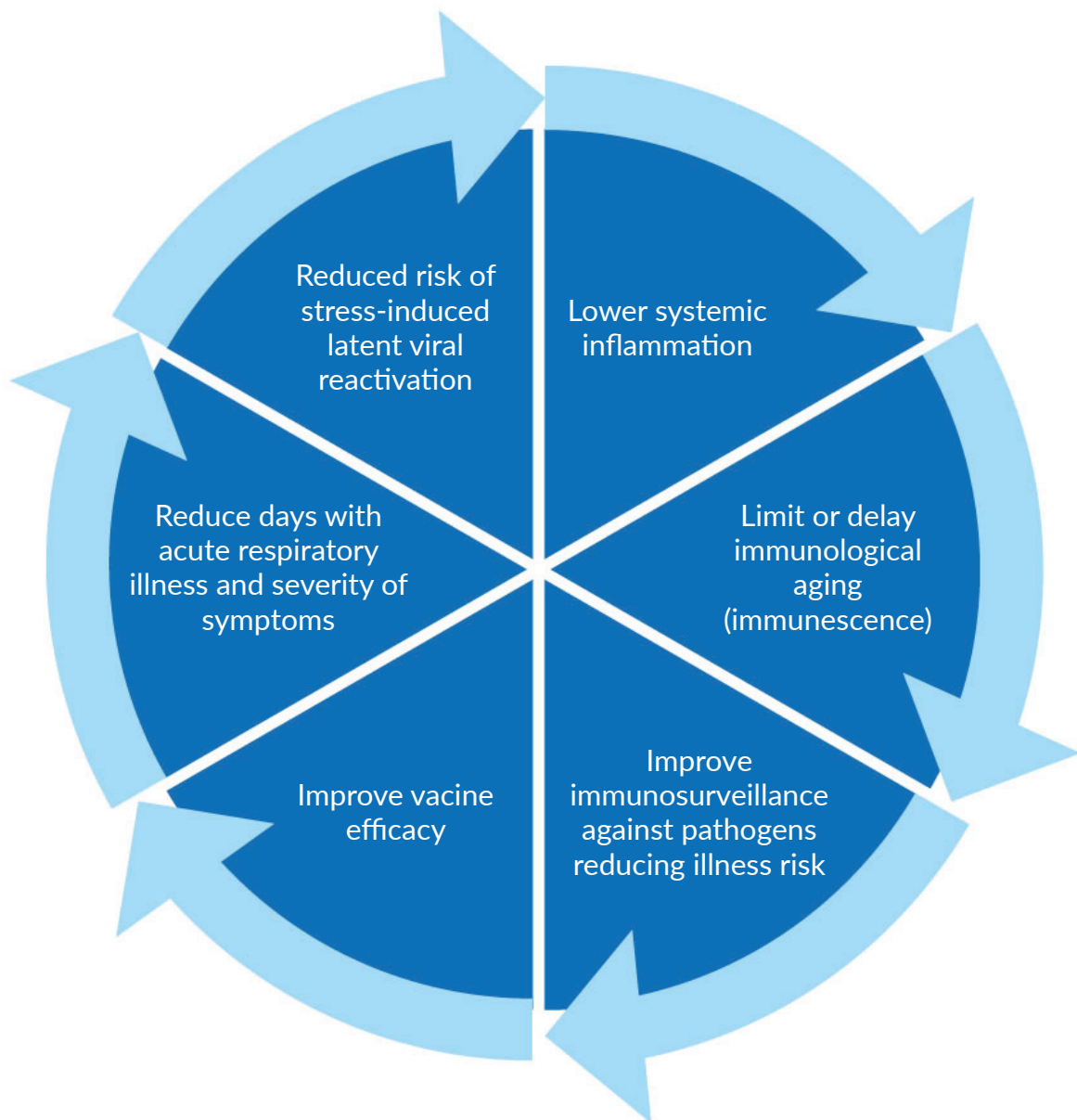


Figure 2: Areas of positive impact of regular exercise improving and reinforcing immune function (Adapted from evidences reported by: Campbell and Turner, 2018; Nieman, Wentz, 2019; Duggall et al., 2019; Zbinden-Foncea et al., 2020; and Nieman, 2020).



“COVID-19 took just a few months to spread to nearly every nation on earth while causing widespread morbidity and mortality. The data support the belief that severe cases of COVID-19 are more likely in older and obese individuals. This is indeed a wake-up call, a tocsin, to the world that primary prevention countermeasures focused on health behaviors and hygiene demand our full attention and support.

Secondary and tertiary prevention approaches centered on vaccine and therapeutics development will take time and may not be fully effective, giving even more urgency to staying fixated on primary prevention”

Nieman, 2020

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