



## Exercise dosing considerations in times of COVID-19 pandemic: A review

Consideraciones sobre la dosificación de ejercicio en tiempos de pandemia de COVID-19: Una revisión

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### Abstract

**Introduction:** During the COVID-19 pandemic, international organizations recommended regular physical exercise to maintain physical and mental health during confinement, however, it is an emerging disease, the evidence is not conclusive regarding the relationship between a physical inactivity and the risk of serious outcomes in patients with COVID-19, therefore, it is essential to identify the contribution of the type of physical exercise modality and the contribution to the immune system. **Objective:** To demonstrate the immunological response of different physical exercise modality in the population between 18 and 84 years of age, the population identified with the highest number of confirmed cases of COVID-19, in the report n°198 of the World Health Organization. **Materials and methods:** A review of the literature was carried out between Central Pubmed, Google Scholar and Scielo from January 2016 to December 2021. **Results:** Of the selected articles, it was possible to identify the main benefits in the immune response with both modalities of physical exercise (aerobic and/or resistance) in the target population. **Conclusion:** At present, the benefits on the immune response in patients with COVID-19 are completely unknown, which is why it is essential to identify the contribution on the immune response in different modalities of physical exercise in the population between 18-84 years of age.

**Keywords:** Physical exercise; strength training; resistance training; immune response; immune system; COVID-19. (Source: DeCS, Bireme).

### Resumen

**Introducción:** Durante la pandemia de COVID-19, organismos internacionales recomendaron ejercicio físico regular para mantener la salud física y mental durante el confinamiento, sin embargo, al tratarse de una enfermedad emergente, la evidencia no es concluyente en relación a una inactividad física y el riesgo de desenlaces graves en estos pacientes con COVID-19. Es fundamental identificar el aporte del tipo de modalidad de ejercicio físico al sistema inmunológico. **Objetivo:** Demostrar la respuesta inmunológica de las diferentes modalidades de ejercicio físico en la población de 18 a 84 años, población identificada con mayor número de casos confirmados de COVID-19, en el informe n°198 de la Organización Mundial de la Salud. **Materiales y métodos:** Revisión de la literatura entre *Pubmed Central*, *Google Scholar* y *Scielo* (enero de 2016 - diciembre de 2021). **Resultados:** De los artículos seleccionados se identificó los principales beneficios en la respuesta inmune con ambas modalidades de ejercicio físico (aeróbico y/o resistencia) en dicha población. **Conclusión:** En la actualidad se desconoce por completo los beneficios sobre la respuesta inmune en pacientes con COVID-19, por ello, es fundamental identificar el aporte sobre la respuesta inmune en diferentes modalidades de ejercicio físico en la población entre 18-84 años de edad.

**Palabras clave:** Ejercicio físico; entrenamiento de fuerza; entrenamiento de resistencia; respuesta inmune; sistema inmune; COVID-19. (Fuente: DeCS, Bireme).

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## Introduction

In late 2019, a new condition caused by SARS-CoV-2 was reported in Wuhan, China, causing a global pandemic problem<sup>(1,2)</sup>. Autopsies of patients who died from COVID-19 identified that the virus invades mainly the lungs, but also affects the cardiovascular system, the liver, the kidneys, and the coagulation system<sup>(3)</sup>. Reported data on morbidity and mortality from COVID-19 in hospitalized patients indicate that 80-85% present asymptotically or with mild or moderate symptoms, 10% with severe infections, and half of the 5% of critical cases resulted in death<sup>(4,5)</sup>.

These data indicate that the severity or mortality rate is low; however, the World Health Organization (WHO) surveillance reports identify that the age distribution of COVID-19 cases is between 25-64 years of age, presenting a higher risk with 64% infection, followed by the third group between 65-84 years of age with a risk of 19.4% of cases<sup>(6)</sup>. During the pandemic, various international organizations, such as the American College of Sports Medicine (ACSM), the American Heart Association (AHA) and the WHO, recommended regular exercise at moderate intensity to maintain physical and psychological health<sup>(7,8)</sup>. In addition, physical exercise is an important immune system booster<sup>(2)</sup>, and although the risk factors associated with severe disease by COVID-19 are still being studied, there is increasing and consistent evidence of the relationship between physical inactivity and an increased risk of severe outcomes, i.e. hospitalization, intensive care unit admission, and/or death, similarly, patients who participated in aerobic and resistance training had a low risk of infection<sup>(9)</sup>. However, the training load dose and its response to the effort performed, as well as the most appropriate exercise modality, are not detailed<sup>(10,11)</sup>.

These elements are key considering the potential effect on patient health, which could put at risk a

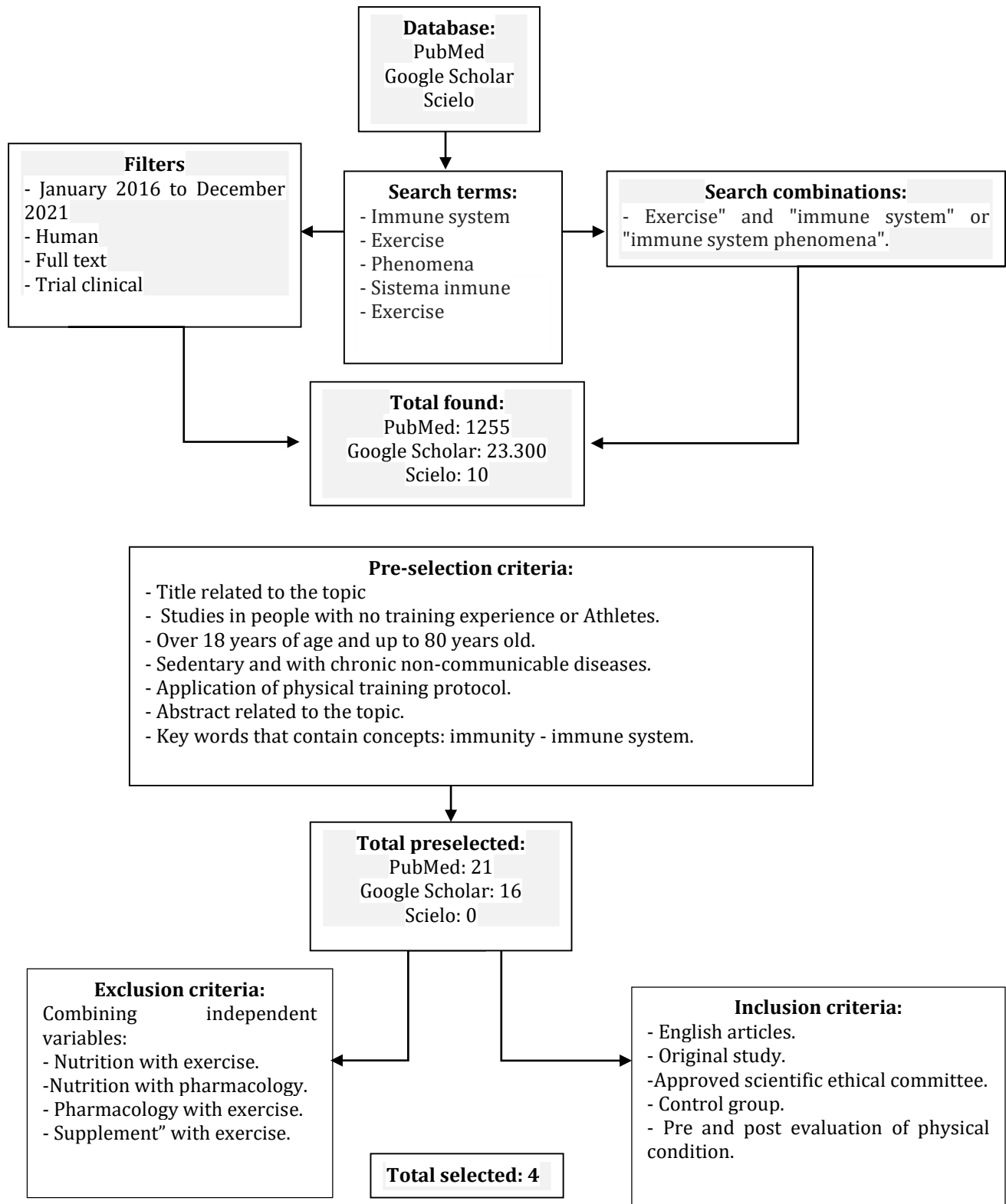
population deconditioned by physical inactivity and nutrition by excess, lack of supervision, and reliance on self-regulation to exercise that could increase the risk of cardiovascular events, alteration of the musculoskeletal system, and a potential immunosuppressive effect when intensity and recovery are not controlled<sup>(12,13)</sup>.

Therefore, when prescribing physical exercise, the following components should be carefully controlled: frequency, intensity, duration of each prescribed session and, above all, the modality of the exercise to be performed; i.e., endurance or resistance or both (concurrent)<sup>(14,15)</sup>. The endurance training mainly emphasizes a prolonged time at a lower intensity of execution, while resistance training, emphasizes high intensities and limited time with respect to resistance exercise and concurrent training involving the aforementioned modalities<sup>(16)</sup>.

These aspects are key when selecting the dose of physical exercise and its physiological contributions according to the individual needs of each person<sup>(17)</sup>. Therefore, this review aims to investigate existing evidence in the last five years (January 2016 through December 2021), on the immunological response of different physical exercise modalities in the population aged 25 to 84 years, identified with the highest number of confirmed cases of COVID-19, declared in the WHO report n°198 of the World Health Organization<sup>(6)</sup>.

## Materials and methods

The following is a flow chart showing the methodology used to carry out bibliographic research and the steps taken to achieve it.



**Figure 1.** Flow diagram of the literature search and article selection process

## Results

Once the search was performed, following the steps explained above, a total of 4 articles were retrieved, all of the original scientific articles. Based on the characteristics of the selected study protocols, we

were able to identify the general characteristics of the participants and the selected studies (Table 1), and the description of the exercise programs, variables, measures, and main results of the selected studies (Table 2).

**Table 1.** General characteristics of the selected studies

First author/years	Main features	Age (Range in years)	Participants (n)	
			EG	CG
Abd El-Kader & Al-Shreef <sup>(18)</sup>	Healthy sedentary people ≥15 minutes of physical activity no more than 2 times a week. Excluding smokers, consumption of any anti-inflammatory and antidepressant medication.	(61-67)	RS: 37 RS: 44 * Randomized gender distribution	---
Bartlett <i>et al.</i> , <sup>(19)</sup>	Sedentary with rheumatoid arthritis No change in medication in the previous 3 months. prednisone ≤5 mg / day. Subjects with diabetes mellitus or any cardiovascular disease are excluded.	(64 ± 7)	Men=1 Women= 11	---
Broadbent & Coutts <sup>(20)</sup>	Sedentary people with chronic fatigue syndrome No diagnosed cardiorespiratory problems No metabolic conditions. No recurrent problems	(18-65)	ET; (Intermittent) = 8	18
Hagstrom <i>et al.</i> , <sup>(21)</sup>	Recovered from Breast Cancer (stage I-III A)	(51.9 ± 8.8)	ET; Gradual= 8 ET; Cycling and regular care = 8 ST: 20	19

EG: experimental group; CG: control group; ET: endurance training; RT: Resistance training.

**Table 2.** Description of the physical exercise programs analyzed and main results

First author/years	Modality Training	Intensity	Duration	Frequency	Session duration	Instruments	Results
Ab d El-Kader & Al-Shreef <sup>(18)</sup>	Endurance	1st stage: 60-70% HRmax	3 months	3 sessions/week	40 min	Treadmill	↓↓ TNF- $\alpha$ , IL-6, CD3, CD4, CD8, CD4/CD8 ↑↑ IL-10
	Resistance	2nd stage 70-80% HRmax 3 sets of 8-12 repetitions at 60% or 80% of 1RM	3 months	3 sessions/week	40 min Individual execution time	Pulley machines	↓ TNF- $\alpha$ , IL-6, CD3, CD4, CD8, CD4/CD8 ↑ IL-10
Bartlett <i>et al.</i> <sup>(19)</sup>	Endurance (HIIT)	Intervals 80-90% VO2 reserve with active recovery 50-60% VO2reserve. Walking speeds range from 1-4.6 mph.	6 months 10 weeks	3 sessions/week	30 min	Treadmill	↓CD14/CD16, CD14/CD16 TLR2, TLR4 and HLA-DR of intermediate monocytes ↑ phagocytosis of monocytes from <i>Escherichia coli</i> ↑ migration of peripheral blood neutrophils isolated from AR towards chemokine CXCL-8 ↑ counts CD3+ y CD4+, CD3-CD16+ CD56 ↑↑NK expressing LAMP- 1 /LAMP- 2
Broadbent & Coutts <sup>(20)</sup>	Endurance (Gradual)	Equivalent workload (w) at 50% of VO2peak or RPE 3 (1-10)	12 weeks	3 sessions/week	25-30 min	Cycloergometer	↑ counts CD3+, CD8+, CD4+, CD3+ CD4+ CD8 +, CD3-CD16+ CD56 +, CD19+ and CD45+ ↑↑NK expressing LAMP- 1 /LAMP- 2
	Endurance (Intermittent)	1 minute at 60% of VO2 peak or RPE 4-5 alternating with 1 minute at 30% of VO2 peak or RPE 1-2		3 sessions/week	25-30 min	Cycloergometer	↑ counts CD3+, CD8+, CD4+, CD3+ CD4+ CD8 +, CD3-CD16+ CD56 +, CD19+ and CD45+ ↑↑NK expressing LAMP- 1 /LAMP- 2
	Usual Care	mobilization by bicycle to the usual care center.				Bicycle	↑↑ CD8+ ↑ NK expressing LAMP- 1 /LAMP- 2
Hagstrom <i>et al.</i> <sup>(21)</sup>	Resistance	3 series of 8-10 repetitions at 80% 1RM	16 weeks	3 sessions/week	Not specified	Free weights	↓ TNF- $\alpha$ in cells NK y NKT

HRmax: Maximum heart rate. HR: Heart rate. 1RM: 1-Maximum repetition. RPE: range of perceived exercise. HIIT: High-Intensity Interval Training. TLR2: Toll-like receptor 2. TLR4: Toll-like receptor 4. HLA-DR: HLA Human Leukocyte Antigen System. IL-6: Interleukin 6. IL-10: Interleukin 10. TNF- $\alpha$ : Tumor necrosis factor. NK: Natural killer cells.

## Discussion

This review aimed to investigate the existing evidence in the last five years (January 2016 through December 2021), regarding the immunological response of different physical exercise modalities in the population aged 25 to 84 years, identified with the highest number of confirmed cases of COVID-19, declared in the WHO report n°198 of the World Health Organization<sup>(2)</sup>.

To propose appropriate physical exercise protocols for the benefit of the population between 25 and 84 years of age, identified as having the highest number of confirmed cases of COVID-19. In general terms, from the articles analyzed in relation to endurance exercise, the volume (duration) of exercise ranged from 20-40 minutes per session with intensities quantified by maximum heart rate (HR<sub>max</sub>), Heart Rate Reserve (HRR), maximal oxygen consumption (VO<sub>2max</sub>) and Perceive Exertion scale (RPE). On the other hand, resistance exercises had a maximum duration of 60 minutes per session, whose intensity was determined based on the percentage of maximum repetition (60-80%1RM).

Specifically, focusing on the main studies, it is of interest to analyze the study by Abd El-Kader *et al.*<sup>(18)</sup>, who studied subjects older than 60 years, sedentary without comorbidities, randomly assigned to two groups exposed to both exercise modalities. One group performed moderate-intensity continuous endurance exercise on a treadmill, and the other group performed resistance exercise with pulley machines, both for the same period and number of weekly sessions. The results showed that endurance exercise was identified to contribute significantly to modulating the immune system and inflammatory markers in elderly subjects. However, resistance exercise can also be an effective method, as an alternative to a shorter endurance effort<sup>(18)</sup>.

Similarly, Bartlett *et al.*<sup>(19)</sup> applied a high intensity treadmill training (HIIT) protocol to a sample of 60+ years of age. The authors found that non-classical monocytes (CD14/CD16) were significantly reduced, as were intermediate monocytes (CD14/CD16). The cell surface expression of toll-like receptors (TLR2, TLR4) and the human leukocyte antigen system (HLA-DR) of intermediate monocytes was significantly reduced. The phagocytosis of *Escherichia coli* monocytes was significantly increased and the migration of peripheral blood

neutrophils isolated from rheumatoid arthritis to the chemokine CXCL8 was enhanced. The described HIIT protocol improved neutrophil migration precision and bactericidal functions in sedentary individuals of both sexes with rheumatoid arthritis. However, no changes were observed in inflammatory markers such as interleukin 1  $\beta$  or IL-1 $\beta$ , interleukin 6 or IL-6, interleukin 8 or IL8 also known as CXCL-8, interleukin 10 or IL-10, C-reactive protein or CRP and tumor necrosis factor or TNF- $\alpha$ <sup>(19)</sup>.

Another study published by Broadbent and Coutts<sup>(20)</sup> analyzed the effect of a gradual and intermittent endurance cycling protocol on lymphocyte cells (CD3+, CD4+, CD25+ and CD134+) counts during 12 weeks. The patients suffered from chronic fatigue syndrome (CFS) and ranged in age from 18 to 65 years. The authors concluded that weeks of training in both aerobic training modalities significantly improved CD4+ lymphocyte activation and aerobic capacity. However, they also suggested that intermittent exercise could improve patients with chronic fatigue syndrome<sup>(20)</sup>.

In addition, Hangstrom *et al.*<sup>(21)</sup>, conducted a resistance exercise intervention in breast cancer survivors (stage I-IIIa) whose ages ranged from 50-60 years, a resistance exercise protocol with free weight lifting was performed for 16 weeks, at a frequency of 3 times per week, at an intensity of 80% of 1RM. These changes were also correlated with an increase in lower body strength, in addition to a reduction in TNF- $\alpha$ , NK and NKT. No modifications were observed for changes in serum markers of inflammation. However, he found correlations between lower extremity strength gain and increased TNF- $\alpha$ , NK, and NKT<sup>(21)</sup>.

However, given the scarcity of controlled studies on physical exercise and COVID-19, future research should focus on the study of the specific effects on the immune response in patients infected with this new viral disease and determine the benefits of physical exercise in its different modalities. Therefore, it is suggested to pay attention to the correct dosage of the different modalities of physical exercise with the help of an exercise professional.

## Conclusion

Based on the different protocols analyzed in the present review, resistance exercise and endurance exercise demonstrate benefits in the immune response in sedentary healthy subjects and/or those with underlying diseases. However, greater specificity and studies in patients who have presented COVID-19 are required.

**Conflict of interest:** Author declared nothing conflict.

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