










REVIEW

Open Access



The influence of structured physical activity on vaccination response from adults to older individuals: a systematic review on the Immunoinflammatory crosstalk of COVID-19

Bruna Maria Palotino-Ferreira¹ , Saulo Vasconcelos Rocha¹ , Albená Nunes-Silva² , Antonio Felipe Souza-Gomes² , Francisco Rodrigues^{3*} , Patrícia Coelho³ , André Luís Lacerda Bachi⁴ , Rodrigo Assunção de Oliveira⁵ , Marcelo Paes de Barros⁵  and Guilherme Eustáquio Furtado^{6,7,8*} 

Abstract

Background Amidst the ongoing COVID-19 pandemic, understanding factors that influence vaccine efficacy is crucial, particularly in older adults. Regular physical exercise and/or structured physical activity (SPA) has emerged as a potential modulator of immune responses, enhancing vaccine effectiveness. This systematic review aims to consolidate current evidence on the impact of SPA/exercise on both immune and inflammatory responses to COVID-19 vaccination in adults and older individuals.

Methods Most relevant studies were extracted from indexed databases using health subject terms in English, Portuguese, and Spanish. Studies that examined the impact of regular exercise or SPA on inflammatory and/or immunological responses in relation to COVID-19 immunization were selected. In particular, all chosen studies included individuals who received vaccinations either prior to or following the exercise regimen or SPA, and the main goal was to evaluate these effects on immunological and/or inflammatory reactions induced by vaccination.

Results Among the 7 studies included ($n = 1149$), the effects of regular exercise or PA on vaccine-induced immune responses while concurrently assessing inflammatory markers were examined. The findings suggest that moderate to high-intensity structured physical activity (50–70% of maximum heart rate for aerobic exercise and 60–80% of 1RM for resistance training), performed 3–5 times per week, was able to enhance immune responses to COVID-19 vaccination, particularly by mitigating chronic low-grade inflammation. Acute exercise can transiently boost immunity, whilst engagement in moderate SPA over a period of six months may contribute to sustained improvements in immune function, especially in older adults. However, these findings should be interpreted with caution due to variability in study design, sample characteristics, and potential confounding factors.

*Correspondence:

Francisco Rodrigues

franciscobrodrigues@ipcb.pt

Guilherme Eustáquio Furtado

guilherme.furtado@ipc.pt; furts2001@yahoo.com.br

Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Conclusion Regular exercise and SPA play a significant role in improving immune/inflammatory responses to COVID-19 vaccination. Older adults, in particular, may benefit from regular SPA and exercise as a strategy to counteract immunosenescence and optimize vaccine efficacy. However, further research is needed to better refine exercise protocols and determine long-term benefits in different populations.

Keywords Upper respiratory tract infectior, J-Shaped curve, Psychobiological stress, Physical exercise, CovFlu vaccines

Introduction

The COVID-19 pandemic, caused by the coronavirus SARS-CoV-2, has brought unprecedented challenges to global healthcare systems and social structures [1]. Although the development and distribution of vaccines have provided a glimmer of light at the end of the tunnel, the full comprehension of the determinants of vaccine efficacy is still ongoing [2]. In this context, the complex interplay between physical activity/exercise, immune/inflammatory responses, and vaccine efficiency is worthy of investigation [3].

Age is one of the most important factors influencing the immune response to infections and vaccination [4]. With aging, the immune system undergoes a process known as immunosenescence, which results in a gradual reduction of responsiveness to pathogens and vaccines, increasing susceptibility to infections, including COVID-19 [5]. This decline in immune function affects both the innate and adaptive immune systems [6], leading to a weakened defense against infectious diseases and an increased risk of chronic conditions in older individuals [7]. It is broadly accepted that some factors, such as genetic predispositions, environmental influences, behavioral habits, and nutrition, contributes to variations in immune responses, as well as sedentary lifestyles can further exacerbate these declines [8]. When combined with comorbidities commonly seen in aging individuals, these factors can lead to a significantly impaired immune response, leading to older individuals more prone to severe disease and complications from infections, as COVID-19 [8, 9]. Therefore, understanding how these age-related changes in immune function influence vaccine responses is critical in developing strategies to protect older populations.

Recent studies have shown that immunosenescence not only results in diminished T-cell production and function but also impacts the efficiency of antibody responses to vaccination and infection [10]. In the context of COVID-19, these age-related changes may contribute to a slower and less robust immune response, leading to reduced vaccine efficacy in older individuals [11]. Based on its data, is essential to consider the role of immune system aging when assessing the effectiveness of COVID-19 vaccines and other interventions [12]. Focusing on the immunological mechanisms underpinning aging, we can better understand the inequalities in COVID-19 results across age groups and adopt more personalized public

health policies to safeguard the most susceptible populations [13].

Regular physical activity (PA) which includes physical exercises is a long-term immune system booster, capable of improving both innate and adaptive responsiveness [14–16]. These responses are characterized by improvements in leukocyte trafficking, optimized immune intern communication (balance between pro- and anti-inflammatory cytokines), proper metabolic modulation (mainly via interleukin 6), and overall immune cell function, which, collectively, contribute to an enhanced state of immune surveillance [17]. Consequently, it is not a surprise the growing evidence of the strong interplay between immune adaptations induced by SPA and the immune/inflammatory responses triggered by COVID-19 vaccines [3, 9, 18].

On the other hand, the balance between the long-term immune improvement induced by exercise and potential immunosuppression (usually due to overtraining or repeated exhaustion) must be carefully considered [9, 19]. In this context, it is worth mentioning that while regular PA is capable of improving or maintaining immunity throughout life [20], prolonged and high-intense exercises, such as endurance events, can trigger transient immunosuppression, generally characterized by an impairment in immune cell function [9]. In fact, this post-exercise “open window” for opportunistic infections has raised questions about whether certain exercise protocols may inadvertently impact the immune response to vaccination, especially against pathogens like SARS-CoV-2 [20]. As the scientific community seeks to optimize COVID-19 vaccination strategies for diverse populations [21], it is crucial to understand how exercise-induced immune adaptations influence the development of protective immunity against respiratory virus [9, 22].

Considering the limited integration of exercise-elicited immune-inflammatory mechanisms and their role in enhancing vaccine efficacy among older adults, this review adopts a systematic approach to address this gap. The aim is to rigorously analyse studies that investigate the concurrent effects of regular PA or structured exercise and COVID-19 vaccination in middle-aged and older individuals. This methodology balances contextual depth with analytical rigor, offering a comprehensive and focused perspective on this complex and evolving topic.

Therefore, this systematic review (SR) aims to present the current state-of-the-art understanding of the complex interplay between regular exercise/PA, age-related immune dysfunction, and inflammatory responses to COVID-19 vaccination. Through synthesis of information from multiple studies, we intend to emphasize the potential of engagement to maximize vaccine response in older adults, identify significant gaps in the existing literature, and recommend paths for future research. Furthermore, this review provides actionable insights for public health strategies aimed at enhancing vaccine efficacy and reducing susceptibility to viral respiratory infections, particularly in aged populations.

Methods

Study design

This is a SR conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [23]. Additionally,

a combined-method approach was used based on the Population, Intervention, Comparison, Outcome, Time, and Settings (PICOTS) framework to develop the conceptual structure of this review (Table 1) [24–26]. The review protocol was registered in PROSPERO (Registration ID: 653698), ensuring methodological transparency and rigor.

Article selection criteria

The PICOTS framework guided the definition of inclusion and exclusion criteria. Expert consultation and systematic searches ensured comprehensive coverage of the topic. The central research question was: *How do PA and exercise interventions influence immune responses to COVID-19 vaccination in adults and older adults?*

Based on this, studies were included if they assessed PA levels or implemented structured, planned, and repetitive exercise interventions aimed at improving physical fitness in adults or older adults, regardless of gender or health status. Eligible studies included those with comparison groups (with or without treatment), PA-only or combined interventions, and outcomes involving pro/anti-inflammatory cytokines or antibody responses. The timing, frequency, and duration of interventions were also considered, along with various settings (e.g., community, healthcare, or social centers).

Only studies in which participants were vaccinated before or after the intervention, and where the primary aim was to assess the effects of PA or exercise on immune and/or inflammatory responses to COVID-19 vaccination, were selected.

Systematic searches

Articles published between March 2020 and January 2025 were selected to ensure coverage of studies on PA and exercise during the COVID-19 pandemic. The search strategy included key terms indexed in MeSH and the Virtual Health Library (in Portuguese, and Spanish) to broaden the scope and accuracy. Only studies published in these three languages were considered. The search focused on articles assessing the impact of exercise interventions on immune and inflammatory responses, particularly in the context of protection against viral respiratory infections.

Screening process

The review process involved several key stages: Keyword Selection, Identification, Screening, and Selection, following the PRISMA statement [23]. During the screening phase, titles and abstracts were reviewed to identify relevant studies, while non-scientific articles (such as congress abstracts, proceedings, editorials, and errata) were systematically excluded. An expert consultation stage was included to identify additional non-indexed

Table 1 Construction strategy for review Preparation based on PICOTS principles

Acronym	Information	Concepts
P	Individuals across all age groups	According to the WHO, encompassing people from different stages of life, including children, adolescents, adults, and older people, without restrictions based on gender, or health status [27]
I	Regular exercise interventions or PA	Planned, repetitive and structured body movement done to improvement one or more components of physical fitness (i.e., muscle strength and resistance; flexibility, body composition) [28]
C	Controls or groups of comparison	Without a specific treatment and/or involving isolated or combined physical exercise interventions [29]
O	Pro/anti-inflammatory cytokines and/or antibodies	Indicators on the changing state of psychosocial, neurocognitive, sensory-motor, social-emotional, sleep, and socio-behavioral domains of an older individual, group of people or populations [30]
T	Time of different types of intervention	Refers to the temporal aspects of exercise interventions, encompassing the duration, frequency, and timing of exercise sessions. It involves specifying how long each exercise session lasts, how often sessions are conducted [31].
S	Community settings or 24-hours healthcare and social support centers	Encompass the environments, contexts, and conditions in which exercise interventions occur. This involves identifying where exercise sessions take place, such as fitness centers, home settings, outdoor locations, or clinical facilities [32].

keywords that could help uncover more relevant articles. The systematic searches were independently and manually conducted by two co-authors (BMPF and AFSG) and supervised by two senior professors in the field (SVR and GEF). The search strategy included combinations such as (“covid19”[Title/Abstract] OR “sarscov2”[Title/Abstract] AND “Physical Activity”[Title/Abstract]) OR “exercise”[Title/Abstract]) AND “vaccination” [Title/Abstract]), AND (“Covid19”[Title] OR “sarscov2”[Title] AND “exercise”[Title] AND “antibodies”[Title]).

Risk of Bias and study quality

To evaluate the methodological rigor and reporting standards of the included studies, the Tool for the Assessment of Study Quality and Reporting in Exercise (TESTEX) was utilized [33]. This instrument was specifically developed and is well-suited to assess research focused on context related to exercise interventions. The TESTEX tool comprises two main domains: one addressing the quality of the study design (maximum of 5 points) and another focused on the completeness and clarity of reporting (up to 10 points), allowing for a total possible score of 15 [34].

Unlike general quality assessment tools, TESTEX places emphasis on aspects particularly relevant to exercise-based studies—such as exercise prescription, adherence monitoring, and reporting of physical outcomes—while deliberately omitting criteria less applicable to this field. Each item is evaluated dichotomously, receiving one point if the criterion is clearly met or zero if not, providing a structured and exercise-specific appraisal of study validity (see Appendix A) [33].

Data synthesis

Given the heterogeneity among the selected studies—including differences in exercise protocols, participant age groups, types of vaccines administered, and the immune and inflammatory biomarkers assessed—a meta-analysis was not feasible. Instead, a narrative synthesis approach was adopted to summarize and interpret the findings. The included studies were grouped based on the type of exercise intervention (acute vs. chronic), population characteristics, and the timing of vaccination in relation to the PA protocol. Key outcomes were categorized according to immune responses and inflammatory profiles.

Where applicable, particular attention was paid to the intensity and duration of PA or exercise, as well as the timing of its application relative to vaccination, as these factors appeared to modulate the immunological outcomes. Studies were also qualitatively assessed for methodological rigor using the TESTEX scale, which supported the reliability of the reported results.

Results

In Fig. 1 is shown the PRISMA flow diagram used to outline the article selection process systematically. A total of 5,088 records were initially identified through database searches. After removing duplicates, 507 records remained for screening. The titles and abstracts of these records were evaluated, leading to the exclusion of 481 articles that did not meet the predefined criteria. After full-text screening, 9 studies were included for meeting the criteria on the role of SPA in modulating immune-inflammatory responses to optimize vaccination outcomes in adults and older adults (Fig. 1).

Summary of included studies

In these 7 studies, a total of 1149 participants were collectively evaluated, with participants ranging in age from 18 to 87 years. The exercise interventions varied in type, including aerobic exercise [35–38], resistance and strength exercises [39], combined aerobic and resistance exercises [37], and questionnaire-based assessments of habitual PA [40, 41]. The studies also differed in duration, frequency, and intensity, ranging from single-session acute exercise to long-term interventions lasting up to 48 weeks. Several experimental designs were employed, including randomized controlled trials, observational studies, and cross-sectional analyses, to assess the effects of PA either acutely or through a longitudinal approach. Participants in these studies received different COVID-19 vaccines, including ChAdOx1 nCoV-19 (AZD1222, AstraZeneca/Oxford), CoronaVac (SinoVac), Pfizer-BioNTech (BNT162b2), and Janssen (Ad26.COV2.S, Johnson & Johnson), and the biomarkers analyzed encompassed different immune and inflammatory types, such as cytokines (IL-6, IL-10, TNF- α , IFN- α), immunoglobulins (IgA, IgG, IgM), total lymphocytes and subpopulations, (CD4+, CD8+, CD28-CD57+), and neutralizing antibodies (NAb, GMT titers). Notably, only the study conducted by Silva *et al.* (2023) exclusively examined older individuals (60–85 years) [37], while the remaining studies included mixed-age populations or younger adults.

Main outputs of included studies

In the study conducted by Hallam and colleagues (2022) explored the effects of light- to moderate-intensity exercise performed after vaccination on serum antibody responses to both COVID-19, using Pfizer-BioNTech (BNT162b2), and influenza vaccines [35]. This study was developed between March and June 2021, during the early phase of the COVID-19 vaccination campaign. The exercise program involved 90 min of exercise, including cycling on a cycle ergometer or engaging in outdoor activities such as walking and games, initiated within 30 min after vaccination. The results showed a

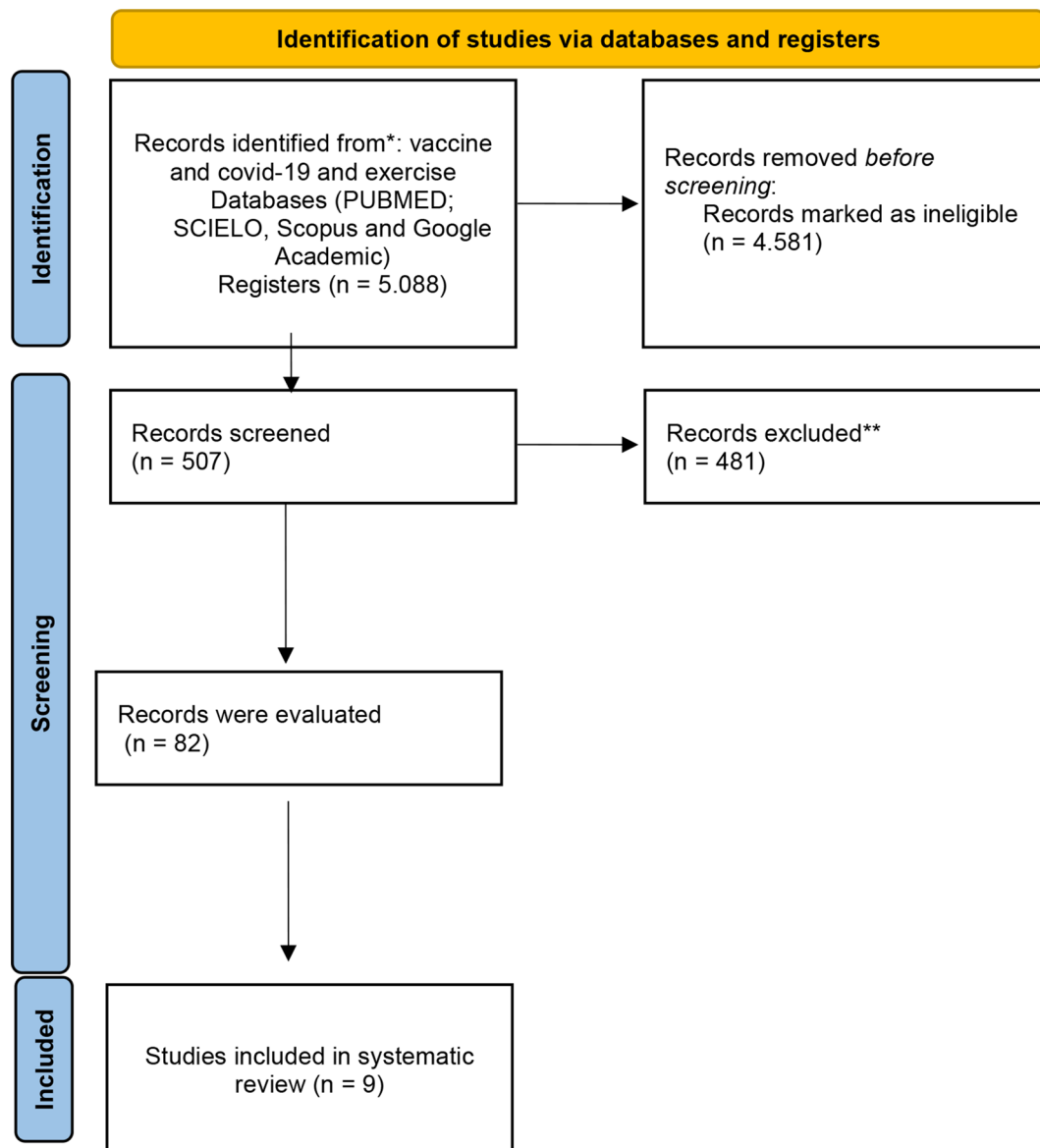


Fig. 1 PRISMA Flowchart of systematic search

light-to-moderate exercise significantly increased serum antibody levels for both influenza and COVID-19 vaccines. This enhancement in antibody response was associated with the role of interferon-alpha (IFN- α), which appears to mediate the exercise-related immunological benefits [35]. These findings have significant public health implications, suggesting that incorporating a light-to-moderate exercise program immediately following vaccination could be an effective strategy to improve immune responses, particularly during mass vaccination campaigns.

Another study explored the effects of regular exercise on vaccine-induced immune responses in active and inactive older adults, considering the impacts of aging and immunosenescence, with a focus on the CoronaVac and

ChadOx-1 vaccines [37]. Participants engaged in a combined training program, which included continuous aerobic and resistance exercises, and their immune responses were assessed pre- and post-vaccination. Results revealed that physically active participants exhibited significantly higher IgG and IgA antibody levels following ChadOx-1 vaccination compared to inactive individuals. Moreover, active participants showed better modulation of T-cell profiles, including CD4+, CD8+, and CD28-CD57+ cells, suggesting that SPA may enhance both humoral and cellular immune responses to vaccines. Interestingly, the group vaccinated with ChadOx-1 that had ceased exercising during the pandemic demonstrated a higher immune response rate (66.7%) compared to those who maintained regular exercise (56.5%), which highlights

the potential adverse impact of discontinuing exercise on vaccine efficacy [37].

A study explored the effects of COVID-19 vaccination on exercise-induced mobilization of SARS-CoV-2-specific T cells and corresponding changes in neutralizing antibody levels [36]. Eighteen healthy participants underwent a 20-minute graded cycling exercise protocol before and/or after immunization with Pfizer 2-dose COVID-19 vaccine. The exercise consisted of 4 incremental 5-minute stages, with power outputs corresponding to 50%, 60%, 70%, and 80% of individual predicted VO₂max. Blood samples were collected at rest, during the 60% and 80% VO₂max stages, and 1 h after exercise cessation. Heart rate and perceived exertion were monitored during each stage. Vaccination had no significant impact on lymphocytes mobilization during exercise. However, post-vaccination, individuals with synthetic immunity (uninfected) showed a reduced mobilization of CD4+ and CD8+ naïve T-cells and CD4+ central memory T-cells. In contrast, those with hybrid immunity (previous SARS-CoV-2 infection) did not show this reduction. Acute exercise post-vaccination led to a significant mobilization of SARS-CoV-2 specific T-cells, particularly those reacting to the spike protein, in both groups. Notably, only the hybrid immunity group mobilized T-cells responsive to membrane and nucleocapsid antigens. Additionally, nAb titers increased significantly during exercise only in the hybrid immunity group [36].

The impact of PA on immunogenicity in seropositive patients with autoimmune rheumatic illnesses was investigated by Smaira and collaborators [40], focusing on the immune response before and after vaccination with the CoronaVac vaccine. The study aimed to evaluate whether PA could influence immune responses in individuals with prior SARS-CoV-2 infection. Levels of PA were assessed using a questionnaire that collected information across four domains: leisure, domestic activities, work, and transportation. Based on their responses, participants were categorized as physically active or inactive. The findings indicated no significant association between PA and improved immune responses after vaccination. Remarkably, 100% of the participants achieved seroconversion for anti-SARS-CoV-2 IgG antibodies, demonstrating a robust immune response. This suggests that prior SARS-CoV-2 infection may override the potential positive effects of PA on antibody production in immunocompromised individuals [40].

Beyond these data, the study conducted by Gualano and colleagues (2022), involving 748 participants in a mass vaccination setting [41], it was examined the association between PA levels and vaccine responses six months after the administration of the second dose of the CoronaVac vaccine. The participants were categorized as physically active (≥ 150 min/week of moderate

to vigorous activity) or inactive. Physically active participants demonstrated significantly higher seroconversion rates (53.1%) compared to inactive individuals (40.7%, $p=0.001$). Additionally, positivity for neutralizing antibodies (NAb) was observed in 31.2% of the active group versus 22.0% of the inactive group ($p=0.007$). Active participants also exhibited a 43% increase in geometric mean titers of antibodies relative to inactive individuals. Furthermore, the odds ratio analysis revealed that active participants were 1.5 times more likely to achieve seroconversion and neutralizing antibody positivity [41].

Another randomized controlled study conducted for Mohamed & Alawna in 2021 examined the effects of moderate-intensity aerobic exercise on immune biomarkers and disease severity in COVID-19 patients [38]. Thirty individuals (aged 24–45) with mild to moderate COVID-19 were randomly assigned to an exercise or control group. The intervention consisted of 40-minute aerobic sessions, three times per week, for two weeks. Post-intervention, the exercise group showed significant increases in leukocytes, lymphocytes, and increased serum antibody to each vaccine four weeks post-immunization ($P<0.05$), along with a reduction in disease severity based on the Wisconsin scale ($P<0.05$). These findings suggest that short-term aerobic exercise enhances immune function and mitigates COVID-19 symptoms [38].

Still in Table 2, Gualano and colleagues developed a study involving patients with autoimmune rheumatic disorders, especially those with spondylarthritis, who were immunized with CoronaVac vaccine [39]. The study included a single-session exercise protocol consisting of 120 min of strength exercises. After the exercise session, participants rested for one hour before administration of COVID-19 vaccine. Pre-vaccination, the seropositivity rates for IgG were 59% in the exercise group ($n=28$) and 57.1% in the control group ($n=27$). Following the booster dose, seropositivity rates increased to 96% in the exercise group and 100% in the control group, with no significant interaction between the groups ($p=0.84$). Regarding neutralizing antibodies (NAb), positivity rates prior to vaccination were 37% in the exercise group and 42.8% in the control group. Post-vaccination results showed rates of 96% and 93%, respectively. These findings indicate that a single session of unilateral strength exercise did not enhance the immunogenicity of the vaccination, as no significant differences in antibody responses or neutralizing antibody activity were identified between the exercise and control groups [39].

Risk of Bias and study quality

The methodological quality of the nine included studies was assessed using the TESTEX scale (Fig. 2). The chart highlights variability in methodological rigor,

Table 2 Characterization of intervention studies related to the effect of exercise modulation on antibody response and inflammation

Author	P	I	C	O	T	S	Main results
Hallam <i>et al.</i> , 2022 [35]	18 to 87 years, both sexes (n=20)	One session, aerobic exercise.	Control group without exercise.	IgG, IFN α , IL-6.	90 min of exercise or instructed to follow their daily routine.	Exercise took place outdoors at the location where participants were vaccinated	The time of 45 min of exercise was insufficient duration to increase the antibody response, and 90 min of exercise showed a increase in IFN α by human plasmacytoid dendritic cells was previously observed.
Silva <i>et al.</i> , 2023 [37].	60 to 85 years, both sexes (n=93)	48-weeks, continuous aerobic and resistance exercises, moderate intensity.	Control group without exercise.	IgA, IgG, T CD4+, T cells, CD8+, CD28-CD57+.	3-days per week, 60 to 75-minutes of exercise.	Geriatrics and Gerontology Discipline of the Federal University of São Paulo (UNIFESP) or from the "Hospital Geriátrico e de Convalescentes Dom Pedro II"	Higher IgG levels and immunogenicity in the ChadOx-1 vaccinated exercise group and non-practitioners vaccinated with ChadOx-1. The group practicing exercises vaccinated with CoronaVac showed a positive correlation between IgA and IgG, and lower levels of IgG after vaccination.
Smith <i>et al.</i> , 2024 [36]	21 to 44 years, both sexes (n=18)	One session, bout of graded cycling exercise before and/or after receiving a COVID-19 vaccine.	Without a control group.	Lymphocytes and subsets of immune cells (lymphocytes CD45+).	One session, 20-minutes of exercise.	The University of Arizona	Uninfected participants had reduced naïve CD4+ and CD8+ T cells and CD4+ central memory T cells after vaccination. Acute exercise after vaccination mobilized SARS-CoV-2 T cells into the blood depending on the intensity.
Smaira <i>et al.</i> , 2023 [40]	≥ 18 years, sex female (n=180)	Questionnaire on physical activity in 4 domains: leisure, domestic activities, work and transport	Without a control group.	anti-SARS-CoV-2 antibodies of IgG GMT total, frequency of positive neutralizing antibodies (NAb)	Physical activity was assessed using a questionnaire.	Tertiary hospital in Sao Paulo, Brazil	There was no association between regular PA and immunogenicity before and after vaccination.
Mo-hamed & Alawna, 2021 [38]	24 to 45 years old, both sex (n=30)	2 weeks of moderate-intensity aerobic exercise for 40 min/session, 3 sessions/week	With a control group.	Leucocytes, Lymphocytes, IL-6, IL-10, Immunoglobulin-A, and TNF- α	The exercise program is walking/running on a treadmill or bicycling on a stationary bicycle.	Turkish hospital in Istanbul	Leucocytes, Lymphocytes, and Immunoglobulin-A increased in the intervention group in comparison to the CG after two weeks of intervention. IL-6, IL-10, and TNF- α showed non-significant differences between both groups after two weeks of intervention

Table 2 (continued)

Author	P	I	C	O	T	S	Main results
Gualano et al., 2022a [41].	≥ 18 years, sex female (n = 748)	Questions addressing 4 different PA domains after 6 months vaccination	Without a control group.	IgG seroconversion and NAb positivity	PA was assessed using a questionnaire.	Tertiary hospital in Sao Paulo, Brazil	PA was associated with an increment in antibody response after 6 months of vaccination
Gualano et al., 2022b [39]	< 50 years, both sexes (n = 60)	One session, Unilateral Strength Exercises.	Control group without exercise.	Anti-SARS-CoV-2 GMT antibodies. Virus SARS-CoV-2 Pass-circulating neutralizing antibodies.	One session, 20-minutes of exercise.	Tertiary hospital in Sao Paulo, Brazil	In the Pre-Exercise Group and the Control Group exhibited seropositivity for IgG and Nab, 1 month after the booster dose, seropositivity occurred in 96% versus 100% of cases. In the post-Graduate period, the GMT increased similarly in both groups.

Notes: IgA=immunoglobulin A, IgM=immunoglobulin M, IgG=immunoglobulin G, T cells=helper T lymphocyte, Nab=frequency of neutralizing antibody positivity, GMT=geometric mean titers of anti-S1/S2 IgG, IFNα= Interferon-α, IL-6=interleukin-6, CD4+/CD8+/- CD28-CD57+ =T-cell Subset

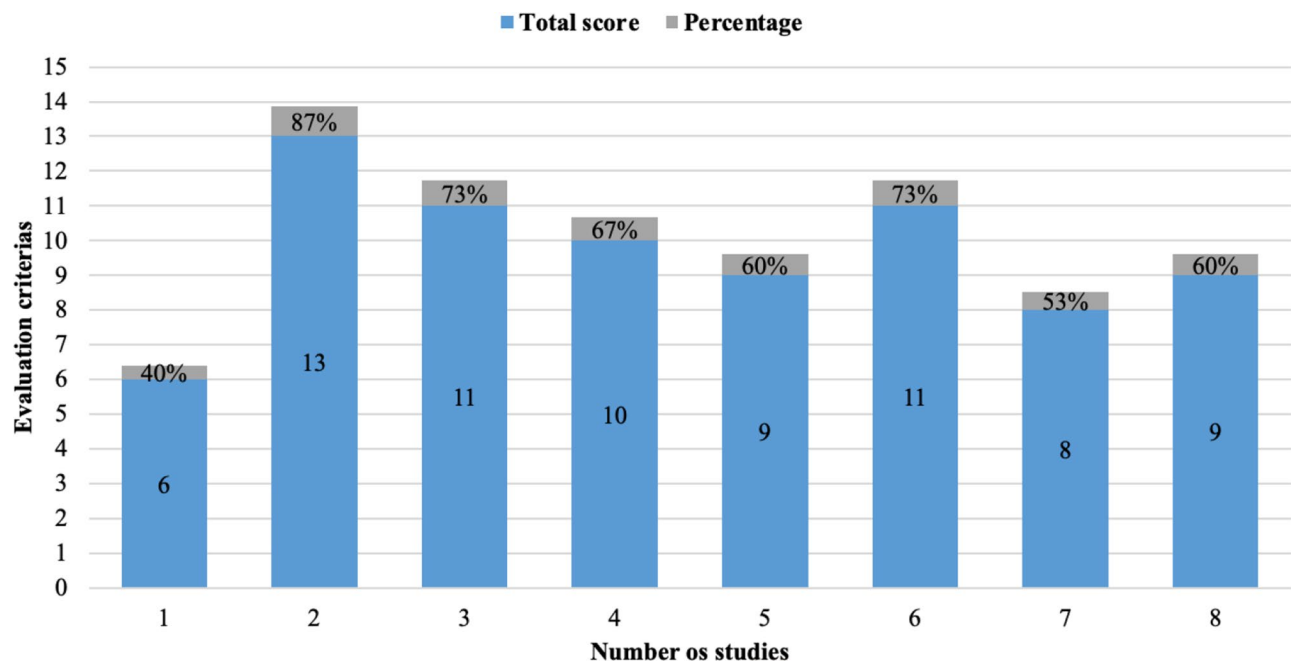


Fig. 2 Methodological quality assessment of the included studies using the TESTEX scale. The scores represent the percentage of the total possible score (15 points) achieved by each study. The articles are ordered as follows: 1: Sevgin et al. (2024); 2: Hallam et al. (2023); 3: Silva et al. (2023); 4: Smith et al. (2024); 5: Smaira et al. (2023); 6: Mohamed & Alawna (2021); 7: Gualano et al. (2022a); 8: Gualano et al. (2022b)

ranging from 40% (6 pts) to 87% (13 pts), with most studies reaching moderate to high quality. The percentage of total score was calculated to provide a clearer interpretation of each study’s quality. One study stood out with a high methodological quality: Hallam et al. (2022) [35], which achieved 87% of the maximum score (13/15). Two studies—Silva et al. (2023) [42], and Mohamed & Alawna (2021)—demonstrated good methodological rigor with scores of 73% (11/15) [38]. Smith et al. (2024) scored 67% (10/15), and Smaira et al. (2023) and Gualano et al. (2022b) scored 60% (9/15) [36, 38, 40, 43],

reflecting moderate quality. Gualano et al. (2022a) presented slightly lower methodological strength with 53% (8/15) [41]. The lowest score was observed in Sevgin et al. (2024), which reached only 40% (6/15), suggesting important limitations in study design and/or reporting [44]. Overall, most studies demonstrated moderate to high methodological quality, although variations in reporting, especially concerning blinding and adherence to exercise protocols, were noted across the studies.

Excluded studies insights

Only 2 studies were excluded since they did not meet one or more inclusion criteria (Table 2). For instance, the study by Sevgin et al. (2021) examined the effects of a 12-week PA on post-vaccination antibody response in older adults who received an inactivated COVID-19 vaccine [44]. The intervention, which included walking, balance exercises, and calisthenics, resulted in significantly higher immunoglobulin levels at both 15 days and 12 weeks post-vaccination. Despite focusing on older individuals, this study was excluded as it did not assess inflammatory markers alongside immune responses [40].

Similarly, the study developed by Batatinha and colleagues in 2022 was excluded due to its focus on athletes, although this study investigated immune/inflammatory biomarkers [45]. This study examined the effects of COVID-19 vaccination on physiological responses on graded exercise. Participants underwent a 20-minute cycling protocol at intensities ranging from 50 to 80% of VO₂max before and 21 days after vaccination with either the Pfizer-BioNTech (two doses) or Janssen (one dose)

vaccines. While vaccination did not significantly affect most physiological markers, including lactate, cortisol, and respiratory gas exchange, it led to a slight but significant increase in heart rate (~5 bpm) and norepinephrine levels during vigorous exercise (70–80% VO₂max), particularly in those receiving the Pfizer-BioNTech vaccine [45].

Many studies have relied on epidemiological data to explore the relationship between the incidence of SARS-CoV-2 infections or reinfections [46–51], pre-illness vaccination profiles, and changes in PA patterns before and after infection or during the pandemic period. However, these studies were excluded from our review as they did not assess both immune/inflammatory biomarkers. Other studies consisted of SRs [52–55], meta-analyses [56, 57], but without a specific focus on immune/inflammatory variables. Additionally, several were narrative reviews [58–60], position statement [61], letters to the editor or short critical commentaries aimed at discussing or hypothesizing the role of regular PA as a protective factor for the immune-inflammatory responses in the context of COVID-19 infections [62].

Author	P	I	C	O	T	S	Main results
Sevgin et al., 2024 [44]	≥ 65 years, both sex	12-weeks cardiovascular exercise	Control group without exercise.	Antibodies IgG, IgA, IgM	45-minutes of exercise	Private nursing home of NP Istanbul Brain Hospital	Exercise can strengthen the antibody response and prolong the vaccine's protection, contributing to improved health and immune response.
Batatinha et al, 2022 [45]	24–43 years old both sex	20-min bout of graded exercise, at intensities corresponding to 50%, 60%, 70%, and 80%	Without a control group.	Lactate, Cortisol and catecholamine release	The graded cycling exercise	Laboratory of University of Arizona	The majority of vaccinated participants (9/12) received the Pfizer mRNA vaccine. A significant increase was observed in heart rate (HR) at 70% of VO ₂ max and in norepinephrine at 80% of VO ₂ max.

Notes: IgA=immunoglobulin A, IgM=immunoglobulin M, IgG=immunoglobulin G, T cells=helper T lymphocyte, Nab=frequency of neutralizing antibody positivity, GMT=geometric mean titers of anti-S1/S2 IgG, IFNα=Interferon-α, IL-6=interleukin-6, CD4+/CD8+/- CD28-CD57 += T-cell Subset; PA=Physical Activity; VO₂max =

Discussion

This systematic review highlights the significant role of PA in enhancing immune-inflammatory responses to COVID-19 vaccination in both adults and older individuals. The included studies demonstrated that acute exercise, particularly single sessions of moderate to vigorous intensity performed before vaccination, was associated

with enhanced mobilization of immune cells, increased cytokine production, and higher antibody titers in the short term. For example, acute protocols were found to temporarily boost levels of IgG and neutralizing antibodies, as well as increase the recruitment of T-cells to peripheral circulation.

In contrast, chronic exercise interventions, involving several weeks of structured aerobic or resistance training, showed sustained benefits, such as elevated immunoglobulin levels over time (e.g., IgG against the SARS-CoV-2 spike protein), improved T-cell function, and a reduction in baseline inflammatory markers such as IL-6 and CRP. These long-term adaptations were particularly evident in older adults and individuals with chronic conditions, suggesting that habitual exercise enhances vaccine responsiveness by mitigating the effects of immunosenescence and chronic low-grade inflammation.

The diversity of subpopulations—including variations in age, health conditions, vaccine types, and factors such as exercise intensity and duration—necessitates caution in interpreting the results. These variables may significantly influence outcomes and limit their generalizability. However, the overall body of evidence strongly supports the notion that PA contributes to enhanced immunogenicity, particularly in individuals with chronic conditions and older adults. The magnitude of these effects may vary, influenced by factors like the specific exercise regimen (type, intensity, duration), as well as individual characteristics such as age and health status.

The studies included in this SR show that both acute and chronic exercise interventions can positively influence various immune markers, such as antibody production, T-cell activation, and immune cell mobilization. However, the specific exercise regimens, including the type, duration, intensity, and frequency, vary widely between studies [35, 36, 38–42]. It is important to consider how these factors influence immune responses, as different forms of exercise or engagement in regular PA might have unique effects on the immune-inflammatory responses to COVID-19 vaccination. For example, prolonged, moderate-intensity exercise could result in sustained improvements in immune function [41, 42], while a single bout of high-intensity exercise may boost acute immune activation [39].

Acute bouts of exercise can temporarily enhance immune surveillance by increasing the circulation of immune cells, such as lymphocytes and natural killer (NK) cells and the oxidative burst of neutrophils [63], while long-term exercise programs contribute to sustained immunomodulation by reducing chronic inflammation and enhancing the adaptive immune response, they can also decrease the production of pro-inflammatory cytokines, improve neutrophil function, and stimulate B lymphocyte proliferation [64–66]. Interestingly, a period of at least two weeks of PA is sufficient to positively stimulate the immune system as a trigger for inducing long-term effects [65]. This adaptation occurs through mechanisms such as enhanced antigen presentation [67], increased circulation of immune cells, and improved communication between innate and adaptive

immunity [63]. Regular engagement in SPA not only boosts the immediate immune response but also fosters long-term immunological memory, potentially enhancing the effectiveness of vaccinations and overall immune resilience [57].

Although acute and chronic exercise have shown benefits in mobilizing immune cells and enhancing antibody production [57], it remains unclear whether these changes impact the duration and strength of immunity after vaccination. Some studies suggest that exercise can enhance the immediate immune response to vaccination [39], but the long-term effects on immune memory and protection against SARS-CoV-2 reinfection are less well understood [63].

This review primarily focuses on the effects of PA on immune responses specifically related to COVID-19 vaccination. It is important to remain focused on how physical activity (or physical exercise), rather than general PA, influences the immune-inflammatory responses to COVID-19 vaccination. Additionally, the age of the participants also plays a crucial role in how exercise influences immune responses, with older adults potentially benefiting more from structured PA due to age-related declines in immune function [44, 68]. Furthermore, the stage of the pandemic during which these studies were conducted could also influence the baseline immune status of the participants, potentially affecting the outcomes.

Additionally, studies included in this SR represent a wide diversity of populations, including differences in age, health status, exercise intensity, and vaccination types [35, 36, 38–42]. These factors significantly influence the outcomes observed, and care should be taken when attempting to generalize the findings across different groups. For example, older adults may benefit more from exercise interventions compared to younger, healthier individuals, as exercise can help mitigate the immunosenescence associated with aging [4, 69]. Additionally, individuals with chronic conditions may experience different immune-enhancing effects from exercise compared to healthy adults [40, 41, 52]. These variations underscore the need for caution when interpreting the generalizability of the results, as individual factors may alter the effectiveness of exercise interventions.

Another key factor to consider is the type of COVID-19 vaccine administered in each study. Vaccines such as mRNA-based vaccines (e.g., Pfizer-BioNTech and Moderna), viral vector vaccines [e.g., ChadOx-1 (AstraZeneca) and Janssen (Johnson & Johnson)], and inactivated virus vaccines (e.g., CoronaVac) may elicit different immune responses [70]. Based on this, such differences could also affect how PA — or even its interruption — influences the immune and inflammatory responses following COVID-19 vaccination, as previously reported [35]. Still in this respect, it has suggested that mRNA

vaccines may trigger a more robust T-cell response, while inactivated vaccines may generate a stronger antibody response [71]. Beyond these facts, the distinct immunological variables examined across studies, including antibodies, T-cells, and cytokines, should be considered in light of the vaccine types used, as these could significantly influence the magnitude and type of immune response that is enhanced by regular exercise and PA. Considering all these data, it is worth highlighting that the interaction between exercise and different vaccine platforms is critical to understanding how PA can boost vaccination efficacy.

The methodological quality assessment of the included studies revealed notable variability in study design and reporting standards. Although all studies contributed valuable insights into the role of PA on the immune response to COVID-19 vaccination, their indicating moderate quality. These methodological differences must be considered when interpreting the results, as they directly impact the robustness and generalizability of conclusions. Therefore, there is a clear need for future randomized controlled trials and longitudinal studies with standardized protocols and improved reporting quality to strengthen the evidence base on how exercise influences vaccine efficacy [72], particularly among older populations.

Another critical issue that warrants further investigation is the potential interaction between PA and vaccine side effects. Although exercise is generally beneficial for health, which includes the improvement of immune responses, post-vaccination side effects, such as fever, muscle soreness, and fatigue, may affect an individual's ability to engage in PA. It is important to determine whether moderate exercise can help reduce the severity of these symptoms or improve recovery time, or even whether intense exercise may exacerbate them. Additionally, some individuals may experience a delayed immune response or more severe side effects, especially if they have underlying health conditions, so understanding how exercise influences this interaction is important for providing appropriate guidance for PA post-vaccination.

Strengths and limitations

The strengths of this study include the comprehensive analysis of main studies investigating the impact of regular physical activity on immune/inflammatory responses to COVID-19 vaccination. The inclusion of different interventions (acute and chronic), vaccine types, and age groups provided valuable insights into how exercise can enhance vaccine efficacy and promote health. Furthermore, the consideration of various immune biomarkers, such as antibodies and T cells, offers a broad perspective on the immune response to vaccination. However, the study also has limitations. The heterogeneity of

methodologies across the studies analyzed, such as variations in the type, intensity, and duration of PA, as well as the populations studied, limits the ability to provide firm generalizations about the universal effectiveness of any specific PA regime. Additionally, most studies focused on short-term interventions, and further longitudinal research is needed to assess the long-term effects of PA on vaccine immunogenicity and the duration of protection against COVID-19.

Future perspectives and Real-World applications

Based on the current evidence, several promising directions emerge for advancing our understanding of how regular PA modulates immune-inflammatory responses to COVID-19 vaccination. First, future longitudinal studies are essential to clarify the sustained impact of regular PA both before and after vaccination, particularly in diverse populations such as older adults and individuals with chronic conditions. Special attention should be given to how immunosenescence affects vaccine efficacy and whether exercise can mitigate its negative effects [73], especially through mechanisms like the peripheral mobilization and apoptotic clearance of senescent cells induced by acute and chronic exercise, respectively.

Second, it remains important to investigate how regular physical activity influences B cell metabolism and function. The potential crosstalk between skeletal muscle (via myokine production) and immune cells—particularly B lymphocytes—may enhance antigen-specific antibody production and improve vaccine immunogenicity [74]. While this muscle-immune interaction has been increasingly studied in oncology, its role in vaccination contexts remains underexplored.

Finally, from a translational perspective, integrating structured PA programs into vaccination campaigns—especially in primary care or public health settings—could serve as a low-cost, scalable strategy to improve vaccine outcomes in vulnerable populations. Tailoring exercise protocols based on age, health status, and type of vaccine could further optimize these benefits. These programs could be implemented in vaccination clinics or as part of public health initiatives, aiming to increase vaccine effectiveness, reduce the risk of post-vaccination complications, and promote overall health in the general population.

Conclusion

This SR highlights the role of PA in enhancing immune/inflammatory responses to COVID-19 vaccination. Evidence from the analyzed studies indicates that both acute and long-term PA interventions can positively influence distinct immunological variables, including antibody production, T-cell activation, and immune cell mobilization. While short-term exercise can act as

an immediate immune stimulant, long-term exercise programs contribute to sustained immunomodulation, reducing chronic inflammation and improving adaptive immune responses. Notably, the effects of exercise vary across populations, with older adults and individuals with chronic conditions particularly benefiting from PA in terms of vaccine-induced immunogenicity. However, the diversity in study designs, exercise modalities, and vaccine types necessitates cautious interpretation of these findings. Moving forward, integrating structured PA strategies into public health policies could be a practical approach to optimizing vaccine efficacy and promoting long-term immune resilience.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12979-025-00515-x>.

Supplementary Material 1

Acknowledgements

Guilherme Furtado thanks the National funding by FCT- Foundation for Science and Technology, Pl., through the institutional scientific employment program-contract (CEECINST/00077/2021). André Bachi was supported by São Paulo Research Foundation (FAPESP, grants nº10/50025-1, 2016/04845-3, and 2019/14115-0), and National Council of Scientific and Technology Development (CNPq, grant nº 307674/2017-7). Bruna Palotino-Ferreira is a master student fellow of the Brazilian National Council for Scientific and Technology Development (CAPES/Brazil: 88887683578/2022-00).

Author contributions

B.M.P.F. contributed to the study conception and design, data analysis, manuscript writing, critical revision, and final approval of the submitted version. S.V.R. also contributed to the study conception, data analysis, manuscript writing, critical revision, and final approval of the submitted version. A.N.S. was responsible for the critical manuscript revision, data analysis, and contributed to manuscript writing. A.F.S.G. assisted with critical manuscript revision, data analysis, and manuscript writing. F.R. contributed to the critical manuscript revision and data analysis. P.C. contributed to the critical manuscript revision and data analysis. A.L.L.B. was involved in data analysis, manuscript writing, and critical manuscript revision. R.A.O. participated in data analysis, manuscript writing, and critical manuscript revision. M.P.B. contributed to data analysis, manuscript writing, and critical manuscript revision. Finally, G.E.F. provided study supervision, critical manuscript revision, and research guidance.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

No datasets were generated or analyzed during the current study.

Declarations

Ethical approval

This article does not involve any studies with human participants or animals conducted by any of the authors.

Consent for publication

As this study does not involve human participants or animals, formal informed consent was not required.

Competing interests

The authors declare no competing interests.

Author details

¹State University of Sudoeste da Bahia, José Moreira Sobrinho Avenue, s/n - Jequiezinho, Jequié, BA 45205-490, Brasil

²Laboratory of Inflammation and Exercise Immunology, Postgraduate Program in Health and Nutrition, Nutrition School, Federal University of Ouro Preto, Ouro Preto, Minas Gerais, Brazil

³SPRINT - Sport Physical activity and health Research & Innovation Center, Polytechnic University of Castelo Branco, Polytechnic University of Castelo Branco, Castelo Branco, Portugal

⁴Postgraduate Program in Health Science, Santo Amaro University (UNISA), São Paulo 04743-030, Brazil

⁵Interdisciplinary Program in Health Sciences, Institute of Physical Activity Sciences and Sports (ICAFE), University Cruzeiro do Sul, São Paulo 01506-000, Brazil

⁶Polytechnic Institute of Coimbra, Rua da Misericórdia, Lagar dos Cortiços S. Martinho do Bispo, Coimbra 3045-093, Portugal

⁷SPRINT - Sport Physical Activity and Health Research & Innovation Center, Polytechnic Institute of Coimbra, Coimbra, Portugal

⁸Research Centre for Natural Resources Environment and Society (CERNAS), Polytechnic Institute of Coimbra, Bencanta, Coimbra 3045-601, Portugal

Received: 14 December 2024 / Accepted: 29 April 2025

Published online: 30 October 2025

References

1. Atzrodt CL, Maknojia I, McCarthy RDP, Oldfield TM, Po J, Ta KTL et al. A Guide to COVID-19: a global pandemic caused by the novel coronavirus SARS-CoV-2. *FEBS J* [Internet]. 2020;287:3633–50. Available from: <https://febs.onlinelibrary.wiley.com/doi/https://doi.org/10.1111/febs.15375>
2. Falahi S, Kenarkoobi A. Host factors and vaccine efficacy: Implications for COVID-19 vaccines. *J Med Virol* [Internet]. 2022;94:1330–5. Available from: <https://onlinelibrary.wiley.com/doi/https://doi.org/10.1002/jmv.27485>
3. Domaszewska K, Boraczyński M, Tang Y-Y, Groniek J, Wochna K, Boraczyński T et al. Protective Effects of Exercise Become Especially Important for the Aging Immune System in The Covid-19 Era. *Aging Dis* [Internet]. 2022;13:129. Available from: <http://www.aginganddisease.org/EN/https://doi.org/10.14336/AD.2021.1219>
4. Zimmermann P, Curtis N. Factors That Influence the Immune Response to Vaccination. *Clin Microbiol Rev* [Internet]. 2019 [cited 2025 Jan 28];32:e00084-18. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6431125/>
5. Rayman MP, Calder PC. Optimising COVID-19 vaccine efficacy by ensuring nutritional adequacy. *British Journal of Nutrition* [Internet]. 2021;126:1919–20. Available from: https://www.cambridge.org/core/product/identifier/S0007114521000386/type/journal_article
6. Calder PC, Ortega EF, Meydani SN, Adkins Y, Stephensen CB, Thompson B, et al. Nutrition, Immunosenescence, and infectious disease: an overview of the scientific evidence on micronutrients and on modulation of the gut microbiota. *Adv Nutr*. 2022;13:S1–26.
7. Pinti M, Appay V, Campisi J, Frasca D, Fülöp T, Sauce D et al. Aging of the immune system: Focus on inflammation and vaccination. *Eur J Immunol* [Internet]. 2016;46:2286–301. Available from: <https://onlinelibrary.wiley.com/doi/https://doi.org/10.1002/eji.201546178>
8. Lindo J, Nogueira C, Soares R et al. Genetic polymorphisms of P2RX7 but not of ADORA2A are associated with the severity of SARS-CoV-2 infection. *Int J Mol Sci* [Internet]. 2024 [cited 2025 Jan 28];25(11):6135. Available from: <https://doi.org/10.3390/ijms25116135>
9. Scheffer DdaL, Latini A. Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease* [Internet]. 2020;1866:165823. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S092544392030168X>
10. Cunha LL, Perazzio SF, Azzi J, Cravedi P, Riella LV. Remodeling of the Immune Response With Aging: Immunosenescence and Its Potential Impact on COVID-19 Immune Response. *Front Immunol* [Internet]. 2020 [cited 2025 Jan 28];11. Available from: <https://pubmed.ncbi.nlm.nih.gov/32849623/>
11. Chen L, Shao C, Li J, Zhu F. Impact of Immunosenescence on Vaccine Immune Responses and Countermeasures. *Vaccines*. 2024, Vol 12, Page 1289 [Internet]. 2024 [cited 2025 Jan 28];12:1289. Available from: <https://www.mdpi.com/2076-393X/12/11/1289/htm>

12. Grifoni A, Alonzi T, Alter G, Noonan DMC, Landay AL, Albini A, et al. Impact of aging on immunity in the context of COVID-19, HIV, and tuberculosis. *Front Immunol*. 2023;14:1146704.
13. Lindo J, Coelho P, Gaviños C, Martins M, Liberal J, Ferreira AJ et al. Health status and COVID-19 epidemiology in an inland region of Portugal: A retrospective study. *Int J Environ Res Public Health* [Internet]. 2024 [cited 2025 Jan 28];21(8):1033. Available from: <https://doi.org/10.3390/ijerph21081033>
14. Improta-Caria AC, Soci ÚPR, Pinho CS, Aras Júnior R, De Sousa RAL, Bessa TCB. Physical Exercise and Immune System: Perspectives on the COVID-19 pandemic. *Rev Assoc Med Bras* [Internet]. 2021;67:102–7. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-42302021000200102&tng=en
15. Silva BR, Monteiro FR, Cezário K, Amaral JB do, Paixão V, Almeida EB et al. Older Adults Who Maintained a Regular Physical Exercise Routine before the Pandemic Show Better Immune Response to Vaccination for COVID-19. *Int J Environ Res Public Health*. 2023;20:1939.
16. Ung T, Rutledge NS, Weiss AM, Esser-Kahn AP, Deak P. Cell-targeted vaccines: implications for adaptive immunity. *Front Immunol*. 2023;14.
17. Sette A, Crotty S. Adaptive immunity to SARS-CoV-2 and COVID-19. *Cell* [Internet]. 2021;184:861–80. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0092867421000076>
18. Barni L, Carrasco-Vega E, Olivieri M, Galán-Mercant A, Guiducci S, Picariello F et al. Does Physical Exercise Enhance the Immune Response after Vaccination? A Systematic Review for Clinical Indications of COVID-19 Vaccine. *Int J Environ Res Public Health* [Internet]. 2023;20:5183. Available from: <https://www.mdpi.com/1660-4601/20/6/5183>
19. Scudiero O, Lombardo B, Brancaccio M, Mennitti C, Cesaro A, Fimiani F et al. Exercise, Immune System, Nutrition, Respiratory and Cardiovascular Diseases during COVID-19: A Complex Combination. *Int J Environ Res Public Health* [Internet]. 2021;18:904. Available from: <https://www.mdpi.com/1660-4601/18/3/904>
20. Azizi GG, Orsini M, Dortas Júnior SD, Vieira PC, De Carvalho RS, Pires CS da R, et al. COVID-19 and physical activity: What is the relation between exercise immunology and the current pandemic situation? *Revista Brasileira de Fisiologia do exercício* [Internet]. 2020;19:20–9. Available from: <https://convergenceseditorial.com.br/index.php/revistafisiologia/article/view/4115>.
21. Dada D, Djioetio JN, McFadden SM, Demeke J, Vlahov D, Wilton L et al. Strategies That Promote Equity in COVID-19 Vaccine Uptake for Black Communities: a Review. *Journal of Urban Health* [Internet]. 2022;99:15–27. Available from: <https://link.springer.com/https://doi.org/10.1007/s11524-021-00594-3>
22. da Silveira MP, da Silva Fagundes KK, Bizuti MR, Starck É, Rossi RC, de Resende e Silva DT. Physical exercise as a tool to help the immune system against COVID-19: an integrative review of the current literature. *Clin Exp Med* [Internet]. 2021;21:15–28. Available from: <https://link.springer.com/https://doi.org/10.1007/s10238-020-00650-3>
23. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JPA et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* [Internet]. 2009;339:b2700–b2700. Available from: <https://www.bmj.com/lookup/doi/https://doi.org/10.1136/bmj.b2700>
24. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev*. 2019;4:2–8.
25. Elias BL, Polancich S, Jones C, Colvin S. Evolving the PICOT method for the digital age: the PICOT-D. *J Nurs Educ*. 2015;54:594–9.
26. Zrubka Z, Champion A, Holtorf A-P, Di Bidino R, Earla JR, Boltyenkov AT, et al. The PICOTS-ComTeC framework for defining digital health interventions: an ISPOR special interest group report. *Value Health*. 2024;27:383–96.
27. Rudnicka E, Napierała P, Podfigurna A, Męczekalski B, Smolarczyk R, Grymowicz M. The world health organization (WHO) approach to healthy ageing. *Maturitas*. 2020;139:6–11.
28. Erickson KI, Liu-Ambrose T, Exercise. Cognition, and health. *Handbook of the psychology of aging*. Elsevier; 2016. pp. 187–201.
29. Kazdin AE. *Research design in clinical psychology*. Cambridge University Press; 2023.
30. Dinarello CA. Proinflammatory cytokines. *Chest*. 2000;118:503–8.
31. Furtado GE, Reis ASLdaS, Braga-Pereira R, Caldo-Silva A, Teques P, Sampaio AR, et al. Impact of exercise interventions on sustained brain health outcomes in frail older individuals: A comprehensive review of systematic reviews. *Healthcare*. 2023;11:3160.
32. WHO. Guidelines on hand hygiene in health care: first global patient safety challenge clean care is safer care. Geneva: World Health Organization; 2009.
33. Smart NA, Waldron M, Ismail H, Giallauria F, Vigorito C, Cornelissen V, et al. Validation of a new tool for the assessment of study quality and reporting in exercise training studies: TESTEX. *Int J Evid Based Healthc*. 2015;13:9–18.
34. Cuthbert M, Ripley N, McMahon JJ, Evans M, Haff GG, Comfort P. The Effect of Nordic Hamstring Exercise Intervention Volume on Eccentric Strength and Muscle Architecture Adaptations: A Systematic Review and Meta-analyses. *Sports Medicine* [Internet]. 2020 [cited 2024 Dec 2];50:83–99. Available from: <https://link.springer.com/article/https://doi.org/10.1007/s40279-019-01178-7>
35. Hallam J, Jones T, Alley J, Kohut ML. Exercise after influenza or COVID-19 vaccination increases serum antibody without an increase in side effects. *Brain Behav Immun*. 2022;102:1–10.
36. Smith KA, Zúñiga TM, Baker FL, Batatinha H, Pedlar CR, Burgess SC, et al. COVID-19 vaccination produces exercise-responsive SARS-CoV-2 specific T-cells regardless of infection history. *J Sport Health Sci*. 2024;13:99–107.
37. Silva BR, Monteiro FR, Cez K, Almeida EB, Andr C, Amirato GR. Older adults who maintained a regular physical exercise routine before the pandemic show better immune response to vaccination for COVID-19. 2023.
38. Mohamed AA, Alawna M. The effect of aerobic exercise on immune biomarkers and symptoms severity and progression in patients with COVID-19: A randomized control trial. *J Bodyw Mov Ther*. 2021;28:425–32.
39. Gualano B, Saad CGS, Sieczkowska SM, Lemes ÍR, da Silva RP, Pinto AJ et al. Effect of an exercise bout before the booster dose of an inactivated SARS-CoV-2 vaccine on immunogenicity in immunocompromised patients. *J Appl Physiol* [Internet]. 2022 [cited 2024 Dec 10];132:682. Available from: <https://pub.ncbi.nlm.nih.gov/articles/PMC8897009/>
40. Smaira FI, Mazzolani BC, Lemes ÍR, da Silva RP, Pinto AJ, Sieczkowska SM, et al. No associations between physical activity and immunogenicity in SARS-CoV-2 seropositive patients with autoimmune rheumatic diseases prior to and after vaccination. *J Phys Act Health*. 2023;20:980–3.
41. Gualano B, Lemes ÍR, da Silva RP, Pinto AJ, Mazzolani BC, Smaira FI, et al. Physical activity and antibody persistence 6 months after the second dose of coronavac in immunocompromised patients. *Scand J Med Sci Sports*. 2022;32:1510–5.
42. Silva BR, Monteiro FR, Cezário K, Amaral JB do, Paixão V, Almeida EB et al. Older Adults Who Maintained a Regular Physical Exercise Routine before the Pandemic Show Better Immune Response to Vaccination for COVID-19. *Int J Environ Res Public Health*. 2023;20.
43. Gualano B, Saad CGS, Sieczkowska SM, Lemes ÍR, da Silva RP, Pinto AJ, et al. Effect of an exercise bout before the booster dose of an inactivated SARS-CoV-2 vaccine on immunogenicity in immunocompromised patients. *J Appl Physiol*. 2022;132:682–8.
44. Şevgin Ö, Özer S. Effect of physical exercise on inactivated COVID-19 vaccine antibody response in the elderly. *Hum Antibodies*. 2024;32:19–24.
45. Batatinha H, Baker FL, Smith KA, Zúñiga TM, Pedlar CR, Burgess SC, et al. Recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people. *J Appl Physiol*. 2022;132:275–82.
46. Lim YH, Lee MH, Jeong S, Han HW. Association of physical activity with SARS-CoV-2 infection and severe clinical outcomes among patients in South Korea. *JAMA Netw Open*. 2023;6:e239840.
47. Sallis R, Young DR, Tartof SY, Sallis JF, Sall J, Li Q, et al. Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: A study in 48 440 adult patients. *Br J Sports Med*. 2021;55:1099–105.
48. Bourdas DI, Bakirtzoglou P, Travlos AK, Andrianopoulos V, Zacharakis E. Analysis of a comprehensive dataset: influence of vaccination profile, types, and severe acute respiratory syndrome coronavirus 2 re-infections on changes in sports-related physical activity one month after infection. *Data Brief*. 2023;51.
49. Collie S, Saggars RT, Bandini R, Steenkamp L, Champion J, Gray G, et al. Association between regular physical activity and the protective effect of vaccination against SARS-CoV-2 in a South African case-control study. *Br J Sports Med*. 2023;57:205–11.
50. Hoang TD, Colebunders R, Fodjo JNS, Nguyen NPT, Tran TD, Van Vo T. Well-being of healthcare workers and the general public during the covid-19 pandemic in Vietnam: an online survey. *Int J Environ Res Public Health*. 2021;18.
51. Senerat AM, Pope ZC, Rydell SA, Mullan AF, Roger VL, Pereira MA. Psychosocial and behavioral outcomes in the adult workforce during the COVID-19 pandemic: a 1-Year longitudinal survey. *BMC Public Health*. 2023;23.
52. Jabbour G, Hermassi S, Bragazzi N. Impact of the COVID-19 pandemic on the physical activity profile and glycemic control among Qatari adults with type 1 diabetes: effect of vaccination status. *Front Public Health*. 2022;10.
53. Barni L, Carrasco-Vega E, Olivieri M, Galán-Mercant A, Guiducci S, Picariello F et al. Does Physical Exercise Enhance the Immune Response after

- Vaccination? A Systematic Review for Clinical Indications of COVID-19 Vaccine. *Int J Environ Res Public Health*. Multidisciplinary Digital Publishing Institute (MDPI); 2023.
54. Nieman DC. Exercise Is Medicine for Immune Function: Implication for COVID-19 [Internet]. 2021. Available from: www.acsm-csmr.org
 55. Marconcin P, Werneck AO, Peralta M, Ihle A, Gouveia ER, Ferrari G et al. The association between physical activity and mental health during the first year of the COVID-19 pandemic: a systematic review. *BMC Public Health*. 2022;22.
 56. Dinas PC, Koutedakis Y, Ioannou LG, Metsios G, Kitas GD. Effects of exercise and physical activity levels on vaccination efficacy: A systematic review and Meta-Analysis. *Vaccines* (Basel). MDPI; 2022.
 57. Chastin SFM, Abaraogu U, Bourgois JG, Dall PM, Darnborough J, Duncan E, et al. Effects of regular physical activity on the immune system, vaccination and risk of Community-Acquired infectious disease in the general population: systematic review and Meta-Analysis. *Sports medicine*. Springer Science and Business Media Deutschland GmbH; 2021. pp. 1673–86.
 58. Furtado GE, Letieri RV, Caldo-Silva A, Sardão VA, Teixeira AM, Barros MP et al. Sustaining efficient immune functions with regular physical exercise in the COVID-19 era and beyond. *Eur J Clin Invest*. 2021.
 59. Pitanga FJG, Pitanga CPS, Beck CC. Can physical activity influence the effect of the covid-19 vaccine on older adults? *Revista Brasileira De Cineantropometria E Desempenho Humano*. 2020;22:1–5.
 60. AL-Mhanna SB, Wan Ghazali WS, Maqsood A, Mohamed M, Ahmed N, Afolabi HA, et al. Physical activities pre- and post-COVID-19 vaccination and its implementations: A narrative review. *SAGE Open Med*. SAGE Publications Ltd; 2023.
 61. Faghy MA, Arena R, Stoner L, Haraf RH, Josephson R, Hills AP, et al. The need for exercise sciences and an integrated response to COVID-19: A position statement from the international HL-PIVOT network. *Prog cardiovasc dis*. W.B. Saunders; 2021. pp. 2–10.
 62. Chen P, Mao L, Nassiss GP, Harmer P, Ainsworth BE, Li F. Coronavirus disease (COVID-19): The need to maintain regular physical activity while taking precautions. *J Sport Health Sci*. Elsevier B.V.; 2020. pp. 103–4.
 63. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. *J Sport Health Sci*. 2019. pp. 201–17.
 64. Drummond LR, Campos HO, Drummond FR, de Oliveira GM, Fernandes JGRP, Amorim RP, et al. Acute and chronic effects of physical exercise on IgA and IgG levels and susceptibility to upper respiratory tract infections: a systematic review and meta-analysis. *Pflugers Arch*. 2022;474:1221–48.
 65. Filgueira TO, Castoldi A, Santos LER, de Amorim GJ, de Sousa Fernandes MS et al. Anastácio W de L do N., The Relevance of a Physical Active Lifestyle and Physical Fitness on Immune Defense: Mitigating Disease Burden, With Focus on COVID-19 Consequences. *Front Immunol* [Internet]. 2021;12. Available from: <https://www.frontiersin.org/articles/https://doi.org/10.3389/fimmu.2021.587146/full>
 66. Seman S, Dražilov SS, Ilić V, Tešić M, Stojiljković S, Arena R, et al. Physical activity and exercise as an essential medical strategy for the COVID-19 pandemic and beyond. *Exp Biol Med*. 2021;246:2324–31.
 67. Mogilenko DA, Shpynov O, Andhey PS, Arthur L, Swain A, Esaulova E, et al. Comprehensive profiling of an aging immune system reveals clonal GZMK+CD8+T cells as conserved hallmark of inflammaging. *Immunity*. 2021;54:99–e11512.
 68. Ponnappan S, Ponnappan U. Aging and Immune Function: Molecular Mechanisms to Interventions. *Antioxid Redox Signal* [Internet]. 2011 [cited 2025 Apr 3];14:1551. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3061194/>
 69. Barni L, Carrasco-Vega E, Olivieri M, Galán-Mercant A, Guiducci S, Picariello F et al. Does Physical Exercise Enhance the Immune Response after Vaccination? A Systematic Review for Clinical Indications of COVID-19 Vaccine. *Int J Environ Res Public Health* [Internet]. 2023 [cited 2024 Dec 11];20:5183. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10049110/>
 70. Patel R, Kaki M, Potluri VS, Kahar P, Khanna D. A comprehensive review of SARS-CoV-2 vaccines: Pfizer, Moderna & Johnson & Johnson. *Hum Vaccin Immunother* [Internet]. 2022 [cited 2025 Apr 3];18:2002083. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8862159/>
 71. Salleh MZ, Norazmi MN, Deris ZZ. Immunogenicity mechanism of mRNA vaccines and their limitations in promoting adaptive protection against SARS-CoV-2. *PeerJ* [Internet]. 2022 [cited 2025 Apr 3];10:e13083. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8917804/>
 72. Schulz R, Langen G, Prill R, Cassel M, Weissgerber TL. Reporting and transparent research practices in sports medicine and orthopaedic clinical trials: a meta-research study. *BMJ Open* [Internet]. 2022 [cited 2025 Apr 23];12:e059347. Available from: <https://bmjopen.bmj.com/content/12/8/e059347>
 73. Yu X, Pei W, Li B, Sun S, Li W, Wu Q. Immunosenescence. Physical Exercise, and their Implications in Tumor Immunity and Immunotherapy. *Int J Biol Sci* [Internet]. 2025 [cited 2025 Apr 12];2025:910–39. Available from: <https://www.ijbs.com//creativecommons.org/licenses/by/4.0/>
 74. Dollet L, Lundell LS, Chibalin AV, Pendergrast LA, Pillion NJ, Lansbury EL, et al. Exercise-induced crosstalk between immune cells and adipocytes in humans: role of oncostatin-M. *Cell Rep Med*. 2024;5:101348.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.