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The role of physical activity in the clinical outcomes of people diagnosed with Covid-19: A systematic review



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ABSTRACT

Keywords: Objective: This review aimed to compile the evidence on PA and clinical outcomes of people receiving a positive Pandemic diagnosis of covid-19. Coronavirus Design: Systematic review. Physical exercise Methods: The search was performed in five databases: EMBASE, MEDLINE via PubMed portal, Scopus, SPORT-General health Discus via EBSCO platform, and Web of Science. In addition, the "gray" literature was searched through Google Scholar and medRxiv published between January 2020 and July 2022. Studies were assessed for risk of bias, with the extraction of relevant data. Our search revealed a total of 10,028 studies. Results: After applying the eligibility criteria 32 studies were included. Thirty-one studies were at low to moderate risk of bias. Physically active individuals, who were diagnosed with covid-19, presented attenuation of clinical outcomes, such as decreased risk of hospitalization, recovery time, number of symptoms, severity, and ICU and death when compared to individuals with low levels of PA or classified as sedentary. Conclusions: Physically active individuals when diagnosed with covid-19 may have decreased risk of several clinical outcomes related to covid-19, including but not limited to hospitalization and number of symptoms. Public health authorities should develop strategies and initiatives that promote safe PA environments to improve the clinical prognosis of people diagnosed with covid-19. Study registration: Open Science Framework (OSF), DOI registry 10.17605/OSF.IO/PV6NF. It can be consulted through the access link: https://doi.org/10.17605/OSF.IO/PV6NF, October 07, 2021.

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Brazil

Summary box

What is already known?

1 Higher levels of PA attenuates clinical outcomes of people diagnosed with covid-19, such as disease severity, admission to the intensive care unit (ICU) and death.

What are the new findings?

- 1 Anthropometric characteristics and fitness level can be used in decision-making scenarios to estimate the risk of complications in patients with covid-19;
- 2 People who walk or run at a pace of 6.8 to 8.2 min/km have a lower risk of hospitalization;
- 3 Athletes were, approximately, 1.5 times less likely to be hospitalized;
- 4 Aerobic and resistance training, and greater muscle strength were associated with lower chances of hospitalization for covid-19;
- 5 Moderate or vigorous PA contributes to the reduction of symptoms and severity of covid-19;
- 6 Tachypnea and fever were more frequent in sedentary people.

1. Introduction

The severity associated with covid-19 includes both endogenous and exogenous factors. Pre-existing conditions such as diabetes, heart diseases, hypertension, obesity, age, race and sex constitute endogenous factors. Exogenous factors include but are not limited to physical activity (PA) [1].

In terms of PA, studies have shown that this behavior was significantly reduced during the first and second wave of the covid-19 pandemic [2-6]. Reductions in PA was already noticeable after the first month of the pandemic [2,3] and PA continued to decline after this period [4], being even lower in countries most affected by the virus, such the United States and United kingdom, Japan, India, Australia, Iran, and several countries across Europe [2,5]. These studies further demonstrated that reductions in PA levels were associated with worsening psychological well-being [7], subjective health [5], leading to chronic disease development, and even premature deaths [8]. Attendance in PA at recommended levels (150–300 min/week) [9,10], is a non-pharmacological approach able to boost the immune system [3,4]. The American College of Sports Medicine recently released a position stand suggesting that an active lifestyle (PA > 150 min/week) should be maintained in the period of isolation and social distancing as a measure to minimize the effects of covid-19 [11].

Adequate levels of PA have been associated with a wide array of benefits that include but are not limited to: reduce the risk of adverse health conditions such as chronic non communicable diseases [8], improve the immune system response, and reduction in viral infections [11]. In fact, engaging in PA on a regular basis contributes to the reduction of numerous chronic diseases such as metabolic syndrome, type 2 diabetes mellitus, cardiovascular diseases, certain types of cancer, reduction of stress, depression and anxiety [8,12-14]. PA has further been positively associated with shorter recovery times, increased macrophage activity, immunoglobulin flux, anti-inflammatory cytokines, neutrophils, natural killer cells, cytotoxic T and immature B [11]. Thus, PA could be a potential strategy to mitigate severe consequences of covid-19 [15], such as hospitalization, respiratory distress, oxygen support, ICU admission, mechanical ventilation, and death [16-22]. Engaging in adequate amounts of PA may mitigate endogenous factors predisposing to covid-19 (i.e., obesity, hypertension, heart and respiratory diseases) [23,24]. In addition, physically active individuals cope better with viral infections [23]. For instance, in a non-pandemic context, the risk of respiratory infections and mortality was reduced by almost half in physically active individuals [25], including the risk of influenza-associated mortality [26]. Collectively, the aforementioned suggests that being physically active decreases the probability of severe symptoms, recovery time and transmissibility of covid-19.

Currently, no studies have clearly, objectively, and systematically compiled the influence of PA on the prognosis of people diagnosed with covid-19. To the best of our knowledge, this is the first study to use a methodological rigor to compile information on the impact of PA on attenuating clinical outcomes of covid-19. To this end, we sought to systematically review the current literature to understand whether different levels of PA are associated with different clinical outcomes of the disease.

2. Methods

We conducted a systematic review of the literature, developed and reported based on the guidelines proposed by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) [27]. The review protocol was registered on the Open Science Framework platform (OSF), under the DOI registration 10.17605/OSF.IO/PV6NF, on October 07, 2021. The review protocol can be verified at: https://doi.org/10.17605/OSF.IO/PV6NF.

The research question ("Do individuals with different levels of PA have different covid-19-related clinical outcomes?") was formulated with the help of the PICO strategy, so that: [1] (*P*)opulation: people with covid-19; [2] (*I*)nterest: PA level; [3] (*C*)omparison: not applicable; [4] (*O*) utcome: clinical outcomes.

The following were considered eligible and included in this review: primary studies with an observational design (cross-sectional, cohort, case–control, case series and case reports) that evaluated the clinical outcomes of people (\geq 18 years) diagnosed with covid-19, according to with their respective PA levels. Secondary studies (other reviews), editorials, books, book chapters, guidelines, expert opinion articles, dissertations, thesis and abstracts presented at congresses on the subject were considered ineligible and therefore excluded from this review.

Article search was conducted in July 2022 using the following databases: Excerpta Medica Data Base (EMBASE), Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed portal, Scopus, SPORTDiscus via EBSCO platform, and Web of Science. In addition, the "grey" literature was consulted through Google Scholar and the medRxiv preprint database.

The search strategy used was formulated through the combination of controlled terms and keywords related to the theme, respecting the specificities of each of the databases (Table 1). Of note, no type of filters was used in the searched databases, nor was the restriction of language or period of publication of the studies applied.

The identified studies were initially exported to the EndNote Basic software, with the purpose of removing duplications between the bases. Then, the studies (without duplication) were exported to the Rayyan software, in which the analysis and selection was carried out, based on the eligibility criteria, in two phases. Phase 1, the analysis and selection was performed by reading the title and abstract of all studies. Phase 2, the analysis and selection was performed by reading the full text only of the studies selected in the previous phase. In addition, in order to identify other eligible studies, a hand search it was made in the references lists of the selected studies in phase 2.

Data from the selected studies were extracted and allocated in a characterization table, containing the following information: [1] Characteristics of the study: study design, objective, country in which the study was developed, follow-up of investigation, and instrument to assess the physical activity level; [2] Characteristics of individuals: sample sizes, sex, average age, comorbidities and physical activity level; [3] Main outcomes:

Table 1

Search strategy used in the databases.

Data base	Search strategies	Number of studies found
PubMed	(covid-19[Mesh] OR covid-19 OR "Coronavirus Disease-19" OR SARS-CoV-2[Mesh] OR SARS-CoV-2 OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "2019-nCoV") AND ("Physical Status" OR "Physical Activity" OR "Physical Activities" OR "Physical Inactivity" OR "Sedentary Behavior"[Mesh] OR "Sedentary Behavior" OR "Sedentary Behaviors" OR "Sedentary Lifestyle" OR "Sedentary") AND (Prognosis[Mesh] OR Prognosis OR Prognoses OR Prognostic OR Signs OR Symptoms OR Complication OR Complications OR Hospitalization[Mesh] OR Hospitalization OR "Hospital Admission" OR "Hospital Admissions" OR "ICU Admission" OR "ICU Admissions" OR "Intensive Care Unit Admission" OR "Intensive Care Unit Admissions" OR Recovery OR Rehabilitation OR "Patient Dropouts"[Mesh] OR Dropout OR Dropouts OR Mortality[Mesh] OR Mortality OR Death[Mesh] OR Death OR Deaths)	1948
Web of Science	(covid-19 OR "Coronavirus Disease-19" OR SARS-CoV-2 OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "2019-nCoV") AND ("Physical Status" OR "Physical Activity" OR "Physical Activities" OR "Physical Inactivity" OR "Sedentary Behavior" OR "Sedentary Behaviors" OR "Sedentary Lifestyle" OR "Sedentary") AND (Prognosis OR Prognoses OR Prognostic OR Signs OR Symptoms OR Complication OR Complications OR Hospitalization OR "Hospital Admission" OR "Hospital Admissions" OR "ICU Admission" OR "ICU Admissions" OR "Intensive Care Unit Admission" OR "Intensive Care Unit Admissions" OR Recovery OR Rehabilitation OR Dropout OR Dropouts OR Mortality OR Death OR Deaths)	1606
Embase	(covid-19 OR "Coronavirus Disease-19" OR SARS-CoV-2 OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "2019-nCoV") AND ("Physical Status" OR "Physical Activity" OR "Physical Activities" OR "Physical Inactivity" OR "Sedentary Behavior" OR "Sedentary Behaviors" OR "Sedentary Lifestyle" OR "Sedentary") AND (Prognosis OR Prognoses OR Prognostic OR Signs OR Symptoms OR Complication OR Complications OR Hospitalization OR "Hospital Admission" OR "Hospital Admissions" OR "ICU Admission" OR "ICU Admissions" OR "Intensive Care Unit Admission" OR "Intensive Care Unit Admissions" OR Recovery OR Rehabilitation OR Dropout OR Dropouts OR Mortality OR Death OR Deaths)	3265
Scopus	(covid-19 OR "Coronavirus Disease-19" OR SARS-CoV-2 OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "2019-nCoV") AND ("Physical Status" OR "Physical Activity" OR "Physical Activities" OR "Physical Inactivity" OR "Sedentary Behavior" OR "Sedentary Behaviors" OR "Sedentary Lifestyle" OR "Sedentary") AND (Prognosis OR Prognoses OR Prognostic OR Signs OR Symptoms OR Complication OR Complications OR Hospitalization OR "Hospital Admission" OR "Hospital Admissions" OR "ICU Admission" OR "ICU Admissions" OR "Intensive Care Unit Admission" OR "Intensive Care Unit Admissions" OR Recovery OR Rehabilitation OR Dropout OR Dropouts OR Mortality OR Death OR Deaths)	1858
SPORTdiscus	 (covid-19 OR "Coronavirus Disease-19" OR SARS-CoV-2 OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "2019-nCoV") AND ("Physical Status" OR "Physical Activity" OR "Physical Activities" OR "Physical Inactivity" OR "Sedentary Behavior" OR "Sedentary Lifestyle" OR "Sedentary") AND (Prognosis OR Prognoses OR Prognostic OR Signs OR Symptoms OR Complication OR Complications OR Hospitalization OR "Hospital Admission" OR "Hospital Admissions" OR "ICU Admission" OR "Intensive Care Unit Admission" OR "Intensive Care Unit Admission" OR Recovery OR Rehabilitation OR Dropout OR Dropouts OR Mortality OR Death OR Deaths) 	93
Google scholar	(covid-19 OR SARS-CoV-2) AND ("Physical Status" OR "Physical Activity" OR "Physical Inactivity" OR "Sedentary") AND (Prognos* OR Sign* OR Symptom* OR Complication* OR Hospitalization* OR Admission* OR Recover* OR Dropout* OR Mortality* OR Death*)	100
medRxiv	(("covid-19") AND ("Exercise") AND ("Treatment Outcome"))	1158

clinical outcomes (recovery time, hospitalization, severity of covid-19, respiratory support, ICU admission, mechanical ventilation, and death) of people diagnosed with covid-19, according to their respective physical activity levels.

The risk of bias assessment was performed using tools provided by the Joanna Briggs Institute (JBI). For each of the topics in the tools, the answers can be "Yes", "No", "It is not clear" or "Not applicable" [22]. Thus, the selected studies were classified as "high risk of bias", "moderate risk of bias" or "low risk of bias".

All study analysis and selection processes, as well as data extraction and risk of bias assessment of eligible studies were performed by two researchers independently and blinded. Any conflict raised during the process was solved by a third researcher.

The present study is characterized as a systematic review and therefore Institutional Review Board approval was not required.

3. Results

Our search identified 10,028 articles. Fig. 1 displays the flowchart adapted from PRISMA, with details of the article selection process. After duplicate studies exclusion, a total of 6782 studies were screened for analysis. These studies were then analyzed by reading the titles and abstracts, and 6726 were excluded because they did not meet the eligibility criteria. Thus, 56 studies were considered eligible, and were analyzed by reading the full text. Of the 56 studies, 24 were excluded due to: 1) study design not compatible with the inclusion criteria (n = 13) and 2) outside of the scope of the potential clinical outcomes (n = 11). At the end of the selection process, 32 studies were considered eligible and were included in the final sample of this systematic review.

The 32 studies included were read in full and carefully analyzed by two researchers, and the main information was extracted. The characteristics of the included studies are summarized in Table 2. A total of 32 studies were included, representing 3.393,105 participants. The mean age reported was 56.4 \pm 10.6 years. The instruments used to measure PA levels included the International PA Questionnaire, accelerometer, self-assessment questionnaire, Global PA Questionnaire, Vital Sign of Exercise, Modified PA classification questionnaire, Data collected (One question), and insurance number of participants in sports club's General health examination. Additional methods included personal medical interview, Questions, interview, WHO recommendation/Health data available Baecke's Habitual PA Questionnaire, PA Rapid Assessment Scale Questionnaire, contact by phone, Questionnaire modified, collection from medical records, Points awarded for performing fitness activities per day and recorded via smart devices, timed attendance at the gym, or participation in mass-registered sporting events, and Estimations of maximal oxygen consumption (VO₂max) from a submaximal cycle ergometer test.

Because we are interested in the association between PA levels and clinical outcomes related to covid-19, the results will be presented in topics to help with visualization and interpretation.

3.1. Recovery (time)

It was observed that sedentary people took an average of six days longer to recover, compared to physically active individuals [28].

3.2. Symptoms (number)

People who had moderate PA had a lower number of symptoms when compared to physically inactive individuals [29]. The same occurred with active people (n = 7 symptoms) vs inactive people (n = 8 symptoms) [30].

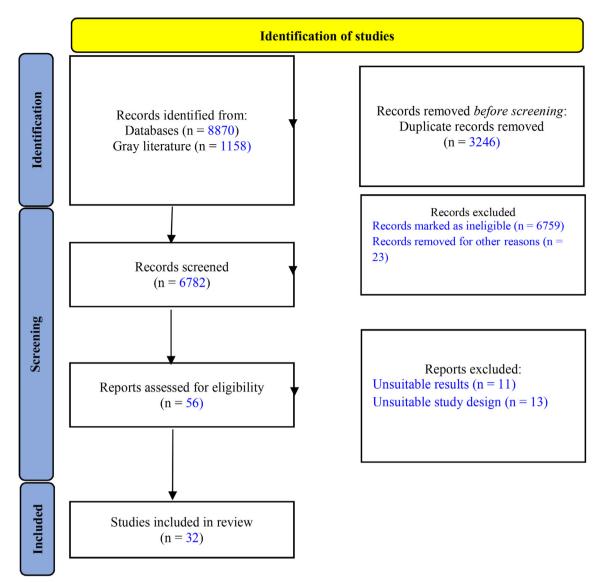


Fig. 1. PRISMA 2020 flowchart for new systematic reviews that only included database and registry searches.

3.3. Hospitalization (time)

In terms of "Hospitalization (time)", no difference was observed between sufficiently active versus inactive individuals [31], between insufficiently active and highly active [32], and with levels of PA related to work, sports, leisure and total PA [33]. However, it was found that individuals who performed PA [34,35] and moderate PA > 150 min per week had shorter hospital stays when compared to sedentary individuals [29]. Additionally, individuals who performed concurrent or non-competing activities of muscle strengthening and/or aerobic exercises showed a reduction in hospitalization time by two days [32]. People who performed moderate PA had a reduction in hospitalization time by 14 days, compared to sedentary people [20].

3.4. Hospitalization (frequency)

When analyzed hospitalization in the context of frequency, individuals partaking in PA [21] and who perform moderate to high-intensity (MHI) [36] did not have a lower frequency of hospitalization for covid-19 compared to inactive people. However, individuals with good cardiorespiratory fitness had a 64% decrease in the frequency of hospitalization compared to individuals with moderate cardiorespiratory fitness [37]. In addition, sufficiently active individuals (726.9 min/week of PA) had a 37.6% lower prevalence of hospitalization when compared to insufficiently active (62.3 min/week of PA) [31]. Athletes had a frequency of hospitalization 1.49 times lower than non-athletes [38]. Physically active individuals have a lower frequency of hospitalization compared to sedentary individuals [39]. Individuals who perform MHI PA have a lower frequency of hospitalization when compared to individuals who perform low-intensity PA [18]. People who performed PA more than once a week and had greater muscle strength had a lower frequency of hospitalization compared to individuals who did not, or rarely, performed PA [40] and high PA was associated with lower rates of hospitalization [18]. Lastly, individuals who engaged in PA regularly were less hospitalized (3.2%) compared to inactive individuals (10,5%) [41].

3.5. Covid-19 severity

Regarding the clinical outcome "Severity", individuals with low, moderate [36,37], good and excellent cardiorespiratory fitness [37], inactive individuals [32], those who performed general PA [42], moderate to vigorous PA (MVPA) [42,43] and who are in the habit of exercising regularly [44] did not present lower severity for covid-19. In other

Table 2
Extraction of the results of the 32 studies included in the systematic review.

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Reference and Country	1,0,		Classification of PA	Recovery (time)	Symptoms (number)	Hospitalization (time)	Hospitalized (frequency)	Severity	RS	ICU	MV	Death		
Alataibi; Boukelia,	Retrospective and	Fitness vs	$n{=}215/36.3{\pm}16.2$	Self-assessment	Sedentary	↑ (-	-	-	-	-	-	-	-
2021 [28] Kingdom of Saudi	prospective NI	duration of symptoms	years/Both sexes	questionnaire	Active	Ļ	-	-	_	-	-	-	-	-
Arabia Brandenburg et al.,	Cross-sectional/	Physical fitness vs	n = 263/227 (86%)	PA-R, online-self-	Low cardiorespiratory	-	\leftrightarrow	-	\leftrightarrow	\leftrightarrow	-	-	-	-
2021 [37] Jorth America, Europe, South America, Asia,	July–October, 2020	symptoms and complications of covid-19	< 65 years 36 (14%) \geq 65 years/Both sexes	report	fitness Moderate cardiorespiratory fitness	-	↔	-	ţ	\leftrightarrow	-	-	-	-
Africa					Good cardiorespiratory	-	\leftrightarrow	-	\leftrightarrow	\leftrightarrow	-	-	-	-
					fitness Excellent cardiorespiratory	-	↔	-	INS	\leftrightarrow	-	-	-	-
Latorre-Román et al.,	Transversal/	PA levels vs	n = 420/33/20-54	IPAQ Spanish version	fitness Sedentary	_	↑.	_	↑	_	_	_	_	_
2021 [29]	May–June, 2020	hospitalizations	years/Both sexes	online-self-report	Walk	-	1 1	_	1	-	_	_	_	_
Spain		for covid-19			MFA	-	Ļ	-	Ļ	-	-	-	-	-
Lee et al., 2021 [32]	Retrospective and	PA Levels vs	$n = 76,395/\ge 20$	General health	VFA Insufficient aerobic	-	1	_ ↑	↑ _	- *	-	-	-	- *
South Korea	Prospective/ January–July 2020	Clinical Outcomes of covid-19	$n = 70,393/ \ge 20$ years	examination, personal medical interview	and muscle strengthening	_	-	I	_	1	-	-	-	I
					Muscle strengthening	-	-	Ļ	-	\downarrow	-	-	-	\downarrow
					Aerobic	-	-	Ļ	-	Ļ	-	-	-	Ļ
					Aerobics and muscle strengthening	-	_	ţ	_	Ļ	-	-	-	Ļ
					Inactive	-	_	↑ ↔	-	1	-	-	-	↑ I
					Insufficiently active Active	_	_	↓	_	↓ I	_	_	_	↓ I
					Highly active	_	_	* ↔	_	Ļ	_	_	_	Ļ
Maltagliati et al., 2021 [40]	Longitudinal and Cross-sectional/	PA vs covid-19 hospitalization	$n = 266/75.4 \pm 10.3$ years/Both sexes	Questions, interview	PA: Almost never or never	-	-	-	↑	-	-	-	-	-
Europe	June–September 2020	-			One to three times a month	-	-	-	\leftrightarrow	-	-	-	-	-
					Once a week	-	-	-	\leftrightarrow	-	-	-	-	-
					More than once a week	-	-	-	Ļ	-	-	-	-	-
					Greater muscle strength	-	_	-	ţ	-	-	-	-	-
Mistry; Natesan;	Case report/U	PA vs	n = 2/40 and 50	GPAQ English version	MFA	-	-	Ļ	-	-	\downarrow	-	-	-
2021 [20] J		hospitalization for covid-19	years, respectively/ Male		Sedentary	-	-	↑	-	-	ſ	-	-	-
Pinto et al.,	Prospective/	PA levels vs covid-	$n = 209/54.9 \pm 14.5$	Baecke's Habitual PA	Work index	-	-	\leftrightarrow	-	-	-	\leftrightarrow	-	\leftrightarrow
2021 [33]	June-October 2020	19 clinical	years/Both sexes	Questionnaire	Sports index Leisure index	-	-	⇔	-	_	-	↔	-	↔
Brazil		outcomes			Total activity index	_	-	⇔ ⇔	_	_	_	↔	_	\leftrightarrow
Samoylov et al., 2020 [61] Russia	Cross/May 2020	PA vs covid-19 hospitalization	$n=144/{\geq}\ 20\ years$	Questionnaire modified, collection from medical records	Active lifestyle	-	-	Ļ	-	-	-	-	-	-
Kontopoulou et al., 2022 [34] Greek	Retrospective/ February 2021 to March 2021	Physical activity vs covid-19 hospitalization	$n=64/62.2\pm13.6/$ Both sexes	Self-reported questionnaire	Physical activity	-	-	ţ	-	-	-	-	-	-

(continued on next page)

Table 2 (continued)

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Reference and Country	Study design/ follow-up	Focus	Sample/age/sex	Instrument to measure PA and form of application	Classification of PA	Recovery (time)	Symptoms (number)	Hospitalization (time)	Hospitalized (frequency)	Severity	RS	ICU	MV	Death
Antunes et al., 2022 [35] Brazil	cross-sectional and quantitative/ September and December 2020		$n=39/{\geq}~65~years/$ Men	IPAQ	Active group Sedentary group	-	-	↓ ↑	-	_	-	¢ ¢	_	_
De Souza et al., 2021 [31] Brazil	Transversal/ June–August, 2020	PA vs covid-19 clinical outcomes	$\begin{array}{l} n = 938 / \\ 6 (0.6\%) = < 18 \\ years \\ 532 (56.8\%) = \\ 18-39 \ years \ old \\ 382 (40.8\%) = \\ 40-64 \ years \\ 17 (1.8\%) = 65-80 \\ years/Both \ sexes \end{array}$	IPAQ, online-self- report	Sufficient PA Insufficient PA	-	-	-	↓ ↑	-	_	-	-	
Halabchi et al.,	Transversal/	Athletes and non-	$n = 4694/42.31 \pm$	Insurance number of	Athletes	-	-	-	Ļ	-	-	-	-	Ļ
2020 [52] Iran	February–April 2020	athletes vs severity of covid- 19	11.92 years/Both sexes	participants in sports clubs	Non athletes	_	_	-	↑ 1	-	-	-	-	ſ
Hamer et al., 2020 [39] UK	Prospective/ March–April 2020	PA levels vs covid- 19 hospitalizations	$\label{eq:n} \begin{split} n &= 760/57.1 \pm 9.0 \\ years/Both \ sexes \end{split}$	IPAQ, UK biobank	Sedentary Active	_	-	-	$\stackrel{\uparrow}{\downarrow}$	_	-	-	-	-
Li; Hua, 2021 [21] Europe/	Cross-sectional/ September 2020	PA vs covid-19 severity	n = 6492/Age: NO/ Gender: Both sexes	Accelerometer	PA	-	-	-	↔	ţ	-	-	-	-
Chen et al.,	Retrospective/NI	MVPA vs covid-19	n=2,586691/Both	PA phenotypes and	MVPA	-	-	-	\leftrightarrow	\leftrightarrow	-	-	-	-
2022 [36]		hospitalization	sexes	accelerometer	Accelerometer	-	-	-	Ļ	\leftrightarrow	-	-	-	-
UK		and severity			Accelerometer- assessed fraction accelerations >425 milligravities	-	-	-	↔	↔	-	-	-	-
Rowlands et al., 2021 [42] UK	Prospective/ March–July 2020	PA vs covid-19 severity	n = 207/64.9 (56.2–73.4)/Both sexes	Pulse accelerometer	General level of PA MVFA	-	-	_	-	$\stackrel{\leftrightarrow}{\leftrightarrow}$	-	-	-	_
Rowlands et al., 2021 [43]	Cross-sectional/ March, 2020-	PA vs clinical outcomes of	n = 2713/40-69 years/Both sexes	Pulse accelerometer	Total PA MVFA			-	-	\downarrow	-	-	-	-
UK Tavakol et al.,	March- 2021 Cross-sectional/	covid-19 Risk factors for	$n = 206/40.9 \pm$	GPAQ, telephone	Short	_	_	_	_	↑	_	_	_	_
2021 [22] Iran	March–April, 2020	the development of severe forms of covid-19, including unhealthy nutrition, obesity and physical inactivity in patients infected with SARS-CoV-2	111.6/Both sexes	interview	Moderate to high	_	_	-	-	ţ	-	_	_	-
Yuan et al.,	Background/	Physical inactivity	$n = 164/61.8 \pm$	VSE, interview	Inactive	-	-	-	-	1	-	-	-	1
2021 [45] China	February–March 2020	vs covid-19 severity	13.6/Both sexes		Active	-	-	-	-	ţ	-	-	-	ţ
Ekblom-Bak et al.,	Case-control/	VO ₂ max vs	n = 857/49.9 years/	Estimations of	Very low VO ₂ max	-	-	-	-	1	-	1	-	1
2021 [16] Sweden	February 2021	hospitalization/ ICU/death	Both sexes	maximal oxygen consumption	Low VO ₂ max Moderate VO ₂ max	-	-	-	-	1	_	1 I	-	↑ I
Sweden		icu/death		(VO ₂ max) from a submaximal	High VO ₂ max	-	-	-	-	ţ	-	Ţ	-	Ţ
Malisoux et al., 2022 [17] Luxemburg	Cross-sectional/ May 2020 and June 2021	PA vs covid-19 severity	n = 452/42 [31–51] years/Both sexes	cycle ergometer test Self-reported e- questionnaire	PA	-	-	-	-	Ļ	-	-	-	-

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Table 2	(continued)
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Reference and Country	Study design/ follow-up	Focus	Sample/age/sex	Instrument to measure PA and form of application	Classification of PA	Recovery (time)	Symptoms (number)	Hospitalization (time)	Hospitalized (frequency)	Severity	RS	ICU	MV	Death
Gundogdu et al., 2022 [44] Turkey	Cross-sectional/ May 2021 and July 2021	Exercise habit vs covid-19 severity	$\begin{array}{l} n = 111 / {\geq} 18 \text{years} / \\ \text{Both sexes} \end{array}$	IPAQ	Exercise habit	_	_	-	-	\leftrightarrow	-	-	-	-
Sallis et al., 2021 [41] USA	Retrospective/ January–October 2020	PA level vs clinical outcomes of covid-19	$\begin{array}{l} n = \textbf{48,440/47.5} \pm \\ \textbf{16.97} \end{array}$	VSE, questions, interview	Consistent PA Inactive	-	-	-	↓ ↑	-	_	↓ ↑	-	↓ ↑
Steenkamp et al., 2020 [18]	Retrospective observational	PA vs hospitalization,	$n = 65,361 \ge 18$ years/Both sexes	Points awarded for performing fitness	Low activity Moderate activity	_	-	-	↑ ↓	-	-	↑ I	↑ I	↑ I
South Africa	study/March 19, 2020 and June 30, 2021	intensive care unit (ICU) admission, ventilation and mortality rates	years, zon ones	activities per day and recorded via smart devices, timed attendance at the gym, or participation in mass-registered sporting events	High activity	-	-	-	Ļ	-	-	Ļ	Ţ	Ļ
Cho et al., 2021 [1]	Retrospective/	PA level vs risk of	$n = 6288/50.7 \pm$	Questionnaire, self-	Physically inactive	-	-			_		_		1
South Korea	January–July, 2020	covid-19 infection	14.3 years/Both	report	LPA	-	-	-	-	-	-	-	-	Ļ
		and mortality	sexes		MPA	-	-	-	-	-	-	-	-	Ļ
					VPA	-	-	-	-	-	-	-	-	Ļ
					MVPA	-	-							Ļ
Cunningham, 2021 [49] USA	Transversal January–November 2020	PA levels vs covid- 19 deaths	n = 3142/65 years and over/Female	Data collected (One question)	Low PA High PA		_	—	_	_		—		↑ ↓
Okeahalam;	Cross-sectional/U	PA and covid-19	$n = 820 \ge 18$ years	WHO	IFA		_	_		_				1
Williams; Otwombe, 2020 [50] African countries		deaths and cases		recommendation∕ Health data available	VFA MFA	-	-	-	-	_	-	-	-	ţ
Salgado-Aranda et al., 2021 [30] Spain	Retrospective/ February–April 2020	PA Level vs clinical outcomes of covid-19	n = 512/18-70 years/Both sexes	RAPA, contact by phone	Sedentary Active	—	—	—		—	-	_	-	↑ ↓
Zhang et al., 2020 [55] UK	Prospective Observational/ March–June 2020	PA vs ICU admission	$\begin{array}{l} n=1596/68.8 \pm \\ 9.2/Both \; sexes \end{array}$	Self-report questionnaire and accelerometer	MVPA AMPA					_		_		↔ ↓
Hamrouni et al.,	Prospective	PA levels vs covid-	n = 259,397/37-73	IPAQ	LPA	_	_	-	_	_				1
2021 [19]	cohort/March 16, 2020 and February 27, 2021	19 mortality	years/Both sexes		MPA HPA	-	-	-	-	-	-	-	-	ţ
Pitanga et al., 2020 [53] Brazil	Cross-sectional/ January 22, 2021	PA vs covid-19 mortality	n = mortality by Covid-19 per 100 thousand inhabitants/NI/Both sexes	NI	Leisure time physical activity	-	-	_	-	-	_	-	-	Ţ
Wang; Sato; Sakuraba, 2021 [51] 186 countries	Datasets/August 20, 2020	Insufficient physical activity vs covid-19 mortality	$n=NI \geq 65 \ years/$ Both sexes	WHO handbooks	Insufficient physical activity	-	-	-	-	-	-	-	-	Ť

Note: RT.

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PA: physical activity; -: It has not been analyzed; NI: not informed; RS: respiratory support; ICU: admission to the Intensive Care Unit; MV: need for mechanical ventilation; INS: Insufficient sample size to generate results; \leftrightarrow : there was no change; \downarrow : decreased; \uparrow : increased; \geq : greater or equal; IPAQ: International PA Questionnaire; PA-R: Modified PA classification questionnaire; PA: physical activity; MPA: moderate PA; VPA: Vigorous PA; IPA: intense PA; LPA: Light PA; MVPA: moderate to vigorous PA; InsPA: Insufficient PA; GPAQ: Global PA Questionnaire; IFA: insufficient physical activity; WHO: World Health Organization; RAPA: PA Rapid Assessment Scale Questionnaire; VSE: Vital Sign of Exercise; AMPA: acceleration vector magnitude PA; VO₂max: maximal oxygen consumption, HPA: high PA.

studies, sedentary people [29], with low level of physical fitness [22] and inactive (25,2% compared with 4.9% for active), had greater disease severity [45]. People who performed aerobic and muscle-strengthening activity had a 57% lower risk of severe forms of covid-19 when compared to people who performed insufficient aerobic and muscle strengthening. Insufficiently active people were 22–35% less likely to have severe forms of covid-19 compared to inactive people. Active people were 38–46% less likely to contract severe forms of covid-19 when compared to their inactive counterpart. Further, highly active people were 21–34% less likely to contract severe forms of covid-19 compared to inactive people [32]. People who performed PA in general [17,21] and, highly active group, had a lower severity for covid-19 compared to a group with low level of PA [32]. People who practice MHI PA and high intensity PA [46] had a lower severity for covid-19.

3.6. Respiratory support (RS)

Regarding the clinical outcome "RS", insufficiently active people [31], sedentary (61.4% vs 69.4% compared to active) [47] or low-intensity PA compared to MHI [18] showed no difference for the need for RS. However, sedentary individuals compared to those who underwent MVPA had a greater need for RS (25% vs 11%), respectively [20].

3.7. Admission to the Intensive Care Unit (ICU)

Regarding the clinical outcome "ICU admission" sedentary and active people [35] (8.8% vs 6.3%) [37] and levels of PA related to work, sports, leisure and total PA [33] were not different regarding ICU admission. However, individuals who perform MHI PA have a low admission in the ICU when compared to individuals who perform low-intensity PA [18]. People who practice regular PA are less likely to be admitted to the ICU (i.e., 1.73 times less likely) [17] compared to inactive people [41]. People who perform moderate physical activity (MPA) and high physical activity (HPA) have a lower risk of being admitted to the ICU compared to people who perform low physical activity (LPA) [18,46].

3.8. Clinical outcomes

Regarding the clinical outcome "need for mechanical ventilation" there were no differences between sufficiently and insufficiently active people [31]. However, people who perform MPA and HPA have a lower risk of using RS compared to people who perform LPA [18].

Regarding the clinical outcome "Death", inactive people [30], with levels of physical activity related to work, sports, leisure and total physical activity [33], and MVPA [48] did not change the risk of death from covid-19. However, people with a low level of PA [19,46,49], LPA [18,19], insufficient PA and inactive [50,51], low and very low VO₂max [46] increased the risk of death from covid-19. Additionally, people who performed MPA and HPA [19], LPA, MPA, VPA and MVPA had 29.3%, 4.3%, 14.1% and 18.5%, respectively, lower chance of risk of death, when compared to inactive people (33.7%) [1]. This decrease in the risk of death was also observed in athletes [52] and people who engage in leisure-time of PA [53]. In addition, people who performed aerobic activity and muscle strengthening had a 0.08% lower risk of death, when compared to people who performed aerobic activity and insufficient muscle strengthening (0.02%). Insufficiently active people had a 19%-40% lower risk of death compared to inactive people and active people had a 65%-83% lower risk of death when compared to inactive people [54]. On the other hand, individuals who perform MHI PA have a low risk of death when compared to individuals who perform low-intensity PA [18]. Compared with inactive people, highly active people had a 21%-63% lower risk of death. The high PA group had a lower risk of death than the inactive group [1]. In addition, people with consistent PA had a 0.4% risk of death, i.e. lower, when compared to inactive people who had a 2.4% risk of death [41]. In the study by Zhang et al., participants in the control group had a longer acceleration vector magnitude PA (AMPA) time, while patients who died of covid-19 had a shorter time [55]. People who perform MPA and HPA have a lower risk of death compared to people who perform LPA [18] and people with very low VO₂max [46] and low level of physical activity [19] had a higher risk of death compared to people with moderate to high VO₂max and MHI PA, respectively.

The results regarding the risk of bias of the studies included in this review, through the analysis of methodological quality, according to each study design, are presented in detail in Table 3. Of the studies included in this systematic review, 12 had a low risk of bias (37.5%), 19 had a moderate risk of bias (59.38%), and one had a high risk of bias (3.13%).

4. Discussion

This systematic review analyzed the association between different levels of PA and clinical outcomes of people diagnosed with covid-19. The main findings were: fitness level can be used to estimate the risk of covid-19 severity [17,28,46]; people who walk or run between 6.8 and 8.2 min/km and who perform MHI PA [18] have a lower risk of hospitalization [37]; athletes have a 1.49 times lower risk of hospitalization [52]; greater muscle strength is associated with lower chances of hospitalization for covid-19 [56]; performing MVPA contributes to the reduction of symptoms and severity of covid-19 [29]; sedentary people more often have tachypnea and fever as symptoms of covid-19 [47]. These positive associations between the level of physical conditioning, walking and/or running, being an athlete, having greater muscle strength, practicing MVPA and not being sedentary, with attenuation of the clinical outcomes of covid-19, can provide scientific knowledge so that society understands the importance of having a physically active life in periods of Pandemic due to a disease similar to the one faced.

4.1. PA and recovery time from covid-19

Relating PA and covid-19 recovery time, physically active people recover faster from covid-19 [28]. This may be because inactive people tend to have a higher body mass index (BMI), and individuals with a higher BMI are more likely to have respiratory symptoms when compared to people with a normal BMI [57,58].

4.2. PA and the number of symptoms of covid-19

Although one study did not show a significant association between the number of covid-19 symptoms and self-reported levels of physical fitness or PA, the outcome may have been influenced by the participant's ability to accurately remember the number of symptoms and the experience of symptoms. It is also possible that the time period of the survey (91 days) influenced the accuracy of symptom recall [37]. Other studies have shown that people who performed moderate-to-vigorous PA [29], or active people [47], had a lower risk factor for the presence of symptoms. The fact that inactive people have fever probably represents a selection bias in relation to the established admission criteria. Absence of fever in active people may reflect advanced age. Researchers highlighted that fever may be absent in 30-50% of older patients [59]. A study by Kostka et al. with 61 elderly patients showed that symptoms of upper respiratory tract infections were inversely related to caloric expenditure from moderate physical exercise [60]. Thus, higher physical activity level seems to be a protect factor against the development of symptoms associated with covid-19.

4.3. PA and length of hospital stay for covid-19

According to the analyzed studies, active [31], insufficiently active and highly active individuals [1], and individuals with levels of work, leisure, sports-related PA and total PA [33] do not report shorter hospitalization time. However, people walk regularly [29], live an active

Table 3

Risk of bias analysis using the JBI Critical Appraisal Tool for Cross-sectional, Case-Control, Cohort, and Case Series analytical studies.

Cross-sectional studies	Questions (Q)											Total	Risk of bias	
	1	2	3	4	5	6	7	8				(% score yes)		
Alataibi; Boukelia (2020) [28]	N	Y	Un	Y	N	N	Y	Y				50%	Moderate	
Brandenburg et al. (2021) [37]	Y	Y	Y	Un	Ν	Ν	Ν	Y				50%	Moderate	
Cunningham (2021) [49]	Ν	Ν	Y	Y	Y	Y	Un	Un				50%	Moderate	
Halabchi et al. (2020) [52]	Y	Y	Y	Y	Y	Y	Y	Un				87,5%	Low	
Hamer et al. (2020) [39]	Ν	Y	Un	Un	Y	Y	Ν	Y				50%	Moderate	
Latorre-Román et al. (2021) [29]	Y	Y	Y	Un	Un	Y	Y	Y				75%	Low	
Lee et al. (2021) [32]	Y	Y	Y	Y	Un	Un	Y	Y				75%	Low	
Li; Hua (2021) [21]	Y	Ν	Un	Un	Y	Y	Un	Y				50%	Moderate	
Maltagliati et al. (2021) [40]	Y	Y	Ν	Ν	Y	Y	Ν	Y				62,5%	Moderate	
Okeahalam; Williams; Otwombe (2020) [50]	Y	NA	S	S	Un	Un	Y	Y				62,5%	Moderate	
Rowlands et al. (2021) [42]	Ν	Y	Un	Un	Y	Y	Y	Y				62,5%	Moderate	
Rowlands et al. (2021) [43]	Y	Y	Un	Un	Y	Y	Y	Y				66,6%	Moderate	
Salgado-Aranda et al. (2021) [30]	Y	Y	Y	Y	Ν	Ν	Ν	S				62,5%	Moderate	
Sallis et al. (2021) [41]	Y	NA	Un	Un	Y	Y	Y	Y				62,5%	Moderate	
Samoylov et al. (2020) [61]	Y	Y	Un	Un	Un	Un	Ν	Un				25%	High	
Souza et al. (2021) [31]	Y	Y	Y	Y	Un	Un	Ν	Y				62,5%	Moderate	
Tavakol et al. (2021) [22]	Y	Y	Y	Y	Y	In	Ν	Y				75%	Low	
Zhang et al. (2020) [55]	Ν	Y	Un	Un	Y	Y	Un	Y				50%	Moderate	
Steenkamp et al. 2021 [18]	Y	Y	Y	Y	Un	Un	Y	Y				75%	Low	
Malisoux et al., 2022 [17]	Y	Ν	Y	Y	Un	Ν	Y	Y				62,5%	Moderate	
Pitanga et al., 2020 [53]	Un	Y	Y	Y	Un	Ν	Y	Y				62,5%	Moderate	
Gundogdu et al., 2022 [44]	Y	Y	Y	Y	Un	Ν	Y	Y				75%	Low	
Antunes et al., 2022 [35]	Y	Y	Y	Y	Un	Un	Y	Y				75%	Low	
Chen et al., 2022 [36]	Un	Y	Y	Y	Un	Un	Y	Y				62,5%	Moderate	
Kontopoulou et al., 2022 [34]	Un	Y	Y	Y	Un	Un	Y	Y				62,5%	Moderate	
Wang; Sato; Sakuraba, 2021 [51]	Y	Un	Y	Y	Un	Un	Y	Y				62,5%	Moderate	
Case-control studies	1	2	3	4	5	6	7	8	9	10				
Cho et al. (2021) [1]	Y	Y	Y	Y	Y	Un	Un	Un	NA	Y		60%	Moderate	
Yuan et al. (2021) [45]	Y	Y	Y	Y	Y	Y	Un	Un	NA	Y		70%	Low	
Ekblom-Bak et al., 2021 [16]	Y	Y	Y	Un	Y	Un	Un	Y	Y	Y		70%	Low	
Cohort studies	1	2	3	4	5	6	7	8	9	10	11			
Pinto et al. (2021) [33]	Y	Y	Y	Y	Y	Y	Y	Un	Un	Y	Y	81,8%	Low	
Hamrouni et al., 2021 [19]	Y	Y	Y	Un	Y	Y	Y	Un	Un	Y	Y	72,7%	Low	
Case series studies	1	2	3	4	5	6	7	8	9	10				
Mistry, Natesan (2021) [20]	Y	Un	Y	Y	Un	Un	Y	Y	Y	Y		70,0%	Low	

Abbreviations: N: no; U: unclear; Y: yes; NA: not applicable.

lifestyle [61], those who performed concurrent or non-competing activities of muscle strengthening and/or aerobic exercises [1], or performed moderate PA [20,34,35] showed a reduction in hospitalization time. This shorter hospital stay may have been influenced by improved immunosurveillance and metabolic health by the increase in immunoglobulins, anti-inflammatory cytokines (interleukin IL-6, IL-1Ra and IL-10), neutrophils, cytotoxic T, immature B and natural killer cell subsets, reduced systemic inflammation promoted by immune cell recirculation, which mediates an anti-inflammatory and antioxidant state through multiple pathways, and better regulation of the immune system and delayed onset of immunosenescence due to PA performance [32,62]. Thus, it is plausible that physically active people present a decrease in hospitalization time, when compared to physically inactive people.

4.4. PA and hospitalized frequency of covid-19

Although people who performed PA did not have a lower frequency of hospitalizations when compared to inactive people [21], people with good cardiorespiratory fitness [37], active people [39], active enough [29], athletes [52], people who trained more than once a week and had greater muscle strength [40], people with high level of physical activity [18], MHI PA [18] and, people who practiced PA consistently [41], had a lower frequency of hospitalizations. Although not conclusive, these results may be related to the levels of cytokines in the body, which play significant roles in immunity and immunopathology [63]. Moderate intensity exercise performed daily reduces susceptibility and morbidity to respiratory viral infections by increasing salivary lactoferrin and

leukocytes and other immunoprotective agents [64]. It has been suggested that PA may reduce the inflammatory response after infection, decreasing the chances of hospitalization [63,64]. Although not conclusive, it appears that physically active people have a lower frequency of hospitalizations when compared to physically inactive people.

4.5. PA and severity of covid-19

Although people with low, moderate, good and excellent cardiorespiratory fitness [37], inactive [32], moderate and high VO₂max [46] with general PA level [37], and who performed PA [17] and MVPA [42, 43] did not present a lower severity of covid-19, sedentary people [29], with low level of physical fitness [22] and inactive (25.2% compared to 4.9% for active) [45], showed greater disease severity. Common to these conditions is a state of chronic low-grade inflammation leading to greater severity of covid-19 [63]. Furthermore, an interruption of PA and a decrease in physical fitness levels can intensify susceptibility to infection and increase various comorbidities related to poor covid-19 outcomes [64]. On the contrary, people who performed aerobic and muscle strengthening activities, people who were insufficiently active, active, highly active, high PA group [32] and, people who underwent PA [30] had a lower chance of contracting severe forms of covid-19.

The severity of symptoms associated with covid-19 and subsequent infection outcomes are associated with the health status of individuals prior to infection [63]. In addition, PA induces angiotensin-converting enzyme 2 (ACE2) expression in skeletal muscle, leading to a reduction in circulating ACE2, which may lead to a protective effect on SARS-CoV-2

susceptibility and covid-19 severity [65]. Isolation increases levels of glucocorticoids, which inhibit critical immune system functions, reduce skeletal muscle activity, increase peripheral insulin resistance, and disrupt mitochondrial homeostasis, systemic inflammation, and increased cytokine levels. This could lead to increased severity of covid-19 in sedentary people [66]. Along with other risk factors (e.g. psychological stress and genetic predisposition), the virus may be associated with a "cytokine storm", contributing to the observed increased risk of severe covid-19 [67]. The role of low-grade inflammation in susceptibility to severe covid-19 infection remains poorly understood. Low-grade inflammation is suggested to be a risk factor for severe covid-19 and partially explains the links between lifestyle behaviors and infection. C-reactive protein plays an important role in immune function [68], therefore, based on these assumptions, it is plausible that active people have a lower severity of covid-19. Decreasing angiotensin II with pharmacological strategies has been reported to improve angiotensin 1-7 and attenuate inflammation, fibrosis, and lung injury [69]. Similarly, regular physical exercise also induces a shift in the Renin Angiotensin System (RAS) to angiotensin 1-7 that could possibly reduce the severity of the clinical outcome of covid-19 infection [47].

Some studies mention that insufficiently active people [31] or sedentary [47] showed no difference for the need for RS. However, when looking at different intensities of PA, people with MVPA required fewer days of oxygen support compared to poor ratings [20]. Aerobic training promotes biochemical changes in the diaphragm muscle phenotype [64]. Adaptations as a result of aerobic training help combat stress on the respiratory system and improve respiratory muscle function, decreasing the need for RS [18]. In a new report, patients with a BMI over 25kg/m2 (clinically overweight) are more than three times more likely to die from covid-19 and seven times more likely to need mechanical ventilation [70]. Presumably, physically active people have lower severity of covid-19 compared to physically inactive people.

4.6. PA and ICU admission in covid-19

Admission to the ICU was not different when comparing sedentary people with active [47] and levels of physical activity related to work, sports, leisure and total physical activity [33]. On the other hand, people with MHI PA [18], moderate-to-high VO₂max [46], active people with HPA and MPA spent less time in the ICU [18,41] compared to their counterparts reporting low levels of PA [46]. It is possible that sedentary people, with a higher burden of comorbidities and a lower probability of recovery, may have been less likely to be selected for ICU admission and, therefore, showing no difference compared to active people [47]. By contrast, higher cardiorespiratory fitness (CRF) may attenuate obesity and hypertension-related risks and, consequently, decreased risk of ICU stay [14]. It appears that moderate levels of PA have a significant protective effect in severe cases of invite-19 with a consequent decrease in ICU time [18].

4.7. PA and need for mechanical ventilation in covid-19

Unlike insufficiently active people, sufficiently active people did not need mechanical ventilation [31] and, people with high level of physical activity and MHI PA needed less mechanical ventilation [18]. Physical activity can help improve the immune system response and lessen viral infection. In addition, exercise prevents and treats numerous complications associated with covid-19, such as heart disease, neurological and metabolic disorders, including the positive effect on the renin-angiotensin system [27]. Reducing the severity of infections, specifically in the lungs, may decrease the severity of the clinical outcome, which may result in patients not needing intervention such as mechanical ventilation [41]. However, more studies are needed to better understand the mechanisms involved in physical activity and its benefits in patients with covid-19.

4.8. PA and death from covid-19

The risk of death was not different in inactive compared to active people [32], with levels of PA related to work, sports, leisure and total physical activity [33] and who performed MVPA [40]. However, the risk of death was higher in people with a low [19,49] and very level of PA [18], with insufficient PA [50] and inactive [45]. By contrast, people with leisure time physical activity [53] who performed MPA and HPA [18], with moderate to high VO₂max [46], LPA MPA, VPA and MVPA [1], athletes [52], who performed aerobic and muscle strengthening activities, insufficiently active, active, highly active, high PA group [32], people with consistent PA [41], and who had a longer AMPA time [55] had a lower risk of death from covid-19. Moderate-intensity exercise can reduce mortality from respiratory viral infections by increasing salivary lactoferrin and leukocytes and other immunoprotective agents [64]. During and after PA, pro and anti-inflammatory cytokines are released, lymphocyte circulation and cellular recruitment increase, which can affect the existence of a viral infection, the intensity of its symptoms and the possibility of mortality as a consequence of the infection in individuals who regularly exercise [71]. Regular aerobic exercise can increase innate immunity and result in greater protection against viral infections [11]. The lower risk of death in active people may also be due to the fact that PA induces ACE2 expression in skeletal muscle and, consequently, decreases circulating ACE2 [65]. Recent research suggests that PA may have protective effects. PA is linked to enhanced immunological markers in a number of covid-19 related diseases, including cardiovascular disease, diabetes, and obesity [72,73]. Thus, the risk of death is possibly lower in people who perform physical activity consistently when compared to people who perform physical activity insufficiently to be classified as physically active people.

4.9. Strength of evidence

Strength of this review is the robustness of the search strategy adopted to retrieve studies from the scientific literature. The non-use of filters related to language and period of publication of the studies in the execution of the search allowed the authors to identify a greater number of potentially eligible studies. In addition, our systematic review was conducted based on internationally accepted theoretical frameworks, which guarantees an unparalleled quality for carrying out all stages of this review.

4.10. Study limitations

This review comes with limitations. Despite the use of a broad and well-directed search strategy, all the scientific literature on the subject, which addresses other outcomes related to the association between PA and covid-19, may not have been included in this review. In addition, due to the considerable heterogeneity between the included studies, and the methodological quality (risk of bias) of them, the quantitative synthesis (meta-analysis) was not possible. Another limitation of the present study lies in the fact that despite our robust search, this review only found and included cross-sectional, case–control, and case studies. No studies using an experimental design were observed. Future studies could be conducted in this direction. Although a meta-analysis would be interesting and strengthen the conclusions of the present study, the heterogeneity observed among studies prevented us from completing such analysis.

4.11. Recommendations for practice

The results of this systematic review suggest that regular PA may be capable of attenuating selected clinical outcomes related to covid-19. Thus, the findings of the present study may help support evidence-based strategies and initiatives aiming at counteracting some of the negative consequences of covid-19.

4.12. Research recommendations

The present systematic review highlighted a number of pertinent considerations for conducting future research. Regarding the outcomes studied, new studies on the subject need to assess PA using a more comprehensive approach taking into account previously established and standardized parameters. Parallel, future studies should jointly assess clinical outcomes related to covid-19, such as severity, signs and symptoms, morbidity and mortality, hospitalization rates, ICU admission, and need for mechanical ventilation. This would create the possibility of a more complete analysis, taking into account short, medium and long term periods.

5. Conclusion

This systematic review showed that physically active individuals diagnosed with covid-19 may show attenuation of severe forms of covid-19, such as decreased risk of hospitalization, recovery time, number of symptoms, severity, ICU and death, when compared to individuals with low levels of PA or classified as sedentary. However, it is important to notice that the included studies used a cross-section design, therefore, examining the association between physical activity and clinical outcomes of the covid-19 rather than establishing a cause-and-effect relationship. Although we included 32 studies, available data from experimental and cohort studies are lacking. Therefore, future studies adopting a more robust design to assess the influence of PA on the clinical outcomes of covid-19, as well as the role played by PA in the period poscovid-19 (i.e. recovery) are needed. Nonetheless, the results of this study reinforce the importance of a physically active lifestyle in mitigating clinical outcomes of covid-19. Public health authorities and health professionals should encourage physical activity at the population level and create strategies and initiatives to promote safe spaces for PA in an attempt to mitigate potential severe consequences of covid-19.

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Informed consent form

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Declaration of data availability

The data is contained in the article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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