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COVID-19

# Association between physical activity and risk of COVID-19 infection or clinical outcomes of the patients with COVID-19: A systematic review and meta-analysis

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Keywords

Exercise • COVID-19 • SARS-CoV-2 • Systematic Review • Meta-analysis

Summary

**Objective**. *The COVID-19 pandemic has caused serious consequences for global health and economy. The important question is whether the level of physical activity might influence the risk of COVID-19 incidence or clinical outcomes, including the severity or mortality of infected patients. The objective of this systematic review and meta-analysis is to evaluate the association between sufficient physical activity and incidence, hospitalization, severity, recovery, and mortality of COVID-19.*
**Methods**. *A systematic search of Web of Sciences, PubMed, and Scopus between December 2019 and November 2021 was conducted. Studies were screened based on the inclusion criteria, i.e. observational studies (case-control, prospective or retrospective longitudinal designs, and cross-sectional studies) which have determined the association of physical activity, exercise, sports participation, or sedentary behavior with COVID-19 incidence or outcomes, including mortality, severity, recovery and hospitalization in healthy population or population with any specific comorbidity.*
**Results**. *Based on eligibility criteria, 27 articles were finally included in the qualitative synthesis. The meta-analysis of five studies evaluating the association of physical activity and COVID-19 mortality showed a weighted OR of OR of 0.61 (CI 95%: 0.50-0.75) with heterogeneity ($I^2$ = 45.8%, P < 0.001) and in seven studies regarding physical activity and COVID-19 hospitalization, weighted OR was 0.541 (CI 95%: 0.491-0.595) with heterogeneity ($I^2$ = 81.7%, P < 0.001).*
**Conclusion**. *Participating in sufficient physical activity might decrease COVID-19 related COVID-19-related hospitalization and mortality. Developing programs to increase physical activity during the COVID-19 pandemic might be an appropriate health strategy.*

## Introduction

The pandemic of COVID-19 has challenged world health systems, economy, and social lifestyles. As a consequence of the frequent lockdowns, public avoidance of social activities and the closure of sports clubs and public venues, physical activity level appears to have declined among different populations [1]. This may lead to short and long-term public health consequences, and an increase in the burden of non-communicable diseases [2]. Participating in regular physical activity improves mental and physical health [3]. Improvement in immunity state in various conditions including cardiovascular disease, insulin resistance state, dementia, and cancer have been indicated in individuals participating in regular exercise [4]. Moderate-intensity physical activity reduces the incidence, prognosis, and severity of viral respiratory infections with several mechanisms affecting the immune system [4-7]. Natural killer (NK) Cells, salivary IgA concentrations, neutrophils, and stress hormones are increased and Th1/Th2 cell responses are regulated via engaging in moderate-intensity physical activity [6].
COVID-19 clinical manifestations consist of a variable spectrum including asymptomatic, mild to moderate, and severe intensity. It is assumed that physical activity may boost immunity in COVID-19 patients and reduce severe outcomes [7]. On the one hand, the physical activity leve&l of the community has been reduced inevitably, due to the COVID-19 preventive protocols (including staying at home, social distancing programs, etc.). On the other hand, physical activity may potentially reduce the incidence of COVID-19 and improve the consequences in COVID-19 patients. A few studies assessing the effects of physical activity on COVID-19 severity, morbidity, mortality, and hospitalization have been conducted [7-9]. Currently, no systematic review has been accomplished in this domain. Indeed, by conducting this systematic review and meta-analysis, we aimed to demonstrate whether if engaging in physical activity is beneficial in COVID-19 control strategies and recommend the policymakers develop proper action plans regarding physical activity in

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the community. [10]. The objective of this study was to perform a systematic review and meta-analysis evaluating the association between physical activity and the risk of COVID-19 infection or clinical outcomes of the patients with COVID-19.

## Methods

### Protocol

The current systematic review and meta-analysis were accomplished according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [11]. The complete study protocol was registered on PROSPERO (protocol number: CRD42021291451).

### Search strategy and information sources

Electronic resources including Web of Sciences, PubMed, and Scopus between December 2019 and November 2021 were searched systematically. In the next stage, in the related studies, references were assessed. Search keywords were as follows: "physical activity" OR "exercise" OR "physical inactivity" OR "sedentary behavior" OR "lifestyle" OR "sports" in combination with "COVID-19" OR "SARS-CoV-2".

### Eligibility criteria and study selection

Inclusion criteria were: 1) observational studies including case-control, prospective or retrospective longitudinal designs, and cross-sectional studies, 2) studies conducted in healthy population or population with any specific comorbidity, 3) COVID-19 patients were detected via diagnostic tests, hospital reports, or deterministic signs or symptoms, 4) studies have tested the association of physical activity, exercise, sports participation, or sedentary behavior with risk of incidence or COVID-19 outcomes, including mortality, severity, recovery, and hospitalization.

Studies qualified based on inclusion criteria were evaluated. Qualitative studies, reviews, commentaries, and editorials were excluded. The studies were not excluded based on the assessment method of physical activity level or diagnostic method of COVID-19 in patients. The screening and study selection process was conducted via wotwo independent reviewers (B.T. & M.S.) and any disagreement was discussed until a settlement was achieved. If no agreement was attained, a third reviewer (B.M.) arbitrated the process.

### Data extraction

Two independent reviewers (B.T. & M.S.), extracted data by applying a standardized data extraction form. Data extraction form consisted of study characteristics including the name of the first author, sample size, physical activity measure, and assessment tool, outcome definition and assessment method, study design, and reported association of physical activity, exercise, sports participation, or sedentary behavior with COVID-19 outcome. A third reviewer (B.M.) evaluated any disparities between results and disagreements were discussed between reviewers until achieving a final agreement.

### Quality assessments of studies

Joanna Briggs Institute (JBI) critical appraisal checklist for cross-sectional, case series, and cohort studies were applied for the quality assessment of studies (Supplementary Table I) [12]. Two reviewers (B.T. & M.S.), applied JBI, and the results were assessed with a third reviewer (B.M). Any disagreement was discussed to achieve a settlement.

### Statistical analysis

Meta-analysis was conducted on studies based on inclusion and exclusion criteria and eligibility of homogenous assessment methods for physical activity and clinical outcomes. Association between physical activity and clinical outcomes including odds ratio, risk ratio, hazards ratio, incidence risk ratio, prevalence ratio, Beta, and correlation coefficient were recorded. Studies containing odds ratio, risk ratio, hazards ratio, incidence risk ratio, and prevalence ratio were meta-analyzed, via STATA (version 13). A random-effect model was applied to evaluate associations between physical activity and clinical outcomes. Assessments of the studies' heterogeneity were via determining the Q-statistic and the I-squared index. A heterogeneity more than 75% was defined as high, and below 40% was insignificant.

## Results

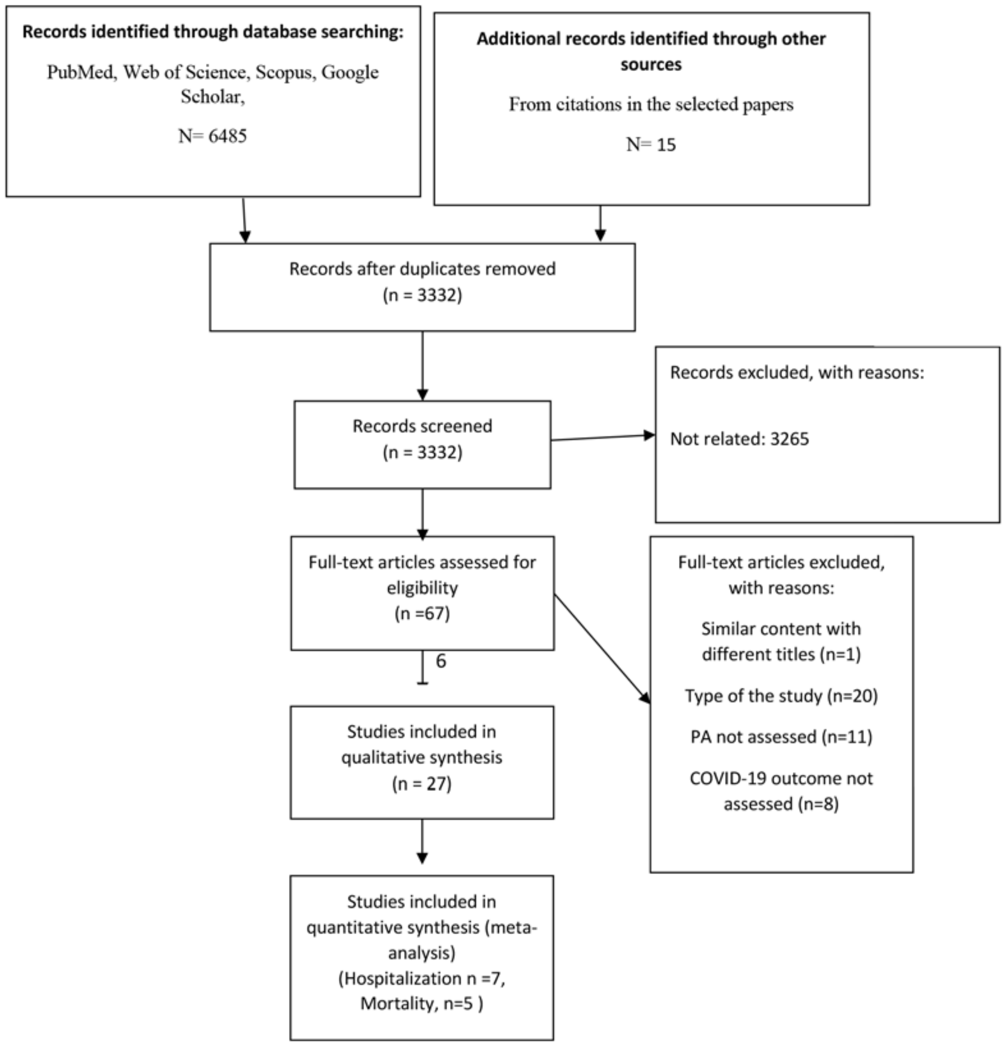
Results of a systematic search through Web of Sciences, PubMed, and Scopus databases for published studies consisted of 6485 studies. After duplicate removal, 3332 studies were evaluated in the primary screening process for subject relativity, and 67 studies were appropriate for complementary full-text assessment**.** After assessing the study according to eligibility criteria**,** 27 articles met the inclusion criteria. PRISMA flowchart is illustrated in Figure 1.

Study characteristics have been reviewed and presented in Table I. Among 27 studies included, patients with COVID-19 were assessed about engaging in physical activity, sports participation, and sedentary behavior.

### Physical activity and COVID-19 infection

Twelve studies have assessed the association between physical activity and COVID-19 infection. Gao et al. suggested that engaging in physical activity more than 5 times a week increased the risk of COVID-19 infection [19]. In studies by Huang et al. and Hamer et al., a sedentary lifestyle and physical inactivity have been proposed as risk factors for COVID-19 infection [20, 22]. Cho et al. indicated that increasing physical activity level per each standard deviation in MET-min/week might reduce the risk of COVID-19 infection [16]. Based on Lee et al. study engaging in sufficient physical activity (aerobic and strengthening exercises) reduces the probability

**Fig. 1.** Flow diagram of systematic literature search on physical activity and COVID-19 outcomes.




of infection compared to inactive individuals (2.6% *vs* 3.1%) [24]. Country-level physical activity reduced the risk of COVID-19 disease in a study by Cunningham et al. [17]. Rowlands et al. suggested that moderate to vigorous physical activity and total physical activity level have no correlations with COVID-19 infection [32]. In a study by Zhang et al. increased physical activity level (based on an acceleration vector scale) reduced the risk of COVID-19 overall infection and outpatients [36]. Bielik et al. did not demonstrate a decreased risk of COVID-19 incidence among cold-water swimmers (physically active individuals). However, an increased probability of asymptomatic COVID-19 and decreased probability of re-infection exceeding twice annually was demonstrated among swimmers [15]. Marcus et al. indicated a reduced risk of incidence of SARS-CoV-2 infection symptoms among individuals participating in the weekly exercise [27]. Also, Nguyen et al. proved that physical activity reduced COVID-19-like symptoms' likelihood [28].

## Physical activity and risk of COVID-19 related hospitalization

Seven studies evaluated the association between physical activity and the risk of hospitalization in patients with COVID-19. An accelerometer was used as an objective physical activity assessment method in a study by Li et al. [25]. No correlation was detected between physical activity predicted genetically (each standard deviation increase) with hospitalization due to COVID-19 [25]. Subjective methods including the international physical activity questionnaire (IPAQ) short version [18, 23], Exercise Vital Sign (EVS) [7, 26], and membership in the sports medicine insurance system [8] were applied in the studies to assess physical activity. De Souza et al. showed a 37.6% reduction in the prevalence of COVID-19 related hospitalization in individuals engaging in sufficient physical activity [18]. In Latorre-Román et al. study, engaging in more than 150 minutes of moderate physical activity per week indicated a negative relation with hospitalization [23].

Tab. I. Characteristics of studies on the association between regular physical activity and clinical outcomes of the patients with COVID-19.

| Results | Outcome | PA assessment tool | Exercise, physical activity, sedentary behavior, etc. | Participants | Study design (type/ registration time) | Study and country |
|---|---|---|---|---|---|---|
| Among physically active individuals decreased mortality was detected (RR: 0.70, 95% CI: 0.54-0.89) | Mortality | Questionnaire (IPAQ short version) | Physical activity | 468,569 participants (mean age: 56.5 ± 8.1) | Cohort study/ March to June 2020 | Ahmadi et al. [13] (2021) United Kingdom |
| Individuals engaging in regular physical activity have a 2.7-time faster recovery process compared to inactive individuals (p = 0.00) | Recovery time | 12 multiple choice questionnaire using a self-rated scale | Fulfilling WHO physical activity recommendation (150 min/w) | 215 (mean age: 36.3 ± 16.2 years) COVID-19 infected participants | Cross sectional | Boukelia & Alataibi [14] (2020) Kingdom of Saudi Arabia |
| Among cold-water swimmers (physically active individuals) lower probability for COVID-19 incidence was not detected (RR:1.07, 95% CI: 0.71-1.62) but increased probability of asymptomatic COVID-19 (RR: 2.32, 95% CI: 0.83-6.44; p < 0.05) was demonstrated | Infection incidence, re-infection, and less severe forms | Adapted version of Questionnaire (IPAQ short version) | Physical activity | 2343 participants [male mean age: 30.5 (29.7-31.3) female mean age:35.1 (34.4-35.8)] | Cross sectional study/7 December-18 December 2020 | Bielik et al. [15] (2021) Slovak Republic |
| Moderate to vigorous physical activity reduced morbidity (adjusted OR:0.90, 95% CI, 0.86-0.95) and mortality (adjusted OR, 0.47; 95% CI, 0.26-0.87) in patients with COVID-19. Each standard deviation increase in physical activity (MET-min/week) reduced risk of infection and mortality of COVID-19 by 4% and 35%, respectively | Morbidity and mortality | Self-reported questionnaire | Leisure time physical activity (Moderate to vigorous PA or MVPA) | 6289 COVID-19 infected participants (mean age: 50.7 ± 14.3 years) & 125,772 Healthy individuals (mean age: 50.7 ± 14.3 y) | Retrospective observational study (Case-Control Study)/ January 1-July 16, 2020 | Cho et al. [16] (2021) South Korea |
| Negative associations between county-level physical activity and COVID-19 infection (r = -0.14) or mortality (r = -0.23) were detected | Mortality | Website databank via a questionnaire | Physical Activity | 3142 counties of USA | Cross sectional/ January 20-November 30, 2020 | Cunningham [17] (2021) United States |
| Engaging in regular physical activity (moderate physical activity for at least 150 minutes weekly or vigorous physical activity for at 75 minutes weekly reduces hospitalizations prevalence among COVID-19 patients (Adjusted PR: 0.65; P = 0.046) | Hospitalization | Online questionnaire (IPAQ short version) | Physical Activity | 938 survivors and fully recovered patients infected with COVID-19 | Cross sectional/ June-August, 2020 (IPAQ short version)] | de Souza et al. [18] (2021) Brazil |

▶

**Tab. I.** *Continues.*

| Results | Outcome | PA assessment tool | Exercise, physical activity, sedentary behavior, etc. | Participants | Study design (type/ registration time) | Study and country |
|---|---|---|---|---|---|---|
| Having physical activity exceeding 5 time a week increased risk of COVID-19 infection (adjusted OR: 2.05, 95% CI: 1.39-3.02) | COVID-19 diagnosis | Questionnaire | Physical activity (frequency per week in latest 2 months) | 105 COVID-19 infected participants (Median age: 55.0 y, IQR: 45.5-66.5) and 210 healthy individuals (Median age: 54.0 y, IQR, 45.0-68.0) | Case-control study/ February 10-March 1, 2020 | Gao et al. [19] (2020) Wuhan, China |
| Regular sports participation significantly reduced severe outcomes (OR: 0.67, 95% CI: 0.46-0.99) | Hospitalization or death (severe outcome) | Membership in the Sports Medicine Insurance system of Tehran province | Regular sports participation | 4,694 (mean age: 42.31 ± 11 years) COVID-19 infected participant | Cross sectional/ February 20-April 20, 2020 | Halabchi et al. [8] (2020) Iran |
| COVID-19 infection risk was augmented in physical inactivity (Adjusted RR: 1.32, 95% CI: 1.10-1.58) | COVID- 19 diagnosis | Questionnaire (IPAQ short version | Physical inactivity | 387,109 (mean age: 56.2 ± 8 y) including 760 COVID-19 infected participants | Prospective cohort/March 16-April 26, 2020 | Hamer et al. [20] (2020) UK |
| Low physical activity increased COVID-19 mortality compared to high physical activity (OR:1.41, 95% CI: 1.09-1.83) | Mortality | Questionnaire (IPAQ short version) | Physical activity | 259 397 participants | Prospective cohort study/16 March 2020-27 February, 2021 | Hamrouni et al. [21] (2021) UK |
| Sedentary lifestyle increases likelihood of COVID-19 infection (OR: 36.05, 95% CI: 3.44-377.44). Low physical activity increases duration of hospital stay(OR: 6.67, 95% CI: 1.61-27.61 | Risk of infection/ Length of hospital stay | Questionnaire (IPAQ short version) | Physical activity based on MET. Minutes/w | 431(228 healthy, 203 COVID-19 infected participants) | Retrospective cohort | Huang et al. [22] (2020) China |
| Engaging in moderate physical activity more than 150 minutes weekly reduces the risk of hospitalization (RR: 0.24, 95% CI: 0.05-1.04) | Hospitalization | Questionnaire (IPAQ short version | Moderate physical activity | ≤ 420 COVID-19 infected participants (Median age: 33 (20-54)) | Cross-sectional | Latorre-Román et al. [23] (2021) Spain |
| Engaging in sufficient physical activity (500-<1000 MET min/week) reduced probability of COVID-19 incidence (aRR: 0.78; 95% CI: 0.66- 0.92), probability of severe infection (aRR: 0.62; 95% CI 0.43-0.90) and mortality (aRR: 0.17; 95% CI: 0.07-0.98) compared to inactivity | Risk of infection, severity, and mortality | Interview based questionnaire | Physical activity | 2295 infected participants | Cross-sectional/ January 1 2020-July 31 2020 | Lee et al. [24] (2021) South Korea |

**Tab. I.** *Continues.*

| Results | Outcome | PA assessment tool | Exercise, physical activity, sedentary behavior, etc. | Participants | Study design (type/ registration time) | Study and country |
|---|---|---|---|---|---|---|
| Lower risk of COVID-19 infection with severe respiratory manifestation was detected with each standard deviation increase in physical activity estimated genetically (OR: 0.19, 95% CI: 0.05-0.74). However, no correlation was demonstrated with hospitalization due to COVID-19 | Severe respiratory COVID-19, COVID-19 hospitalization | Accelerometer-measured PA | Physical activity | Data from 2 genome-wide association studies (GWAS) including 9464 hospitalized patients with COVID-19 and 1,297,281 healthy controls | Cross-sectional (Mendelian randomization study) | Li et al. [25] (2021) UK |
| Inactive individuals were more likely to be hospitalized due to COVID-19 (adjusted OR: 1.25, 95% CI: 1.03-1.51) | Hospitalization | Exercise Vital Sign (EVS), (self-reported PA) | Physical inactivity for those self-reporting < 10 min of exercise/week | 5712 COVID-19 infected participants (mean age: 44.81 ± 5.7) | Retrospective cohort study/ March 3-October 29, 2020 | Lobelo et al. [26] (2021) United States |
| Weekly exercise reduced risk of incidence of SARS-CoV-2 infection's symptoms (OR: 0.57, 95% CI: 0.47-0.70) | SARS-CoV-2 infection incidence | Mobile application | Physical activity | 14,335 participants | Prospective cohort study/March 26-May 3, 2020 | Marcus et al. [27] (2021) United States and 93 countries outside the US |
| Physical activity reduced COVID-19-like Symptoms' likelihood (OR: 0.69; p < 0.001) | COVID-19-like Symptoms | Questionnaire (IPAQ short version) | Physical activity | 3947 outpatients (mean age: 44.4 ± 17.0 y) | Cross sectional study/14 February to 2 March 2020 | Nguyen et al. [28] (2021) Vietnam |
| Increased prevalence of inadequate physical activity augmented the probability of COVID-19 mortality [Beta (SE): 0.08 (0.0333), p = 0.0127] | Mortality | WHO Global Health Observatory Repository | Insufficient physical activity (not meeting the WHO physical activity recommendations) | Publicly available core health data for 53 sub-Saharan African countries | Cross sectional | Okeahalam et al. [29] (2020) sub-Saharan Africa |
| No associations between total physical activity and duration of hospital stay due to COVID-19 infection (β = 0.20, 95% CI: -0.48-0.87, p = 0.563), mortality (OR: 0.7, 95% CI: 0.4-1.3, p = 0.272), ICU admission (OR: 0.9, 95% CI: 0.7-1.2, p = 0.459), and need to mechanical ventilation (OR: 0.8, 95% CI: 0.5-1.2, p = 0.214) were detected | Length of hospital stay, mortality, ICU admission, need to mechanical ventilation | Baecke Questionnaire of Habitual Physical Activity | Physical activity | 209 hospitalized patients with severe COVID-19 (mean age: 54.9 ± 14.5 y) | Prospective cohort/June 2-October 7, 2020 | Pinto et al. [30] (2020) Brazil |
| Recreational physical activity has an inverse association with mortality rate per 100,000 individuals (r: -0.43, p = 0.02), disease lethality (r: -0.51, P = 0.01), and the accumulated deaths (r: -0.44, p = 0.03) | Accumulated deaths, disease lethality and mortality rate | Data through the Risk Factor Surveillance System for chronic non-communicable diseases (VIGITEL 2019) | Leisure time physical activity (LTPA) | 26 Brazilian capitals and the Federal District | Cross-sectional/ January 22, 2021 | Pitanga et al. [31] (2021) Brazil |

**Tab. I.** *Continues.*

| Results | Outcome | PA assessment tool | Exercise, physical activity, sedentary behavior, etc. | Participants | Study design (type/ registration time) | Study and country |
|---|---|---|---|---|---|---|
| No associations between moderate to high physical activity or total physical activity level with the COVID-19 infection or severe manifestation of COVID-19 were demonstrated. Increased waking time physical activity reduces the risk (OR, 0.75, 95% CI: 0.61-0.93) | SARS-CoV-2 positivity and COVID-19 severity. | Accelerometer data from Biobank | Physical activity | 207 COVID-19 infected participants (including 124 patients with severe infection) | Cross-sectional/ March 16-July 19, 2020 | Rowlands et al. [32] (2020) UK |
| Sedentary lifestyle enhances the mortality due to COVID-19 infection. (Adjusted hazard ratio: 5.91, 95%CI: 1.80-19.41) | Mortality | Rapid Assessment of Physical Activity Scale questionnaire | Baseline physical activity level (BPAL) | 520 patients hospitalized COVID-19 infected participants (mean age: 54.6, range: 42.9-64.6) | Retrospective cohort Study/ February 15-April 15, 2020 | Salgado-Aranda et al. 33 (2021) Spain |
| Inactive individuals with COVID-19 have higher risk of hospitalization (OR 2.26; 95% CI: 1.81, 2.83), ICU admission (OR = 1.73; 95% CI: 1.18, 2.55) and mortality (OR 2.49; 95% CI: 1.33, 4.67) | Hospitalization, ICU admission and mortality | Exercise Vital Sign (EVS), (self-reported PA) | Physical inactivity | 48440 COVID-19 infected participants (median age: 47) | Retrospective observational study/January 1-October 21, 2020 | Sallis et al. [7] (2021) United States |
| Moderate to vigorous physical activity reduces the COVID-19 severe manifestations (OR: 0.28, p = 0.05) | Severe COVID-19 disease | GPAQ | Physical activity | 206 COVID-19 infected participants (mean age: 40.9 ± 11.6 y) | Cross-sectional/ March 20-April 24 | Tavakol et al. [9] (2020) Iran |
| COVID-19 mortality indicated positive correlations with insufficient physical activity ($R^2$:0.04, p = 0.007) | Mortality | 2015/2016 WHO handbooks | Insufficient physical activity | Data from 2015/2016 WHO handbooks | Cross sectional study/August 20, 2020 | Wang et al. [34] (2021) 186 countries from Africa (55), Asia/Oceania (45), Europe (45), North/Central America (28), and South America (13) |
| No associations between insufficient aerobic activity and hospitalization rate (Crude OR 1.06; CI 95%: 0.48, 2.34) | Hospitalization | Periodic Health Assessment Questionnaire | Physical activity | 93 hospitalized and 372 ambulatory COVID-19 military personnel (median age = 26) | Case-control study/between March 5, 2020, and March 10, 2021 | Webber et al. [35] (2021) United States |
| Increased physical activity level (based on accelerometer) reduces the risk of COVID-19 overall infection and outpatients [36]. However, no association have been demonstrated between physical activity (based on accelerometer) and inpatients or MVPA (based on touch screen questionnaire) and COVID-19 consequences | Overall COVID-19, inpatients and outpatients | Self-reported moderate-to-vigorous PA (MVPA) and acceleration vector magnitude PA (AMPA) | Physical activity | 7187 inpatients and 2307 out patients (mean age: 68.8 ± 9.2 y) | Cross-sectional (Mendelian randomization study)/March 16-June 29,2020 | Zhang et al. [36] (2020) UK |

Halabchi et al. proposed that hospitalization was 1.49 times less probable among athletes participating in regular sports [8]. Physical inactivity was proposed as a major risk factor for hospitalization due to COVID-19 in Sallis et al. and Lobelo et al. studies [7, 26]. Webber et al. did not show an association of between insufficient aerobic physical activity and COVID-19 hospitalization rate among military personnel [35].

Overall, most studies demonstrated the significant impact of physical activity in reducing hospitalization due to COVID-19. The results of a meta-analysis on seven studies evaluating the association of physical activity and COVID-19 hospitalization showed weighted OR= 0.541 (CI 95%: 0.49-0.6) with heterogeneity ($I^2$ = 81.7%, P < 0.001) (Fig. 2).

## Physical activity and COVID-19 related mortality

Eleven studies evaluated the association of physical activity with mortality in patients with COVID-19. Questionnaires [13, 16, 21, 24, 30, 33], exercise vital signs [7], website databank [17], Global Health Observatory Data Repository [29], and surveillance systems [31, 34] were applied to assess the physical activity status. Cho et al. proposed that the higher physical activity level was associated with lower mortality risk due to COVID-19 [16]. Physical inactivity and sedentary behaviour increased mortality risk in COVID-19 patients [7, 29, 33]. In Cunningham's study, country-level physical activity had a negative correlation with COVID-19 mortality [17] and in Pinto et al. study no associations were detected between work-related physical activity, leisure-time physical activity, sport index, and total activity with mortality [30]. Leisure-time physical activity reduced COVID-19 mortality risk [31]. Ahmadi et al. and Lee et al. indicated decreased mortality among physically active individuals [13, 24]. Hamrouni et al. and Wang et al. demonstrated that low and insufficient physical activity increased COVID-19 mortality [21, 34]. Overall, most studies indicated that sufficient physical activity reduces COVID-19 mortality. The results of a meta-analysis on five studies assessing the association of physical activity and COVID-19 mortality showed a weighted OR of 0.61 (CI 95%: 0.50-0.75) with heterogeneity ($I^2$ = 45.8%, P < 0.001) (Fig. 3).

### Physical activity and COVID-19 recovery, hospital stay, and severity

Seven studies evaluated the association of physical activity with COVID-19 recovery, hospital stay, and severity. Alataibi and Boukelia indicated that engaging in regular physical activity leads to 2.7 times faster recovery [14]. Huang et al. suggested that low physical activity increases the duration of hospital stay compared to high-intensity physical activity based on METs [22]. In another study by Pinto et al., no associations were detected between physical activity indexes with the duration of hospital stay, ICU admission, and the necessity of mechanical ventilation [30]. Li et al. indicated that with each standard deviation increase in physical activity estimated genetically, a lower risk of severe respiratory manifestation in COVID-19 patients was detected [25]. Rowlands et al. proposed that no associations exist between total or moderate to high physical activity and COVID-19 infection with severe manifestation [32]. However, increased daytime physical activity reduced the risk [32]. Tavakol et al. suggested that moderate to vigorous physical activity decreases the probability of severe COVID-19 infection and similar findings was detected in Lee et al. study in individuals engaging in aerobics and strengthening exercises [9, 24].

### Quality assessment

Results for the quality assessment of the studies applying Joanna Briggs Institute (JBI) critical appraisal checklist are illustrated in Supplementary Table II (The tools are illustrated in Supplementary Table I) [12].

Results for quality assessment of the studies applying Joanna Briggs Institute (JBI) critical appraisal checklist for cross sectional studies in Q1 were no in Boukelia and Alataibi (2020), Cunningham (2021), Li et al. (2021), Okeahalam et al. (2020), Pitanga et al. (2021), and Wang et al. (2020) studies. The results of question 2 was no in Pitanga et al. (2021) and Latorre-Román et al. (2021) studies. The results of question 3 was no in Bielik et al. (2021), Latorre-Román et al. (2021), and Wang et al. (2020) studies and unclear in Okeahalam et al. (2020) and Pitanga et al. (2021) studies. The no answer for question 4 was in Okeahalam et al. (2020) and Pitanga et al. (2021) studies, for question 5 in Bielik et al. (2021) and for question 7 in Bielik et al. (2021), Boukelia and Alataibi (2020), Cunningham (2021), de Souza et al. (2021), Latorre-Román et al. (2021), and Sallis et al. (2021) studies. The answers to other questions were yes (Supplementary Table II).

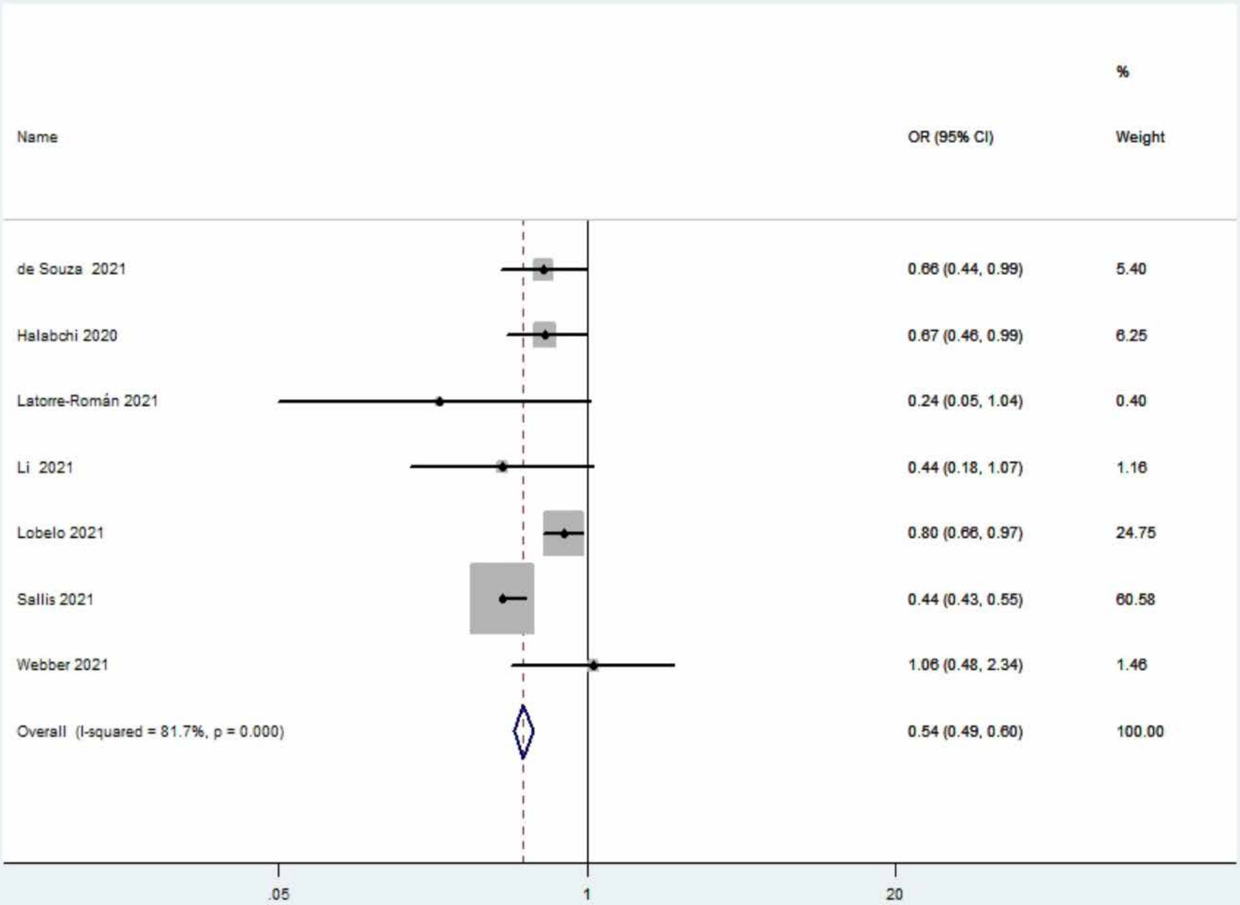
In the cohort studied the negative answer in question 1 was in Hamer et al. (2020), and Lobelo et al. (2021) and Marcus et al. (2021) studies and in question 2 was in Pinto et al. (2020) and Lobelo et al. (2021) studies. Question 8 and 10 was unclear in all cohort studies. In case-control studies, results of question 8 was no in all studies and in question 9 unclear in all studies (Supplementary Table II).

## Discussion

A high proportion of studies indicated that engaging in physical activity might reduce the risk of COVID-19 infection, hospitalization, and mortality due to COVID-19. The results of the meta-analysis regarding the association of physical activity and COVID-19 hospitalization and mortality showed statistically meaningful differences in favour of physically active patients.

In a systematic review by Song et al., the association between physical activity and influenza/pneumonia was evaluated [37]. The overall conclusion of the studies indicated that engaging in regular exercise might be a protective factor against influenza-related infection in

**Fig. 2.** Forest plot of the association between physical activity and COVID-19 hospitalization.




older populations [37]. Simultaneously, the benefits of engaging in Asian martial arts on the immunological state of the older individuals were suggested [37].

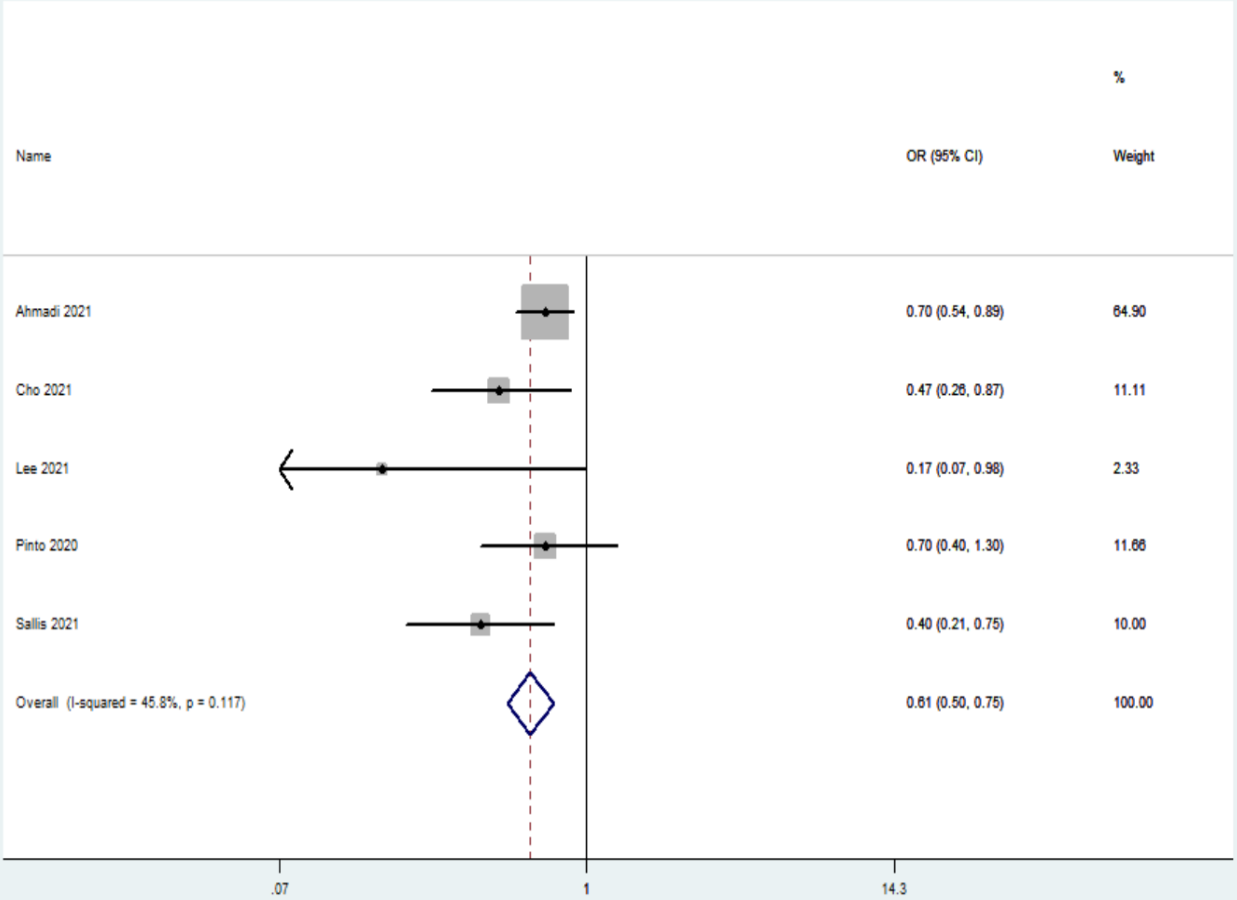
It has been proposed that engaging in regular exercise programs might be a protective factor against the risk of viral infection, duration, and clinical outcome of the viral diseases [38]. Higher level of habitual physical activity reduces the risk of community-acquired infectious disease by about 31% and reduces the risk of infectious disease mortality by about 37% [39].

Engaging in moderate- to vigorous-intensity exercise programs regularly improve the respiratory system's function and a 20-30 percent reduction in upper respiratory infections is detected [6]. In a study by Nienman et al., physical fitness level and number of aerobic exercise sessions during the week were inversely correlated to the duration and severity of upper respiratory tract infection [40]. Individuals exercising ≥ 5 days/week indicated a 43% reduction in upper respiratory tract infection duration compared to sedentary individuals [40]. Individuals exercising ≥ 5 days/week indicated about a 43% reduction in duration of upper respiratory tract infection compared to sedentary individuals [40]. Physical fitness can also reduce COVID-19 related risk factors including hypertension, diabetes, cardiovascular diseases.[41].

Engaging in moderate intensity exercise regularly, balances immunity function in inflammatory related disease including type 2 diabetes, obesity, and cardiovascular diseases, and stabilizes hallmarks of immunosenescence [42]. Simultaneously, the positive effect of exercise on the function of different leukocyte subtypes and the arrangement of the T cell compartment havehas been shown leading to improved adaptive immunity [42]. Moderate intensity exercise shifts immunity responses towards a T-helper type 1 pattern and decreases the probability of infection [43]. In a study by Terra et al., 12 weeks of exercise in mice led to increased interferon-gamma (IFN-γ) and TNF-α levels and a reduction in IL-4 and IL-10 levels. Based on the results of the systematic review by Chastin et al., physical activity-increasing interventions increase CD4 cell counts and salivary immunoglobulin A concentration and reduce neutrophil counts [39].

Among individuals infected with COVID-19, the severe clinical presentation of the disease in some patients appears approximately 7 to 10 days after the onset. This delayed manifestation of COVID-19 is a consequence of the over-activity of the immune system "cytokine storm syndrome" aiming lungs [4]. The anti-inflammatory effect of exercise is a consequence of increased mediators including IL-1 receptor antagonist, IL-10, and IL-6 [44].

**Fig. 3.** Forest plot of the association between physical activity and COVID-19 mortality.




During exercise, skeletal muscles produce and release IL-6, which is one of the leading determinants of exercise's anti-inflammatory mechanism [45]. Another suggested anti-inflammatory effect of exercise is the reduction of Toll-like receptor 4 (TLR4) expression on the monocytes following aerobic training and resistance exercises specifically in individuals with diabetes and obesity [4].

One of the causes of COVID-19 related mortality is coagulopathy. COVID-19 leads to a cascade of pro-inflammatory cytokines, which damages the hematological system. The cytokine storm leads to an increased risk of coagulation and endothelial dysfunction. This cascade results in the enhanced probability of thrombosis in veins and arteries. Physical inactivity is one of the leading risk factors of coagulopathy, which exacerbatesa leading risk factor of coagulopathy, exacerbating the COVID-19 patients' condition [46].

Considering the protective role of physical activity against COVID-19, policymakers and governments should develop adapted action plans according to different countries' COVID-19 situation to increase physical activity during the COVID-19 pandemic [10]. Improved levels of physical activity could lead to lower COVID-19 hospitalization and the financial burden on the health system will be reduced.

### Limitations

Studies evaluating the associations between physical activity and COVID-19 are limited and heterogeneous**.** Further high-quality studies in this domain is mandated to make more definite conclusions.

## Conclusion

Engaging in regular physical activity may reduce the incidence of COVID-19 infection and severe outcomes including COVID-19 related hospitalization and death. Developing action plans to increase physical activity could be an appropriate preventive strategy.

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## Informed consent statement

Not applicable

## Conflict of interest statement

Authors state no conflict of interests.

## Authors' contributions

FH: Conceptualization, methodology, investigation (quality assessment), revise the first draft, critical review of the final draft. BM: Design the study, investigation (data collection and extraction), critical review of the final draft. BT: Investigation (data collection and extraction), critical review of the final draft. MS: Writing original draft, Investigation (data collection and extraction), review & editing, critical review of the final draft. SSh: Formal analysis, critical review of the final draft.

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## Supplementary Tables

**Supplementary Table I. Joanna** Briggs Institute (JBI) critical appraisal checklist for cross sectional, cohort, and case control studies.

| **Joanna Briggs Institute (JBI) critical appraisal checklist for cross sectional studies** | Yes | No | Unclear | Not applicable |
|---|---|---|---|---|
| 1. Were the criteria for inclusion in the sample clearly defined? | ▢ | ▢ | ▢ | ▢ |
| 2. Were the study subjects and the setting described in detail? | ▢ | ▢ | ▢ | ▢ |
| 3. Was the exposure measured in a valid and reliable way? | ▢ | ▢ | ▢ | ▢ |
| 4. Were objective, standard criteria used for measurement of the condition? | ▢ | ▢ | ▢ | ▢ |
| 5. Were confounding factors identified? | ▢ | ▢ | ▢ | ▢ |
| 6. Were strategies to deal with confounding factors stated? | ▢ | ▢ | ▢ | ▢ |
| 7. Were the outcomes measured in a valid and reliable way? | ▢ | ▢ | ▢ | ▢ |
| 8. Was appropriate statistical analysis used? | ▢ | ▢ | ▢ | ▢ |
| **Joanna Briggs Institute (JBI) critical appraisal checklist for cohort studies** | Yes | No | Unclear | Not applicable |
| 1. Were the two groups similar and recruited from the same population? | ▢ | ▢ | ▢ | ▢ |
| 2. Were the exposures measured similarly to assign people to both exposed and unexposed groups? | ▢ | ▢ | ▢ | ▢ |
| 3. Was the exposure measured in a valid and reliable way? | ▢ | ▢ | ▢ | ▢ |
| 4. Were confounding factors identified? | ▢ | ▢ | ▢ | ▢ |
| 5. Were strategies to deal with confounding factors stated? | ▢ | ▢ | ▢ | ▢ |
| 6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? | ▢ | ▢ | ▢ | ▢ |
| 7. Were the outcomes measured in a valid and reliable way? | ▢ | ▢ | ▢ | ▢ |
| 8. Was the follow up time reported and sufficient to be long enough for outcomes to occur? | ▢ | ▢ | ▢ | ▢ |
| 9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored? | ▢ | ▢ | ▢ | ▢ |
| 10. Were strategies to address incomplete follow up utilized? | ▢ | ▢ | ▢ | ▢ |
| 11. Was appropriate statistical analysis used? | ▢ | ▢ | ▢ | ▢ |
| **Joanna Briggs Institute (JBI) critical appraisal checklist for case control studies** | Yes | No | Unclear | Not applicable |
| 1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls? | ▢ | ▢ | ▢ | ▢ |
| 2. Were cases and controls matched appropriately? | ▢ | ▢ | ▢ | ▢ |
| 3. Were the same criteria used for identification of cases and controls? | ▢ | ▢ | ▢ | ▢ |
| 4. Was exposure measured in a standard, valid and reliable way? | ▢ | ▢ | ▢ | ▢ |
| 5. Was exposure measured in the same way for cases and controls? | ▢ | ▢ | ▢ | ▢ |
| 6. Were confounding factors identified? | ▢ | ▢ | ▢ | ▢ |
| 7. Were strategies to deal with confounding factors stated? | ▢ | ▢ | ▢ | ▢ |
| 8. Were outcomes assessed in a standard, valid and reliable way for cases and controls? | ▢ | ▢ | ▢ | ▢ |
| 9. Was the exposure period of interest long enough to be meaningful? | ▢ | ▢ | ▢ | ▢ |
| 10. Was appropriate statistical analysis used? | ▢ | ▢ | ▢ | ▢ |

**Supplementary Table II.** Results of quality assessment of the studies via Joanna Briggs Institute (JBI) critical appraisal checklist for cross sectional, cohort, case control, and case series studies.

| **Cross sectional studies** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Bielik et al. (2021) | Yes | Yes | No | Yes | No | Yes | No | Yes | | | |
| Boukelia & Alataibi (2020) | No | Yes | Yes | Yes | Yes | Yes | No | Yes | | | |
| Cunningham (2021) | No | Yes | Yes | Yes | Yes | Yes | No | Yes | | | |
| de Souza et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | | | |
| Halabchi et al. (2020) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| Latorre-Román et al. (2021) | Yes | No | No | Yes | Yes | Yes | No | Yes | | | |
| Lee et al.(2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| Li et al. (2021) | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| Nguyen et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| Okeahalam et al. (2020) | No | Yes | U | No | Yes | Yes | Yes | Yes | | | |
| Pitanga et al. (2021) | No | No | U | No | Yes | Yes | Yes | Yes | | | |
| Rowlands et al. (2020) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| Sallis et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | | | |
| Tavakol et al. (2020) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| Wang et al. (2020) | No | Yes | No | Yes | Yes | Yes | Yes | yes | | | |
| Zhang et al. (2020) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | | | |
| **Cohort studies** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** | **Q9** | **Q10** | **Q11** |
| Ahmadi et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | U* | Yes | U | Yes |
| Hamer et al. (2020) | No | Yes | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| Hamrouni et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| Huang et al. (2020) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| Lobelo et al. (2021) | No | No | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| Marcus et al. (2021) | No | Yes | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| Pinto et al. (2020) | Yes | No | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| Salgado-Aranda et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | U | Yes | U | Yes |
| **Case control studies** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** | **Q9** | **Q10** | |
| Cho et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | U | Yes | |
| Gao et al. (2020) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | U | Yes | |
| Webber et al. (2021) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | U | Yes | |

* U: unclear.