Brief Summary of Findings on the Association Between Physical Inactivity and Severe COVID-19 Outcomes

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Brief Summary of Findings on the Association Between Physical Inactivity and Severe COVID-19 Outcomes

Twenty-five studies, 15 cohort, 5 cross-sectional, 4 ecological and one case-control, reported data on physical inactivity or physical activity and severe COVID-19 outcomes and were included in this analysis. Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure. Physical inactivity is defined as the lack of physical activity. Both may vary, depending on the context.

- The data indicate an association between increased mortality[1-12] and hospitalization[8,13-18] due to COVID1-19 infection and physical inactivity, and a possible association between increased ventilation[1,6,9] due to COVID1-19 infection and physical inactivity. Limited data is insufficient on the association between physical inactivity and ICU admission[6,9]. Limited data from only one study is insufficient to determine if there is an association between physical inactivity and intubation[17]. The data suggest an increased risk of mortality[19-22] and hospitalization[15,17,18,22-25] due to COVID1-19 infection with decreased duration or frequency of physical activity.

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A. Methods

The aim of this review is to identify and synthesize the best available evidence on the association between underlying disabilities and severe COVID-19 to update the Centers for Disease Control and Prevention (CDC) website on underlying conditions and add to the provider-specific website.
The methods for all underlying conditions and risk factors are outlined in the webpage, https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/systematic-review-process.html. These methods were established in May 2021 and are standard for all conditions and risk factors on the CDC COVID-19 response underlying medical conditions page.

Below are methodologic highlights and additional methods unique to this review. For more information, please visit https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/systematic-review-process.html

A.1. Literature Search

A list of search terms was developed to identify the literature most relevant to the population, exposure, comparator, outcomes (PECO) question. Subject matter experts and library scientists were consulted to develop a robust list of search terms. These terms were then incorporated into search strategies, and these searches were performed in OVID using the COVID-19 filter for all articles from the beginning of each data base until August 26, 2021. The publications span before and after the availability of vaccines. Vaccination was not a criteria for selection. The detailed search strategies for identifying primary literature and the search results are provided in Part B. References were included if retrieved by the literature search and reported exposures and outcomes relevant to this review.

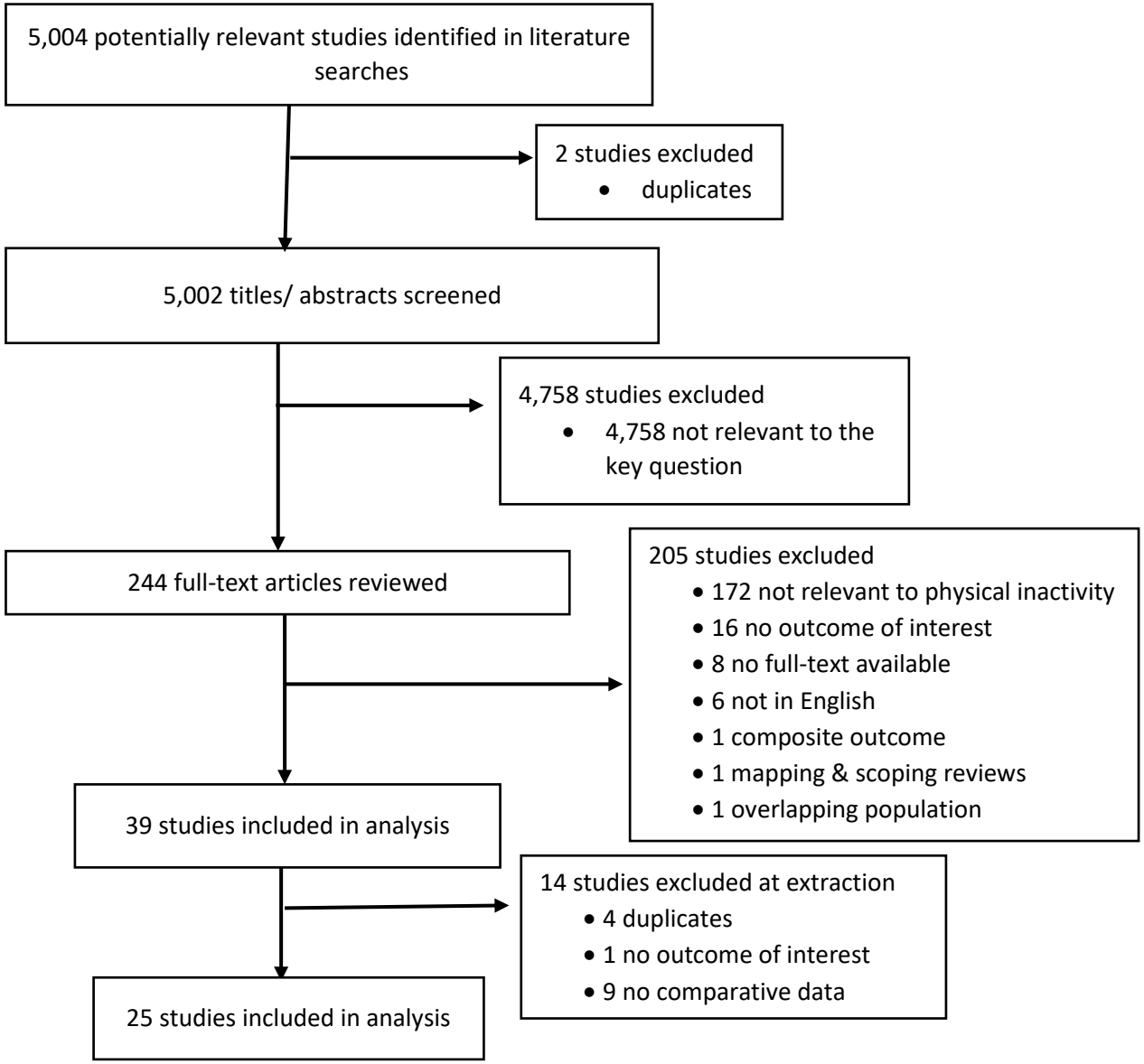
A.2. Study Selection

Titles and abstracts from references were screened by dual review (A.H., M.M., D.O.S., E.C.S, C.N.S., M.W., M.C., T.R. or J.K.). Full-text articles were retrieved if they were:

1. relevant to the PECO question;
2. primary research; and
3. written in English.

Part B presents the full list of exclusion criteria. The full texts of selected articles were then screened by two independent reviewers, and disagreements were resolved by discussion (A.H., M.M., D.O.S., E.C.S, C.N.S., M.W., M.C., T.R. or J.K.). The results of the study selection process are depicted in Figure 1.

Figure 1. Results of the Study Selection Process



A.4. Data Extraction and Synthesis

Methodologic data and results of relevant outcomes from the studies meeting inclusion criteria were extracted into standardized evidence tables. Data and analyses were extracted as presented in the studies. For the purposes of this review, statistical significance was defined as $p \leq 0.05$. Wide confidence intervals were defined as upper tertiles that exceeded the average median of all confidence intervals reported. Small sample sizes were defined as sample sizes that were less than the average sample size from all studies included.

A.5. Internal Validity Assessment

The internal validity associated with each study was assessed using scales developed by the Division of Healthcare Quality Promotion and scores were recorded in the evidence tables. Part B includes the questions used to assess the quality of each study design. The strength, magnitude, precision, consistency, and applicability of results were assessed for all comparators. The overall confidence in the evidence base is reported in the aggregation tables in the Part B. The denominators used in the aggregation tables are of people diagnosed with COVID-19. If the number was not given, the denominator was listed as "not reported" (NR).

A.6. Reviewing and Finalizing the Systematic Review

Draft findings, aggregation tables, and evidence tables were reported to a CDC subject matter for review and input.

B. Systematic Literature Review Results

B.1. Search Strategies and Results

Table 1 Physical Inactivity / Activity Search Conducted August 26, 2021.

Database	**Strategy**	**Records** 08/26/2021
Medline (OVID) 1946-	Physical activit* OR Physically active OR (Physical* ADJ3 inactiv*) OR sedentary OR immobil* OR (sitting ADJ3 time) OR (sitting ADJ3 behavior*) OR (activity ADJ3 level) OR (activity ADJ3 behavior) OR (daily ADJ3 activit*) OR (routine* ADJ3 activit*) OR (leisure* ADJ3 activit*) OR recreation* OR leisure-time OR (household ADJ3 activit*) OR (activ* ADJ3 lifestyle*) AND Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR intensive care OR oxygen OR respirat* OR vaccin* OR immun* OR titer* Limit COVID-19 (validated filter)	1897
Embase (OVID) 1988-	Physical activit* OR Physically active OR (Physical* ADJ3 inactiv*) OR sedentary OR immobil* OR (sitting ADJ3 time) OR (sitting ADJ3 behavior*) OR (activity ADJ3 level) OR (activity ADJ3 behavior) OR (daily ADJ3 activit*) OR (routine* ADJ3 activit*) OR (leisure* ADJ3 activit*) OR recreation* OR leisure-time OR (household ADJ3 activit*) OR (activ* ADJ3 lifestyle*) AND Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR intensive care OR oxygen OR respirat* OR vaccin* OR immun* OR titer* Limit COVID-19 (validated filter)	2722 -1188 duplicates =1534 unique items

Global Health (OVID)	(novel coronavir* OR novel corona virus* OR 2019 coronavirus OR coronavirus disease OR coronavirus 2019 OR betacoronavir* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR sars-cov OR sarscov OR 2019nCoV OR 2019-nCoV OR wuhan virus*) AND Physical activit* OR Physically active OR (Physical* ADJ3 inactiv*) OR sedentary OR immobil* OR (sitting ADJ3 time) OR (sitting ADJ3 behavior*) OR (activity ADJ3 level) OR (activity ADJ3 behavior) OR (daily ADJ3 activit*) OR (routine* ADJ3 activit*) OR (leisure* ADJ3 activit*) OR recreation* OR leisure-time OR (household ADJ3 activit*) OR (activ* ADJ3 lifestyle*) AND Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR intensive care OR oxygen OR respirat* OR vaccin* OR immun* OR titer*	854 -477 duplicates =377 unique items
CAB Abstracts (OVID)	(novel coronavir* OR novel corona virus* OR 2019 coronavirus OR coronavirus disease OR coronavirus 2019 OR betacoronavir* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR sars-cov OR sarscov OR 2019nCoV OR 2019-nCoV OR wuhan virus*) AND Physical activit* OR Physically active OR (Physical* ADJ3 inactiv*) OR sedentary OR immobil* OR (sitting ADJ3 time) OR (sitting ADJ3 behavior*) OR (activity ADJ3 level) OR (activity ADJ3 behavior) OR (daily ADJ3 activit*) OR (routine* ADJ3 activit*) OR (leisure* ADJ3 activit*) OR recreation* OR leisure-time OR (household ADJ3 activit*) OR (activ* ADJ3 lifestyle*) AND Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR intensive care OR oxygen OR respirat* OR vaccin* OR immun* OR titer*	473 -472 duplicates =1 unique items
PsycInfo (OVID) 1987-	(novel coronavir* OR novel corona virus* OR 2019 coronavirus OR coronavirus disease OR coronavirus 2019 OR betacoronavir* OR covid19 OR covid 19 OR nCoV OR novel CoV OR CoV 2 OR CoV2 OR sarscov2 OR sars-cov OR sarscov OR 2019nCoV OR 2019-nCoV OR wuhan virus*) AND	179 -135 duplicates =44

	Physical activit* OR Physically active OR (Physical* ADJ3 inactiv*) OR sedentary OR immobil* OR (sitting ADJ3 time) OR (sitting ADJ3 behavior*) OR (activity ADJ3 level) OR (activity ADJ3 behavior) OR (daily ADJ3 activit*) OR (routine* ADJ3 activit*) OR (leisure* ADJ3 activit*) OR recreation* OR leisure-time OR (household ADJ3 activit*) OR (activ* ADJ3 lifestyle*) AND Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR intensive care OR oxygen OR respirat* OR vaccin* OR immun* OR titer*	unique items
CINAHL (EbscoHost)	(“novel coronavir*” OR “novel corona virus*” OR “2019 coronavirus” OR betacoronavir* OR covid19 OR “covid 19” OR nCoV OR “novel CoV” OR “CoV 2” OR CoV2 OR sarscov2 OR sars-cov OR sarscov OR 2019nCoV OR 2019-nCoV OR “wuhan virus*”) AND ("Physical activit*" OR "Physically active" OR (Physical* N3 inactiv*) OR sedentary OR immobil* OR (sitting N3 time) OR (sitting N3 behavior*) OR (activity N3 level) OR (activity N3 behavior) OR (daily N3 activit*) OR (routine* N3 activit*) OR (leisure* N3 activit*) OR recreation* OR leisure-time OR (household N3 activit*) OR (activ* N3 lifestyle*)) AND (Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR "intensive care" OR oxygen OR respirat* OR vaccin* OR immun* OR titer*)	534 -380 duplicates =154 unique items
Academic Search Complete	(“novel coronavir*” OR “novel corona virus*” OR “2019 coronavirus” OR betacoronavir* OR covid19 OR “covid 19” OR nCoV OR “novel CoV” OR “CoV 2” OR CoV2 OR sarscov2 OR sars-cov OR sarscov OR 2019nCoV OR 2019-nCoV OR “wuhan virus*”) AND ("Physical activit*" OR "Physically active" OR (Physical* N3 inactiv*) OR sedentary OR immobil* OR (sitting N3 time) OR (sitting N3 behavior*) OR (activity N3 level) OR (activity N3 behavior) OR (daily N3 activit*) OR (routine* N3 activit*) OR (leisure* N3 activit*) OR recreation* OR leisure-time OR (household N3 activit*) OR (activ* N3 lifestyle*))	1093 -734 duplicates =359 unique items

	AND (Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR "intensive care" OR oxygen OR respirat* OR vaccin* OR immun* OR titer*)	
Scopus	TITLE-ABS-KEY(“novel coronavir*” OR “novel corona virus*” OR “2019 coronavirus” OR betacoronavir* OR covid19 OR "covid 19" OR ncov OR "CoV 2" OR cov2 OR sarscov2 OR sars-cov OR sarscov OR 2019ncov OR 2019-nCoV OR "novel CoV" OR "wuhan virus") AND TITLE-ABS-KEY("Physical activit*" OR "Physically active" OR (Physical* W/3 inactiv*) OR sedentary OR immobil* OR (sitting W/3 time) OR (sitting W/3 behavior*) OR (activity W/3 level) OR (activity W/3 behavior) OR (daily W/3 activit*) OR (routine* W/3 activit*) OR (leisure* W/3 activit*) OR recreation* OR leisure-time OR (household W/3 activit*) OR (activ* W/3 lifestyle*)) AND TITLE-ABS-KEY(Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR "intensive care" OR oxygen OR respirat* OR vaccin* OR immun* OR titer*) AND NOT INDEX(medline)	1227 -950 duplicates =277 unique items
WHO Global COVID Literature Database	"physical activity" OR "physically active" OR "physical inactivity" OR sedentary OR "active lifestyle" OR "routine activity" OR immobility OR (sitting AND time) OR (sitting AND behavior) OR "level of activity" OR (activity AND behavior*) OR "daily activity" OR "leisure activity" OR recreation* OR leisure-time OR "household activity" OR "household activities" AND (Severe* OR severity OR moderate OR outcome* OR hospital* OR symptom* OR ventilat* OR intubat* OR mortality OR morbidit* OR death* OR fatalit* OR risk* OR ICU* OR "intensive care" OR oxygen OR respirat* OR vaccin* OR immun* OR titer*)	539 -178 duplicates =361 unique items

B.2. Study Inclusion and Exclusion Criteria

Inclusion Criteria: Studies were included at the title and abstract screen if they:

- were relevant to the key (PECO)question “What is the association between physical inactivity and severe COVID-19?”;
    - exposures: physical inactivity, physical activity, activity, inactivity, exercise, sedentary, sedentary behavior, sitting

- outcomes: mortality, ICU admission, intubation (invasive ventilation, ECMO), ventilation (non-invasive ventilation, mechanical ventilation), hospitalization, and re-admission
- were primary research, systematic reviews, meta-analysis, or guidelines based on systematic reviews;
- were written in English (can be seen as [language] in title);
- examined humans only;
- were in a community setting; and
- notably, descriptive data or comparative data where n < 5 with the exposure of interest were included only when comparative data was unavailable for an exposure of interest.

Exclusion Criteria: Studies were excluded at full text review if they:

- were not available as full-text;
- were a conference abstract, poster, or reply letter;
- were mapping and scoping reviews;
- reported autopsy results;
- reported on a population that overlapped with a larger study using the same data set; and
- reported only composite outcome measures for "severe COVID-19".

B.3. Evidence Review: Physical Inactivity and Severe COVID-19

B.3.a. Strength & Direction of Evidence

Table 2 The Association Between Physical Activity / Inactivity and Severe COVID-19 Outcomes.

Outcome	Results
Mortality	The data from 12 studies[1-12] suggests that physical inactivity is associated mortality; physical inactivity is associated with an increase in mortality whereas physical activity is associated with a decrease in mortality, among people with COVID-19. Ten studies were found to have a moderate threat to internal validity, and 2 studies[5,11] had a high threat to internal validity. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity.

Outcome	Results

	• Strength of Association: Five studies reported measures of association. Four reported physical activity adjusted measures of 0.70 – 0.97, and one reported a physical inactivity adjusted measure of 5.91.
	• Precision of Association: Five studies reported confidence intervals: 1 reported physical inactivity[6] and 4 reported physical activity[7-10]. Confidence intervals for the 4 studies reporting physical activity spanned the null.
	• Consistency of Association: Results were consistent.
	• Applicability of Association: Settings were applicable across studies. Six studies[1,6-8,11,12] were conducted in high income countries (HIC), 3 studies[3,9,10] were conducted in low- and middle-income countries (LMIC), and 3 studies[2,4,5] were conducted across resource settings.
	
	Summary of Evidence:
	• Twelve studies[1-12] (N = 4,690,953) reported data suggesting an association between physical activity or physical inactivity and mortality among people with COVID-19.
	  • Seven studies reported the measure of physical inactivity.
	  • Two cohort studies[1,6] (N = 684), 2 cross-sectional studies[2,3] (N = 4,670,832), and 3 ecological studies [4,5,12] (N = 517 countries, countries may overlap) reported measures of association, correlation measures, or proportions suggesting a possible association between physical inactivity and increased mortality among people with COVID-19 [aHR: 5.91 (95% CI: 1.80 – 19.41), p < 0.01][6].
	  ○ Study limitations include wide confidence intervals[6], small sample sizes[1,6], low number of deaths[1,6], insufficient follow up[1], and heterogeneous measures for physical activity[12]. The use of multiple datasets resulting in the comparison of heterogeneous exposure and outcome measurements[5]. Perhaps most importantly, sedentary patients, defined as those engaging in light physical activity, from the study[6] reporting the aHR, had a higher median age, more comorbidities, and were more commonly physically dependent.
	  • Five studies reported the measure of physical activity.
	  • Three cohort studies[8-10] (N = 17,484) and one ecological study[11] (N = 3,142 counties) reported measures of association or estimates suggesting that physical activity is associated with a decrease in mortality among people with COVID-19. ([aOR: 0.70 (95% CI: 0.40 – 1.30), p = 0.27][9] to [aHR: 0.94 (95% CI: 0.90 – 0.99), p < 0.02][10]; [estimate: -0.72 (SE = 0.27), p<0.01]).
	  ○ Of these studies, one confidence interval was wide and spanned the null[8]. Other limitations include the use data acquired from 2006-2010[8] affecting confidence in the results. Furthermore,

Outcome	Results
	one study[10] reported a small number of deaths and did not report which confounders were used to adjust results. • One cohort study[7] (N = 1,953) reported adjusted measures of association suggesting that physical activity, even when stratified by walking as the primary mode of transport, is not associated with mortality among people with COVID-19 [aHR: 0.97 (95% CI: 0.76 – 1.23), p = 0.79] to [aHR: 1.06 (95% CI: 0.85 – 1.32, p = 0.61)]. ▪ This study[7] had wide confidence intervals that spanned the null and did not report the number of participants that were physically active.
ICU Admission	The data from 2 studies[6,9] is insufficient to determine an association between physical inactivity or activity and ICU admission in patients with COVID-19. Both studies were found to have a moderate threat to internal validity. Self-reported data is considered to introduce reporting bias, however this data is considered normative in the field of physical activity • Strength of Association: One study reported adjusted effect measures ranging from 0.90 – 1.10. • Precision of Association: One study reported wide confidence intervals that crossed the null. • Consistency of Association: The data is inconsistent. • Applicability of Association: One study[6] was conducted in a HIC and 1[9] was conducted in a LMIC. Summary of Evidence: • Two cohort studies[6,9] (N = 520) reported inconsistent results for ICU admission among patients with COVID-19 who reported physical inactivity or activity. ▪ One cohort study[6] (N = 520) of hospitalized COVID-19 patients 18- to 70-years-old in Spain reported a higher proportion of ICU admission in patients with a sedentary lifestyle compared to those with an active lifestyle [8.8% (26/297) vs. 6.3% (14/223), p = 0.29]. Additionally, sedentary patients had a higher median age, more comorbidities, and were more commonly physically dependent. ▪ One study[9] (N = 209) of hospitalized patients with COVID-19 in Brazil suggested that there is no association between total activity and ICU admission [aOR: 0.90 (95% CI: 0.70 – 1.20), p = 0.46]. The effect measures were adjusted for age, sex, BMI, and presence of comorbidities.

Outcome	Results
Intubation	Limited data from only one study[17] is insufficient to suggest an association between physical inactivity and intubation. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • One study[17] (N = 938) reported proportions of intubation among people reporting physical activity with COVID-19. ▪ One cross-sectional study[17] (N = 938) of people who survived COVID-19 in Brazil reported higher, non-significant rates of intubation among people reporting insufficient physical activity compared to those reporting sufficient physical activity [14.3% (6/42) vs. 6.1% (3/49), p = 0.29]. The study stratified analysis by time spent sitting each day and reported no difference in intubation whether participants sat for more or less than 7.4 hours per day [10.5% (2/19) vs. 9.7% (7/72), p = 1.00], or 4.7 hours per day [11.8% (6/51) vs. 7.5% (3/40), p = 0.73]. The study included people who survived or fully recovered from COVID-19 and did not capture the most severe cases. Additionally, the number of intubation events were small, and the proportions were not statistically significant decreasing confidence in these results.
Ventilation	Data from three studies[1,6,9] suggest a possible association between physical inactivity and increased ventilation, or physical activity and decreased ventilation among patients with COVID-19. The three studies[1,6,9] were found to have a moderate threat to internal validity. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • Strength of Association: One study[9] reported adjusted effect measures from 0.60 – 0.90. • Precision of Association: One study[9] reported wide confidence intervals that cross the null. • Consistency of Association: The data is consistent. • Applicability of Association: Two studies[1,6] were conducted in HIC and 1 study[9] was conducted in a LMIC. Summary of Evidence: • Two cohort studies[1,6] (N = 684) reported a non-statistically significant higher proportion of ventilation among those with COVID-19 who reported physical inactivity. ▪ One cohort study[1] (N = 164) of patients with COVID-19 in China reported higher rates of invasive ventilation among patients that were physically inactive compared to patients that were physically active [2.9% (3/103) vs. 0% (0/61), p = NR]. This study had a small sample size and a low number of events.

Outcome	Results
	▪ One cohort study[6] (N = 520) of hospitalized COVID-19 patients 18- to 70-years-old in Spain reported higher rates of invasive ventilation, and a lower rate of non-invasive ventilation in patients with a sedentary lifestyle compared to those with an active lifestyle ([7.7% (23/297) vs. 4.5% (10/223), p = 0.14], and [16.2% (48/297) vs. 22.4% (50/223), p = 0.07]). Sedentary patients had a higher median age, more comorbidities, and were more commonly physically dependent. • One cohort study[9] (N = 209) suggested that physical activity is associated with a decrease in ventilation among patients with COVID-19. ▪ One cohort study[9] (N = 209) of hospitalized patients with COVID-19 in Brazil suggested that physical activity has a protective effect, decreasing the odds of ventilation [aOR: 0.80 (95% CI: 0.50 – 1.20), p = 0.21], and the measure of effect was larger for those with increased work levels. All models were adjusted for age, sex, BMI, and presence of comorbidities. This study reported a small sample size which likely contributed to wide confidence intervals that span the null across analyses.
Hospitalization	Data from 7 studies[8,13-18] (N = 18,124) indicates physical inactivity is associated with an increase and physical activity is associated with a decrease in hospitalization in people with COVID-19. All studies were found to have a moderate threat to internal validity. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • Strength of Association: Seven studies reported measures of association of 0.44 – 0.85 for physical activity and 1.25 – 4.12 for physical inactivity. • Precision of Association: Seven studies reported wide confidence intervals, and 4 confidence intervals included the null. • Consistency of Association: Results were consistent. • Applicability of Association: Settings were applicable across studies. One study[17] was conducted in a LMIC and 6 studies[13-15,18 8,16] were conducted in HIC. Summary of Evidence: • Seven studies[8,13-18] (N = 18,124) reported an increase in hospitalization with physical inactivity among people with COVID-19. • Three studies reported on the measure of physical inactivity.

Outcome	Results
	• Two cohort studies[13,14] (N = 5,712) and 1 cross-sectional study[18] (N = NR) reported adjusted effect measures indicating that physical inactivity is associated with increased hospitalization among people with COVID-19. (aOR: 1.25 (95% CI: 1.03 – 1.51, p ≤ 0.05][14] to [aRR: 4.12 (95% CI: 0.95 - 17.76), p = 0.05][18]) ○ One study reported wide confidence intervals that spanned the null[18]. One study[13] was restricted to white participants and another study[14] was restricted to Kaiser Permanente insurance patients of Georgia who had ready access to healthcare services. • Four studies reported on the measure of physical activity. • Three cohort studies[8,15,16] (N = 11,474) and one cross-sectional study[17] (N = 938) reported effect measures suggesting that physical activity is associated with decreased hospitalization among people with COVID-19. (unadjusted [OR: 0.44 (95% CI: 0.18 – 1.07), p = 0.07] (Li 2021) to [OR: 0.83 (95% CI: 0.68 – 1.00, p = 0.06])[8] and adjusted ([aOR: 0.59 (95% CI: 0.39-0.89), p = 0.01][15] to [aOR: 0.85 (95% CI: 0.69 - 1.05), p < 0.13])[8] ○ All studies reported wide confidence intervals and 3 of these wide confidence intervals span the null[8,16,17]. Furthermore, studies used physical activity data acquired from 2006 to 2010[8], decreasing confidence in the results.

**Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure.*

** Physical inactivity is defined as reporting no physical activity in the given questionnaire Both terms may vary by context of activity.*

Table 3 The Association Between Physical Activity/ Inactivity and Risk Markers and Severe COVID-19 Outcomes.

Outcome	Results

Hospitalization	Limited data from only one study[14] is insufficient to determine an association between physical inactivity, gender, and hospitalization among people with COVID-19. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only one study. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • One study[14] (N = 5,712) reported effect measures suggesting that physical inactivity and female gender are associated with an increase in hospitalization among people with COVID-19. ▪ One cohort study[14] (N = 5,712) reported increased odds of hospitalization in physically inactive female patients compared to physically inactive male patients when adjusting for age, COVID-19 status, and race/ethnicity. ([aOR: 1.45 (95%CI: 1.12 – 1.89), p ≤ 0.05])

Table 4 The Association Between the Duration or Frequency of Physical Activity/ Inactivity and Severe COVID-19 Outcomes.

Outcome	Results
Mortality	Data from 4 studies[19-22] (N =60,905) suggests that the duration of physical inactivity is associated with mortality among people with COVID-19; duration of physical inactivity is associated with increased mortality whereas duration of physical activity is associated with decreased mortality. All studies were found to have a moderate threat to internal validity. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • Strength of Association: Four studies reported adjusted measures of association from 0.28 – 0.90 for physical activity and 1.32 – 2.49 for physical inactivity. • Precision of Association: Four studies reported wide confidence intervals and 3 studies[19-21] included the null. • Consistency of Association: Results were consistent. • Applicability of Association: Four studies[19-22] were conducted in HIC. Summary of Evidence: • Four studies[19-22] (N = 60,905) reported data suggesting that increased mortality is associated with increased duration or frequency of physical inactivity and decreased duration of physical activity in people with COVID-19. • One study reported on the measure of physical inactivity. • One cohort study[22] (N = 48,440) stratified the population by number of minutes of physical inactivity per week and reported the odds of mortality increases as the minutes of physical inactivity per week increases among people with COVID-19. ([aOR: 1.32 (95% CI: 1.09 – 1.60), p = NR] to [aOR: 2.49 (95% CI: 1.33 – 4.67), p = NR])

Outcome	Results
	○ Some confidence intervals were wide, and the study population was limited to managed care organization members, decreasing confidence and generalizability of the results. • Three studies reported on the measure of physical activity. • Two cohort studies[19,21] (N = 6,177) and one case-control[20] (N = 6,288) reported a decrease in the odds of mortality as the minutes of physical activity per week increases when stratifying the population by number of minutes of physical activity per week and among patients with COVID-19. ([aOR: 0.28 (95% CI: 0.06 – 1.20), p = NR][21] to [aRR: 0.90 (95% CI: 0.68 – 1.90), p = NR][19]) ○ Some confidence intervals were wide, included the null, and one study[21] limited the population to those that received COVID-19 testing by medical or Korean Disease Control and Prevention Agency (KDCA) referral.
ICU admission	Limited data from only one study[22] is insufficient to determine an association between the frequency of physical inactivity and ICU admission. The study was found to have a moderate threat to internal validity. Aggregation indices are not assessed for outcomes reported by only 1 study. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • One cohort study[22] (N = 48,440) reported adjusted effect measures suggesting increased ICU admission is associated with increased duration of physical inactivity among people with COVID-19. ▪ One cohort study[22] (N = 48,440) of HMO members with COVID-19 suggested that the odds of ICU admission increase as the duration of physical inactivity increases. Participants who were consistently active had a lower odds of ICU admission compared with participants who were inconsistently active [aOR 1.58 (95% CI: 1.10 – 2.27), p = NR] and those who were consistently inactive [aOR 1.73 (95% CI: 1.18 – 2.55), p = NR] when adjusting for demographics and other risk factors for severe COVID-19. While the odds of ICU admission were greater among those who were consistently inactive, there was no difference in ICU admission when comparing participants who were consistently inactive to those who were inconsistently active [aOR 1.10 (95% CI: 0.93 – 1.29), p = NR]. This study reported wide confidence intervals.
Hospitalization	Data from 7 studies[15,17,18,22-25] indicates that the duration of physical inactivity is associated with the need for hospitalization among patients with COVID-19; duration of physical inactivity is associated with increased need for hospitalization whereas duration of physical activity is associated decreased for hospitalization. All the studies all were found to have a moderate threat to internal validity. Self-reported data is considered to introduce reporting bias; however, this data is considered normative in the field of physical activity. • Strength of Association: Seven studies reported adjusted measures of association from 0.13 – 0.76 for physical activity and 1.22 – 2.26 for physical inactivity.

Outcome	Results

	• Precision of Association: Five studies[15,17,18,22,23] reported wide confidence intervals and 6 studies[15,17,18,23-25] reported confidence intervals that included the null.
	• Consistency of Association: Results were consistent.
	• Applicability of Association: Six studies[15,18,22-25] were conducted in high-income countries a and one[17] in a middle-income country.
	
	Summary of Evidence:
	
	• Seven studies[15,17,18,22-25] (N = 53,840) reported data indicating that increased hospitalization is associated with increased duration of physical inactivity or decreased intensity or duration of physical activity among people with COVID-19.
	  • Three studies reported on the measure of physical inactivity.
	  • Three cohort studies[22,24,25] (N = 49,080) stratified the population by number of minutes of physical inactivity per week and reported that the odds of hospitalization increase as the minutes of physical inactivity per week increases in people with COVID-19. ([aRR: 0.98 (95% CI: 0.83 – 1.17), p = NR][24] to [aOR: 2.26 (95% CI: 1.81 – 2.83), p = NR][22])
	  ○ One study[22] reported a wide confidence interval and 2 studies[24,25] reported confidence intervals that included the null.
	  • Four studies reported on the measure of physical activity.
	  • One cohort study[15] (N = 3,139) and 3 cross-sectional studies[17,18,23] (N = 1,621) stratified the population by duration of physical activity per week and reported that the odds of hospitalization decrease as the duration of physical activity per week increases. ([OR: 0.41 (95% CI: 0.22 – 0.74), p < 0.01][15] to [PR: 0.72 (95% CI: 0.43 – 1.21), p = 0.21][17], or adjusted [aRR: 0.13 (95% CI: 0.01 – 1.17), p = 0.07][18] to [aOR: 0.76 (95% CI: 0.26 – 1.84), p = 0.58][15])
	  ○ All 4 studies reported confidence intervals that included the null[15,17,18,23].

B.3.b. Extracted Evidence

Table 5 Extracted Studies Reporting the Association Between Physical Activity/ Inactivity and Severe COVID-19 Outcomes.

Study	Population and Setting	Exposure	Definitions	Results
Author: Ahmadi[19] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To examine the association of combined lifestyle risk factor indexes and risk of infectious disease mortality, including mortality due to pneumonia and COVID-19. **IVA Score:** 24 (Moderate)	**Population:** N = 468,569 COVID-19 positive N = NR **Setting:** Assessment centers **Data Source:** UK National Health Service (NHS) **Location:** United Kingdom **Study Dates:** NA – June 28, 2020 **Inclusion Criteria:** Adults aged between 40 and 69 years who were registered with NHS. **Exclusion Criteria:** Participants who did not have usable physical activity, sedentary behavior, sleep, diet, alcohol consumption, and smoking history information and any remaining participants with an incomplete covariate profile.	**Condition, n/N (%):** Insufficient physical activity: 140,609/468,569 (30%) Sufficient physical activity: 232,613/468,569 (50%) Moderate sedentary behavior: 249,929/468,569 (53.3%) Low sedentary behavior: 161,029/468,569 (34.3%) **Control/Comparison Group, n/N (%):** Physically inactive: 95,221/468,569 (20.3%) High sedentary behavior: 57,485/468,569 (12.3%)	**Condition(s):** NR **Severity Measure(s):** *Inactive: 0 min/week of activity* *Insufficient physical activity:* <600 MET-min/week *Sufficient physical activity:* at least 600 MET-min/week *High sedentary behavior:* >7 h/d of daily TV, PC, screen-based activities and driving *Moderate sedentary behavior:* 4 to 7 h/d of TV, PC screen-based activities and driving *Low sedentary behavior:* <4 h/d of TV, PC screen-based activities and driving **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* COVID-19 mortality was identified using ICD-10 codes U07.1-U07.2 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** NR **Severity of Condition:** *aRR: fully adjusted Risk Ratio model* *RR: Risk Ratio* *Mortality, n/N (%):* Insufficient physical activity: • aRR: 0.87 (95% CI: 0.67 –1.14) • RR: 0.75 (95% CI: 0.58 – 0.97) • Insufficient PA: 115/140,609 (0.08%) • Inactive: 112/95,221 (0.11%) Sufficient physical activity: • aRR: 0.70 (95% CI: 0.54 – 0.89) • RR: 0.57 (95% CI: 0.44 – 0.72) • Sufficient PA: 160/232,613 (0.06%) • Inactive: 112/95,221 (0.11%) Moderate sedentary behavior: • aRR: 0.90 (95% CI: 0.68 – 1.90) • RR: 0.72 (95% CI: 0.55 – 0.95) • Moderate sedentary: 217/249,929 (0.08%) • High sedentary: 68/57,485 (0.11%) Low sedentary behavior: • aRR: 0.87 (95% CI: 0.64 – 1.20) • RR: 0.65 (95% CI: 0.48 – 0.89) • Low sedentary: 102/161,029 (0.06%) • High sedentary: 68/57,485 (0.11%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Exposure	Definitions	Results
Author: Brandenburg[23] **Publication:** 2021 **Data Extractor:** MC **Reviewer:** MW **Study Design:** Cross-sectional **Study Objective:** To understand whether physical activity and physical fitness levels are related to COVID-19 symptom characteristics and any adverse complications resulting from infection. **IVA Score:** 22 (Moderate)	**Population:** N = 263 **Setting:** NA **Data Source:** Self-report survey, self-report cardiorespiratory and physical fitness assessment **Location:** Canada **Study Dates:** early July - mid-October 2021 **Inclusion Criteria:** Over the age of 18 years, and a confirmed/positive SARS-CoV-2test result. **Exclusion Criteria:** Respondents that did not indicate positive test result for COVID-19, and respondents with missing data on COVID-19 characteristics, CR fitness, physical activity, and demographics.	**Condition, n/N (%):** Physical activity: • Moderate: 73/263 (28%) • < 1 hour, vigorous: 49/263 (18%) • > 1 hour, vigorous: 102/263 (39%) **Control/Comparison Group, n/N (%):** No/low physical activity: 39/263 (15%)	**Condition(s):** *Physical activity:* modified physical activity rating (PA-R) questionnaire, which asked participants to rate their physical activity level, using a 0 to 7 scale, over the 6 months prior to the COVID-19 diagnosis **Severity Measure(s):** *Physical activity:* • *No/low:* no regular physical activity (score: 0-1) • *Moderate: participation in moderate-intensity activity of any duration (score: 2-3)* • *< 1 hour, vigorous:* regular participation in vigorous intensity activity for <1 hour per week (score: 4-5) • *> 1 hour, vigorous:* regular participation in vigorous-intensity activity for a weekly duration greater than 1 hour (score: 6-7) **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* required hospitalization (not including emergency room visits) *Non-elective readmissions*: NR	**Severe COVID-19:** **Severity of Condition:** *aOR1: Odds Ratio (adjusted for age, BMI, pre-existing condition, and time between recovery from COVID-19 and completion of the online survey)* *aOR2: Odds Ratio (adjusted for age, BMI, and preexisting conditions)* *Hospitalization, n/N (%):* Physical activity, no/low: Ref Physical activity, moderate: • aOR1: 1.1 (95% CI: 0.50 – 2.59), p = 0.8 • aOR2: 1.43 (95% CI: 0.42 – 4.84), p = 0.6 Physical activity, < 1 hour, vigorous: • aOR1: 1.4 (95% CI: 0.55 – 3.49), p = 0.5 • aOR2: 1.05 (95% CI: 0.22 – 5.0), p = 0.9 Physical activity, > 1 hour, vigorous: • aOR1: 0.55 (95% CI: 0.24 – 1.28), p = 0.2 • aOR2: 1.06 (95% CI: 0.23 – 4.79), p = 0.6 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
			Comments: None	
Author: Burden[2] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** MC **Study Design:** Cross-sectional **Study Objective:** To collate data and establish whether modifiable risk factors and country-specific characteristics are associated with the number of COVID-19 cases and deaths. **IVA Score:** 21 (Moderate)	**Population:** N = 181 countries COVID-19 positive cases = 4,670,832 **Setting:** Population **Data Source:** European Centre for Disease Prevention and Control (ECDC) **Location:** Worldwide **Study Dates:** NR - May 18, 2020 **Inclusion Criteria:** NR **Exclusion Criteria:** NR	**Condition, n/N (%):** NR **Control/Comparison Group, n/N (%):** NR	**Condition(s):** *Excess deaths:* the number of deaths above or below those linearly predicted by case number for the whole population **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality: ND* *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *multivariable logistic regression; included model variables: gross domestic product per person (GDPP), population, land mass, healthcare access and quality index (HAQ) and agedness* *Mortality:* Physical inactivity was associated with excess deaths, and this remained significant after adjustment for confounders • $p < 0.05$ **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Mortality:* Physical inactivity was associated with excess deaths in both men and women, and this remained significant after adjusting for GDPP, population, land mass, HAQ and agedness, • $p < 0.05$ **Long-term Sequelae:** Non-elective readmissions: NR
Author: Cho[20] **Publication:** 2021	**Population:** N =132,060 Cases: n = 6,288 Controls: n = 125,772	**Medical Condition, n/N (%):** Physical activity, by intensity: • Light intensity: 1752/6288 (27.9%)	**Medical Condition(s):** NR **Severity Measure(s):** *Physical inactivity*: Sedentary	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: age, sex, income, medical history (obesity, hypertension,*

Study	Population and Setting	Exposure	Definitions	Results
Data Extractor: AH **Reviewer:** CS **Study Design:** Case-Control **Study Objective:** To examine the associations between regular physical activity and the risk of COVID-19 and mortality. **IVA Score:** 25 (Moderate)	**Setting:** Nationwide, population-based **Data Source:** Electronic medical records **Location:** South Korea **Study Dates:** January 1 – July 16, 2020 **Inclusion Criteria:** The study included all Koreans over 18 years of age who tested positive for SARS-CoV-2 by TR-PCR of pharyngeal and nasal swab samples and underwent national health screening between 2014 and 2017. For every case patient, 20 random controls from the target population who underwent the national health screening was selected. **Exclusion Criteria:** People missing data of physical activity were excluded.	• Moderate intensity: 861/6288 (13.7%) • Vigorous intensity: 2362/6288 (37.6%) Physical activity, by level of MET-min/week: • <500 MET-min / week: 1889/6288 (30.0%) • 500-999 MET-min / week: 1973/6288 (31.4%) • 1000-1499 MET-min / week: 752/6288 (12.0%) • ≥1500 MET-min / week: 364/6288 (5.8%) **Control/Comparison Group, n/N (%):** Physical inactivity: 1,313/6,288 (20.9%)	*Light intensity:* Walking at own pace at slow speed *Moderate intensity:* Brisk walking, playing tennis, or slow cycling *Vigorous intensity:* Running, jogging, climbing, or bicycling or fast cycling *Physically Inactive:* 0 METs-min/week *<500 MET-min / week*: physical activity <500 METs-min/week *500-999 MET-min / week:* 500 ≤ physical activity < 1000 METs-min/week *1000-1499 MET-min / week:* 1000 ≤ physical activity < 1500 METs-min/week *≥1500 MET-min / week:* physical activity ≥ 1500 METs-min/week **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* COVID-19 related mortality was defined as the termination of isolation due to death *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	*diabetes, dyslipidemia, ischaemic heart disease, and stroke), smoking status, and alcohol consumption.* **Severity of Condition:** *Mortality, n/N (%):* *Physically inactive (ref):* • 31/1344 (2.3%) *Light intensity:* • aOR: 0.57 (95% CI: 0.31 – 1.04) • 27/1779 (1.5%) *Moderate intensity:* • aOR: 0.26 (95% CI: 0.08 – 0.81) p<0.05 • 4/865 (0.5%) *Vigorous intensity:* • aOR: 0.38 (95% CI: 0.18-0.81) p< 0.05 • 13/2375 (0.5%) *Moderate to vigorous intensity:* • aOR: 0.47 (95% CI: 0.26-0.87) p < 0.05 • 17/3240 (0.5%) *<500 MET-min / week:* • aOR: 0.54 (95% CI: 0.28 – 1.08) • 19/1905 (1.0%) *500-999 MET-min / week:* • aOR: 0.42 (95% CI: 0.21 – 0.83) p < 0.05 • 16/1989 (0.8%) *1000-1499 MET-min / week:* • aOR: 0.56 (95% CI: 0.21 – 1.49) • 6/758 (0.8%) *≥1500 MET-min / week:* • aOR: 0.23 (95% CI: 0.06-0.85) p < 0.05 • 3/367 (0.8%) **Duration of Condition:** NR **Comorbid Conditions:** NR

Study	Population and Setting	Exposure	Definitions	Results
				Risk Markers: NR **Long-term Sequelae:** NR
Author: Cunningham[11] **Publication:** 2021 **Data Extractor:** DOS **Reviewer:** AH **Study Design:** Ecological study **Study Objective:** To examine through an analysis of county-level data the possibility that communities with higher levels of physical activity might also see fewer COVID-19 cases and deaths. **IVA Score:** 17 (High)	**Population:** N = 3,142 counties and county-equivalents **Setting:** Nationwide **Data Source:** 1) USA Facts 2) 2020 County Health Ranking and Roadmaps **Location:** US **Study Dates:** January 20 – November 30, 2020 **Inclusion Criteria:** Data related to COVID-19 cases and deaths, physical activity, subjective health rating, lack of insurance, unemployment, median household income, sex, race, age, and rural designation in counties and county-equivalents (boroughs, parishes,	**Condition, n/N (%):** Physical activity: 76.63% **Control/Comparison Group, n/N (%):** No physical activity: 23.37%	**Condition(s):** *Physical activity:* percentage who had any level of activity assessed via the following survey question: "During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?"; this measure represents the lowest possible threshold of physical activity **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* COVID-19 deaths per 100,000 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *County- and state-level random intercept model with county-level physical activity predicting COVID-19 deaths; model included covariates for fair or poor health, uninsured, natural log of the median household income, unemployed, female residents, White residents, 65 or older, and rural.* *Mortality:* Physical activity was negatively correlated with COVID-19 deaths per 100,000 (correlation coefficient, r: -0.23). In the random intercept model, physical activity was negatively associated with COVID-19 deaths per 100,000 (estimate = -0.72, SE = 0.27, $p<0.01$). Physical activity appears to be a moderator for the relationship between cases and deaths as this relationship is stronger when physical activity was low than when it was high. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Exposure	Definitions	Results
	and the District of Columbia). **Exclusion Criteria:** NR			
Author: de Souza[17] **Publication:** 2021 **Data Extractor:** CS **Reviewer:** TR **Study Design:** Cross-sectional **Study Objective:** To assess the association of physical activity before the pandemic and quarantine measures with the prevalence of hospitalizations in surviving patients infected with SARS-CoV-2. **IVA Score:** 24 (Moderate)	**Population:** N = 938 **Setting:** Nationwide, community **Data Source:** Electronic link to questionnaires spread through social media, newscasts, hospitals, medical care providers, and disease control centers in some cities **Location:** Brazil **Study Dates:** March-August 2020 **Inclusion Criteria:** Survivors (after hospital discharge) and fully recovered patients (outpatient without symptoms) of all ages, with or without symptoms/hospitalization, with confirmed quantitative PCR viral tests, blood test (serology), and a rapid	**Condition, n/N (%):** Sufficient physical activity: 611/938 (65.1%) Sitting time: • ≥4.7: 475/938 (50.6%) • ≥7.4: 228/938 (24.3%) Number of physical activities performed: • 2 or more: 261/938 (27.8%) • 1: 192/938 (20.5%) **Control/Comparison Group, n/N (%):** Insufficient physical activity: 327/938 (34.9%) Sitting time: • <4.7: 463/938 (49.4%) • <7.4: 710/938 (75.7%) No physical activities performed: 485/938 (51.7%)	**Condition(s):** *Sufficient physical activity:* at least 150 minutes per week of moderate physical activity and/or at least 75 minutes of vigorous physical activity *Sitting time:* in hours/day **Severity Measure(s):** *Number of physical activities performed:* 2 or more, 1, or no physical activities performed **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* mechanical ventilation *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aPR: Adjusted Prevalence Ratio; Poisson multivariate regression model; included model variables: age, sex, and pre-existing diseases* *PR: Prevalence ratio; Univariable Poisson regression* *Intubation, n/N (%):* Physical activity: • Sufficient: 3/49 (6.1%) • Insufficient: 6/42 (14.3%) • p = 0.293 Sitting time ≥4.7: • <4.7: 6/51 (11.8%) • ≥4.7: 3/40 (7.5%) • P = 0.726 Sitting time ≥7.4: • <7.4: 7/72 (9.7%) • ≥7.4: 2/19 (10.5%) • p > 0.999 *Hospitalization, n/N (%):* Physical activity: • aPR: 0.66 (95% CI: 0.44 – 0.99), p = 0.05 • PR: 0.624 (95% CI: 0.423 – 0.922), p = 0.02 • Sufficient: 49/611 (8.0%) • Insufficient: 42/327 (12.8%) • p = 0.02 Sitting time ≥4.7: • aPR: 1.24 (95% CI: 0.84 – 1.84), p = 0.28 • PR: 1.31 (95% CI: 0.88 – 1.94), p = 0.18 • <4.7: 51/463 (11.0%)

Study	Population and Setting	Exposure	Definitions	Results
	antibody test for SARS-CoV-2were included. Those with or without drug treatment, and with any chronic disease, such as diabetes, hypertension, coronary artery disease, obesity, metabolic syndrome, cancer, among others were also included. **Exclusion Criteria:** Illiterate patients who had difficulty filling out the electronic form, patients still hospitalized or with symptoms of COVID-19, duplicate responses, people without any diagnostic tests for SARS-CoV-2, children under the age of 10, and participants with inconsistent answers were excluded.			• ≥4.7: 40/475 (8.4%) • p = 0.218 Sitting time ≥7.4: • aPR: 1.14 (95% CI: 0.71 – 1.84), p = 0.59 • PR: 1.22 (95% CI: 0.75 – 1.97), p = 0.43 • <7.4: 72/710 (10.1%) • ≥7.4: 19/228 (8.3%) • p = 0.50 **Severity of Condition:** *Hospitalization, n/N (%):* PR by Number of physical activities performed: • PR, ≥2: 0.54 (95% CI: 0.35 – 0.83), p = 0.01 • PR, 1: 0.72 (95% CI: 0.43 – 1.21), p = 0.21 • ≥2: 36/261 (7.4%) • 1: 19/192 (9.9%) • None, ref: 36/485 (13.8%) • p = 0.020 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Hamer[13] **Publication:** 2020	**Population:** N = 334,329 COVID-19 positive cases = NR **Setting:** Community	**Condition, n/N (%):** Physical (in)activity: 78/19,690 **Control/Comparison Group, n/N (%):** NR	**Condition(s):** *Physical (in)activity:* measured by physical activity in the last 4 weeks: none, walking, exercise and sport, household maintenance work and gardening	**Severe COVID-19:** *aOR: Odds Ratio, adjusted for age (per 5 years), sex, smoking, physical activity, alcohol consumption, education, ethnicity, diabetes, hypertension, and CVD* *Hospitalization, n/N (%):*

Study	Population and Setting	Exposure	Definitions	Results
Data Extractor: MC **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To attempt to discover if a potential obesity–COVID-19 association is driven by underlying morbidity or other biological mechanisms, and to examine the aetiological relation of overweight and obesity with new cases of COVID-19 hospitalizations in a general population-based cohort study with available biomarker data.	**Data Source:** UK Biobank **Location:** UK **Study Dates:** March 16 - April 26, 2020 **Inclusion Criteria:** Participants who were alive prior to COVID-19 testing (5 March 2020) and had available data on BMI and covariates. **Exclusion Criteria:** Participants residing in Scotland and Wales.		**Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** Given the reported increased risk of COVID-19 in ethnic minority groups, analysis was restricted to White participants.	• aOR: 1.52 (95% CI: 1.19 - 1.95) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
IVA Score: 21 (Moderate)				
Author: Hamer M[13] **Publication:** 2020 **Data Extractor:** MW **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To examine the association of lifestyle risk factors with new cases of COVID-19 hospitalizations in a general population-based cohort study. **IVA Score:** 23 (Moderate)	**Population:** N= 387,109 COVID-19 positive cases, N = NR **Setting:** Research assessment centers **Data Source:** UK Biobank **Location:** United Kingdom **Study Dates:** March 16 – April 26, 2020 **Inclusion Criteria:** Participants who were alive up to March 5th, 2020 and had available data on lifestyle exposures and covariates. Baseline data was collected among people aged 40-69 years between 2006 and 2010. **Exclusion Criteria:** NR	**Condition, n/N (%):** Insufficient physical activity: 108,707/387,109 (28.1%) Nonphysical activity: 68,913/387,109 (17.8%) **Control/Comparison Group, n/N (%):** Sufficient physical activity: 209,489/387,109 (54.1%)	**Condition(s):** *Physical activity:* Was assessed using the International Physical Activity Questionnaire (IPAQ) short form that measures duration and frequency of moderate-to-vigorous physical activity (MVPA) from all domains in the last week. **Severity Measure(s):** *Sufficient physical activity:* ND *Insufficient physical activity:* ND **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* ND *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aRR1: adjusted Relative Risk, model adjusted for age, sex, education, ethnicity, diabetes, hypertension, cardiovascular disease (heart attack, angina, or stroke)* *aRR2: adjusted Relative Risk, model adjusted for age and sex* **Severity of Condition:** *Hospitalization, n/N (%):* Insufficient physical activity: • aRR1: 0.99 (95% CI: 0.84 – 1.18) • aRR2: 0.98 (95% CI: 0.83 – 1.17) • Insufficient PA: 192/108,707 (0.17%) • Sufficient PA: 382/209,489 (0.18%) Nonphysical activity: • aRR1: 1.38 (95% CI: 1.15 – 1.64) • aRR2: 1.51 (95% CI: 1.27 – 1.81) • None: 186/68,913 (0.27%) • Sufficient PA: 382/209,489 (0.18%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Lassale[25]	**Population:** N = 427,594 Analyzed, n = 340,966	**Condition, n/N (%):** **Numerators calculated using percentages reported among*	**Condition(s):** NR **Severity Measure(s):**	**Severe COVID-19:** *aOR: Adjusted Odds Ratio; fitted logistic regression model include age, sex,*

Study	Population and Setting	Exposure	Definitions	Results
Publication: 2020 **Data Extractor:** AH **Reviewer:** DOS **Study Design:** Cohort **Study Objective:** To assess the ethnic differences in serious cases of COVID-19 in a well characterized, large, community-based cohort and to investigate which underlying factors drive the observed associations. **IVA Score:** 19 (Moderate)	COVID-19 positive cases, n = 640 **Setting:** Community **Data Source:** UK Biobank & Public Health England **Location:** UK **Study Dates:** March 16 – April 26, 2020 **Inclusion Criteria:** Participants aged 40-69 years when recruited in 2006 – 2010. Recruitment relied on mailed invitations. **Exclusion Criteria:** Participants residing in Scotland and Wales were excluded as SARS-CoV-2 test data were only available for England.	*those not hospitalized; prevalence data reported among entire study population* Active > 10 min not reaching guideline: 119,550/428,494 (27.9%) Inactive: 77,986/428,494 (18.2%) **Control/Comparison Group, n/N (%):** Physical activity meeting guideline: 230,958/428,494 (53.9%)	*Physical activity meeting guideline:* ≥150 min/week moderate-to-vigorous physical activity or ≥ 75 min/week vigorous activity *Active > 10 min not reaching guideline*: > 10 min of physical activity but not below guidelines *Inactive*: < 10 min of physical activity **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* real-time PCR confirmed COVID-19 via combined nose/throat swab used as a proxy for hospitalizations for severe COVID-19 cases as testing was largely restricted to those with symptoms in hospital *Non-elective readmissions*: NR **Comments:** Real-time PCR confirmed COVID-19 used as a proxy for hospitalization.	*socioeconomic covariates, lifestyle covariates, comorbidities, and biomarkers* **Severity of Condition:** *Hospitalization, (%):* Physical activity meeting guideline: ref Active > 10 min not reaching guideline: • aOR: 0.93 (95% CI: 0.77 – 1.13), p = 0.47 Inactive: • aOR: 1.22 (95% CI: 1.00 – 1.48), p = 0.05 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Latorre-Roman[18] **Publication:** 2021 **Data Extractor:**	**Population:** N = 420 COVID-19 positive cases, n = NR **Setting:** Community	**Medical Condition, n/N (%):** Moderate physical activity (PA): 243/420 (58.0%) **Control/Comparison Group, n/N (%):**	**Medical Condition(s):** *Physical activity:* The level of self-reported engagement in moderate or vigorous activity in a typical week, measured in days per week and hours per week, as well as	**Severe COVID-19:** *aRR: Adjusted Risk ratio; adjusted by sex and age* *Hospitalization:* Performing moderate PA: ref Not performing PA:

Study	Population and Setting	Exposure	Definitions	Results
MM **Reviewer:** MW **Study Design:** Cross-sectional **Study Objective:** To determine the association of physical activity patterns prior to COVID-19 confinement and severe respiratory symptoms consistent with COVID-19. **IVA Score:** 22 (Moderate)	**Data Source:** Online questionnaire **Location:** Spain **Study Dates:** May – June 2020 **Inclusion Criteria:** People ≥ 18 years-old residing in Spain that had reliable internet access were included. **Exclusion Criteria:** People that were unable to give consent, had intellectual limitations, or had no internet access were excluded	Not performing PA: 84/420 (20.0%)	how many days per week the individual walks for 10 minutes **Severity Measure(s):** *Moderate physical activity*: An activity that causes heavier than normal breathing and may include carrying light weights, riding a bicycle at normal speed, and engaging in sports, but does not include walking **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* admission for respiratory symptoms compatible with COVID-19 *Non-elective readmissions*: NR **Comments:** Measures are not adjusted and are self-reported	• aRR: 4.12 (95% CI: 0.95 – 17.76), p = 0.05 **Severity of Condition:** *Hospitalization:* • Moderate PA, <30 min/week: ref Moderate PA, >150 min/week: aRR: 0.24 (95% CI: 0.05 – 1.04), p = 0.05 Moderate PA, 30-150 min/week: aRR: 0.13 (95% CI: 0.01 – 1.17), p = 0.07 **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Lee SW[21] **Publication:** 2021 **Data Extractor:** DOS **Reviewer:** TR	**Population:** N = 212,768 Two cohorts: *Activity recommendations*: COVID-19 positive cases, N = 2,295 *MET score:* COVID-19 positive cases, N = 3,882	**Condition, n/N (%):** *Activity recommendations:* Muscle strengthening only: 150/2,295 (6.5%) Aerobic only: 561/2,295 (24.4%) Aerobic and muscle strengthening: 291/2,295 (12.7%) *MET score* Insufficiently active: 1,641/3,882 (42.3%)	**Condition(s):** NR **Severity Measure(s):** *Activity recommendations:* • *Insufficient aerobic activity and muscle strengthening:* <150 min/week of moderate intensity activity (exercise that causes mild shortness of breath such as risk walking and bicycling), <75 min/week of	**Severe COVID-19:** *aRR: Adjusted Relative Risk; modified Poisson regression adjusted for age, sex, region of residence, Charlson comorbidity index, history of diabetes mellitus, tuberculosis, stroke and cardiovascular disease, BMI, systolic blood pressure, diastolic blood pressure, fasting blood glucose, serum total cholesterol, glomerular filtration rate, household income, smoking, alcoholic drinks, and medication for*

Study	Population and Setting	Exposure	Definitions	Results
Study Design: Cohort **Study Objective:** To investigate whether sufficient physical activity reduces the risk of COVID-19 infectivity, severity, and its related mortality among patients who underwent SARS-CoV-2 testing or decrease the length of hospital stay among patients confirmed with COVID-19. **IVA Score:** 25 (Moderate)	**Setting:** Nationwide **Data Source:** Korean National Health Insurance Survey, national COVID-19 related registers generated by the Korean Disease Control and Prevention Agency (KDCA), and national general health examination and health insurance data from the Ministry of Health and Welfare, South Korea **Location:** South Korea **Study Dates:** January 1 – July 31, 2020 **Inclusion Criteria:** All Korean people aged ≥20 years who underwent SARS-CoV-2 testing between January 1 – May 15, 2020 by medical or KDCA referral. SARS-CoV-2 infection was confirmed by nasal and pharyngeal swabs using the laboratory real-time rt-PCR assay.	Active: 816/3,882 (21.0%) Highly active: 622/3,882 (16.0%) **Control/Comparison Group, n/N (%):** *Activity recommendations:* Insufficient aerobic activity and muscle strengthening: 1,293/2,295 (56.3%) *MET score* Inactive: 803/3,882 (20.7%)	vigorous intensity activity (intense exercise that causes severe shortness of breath such as running), and less than an equivalent combination (equivalent combination was calculated using the general rule that 2 min of moderate counts as 1 min of vigorous intensity activity) plus <2 times/week of muscle strengthening activity • *Muscle strengthening only:* <150 min/week of moderate intensity activity, <75 min/week of vigorous intensity activity, and less than an equivalent combination plus ≥2 times/week of muscle strengthening activity • *Aerobic only:* ≥150 min/week of moderate intensity activity or ≥75 min/week of vigorous intensity activity or greater than an equivalent combination plus <2 times/week of muscle strengthening activity • *Aerobic and muscle strengthening:* ≥150 min/week of moderate intensity activity or ≥75 min/week of vigorous intensity activity or great than an equivalent combination plus ≥2 times/week of muscle strengthening activity *MET score:*	*hypertension, diabetes mellitus, and cardiovascular disease* **Severity of Condition:** *Mortality, n/N (%):* Muscle strengthening only: • Muscle strengthening only: 0/150 (0%) • Insufficient aerobic activity and muscle strengthening: 32/1,293 (2.5%) Aerobic only: • aRR: 0.71 (95%CI: 0.35 – 1.42) • Aerobic only: 11/561 (2.0%) • Insufficient aerobic activity and muscle strengthening: 32/1,293 (2.5%) Aerobic and muscle strengthening: • aRR: 0.28 (95%CI: 0.06 – 1.20) • Aerobic and muscle strengthening: 2/291 (0.69%) • Insufficient aerobic activity and muscle strengthening: 32/1,293 (2.5%) Insufficiently active: • aRR: 0.74 (95%CI: 0.49 – 1.06) • Insufficiently active: 53/1,641 (3.2%) • Inactive: 39/803 (4.9%) Active: • aRR: 0.49 (95%CI: 0.27 – 0.82) • Active: 17/816 (2.1%) • Inactive: 39/803 (4.9%) Highly active: • aRR: 0.43 (95%CI: 0.22 – 0.83) • Highly active: 13/622 (2.1%)

Study	Population and Setting	Exposure	Definitions	Results
	Exclusion Criteria: Patients that self-referred for SARS-CoV-2 testing.		*Metabolic equivalent task (MET) score:* each category of activity was assigned a MET score on the energy cost and the weighted MET-minutes per week was calculated by multiplying the standard MET score, duration, and frequency per week; rating of 4.0 and 8.0 METs were assigned for moderate and vigorous intensity activity, respectively • *Inactive:* 0 MET min/week • *Insufficiently active:* 0 to <500 MET min/week • *Active:* 500 to <1,000 MET min/week • *Highly active:* more than 1,000 MET min/week **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* COVID-19 related death *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• Inactive: 39/803 (4.9%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Li[12] **Publication:** 2020	**Population:** N = 217 counties **Setting:** Counties from 37 states and the District of Columbia	**Condition, n/N (%):** Physical inactivity: NR **Control/Comparison Group, n/N (%):**	**Condition(s):** *Physical inactivity:* ND **Severity Measure(s):** NR **Clinical Marker:** NR	**Severe COVID-19:** *Mortality comparing top 50% of counties reporting deaths per 100,000 vs. bottom 50% of counties reporting deaths per 100,000 (standard error of the mean):* • Top 50%: 25.01% (0.48%)

Study	Population and Setting	Exposure	Definitions	Results
Data Extractor: CS **Reviewer:** AH/DOS **Study Design:** Ecological **Study Objective:** To analyze data for COVID-19 in United States counties and ground them in the larger context of patient demographics, underlying health conditions, social determinants of health, environmental variables, and social distancing adherence. **IVA Score:** 18 (Moderate)	**Data Source:** County-level data obtained from Center for Systems Science and Engineering (CSSE) Coronavirus Resource Center at Johns Hopkins University, census data, County Health Rankings and Roadmaps Program Database, National Oceanic and Atmospheric Administration, research agreements with companies, and other publicly available data sources **Location:** U.S. **Study Dates:** Through April 14, 2020 **Inclusion Criteria:** All COVID-19 confirmed case number and death numbers from each U.S. county through the study date. **Exclusion Criteria:** Counties were excluded from death	NA as exposure is a continuous variable	**Outcome Definitions:** *Mortality:* COVID-19 confirmed deaths per 100,000 *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• Bottom 50%: 21.73% (0.46%) • $p < 0.001$ The percentage of physical inactivity was higher (25.01%) in the top 50% of counties reporting deaths per 100,000 due to COVID-19 compared to the percentage of physical inactivity in the bottom 50% of counties (21.73%). **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
	analyses if they reported fewer than 50 cases and fewer than 10 deaths or the first death had occurred fewer than 2 weeks prior to the end of the study.			
Author: Li[16] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** DOS **Study Design:** Cohort using Mendelian randomization **Study Objective:** To investigate the causality between four lifestyle factors, namely BMI, smoking, physical activity and alcohol consumption, and severe illness of COVID-19 using a large	**Population:** N = 941,280 COVID-19 positive cases, n: 9,462 **Setting:** NR **Data Source:** Two genome-wide association study (GWAS) analyses by the COVID-19 Host Genetic Initiative **Location:** Europe **Study Dates:** Up to September 2020 **Inclusion Criteria:** One analysis included very severe respiratory confirmed COVID-19 cases defined as hospitalized laboratory confirmed SARS CoV-2 infection via RNA or serology with death or respiratory support,	**Condition, n/N (%):** Genetically predicted physical activity: NR **Control/Comparison Group, n/N (%):** No genetically predicted physical activity: NR	**Condition(s):** *Genetically predicted physical activity:* five genetic variants identified to be associated with accelerometer-measured overall physical activity (measured as average vector magnitude) in a sample of up to 91,105 UK Biobank people, explaining ~0.2% variation in overall physical activity **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* COVID-19 hospitalization *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *Per-SD OR: Odds Ratio using inverse-variance weighted method under random-effects model calculating odds of COVID-19 hospitalization for per-standard deviation (SD) increase accelerometer-measured physical activity* *Hospitalization:* Genetically predicted physical activity: • Per-SD OR = 0.44 (95% CI: 0.18 – 1.07), p = 0.07 Genetically predicted physical activity was found to be associated with a decreased risk of COVID-19 hospitalization, however the 95% CI did include one and the finding was not statistically significant. There might be weak instrument bias as the five genetic instrumental variables for physical activity only explained ~0.2% variation in accelerometer-measured physical activity. There might be horizontal pleiotropy of the physical activity genetic instrumental variables, potentially biasing results. There was no evidence of heterogeneity between genetic variants of physical activity. **Severity of Condition:** NR

Study	Population and Setting	Exposure	Definitions	Results
sample size and the two-sample Mendelian randomization approach. **IVA Score:** 20 (Moderate)	and hospitalization with COVID-19 as primary reason for admission. The other analysis included hospitalized confirmed COVID-19 defined as hospitalized laboratory confirmed SARS-CoV-2 via RNA or serology and hospitalization due to corona-related symptoms. Both analyses included population controls. **Exclusion Criteria:** NR			**Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Lobelo[14] **Publication:** 2021 **Data Extractor:** DOS **Reviewer:** TR **Study Design:** Retrospective cohort **Study Objective:** To determine if racial disparities exist among	**Population:** N = 5,712 **Setting:** Regional integrated healthcare system **Data Source:** Electronic health records (EHR) and ESRI Business Analyst data **Location:** GA, US **Study Dates:** March 3 – October 29, 2020 **Inclusion Criteria:** Patients who were members of the study healthcare system with	**Condition, n/N (%):** Physically inactive: 1,648/5,712 (28.9%) **Control/Comparison Group, n/N (%):** Not physically inactive: 4,073/5,712 (71.3%)	**Condition(s):** *Physically inactive:* self-reported exercise <10 min assessed at the most recent clinical encounter within the last 12 months **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation: NR* *Hospitalization:* hospitalized at hospital affiliated with study healthcare system *Non-elective readmissions*: NR	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression model included age, sex, race/ethnicity, BMI, comorbidity burden, and therapeutic management* *Hospitalization:* Physically inactive: • aOR: 1.25 (95%CI: 1.03 – 1.51), p ≤ 0.05 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** *Hospitalization among female patients:* Physically inactive: • aOR: 1.45 (95%CI: 1.12 – 1.89), p ≤ 0.05

Study	Population and Setting	Exposure	Definitions	Results
patients with COVID-19, with respect to demographic and social determinants of health (SDOH), pre-pandemic comorbidities/underlying conditions, quality of care metrics and lifestyle behaviors as well as COVID-19-related clinical outcomes and to explore the roles of these clinical behavioral and SDOH factors as potential drivers of racial disparities for COVID-19 hospitalization. **IVA Score:** 23 (Moderate)	a documented diagnosis or laboratory-confirmed SARS-CoV-2 PCR test in their EHR. Tests were prioritized among symptomatic healthcare workers and patients requiring hospital admission. Testing was progressively expanded to high-risk symptomatic patients and symptomatic patients with public health implications. Patients were tested if recommended after in-person or telemedicine evaluation. **Exclusion Criteria:** Patients with COVID-19 seen during study period in the 'Other', 'unknown', and 'declined to report' race/ethnicity categories.		**Comments:** None	The effect estimate of physical inactivity was even more pronounced for female patients **Long-term Sequelae:** NR

Study	Population and Setting	Exposure	Definitions	Results
Author: Madakkatel[7] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** DOS **Study Design:** Cohort **Study Objective:** To identify possible predictors for long-term susceptibility to severe COVID-19 infection and mortality. **IVA Score:** 20 (Moderate)	**Population:** N = 421,111 COVID-19 positive, n = 1,953 **Setting:** Community **Data Source:** UK Biobank **Location:** England **Study Dates:** Up to July 26, 2020 **Inclusion Criteria:** Participants aged 37-73 years recruited between March 13, 2006 – October 1, 2010 from assessment centers across England. COVID-19 diagnosis was made based on a positive RT-PCR test. **Exclusion Criteria:** Participants who died before January 2020 or were not from England.	**Medical Condition, n/N (%):** Physical activity: NR Walking as transport: NR Number days/week walked≥10 min: NR Time spent watching TV: NR **Control/Comparison Group, n/N (%):** No physical activity: NR No walking as transport: NR No comparison for number day/week walked ≥10 min or time spent watching TV as these are continuous variables	**Medical Condition(s):** NR *Physical activity:* within the last 4 weeks measured at baseline recruitment (March 13, 2006 – October 1, 2010) *Walking as transport:* ND *Time spent watching TV:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ICD-10 code U07.2 (recorded up to June 28, 2020) *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; model included age, sex, UK Biobank assessment center, Townsend deprivation index, ethnicity, BMI, smoking, and long-standing illness* *Mortality:* Physical activity (past 4 weeks): • aHR: 0.97 (95% CI: 0.76 – 1.23), p = 0.79 Walking as transport: • aHR: 1.06 (95% CI: 0.85 – 1.32), p = 0.61 Time spent watching TV: • aHR: 1.04 (95% CI: 0.98 – 1.10), p = 0.18 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Maltagliati[15] **Publication:** 2021	**Population:** N =3,139 COVID-19 positive, n = 266 **Setting:** NR	**Condition, n/N (%):** Physical activity, any intensity: • More than once a week: 1161/3139 (37.0%)	**Condition(s):** *Muscle strength:* hand grip strength measured by handheld dynamometer	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: age, height, sex, body mass index, cardiovascular disease, diabetes, cancer, chronic kidney*

Study	Population and Setting	Exposure	Definitions	Results
Data Extractor: CS **Reviewer:** AH **Study Design:** Cohort **Study Objective:** To test the association between physical activity and the odds of COVID-19 hospitalization, and to investigate whether this association is explained by established risk factors for COVID-19 hospitalization. **IVA Score:** 20 (Moderate)	**Data Source:** Longitudinal, cross-national information from people aged 50 or older; SHARE and SHARE COVID-19 **Location:** 27 European countries **Study Dates:** NR **Inclusion Criteria:** Participants 50 years or older who completed at least one health questionnaire in SHARE over the 7 survey waves (2004-2017), and provided an answer to "Have you, or anyone close to you, been tested for the coronavirus and the result was positive, meaning that the person had the COVID disease?" from the COVID-19 questionnaire. Patients who did not answer that question but indicated they were hospitalized for COVID-19 were also included in the analysis.	• Once a week: 541/3139 (17.2%) • Once to three times a month: 270/3139 (8.6%) Muscle strength: NR **Control/Comparison Group, n/N (%):** Physical activity, any intensity: • Hardly ever or never: 1167/3139 (37.2%) Low muscle strength: NR	**Severity Measure(s):** *Physical activity:* self-reported low-to-moderate or vigorous physical activity intensity more than once a week, once a week, one to three times a month, or hardly ever/never **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* self-reported hospitalization due to COVID-19 *Non-elective readmissions*: NR **Comments:** None	*disease, rheumatoid arthritis, respiratory disease, and muscle strength* *OR: Univariable (Univariate) Logistic Regression* *Hospitalization:* Muscle strength: • aOR: 0.59 (95% CI: 0.39 – 0.89), p = 0.01 **Severity of Condition:** *Hospitalized, n/N (%):* Physical activity, more than once a week: • aOR: 0.64 (95% CI: 0.32 – 1.20), p = 0.17 • OR: 0.41 (95% CI: 0.22 – 0.74), p < 0.01 • More than once a week: 15/66 (23.0%) • Hardly ever or never (ref): 36/66 (54.5%) Physical activity, once a week: • aOR: 0.78 (95% CI: 0.36 – 1.56), p = 0.50 • OR: 0.59 (95% CI: 0.28 – 1.16), p = 0.15 • Once a week: 10/66 (15.2%) • Hardly ever or never (ref): 36/66 (54.5%) Physical activity, one to three times a month: • aOR: 0.76 (95% CI: 0.26 – 1.84), p = 0.58 • OR: 0.59 (95% CI: 0.20 – 1.29), p = 0.28 • One to three times a month: 5/66 (7.6%) • Hardly ever or never (ref): 36/66 (54.5%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
	Exclusion Criteria: Participants without all covariate measurements recorded.			
Author: Okeahalam[3] **Publication:** 2020 **Data Extractor:** MM **Reviewer:** MC **Study Design:** Cross-sectional **Study Objective:** To determine risk factors for cumulative COVID-19 deaths and cases per million in all countries in the continent of Africa. **IVA Score:** 21 (Moderate)	**Population:** N = 53 countries **Setting:** Population **Data Source:** WHO Global Health Observatory Repository and *2018* Global Reference List of 100 Core Health Indicators **Location:** Africa **Study Dates:** NR **Inclusion Criteria:** NR **Exclusion Criteria:** NR	**Condition, n/N (%):** Insufficient physical activity: NR **Control/Comparison Group, n/N (%):** Sufficient physical activity: NR	**Condition(s):** *Insufficient physical activity*: adults who do not meet the WHO recommendations on PA for health: 150 min of moderate intensity, or 75 min of vigorous intensity PA per week **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *aOR: Multivariable logistic regression; included model variables: age, sex, mortality by cause, morbidity, nutrition, environmental risk factors, noncommunicable diseases, immunization, essential health services, utilization and access, health workforce, health information and health financing* *OR: Univariable (Univariate) Logistic Regression* *SE: Standard error* *Mortality:* • aOR = 0.08 (SE: 0.03), p = 0.01 • OR: 0.12 (SE: 0.02), p < 0.01 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
Author: Pinto[9] **Publication:** 2021 **Data Extractor:** MM **Reviewer:** MW/CS **Study Design:** Cohort **Study Objective:** To investigate the possible associations between physical activity (PA) levels and clinical outcomes among hospitalized patients with moderate to severe COVID-19. **IVA Score:** 22 (Moderate)	**Population:** N = 209 **Setting:** Hospital **Data Source:** Medical records **Location:** Brazil **Study Dates:** June 2 – October 7, 2020 **Inclusion Criteria:** Patients aged 18 years or older with a diagnosis of COVID-19 by PCR or CT scan and a diagnosis of flu syndrome, i.e., presenting with respiratory rate of 24 breaths per minute and saturation of <93% on room air, or have risk factors for complications, such as heart disease, diabetes mellitus, systemic arterial hypertension, neoplasms, immunosuppression, pulmonary tuberculosis, and obesity, followed by COVID-19 confirmation were included.	**Medical Condition, n/N (%):** Physical activity levels: 209/209 (100%) **Control/Comparison Group, n/N (%):** NA	**Medical Condition(s):** *Physical activity levels*: assessed using the Baecke Questionnaire of Habitual Physical Activity consisting of 3 sections: work, sport, and leisure-time activity. Scores in each section range between 0 and 5, where higher scores indicate a higher PA level. A total activity index is obtained by summing all scores (maximum score = 15) **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* mechanical ventilation *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None.	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression; included model variables: age, sex, BMI, and presence of comorbidities* *OR: Univariable (Univariate) Logistic Regression* *Mortality:* Work index • aOR: 1.10 (95% CI: 0.30 – 3.80), p = 0.94 • OR: 2.40 (95% CI: 0.90 – 6.50), p = 0.07 Sport index • aOR: 0.40 (95% CI: 0.10 – 1.50), p = 0.19 • OR: 0.90 (95% CI: 0.30 – 2.30), p = 0.81 Leisure-time index • aOR: 0.50 (95% CI: 0.10 – 2.10), p = 0.34 • OR: 1.20 (95% CI: 0.40 – 3.30), p = 0.76 Total activity index • aOR: 0.70 (95% CI: 0.40 – 1.30), p = 0.27 • OR: 1.30 (95% CI: 0.80 – 2.10), p = 0.27 *ICU admission:* Work index: • aOR: 1.10 (95% CI: 0.60 – 2.00), p = 0.70 • OR: 1.50 (95% CI: 0.9 – 2.4), p = 0.10 Sport index: • aOR: 0.90 (95% CI: 0.50 – 1.80), p = 0.87 • OR: 1.10 (95% CI: 0.70 – 2.00), p = 0.64 Leisure-time index • aOR: 0.50 (95% CI: 0.30 – 1.10), p = 0.08 • OR: 0.80 (95 % CI: 0.40 – 1.30), p = 0.34 Total activity index: • aOR: 0.90 (95% CI: 0.70 – 1.20), p = 0.46 • OR: 1.10 (95% CI: 0.80 – 1.40), p = 0.47

Study	Population and Setting	Exposure	Definitions	Results
	Exclusion Criteria: Patients were excluded if they were unable to read and sign the written informed consent, were already admitted under invasive mechanical ventilation, had a previous vitamin D3 supplementation (>1000 IU/day), have renal failure requiring dialysis, pregnant or lactating women, and/or had an expected hospital discharge of less than 24 h from admission.			*Ventilation, n/N (%), or Median (IQR):* Work index: • aOR: 0.60 (95% CI: 0.30 – 1.20), p = 0.18 • OR: 1.1 (95% CI: 0.60 – 1.90), p = 0.81 Sport index: • aOR: 0.90 (95% CI: 0.40 – 2.00), p = 0.84 • OR: 1.10 (95% CI: 0.50 – 2.10), p = 0.85 Leisure-time index: • aOR: 0.70 (95% CI: 0.30 – 1.60), p = 0.41 • OR: 0.90 (95 % CI: 0.40 – 1.70), p = 0.68 Total activity index • aOR: 0.80 (95% CI: 0.50 – 1.20), p = 0.21 • OR: 1.00 (95% CI: 0.70 – 1.40), p = 0.97 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Prado-Galbarro[10] **Publication:** 2020 **Data Extractor:** CS **Reviewer:** TR **Study Design:** Cohort	**Population:** N = 15,529 **Setting:** Healthcare units and hospitals **Data Source:** Nationwide COVID-19 data from the Mexican Secretary of Health **Location:** Mexico **Study Dates:** January 13-April 28, 2020	**Condition, n/N (%):** Walking: NR **Control/Comparison Group, n/N (%):** Driving or public transport: NR	**Condition(s):** *Walking:* as the participant's main mode of transport **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio; Cox proportional hazards ratio; included model variables: NR* *Mortality, n/N (%):* Walking, overall sample: • aHR: 0.95 (95% CI: 0.91 – 1.00), p = 0.04 Walking, outpatients: • aHR: 0.94 (95% CI: 0.90 - 0.99), p = 0.02 Walking, hospitalized patients: • aHR: 0.99 (95% CI: 0.86 – 1.14), p = 0.87

Study	Population and Setting	Exposure	Definitions	Results
Study Objective: To evaluate the association of the chronic disease profile and indigenous ethnicity on the poor prognosis of outpatients with COVID-19 and hospitalized patients in Mexico. **IVA Score:** 25 (Moderate)	**Inclusion Criteria:** Patients in the nationwide COVID-19 data set with confirmed SARS-CoV-2 using RT-PCR. **Exclusion Criteria:** NR		*Non-elective readmissions*: NR **Comments:** None	Living in Mexico City or the State of Mexico and walking as the mode of transport (rather than driving or getting public transport) were negatively associated with mortality after SARS-CoV-2 infection. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Salgado-Aranda[6] **Publication:** 2021 **Data Extractor:** MW **Reviewer:** MC **Study Design:** Cohort study **Study Objective:** To analyze retrospectively the influence of baseline physical activity level (BPAL) on the	**Population:** N=520 **Setting:** Hospital **Data Source:** Telephone interviews **Location:** Spain **Study Dates:** February 15 - April 15, 2020 **Inclusion Criteria:** Consecutive patients between 18 and 70 years of age who were hospitalized in the center between the study dates during Spain's first wave of	**Condition, n/N (%):** Sedentary group: 297/520 (57.1%) **Control/Comparison Group, n/N (%):** Active group: 223/520 (42.9%)	**Condition(s):** *Sedentary group:* Sedentary or light physical activity, never to light physical activity each week *Active group:* Moderate activity <30 minutes/day 5 days/week to vigorous physical activities (PA) for <20 minutes/day <3 days/week, and ≥30 minutes/day of moderate PA ≥ 5 days/week, or ≥20 minutes/day of vigorous PA ≥3 days/week **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* Critical care unit admission	**Severe COVID-19:** *aHR: Adjusted Hazard Ratio* *HR: Hazard Ratio* *Mortality (among all COVID-19 patients):* Sedentary lifestyle: • aHR: 5.91 (95% CI: 1.80 - 19.41), p = 0.003 • HR: 8.13 (95% CI: 2.91 - 22.70), p < 0.001 • Sedentary group: 41/297 (13.8%) • Active group: 4/223 (1.8%) • p<0.01 *ICU admission, n/N (%):* • Sedentary group: 26/297 (8.8%) • Active group: 14/223 (6.3%) • p = 0.29 *Invasive mechanical ventilation, n/N (%):* • Sedentary group: 23/297 (7.7%) • Active group: 10/223 (4.5%)

Study	Population and Setting	Exposure	Definitions	Results
course of SARS-CoV-2 and COVID-19 mortality. **IVA Score:** 23 (Moderate)	the pandemic were included. **Exclusion Criteria:** Patients who were managed on an outpatient basis, who died before obtaining medical attention. patients for in whom the diagnosis of COVID-19 could not be confirmed by PCR, patients with compatible symptomatology but negative polymerase chain reaction (PCR) and elderly patients (over 70 years old).		*Intubation:* NR *Ventilation:* Invasive and non-invasive mechanical ventilation *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	• p = 0.14 *Non-invasive mechanical ventilation, n/N (%):* • Sedentary group: 48/297 (16.2%) • Active group: 50/223 (22.4%) • p = 0.07 **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Sallis[22] **Publication:** 2021 **Data Extractor:** MC **Reviewer:** MM **Study Design:** Cohort **Study Objective:** To compare hospitalization rates, intensive	**Population:** N = 48,440 **Setting:** Kaiser Permanente Southern California (KPSC) **Data Source:** Electronic health records **Location:** California, USA **Study Dates:** January 1 - October 21, 2020	**Condition, n/N (%):** Consistently inactive: 6,984/48,440 (14.4%) Inconsistently active: 38,338/48,440 (79.2%) **Control/Comparison Group, n/N (%):** Consistently active: 3,118/48,440 (6.4%)	**Condition(s):** NR **Severity Measure(s):** Exercise level: • *Consistently inactive: EVS* 0-10 minutes of activity per week at all assessments • *Inconsistently active: EVS* 11-149 minutes of activity per week or those with variability in their EVS measures • *Consistently active: EVS* ≥150 minutes of activity per week at all assessments during the study period	**Severe COVID-19:** NR **Severity of Condition:** *OR: odds ratio* *Mortality, n/N (%):* Consistently active [reference]: • 11/3,118 (0.4%) Consistently inactive: • OR: 2.49 (95% CI: 1.33 – 4.67) • 170/6,984 (2.4%) Inconsistently active: • OR: 1.88 (95% CI: 1.02 – 3.47) • 590/38,338 (1.5%) *ICU admission, n/N (%):*

Study	Population and Setting	Exposure	Definitions	Results
care unit (ICU) admissions and mortality for patients with COVID-19 who were consistently inactive, doing some activity or consistently meeting physical activity. **IVA Score:** 24 (Moderate)	**Inclusion Criteria:** KPSC health plan members aged 18 years and older with a positive SARS-CoV-2 test or diagnosis between the study dates were included. Participants were also required to have at least three outpatient visits with an exercise vital sign (EVS) measure between March 19, 2018 and March 19, 2020 to be included. **Exclusion Criteria: NR**		**Clinical Marker:** NR **Outcome Definitions:** *Mortality:* ND *ICU admission:* ND *Intubation:* NR *Ventilation:* NR *Hospitalization:* *Non-elective readmissions*: NR **Comments:** None	Consistently active [reference]: • 32/3,118 (1%) Consistently inactive: • OR: 1.73 (95% CI: 1.18 – 2.55) • 195/6,984 (2.8%) Inconsistently active: • OR: 1.58 (95% CI: 1.10 – 2.27) • 972/38,338 (2.5%) *Hospitalization, n/N (%):* Consistently active [reference]: • 99/3,118 (3.2%) Consistently inactive: • OR: 2.26 (95% CI: 1.81 – 2.83) • 732/6,984 (10.5%) Inconsistently active: • OR: 1.89 (95% CI: 1.53 – 2.33) • 3,405/38,338 (8.9%) **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR
Author: Urashima[4] **Publication:** 2020 **Data Extractor:** MC	**Population:** N = 173 countries **Setting:** NR **Data Source:** Open resources, Worldometer COVID-19 Data	**Condition, n/N (%):** Insufficient physical activity: NR **Control/Comparison Group, n/N (%):** NR	**Condition(s):** *Insufficient physical activity:* Percent of defined population attaining less than 150 minutes of moderate-intensity physical activity per week, or less than 75 minutes of vigorous-intensity physical activity per week, or equivalent	**Severe COVID-19:** *aR^2: Multi-linear regression adjusting for PCR-test numbers and COVID-19 morbidity per million population* *Mortality:* • Insufficient physical inactivity had a strong and positive association with morbidity, but not with mortality (aR^2: 0.7270)

Study	Population and Setting	Exposure	Definitions	Results
Reviewer: MW **Study Design:** Ecological **Study Objective:** To explore whether recent Bacillus Calmette–Guérin (BCG) vaccine coverage is associated with COVID-19 morbidity and/or mortality rates, using linear regression models to explore associations between the two continuous random variables adjusted for a variety of potential confounders, such as median age and body mass index (BMI) in individual countries. **IVA Score:** 21 (Moderate)	**Location:** 173 countries **Study Dates:** Unknown - July 17,2020 **Inclusion Criteria:** Only countries that had data of both total deaths and BCG vaccine coverage were included for analyses in this study. **Exclusion Criteria:** NR		**Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* Total COVID-19-related deaths per million population *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** Non-elective readmissions: NR

Study	Population and Setting	Exposure	Definitions	Results
Author: Wang[5] **Publication:** 2021 **Data Extractor:** TR **Reviewer:** CS/DOS **Study Design:** Ecological study **Study Objective:** To investigate the worldwide association between lifestyle-related disease burden and COVID-19 mortality. **IVA Score:** 15 (High)	**Population:** N =186 countries **Setting:** NR **Data Source:** 2015/2016 WHO handbooks, 2019 World bank, 2019 International Diabetes Federation, and Worldometer **Location:** Worldwide **Study Dates:** through August 20, 2020 **Inclusion Criteria:** Countries with data on mortality due to COVID-19 and at least one of the variables (lifestyle-related factors of hypertension, hyperlipidaemia, smoking, overweight, diabetes, and insufficient physical activity, age ≥ 65). **Exclusion Criteria:** NR	**Condition, n/N (%):** Insufficient physical activity: NR **Control/Comparison Group, n/N (%):** NA	**Condition(s):** *Insufficient physical activity:* ND **Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* deaths per million population *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None *Mortality:* deaths per million population *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* NR *Non-elective readmissions*: NR **Comments:** None	**Severe COVID-19:** *R^2: Bonferroni multiple comparison test* *Mortality:* Insufficient physical activity: • R^2: 0.04, p = 0.01 COVID-19 mortality showed significant positive association with insufficient physical activity. **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR Non-elective readmissions: NR
Author: Yuan[1] **Publication:** 2021	**Population:** N = 164 **Setting:** Tumor Center at one hospital	**Condition, n/N (%):** Physical inactivity: 103/164 (62.8%)	**Condition(s):** *Physical inactivity:* <150 min/week of moderate activity or <75 min/week of vigorous activity	**Severe COVID-19:** *Mortality, n/N (%):* • *Physical inactivity:* 6/103 (5.8%)

Study	Population and Setting	Exposure	Definitions	Results
Data Extractor: AH **Reviewer:** DOS **Study Design:** Cohort **Study Objective:** To investigate the association between pre-existent physical inactivity and severe COVID-19 retrospectively. **IVA Score:** 18 (Moderate)	**Data Source**: Digital database of medical records **Location:** China **Study Dates:** February 15 – March 14, 2020 **Inclusion Criteria:** Consecutive hospitalized patients with laboratory confirmation of SARS-CoV-2 via real-time RT-PCR of viral RNA extracted from nasopharynx and oropharynx swab. **Exclusion Criteria:** NR	**Control/Comparison Group, n/N (%):** Physical activity: 61/164 (37.2%)	**Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* NR *ICU admission:* NR *Intubation:* NR *Ventilation:* Invasive ventilation *Hospitalization:* Hospitalized due to COVID-19. *Non-elective readmissions*: NR **Comments:** None	• *Physical activity:* 0/61 (0.0%) • p = 0.09 *Ventilation, n/N (%):* • *Physical inactivity:* 3/103 (2.9%) • *Physical activity:* 0/61 (0.0%) • p = NR **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR
Author: Zhang[8] **Publication:** 2020 **Data Extractor:** TR **Reviewer:** DOS **Study Design:** Prospective cohort **Study Objective:**	**Population:** N = 339,256 COVID-19+, n = 1,746 **Setting:** Community **Data Source:** UK Biobank **Location:** United Kingdom **Study Dates:** March 16 – June 29, 2020	**Condition, mean (SD):** Moderate-to-vigorous physical activity (MVPA), MET-min/week: 990.4 (1310.8) Acceleration vector magnitude physical activity (AMPA), milli-gravities: 26.7 (8.6) (n = 215) **Control/Comparison Group, mean (SD):** NA as MVPA and AMPA are continuous variables	**Condition(s):** *MVPA:* Self-reported physical activity mainly acquired during 2006 to 2010 through touch screen questionnaire; calculated by taking the sum of total min/week of moderate physical activity multiplied by four and the total number of vigorous physical activity min/week multiplied by eight *AMPA*: collected from participants wearing an accelerometer for 7 days between 2013 and 2015	**Severe COVID-19:** *aOR: Adjusted odds ratio; multivariable logistic regression model includes age, sex, waist circumference, hip circumference, BMI, and smoking status* *OR: Univariable (Univariate) Logistic Regression* *Mortality, Mean (SD):* MVPA, MET-min/week: • aOR: 1.00 (95% CI: 0.90 – 1.11), p = 0.97 • OR: 1.03 (95% CI: 0.94 – 1.14), p = 0.49 • COVID-19 deaths: 1017.0 (1057.9) • COVID-19 survivals: NR

Study	Population and Setting	Exposure	Definitions	Results
To analyze whether PA influences the risk of COVID-19 in a prospective observational study by adjusting measures of obesity and smoking status. **IVA Score:** 23 (Moderate)	**Inclusion Criteria:** Patients included in the prospective cohort were aged 40 to 69 years. COVID-19 inpatients included all inpatients with at least one positive SARS-CoV-2 testing result. COVID-19 outpatients included outpatients who tested SARS-CoV-2 positive at least once. Controls consisted of participants who have not tested positive for SARS-CoV-2 and have not died of COVID-19 **Exclusion Criteria:** Participants were excluded due to consent withdrawals, non-white British ethnic background, sex mismatch, sex aneuploidy, high missing rate/outlier, and kinship inference. Participants who tested negative (as these results could have been false negatives), those who are not from England (as all SARS-CoV-2 test		**Severity Measure(s):** NR **Clinical Marker:** NR **Outcome Definitions:** *Mortality:* deaths caused by clinical and epidemiological diagnosed COVID-19 (both primary and contributory causes of death) *ICU admission:* NR *Intubation:* NR *Ventilation:* NR *Hospitalization:* inpatient COVID-19 cases *Non-elective readmissions*: NR **Comments:** None	AMPA, milli-gravities (n = 36): • aOR: 0.74 (95% CI: 0.48 – 1.14), p = 0.17 • OR: 0.56 (95% CI: 0.38 – 0.83), p < 0.01 • COVID-19 deaths: 24.1 (8.1) • COVID-19 survivals: NR *Hospitalization, Mean (SD):* MVPA, MET-min/week: • aOR: 1.05 (95% CI: 0.98 – 1.11), p = 0.17 • OR: 1.05 (95% CI: 0.99 – 1.11), p = 0.10 • COVID-19 inpatients: 1039.0 (1356.1) • COVID-19 outpatients: 898.7 (1236.7) AMPA, milli-gravities (n = 201): • aOR: 0.85 (95% CI: 0.69 – 1.05), p = 0.13 • OR: 0.83 (95% CI: 0.68 – 1.00, p = 0.06 • COVID-19 inpatients: 26.6 (8.9) • COVID-19 outpatients: 27.4 (8.1) **Severity of Condition:** NR **Duration of Condition:** NR **Comorbid Conditions:** NR **Risk Markers:** NR **Long-term Sequelae:** NR

Study	Population and Setting	Exposure	Definitions	Results
	results were provided by NHS England only), and those who died before January 1, 2020 were excluded from the non-COVID-19 control group.			

B.3.c. Internal Validity Assessments of Extracted Studies

Table 6 Internal Validity Assessments of Extracted Studies Reporting the Association Between Physical Activity / Inactivity and Severe COVID-19 Outcomes.

	Author Publication Year	Ahmadi 2021[19]	Brandenburg 2020[23]	Burden 2020[2]	Cho 2020[20]	Cunningham 2021[11]	de Souza 2020[17]
	Outcome(s)	Mortality	Hospitalization	Mortality	Mortality	Mortality	Intubation, Hospitalization
Domain	**Signaling question**						
Study Elements	Design appropriate to research question	1	1	1	1	0	1
	Well described population	1	1	1	1	0	1
	Well described setting	0	0	1	1	1	1
	Well described intervention/ exposure	1	1	0	1	1	1
	Well described control/ comparator	1	1	0	1	1	1
	Well described outcome	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	0	1	0	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	0	1
	Attrition <10-15% of population	1	1	1	1	0	1
	Attrition appropriately analyzed	1	1	1	0	0	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	1	1	0	0	0
	Measure of outcome is valid	1	1	1	1	1	0
	Fidelity to intervention is measured	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1
	Adequately powered to detect result	1	0	0	1	0	1

	Author **Publication Year**	Ahmadi 2021[19]	Brandenburg 2020[23]	Burden 2020[2]	Cho 2020[20]	Cunningham 2021[11]	de Souza 2020[17]
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1
	Data collection methods appropriate	1	0	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1	1
	Confidence interval is narrow	0	0	0	1	0	1
Confounding	Potential confounders identified	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	1	1	0	0
	Adjustment for confounders in data analysis phase	1	1	1	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	0	1	1	1
SCORE	Threat to internal validity	24	22	21	25	17	24
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	High	Moderate

	Author **Publication Year**	Hamer. M. 2020[24]	Hamer 2020[13]	Lassale 2020[25]	Latorre-Roman 2021[18]	Lee SW 2021[21]	Li 2020[12]
	Outcome(s)	Hospitalization	Hospitalization	Hospitalization	Hospitalization	Mortality	Mortality
Domain	**Signaling question**						

	Author **Publication Year**	Hamer. M. 2020[24]	Hamer 2020[13]	Lassale 2020[25]	Latorre-Roman 2021[18]	Lee SW 2021[21]	Li 2020[12]
Study Elements	Design appropriate to research question	1	1	1	1	1	0
	Well described population	1	1	1	1	1	1
	Well described setting	1	1	1	1	1	1
	Well described intervention/ exposure	1	1	0	1	1	0
	Well described control/ comparator	1	0	0	0	1	0
	Well described outcome	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	0	1	1	1	1
	Attrition <10-15% of population	1	0	0	1	1	1
	Attrition appropriately analyzed	1	0	0	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	0	1	0	1	1	0
	Measure of outcome is valid	1	1	0	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1
	Adequately powered to detect result	0	0	1	0	1	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1	1
	Data collection methods appropriate	1	1	1	0	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1	1
	Confidence interval is narrow	0	1	0	0	0	0

	Author **Publication Year**	Hamer. M. 2020[24]	Hamer 2020[13]	Lassale 2020[25]	Latorre-Roman 2021[18]	Lee SW 2021[21]	Li 2020[12]
Confounding	Potential confounders identified	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	1	1	1	1	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	0
SCORE	Threat to internal validity	23	21	19	22	25	18
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

	Author **Publication Year**	Li 2021[16]	Lobelo 2021[14]	Madakkattel 2020[7]	Maltagliati 2021[15]	Okeahalam 2020[3]
	Outcome(s)	Hospitalization	Hospitalization	Hospitalization	Hospitalization	Mortality
Domain	**Signaling question**					
Study Elements	Design appropriate to research question	0	1	1	1	1
	Well described population	1	1	1	1	0
	Well described setting	0	1	1	0	0
	Well described intervention/ exposure	0	1	0	1	0
	Well described control/ comparator	1	1	0	1	0
	Well described outcome	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	0	1	1	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1

	Author **Publication Year**	Li 2021[16]	Lobelo 2021[14]	Madakkattel 2020[7]	Maltagliati 2021[15]	Okeahalam 2020[3]
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1
	Attrition <10-15% of population	1	1	1	1	1
	Attrition appropriately analyzed	1	1	1	1	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	0	0	0	1
	Measure of outcome is valid	1	1	1	0	1
	Fidelity to intervention is measured	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0
	Prospective study	1	1	1	1	1
	Adequately powered to detect result	1	0	0	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0	0	0	0
	Study participant blinded	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0
	Data collection methods described in sufficient detail	1	1	1	1	1
	Data collection methods appropriate	1	1	1	1	1
	Sufficient follow up to detect outcome	1	1	1	0	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1
	Confidence interval is narrow	0	0	0	0	0
Confounding	Potential confounders identified	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	1
	Adjustment for confounders in data analysis phase	1	1	1	1	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1
Other Bias	No other sources of bias	0	1	1	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	0	1	1
SCORE	Threat to internal validity	20	23	20	20	21
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate

	Author Publication Year	Pinto 2021[9]	Prado-Galbarro 2020[10]	Salgado-Aranda 2021[6]	Sallis 2021[22]	Urashima 2020[4]	Wang 2021[5]
	Outcome(s)	Mortality, ICU admission, ventilation	Mortality	Mortality, ICU admission, Ventilation	Mortality, ICU admission, Hospitalization	Mortality	Mortality
Domain	**Signaling question**						
Study Elements	Design appropriate to research question	1	1	1	1	1	0
	Well described population	0	1	1	1	1	1
	Well described setting	1	1	1	1	0	0
	Well described intervention/ exposure	1	1	1	1	1	0
	Well described control/ comparator	0	1	1	1	0	0
	Well described outcome	1	1	1	1	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1	1	1	0	1
Selection Bias: Sampling	Randomization appropriately performed	0	0	0	0	0	0
	Allocation adequately concealed	0	0	0	0	0	0
	Population sampling appropriate to study design	1	1	1	1	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	1	1	1	1	1	0
	Attrition <10-15% of population	1	1	1	1	1	0
	Attrition appropriately analyzed	1	1	1	1	1	0
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	1	0	1	1	1	0
	Measure of outcome is valid	1	1	1	1	1	1
	Fidelity to intervention is measured	0	0	0	0	0	0
	Fidelity to intervention is valid	0	0	0	0	0	0
	Prospective study	1	1	1	1	1	1
	Adequately powered to detect result	0	1	0	0	1	0
Information Bias:	Outcome assessor blinded	0	0	0	0	0	0
	Study participant blinded	0	0	0	0	0	0
	Investigator/ data analyst blinded	0	0	0	0	0	0

	Author **Publication Year**	Pinto 2021[9]	Prado-Galbarro 2020[10]	Salgado-Aranda 2021[6]	Sallis 2021[22]	Urashima 2020[4]	Wang 2021[5]
Performance & Detection	Data collection methods described in sufficient detail	1	1	1	1	1	1
	Data collection methods appropriate	1	1	0	1	1	1
	Sufficient follow up to detect outcome	1	1	1	1	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1	1	1	1	1
	Appropriate statistical analyses are conducted correctly	1	1	1	1	1	1
	Confidence interval is narrow	0	1	0	0	0	0
Confounding	Potential confounders identified	1	1	1	1	1	1
	Adjustment for confounders in study design phase	0	0	0	0	0	0
	Adjustment for confounders in data analysis phase	1	1	1	1	1	0
Reporting Bias	All pre-specified outcomes are adequately reported	1	1	1	1	1	1
Other Bias	No other sources of bias	1	1	1	1	0	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1	1	1	1	1
SCORE	Threat to internal validity	22	25	23	24	21	15
	Low, Moderate, High	Moderate	Moderate	Moderate	Moderate	Moderate	High

	Author **Publication Year**	Yuan 2021[1]	Zhang 2020[8]
	Outcome(s)	Mortality, ventilation	Mortality, hospitalization
Domain	**Signaling question**		
Study Elements	Design appropriate to research question	1	1
	Well described population	1	1
	Well described setting	1	1

	Author **Publication Year**	Yuan 2021[1]	Zhang 2020[8]
	Well described intervention/ exposure	1	1
	Well described control/ comparator	1	1
	Well described outcome	1	1
	Clear timeline of exposures/ interventions and outcomes	1	1
Selection Bias: Sampling	Randomization appropriately performed	0	0
	Allocation adequately concealed	0	0
	Population sampling appropriate to study design	1	1
Selection Bias: Attrition	Attrition not significantly different between groups	0	1
	Attrition <10-15% of population	0	1
	Attrition appropriately analyzed	0	1
Information Bias: Measurement and Misclassification	Measure of intervention/ exposure is valid	0	0
	Measure of outcome is valid	1	1
	Fidelity to intervention is measured	0	0
	Fidelity to intervention is valid	0	0
	Prospective study	0	1
	Adequately powered to detect result	0	0
Information Bias: Performance & Detection	Outcome assessor blinded	0	0
	Study participant blinded	0	0
	Investigator/ data analyst blinded	0	0
	Data collection methods described in sufficient detail	1	1
	Data collection methods appropriate	1	1
	Sufficient follow up to detect outcome	1	1
Information Bias: Analytic	Appropriate statistical analyses for collected data	1	1
	Appropriate statistical analyses are conducted correctly	1	1
	Confidence interval is narrow	0	0
Confounding	Potential confounders identified	1	1
	Adjustment for confounders in study design phase	0	0

	Author **Publication Year**	Yuan 2021[1]	Zhang 2020[8]
	Adjustment for confounders in data analysis phase	0	1
Reporting Bias	All pre-specified outcomes are adequately reported	1	1
Other Bias	No other sources of bias	1	1
COI	Funding sources disclosed and no obvious conflict of interest	1	1
SCORE	Threat to internal validity	18	23
	Low, Moderate, High	Moderate	Moderate

C. References

D. Abbreviations

Table 7 Abbreviations.

Acronym	Full
95% CI	95% confidence interval
aHR	adjusted hazard ratio
aOR	adjusted odds ratio
aPR	adjusted prevalence ratio
aRR	adjusted risk ratio
BCG	bacille Calmette–Guérin
BMI	body mass index
BPAL	baseline physical level
CDC	centers for disease control and prevention
CI	confidence interval
COI	conflict of interest
COVID-19	2019 Novel Coronavirus
CR	cardiorespiratory
CSSE	center for systems science and engineering
CVD	cardiovascular disease
ECDC	European Centre for disease prevention and control
ECMO	extracorporeal membrane oxygenation
EHR	electronic health record
EMR	electronic medical record
EVS	exercise vital sign
GDPP	gross domestic product per person
GWAS	genome-wide association study
HAQ	healthcare access and quality index
HIC	high-income country
HR	hazard ratio
ICD10	international classification of diseases 10

ICU	intensive care unit
IPAQ	international physical activity questionnaire
IQR	interquartile range
IU	international unit
IVA	internal validity assessments
KDCA	Korean disease control and prevention agency
KPSC	Kaiser Permanente southern California
LIC	low-income country
MET	metabolic equivalent of task
MIC	middle-income country
MR	mortality rate
MVPA	moderate-to-vigorous physical activity
NA	not applicable
ND	not defined
NHS	national health service
NR	not reported
OR	odds ratio
PA	physical activity
PC	personal computer
PCR	polymerase chain reaction
PECO	population, exposure, comparator, and outcomes
PR	prevalence ratio
PUI	person under investigation
R^2	r-squared
RNA	ribonucleic acid
RR	risk ratio
RT-PCR	real time polymerase chain reaction
SD	standard deviation
SDOH	social determinants of health
SE	standard error
SHARE	the survey of health, ageing and retirement in Europe
WHO	world health organization

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