



Muscle strength explains the protective effect of physical activity against COVID-19 hospitalization among adults aged 50 years and older

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ABSTRACT

Physical activity has been proposed as a protective factor for COVID-19 hospitalisation. However, the mechanisms underlying this association are unclear. We examined the association between physical activity and COVID-19 hospitalisation and whether this relationship was explained by risk factors (chronic conditions, weak muscle strength). We used data from adults over 50 years from the Survey of Health, Ageing and Retirement in Europe. The outcome was self-reported hospitalisation due to COVID-19, before August 2020. The main exposure was physical activity, self-reported between 2004 and 2017. Among the 3139 participants included (69.3 ± 8.5 years, 1763 women), 266 were tested positive for COVID-19, 66 were hospitalised. Logistic regression models showed that individuals who engaged in physical activity more than once a week had lower odds of COVID-19 hospitalisation than individuals who hardly ever or never engaged in physical activity (odds ratios = 0.41, 95% confidence interval = 0.22–0.74, $p = .004$). This association between physical activity and COVID-19 hospitalisation was explained by muscle strength, but not by other risk factors. These findings suggest that, after 50 years, engaging in physical activity is associated with lower odds of COVID-19 hospitalisation. This protective effect of physical activity may be explained by muscle strength.

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KEYWORDS

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The coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On 30 January 2020, the COVID-19 outbreak was declared a public international health emergency of international concern, highest level of alarm of the World Health Organization (World Health Organization, 2020a). To reduce the number of hospitalisations and deaths due to COVID-19, a massive effort has been invested on public health measures (World Health Organization, 2020b), pharmacological treatments (Lam et al., 2020) and vaccines (Dong et al., 2020). In the meantime, a large amount of research has quickly identified risk factors for severe COVID-19 (Center for Disease Control and Prevention, 2020). These risk factors include not only older age, male sex, and underlying chronic conditions (i.e., obesity, cardiovascular disease, lung disease, kidney disease, diabetes, and cancer) (Jordan et al., 2020; Li et al., 2020), but also lower physical fitness, as indexed by weaker muscle strength (Cheval, Sieber et al., 2021), by lower maximal exercise capacity (Brawner et al., 2020) or lower walking speed (Yates et al., 2021). However, less attention has been paid to behavioural protective factors, which may yet represent modifiable and low-cost levers to support health policies. In particular, physical activity has recently been suggested as a protective factor for severe

COVID-19 (Burtscher, Millet et al., 2020; Woods et al., 2020; Zbinden-Foncea et al., 2020).

The hypothesised protective effect of physical activity may be explained by at least two pathways. First, physical activity has been associated with a greater functioning of the immune system (Nieman & Wentz, 2019), which may in turn decrease the odds for severe illness following respiratory tracts infections (Gleeson et al., 2011). Second, physical activity can affect underlying chronic conditions that have been identified as risk factors for COVID-19 hospitalisation. Specifically, studies showed that physical activity reduces the risk of developing several chronic conditions including cardiovascular diseases, type 2 diabetes, cancer, and obesity (e.g., Warburton, 2006). Moreover, physical activity, and especially certain forms of exercise, such as resistance training (e.g., Gentil et al., 2020), has been associated with higher physical fitness, as indexed by greater muscle strength (Dodds et al., 2013). These effects of physical activity on chronic conditions or muscle strength, for instance, using resistance training, may indirectly reduce the risk for severe COVID-19.

To the best of our knowledge, only a few studies have assessed the association between physical activity and severe COVID-19, as indexed by risks for hospitalisation (Batty et al., 2020; Halabchi et al., 2021; Hamer et al., 2020; Sallis et al., 2021;

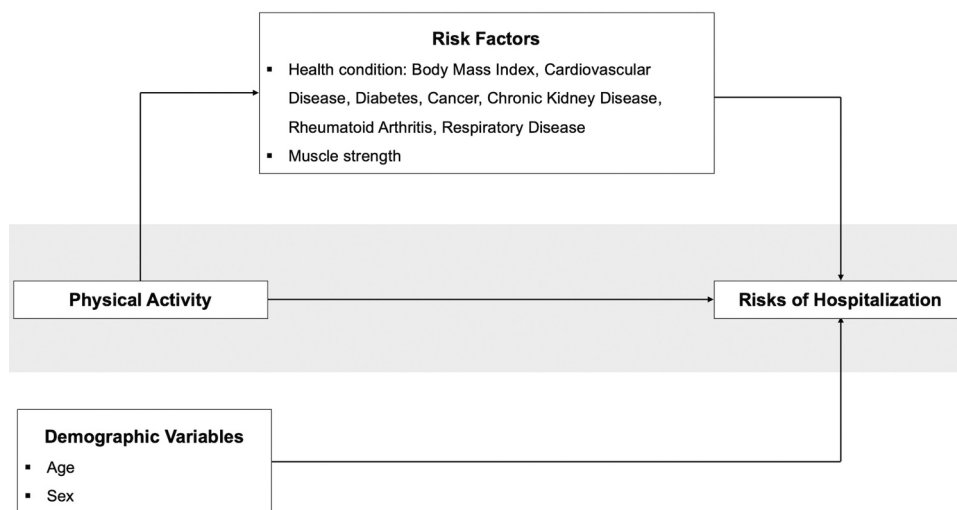


Figure 1. Tested model.

Tavakol et al., 2021). These studies showed that a higher level of physical activity was associated with a lower risk for COVID-19 hospitalisation. However, two of these studies were cross-sectional and conducted in a sample of COVID-19 patients (Halabchi et al., 2021; Tavakol et al., 2021). Moreover, these studies only adjusted for a restricted number of risk factors for COVID-19 hospitalisation and did not include muscle strength (Batty et al., 2020; Halabchi et al., 2021; Hamer et al., 2020; Sallis et al., 2021; Tavakol et al., 2021). Finally, these studies did not assess whether the association between physical activity and COVID-19 hospitalisation was explained by these risk factors. In sum, the mechanisms underlying the association between physical activity and COVID-19 hospitalisation remain unclear.

The objectives of the current study are to test the association between physical activity and the odds of COVID-19 hospitalisation, and to investigate whether this association is explained by established risk factors for COVID-19 hospitalisation (Figure 1).

Materials and methods

Procedure

Data were drawn from the Survey of Health, Ageing and Retirement in Europe (SHARE), a longitudinal population-based study on European adults 50 years of age or older. All procedures and measures of SHARE were described in detail elsewhere (Börsch-Supan et al., 2013). In short, data are collected every two years on seven waves, between 2004 and 2017 using computer-assisted personal interviewing (CAPI) in participants' homes. Wave 3 (2008–2009) was devoted to retrospective data collection related to childhood and life histories (SHARELIFE). This wave did not contain any data related to physical activity and other health-related variables (e.g., cancer, diabetes) and was therefore not used in the current study. In June 2020, a special "SHARE COVID-19" questionnaire was disseminated, assessing social, health, and economic data on ~52,000 individuals. Critically, this questionnaire assessed whether participants were tested positive for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and whether

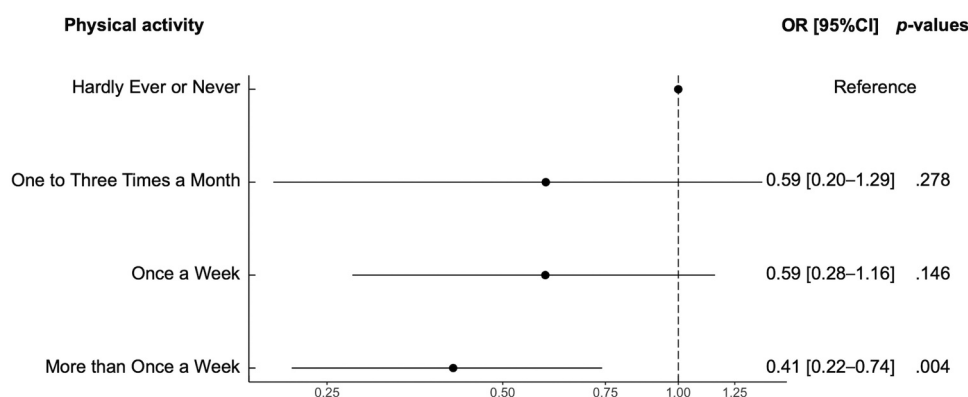


Figure 2. Odds ratios for the different levels of physical activity. Note: OR: Odds Ratio; [95%CI]: 95% Confidence Interval. Odds ratios were computed from unadjusted model (Model 0). *Hardly ever or never* served as the reference category.

they were hospitalised because of this disease. The present study combines data from these two datasets (i.e., SHARE and SHARE COVID-19) to examine the potential association between health-related information (i.e., assessed across the SHARE questionnaires from 2004 to 2017) with COVID-19 hospitalisation (i.e., assessed in the SHARE COVID-19 questionnaire in 2020). To be included in the current analysis, participants had to be 50 years or older, had completed at least one health questionnaire over the seven survey waves, and had provided an answer to the question “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. If the patient indicated that their “spouse or partner” was hospitalized, the spouse or partner was included in the analyses. Patients who did not answer this question but indicated that they were hospitalized for COVID-19 were also included in the analysis.

Measures

Primary outcome: COVID-19 hospitalizations

COVID-19 hospitalisation was measured during the special “SHARE COVID-19” questionnaire, in 2020 and used as an indicator of severe COVID-19. It was determined using the following question: “Have you or anyone close to you been hospitalised due to an infection from the Corona virus?”. If the patient answered “yes”, the interviewer asked who was hospitalised. Individuals who indicated they were hospitalised were included in the analyses as COVID-19 hospitalised. If the patient indicated that their “spouse or partner” was hospitalised, the spouse or partner was included in the analyses.

Exposure: physical activity

Physical activity was measured across the seven waves (except wave 3) of the SHARE survey, and the most recent measure of physical activity was used in the analyses, regardless the timespan between this measure and the potential COVID-19 hospitalisation. This strategy allowed to increase the sample size and the number of participants who were hospitalised after becoming infected with the COVID-19. However, a sensitivity analysis with a more restrictive inclusion criterion was also conducted in order to reduce the timespan between the measure of physical activity and the potential COVID-19 hospitalisation (see sensitivity analysis). Physical activity was assessed using two items, beginning with the stem “We would like to know about the type and amount of physical activity you do in your daily life.”. This stem was intended to ensure that the participants understood that the question focus on usual rather than recent (i.e., last past weeks) physical activity. Then, items, respectively, measured the frequency of low-to-moderate and vigorous physical activity: “How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or doing a walk?” and “How often do you engage in vigorous physical activity, such as sports, heavy housework, or a job that involves physical labor?”. Patients answered on a four-point scale ranging from (1, More than once a week; 2, Once a week; 3, One to three times a month; 4, Hardly ever or never). Scores

were reversed so that so that higher scores reflected higher levels of physical activity. In the main analysis, the upper score between low-to-moderate and vigorous physical activity was retained in the analysis. This variable was treated as a four-level categorical variable, with *Hardly ever, or never* serving as the reference category. This two-item scale has been widely used to predict multiple health outcomes, including, for example, chronic diseases (De Souto Barreto et al., 2017), cognitive functions (Cheval, Orsholits et al., 2020; Cheval et al., 2019), depressive symptoms (Boisgontier et al., 2020) or diabetes (Cheval, Cheval, Maltagliati et al., 2021). Moreover, similar one- or two-items scales have provided acceptable validity regarding the assessment of physical activity (Milton et al., 2011), including among older adults (Gill et al., 2012).

Other risk factors

We included three covariates related to participants sociodemographic characteristics: *Age* (in 2020, when answering to the SHARE COVID-19 questionnaire), *height*, and *sex* (male, female). Height was adjusted to ensure that the associations between muscle strength and COVID-19 would not simply reflect differences in height (Wearing et al., 2018). We also included eight covariates related to the previously established risk factors for COVID-19 hospitalisation: *higher body mass index* (BMI), *cardiovascular disease* (heart attack, including myocardial infarction or coronary thrombosis or any other cardiovascular problem including congestive heart failure, high blood cholesterol, high blood pressure or hypertension, stroke or cerebral vascular disease), *diabetes*, *cancers*, *chronic kidney disease*, *rheumatoid arthritis*, *respiratory disease*, and *muscle strength*.

Muscle strength was indexed by hand grip strength, which was measured using a handheld dynamometer (Smedley, S Dynamometer, TTM, Tokyo, 100 kg) (see 8 for a detailed description of the procedure). The other covariates were measured using self-reported questionnaires. In the case of variables repeatedly assessed across waves, the most recent measures were included in the analyses.

Statistical analysis

Univariable and multivariable logistic regression models were used to test the association between the exposure of interest (physical activity) and the primary outcome (COVID-19 hospitalisation). Model 0 tested the unadjusted association between physical activity and odds of COVID-19 hospitalisation. Model 1 tested the associations between physical activity and odds of COVID-19 hospitalisation when adjusting for the demographic covariates (i.e., age, height, and sex). These variables were included in Model 1 because they could not explain the potential associations between physical activity and COVID-19 hospitalisations (i.e., physical activity cannot causally predict age, height, or sex). Model 2 added to Model 1 the risk factors (i.e., higher body mass index, cardiovascular disease, diabetes, cancer, chronic kidney disease, rheumatoid arthritis, respiratory disease and weak muscle strength). The *p*-values for global effects were calculated using likelihood ratio tests. To estimate the association of physical activity with COVID-19 hospitalisation explained by other risk factors, we computed additional

models in which significant risk factors were removed from the equation. In line with previous studies (Cheval et al., 2018; Cheval; Cheval, Maltagliati et al., 2021), the decrease in the percentage of the association between physical activity and COVID-19 hospitalisations was calculated as follows: $\frac{b_{\text{model without the risk factor}} - b_{\text{model with the risk factor}}}{b_{\text{model without the risk factor}}}$, with b representing the estimates of physical activity on COVID-19 hospitalisations. Statistical analyses were conducted in R using the `glm` function. Statistical assumptions associated with general logistic models were met (i.e., normality of the residuals, multicollinearity, and undue influence).

Sensitivity analyses

Three sensitivity analyses were conducted. In the first two sensitivity analyses, we examined the distinct association of low-to-moderate and vigorous physical activity with COVID-19 hospitalisation. These analyses aimed to reduce the potential bias related to the aggregated score between low-to-moderate and vigorous physical activity. In the third sensitivity analysis, we relied on a sample of participants having responded to wave 7 (i.e., last wave in 2017) or wave 6 (i.e., second last wave in 2015).¹ This analysis aimed to reduce the timespan between the measurement of the exposure (i.e., physical activity) and the potential occurrence of the outcome (i.e., COVID-19 hospitalisation).

Robustness analyses

The dataset was analysed using a rare-events logistic regression (King & Zeng, 2001), which corrects for the bias associated with rare events. To account for the estimated fraction of patients hospitalised due to COVID-19 in the European population from June to September 2020, we used a tau parameter of 84/100,000 based on COVID-19 hospitalisation data that were available from May 2020 (see Cheval, Sieber et al., 2021 for a detailed description of the procedure). In addition, we corrected for our case-control sampling design using the weight method of the `Zelig` package (Choirat et al., 2018).

Results

The final study sample included 3139 individuals (69.3 ± 8.5 years, 1763 women) (Figure S1), from which 266 were tested positive and 66 were hospitalised for COVID-19 (75.4 ± 10.3 years, 36 women). The number of participants who completed their last measure of usual physical activity in 2004, 2006–2007, 2010–2011, 2012–2013, 2014–2015, and 2017 was 10, 10, 43, 237, 2099, and 740, respectively. Bivariable associations, computed using chi-square tests and correlation tests, showed that physical activity ($p = .024$), higher age ($p < .001$), cardiovascular disease ($p = .044$), and muscle strength ($p = .003$) were associated with COVID-19 hospitalisation (vs. no hospitalisation). Table 1 summarises the characteristics of the participants, stratified by COVID-19 hospitalisation status.

Unadjusted association between physical activity and odds of COVID-19 hospitalization (Model 0)

Model 0 showed that physical activity was associated with odds of COVID-19 hospitalisation ($p < .001$ for global effect). Compared with participants who *hardly ever or never* engaged in physical activity, the odds of COVID-19 hospitalisation were lower for those who engaged in physical activity *more than once a week* (odds ratio [OR] = 0.41, 95% Confidence Interval [95%CI] = 0.22–0.74, $p = .004$). The other comparisons were not statistically significant ($ps > .146$) (Table 2 and Figure 2).

Physical activity, demographic variables and odds of COVID-19 hospitalization (Model 1)

Model 1 showed that physical activity remained associated with COVID-19 hospitalisation (p for global effect = .042). Consistent with the previous model, the odds of COVID-19 hospitalisation were lower for participants who engaged in physical activity *more than once a week* than participants who engaged in physical activity *hardly ever or ever* (OR = 0.48, 95% CI = 0.25–0.87, $p = .020$). Moreover, the odds of COVID-19 hospitalisation were greater in older participants ($p < .001$ for global effect). Compared to participants aged 50–64 years, participants aged 65–75 years (OR = 2.20, 95%CI = 1.03–5.09, although $p = .050$) and 75–96 years (OR = 4.44, 95%CI = 2.19–9.97, $p < .001$) had greater odds of COVID-19 hospitalisation.

Physical activity, demographic variables, established risk factors and odds of COVID-19 hospitalisation (Model 2)

Model 2 showed that physical activity was no longer associated with odds of COVID-19 hospitalisation, after adjustment with the other risk factors ($p = .569$ for global effect). Older age remained associated with the odds of COVID-19 hospitalisation (p for global effect $< .001$; OR for 75–96 years = 3.17, 95% CI = 1.50–7.36, $p = .004$). Moreover, higher muscle strength was associated with lower odds of COVID-19 hospitalisation (OR = 0.59, 95%CI = 0.39–0.89, $p = .011$). In contrast, the other relevant risk factors were not significantly associated with the odds of COVID-19 hospitalisation ($ps > .092$). Further analyses revealed that muscle strength explained ~20% of the association between physical activity and COVID-19 hospitalisation.

Sensitivity analyses

Results of the sensitivity analyses yielded similar results as the main analysis. Specifically, results of the two first sensitivity analysis showed that both low-to-moderate and vigorous physical activity were associated with COVID-19 hospitalisation in unadjusted models and in models adjusted for demographic variables, and that this association was explained by muscle strength. Similarly, results of the sensitivity analysis including participants having responded to waves 6 or 7 showed that physical activity was associated with COVID-19 hospitalisation in unadjusted models and in models adjusted for demographic variables. Of note, unlike the results of the main analysis, physical activity remained significantly associated with COVID-19

¹: We included individuals having responded to wave 6 in 2015 in order to keep a sufficient sample size and a sufficient number of occurrences in the outcome, which was not the case if we only included participants who participated in the last wave 7. In total, 2839 individuals were included in this second sensitivity analysis, among whose 57 were hospitalized due to COVID-19.

Table 1. Descriptive statistics stratified by hospitalisation status.

	Not Hospitalized (N = 3073)		Hospitalized (N = 66)		p-values
	N	%	N	%	
Physical activity					
<i>Hardly ever or never</i>	1131		54		.024
		37	36		
<i>Once to three times a month</i>	265		8		
		9	5		
<i>Once a week</i>	531		15		
		17	10		
<i>More than once a week</i>	1146		23		
		37	15		
Established risk factors					
Age (years)					
<i>50–64</i>	1062		14		< .001
		35	9		
<i>65–74</i>	1106		32		
		36	21		
<i>75–96</i>	905		54		
		29	36		
Sex					
			0,00		
<i>Women</i>	1726		56		.999
		56	37		
<i>Men</i>	1347		44		
		44	29		
Body mass index (kg/m²)					
<i>Normal: <25</i>	1261		30		.142
		41	20		
<i>Overweight: ≥25 and <30</i>	1249		25		
		31	17		
<i>Obese: ≥30</i>	563		44		
		18	29		
Cardiovascular disease					
<i>No</i>	1526		36		.044
		50	24		
<i>Yes</i>	1547		64		
		50	42		
Respiratory disease					
<i>No</i>	2911		89		.999
		95	59		
<i>Yes</i>	162		11		
		5	7		
Diabetes					
<i>No</i>	2782		85		.180
		91	56		
<i>Yes</i>	291		15		
		9	10		
Cancer					
<i>No</i>	2938		95		.999
		96	63		
<i>Yes</i>	135		5		
		4	3		
Rheumatoid arthritis					
<i>No</i>	2825		84		.065
		92	56		
<i>Yes</i>	248		15		
		8	10		
Chronic kidney disease					
<i>No</i>	3033		95		.088
		99	63		
<i>Yes</i>	40		5		
		1	3		
Muscle strength (kg) (Mean ± SD)	34.57 ± 11.79				
	30.32 ± 10.89				.004

Note: For muscle strength, mean and standard deviations (SD) are reported. p-values are based on the analysis of variance and chi-square tests for continuous and categorical variables, respectively, testing the bivariate association between hospitalization (vs. no hospitalization) and these variables.

hospitalisation, after adjustment for muscle strength. In comparison with participants who engaged in physical activity *hardly ever or ever*, the odds of COVID-19 hospitalisation were lower for participants who engaged in physical activity *more than once a week* (OR = 0.52, 95%CI = 0.27–0.99, $p = .049$) (Table S3). However, the reduction of the association between physical activity and odds of COVID-19 hospitalisation was similar with that observed in the main analysis (about 15%). This latter result consistently suggests that muscle strength at least partly explains the association of physical activity with odds of COVID-19 hospitalisation.

Robustness analyses

The rare-events logistic regression yielded similar results as the main analysis (Table S4).

Discussion

In this study, included 3139 participants, we found that higher physical activity was associated with lower odds of COVID-19 hospitalisation. In particular, individuals who usually engaged in physical activity more than once a week had lower odds to be hospitalised due to COVID-19 than those who hardly ever or never engaged in physical activity. Furthermore, after adjustment for a wide range of established risk factors, we found that muscle strength was the main factor explaining this association. This study adds to the growing literature that has hypothesised a link between physical activity and severe forms of COVID-19 (Burtscher, Millet et al., 2020; Woods et al., 2020). Crucially, our findings not only support this protective association but also suggest that muscle strength can underlie it.

Our results are consistent with previous studies observing a negative association between physical activity and the odds of COVID-19 hospitalisation (Batty et al., 2020; Halabchi et al., 2021; Hamer et al., 2020; Sallis et al., 2021; Tavakol et al., 2021). This relationship can be explained by the effect of physical activity on the functioning of the immune system (Nieman & Wentz, 2019). As such, physical activity decreases the risk of severe forms of diseases causing respiratory distress (e.g., upper respiratory tracts infections) (Gleeson et al., 2011). In the case of COVID-19, it has been suggested that physical activity may reduce the inflammatory response after the infection, thereby exposing individuals to lower the odds of hospitalisation (Burtscher, Millet et al., 2020; Woods et al., 2020; Zbinden-Foncea et al., 2020). Of note, in our study, we only observed a significant difference between participants who engaged in physical activity *more than once week* vs. those who *hardly ever or never* engaged in physical activity. Yet, this lack of significant difference between the different strata of physical activity may be attributed to the low number of observations in some stratum, thereby generating a large variability in estimated coefficients. For example, although the estimated odds ratios were descriptively in the expected direction (OR = .59 for *once to three times a month*), in comparison with *hardly ever or never*), only five individuals were hospitalised in the stratum *once to three times a month*.

Table 2. Results of the general logistic models testing the associations of physical activity and other risk factors with COVID-19 hospitalisations.

Predictors	Model 0			Model 1			Model 2		
	OR	95 CI	p	OR	95 CI	p	OR	95 CI	p
Intercept	0.03	0.02–0.04	<.001	0.01	0.01–0.03	<.001	0.01	0.00–0.02	<.001
Physical activity (Ref: <i>Hardly ever or never</i>)									
<i>Once to three times a month</i>	0.59	0.20–1.39	.278	0.64	0.22–1.52	.356	0.76	0.26–1.84	.583
<i>Once a week</i>	0.59	0.28–1.16	.146	0.64	0.30–1.27	.226	0.78	0.36–1.56	.503
<i>More than once a week</i>	0.41	0.22–0.74	.004	0.48	0.25–0.87	.020	0.64	0.32–1.20	.172
Age (Ref: <i>50–64 years</i>)									
<i>65–74 years</i>				2.20	1.03–5.09	.050	1.87	0.86–4.37	.127
<i>75–96 years</i>				4.44	2.19–9.97	<.001	3.17	1.50–7.36	.004
Sex (Ref: <i>Women</i>)				0.76	0.39–1.47	.415	1.18	0.54–2.52	.681
Height				1.23	0.87–1.74	.232	1.46	1.02–2.09	.040
Muscle strength							0.59	0.39–0.89	.011
Body Mass Index (Ref: <i>Normal weight</i>)									
<i>Obese</i>							1.81	0.90–3.59	.092
<i>Overweight</i>							1.46	0.81–2.68	.212
Lung Disease (Ref: <i>No</i>)							1.49	0.59–3.21	.348
Cardiovascular disease (Ref: <i>No</i>)							1.08	0.63–1.89	.772
Diabetes (Ref: <i>No</i>)							1.08	0.50–2.14	.826
Cancer (Ref: <i>No</i>)							0.77	0.18–2.18	.670
Arthritis (Ref: <i>No</i>)							1.27	0.58–2.52	.520
Kidney Disease (Ref: <i>No</i>)							2.06	0.46–6.36	.266

Note: Odds ratios (OR), 95% Confidence Intervals (95 CI), and *p*-values (*p*) are reported.

When examining the potential mechanisms underlying the relationship between physical activity and COVID-19 hospitalisation, we found that this association was no longer significant, after adjustment for other risk factors (i.e., chronic conditions, weak muscle strength). In particular, because muscle strength was associated with odds of COVID-19 hospitalisation, our results suggest that this factor may play a pivotal role in explaining the protective effect of physical activity on COVID-19 hospitalisation. These findings are consistent with previous studies showing that, on the one hand, engaging in regular physical activity reduces sarcopenia (Dodds et al., 2013; Meier & Lee, 2020) and that, on the other hand, a greater physical fitness, as indexed by muscle strength, reduced the odds of COVID-19 hospitalisation (Cheval, Sieber et al., 2021). Particularly, muscle strength has been shown to affect the immune function through its involvement in the motor and respiratory functions (e.g., Okazaki et al., 2020). It contributes to the regulation of the inflammatory response after an infection, as suggested by the observed inverse association between muscle strength and inflammatory markers (e.g., levels of C-reactive protein) (see Tuttle et al., 2020 for a meta-analysis), thereby explaining the evidenced association with odds of COVID-19 hospitalisation (Cheval, Sieber et al., 2021). It should be noted that, in sensitivity analyses, when including participants having responded to the most recent waves of measurement (wave 6 in 2015 or wave 7 in 2017), the association between physical activity and odds of COVID-19 hospitalisation remained significant. However, the reduction in the association of physical activity was similar with that observed in the main analysis (i.e., about 15%), lending support to the fact that muscle strength at least partly explains the association between physical activity and odds of COVID-19 hospitalisation. Nonetheless, the association of physical activity with odds of COVID-19 hospitalisation, after adjustment for other risk factors, needs to be interpreted in the light of our measurement and of the design limitations, which are detailed below.

Regardless of these features, our study was the first to test and demonstrate that the link between physical activity and COVID-19 hospitalisation was explained by muscle strength.

The present study has several strengths, including its prospective design and the adjustment for a wide range of established risk factors for COVID-19 hospitalisation. Moreover, the results of the sensitivity and robustness analyses were overall consistent with the main analysis, strengthening the present findings. However, this work also presents some limitations. First, the measure of physical activity was self-reported, which may have reduced both its validity and its sensitivity, in comparison with device-based measures (Prince et al., 2008). Second, our study had a relatively long timespan between the assessment of exposures (i.e., physical activity and other risk-factor measurement) and the outcome (i.e., COVID-19 hospitalisation). Hence, although trajectories of physical activity have been shown to be relatively stable over time in this database (Cheval, Csajbók et al., 2021), some individuals may have increased or decreased their physical activity level from its assessment to the outbreak of the COVID-19 pandemic. In the same perspective, participants may have contracted a disease between the assessment of risk factors and their potential infection by COVID-19. Accordingly, though other prospective studies results point in the same direction with a rather equivalent timespan between the exposures and the outcome (Hamer et al., 2020; Sallis et al., 2021), this temporal gap may have affected observed associations. To minimize this bias, a sensitivity analysis including only participants having responded to waves 6 or 7 has been conducted (i.e., in 2015 or in 2017, respectively), and yielded consistent results to those of the main analyses. In order to obtain more accurate estimates, future studies should rely on device-based measures of physical activity and on a design with a shorter timespan between the measure of physical activity and COVID-19-related outcomes. Third, because physical activity and other risk factors could have been assessed at a same time, we cannot

infer a causal relationship between these variables (i.e., physical activity can affect certain chronic conditions or muscle strength, and vice versa). Fourth, our study focused on the potential protective role of usual or long-term physical activity patterns, but did not investigate how acute and/or excessive levels of physical activity at the time of the potential infection can also influence odds of hospitalisation (Gleeson et al., 2011). Future studies should determine whether current levels of physical activity are more closely related to risks for COVID-19 hospitalisation, than usual physical activity. Fifth, established risk factors for COVID-19 hospitalisation were self-reported, which may have decreased the validity of these measures. These latter limitations may explain the non-significant associations between these established risk factors and odds of COVID-19 hospitalisation. Future larger-scale studies are needed to examine whether the associations of physical activity with severe COVID-19 may be also explained by the links between physical activity and other relevant chronic conditions (e.g., diabetes, Cheval, Cheval, Maltagliati et al., 2021).

Conclusion

This study shows that physical activity is associated with lower odds of COVID-19 hospitalisation in adults aged 50 years and older. This association was explained by muscle strength, but not by the other established risk factors for COVID-19 hospitalisation. Because of the high prevalence of physical inactivity in the general population (Guthold et al., 2018), especially at older age (Cheval, Orsholits et al., 2020; Cheval et al., 2018; Sun et al., 2013) and during the COVID-19 pandemic (Burtscher, Burtscher et al., 2020; Cheval, Sivaramakrishnan et al., 2020; Dunton et al., 2020; Maltagliati et al., 2021), the present findings highlight the need to encourage older adults to regularly practice physical activity. In particular, engaging in strength training may be particularly beneficial to decrease odds of COVID-19 hospitalisations (e.g., Gentil et al., 2020).

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References

- Batty, G. D., Deary, I. J., Luciano, M., Altschul, D. M., Kivimäki, M., & Gale, C. R. (2020). Psychosocial factors and hospitalisations for COVID-19: Prospective cohort study based on a community sample. *Brain, Behavior, and Immunity*, 89, 569–578. <https://doi.org/10.1016/j.bbi.2020.06.021>
- Boisgontier, M. P., Orsholits, D., von Arx, M., Sieber, S., Miller, M. W., Courvoisier, D., Iversen, M. D., Cullati, S., & Cheval, B. (2020). Adverse childhood experiences, depressive symptoms, functional dependence, and physical activity: A moderated mediation model. *Journal of Physical Activity & Health*, 17(8), 790–799. <https://doi.org/10.1123/jpah.2019-0133>
- Börsch-Supan, A., Brandt, M., Hunkler, C., Kneip, T., Korbacher, J., Malter, F., Schaan, B., Stuck, S., & Zuber, S. (2013). Data resource profile: The survey of health, ageing and retirement in Europe (SHARE). *International Journal of Epidemiology*, 42(4), 992–1001. <https://doi.org/10.1093/ije/dyt088>
- Brawner, C. A., Ehrman, J. K., Bole, S., Kerrigan, D. J., Parikh, S. S., Lewis, B. K., Gindi, R. M., Keteyian, C., Abdul-Nour, K., & Keteyian, S. J. (2020). Maximal exercise capacity is inversely related to hospitalization secondary to coronavirus disease 2019. *Mayo Clinic Proceedings*, 96(1), 32–39. <https://doi.org/10.1016/j.mayocp.2020.10.003>
- Burtscher, J., Burtscher, M., & Millet, G. P. (2020). (Indoor) isolation, stress, and physical inactivity: Vicious circles accelerated by COVID-19? *Scandinavian Journal of Medicine & Science in Sports*, 30(8), 1544–1545. <https://doi.org/10.1111/sms.13706>
- Burtscher, J., Millet, G. P., & Burtscher, M. (2020). Low cardiorespiratory and mitochondrial fitness as risk factors in viral infections: Implications for COVID-19. *British Journal of Sports Medicine*, 55(8), 413–415. <https://doi.org/10.1136/bjsports-2020-103572>
- Center for Disease Control and Prevention. (2020). <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html#smoking>
- Cheval, B., Csajbók, Z., Formánek, T., Sieber, S., Boisgontier, M. P., Cullati, S., & Cermakova, P. (2021). Association between physical-activity trajectories and cognitive decline in adults 50 years of age or older. *MedRxiv*. <https://doi.org/10.1101/2021.04.13.21255381>
- Cheval, B., Maltagliati, S., Sieber, S., Beran, D., Chalabaev, A., Sander, D., Cullati, S., & Boisgontier, M. P. (2021). Why are individuals with diabetes less active? The mediating role of physical, emotional, and cognitive factors. *Annals of Behavioral Medicine*. <https://doi.org/10.1093/abm/kaa120>
- Cheval, B., Orsholits, D., Sieber, S., Courvoisier, D., Cullati, S., & Boisgontier, M. P. (2020). Relationship between decline in cognitive resources and physical activity. *Health Psychology*, 39(6), 519–528. <https://doi.org/10.1037/hea0000857>
- Cheval, B., Rebar, A. L., Miller, M. W., Sieber, S., Orsholits, D., Baranyi, G., Courvoisier, D., Cullati, S., Sander, D., Chalabaev, A., & Boisgontier, M. P. (2019). Cognitive resources moderate the adverse impact of poor perceived neighborhood conditions on self-reported physical activity of older adults. *Preventive Medicine*, 126, 105741. <https://doi.org/10.1016/j.ypmed.2019.05.029>
- Cheval, B., Sieber, S., Guessous, I., Orsholits, D., Courvoisier, D. S., Kliegel, M., Stringhini, S., Swinnen, S. P., Burton-Jeangros, C., Cullati, S., & Boisgontier, M. P. (2018). Effect of early- and adult-life socioeconomic circumstances on physical inactivity. *Medicine and Science in Sports and Exercise*, 50(3), 476–485. <https://doi.org/10.1249/MSS.0000000000001472>
- Cheval, B., Sieber, S., Maltagliati, S., Millet, G. P., Formánek, T., Chalabaev, A., Cullati, S., & Boisgontier, M. P. (2021). Muscle strength is associated with COVID-19 hospitalization in adults 50 years of age and older. *MedRxiv*, (2021)2, 02.21250909. <https://doi.org/10.1101/2021.02.02.21250909>
- Cheval, B., Sivaramakrishnan, H., Maltagliati, S., Fessler, L., Forestier, C., Sarrazin, P., Orsholits, D., Chalabaev, A., Sander, D., Ntoumanis, N., & Boisgontier, M. P. (2020). Relationships between changes in self-reported physical activity, sedentary behaviour and health during the coronavirus (COVID-19) pandemic in France and Switzerland. *Journal of Sports Sciences*, 1–6. <https://doi.org/10.1080/02640414.2020.1841396>
- Choirat, C., Gandrud, C., Honaker, J., Imai, K., & King, G. L. O. (2018). rrelogit: Rare events logistic regression for dichotomous dependent variables. *Everyone's statistical software* <http://zeligproject.org>. 2018.
- de Souto Barreto, P., Cesari, M., Andrieu, S., Vellas, B., & Rolland, Y. (2017).

- Physical activity and incident chronic diseases: A longitudinal observational study in 16 European countries. *American Journal of Preventive Medicine*, 52(3), 373–378. <https://doi.org/10.1016/j.amepre.2016.08.028>
- Dodds, R., Kuh, D., Aihie Sayer, A., & Cooper, R. (2013). Physical activity levels across adult life and grip strength in early old age: Updating findings from a British birth cohort. *Age and Ageing*, 42(6), 794–798. <https://doi.org/10.1093/ageing/af124>
- Dong, Y., Dai, T., Wei, Y., Zhang, L., Zheng, M., & Zhou, F. (2020). A systematic review of SARS-CoV-2 vaccine candidates. *Signal Transduction and Targeted Therapy*, 5(1), 237. <https://doi.org/10.1038/s41392-020-00352-y>
- Dunton, G. F., Wang, S. D., Do, B., & Courtney, J. (2020). Early effects of the COVID-19 pandemic on physical activity locations and behaviors in adults living in the United States. *Preventive Medicine Reports*, 20, 101241. <https://doi.org/10.1016/j.pmedr.2020.101241>
- Gentil, P., Ramirez-Campillo, R., & Souza, D. (2020). Resistance training in face of the coronavirus outbreak: Time to think outside the box. *Frontiers in Physiology*, 11, 859. <https://doi.org/10.3389/fphys.2020.00859>
- Gill, D. P., Jones, G. R., Zou, G., & Speechley, M. (2012). Using a single question to assess physical activity in older adults: A reliability and validity study. *BMC Medical Research Methodology*, 12(1), 20. <https://doi.org/10.1186/1471-2288-12-20>
- Gleeson, M., Bishop, N. C., Stensel, D. J., Lindley, M. R., Mastana, S. S., & Nimmo, M. A. (2011). The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. *Nature Reviews. Immunology*, 11(9), 607–615. <https://doi.org/10.1038/nri3041>
- Guthold, R., Stevens, G. A., Riley, L. M., & Bull, F. C. (2018). Worldwide trends in insufficient physical activity from 2001 to 2016: A pooled analysis of 358 population-based surveys with 1.9 million participants. *The Lancet Global Health*, 6(10), e1077–e1086. [https://doi.org/10.1016/S2214-109X\(18\)30357-7](https://doi.org/10.1016/S2214-109X(18)30357-7)
- Halabchi, F., Mazaheri, R., Sabeti, K., Yunesian, M., Alizadeh, Z., Ahmadijad, Z., Aghili, S. M., & Tavakol, Z. (2021). Regular sports participation as a potential predictor of better clinical outcome in adult patients with COVID-19: A large cross-sectional study. *Journal of Physical Activity & Health*, 18(1), 8–12. <https://doi.org/10.1123/jpah.2020-0392>
- Hamer, M., Kivimäki, M., Gale, C. R., & Batty, G. D. (2020). Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. *Brain, Behavior, and Immunity*, 87, 184–187. <https://doi.org/10.1016/j.bbi.2020.05.059>
- Jordan, R. E., Adab, P., & Cheng, K. K. (2020). Covid-19: Risk factors for severe disease and death. *BMJ*, 368, 1198. <https://doi.org/10.1136/bmj.m1198>
- King, G., & Zeng, L. (2001). Logistic regression in rare events data. *Political Analysis*, 9(2), 137–163. <https://doi.org/10.1093/oxfordjournals.pan.a004868>
- Lam, S., Lombardi, A., & Ouanounou, A. (2020). COVID-19: A review of the proposed pharmacological treatments. *European Journal of Pharmacology*, 886, 173451. <https://doi.org/10.1016/j.ejphar.2020.173451>
- Li, X., Xu, S., Yu, M., Wang, K., Tao, Y., Zhou, Y., Shi, J., Zhou, M., Wu, B., Yang, Z., Zhang, C., Yue, J., Zhang, Z., Renz, H., Liu, X., Xie, J., Xie, M., & Zhao, J. (2020). Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *Journal of Allergy and Clinical Immunology*, 146(1), 110–118. <https://doi.org/10.1016/j.jaci.2020.04.006>
- Maltagliati, S., Rebar, A., Fessler, L., Forestier, C., Sarrazin, P., Chalabaev, A., Sander, D., Sivaramakrishnan, H., Orsholits, D., Boisgontier, M. P., Ntoumanis, N., Gardner, B., & Cheval, B. (2021). Evolution of physical activity habits after a context change: The case of COVID-19 lockdown. *British Journal of Health Psychology*, 12524. <https://doi.org/10.1111/bjhp.12524>
- Meier, N. F., & Lee, D. (2020). Physical activity and sarcopenia in older adults. *Aging Clinical and Experimental Research*, 32(9), 1675–1687. <https://doi.org/10.1007/s40520-019-01371-8>
- Milton, K., Bull, F. C., & Bauman, A. (2011). Reliability and validity testing of a single-item physical activity measure. *British Journal of Sports Medicine*, 45(3), 203–208. <https://doi.org/10.1136/bjism.2009.068395>
- Nieman, D. C., & Wentz, L. M. (2019). The compelling link between physical activity and the body's defense system. *Journal of Sport and Health Science*, 8(3), 201–217. <https://doi.org/10.1016/j.jshs.2018.09.009>
- Okazaki, T., Ebihara, S., Mori, T., Izumi, S., & Ebihara, T. (2020). Association between sarcopenia and pneumonia in older people. *Geriatrics & Gerontology International*, 20(1), 7–13. <https://doi.org/10.1111/ggi.13839>
- Prince, S. A., Adamo, K. B., Hamel, M., Hardt, J., Connor Gorber, S., & Tremblay, M. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: A systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, 5(1), 56. <https://doi.org/10.1186/1479-5868-5-56>
- Sallis, R., Young, D. R., Tartof, S. Y., Sallis, J. F., Sall, J., Li, Q., Smith, G. N., & Cohen, D. A. (2021). Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: A study in 48 440 adult patients. *British Journal of Sports Medicine*, 104080. <https://doi.org/10.1136/bjsports-2021-104080>
- Sun, F., Norman, I. J., & While, A. E. (2013). Physical activity in older people: A systematic review. *BMC Public Health*, 13(1), 449. <https://doi.org/10.1186/1471-2458-13-449>
- Tavakol, Z., Ghannadi, S., Tabesh, M. R., Halabchi, F., Noormohammadpour, P., Akbarpour, S., Alizadeh, Z., Nezhad, M. H., & Reyhan, S. K. (2021). Relationship between physical activity, healthy lifestyle and COVID-19 disease severity; a cross-sectional study. *Journal of Public Health*, 4, 1–9. <https://doi.org/10.1007/s10389-020-01468-9>
- Tuttle, C. S. L., Thang, L. A. N., & Maier, A. B. (2020). Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis. *Ageing Research Reviews*, 64, 101185. <https://doi.org/10.1016/j.arr.2020.101185>
- Warburton, D. E. R. (2006). Health benefits of physical activity: The evidence. *Canadian Medical Association Journal*, 174(6), 801–809. <https://doi.org/10.1503/cmaj.051351>
- Wearing, J., Konings, P., Stokes, M., & De Bruin, E. D. (2018). Handgrip strength in old and oldest old Swiss adults – A cross-sectional study. *BMC Geriatrics*, 18(1), 266. <https://doi.org/10.1186/s12877-018-0959-0>
- Woods, J. A., Hutchinson, N. T., Powers, S. K., Roberts, W. O., Gomez-Cabrera, M. C., Radak, Z., Berkes, I., Boros, A., Boldogh, I., Leeuwenburgh, C., Coelho-Junior, H. J., Marzetti, E., Cheng, Y., Liu, J., Durstine, J. L., Sun, J., & Ji, L. L. (2020). The COVID-19 pandemic and physical activity. *Sports Medicine and Health Science*, 2(2), 55–64. <https://doi.org/10.1016/j.smhs.2020.05.006>
- World Health Organization. (2020a). [https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-ihf-emergency-committee-on-novel-coronavirus-\(2019-ncov\)](https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-ihf-emergency-committee-on-novel-coronavirus-(2019-ncov))
- World Health Organization, (2020b). <https://www.who.int/publications/i/item/overview-of-public-health-and-social-measures-in-the-context-of-covid-19>
- Yates, T., Razieh, C., Zaccardi, F., Rowlands, A. V., Seidu, S., Davies, M. J., & Khunti, K. (2021). Obesity, walking pace and risk of severe COVID-19 and mortality: Analysis of UK Biobank. *International Journal of Obesity*, 45(5), 1155–1159. <https://doi.org/10.1038/s41366-021-00771-z>
- Zbinden-Foncea, H., Francaux, M., Deldicque, L., & Hawley, J. A. (2020). Does high cardiorespiratory fitness confer some protection against proinflammatory responses after infection by SARS-CoV-2? *Obesity*, 28(8), 1378–1381. <https://doi.org/10.1002/oby.22849>