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# Journal Pre-proof

Risk factors of post-COVID-19 condition attributed to COVID-19 disease in people aged 50+ in Europe and Israel

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**Title:** Risk factors of post-COVID-19 condition attributed to COVID-19 disease in people aged 50+ in Europe and Israel

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**Key points:**

- This study examines the risk-factors of post-COVID-19 condition among Europeans aged 50 years or more who tested positive for COVID-19
- Higher age, low and medium educational level and prior COVID-19 related hospitalisation are risk factors of post COVID-19 condition
- This study suggests policy makers to increase their focus on educational interventions towards increasing health literacy

## Abstract

**Objectives:** High age, male sex, and pre-existing comorbidities are risk factors for a more severe development of COVID-19, and individuals surviving COVID-19 may experience persistent symptoms afterwards referred to as “Post COVID-19 condition”, which represents a range of symptoms after recovering from COVID-19. This study aims at identifying risk factors of post-COVID-19 conditions among 50+ year olds.

**Study design:** We conducted a cross-sectional study based on data from the Survey of Health, Ageing and Retirement in Europe.

**Methods:** A multiple logistic regression model was used to investigate age, sex, education, comorbidities, smoking, BMI, and COVID-19 hospitalisation as risk-factors of post-COVID-19 condition.

**Results:** Participants aged 70+ (OR 1.61), with medium (OR 2.38) and lower (OR 2.14) educational level have a higher risk of post-COVID-19 conditions. Additionally, when considering the severity of the COVID-19 disease, those who were hospitalised due to COVID-19 had a 26 times higher risk of post-COVID-19 conditions compared to those who were only tested positive (OR 25.9).

**Conclusions:** This study supports that health inequalities exist across educational levels with respect to post-COVID-19 conditions, although misclassification may be more common among lower educated participants. The results suggest that policy makers should increase educational interventions towards increasing health literacy.

## Introduction

By fall 2022 the COVID-19 pandemic has been present for more than two years and repercussions of COVID-19 may well be observed. Although COVID-19 strikes at all ages, older people are at increased risk of a critical course of disease, as are people with pre-existing comorbidities<sup>1</sup>. Following COVID-19 disease, lingering symptoms lasting from weeks to months, may be experienced. The World Health Organisation has recently coined this as “post-COVID-19 condition”, defined as a condition that “occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis”<sup>2</sup>.

Studies describing risk factors of post-COVID-19 health conditions are limited and show conflicting results, but increasing age, female gender, multimorbidity, high BMI, lower educational level, having several symptoms during COVID-19 infection, and a more severe acute phase of COVID-19 disease, have all been associated with post-COVID-19 condition<sup>3,4</sup>. Full recovery from COVID-19 is important to keep people’s work capacity, productivity, and ability to return to normal everyday activities and thus, risk factors of post-COVID-19 must be explored. To our knowledge, no previous studies have explored the possible risk factors in a large population-based sample of middle-aged and older adults comparing several countries. Thus, the aim of the study was to investigate risk factors of post-COVID-19 conditions among 50+ year olds within 27 European countries and Israel.

## Methods

We used data from the second wave of the Survey of Health, Ageing and Retirement in Europe (SHARE) COVID-19 survey (SCS2) conducted in June-August 2021<sup>5</sup>. Participants, who had tested positive with COVID-19 (Supplementary figure F1), were asked “*Have you experienced any long-term or lingering effects that you attribute to your Covid Illness?*”, with the following answer options: ‘fatigue’, ‘cough, congestion, shortness of breath’, ‘loss of taste or smell’, ‘headache’, ‘body aches, joint pain’, ‘chest or abdominal pain’, ‘diarrhoea, nausea’, ‘confusion’, and ‘other’. Based on this question, an outcome variable was created and dichotomised, indicating whether the respondents had ‘no symptoms’ or ‘one or more’. The following variables were selected as the primary potential risk factors for post-COVID-19 condition: age (50-69 and 70+ years), sex (male, female), and educational level ([according to the International Standardized Classification of Education (ISCED) classified into lower (ISCED groups 0–2), medium (ISCED groups 3–4) and higher (ISCED groups 5–6)]), comorbidity (‘no diseases’, ‘one or two diseases’, and ‘three or more diseases’), smoking (‘not smoking’, ‘smoking now’, ‘previous smoker’), BMI (‘normal weight’ (BMI $\geq$ 18.5 and  $<$ 25 kg/m<sup>2</sup>), ‘underweight’ (BMI  $<$  18.5 kg/m<sup>2</sup>), ‘overweight’ (BMI  $\geq$  25 and  $<$  30 kg/m<sup>2</sup>) and ‘obese’ (BMI $\geq$  30 kg/m<sup>2</sup>)), and a COVID-19 hospitalisation variable indicating if respondents have been hospitalised due to COVID-19 (‘yes’ or ‘no’) and

serves as a proxy of the severity of the COVID-19 disease. Moreover, the variable 'country', representing the 28 SHARE countries was included (Germany, The Netherlands, Belgium, Luxembourg, Switzerland, Austria, France, Spain, Portugal, Malta, Italy, Greece, Cyprus, Estonia, Latvia, Lithuania, Poland, Czech Republic, Slovakia, Slovenia, Hungary, Croatia, Romania, Bulgaria, Denmark, Sweden, Finland, and Israel) (supplementary table S2). Age, sex, diseases, and COVID-19 hospitalisation were drawn from SCS2, and all other variables were drawn from SHARE wave 8 (conducted in 2020)<sup>6</sup> or the latest wave possible.

Multiple logistic regression models were used to study the risk factors of post-COVID-19 conditions, and the analyses were performed in three steps. First, we included age, gender, education, comorbidity, smoking and BMI (model 1), secondly, we added a 'country' variable (model 2), and finally we included the 'COVID-19-hospitalisation' variable (model 3). In all analyses, the cross-sectional individual weights supplied by SHARE were applied to yield a representative sample.

## Results

Of all SCS2 participants aged 50 years or more ( $n=49,044$ ), 6.5% ( $n=3,156$ ) reported having tested positive for COVID-19 and were thus included in the final analysis (supplementary figure F1). In the final sample 42.4% were aged 70 years or more, and 61.6% were females. The proportion of people with a high educational level was 19.2%, 45.1% with a medium level, and 30.4% had a lower educational level (10% were missing). Among the respondents, 19.4% had three or more comorbidities and 24.1% had none, and 39.1% were overweight and 28.4% had a normal BMI. Only 7.9% reported to be smokers and 16.4% were hospitalised due to COVID-19 disease (supplementary table S3).

Of those who tested positive almost one quarter (23.5%) reported at least one post-COVID-19 condition, the most common being 'fatigue' (18.8%), followed by 'cough, congestion or shortness of breath' (13.5%), and 'body aches or joint pain' (13.2%) (Supplementary table S4). In the crude analysis, respondents with higher age (70+), medium or low education, multimorbidity, and obesity were at higher risk of post-COVID-19 condition. However, in the adjusted model (model 1), only older participants (70+) (OR 1.58, 95% CI 1.06-2.34), and those with a medium (OR 2.46, 95% CI 1.46-4.16) or low education (OR 2.42, 95% CI 1.37-4.25), had a higher risk of post-COVID-19 condition. When adding the country variable to the model (model 2), the risk persisted for those aged 70+ (OR 1.61, 95% CI 1.08-2.41), and with a medium (OR 2.38, 95% CI 1.39-4.09) or lower (OR 2.14, 95% CI 1.18-3.86) educational level, but the effect attenuated. Additionally, when considering the severity of the COVID-19 disease (model 3), those who were hospitalised due to COVID-19 had a 26 times higher risk of post-COVID-19 condition compared to those who were not hospitalised (OR 25.9, 95% CI 15.64-42.79) and the effect of educational level persisted (medium (OR 2.69, 95% CI 1.48-4.89),

lower (OR 2.30, 95% CI 1.22-4.35) (Table 1). Sex, comorbidity, BMI, and smoking did not show any association with post-COVID-19 conditions.

[ Please insert table 1 here]

## Discussion

Post-COVID-19 conditions are common among COVID-19 infected 50+ year old people living in the 28 SHARE countries and affects in particular older people and those with lower educational level. The association to lower educational level has not been described previously in a European population. However, educational attainment is a social determinant of health, as well as a predictor of the severity of COVID-19 disease<sup>7</sup>. Low educational level is also associated with low health literacy<sup>8</sup>, i.e., the ability to reflect upon one's illness and understand how to distinguish between symptoms from chronic disease and symptoms related to COVID-19, and poorer health literacy may explain an over-reporting of symptoms.

Not only is increasing age associated with COVID-19 disease severity<sup>1</sup>, but it is also associated with higher risk of post-COVID-19 conditions<sup>4</sup>, and in line with our findings. This may be explained by an age-associated adverse immunological response as specific cell-changes persist longer in older compared to younger individuals<sup>9</sup> and therefore the symptoms may be more persistent.

The most salient predictor of post COVID-19 condition in our study was the COVID-19 hospitalisation, which may represent the severity of the COVID-19 disease and is in keeping with other studies (4). However, as intensive treatment during hospital stay can cause similar symptoms<sup>10</sup>, it may be difficult to determine if the symptoms are attributed to the in-hospital treatment, COVID-19, or a combination.

The strength of this study was the large and representative sample of 28 countries using standardised methods for data collection. Also, this study comprised both hospitalised and non-hospitalised participants. However, it is a weakness that SHARE did not collect information on the duration of the post-COVID-19 symptoms to account for the extent of the post-COVID-19 condition. A time frame for long-term or lingering symptoms would have improved the comparability across individuals. In general, we cannot exclude residual confounding; for instance, both hospitalisations and post-COVID-19 condition may be correlated with vaccination status. Finally, as a self-reported questionnaire, the post-COVID-19 conditions may be over- or underreported due to information bias.

## Conclusion

The results indicate that lower educational level, higher age, and prior hospitalisation for COVID-19 disease increase the risk of post-COVID-19 conditions. While biological mechanisms may explain the adverse effects

of higher age and disease severity, the effect of a lower educational level for post-COVID-19 conditions is more likely explained by lower health literacy. In conclusion, these findings have implications for public policies in Europe and Israel, as we shed light on the social inequalities in health, which still exist at large. We encourage policy makers to increase their focus on educational interventions and implement programmes and policies to increase health literacy and hereby reduce inequalities in health.

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### Data source

*This paper uses data from SHARE Waves 1, 2, 3, 4, 5, 6, 7, 8 and 9 (DOIs: [10.6103/SHARE.w1.800](https://doi.org/10.6103/SHARE.w1.800), [10.6103/SHARE.w2.800](https://doi.org/10.6103/SHARE.w2.800), [10.6103/SHARE.w3.800](https://doi.org/10.6103/SHARE.w3.800), [10.6103/SHARE.w4.800](https://doi.org/10.6103/SHARE.w4.800), [10.6103/SHARE.w5.800](https://doi.org/10.6103/SHARE.w5.800), [10.6103/SHARE.w6.800](https://doi.org/10.6103/SHARE.w6.800), [10.6103/SHARE.w7.800](https://doi.org/10.6103/SHARE.w7.800), [10.6103/SHARE.w8.800](https://doi.org/10.6103/SHARE.w8.800), [10.6103/SHARE.w8ca.800](https://doi.org/10.6103/SHARE.w8ca.800), [10.6103/SHARE.w9ca800](https://doi.org/10.6103/SHARE.w9ca800)), see Börsch-Supan et al. (2013) for methodological details.*

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Table 1. The risk of having Post-COVID-19 condition

Variables	Crude		Model 1 <sup>a</sup>		Model 2 <sup>a+b</sup>		Model 3 <sup>a+b+c</sup>	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age								
50-69	-		-		-		-	
70+	1.57*	1.05 - 2.35	1.58*	1.06 - 2.34	1.61*	1.08 - 2.41	1.07	0.64 - 1.80
Sex								
Male	-		-		-		-	
Female	0.98	0.58 - 1.64	1.14	0.76 - 1.72	1.18	0.79 - 1.76	1.31	0.81 - 2.13
Education								
High	-		-		-		-	
Medium	3.13***	1.77 - 5.56	2.46***	1.46 - 4.16	2.38**	1.39 - 4.09	2.69***	1.48 - 4.89
Low	3.43***	1.96 - 6.01	2.42**	1.37 - 4.25	2.14*	1.18 - 3.86	2.30**	1.22 - 4.35
Comorbidity								
0	-		-		-		-	
1-2	1.68	0.93 - 3.01	1.28	0.73 - 2.25	1.23	0.71 - 2.12	0.99	0.58 - 1.70
3 +	3.40**	1.43 - 8.08	1.75	0.89 - 3.46	1.76	0.92 - 3.37	1.74	0.82 - 3.67
Smoking								
Not smoking	-		-		-		-	
Previous smoker	1.16	0.75 - 1.81	1.11	0.74 - 1.66	1.11	0.74 - 1.67	1.07	0.64 - 1.78
Smoker	2.10	0.92 - 4.77	2.20	0.97 - 4.98	2.25	0.97 - 5.18	1.68	0.72 - 3.94
BMI								
Normal	-		-		-		-	
Underweight	0.28	0.04 - 1.88	0.27	0.04 - 1.76	0.23	0.03 - 1.67	0.35	0.05 - 2.64
Overweight	1.15	0.68 - 1.93	1.18	0.76 - 1.83	1.22	0.78 - 1.91	1.14	0.69 - 1.88
Obese	1.86**	1.17 - 2.94	1.59	0.98 - 2.59	1.61	0.98 - 2.67	1.31	0.69 - 2.46
COVID-19 hospitalisation								
No							ref	
Yes							25.9***	15.64-42.79
Pseudo R <sup>2</sup>			0.059		0.081		0.274	
Observations			2,817		2,817		2,817	

a: adjusted for age, sex, education, comorbidity, smoking, BMI; b: adjusted for country (Germany used as reference); c: adjusted for COVID-19 hospitalisation

\*\*\* p<0.001, \*\* p<0.01, \* p<0.05