

Letters

RESEARCH LETTER

Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers

Approximately 80% of hospitalized patients with COVID-19 report persistent symptoms several months after infection onset.^{1,2} However, knowledge of long-term outcomes among individuals with mild COVID-19 is scarce, and prevalence data are hampered by selection bias and suboptimal control groups.^{3,4} This cohort study investigated COVID-19-related long-term symptoms in health care professionals.



[Supplemental content](#)

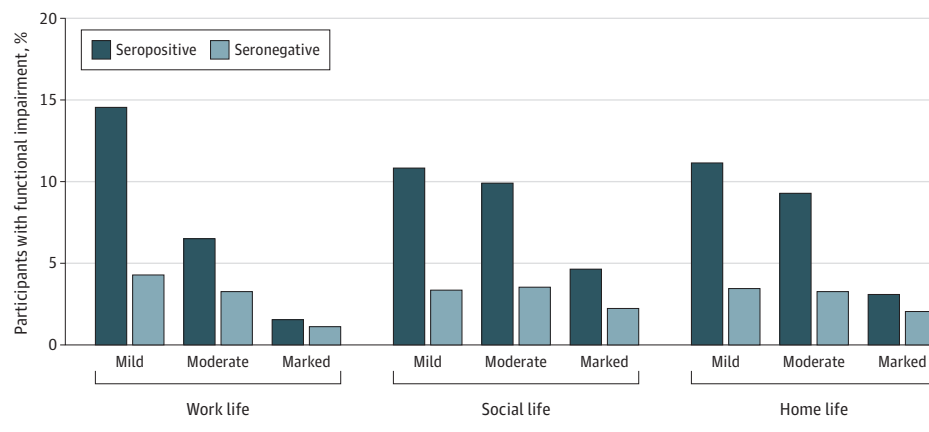
Methods | The COMMUNITY (COVID-19 Biomarker and Immunity) study investigates long-term immunity after mild COVID-19⁵ (eMethods in the [Supplement](#)). Between April 15, 2020, and May 8, 2020, health care professionals at Danderyd Hospital, Stockholm, Sweden, were invited to participate, with a limit of approximately 2000 participants because of testing restrictions. Participants had blood sampling performed every 4 months. Demographics, symptoms and severity (mild or severe), and chronic diseases were obtained through questionnaires at baseline. Participants who were seropositive for SARS-CoV-2 anti-spike IgG at baseline and who reported severe symptoms were excluded, as were initially seronegative participants who seroconverted during follow-up. At the 8-month follow-up (January 11-29, 2021), participants reported via smartphone app the presence, duration (<2 months, ≥2 months, ≥4 months, ≥8 months), and severity (mild, moderate, or severe) of 23 predefined symptoms. For participants reporting at least 1 symptom persistent for at least 2 months, the Sheehan Disability Scale⁶ was used to score functional impairment from present or prior long-term symptoms (0, not at all; 1-3, mild; 4-6, moderate; and 7-10, marked) in 3 interrelated domains (work, social, and home life). Associations between categorical variables were assessed using the χ^2 test of independence. Risk ratios (RRs) and their corresponding 95% CIs were calculated comparing seropositive and seronegative participants for moderate to severe symptoms lasting 2 or more or 8 or more months and for moderate to marked disruption on the Sheehan Disability Scale, using the STATA command `cs`. Statistical analyses were performed using STATA, version 16.1 (StataCorp LP). A 2-sided *P* value <.05 was considered statistically significant. The study was approved by the Swedish Ethical Review Authority, and informed written consent was obtained from all participants.

Results | Participant enrollment was closed after 2149 of 4375 health care professionals (49%) enrolled; 393 were

Table. The 10 Most Common Moderate to Severe Long-term Symptoms in Seropositive and Seronegative Participants

Duration of symptom, mo	No. (%)	
	Seropositive (n = 323)	Seronegative (n = 1072)
Any symptom		
≥2	84 (26.0)	95 (8.9)
≥4	69 (21.4)	77 (7.2)
≥8	48 (14.9)	36 (3.4)
Anosmia		
≥2	47 (14.6)	6 (0.6)
≥4	35 (10.8)	4 (0.4)
≥8	29 (9.0)	1 (0.1)
Fatigue		
≥2	27 (8.4)	57 (5.3)
≥4	22 (6.8)	47 (4.4)
≥8	13 (4.0)	16 (1.5)
Ageusia		
≥2	25 (7.7)	6 (0.6)
≥4	17 (5.3)	3 (0.3)
≥8	12 (3.7)	1 (0.1)
Dyspnea		
≥2	14 (4.3)	12 (1.1)
≥4	11 (3.4)	10 (0.9)
≥8	6 (1.9)	3 (0.3)
Sleeping disorder		
≥2	10 (3.1)	21 (2.0)
≥4	9 (2.8)	19 (1.8)
≥8	7 (2.2)	9 (0.8)
Headache		
≥2	9 (2.8)	34 (3.2)
≥4	8 (2.5)	24 (2.2)
≥8	5 (1.5)	11 (1.0)
Palpitations		
≥2	8 (2.5)	18 (1.7)
≥4	7 (1.9)	13 (1.2)
≥8	2 (0.6)	7 (0.7)
Concentration impairment		
≥2	7 (2.2)	12 (1.1)
≥4	6 (1.9)	9 (0.8)
≥8	2 (0.6)	2 (0.2)
Muscle/joint pain		
≥2	6 (1.9)	19 (1.8)
≥4	5 (1.5)	10 (0.9)
≥8	2 (0.6)	4 (0.4)
Memory impairment		
≥2	5 (1.5)	11 (1.0)
≥4	4 (1.2)	6 (0.6)
≥8	1 (0.3)	3 (0.3)

Figure. COVID-19-Related Long-term Functional Impairment



The percentage of seropositive (n = 323) and seronegative (n = 1072) participants reporting symptoms lasting at least 2 months and their related functional impairment in their work, social, and home life using the Sheehan Disability Scale (1-3, mild; 4-6, moderate; and 7-10, marked).

seropositive. Fifty seropositive participants with severe symptoms and 404 seronegative participants who seroconverted were excluded. Twenty seropositive and 280 seronegative participants did not complete the 8-month follow-up, leaving 323 (94%) seropositive and 1072 (84%) seronegative participants. Seropositive participants who reported no or mild prior symptoms had a median (interquartile range) age of 43 (33-52) years and 268 (83%) were women; continuously seronegative participants had a median (interquartile range) age of 47 (36-56) years and 925 (86%) were women. Underlying chronic disease was reported by 71 (22%) seropositive participants vs 254 (24%) seronegative participants.

Comparing seropositive vs seronegative participants, 26% vs 9% reported at least 1 moderate to severe symptom lasting for at least 2 months (RR, 2.9 [95% CI, 2.2-3.8]) and 15% vs 3% reported at least 1 moderate to severe symptom lasting for at least 8 months (RR, 4.4 [95% CI, 2.9-6.7]) (Table). The most common moderate to severe symptoms lasting for at least 2 months in the seropositive group were anosmia, fatigue, ageusia, and dyspnea.

Of the seropositive participants, 8% reported that their long-term symptoms moderately to markedly disrupted their work life, compared with 4% of the seronegative participants (RR, 1.8 [95% CI, 1.2-2.9]); 15% reported their long-term symptoms moderately to markedly disrupted their social life, compared with 6% of the seronegative participants (RR, 2.5 [95% CI, 1.8-3.6]); and 12% reported that their long-term symptoms moderately to markedly disrupted their home life, compared with 5% of the seronegative participants (RR, 2.3 [95% CI, 1.6-3.4]) (Figure). Furthermore, 11% of the seropositive participants reported moderate to marked disruption in any Sheehan Disability Scale category as well as having at least 1 moderate to severe symptom lasting for at least 8 months, compared with 2% of the seronegative participants (RR, 4.5 [95% CI, 2.7-7.3]).

Discussion | The results of this study showed that a considerable portion of low-risk individuals with mild COVID-19

reported a diversity of long-term symptoms, and that these symptoms disrupted work, social, and home life. Limitations of the study include the possibility of recall bias and the subjective rating of symptoms. Further research is needed to understand the mechanisms underlying COVID-19-related long-term sequelae.

Sebastian Havervall, MD
Axel Rosell, MD
Mia Phillipson, PhD
Sara M. Mangsbo, PhD
Peter Nilsson, PhD
Sophia Hober, PhD
Charlotte Thålin, MD, PhD

Author Affiliations: Danderyd Hospital, Karolinska Institute, Stockholm, Sweden (Havervall, Rosell, Thålin); SciLifeLab, Uppsala University, Uppsala, Sweden (Phillipson, Mangsbo); SciLifeLab, KTH Royal Institute of Technology, Stockholm, Sweden (Nilsson, Hober).

Corresponding Author: Charlotte Thålin, MD, PhD, Department of Clinical Sciences, Danderyd Hospital, Karolinska Institutet, 18288 Stockholm, Sweden (charlotte.thalin@sl.se).

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Concept and design: Havervall, Phillipson, Mangsbo, Nilsson, Hober, Thålin.
Acquisition, analysis, or interpretation of data: Havervall, Rosell, Mangsbo, Nilsson, Hober, Thålin.

Drafting of the manuscript: Havervall, Nilsson, Thålin.

Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Havervall, Rosell, Nilsson.

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Supervision: Phillipson, Mangsbo, Nilsson, Hober, Thålin.

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1. Carfi A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. *JAMA*. 2020;324(6):603-605. doi:10.1001/jama.2020.12603
2. Arnold DT, Hamilton FW, Milne A, et al. Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort. *Thorax*. Published online December 3, 2020. doi:10.1136/thoraxjnl-2020-216086
3. Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in adults at 6 months after COVID-19 infection. *JAMA Netw Open*. 2021;4(2):e210830. doi:10.1001/jamanetworkopen.2021.0830
4. Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nat Med*. Published online March 10, 2021. doi:10.1038/s41591-021-01292-y
5. Rudberg AS, Havervall S, Månberg A, et al. SARS-CoV-2 exposure, symptoms and seroprevalence in healthcare workers in Sweden. *Nat Commun*. 2020;11(1):5064. doi:10.1038/s41467-020-18848-0
6. Sheehan KH, Sheehan DV. Assessing treatment effects in clinical trials with the discan metric of the Sheehan Disability Scale. *Int Clin Psychopharmacol*. 2008;23(2):70-83. doi:10.1097/YIC.0b013e3282f2b4d6