# Journal: Infection

# Supplementary material to

# Definition of the Post-COVID syndrome using a symptom-based Post-COVID score in a prospective, multi-center, cross-sectoral cohort of the German National Pandemic Cohort Network (NAPKON)

Katharina S. Appel<sup>1,2\*</sup>, Carolin Nürnberger<sup>3,4\*</sup>, Thomas Bahmer<sup>5,6</sup>, Christian Förster<sup>7</sup>, Maria Cristina Polidori<sup>8,9</sup>, Mirjam Kohls<sup>3</sup>, Tanja Kraus<sup>7</sup>, Nora Hettich-Damm<sup>10</sup>, Julia Petersen<sup>10</sup>, Sabine Blaschke<sup>11</sup>, Isabel Bröhl<sup>2</sup>, Jana Butzmann<sup>12</sup>, Hiwa Dashti<sup>13</sup>, Jürgen Deckert<sup>14</sup>, Michael Dreher<sup>15</sup>, Karin Fiedler<sup>1,2</sup>, Carsten Finke<sup>16</sup>, Ramsia Geisler<sup>1,2</sup>, Frank Hanses<sup>17</sup>, Sina M. Hopff<sup>18</sup>, Björn-Erik O. Jensen<sup>19</sup>, Margarethe Konik<sup>20</sup>, Kristin Lehnert<sup>21,22</sup>, Susana M. Nunes de Miranda<sup>2</sup>, Lazar Mitrov<sup>18</sup>, Olga Miljukov<sup>3,4</sup>, Jens-Peter Reese<sup>3,4</sup>, Gernot Rohde<sup>23</sup>, Margarete Scherer<sup>1</sup>, Kristin Tausche<sup>24</sup>, Johannes J. Tebbe<sup>25</sup>, Jörg Janne Vehreschild<sup>1,2,26</sup>, Florian Voit<sup>27</sup>, Patricia Wagner<sup>2</sup>, Martin Weigl<sup>28</sup>, Christina Lemhöfer<sup>29</sup> on behalf of the NAPKON Study Group

#### \*Contributed equally

1 Goethe University Frankfurt, University Hospital, Center for Internal Medicine, Medical Department 2 (Hematology/Oncology and Infectious Diseases), Frankfurt, Germany

2 University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Cologne, Germany

3 University of Würzburg, Institute for Clinical Epidemiology and Biometry, Würzburg, Germany

4 University Hospital Würzburg, Institute for medical Data Science, Würzburg, Germany

5 Internal Medicine Department I, University Hospital Schleswig-Holstein Campus Kiel, Kiel, Germany

6 Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshansdorf, Germany

7 Institute of General Practice and Interprofessional Care, University Hospital Tübingen, Tübingen, Germany

8 Department II of Internal Medicine and Center for Molecular Medicine Cologne, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

9 CECAD, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany

10 Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Mainz, Mainz, Germany

11 Emergency Department, University Medical Center Goettingen, Göttingen, Germany

12 Institute of Medical Microbiology and Hospital Hygiene, University Hospital Magdeburg, Medical Faculty, Otto-von-Guericke University Magdeburg, Magdeburg, Germany

13 Practice for general medicine Dashti, Eberswalde, Germany

14 University Hospital Würzburg, Center of Mental Health, Department of Psychiatry, Psychosomatics and Psychotherapy, Würzburg, Germany

15 Department of Pneumology and Intensive Care Medicine, University Hospital RWTH Aachen, Aachen, Germany

16 Department of Neurology, Charité Berlin, Berlin, Germany

17 Emergency Department and Department for Infection Control an Infectious Diseases, University Hospital Regensburg, Regensburg, Germany

18 University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf, Cologne, Germany

19 Department of Gastroenterology, Hepatology and Infectious Diseases, Düsseldorf University Hospital, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany

20 Department of Infectious Diseases, West German Centre of Infectious Diseases, University Medicine Essen, University Duisburg-Essen, Essen, Germany

21 DZHK (German Center for Cardiovascular Research), University Medicine Greifswald, Greifswald, Germany

22 Department of Internal Medicine B, University Medicine Greifswald, Greifswald, Germany

23 Goethe University Frankfurt, University Hospital, Medical Clinic I, Department of Respiratory Medicine, Frankfurt/Main, Germany

24 Department of Internal Medicine I, University Hospital Carl Gustav Carus TU Dresden, Dresden, Germany

25 Klinikum Lippe, Department of Gastroenterology and Infectious Diseases, Lippe, Germany

26 German Centre for Infection Research (DZIF), partner site Bonn-Cologne, Cologne, Germany

27 Department of Internal Medicine II, University hospital rechts der Isar, Technical University of Munich, School of Medicine, Munich, Germany

28 Department of Orthopaedics and Trauma Surgery, Musculoskeletal University Center Munich (MUM), University Hospital, LMU Munich, Munich, Germany

29 Institute of Physical and Rehabilitation Medicine, Jena University Hospital/Friedrich-Schiller-University Jena, Jena, Germany

#### **Corresponding author**

Katharina S. Appel

Goethe University Frankfurt, University Hospital, Center for Internal Medicine, Medical Department 2 (Hematology/Oncology and Infectious Diseases), Frankfurt, Germany

Email: appel@med.uni-frankfurt.de



Figure S1: Study Flow Chart.

\* at lest one criteria was not present; \*\* review A status means that a monitoring has been performed at the study sites, which recruited the patient and entered study data; this is a standard data export criterion for NAPKON data; \*\*\* PCS at 12MFU was only calculated for patients with PCS including PROMs at 3MFU

	Item No	Recommendation	Page No
Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	( <i>a</i> ) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(b) For matched studies, give matching criteria and number of exposed and unexposed	/
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	( <i>a</i> ) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	4
		( <u>e</u> ) Describe any sensitivity analyses	6

# File S1: continued

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	14- 16
		(c) Summarise follow-up time (eg, average and total amount)	/
Outcome data	15*	Report numbers of outcome events or summary measures over time	5-6
Main results	16	( <i>a</i> ) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14- 15
		(b) Report category boundaries when continuous variables were categorized	4-5
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

\*Give information separately for exposed and unexposed groups.

 Table S1: Variable selection for PCS score mapping.

No.	Complex PCS	Description PCS	Symptom	Query	Form	Variables
1	Chemosensory	Smelling disturbance,	Taste disorders	Symptoms	fv3_3	gec_sy_ne_taste
	deficits	impaired sense of	Odor disorders	Symptoms	fv3_3	gec_sy_ne_smell
		taste				
2	Fatigue	Fatigue	Fatigue ("Fatigue")	Symptoms	esyoth	sy_oth_icd11name
			Chronic Fatigue Syndrome (Persistent or frequent	PROM	prom	cfs
			fatigue)			
			Chalder Fatigue Scale	PROM	promext	cfs_seid_1 to cfs_seid_13
			PROMIS 29 – Fatigue	PROM	promext	pro_29_hi7, pro_29_an3,
						pro_29_fatexp41, pro_29_fatexp40
3	Exercise	Shortness of breath,	Dyspnea	Symptoms	fv3_3	gec_sy_pd_dysp
	intolerance	reduced exercise	Dyspnea (screening question)	PROM	prom	dysp
		capacity	PROMIS Dyspnea	PROM	promext	pro_dysfl001 to pro_dysfl10
			Fatigue – diagnostic criteria	PROM	promext	cfs_seid_crit2
			(Feeling sick after physical exertion)			
4	Joint or muscle	Muscle pain, joint	Joint pain	Symptoms	fv3_1	sy_arthr
	pain	pain	Muscle pain	Symptoms	fv3_1	sy_myalg
5	Ear-nose-throat	Hoarseness, sore	Runny nose	Symptoms	fv3_2	sy_pd_rhin
	ailments	throat, running nose	Nasal congestion	Symptoms	fv3_2	sy_pd_stuf
			Sneezing	Symptoms	fv3_2	sy_pd_sneez
			Sore throat	Symptoms	fv3_2	sy_pd_sore
6	Coughing,	Coughing, wheezing	Coughing	Symptoms	fv3_2	gec_sy_pd_cough
	wheezing		Wheezing	Symptoms	fv3_2	sy_pd_wheez
7	Chest pain	Chest pain	Chest pain	Symptoms	fv3_1	sy_breastp
			Pain, location: chest	PROM	prom	pain_loc_chest
8	Gastrointestinal	Stomach pain,	Stomach ache	Symptoms	fv3_2	gec_sy_gi_abdp
	ailments	diarrhea, vomiting,	Pain, location: abdomen	PROM	prom	pain_loc_abd
		nausea	Diarrhea	Symptoms	fv3_2	gec_sy_gi_diar
			Vomiting	Symptoms	fv3_2	gec_sy_gi_vom
			Nausea	Symptoms	fv3_2	gec sy gi naus

# Table S1: continued

No.	<b>Complex PCS</b>	<b>Description PCS</b>	Symptom	Query	Form	Variables
9	Neurological	Confusion, vertigo,	Orientation disorder or confusion	Symptoms	fv3_3	gec_sy_ne_conf
	ailments	headache, motor	Cognitive impairments	Symptoms	Fv3_3	sy_ne_cogn
		deficits, sensory	Fatigue - diagnostic criteria	PROM	promext	cfs_seid_crit5
		deficits, numbness,	(Orthostatic intolerance - dizziness when standing			
		tremor, deficits of	up/walking)			
		concentration,	Vertigo	Symptoms	fv3_1	sy_dizzi
		cognition or speech	Headache	Symptoms	fv3_1	gec_sy_heada
			Pain, location: head	PROM	prom	pain_loc_head
			In the same area of the body: numbness (in case of	PROM	promext	pain_dn2_6
			pain)			
			Fatigue - diagnostic criteria	PROM	promext	cfs_seid_crit4
			(cognitive (concentration or word-finding)			
			disorders)			
			PROMIS cognitive function	PROM	prom	pro_pc2r
						pro_pc35r
						pro_pc36r
10		TT 1 1		<b>G</b> (	6.2.1	pro_pc42r
10	Dermatological	Hair loss, rash,	Change in the skin or mucous membranes	Symptoms	fv3_1	sy_skin
11	aliments	Chille force and a	$E_{-1}$ = -14 (%Ch:11-2)	C	41-	41 :
11	Infection signs	cinins, lever, general	Feeling cold ( Chills )	Symptoms	Esyoth	sy_our_learmane
		sumptoms	rever	Symptoms	IV3_1	gec_sy_lever
		symptoms	Anorexia	Symptoms	IV3_1	
			Compared side swelling	Symptoms	1V3_1	sy lympn
10	Sleen disturbance	Incomplete supported	General sickness/flulike symptoms ("Feeling III")	Symptoms	esyoth	sy oth icd liname
12	Sleep disturbance	insomnia, unrestful	Steep disturbance (,,,Steep alsturbance, not	Symptoms	esyoth	sy_oin_ical iname
		sieep	BROMIS 20: Sloop disturbance	PROM	nromayt	nro 20 sloon100
			r KOWIS-29: Sleep disturbance	FKOW	promext	$pio_29$ _sieepi09, pro 20 sleepi16 pro 20 sleep20
						pro_29_sleep110, pro_29_sleep20,
						pro_29_sieep44,

The complete data dictionary is available in German here.

**Table S2**: Post hoc test results for sex (male vs. female), smoker (yes or former vs. no), hospitalization (yes vs. no), administration to ICU (never vs. at least once), Vaccination against SARS-CoV-2 prior to study inclusion (yes vs. no).

	p value											
			PCC s	everity								
	None vs.	None vs.	None vs.	Mild vs.	Mild vs.	Moderat						
	mild	moderate	severe	moderate	severe	e vs.						
						severe						
Age	.625	.718	.293	.373	.175	.430						
Sex	.192	.078	<.001*	.972	.039*	.032*						
Smoker	.655	.570	.760	>.999	>.999	>.999						
Hospitalization	.738	.004*	.164	.051	.314	>.999						
Admission to ICU	.456	.753	.514	.697	.208	.353						
At least one vaccination against	.132	.366	.156	.496	.816	.403						
SARS-CoV-2 prior to study inclusion												
All vaccinations against SARS-CoV-	.019*	.013*	.929	.825	.110	.131						
2 prior to study inclusion												
PROMIS-29 Ability to participate in	.004*	<.001*	<.001*	<.001*	<.001*	.054						
social roles and activities												
<b>PROMIS-29</b> Physical Function	<.001*	<.001*	<.001*	.001*	.001*	.356						

**Table S3**: Post hoc test results for comparison between PCC severity groups of age, BMI, number of comorbidities, PROMIS-29 Ability to participate in social roles and activities, PROMIS-29 physical function, number of vaccinations against SARS-CoV-2, EQ-5D-5L index and VAS at 3 and 12MFU, adjusted for multiple testing using Bonferroni correction.

	p value	power
Difference in mean age between PCC groups		
None vs. mild	.731	
None vs. moderate	.281	
None vs. severe	>.999	
Mild vs. moderate	>.999	
Mild vs. severe	>.999	
Moderate vs. severe	>.999	
Difference in mean BMI between PCC groups		
None vs. mild	>.999	
None vs. moderate	.442	
None vs. severe	.448	
Mild vs. moderate	.397	
Mild vs. severe	.361	
Moderate vs. severe	>.999	
Difference in mean number of comorbidities between PCC groups	0.05	
None vs. mild	.095	120
None vs. moderate	.045*	.128
None vs. severe	.263	
Mild vs. moderate	>.999	
Mild vs. severe	>.999	
Differences in mean of DDOMIS 20 Ability to norticinate in social value and	>.999	
Difference in mean of FROMIS-29 Adding to participate in social roles and		
Activities sum score	< 001*	212
None vs. mildi	<.001 < 001*	312
None vs. moderate	<.001*	073
None vs. severe	<.001*	/3/
Mild vs. moderate	<.001*	350
Mild vs. severe	<.001*	494
Moderate vs. severe	.431	
Difference in mean of PROMIS-29 Physical function sum score		
None vs. mild	<.001*	332
None vs. moderate	<.001*	616
None vs. severe	<.001*	696
Mild vs. moderate	<.001*	275
Mild vs. severe	<.001*	437
Moderate vs. severe	.235	
Difference in mean of number of vaccinations against SARS-CoV-2		
None vs. mild	>.999	
None vs. moderate	>.999	
None vs. severe	> 999	
Mild via medenete	> 000	
	~.999	
Mild vs. severe	>.999	
Moderate vs. severe	>.999	
Difference in mean of EQ-5D-5L Index at 3MFU		
None vs. mild	.006*	202
None vs. moderate	<.001*	542
None vs. severe	<.001*	597
	< 001*	_ 373
		525
Ivilia vs. severe	<.001*	4/8
Moderate vs. severe	.014*	146

# Table S3: continued

	p value	power
Difference in mean of EQ-5D-5L VAS at 3MFU		
None vs. mild	<.001*	280
None vs. moderate	<.001*	557
None vs. severe	<.001*	578
Mild vs. moderate	<.001*	260
Mild vs. severe	<.001*	385
Moderate vs. severe	.435	
Difference in mean of EQ-5D-5L Index at 12MFU		
None vs. mild	<.001*	343
None vs. moderate	<.001*	721
None vs. severe	<.001*	719
Mild vs. moderate	<.001*	358
Mild vs. severe	<.001*	503
Moderate vs. severe	.327	
Difference in mean of EQ-5D-5L VAS at 12MFU		
None vs. mild	.006*	233
None vs. moderate	<.001*	619
None vs. severe	<.001*	612
Mild vs. moderate	<.001*	367
Mild vs. severe	<.001*	484
Moderate vs. severe	.668	

	p value													
	Clinical severity during acute infection													
PCC severity	Mild vs. moderate	Mild vs. severe	Moderate vs severe											
None vs. mild	.995	.245	.198											
None vs. moderate	.007*	.014*	.613											
None vs. severe	.147	.505	.806											
Mild vs. moderate	.036*	.402	.439											
Mild vs. severe	.214	>.999	.255											
Moderate vs. severe	>.999	.763	.530											

Table S4: Post hoc test results for clinical severity (mild, moderate, severe) during acute infection.

_	p value <sup>a</sup>													
	Number of vaccinations against SARS-CoV-2 b													
PCC severity	0 vs. 1 0 vs. 2 0 vs. 3+ 1 vs. 2 1 vs. 3+													
None vs. mild	.438	.991	.762	.552	.739	.906								
None vs. moderate	.353	.064	.154	.635	.894	.806								
None vs. severe	.606	.181	.325	.749	.984	.941								
Mild vs. moderate	>.999	.192	.489	.245	.548	.654								
Mild vs. severe	.267	.187	.231	>.999	>.999	>.999								
Moderate vs. severe	.228	.011*	.050	.503	.852	.782								

**Table S5:** Post hoc test results for number of vaccinations against SARS-CoV-2 (0, 1, 2, 3 or more)

		Female																
					<65 y	ears								>= 65	years			
				Р	CC Se	verity				PCC Severity								
	None		Mild		Moderate		Se	vere	p value <sup>a</sup>	N	lone	Ν	1ild 🛛	Moderate		Se	vere	p value <sup>a</sup>
n (%)	52	(28.7)	35	(19.3)	71	(39.2)	23	(12.7)		18	(32.1)	13	(23.2)	20	(35.7)	5	(9.0)	
BMI	26.7	(6.9)	26.2	(6.4)	29.3	(8.0)	29.9	(6.6)	.052	25.5	(6.3)	25.7	(7.1)	26.6	(4.4)	22.3	(3.1)	.377
[ <b>kg/m<sup>2</sup>]</b> , mean (SD) <sup>b,c</sup>																		
<b>Smoker</b> , <i>n</i> (%)	b																	
Never	39	(78.0)	21	(60.0)	46	(65.7)	15	(65.2)	.311	8	(47.1)	10	(76.9)	13	(65.0)	2	(40.0)	.309
Yes or	11	(22.0)	14	(40.0)	24	(34.3)	8	(34.8)		9	(52.9)	3	(23.1)	7	(35.0)	3	(60.0)	
former		. ,						. ,										
<b>Clinical Sever</b>	ity (fol	lowing W	/HO cr	iteria) <sup>b, f</sup>	2													
Mild	20	(38.5)	12	(35.3)	12	(16.9)	2	(8.7)	.514	1	(5.6)	0		0		0		.162
disease, $n$																		
 Moderate	28	(53.8)	19	(55.9)	54	(76.1)	19	(82.6)		17	(94.4)	10	(76.9)	16	(80.0)	5	(100.0)	
disease n	20	(55.0)	17	(33.7)	54	(70.1)	17	(02.0)		17	()-1.1)	10	(70.))	10	(00.0)	5	(100.0)	
(%)																		
Severe	4	(7.7)	3	(8.8)	5	(7.0)	2	(8.7)		0		3	(23.1)	4	(20.0)	0		
disease. n		(,.,)	5	(0.0)	5	(7.0)	2	(0.7)		0		5	(23.1)	•	(20.0)	Ū		
(%)																		
Hospitalized.	n (%) <sup>b</sup>																	
No	20	(38.5)	12	(35.3)	12	(16.9)	2	(8.7)	.035*	1	(5.6)	0		0		0		.643
Yes	32	(61.5)	22	(64.7)	59	(83.1)	21	(91.3)		17	(94.4)	13	(100.0)	20	(100.0)	5	(100.0)	
Admission to	ntensiv	ve care u	nit (IC	Ū) <sup>b</sup>													/	
Never, n	28	(87.5)	16	(84.2)	47	(81.0)	18	(90.0)	.795	17	(100.0)	11	(84.6)	17	(85.0)	5	(100.0)	.323
<u>(%)</u>		(10.5)	2	(1.5.0)	1.1	(10.0)		(10.0)		0			(1.5.4)	2	(1.5.0)	0		
At least once, <i>n</i> (%)	4	(12.5)	3	(15.8)	11	(19.0)	2	(10.0)		0		2	(15.4)	3	(15.0)	0		
										Male								
					< 65 y	ears								>= 65	years			
				Р	CC Se	verity							]	PCC Se	verity			
	N	one	Ν	1ild 🛛	Mo	derate	Se	vere	p value <sup>a</sup>	N	one	Ν	<b>fild</b>	Mo	derate	Se	vere	p value <sup>a</sup>
n (%)	103	(40.1)	47	(18.3)	92	(35.8)	15	(5.8)		42	(39.3)	24	(22.4)	37	(34.6)	4	(3.7)	

Table S6: Group comparisons between PCC severity groups none, mild, moderate and severe stratified by sex and age groups.

#### BMI 28.4 (5.4) 28.1 (5.9) 28.1 29.5 (4.5) .573 (6.1) 27.9 28.2 27.3 (4.1)(4.3)26.8 (4.6) (6.5) .452 $[kg/m^2],$ mean (SD) b,c

### Table S6: continued

											Male								
						< 65 y	vears								>= 65	years			
					Р	CC Se	everity				PCC Severity								
	_	N	one	Ν	Aild	Mo	derate	Se	evere	p value <sup>a</sup>	Ν	None Mild		Mild	ild Moderate		Severe		p value <sup>a</sup>
Smoker, n (	%) <sup>b</sup>	1								-									
Never		60	(59.4)	23	(48.9)	51	(56.0)	7	(46.7)	.587	19	(50.0)	14	(60.9)	16	(43.2)	3	(75.0)	.439
Yes	or	41	(40.6)	24	(51.1)	40	(44.0)	8	(53.3)		19	(50.0)	9	(39.1)	21	(56.8)	1	(25.0)	
former									. ,			. ,		. ,		. ,		· /	
Clinical Sev	erit	y (foll	owing Wl	HO cr	iteria) <sup>b,</sup>														
Mild		27	(26.2)	11	(23.4)	13	(14.4)	4	(26.7)	.327	2	(4.8)	2	(8.3)	2	(5.4)	0		.973
disease,	п																		
(%)																			
Moderate	•	63	(61.2)	26	(55.3)	59	(65.6)	8	(53.3)	•	32	(76.2)	17	(70.9)	28	(75.7)	4	(100.0)	
disease,	n																		
(%)																			
Severe		13	(12.6)	10	(21.3)	18	(20.0)	3	(20.0)		8	(19.0)	5	(20.8)	7	(18.9)	0		
disease,	n																		
(%)																			
Hospitalized	<b>d</b> , <i>n</i>	(%) <sup>b</sup>																	
No		27	(26.2)	11	(23.4)	13	(14.4)	4	(26.7)	.196	2	(4.8)	2	(8.3)	2	(5.4)	0		.810
Yes		76	(73.8)	36	(76.6)	77	(85.6)	11	(73.3)	•	40	(95.2)	22	(91.7)	35	(94.6)	4	(100.0)	
Admission t	to in	tensiv	e care un	it (ICI	U) <sup>b</sup>														
Never,	п	60	(83.3)	26	(74.3)	61	(80.3)	9	(81.8)	.733	30	(76.9)	17	(81.0)	30	(88.2)	4	(100.0)	.549
(%)																			
At lea	ist	12	(16.7)	9	(25.7)	15	(19.7)	2	(18.2)	-	9	(23.1)	4	(19.0)	4	(11.9)	0		•
once n (%	6)																		

<sup>a</sup> group differences assessed by Chi2, Fishers- or Kruskal-Wallis test, as appropriate; normally significant values were Bonferroni-adjusted by multiplication with the size of the respective group characteristics (i.e. 6 or 18), if the unadjusted p value already exceeded 0.050, no adjustment was done

<sup>b</sup> all analyses were conducted for patients with available data (female missing data <65 years/>=65 years: BMI 16/6, smoker 3/1, admission to ICU 44/2, clinical severity 1/0, vaccination against Sars-COV-2 21/5; male missing data <65 years/>=65 years: BMI 21/8, smoker 3/5, hospitalization 1/0, admission to ICU 54/4, clinical severity 2/0, vaccination against SaSARS-CoV-2 32/15, PROMIS-29 Ability to participate in social roles and activities 74/35, PROMIS-29 Physical Function 71/34)

Table S7: Post hoc test results for smoker (yes or former vs. no), hospitalization (yes vs. no), administration to ICU (never vs. at least once) stratified by sex and age groups.

		Female											
		p value											
	< 65 years							>= 65 years					
	PCC severity						PCC severity						
	None vs.	None vs.	None vs.	Mild vs.	Mild vs.	Moderate	None vs.	None vs.	None vs.	Mild vs.	Mild vs.	Moderate	
	mild	moderate	severe	moderate	severe	vs. severe	mild	moderate	severe	moderate	severe	vs. severe	
Smoker	.121	.209	.385	.720	.901	>.999	.201	.444	>.999	.701	.268	.358	
Hospitalization	.945	.013*	.020*	.064	.048*	.505	>.999	.474	>.999	-	-	-	
Administration to	>.999	.622	>.999	>.999	.661	.496	.179	.234	-	>.999	>.999	>.999	
ICU													
						Ma	ale						

	p value												
	< 65 years								>= 65 years				
	PCC severity							PCC severity					
	None vs.	None vs.	None vs.	Mild vs.	Mild vs.	Moderate	None vs.	None vs.	None vs.	Mild vs.	Mild vs.	Moderate	
	mild	moderate	severe	moderate	severe	vs. severe	mild	moderate	severe	moderate	severe	vs. severe	
Smoker	.309	.745	.514	.540	>.999	.692	.575	.723	.608	.288	>.999	.321	
Hospitalization	.869	.067	>.999	.283	>.999	.259	.618	>.999	>.999	.643	>.999	>.999	
Administration to	.398	.787	>.999	.644	>.999	>.999	>.999	.340	.564	.464	>.999	>.999	
ICU													

	Female					Male					
	Т	otal	< 65	years	>= 65	5 years	< 65	years	>= 6	5 years	
	rho	p value	rho	p value	rho	p value	rho	p value	rho	p value	
Age	0.072	.077	-	-	-	-	-	-	-	-	
BMI	0.121	.004*	0.249	.001*	0.023	.875	0.036	.584	0.196	.054	
Clinical Severity	0.104	.011*	0.226	.002*	0.244	.070	0.106	.090	-0.017	.861	
Number of pre- existing comorbidities	0.116	.004*	0.092	.216	0.093	.494	0.170	.006*	0.229	.018*	
Number of vaccinations against SARS- CoV-2	0.036	.393	-0.042	.588	0.252	.069	0.009	.890	0.117	.254	
Quality of Life (EQ-5D-5L) at 3MFU											
Index	-0.558	<.001*	-0.686	<.001*	-0.277	.068	-0.551	<.001*	-0.428	<.001*	
VAS	-0.531	<.001*	-0.598	<.001*	-0.278	.065	-0.554	<.001*	-0.555	<.001*	
Quality of Life (EQ-5D-5L) at 12MFU											
Index	-0.691	<.001*	-0.756	<.001*	-0.244	.179	-0.698	<.001*	-0.714	<.001*	
VAS	-0.594	<.001*	-0.592	<.001*	-0.416	.018*	-0.602	<.001*	-0.743	<.001*	
PROMIS-29 Ability to participate in social roles and activities <sup>1</sup>	-0.635	<.001*	-0.668	<.001*	-0.414	.018*	-0.688	<.001*	-0.520	<.001*	
PROMIS-29 Physical	-0,593	<.001 <sup>*</sup>	-0.646	< <b>.001</b> *	-0.466	.006*	-0.607	<.001*	-0.520	<.001*	

Table S8: Correlations with Post-COVID-Sum-Score.

function<sup>1</sup> <sup>1</sup> the lower the sum score, the higher the social or functional impairments

	Worse PCS		No s	hift in PCS	Better PCS		
	73	(12.1)	232	(38.5)	85	(14.1)	
Sex, n (%)							
Women	29	(39.7)	96	(41.6)	31	(36.5)	
Men	44	(60.3)	135	(58.4)	54	(63.5)	
Age [years], mean (SD)	57.2	(16.8)	53.6	(15.5)	49.9	(14.6)	
Age groups, n (%)							
< 65 years	45	(61.6)	174	(75.7)	69	(81.2)	
>= 65 years	28	(38.4)	56	(24.3)	16	(18.8)	
<b>Pre-existing comorbidities</b> , <i>n</i> (%)		· · ·					
Cardiovascular diseases	38	(52.1)	109	(47.0)	29	(34.1)	
Diabetes	15	(20.5)	40	(17.3)	9	(10.6)	
Cancer	15	(20.5)	29	(12.6)	8	(9.4)	
Nephrological diseases	12	(16.4)	14	(6.0)	10	(11.8)	
Allergies	11	(15.3)	39	(16.9)	16	(18.8)	
Respiratory diseases	7	(9.6)	27	(11.6)	15	(17.6)	
Gastrointestinal or hepatic diseases	6	(8.2)	18	(7.8)	3	(3.5)	
Psychiatric diseases	4	(5.5)	11	(4.7)	3	(3.5)	
Organ transplant	3	(4.1)	9	(3.4)	5	(5.9)	
Neurological diseases	2	(2.7)	7	(3.0)	3	(3.5)	
Rheumatologic or immunologic diseases	1	(1.4)	7	(3.0)	2	(2.4)	
No. of pre-existing comorbidities, Mean (SD)	2.0	(2.0)	1.7	(1.8)	1.5	(1.7)	
0, <i>n (%)</i>	19	(26.0)	68	(29.3)	31	(36.5)	
1-2, <i>n (%)</i>	30	(41.1)	105	(45.3)	36	(42.4)	
3-5, n (%)	18	(24.7)	47	(20.3)	14	(16.5)	
6 or more, <i>n (%)</i>	6	(8.2)	12	(5.2)	4	(4.7)	
<b>No. of vaccinations per patient,</b> <i>Mean (SD)</i>	1.4	(1.1)	1.5	(1.1)	1.5	(1.1)	
<b>0</b> , <i>n</i> (%) <sup>b</sup>	19	(26.8)	56	(25.3)	21	(27.3)	
<b>1</b> , <i>n</i> (%) <sup>b</sup>	18	(25.4)	40	(18.1)	13	(16.9)	
<b>2</b> , <i>n</i> (%) <sup>b</sup>	22	(31.0)	77	(34.8)	28	(36.4)	
<b>3 or more</b> , <i>n (%)</i> <sup>b</sup>	12	(16.9)	48	(21.7)	15	(19.5)	

Table S9: Patient characteristics of patients with changed PCS from 3 to 12MFU.

No.	Symptom complex	Self-reported sub-symptoms	Witl PR(	hout DMs	With PROMs	
			n	(%)	n	(%)
1	Chemosensory deficits <sup>a, b</sup>	Smelling disturbance, impaired sense of taste	45	(8.4)	45	(8.4)
2	Fatigue <sup>b</sup>	Fatigue	52	(9.2)	244	(42.6)
3	Exercise intolerance	Shortness of breath	96	(19.0)	205	(39.0)
4	Joint or muscle pain <sup>a,b</sup>	Muscle pain, joint pain	39	(7.4)	39	(7.4)
5	Ear-Nose-Throat (ENT) ailments <sup>a,b</sup>	Sneezing, sore throat, running nose, stuffy nose	16	(3.0)	16	(3.0)
6	Coughing, wheezing <sup>a,b</sup>	Coughing, wheezing	35	(6.5)	35	(6.5)
7	Chest pain <sup>b</sup>	Chest pain	11	(2.1)	63	(11.9)
8	Gastrointestinal ailments <sup>b</sup>	Stomach pain, diarrhea, vomiting, nausea	11	(2.0)	51	(9.0)
9	Neurological ailments <sup>b</sup>	Confusion, vertigo, headache, deficits of cognition	77	(14.0)	244	(43.3)
10	Dermatological ailments <sup>a,b</sup>	Skin or mucous membrane change	7	(1.3)	7	(1.3)
11	Infection signs <sup>a,b</sup>	Chills, fever, feeling ill, lymph node swelling, loss of appetite	14	(2.5)	14	(2.5)
12	Sleep disturbance <sup>b</sup>	Sleep disturbance, not elsewhere classified	0	-	78	(13.4)

**Table S10:** Symptom complexes with symptoms present for at least two months at 12MFU visit following the recommendations by Bahmer et al. (2022)

<sup>a</sup> no adjustment with patient reported outcome measures (PROMs)

<sup>b</sup> percentages relate to number of patients with available data (missing data: chemosensory deficits 50, Fatigue without/with PROMs 17/12, exercise and intolerance without/with PROMs 81/59, joint or muscle pain 57, ENT ailments 48, coughing/ wheezing 43, chest pain without/with PROMs 63/57, gastrointestinal ailments without/with PROMs 21/20, neurological ailments without/with PROMs 36/22, dermatological ailments 53, infection signs 21, sleep disturbance without/with PROMs 2/2)

		<u>PCC severity = "None"</u>							
		PROMIS-29 Ability	y to participate in	PROMIS-29 Phy	sical Function <sup>a</sup>				
		social roles an	d activities <sup>a</sup>						
	Total	No impairments	Impairments	No impairments	Impairments				
Pre-existing comorbidities, <i>n (%)</i> <sup>b</sup>	854	113 (13.2)	2 (0.23)	111 (13.0)	8 (0.94)				
Respiratory diseases	10 (4.7)	2 (1.8)	0	2 (1.8)	0				
Cardiovascular diseases	94 (43.7)	42 (37.2)	2 (100.0)	40 (36.0)	6 (75.0)				
Neurological diseases	7 (3.3)	2 (1.8)	0	2 (1.8)	0				
Psychiatric diseases	7 (3.3)	2 (1.8)	0	2 (1.8)	0				
Gastrointestinal or hepatic diseases	11 (5.1)	5 (4.4)	0	7 (6.3)	0				
Diabetes	29 (13.5)	14 (12.4)	0	14 (12.6)	2 (25.0)				
Rheumatologic or immunologic	1 (0.5)	1 (0.9)	0	1 (0.9)	0				
diseases									
Nephrological diseases	19 (8.8)	8 (7.1)	1 (50.0)	8 (7.2)	2 (25.0)				
Allergies <sup>j</sup>	29 (13.5)	20 (17.7)	0	19 (17.1)	1 (12.5)				
Cancer <sup>j</sup>	35 (16.3)	13 (11.5)	1 (50.0)	13 (11.7)	2 (25.0)				
Organ transplant <sup>j</sup>	14 (6.5)	7 (6.2)	0	7 (6.3)	1 (12.5)				

Table S11: Connection between social or functional impairments and pre-existing comorbidities for patients with no Post-COVID.

<sup>a</sup> all analyses were conducted for patients with available data (missing data: PROMIS-29 ability to participate in social roles and activities 172, PROMIS-29 Physical Function 166) <sup>b</sup> all analyses were conducted for patients with available data (missing data: psychiatric diseases 1, diabetes 3, allergies 6, cancer 4) **Table S12:** Sensitivity analysis treating a missing in a symptom complex as 0 points: Group comparisons between PCC severity groups none, mild, moderate and severe.

		p value °				
	0	>0 to <u>&lt;</u> 10.75	>10.75 to <26.25	>26.25		
	(none)	(mild)	(moderate)	(severe)	unadjusted	adjusted
n (%)	318 (37.2)	173 (20.3)	301 (35.2)	62 (7.3)		
Age [years], Mean (SD) <sup>b,d</sup>	52.6 (17.1)	55.3 (16.7)	54.7 (14.9)	53.4 (13.8)	.218	n.a
Age groups, n (%) <sup>b,d</sup>						
< 65 years	226 (71.1)	122 (70.9)	224 (74.7)	51 (82.3)	.251	n.a
>= 65 years	92 (28.9)	51 (29.1)	76 (25.3)	11 (17.7)		
<b>Sex</b> <i>n</i> (%) <sup>b,d</sup>						
Women,	119 (37.4)	65 (37.8)	127 (42.2)	35 (56.5)	.034*	.204
Men	199 (62.6)	107 (62.2)	174 (57.8)	27 (43.5)		
BMI [kg/m <sup>2</sup> ], mean (SD) <sup>b,d</sup>	27.6 (5.9)	28.2 (7.7)	28.4 (6.0)	29.1 (6.0)	.078	n.a
<b>Smoker</b> , <i>n</i> (%) <sup>b,d</sup>						
Never	179 (60.9)	100 (58.5)	166 (55.9)	35 (56.5)	.659	n.a
Yes or former	115 (39.1)	71 (41.5)	131 (44.1)	27 (43.5)		
Clinical Severity (following WHO criteria) <sup>b,d</sup>						
Mild disease (no hospitalization), n (%)	64 (20.3)	31 (18.0)	35 (11.7)	7 (11.3)	.026*	.466
Moderate disease (hospitalized, no oxygen or oxygen						
by mask or nasal prongs (< 15 l/min)), n (%)	204 (64.6)	105 (61.0)	208 (69.8)	48 (77.4)		
Severe disease (hospitalized, oxygen by NIV or high						
flow (> 15 l/min)), n (%)	48 (15.2)	36 (20.9)	55 (18.5)	7 (11.3)		
Hospitalized, n (%) <sup>b,d</sup>						
No	64 (20.3)	31 (18.0)	35 (11.7)	7 (11.3)	.021*	.126
Yes	252 (79.7)	141 (82.0)	263 (88.3)	55 (88.7)		
Admission to intensive care unit (ICU) <sup>b,d</sup>						
Never, <i>n</i> (%)	202 (82.1)	104 (76.5)	209 (80.7)	46 (86.8)	.369	n.a
At least once, n (%)	44 (17.9)	32 (23.5)	50 (19.3)	7 (13.2)		
Vaccination against SARS-CoV-2 prior to study						
inclusion <sup>b,e</sup>						
<b>No</b> , <i>n</i> (%)	159 (57.8)	106 (67.5)	170 (60.7)	35 (60.3)	.262	n.a
Yes, n (%)	116 (42.2)	51 (32.5)	110 (39.3)	23 (39.7)		
No. of pre-existing comorbidities, Mean (SD) <sup>b,d</sup>	1.6 (1.8)	2.0 (2.1)	2.0 (2.0)	2.3 (2.3)	.053	n.a
<b>0</b> , <i>n</i> (%)	106 (33.3)	56 (32.4)	83 (27.6)	15 (24.2)	.276	n.a
<b>1 or more,</b> <i>n (%)</i>	212 (66.7)	117 (67.6)	218 (72.4)	47 (75.8)		

# Table S12: continued

		p val	ue <sup>c</sup>			
	0	>0 to <u>&lt;</u> 10.75	>10.75 to <u>&lt;</u> 26.25	>26.25		
	(none)	(mild)	(moderate)	(severe)	unadjusted	adjusted
<b>Pre-existing comorbidities</b> <i>n</i> (%) <sup>b,f</sup>						
Cardiovascular diseases	140 (44.0)	84 (48.6)	139 (46.2)	26 (41.9)	.729	n.a
Diabetes	44 (14.0)	40 (23.3)	42 (14.0)	11 (17.7)	.035*	.210
Cancer	47 (15.0)	20 (11.6)	53 (17.7)	15 (24.6)	.083	n.a
Allergies	43 (13.8)	26 (15.0)	45 (15.1)	9 (14.5)	.969	n.a
Respiratory diseases	24 (7.6)	21 (12.1)	52 (17.3)	14 (22.6)	<.001*	.002*
Nephrological diseases	28 (8.8)	19 (11.0)	32 (10.6)	10 (16.1)	.356	n.a
Gastrointestinal or hepatic diseases	21 (6.6)	11 (6.4)	21 (7.0)	6 (9.7)	.794	n.a
Organ transplant	20 (6.3)	9 (5.2)	14 (4.7)	4 (6.5)	.773	n.a
Psychiatric diseases	11 (3.5)	5 (2.9)	26 (8.7)	5 (8.3)	.009*	.055
Neurological diseases	12 (3.8)	8 (4.6)	11 (3.7)	7 (11.3)	.087	n.a
Rheumatologic or immunologic diseases	5 (1.6)	4 (2.3)	17 (5.7)	2 (3.2)	.033*	.200
PROMIS-29 Ability to participate in social roles and	18.9 (2.0)	16.9 (3.8)	13.1 (4.3)	11.3 (3.9)	<.001*	<.001*
activities <sup>b,d</sup>						
No social impairments, n (%)	144 (98.6)	104 (89.7)	128 (53.6)	17 (32.7)	<.001*	<.001*
Social impairments, n (%)	2 (1.4)	12 (10.3)	111 (46.4)	35 (67.3)		
PROMIS-29 Physical function <sup>b,d</sup>	19.4 (1.6)	17.6 (3.5)	15.2 (4.2)	13.7 (4.2)	<.001*	<.001*
No physical impairments, <i>n</i> (%)	140 (44.0)	81 (46.8)	93 (30.9)	13 (21.0)	<.001*	<.001*
Physical impairments, n (%)	12 (3.8)	38 (22.0)	148 (49.2)	38 (61.3)		

<sup>a</sup> PCC-Groups including PROMs; missing values: 22; missings in symptom complexes were ignored (represented 0 points for the complex)

<sup>b</sup> all analyses were conducted for patients with available data (missing data by PCC-group:, age/age groups 2, sex: 1, BMI 82, smoker 30, clinical severity 6, hospitalization 6, admission to ICU 127, vaccination against SARS-CoV-2 prior to study inclusion 84, PROMIS-29 Ability to participate in social roles and activities 301, PROMIS-29 Physical function 291, diabetes 6, cancer 7, allergies 9, respiratory diseases 1, psychiatric diseases 5)

<sup>c</sup> group differences assessed by Chi2, Fishers- or Kruskal-Wallis test, as appropriate; normally significant values were Bonferroni-adjusted by multiplication with the size of the respective group characteristics (i.e. 6 or 18), n.a: not applicable because the unadjusted p value already exceeded 0.050

<sup>d</sup> for post-hoc test results see Figure 3 (age), Figure 4 (BMI), Table 4 (age groups (< or >= 65 years), sex, smoker, hospitalization, administration to ICU), Table 5 (clinical severity) <sup>e</sup> "No" includes all patients without any SARS-CoV-2 vaccination

<sup>f</sup> pre-existing comorbidities were either diagnosed or not diagnosed

# Supplementary text 1: Version numbers of PROMs

In the SUEP, PROMIS were assessed in the following versions: PROMIS-29 Fatigue 4a – Adult v1.0, PROMIS-29 Dyspnea Functional Limitations 10a – Adult v1.0, PROMIS Cognitive Function 4a – Adult v2.0, PROMIS-29 Sleep Disturbance 4a.