

Online supplement

Post COVID-19 symptoms are common, also among young adults in the general population

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Definition of co-variables and chronic diseases

Baseline questionnaire

Maternal smoking: the mother smoked at least one cigarette per day at any point of time during pregnancy and/or in infancy

1–2-year follow-up questionnaire

Bronchitis first 2 years: parental-reported doctor's diagnosis of bronchitis reported in the 1-year and/or 2-year questionnaire

Pneumonia first 2 years: parental-reported doctor's diagnosis of pneumonia reported in the 1-year and/or 2-year questionnaire

Wheeze first 2 years: at least one episode of wheeze (after 3 months of age) reported in the 1-year and/or 2-year questionnaire

24-year follow-up questionnaire

Smoking: self-reported based on the question “do you smoke”, with the answer alternatives ‘No’, ‘No, but I have smoked before’ (referred to as ex-smoker), ‘Yes, sometimes’, ‘Yes, every day’. Smoking was also categorized as yes/no in some analyses due to low numbers.

Snuff use: self-reported based on the question “do you use snuff”, with the answer alternatives ‘No’, ‘No, but I have used snuff before’ (referred to as ex-user), ‘Yes, sometimes’, ‘Yes, every day’. Snuff use was also categorized as yes/no in some analyses due to low numbers.

Asthma: doctor's diagnosis of asthma (ever) together with symptoms of breathing difficulties or asthma medication occasionally or regularly in the last 12 months.

Chronic bronchitis: cough and mucus production in the morning during winter.

Rhinitis: symptoms from eyes or nose after exposure to furred animals or pollen (without having a flu) in the last 12 months

Migraine, Depression and ADHD or ADD: self-reported doctor's diagnosis (ever) of “Migraine”, “Depression”, “ADHD or ADD”, respectively.

Consider themselves completely health: answering “Completely healthy” to the question “How healthy would you say that you are?”

24-year follow-up examination

Overweight: defined from measured weight and height as a body mass index ≥ 25 kg/m².

Sensitization to airborne allergens were analyzed from the blood samples using the Phadiatop mix (cat, dog, horse, timothy, birch, mug wort, house dust mite and mold). IgE values ≥ 0.35 kU/L were considered positive.

Lung function: lung function testing was performed with spirometry (Vyaire Vyntus system, Vyair Medical, IL, USA, according to the ATS/ERS guidelines ¹; bronchodilation with four puffs of Salbutamol in spacer with new measurements 15 minutes later). Measured values were expressed as percent of predicted (pp) using the Global Lung Initiative reference

material². Multiple breath nitrogen wash out test was performed at least twice with an Exhalyzer D (Ecomedics Technologies™, San Diego, CA) according to ERS guidelines³. As software, Spiroware 3.2.0 was used, and migrated to Spiroware 3.3.1 to correct for previously reported calculation errors⁴⁻⁶.

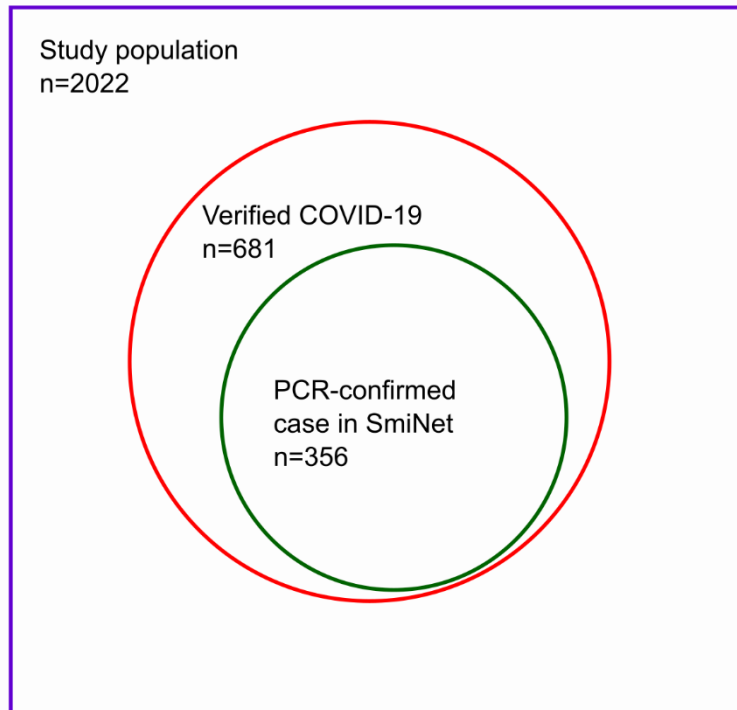
COVID-19 follow-up questionnaire

Education: self-reported highest completed education at the time of the phase 3 questionnaire. Categorized as elementary school, high school/upper secondary school, university/College <3 years/folk high school and university ≥ 3 years.

Occupation: self-reported occupation at the time of the phase 3 questionnaire and categorized as studying, working, other (including the answer alternatives “parental leave or unpaid leave”, “unemployed”, “furloughed due to the current pandemic” or “other”)

Living area: based on the registered postal address at the time of questionnaire 3, categorized as Stockholm County or outside of Stockholm County

Bedbound during COVID-19: bedbound during the COVID-19 infection with the answer alternatives “no”, “yes, 1-6 days”, “yes, ≥ 1 week”



Supplementary Figure 1. Proportional Venn-diagram showing PCR-confirmed cases in the SmiNet register (a national register covering all positive PCR-tests for SARS-CoV-2 conducted in Sweden) and total number of confirmed cases of COVID-19 (PCR-verified in SmiNet and/or reported positive PCR and/or reported positive antigen test and/or reported IgG if unvaccinated during the clinical examination). Figure created in Stata and Inkscape.

Supplementary Table S1. Description of sociodemographic factors, disease severity and vaccination against COVID-19 among participants with and without confirmed COVID-19¹ (n=2022)

	No confirmed COVID-19 (n=1341)	Confirmed COVID- 19 (n=681)	
	n (%)	n (%)	P-value ²
Sex (n=2022)			0.76
- Female	788 (58.8)	405 (59.5)	
- Male	553 (41.2)	276 (40.5)	
COVID-19 follow-up variables	n (%)	n (%)	P-value²
Education (n=1948)			0.68
- Elementary school	26 (2.0)	11 (1.7)	
- High school/upper secondary school	373 (28.7)	184 (28.4)	
- University/College <3 years or folk high school	194 (14.9)	110 (17.0)	
- University ≥ 3 years	706 (54.4)	344 (53.0)	
Occupation (n=1953)			0.79
- Studying	364 (27.9)	183 (28.0)	
- Working	844 (64.8)	426 (65.5)	
- Other	95 (7.3)	42 (6.5)	
Living area (n=2022)			<0.001
- Stockholm County	986 (73.5)	565 (83.0)	
- Outside of Stockholm County	355 (26.5)	116 (17.0)	

¹ Confirmed COVID-19 self-reported SARS-CoV-2 positive PCR-test, antigen test or IgG test before vaccination and/or positive PCR-test in the database SmiNet (a national register covering all positive PCR-tests for SARS-CoV-2 conducted in Sweden).

² P-value obtained by chi-2 test

Supplementary Table S2. Description lifestyle and chronic diseases before the pandemic among participants with and without confirmed COVID-19¹ (n=2022)

	No confirmed COVID-19 (n=1341)	Confirmed COVID-19 (n=681)	
	n (%)	n (%)	P-value²
Early factors (1-2 year questionnaire)			
Maternal smoking in pregnancy and/or infancy (n=2021)	151 (11.3)	94 (13.8)	0.10
Pneumonia first 2 years (n=1948)	100 (7.8)	49 (7.5)	0.81
Wheeze first 2 years (n=1948)	315 (24.4)	180 (27.3)	0.17
Bronchitis first 2 years (n=1943)	180 (14.0)	104 (15.8)	0.28
24- year follow-up variables	n (%)	n (%)	P-value²
Smoking (n=2018)			<0.001
- No	960 (71.8)	430 (63.1)	
- Ex-smoker	151 (11.3)	97 (14.2)	
- Yes, sometimes	134 (10.0)	113 (16.6)	
- Yes, everyday	92 (6.9)	41 (6.0)	
Snuff use (n=2020)			0.20
- No	1117 (83.4)	560 (82.2)	
- Ex-user	35 (2.6)	28 (4.1)	
- Yes, sometimes	54 (4.0)	33 (4.9)	
- Yes, everyday	133 (9.9)	60 (8.8)	
Overweight (n=1675)	239 (21.7)	125 (21.7)	1.00
Asthma (n=2017)	154 (11.5)	75 (11.1)	0.76
Chronic bronchitis (n=1972)	71 (5.4)	36 (5.5)	0.98
Rhinitis (n=2001)	408 (30.8)	210 (31.1)	0.88
Sensitization to airborne allergens (n=1656)	472 (43.5)	240 (42.1)	0.60
Migraine doctors diagnosed (n=1970)	74 (5.7)	53 (8.0)	0.049
Depression doctors diagnosed (n=1971)	202 (15.5)	75 (11.3)	0.01
ADHD or ADD doctors diagnosed (n=1973)	74 (5.7)	22 (3.3)	0.02
Consider themselves completely healthy (n=1981)	823 (62.7)	432 (64.7)	0.39

¹ Confirmed COVID-19: self-reported SARS-CoV-2 positive PCR-test, antigen test or IgG test before vaccination and/or positive PCR-test in the database SmiNet (a national register covering all positive PCR-tests for SARS-CoV-2 conducted in Sweden).

² P-value obtained by chi-2 test

Supplementary Table S3. Description of disease severity (being bedbound during the COVID-19 disease) among participants with confirmed COVID-19 with and without post COVID-19, as well as for the groups with the three most common specific symptoms of post COVID-19 (altered smell and taste, dyspnea, and fatigue).

	No post COVID-19 (n=518)	Post COVID-19 (n=112)	Altered smell/taste (n=76)	Dyspnea (n=34)	Fatigue (n=33)
	n (%)	n (%)	n (%)	n (%)	n (%)
Bedbound during disease (n=)					
- No	222 (42.9)	35 (31.5)	28 (36.8)	6 (17.7)	4 (12.1)
- Yes, 1-6 days	246 (47.5)	59 (53.2)	40 (52.6)	20 (58.8)	16 (48.5)
- Yes, ≥ 1 week	50 (9.7)	17 (15.3)	8 (10.5)	8 (23.5)	13 (39.4)
P-value ¹		0.044	0.61	0.003	<0.001

¹ All groups as compared to the groups with no post COVID-19 symptoms using chi-2 test.

Supplementary Table S4. Description lifestyle and chronic diseases before the pandemic (at the 24-year follow-up among participants with confirmed COVID-19 with or without post COVID-19

	Confirmed COVID-19 ¹ without post COVID (n=569)	Confirmed COVID-19 ¹ with post COVID-19 (n=112)	P-value ²
Early factors (1–2-year follow-up)	n (%)	n (%)	
Maternal smoking in pregnancy and/or infancy (n=681)	76 (13.4)	18 (16.1)	0.45
Pneumonia first 2 years (n=658)	37 (6.7)	12 (11.2)	0.11
Wheeze first 2 years (n=659)	154 (27.9)	26 (24.5)	0.48
Bronchitis first 2 years (n=657)	90 (16.3)	14 (13.2)	0.42
24- year-follow-up variables	n (%)	n (%)	P-value²
Smoking (n=681)	128 (22.5)	26 (23.3)	0.87
Snuff use (n=681)	79 (13.9)	14 (12.5)	0.70
Overweight (n=575)	104 (21.6)	21 (22.6)	0.83
Asthma (n=678)	59 (10.4)	16 (14.4)	0.22
Chronic bronchitis (n=661)	29 (5.2)	7 (6.5)	0.60
Rhinitis (n=675)	174 (30.8)	36 (32.7)	0.69
Sensitization to airborne allergens (n=570)	196 (41.1)	44 (47.3)	0.27
Migraine doctors diagnosed (n=665)	40 (7.2)	13 (11.7)	0.11
Depression doctors diagnosed (n=666)	62 (11.2)	13 (11.7)	0.87
ADHD or ADD doctors diagnosed (n=666)	16 (2.9)	6 (5.4)	0.18
Consider themselves completely healthy (n=668)	370 (66.2)	62 (56.9)	0.06

¹ Confirmed COVID-19: confirmed case in SmiNet (PCR-verified) and/or reported positive PCR and/or reported positive antigen test and/or reported IgG if unvaccinated during the clinical examination (all from the questionnaire in phase 3)

² P-value obtained by chi-2 test or Fischer's exact test depending on size of the groups

Supplementary Table S5. Description of lung function before the pandemic (at the 24-year follow-up) among participants with confirmed COVID-19 with or without post COVID-19

	No post COVID-19 Pre BD: n=440 Post BD: n=420	Post COVID-19 Pre BD: n=84 Post BD: n=79	P-value¹
	mean (SD)	mean (SD)	
FEV1pp pre BD	97.0 (9.5)	97.1 (9.9)	0.93
FEV1pp post BD	100.4 (9.3)	101.0 (9.8)	0.59
FVCpp pre BD	100.1 (9.8)	100.3 (9.8)	0.86
FVCpp post BD	99.6 (9.9)	100.5 (9.9)	0.44
FEV1/FVC pre BD	0.83 (0.058)	0.83 (0.064)	0.94
FEV1/FVC post BD	0.86 (0.049)	0.86 (0.056)	0.72
	n=246	N=51	
LCI	6.09 (0.41)	6.03 (0.37)	0.31

¹ P-value obtained by the t-test

BD: Bronchodilation; pp: percent of predicted; FEV1: forced exhaled volume the first second; FVC: forced vital capacity; LCI: lung clearance index

Supplementary Table S6. Description of lung function before the pandemic (at the 24-year follow-up) in participants without post COVID-19 compared with participants with post COVID-19 symptom of dyspnea

	No post COVID-19	No post COVID-19 dyspnea	P-value ¹
	Pre BD: n=440 Post BD: n=420	Pre BD: n=28 Post BD: n=25	
	mean (SD)	mean (SD)	
FEV1pp pre BD	97.0 (9.5)	97.3 (9.0)	0.86
FEV1pp post BD	100.4 (9.3)	100.9 (10.2)	0.79
FVCpp pre BD	100.1 (9.8)	101.5 (10.3)	0.45
FVCpp post BD	99.6 (9.9)	102.3 (10.6)	0.19
FEV1/FVC pre BD	0.83 (0.058)	0.82 (0.068)	0.51
FEV1/FVC post BD	0.86 (0.049)	0.85 (0.059)	0.088
	n=246	n=23	
LCI	6.09 (0.41)	6.15 (0.40)	0.50

Pre: n=440+28 Post: n=420+25

¹ P-value obtained by the t-test

BD: Bronchodilation; pp: percent of predicted; FEV1: forced exhaled volume the first second; FVC: forced vital capacity; LCI: lung clearance index

Supplementary Table S7. Association between sociodemographic factors during the pandemic as well as chronic diseases before the pandemic and post COVID-19 defined as symptoms lasting for at least 3 months after COVID-19 in combination with confirmed COVID-19, analyzed by a mutually adjusted multivariable logistic regression analysis (n=510)

	Post COVID-19	
	OR	95% CI
Sex		
Females	Referent	-
Males	0.93	0.56-1.56
Living area		
Outside of Stockholm County	Referent	-
Stockholm County	1.04	0.53-2.05
Education		
Elementary school, high school, or upper secondary school	Referent	-
University/College	0.78	0.47-1.29
Occupation		
Student	Referent	-
Worker	0.67	0.39-1.14
Other	0.87	0.32-2.38
Bedbound during COVID-19		
No	Referent	-
Yes, 1-6 days	1.27	0.74-2.16
Yes, ≥ 1 week	1.57	0.72-3.45
BMI status at 24 years		
Normal weight	Referent	-
Overweight	0.80	0.43-1.49
Smoking at 24 years		
No	Referent	-
Yes	0.82	0.45-1.50
Asthma at 24 years		
No	Referent	-
Yes	1.09	0.52-2.31
Consider themselves completely healthy		
No	Referent	-
Yes	0.62	0.38-1.01

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