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Title

Impact of post-covid-19 condition on health status and activities of daily living: The PRIME post-COVID study

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Summary boxes

What is already known on this topic

- A substantial proportion of SARS-CoV-2 infected people develop post-covid-19 condition (PCC)
- PCC impacts health and activities of daily living (ADL)
- Published studies were prone to selection bias, lacked controls, and used different criteria to define the same condition hampering comparison between studies and undermines the validity of the evidence

What this study adds

- PCC has a substantial impact on health and performance of ADL compared with negative controls, this irrespective of the case definition used

How this study might affect research, practice or policy

- Irrespective of the case definition there is an associated burden of PCC which requires an adequate response by authorities in terms of informing the public and enabling support
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Abstract

Objective: To assess health and Activities of Daily Living (ADL) in SARS-CoV-2 positive adults with and without post-covid-19 condition (PCC), and compare this with negative tested individuals. Further, different PCC case definitions were compared with SARS-CoV-2 negative individuals.

Methods: All adults tested PCR positive for SARS-CoV-2 at the Public Health Service South Limburg (Netherlands) between June 2020 and November 2021 (n=41,780) and matched PCR negative individuals (2:1, on age, sex, year-quarter test, municipality; n=19,875) were invited by email. Health (5-level EuroQol 5-Dimension; EQ5D index and EQVAS) and ADL impairment were assessed. PCC classification was done using the WHO case definition and 5 other common definitions.

Results: In total, 8,409 individuals (6,381 SARS-CoV-2 positive; 53±15 years; 57% female; 9[7-11] months since test) were included. 39.4% of positives had PCC by WHO case definition (EQVAS: 71±20; EQ5D index: 0.800±0.191; ADL impairment: 38±32%) and perceived worse health and more ADL impairment than negatives, i.e., difference of -8.50 (95%CI[-9.71;-7.29];p<.001) for EQVAS which decreased by 1.49 (95%CI[0.86;2.12];p<.001) in individuals with PCC for each comorbidity present, and differences of -0.065 (95%CI[-0.074;-0.056];p<.001) for EQ5D index, and +16.7% (95%CI[15.0;18.4];p<.001) for ADL impairment. Health and ADL impairment were similar in negatives and positives without PCC. Replacing the WHO case definition by other PCC definitions yielded comparable results.

Conclusions: Individuals with PCC have substantially worse health and more ADL impairment than individuals without PCC and negative controls, this irrespective of the case definition. Authorities should inform the public about the associated burden of PCC and enable adequate support.

Introduction

A substantial proportion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected people report lasting symptoms (1, 2), initially referred to as 'long covid' (3). This was later updated by the World Health Organization (WHO) to 'post-covid-19 condition'(PCC) which is defined as *"a history of probable or confirmed SARS-CoV-2 infection usually 3 months from onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis"* (4).

Several studies have reported on the impact of PCC (5, 6). Patients with PCC were found to have comparable health to that of people with chronic obstructive pulmonary disease and rheumatic arthritis (7). Furthermore, a negative impact of PCC upon quality of life (8, 9), and activities of daily living (ADL) was found (10, 11). However, study populations in these studies were often recruited via online support groups and therefore prone to selection bias. Additionally, studies often lack controls (12). Consequently, the true burden of PCC on health and ADL remains poorly reported in the general population at the time of writing. Moreover, the lack of clear diagnostic criteria for PCC (4), and use of different terminologies and criteria to define the same condition hampers comparison between studies and undermines the validity of the evidence (13). In addition, little is known about other factors (such as sex, age, comorbidities) that potentially affects impact of PCC on ADL and health (14).

Therefore, the aims of the current study were (1) to assess experienced health and ADL in SARS-CoV-2 positive adults with and without PCC, and compare this with SARS-CoV-2 negative individuals), and (2) to compare these outcomes between SARS-CoV-2 negative individuals and various commonly used case definitions for PCC while accounting for potential confounding factors.

Methods

Data from the first wave of a longitudinal open cohort study, the Prevalence, Risk factors, and Impact Evaluation of post-COVID-19 condition (PRIME post-COVID). The protocol of the study was published elsewhere (15). Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study design

In short, adults tested for SARS-CoV-2 at the Public Health Service (PHS) South Limburg in the Netherlands, with a valid Polymerase Chain Reaction (PCR) test result (positive/negative) between June 1 2020 and November 1 2021, and a valid email address were retrieved from test records in the registry. In November 2021, all PCR positive individuals (n=41,780) and a group of PCR negative individuals (who only had negative test result(s); n=19,875) matched (2:1 ratio) by age, sex, year-quarter of test, and municipality of residence, were invited for participation by email. Of note: when people tested negative multiple times, the last negative PCR test date was used. The online survey lasted 30-45 minutes and was available from November 17 2021 to January 9 2022. Digital informed consent for the use and storage of data for research was asked prior to the start of the survey. The invitee could participate in the questionnaire after consent was provided on participation in the study and on the use of the data for research (15).

Population in the current analysis

Individuals were excluded from the current study when they were tested less than three months prior to participation to the survey, sex was not reported, PCR negative individuals in the registry self-reported seropositivity for SARS-CoV-2 before vaccination (because of missing relevant infection-related information), or if the health section of the survey was not completed. Further, PCR negative individuals (i.e., SARS-CoV-2 negative individuals in the registry) were attributed to the SARS-CoV-2 positive group if they self-reported a positive test not in the registry (e.g., tested in hospital, outside

geographical service area, rapid antigen testing). This was the case in 87 individuals. Besides that, 166 individuals gave no consent for matching registry data with their questionnaire data. In these individuals, we used self-reported data only.

Main outcome variables

Experienced health EQ5D index

Experienced health was assessed using the 5-level EuroQol 5-dimensions version (EQ5D5L) which includes five health dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) each on a 5-level scale (1: no problems, 2: slight problems, 3: moderate problems, 4: severe problems, and 5: extreme problems/unable to) (16). An EQ5D index score was calculated by attaching weights to each level in each dimension. The attached weights were obtained by Versteegh and colleagues for the Dutch population via a standardized valuation study protocol by the EuroQol Group (17). Index scores could range between -0.446 (worst health) and 1.000 points (best health), whereas 0 is the value of a health state equivalent to dead (17).

Experienced health EQVAS

Additionally, the EQ5D5L includes a vertical visual analogue scale (EQVAS) ranging from 0 (worst health you can imagine) to 100 points (best health you can imagine), to obtain respondent's current perceived health (16).

Impairment in activities of daily living (ADL)

Illness-related impairment in regular activities other than work (in the past 7 days) was assessed using a selected item of the Work Productivity and Activity Impairment questionnaire. Individuals were asked to indicate the degree their health affected productivity in regular unpaid activities using a 0 (no effect) to 10 (completely prevented me from doing my daily activities) scale. The degree of ADL impairment is expressed as a percentage, and higher percentages indicate a higher overall impairment (18).

Case definitions for post-covid-19 condition (PCC)

SARS-CoV-2 positive individuals were grouped in 'PCC' group (yes/no) based on the WHO case definition (here used as main PCC definition) and 5 alternative, commonly used definitions including an adapted WHO case definition to take into account advances in scientific knowledge regarding this definition. All SARS-CoV-2 positive individuals included in analyses were at least 3 months after their initial SARS-CoV-2 infection. A detailed description of the definitions and questions used can be found in the **online supplement (eMethods 1)**.

1. **WHO case definition for PCC**: fulfilling current WHO case definition referring to a condition that occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually three months from the onset of COVID-19, with symptoms that last for at least two months and cannot be explained by an alternative diagnosis (4).
   In concrete terms, this means experiencing ≥1 symptom, symptom(s) is/are present for ≥1 month, the time since test is longer than or equal to the presence of symptom(s), and no new diagnoses are confirmed since the test.
2. **Adapted WHO case definition for PCC:** fulfilling all criteria of current WHO case definition (4), except for criterion of an alternative diagnosis that could explain the symptoms, as recent studies showed associations between COVID-19 and new-onset illnesses (19-21).
3. **Symptom present:** having ≥1 symptom present (22).
4. **Differentiating symptom present:** having ≥1 symptom present that is observed to be significantly different between SARS-CoV-2 positives and negatives (1, 23).
5. **Differentiating symptom present with at least a moderate severity:** Having ≥1 symptom present that is observed to be significantly different between SARS-CoV-2 positives and negatives with a severity score of ≥5/10 (1, 23).
6. **Not recovered:** Indicating not feeling (fully) recovered (24).

Of note, the following 44 prelisted symptoms (in alphabetical order) were considered: amnesia, brain fog, burning sensation in the trachea, chest tightness, cold, concentration difficulties, confusion, cough, coughing up mucus, diarrhea, dizziness, dreariness/depression, earache, elevated body temperature, eye difficulties, fatigue, fear, fever, hair loss, headache, heat flushes, increased resting heart rate, irritability, joint pain, loss of appetite, loss/change of smell, loss/change of taste, muscle pain or weakness, nausea, nerve pain, pain between shoulder blades, pain or burning sensation in the lungs, palpitations, runny nose, shortness of breath, skin rashes/red spots on toes or feet, sleeping problems, sneezing, sore throat, stomach ache, sudden weight loss, tinnitus, voice difficulties, vomiting (23).

Baseline characteristics

Other factors include sex, age, education level, and body weight and height to calculate body mass index (BMI). Furthermore, date of test to calculate time since test and information about hospital admission during acute infection (yes/no; in PCR positives only) were surveyed. The number of (pre-existing) comorbidities present (before the test) were determined using a predefined list of comorbidities (**eMethods 2**) and a question on whether this specific comorbidity was present before the SARS-CoV-2 test. Perceived health the year prior to testing was assessed using EQVAS (retrospectively).

Statistical analysis

Descriptive statistics were presented for the 3 groups (i.e., positives with PCC, positives without PCC, and SARS-CoV-2 negatives). Categorical data was reported as number (frequencies), and ordinal data as medians (IQRs). Continuous data was checked for normality using histograms and QQ-plots, and reported as mean (standard deviations) or median (IQRs) as appropriate.

Univariable and multivariable regression models were performed for the main continuous outcomes (i.e., EQVAS, EQ5D index and ADL impairment) with ordinary least squares linear regression to assess the main determinant (i.e., PCC, no PPC, SARS-CoV-2 negatives). The multivariable analyses were adjusted for a minimally sufficient set of confounders identified in the literature: age, sex, pre-existing comorbidities when tested, time since test, and health the year prior to test (2, 22, 23). The 3 groups were modeled as two dummy variables in this analysis with the SARS-CoV-2 negatives as reference group. The WHO case definition was used to classify SARS-CoV-2 positive individuals into the (no) PCC group. If multicollinearity was present (Variance Inflation Factor, VIF >5), variables were identified and removed from the model. Interaction terms for sex, age, health before test, comorbidities before test on one hand and time since test and the two dummy variables (i.e., group variables) on the other hand were explored, as a potential effect of the group variables on health and ADL might depend on these confounders included in the model (2, 23, 25). When found statistically significant, the intercation term was included in the final models.

Furthermore, analysis of covariance (ANCOVA) adjusting for time since test and health the year prior to test were performed for subgroups by sex (male/female), age (18-40, 41-60, and +60 years) and presence of pre-existing comorbidities at the test (yes/no). This was done for positives with and without PCC according the WHO case definition and the SARS-CoV-2 negative group, and for the various commonly used definitions for PCC.

A priori, the level of significance was set at 0.01 (2-tailed) to account for multiple testing in this study and account for high sample size in the multivariable regression analyses. Model assumptions were checked when performing the analyses. Tables and figures include 95% confidence intervals (95%CIs). Statistical analyses were performed using SPSS v27.0 (IBM Corp., Armonk, NY, USA). Visualizations were made using Graphpad Prism 9.3.1 (GraphPad Software, La Jolla, CA, USA).

Results

61,655 adults were invited by email to participate. From the 18,859 respondents, 12,453 were eligible as they provided minimal data and showed sufficient certainty to be the intended invitee (23). Individuals were excluded if they were tested <3 months prior to participation (n=2,656), did not complete the health section of survey (n=1,331), were PCR negative but reported to have SARS-CoV-2 antibodies before vaccination (n=56) or did not report sex (n=1). Consequently, 8,409 individuals (6,381 SARS-CoV-2 positive and 2,028 negative) were included (**Figure 1**). Age and sex data of all invitees, and invitees (not) included in the analysis are reported in the online supplement (**eTable 1**).

Description of the study population

In total, 39.4% of positive individuals (n=2,513) had PCC according the WHO case definition. Demographical and clinical data of the SARS-CoV-2 positives with PCC, positives without PCC, and negatives are shown in **Table 1.** In short, the positives with and without PCC had a similar sex distribution (62% and 57% females, respectively), mean age (51±15 years), and median time since infection of 10 [7-11] months. Positives without PCC had on average a better perceived health the year prior to test and less often comorbidities present when tested than positives with PCC and negatives. Further, the negative group was on average 7 years older and had a lower proportion of females (49%) than both positive groups.

Differences in health and ADL

SARS-CoV-2 positives with PCC reported a higher median ADL impairment due to health (30% *vs.* 0% and 0%) and a worse average perceived health at this moment (EQVAS: 70.8 *vs.* 81.5 and 79.2; EQ5D index: 0.800 *vs.* 0.896 and 0.878) compared with positives without PCC and negatives respectively. The greatest impairments in positives with PCC were observed for the domain's usual activities and

pain/discomfort (**Table 1**). A more detailed overview of the extent of impairment across the several health domains can be found in **online supplement (eFigure 1)**.

Results of the univariable and multivariable regression models can be found in **Table 2**. Adjusted EQ5D index was significantly lower in positives with PCC compared with negatives (-0.065, 95%CI[-0.074;-0.056]; p<.001). No significant difference between positives without PCC and negatives was observed (-0.003 points, 95%CI[-0.011;0.005]; p=.492).

Also EQVAS was 8.50 points (95%CI[-9.71;-7.29]; p<.001) lower in positives with PCC than in negatives. While the EQVAS was not statistically significant higher in positives without PCC than in negatives (0.26 points, 95%CI[-0.68;1.19]; p=.593). Our model indicated that the presence of PCC and comorbidities together has a smaller effect on EQVAS than the sum of each. Specifically, the associated burden of PCC on EQVAS decreases by 1.49 95%CI[0.86;2.12] for each comorbidity present (p<.001). The specific models for EQVAS for people without comorbidities, with 1 comorbidity and with ≥2 or more comorbidities are reported in **online supplement (eTable 2)**. The beta coefficient for PCC and no PCC (versus reference: negatives) in abovementioned models are -9.00 (95%CI[-10.47;-7.53]; p<.001), and -0.46 (95%CI[-1.72;0.80]; p=.476); -6.64 (95%CI[-8.54;-4.74]; p<.001), and 0.99 (95%CI[-0.80;2.77]; p=.278); and -3.73 (95%CI[-5.91;-1.55]; p<.001), and 1.47 (95%CI[-0.80;3.73]; p=.204), respectively.

Further, ADL impairment due to health problems was 16.7% (95%CI[15.0;18.4]; p<.001) higher in positives with PCC compared with negatives. The ADL impairment observed in positives without PCC was not significantly higher than those observed in negatives (2.0%, 95%CI[0.4;3.5]; p=.014).

A sensitivity analysis in 8,156 individuals was performed for the abovementioned multivariable models (253 individuals with a self-reported test-result were excluded from the analyses). The results can be found in **eTable 3**. In short, similar direction and extent of findings were observed compared to the analyses in 8,409 individuals.

Differences in health and ADL stratified for sex, age and presence of comorbidities

Results of analyses for EQVAS, EQ5D index and ADL impairment due to health after stratification upon sex, age and presence of pre-existing comorbidities and adjusted for health prior to test and time since test can be found in **Figure 2**. Briefly, significantly worse health and larger ADL impairment were observed in the PCC group compared with the positive group without PCC and negative group, this in nearly all strata.

Differences between PCC definitions in health and ADL

In general, the participants meeting criteria for WHO case definition and the definition based upon the presence of ≥1 symptom presented the best health and least ADL impairment of all definitions (i.e., smallest differences with SARS-CoV-2 negative group). Contrary, those meeting the criteria for the definition based upon the presence of ≥1 differentiating symptom between SARS-CoV-2 positive and negative individuals with at least a moderate severity and the definition based on the feeling not being recovered presented the worst health and highest ADL impairment of all definitions.

Results for EQVAS were comparable for all PCC definitions after stratification for age, sex and comorbidities, except for certain case definitions in the stratum males aged 41-60 years without comorbidities (**Figure 3**). Further, slight differences between certain case definitions were found for the outcomes EQ5D index and ADL impairment. These differences were mainly located in the strata with men and women without comorbidities and between above-mentioned PCC definitions.

Discussion

In this population-based cohort study, the impact of PCC on health and impairment in ADL was studied in adults tested positive for SARS-CoV-2 and controls. The associated burden of PCC on health and impairment in ADL is meaningful, irrespective of the case definition used or age, sex, presence of pre-existing comorbidities, time since test or health status prior to test.

Findings from the current study confirm previous reports that PCC affects health and ADL (6, 8, 9). Nevertheless, findings are difficult to compare, as most studies used other measures or reported findings of all SARS-CoV-2 positive individuals, without presenting results for PCC separately (6, 25, 26). Studies that specifically reported on PCC found values that were considerably worse in terms of health and ADL (6, 10, 11, 27, 28). Vaes et al. for example used the same outcome measures and found a mean EQVAS of 56 points and ADL impairment of 60% around 6 months after infection (11). A conceivable explanation for this is that previous studies mainly reported on individuals recruited via online support groups or clinics describing a subgroup of the population with a possible bias resulting in an overestimation of the burden (10, 11, 28, 29). Still, an associated burden of PCC is found when values are compared with Dutch population norms (EQVAS: 70.8 *vs.* 81.4; and EQ5D index: 0.800 *vs.* 0.869, respectively), while positives without PCC and negatives show similar values to the Dutch population norms (17, 30). After controlling for possible confounders, the PCC group had on average 8.50 and 0.065 points lower EQVAS and EQ5D index score, respectively, and 16.7% higher ADL impairment than the negative group. In the literature difference of 7 points for EQVAS (cancer patients), 0.063 points for EQ5D index (EQ5D5L value set for England), and 20% for ADL impairment (psoriasis patients) is established as meaningful (31-33)

To date, the WHO case definition for PCC is considered the golden standard in absence of a laboratory test to diagnose PCC (4). Though the different definitions for PCC found comparable results for health and ADL impairment indicating that although the heterogeneity in case definitions the same conclusion upon the impact of PCC on health and ADL can be drawn. Slight differences

observed between definitions can be due to misclassification as evidence emerges that a SARS-CoV-2 infection and PCC is associated with new-onset illnesses in case of the WHO case definition for example (34), or in case of a definition using the presence of ≥1 symptom, as (generic) symptoms (e.g., fatigue, pain) are also present in chronic diseases and the general population (1, 35, 36).

The associated burden on perceived health (i.e., EQVAS) decreases with the presence of comorbidities, presumably because the room to deteriorate in terms of health is smaller when having more comorbidities. In addition, no interactions between presence of comorbidities and PCC were observed for EQ5D index (and ADL impairment). This has to do with the nature of both health measures as EQVAS assesses the perceived health of an individual while EQ5D index is a score based on limitations in 5 domains. Until today it remains unknown PCC is a unique condition, an illness similar to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and other post-infectious illnesses, or even a combination of conditions. To determine this, a comparison with ME/CFS and other post-infectious illnesses is needed.

The major strengths of this study are the large sample size and population-based study design as the recruitment of individuals was done using the Dutch COVID-19 PCR test registry. By inviting all PCR positive individuals and matched negative controls we were able to compare results with a reference group and consider (non-)pandemic-related factors. Further, various definitions for PCC were used and compared in the current study as well as standardized and validated questionnaires.

This study has a number of limitations. Only individuals with a valid e-mail address were invited for this online study. This may have resulted in a potential selection bias of digital illiterate individuals as they were not invited or did not complete the study. Likewise, this may have been the case for people with disability or severe disease. In total, 14% of invitees are included in the current study, although this response rate would be higher if individuals were not excluded for several reasons (15). Similar rates were reported in other population-based studies regarding PCC with the same recruitment strategy (e.g., Whitaker et al., 26-29%, Hastie et al., 16%) (2, 25) and what is expected in

email surveys in general (37). Further, an under-representation of 18-40y, and over-representation of 50-80y old invitees is observed in the current sample and was more pronounced in the negative invitees. In the current study less than 2% of the population was hospitalized for COVID-19. It is possible that people went directly to the hospital instead of being tested at the PHS, and are therefore underrepresented in our sample. Further, misclassification bias regarding (confirmed) SARS-CoV-2 diagnosis is inevitable as in the early phase of the pandemic the availability and access of testing was limited (38). As a consequence, individuals that had SARS-CoV-2 in the early phase of the pandemic (before June 1 2020) or were asymptomatic could be present in the negative reference group. Nevertheless, the potential misclassification of SARS-CoV-2 positives in the negative group would not change the direction of the findings. Another potential limitation is that data gathering was done by self-report leaving potentially relevant information missing (e.g., comorbidities). To fulfill the WHO case definition alternative diagnoses that could explain symptoms need to be excluded. Our study did not include clinician reported information, or information on alternative diagnosis based on medical records. The self-reported data regarding (pre-existing) comorbidities in our study may have a potential recall and misclassification bias. Furthermore, certain questions were prone to recall bias (e.g., health the year prior to test). The study includes test-results until the last quarter of 2021 (i.e., before the omicron wave). Therefore, results cannot be generalized to vaccinated individuals that developed PCC by a break-through infection as the majority was unvaccinated when they were infected with SARS-CoV-2 nor to PCC by the omicron variant. Hence, recent research suggests there is no difference in PCC sequela between SARS-CoV-2 variants (39, 40). Of note, this study was limited to adults, however PCC is also present in children and adolescents (34).

Conclusion

Individuals with PCC have substantial and clinically meaningful worse health and more impairment in ADL than individuals without PCC and negative controls, irrespective of sex, age, pre-existing comorbidities, time since test and health status prior to test and regardless of the case definition used to define PCC.

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Contributorship

MVH, DP, CvB, SB, KK, CdH, SM, HtW, CH, MAS, ND designed the study. DP, CvB and SB actively participated in data collection. MVH performed the data analysis and wrote the first draft of the manuscript. DP, CvB, SB, KK, CdH, SM, CB, DJA, MS and ND supervised data analysis. All authors were involved in data interpretation, revised the manuscript critically for important intellectual content, approved the final version, and agreed to be accountable for all aspects of the manuscript.

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Competing of interests

No conflicts of interest have been declared.

Ethics approval

The medical ethics committee of Maastricht University Medical Centre+ waived this study (Maastricht, the Netherlands; METC2021-2884), as the Medical Research Involving Human Subjects Act did not apply to this study.

Data availability statement

Data cannot be shared publicly because the data contains potentially identifying patient information. Data are available on request from the head of the data-archiving South Limburg Public Health Service (contact via Helen.Sijstermans@ggdzl.nl) for researchers who meet the criteria for access to confidential data.

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Table 1. Characteristics of SARS-CoV-2 negatives and SARS-CoV-2 positives stratified for post-covid-19 condition (PCC) according the WHO case definition.

	SARS-CoV-2 negatives (n=2,028)	**SARS-CoV-2 positives**	
		No PCC (n=3,868)	**PCC** (n=2,513)
Female, No. (%)	991 (48.9)	2,212 (57.2)	1,564 (62.2)
Age, mean (SD), years	58.1 (14.7)	51.3 (15.2)	51.4 (14.7)
BMI, mean (SD), kg/m^2	26.3 (4.7)	26.6 (4.9)	27.2 (5.2)
Level of education, No. (%)			
Studying	22 (1.1)	102 (2.6)	62 (2.5)
Low	223 (11.0)	360 (9.3)	242 (9.6)
Medium	885 (43.6)	1,801 (46.6)	1,262 (50.2)
High	898 (44.3)	1,605 (41.5)	947 (37.7)
Comorbidities reported at moment of test, No. (%)			
None	959 (47.3)	2,306 (59.6)	1,047 (41.7)
1	619 (30.5)	970 (25.1)	752 (29.9)
≥2	450 (22.2)	592 (15.3)	714 (28.4)
Time between survey and test, median [IQR], months	8 [6-11]	10 [7-11]	10 [7-11]
Hospital admission in acute phase of infection, No. (%)	NA	50 (1.5)[a]	47 (2.0)[b]
Experienced health			
Health the year prior to test (EQVAS), mean (SD), points	82.7 (15.8)	85.9 (14.3)	81.9 (16.0)
Health at the moment of survey (EQVAS), mean (SD), points	79.2 (20.7)	81.5 (19.0)	70.8 (19.8)
EQ5D index, mean (SD), points	0.878 (0.167)	0.896 (0.164)	0.800 (0.191)
Mobility (no problems), No. (%)	1,547 (76.3)	3,164 (81.8)	1,619 (64.4)
Self-care (no problems), No. (%)	1,919 (94.6)	3,721 (96.2)	2,294 (91.3)
Usual activities (no problems), No. (%)	1,546 (76.2)	3,064 (79.2)	1,226 (48.8)
Pain/ discomfort (no problems), No. (%)	1,169 (57.6)	2,527 (65.3)	870 (34.6)
Anxiety/ depression (no problems), No. (%)	1,562 (77.0)	3,082 (79.7)	1,599 (63.6)
Non-work related impairment due to health (WPAI)			
Overall activity impairment due to health, mean (SD), %	0 [0-30]	0 [0-30]	30 [10-70]

Data are presented as frequency and proportion, mean and (standard deviation) or median and [interquartile range]. [a]n=3399, and [b] n=2374, as only PCR positive invitees were asked about hospital admission in survey. Abbreviations: EQ5D, EuroQol 5 dimension; EQVAS, EuroQol Visual Analogue Scale; SARS-CoV-2; Severe Acute Respiratory Syndrome Coronavirus 2; No., number; NA, Not Applicable; post-covid-19 condition, PCC; WPAI, Work Productivity and Activity Impairment.

Table 2. Unadjusted and adjusted regression models for health and ADL impairment adjusted for age, sex, comorbidities at test, health status year prior to test and time since test, with SARS-CoV-2 negatives as reference group and post-covid-19 condition (PCC) according the WHO case definition.

Variables	Unadjusted unstandardized Coefficient β [95%CI]	p-value	Adjusted unstandardized Coefficient β [95%CI]	p-value
1. Unadjusted and adjusted linear regression results for perceived health at the moment (EQVAS)				
Group (PCC by WHO)	-8.44 [-9.59;-7.29]	**<.001**	-8.50 [-9.71;-7.29]	**<.001**
Group (No PCC by WHO)	2.27 [1.21;3.33]	**<.001**	0.26 [-0.68;1.19]	.593
Interaction Group (PCC by WHO)*Comorbidities at test	NA	NA	1.49 [0.86;2.12]	**<.001**
2. Unadjusted and adjusted linear regression results for health at the moment (EQ5D index)				
Group (PCC by WHO)	-0.079 [-0.089;-0.068]	**<.001**	-0.065 [-0.074;-0.056]	**<.001**
Group (No PCC by WHO)	0.018 [0.009;0.028]	**<.001**	-0.003 [-0.011;0.005]	.492
3. Unadjusted and adjusted linear regression results for ADL impairment due to health				
Group (PCC by WHO)	18.57 [16.78;20.37]	**<.001**	16.72 [15.01;18.43]	**<.001**
Group (No PCC by WHO)	-0.64 [-2.29;1.01]	.448	1.97 [0.40;3.54]	.014

Figure 1. Flowchart of invitees, respondents, participants eligible for inclusion, and study population included in the analysis.

Figure 2. Health and ADL impairment for SARS-CoV-2 negatives, positives with and without post-covid-19 condition according the WHO case definition, stratified for sex, age and pre-existing comorbidities and adjusted for time since test and health prior to test. **Legend Figure 2.** From left to right: ●: SARS-CoV-2 positives with post-covid-19 condition, ●: SARS-CoV-2 positives without post-covid-19 condition; ●: SARS-CoV-2 negatives. Whiskers are 95%CI. # indicates p<.01 and * p<.001.

Figure 3. Health and ADL impairment for SARS-CoV-2 negatives and different PCC case definitions stratified for sex, age and pre-existing comorbidities. **Legend Figure 3.** From left to right: ●: WHO case definition, ●: WHO case definition except for criterion of alternative diagnosis, ●: ≥1 symptom, ●: ≥ 1 symptom that differ between SARS-CoV-2 positives & negatives, ●: ≥1 symptom that differ between SARS-CoV-2 positives & negatives with a severity ≥5/10; ●: feeling not recovered; ●: SARS-CoV-2 negatives. Whiskers are 95%CI, # indicates p<.01 and * p<.001 from SARS-CoV-2 negatives, and horizontal brackets indicates absence of overlap in 95%CI.