Differences in physical health, mental health, fatigue and quality of life between COVID-19 seronegatives and seropositive

Long-term health-related quality of life in non-hospitalised COVID-19 cases with confirmed SARSCoV-2 infection in England: Longitudinal analysis and cross-sectional comparison with controls

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Abstract

Background:

Method:

Result:

Conclusion:

1. SARS-CoV-2
    a. Current infection and mortality numbers
    b. Impact in general > societal, economical, financial
    c. Clinical picture
    d. Morbidity > Impact on health
2. Differentiate between acute and long term impact on health
3. Introduce long COVID
    a. Terminology
    b. WHO case definition?
    c. Associated symptoms
    d. Incidence estimates so far
4. Little is known about the impact of COVID on health status among all cases ranging from asymptomatic disease to IC admissions to long term symptoms
5. Aim: Investigate the impact of SARS-CoV-2 infections up to one year post-infection on health related quality of life and identify interrelations with general health, physical health, mental health and fatigue.

Introduction

Since the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and it's spread across the globe in early 2020, the World Health Organization (WHO) reported more than 270 million confirmed cases and more than 5 million deaths worldwide related to coronavirus disease 2019 (COVID-19) as of 14 December 2021 (1). With societal, economical and financial consequences all over the world, the impact of the COVID-19 pandemic thus far has been unparalleled (2-8).

The clinical picture of COVID-19 varies from asymptomatic infections to fatal disease (9). At least one third of the SARS-CoV-2 infections develops into symptomatic COVID-19 (10,11), ranging from a mild to more severe disease course requiring hospital or even ICU admission (REF?). This indicates that acute COVID-19, at least temporarily, has an impact on people's health. However, it remains unclear to what extent and duration this affects health related quality of life (HRQoL).

Generally, COVID-19 symptoms reduce over time and disappear within 4 weeks (REF?). However, it has become clear that some COVID-19 patients still experience symptoms after the acute phase of infection (REF?). This clinical picture, initially termed *"Long COVID"* has been an increasingly interesting topic of research. Recently, the WHO published a case definition referring to the condition as post COVID-19 condition which "occurs in individuals with a history of probably 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" (12). Numerous symptoms have been associated with post COVID-19 condition, involving various organ systems (13). Common symptoms include fatigue, dyspnea and cognitive dysfunction as well as memory issues, sleep disorders and post-exertional malaise (12). These post-acute COVID-19 symptoms have been observed from mild to severe cases of acute COVID-19 (REF?). Analyses regarding incidence estimates of post COVID-19 condition vary, but approximately 20-25% of COVID-19 patients still experiences symptoms after 4-5 weeks and 1 in 10 still reports symptoms after 12 weeks (REF?). However, usually these estimates do not include SARS-CoV-2 infections with an asymptomatic acute phase. Therefore little is known about the overall impact of post COVID-19 condition on health status.

Since knowledge about the overall impact of COVID-19 on health status among all SARS-CoV-2 infections (ranging from acute to long term symptoms and from asymptomatic disease to ICU admissions) is lacking, the aim of this study is to investigate the impact of SARS-CoV-2 infections on HRQoL up to one year post-infection and identify interrelations with general health, physical health, mental health and fatigue.

Objectives

1. Is there a difference in health related quality of life, fatigue, physical and/or mental health between SARS-CoV-2 infected and non-SARS-CoV-2 infected participants?
2. Is there a difference in health related quality of life, fatigue, physical and/or mental health between participants with recent SARS-CoV-2 infections and participants that were infected with SARS-CoV-2 at least 4 months ago?

References

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Methods

Study design and population

The Pienter-Corona study, is a nationwide serosurveillance prospective cohort study that was started in April 2020 to investigate the immunity of the Dutch population to SARS-CoV2 (website RIVM ref). The study consists of a data from a previous serosurveillance study that aimed to gain insights regarding protection against vaccine preventable diseases by the National Immunisation Programme in the Netherlands(Vos, den Hartog et al. 2020). The study shows which part of the Dutch population has developed antibodies against SARS-CoV-2 and hence allows for estimates to be made regarding built up resistance due to infection and vaccination (ref RIVM website). Further details of the study are described elsewhere(ref XXX).

Data of participants aged 15 and above, who had blood test results that tested for the presence of SARS-CoV-2 spike S1-specific IgG antibodies were used for analyses. In addition participants were required to have completed the SF-12 and the CIS fatigue questionnaires at the fourth round (PICO 4). A total sample size of 5630 participants were included in the study. Participants were divided into cases (those whose blood test results showed the presence of SARS-CoV-2 spike S1-specific IgG antibodies) and controls whose blood test results showed no presence of SARS-CoV-2 spike S1-specific IgG antibodies. A more detailed description of the PIENTER study can be found elsewhere (ref XXX).

SARS-CoV-2 negative controls

Participants that tested negative on all four PICO rounds constituted the control group. In addition individuals who had one missing test result in one of the rounds(PICO 1, 2, or 3), that was followed by a negative test result in the next round were added to the control group as controls. The rational was that if these individuals had tested positive, the antibodies would have been detected in the blood in the next round since antibodies can remain in the body for a period of XXXmonths (ref). Self-reported PCR tests and other reported corona tests were checked to ensure that controls had not previously tested positive to SARS-CoV-2. Participants in the control group with self-reported PCR tests and other reported corona tests were excluded from the control group.

SARS-CoV-2 cases

Individuals that had a positive test result in any of the rounds were considered to be cases. The cases group was further divided into acute cases and long COVID cases. Acute cases were participants that had a follow up time of less than 12 weeks(ref). Participants with a follow up time of 12 weeks or more were termed long COVID cases. Follow up time was calculated at moment of

testing positive (antibody test) minus 14 days for participants that seroconverted in PICO 1,2 and 3. For participants that seroconverted, the follow up time was calculated based on the date of a positive PCR. In the event that a positive PCR test was not available, follow up time was calculated based from the date of the positive PCR test. Participants that tested positive in PICO round 4 and had no PCR test formed a separate group and were analyzed as part of the sensitivity analyses.

Recruitment Figure(How the participants are recruited into the study) Figure(insert)

Outcome Measures

Every 4 months (i.e. during each PICO round) blood samples were collected and questionnaires were completed online. Data regarding comorbidities, sociodemographic factors, COVID-19-related symptoms, potential determinants for SARS-CoV-2 seropositivity, such as, medication use and behavioral factors were collected (Vos 2021). All participants provided written informed consent. From PICO round 4, data regarding HRQoL questionnaire (SF-12) and the fatigue(CIS) were collected. HRQoL and fatigue are important factors participants that experience prolonged symptoms following SARS-CoV-2 infection.

Health related quality of life (SF-12)

The SF-12/Rand-12, a shorter version of the Rand-36/SF-36 health related quality of life questionnaire and consists of 12 questions from the following 8 domains; physical functioning, physical role, emotional role limitations, social functioning, physical pain, general mental health, vitality and general health perception. The 8 domains can be summarized into a physical and mental health domain (Xuemei 2003). Health scores were converted into utility scores using the SF-6D (Short-Form Six-Dimension). Scores range from -0.333 to 1 with a score of 1 indicating perfect health and scores less than zero indicating a health status worse than death(ref).

Mental and Physical Health

Mental and physical summary scales were calculated using the SF-12/Rand-12. The scores range from 0 (lowest general health) to (100 highest general health). Higher scores indicate better health. The recommended cut-off score for physical health (PCS-12) is 50. A score of 50 or less indicates a physical condition, whereas a score of 42 or less on the MCS-12 may indicate a mental condition such as clinical depression (Ware 1995).

Fatigue (Checklist Individual Strength [CIS])

Fatigue severity is assessed using the subscale fatigue of the Checklist Individual Strength (CIS). The CIS subscale fatigue is a 8-item fatigue questionnaire (Vercoulen 1994). Each item is scored on a 7-point Likert scale. Scores range from 8 to 56, and normal scores are indicated by values less than 27, verhooged fatigue by values between 27-35 and severe fatigue by score above 35.

Statistical analysis

Baseline characteristics of the participants in all groups (cases and controls) were presented using descriptive statistics [mean (standard deviation), median (range), or proportion] to assess if there is a balance in the groups regarding distribution of prognostic factors such as age, gender, co-morbidity and education. Further symptoms related to COVID-19 and vaccination status were described including cut-off measures of fatigue, physical health and mental health. Only outcome data for participants that completed the LongCovid questionnaires was used, hence there was hardly any missing outcome data.

To answer the research question, regarding significance of association between cases/controls with HRQoL, fatigue, physical and mental health, permutation tests were performed based on the so called 'sum statistics' (Rosebaum 2009) and blocked by strata. The strata were determined by confounders. Confounders included in our permutation tests were, the number of comorbidities, age, sex, education level and vaccination status. Permutation tests provide estimates of the distribution of a test statistic, conditioned on the observed data, under the null hypothesis. Observations are permuted randomly and the test statistic is re-estimated after each permutation. By repeating this procedure a number of times (1000 and 10 000 times in this study) and ordering the set of permuted test statistics that results, the distribution of the test statistic under the null hypothesis is sampled and from it critical values for valid hypothesis testing are derived. A p-value is then obtained by comparing number of times that the permutation test statistic was greater than the observed test statistic (from our initial data) divided by the number of permutations done. The p value of the independent test reflects a significant relationship between the groups (controls/cases and acute/longCOVID cases) and fatigue, health related quality of life, physical health and mental health. Data in this study was cleaned and analyzed using SAS version….. and R.

Sensitivity analysis

Two sensitivity analysis were performed:

1. Case were divided into acute case and LongCovid cases. The significance of association between acute cases/LongCOVID cases with HRQoL, fatigue, physical and mental health was tested using permutation tests.
2. Descriptive statistics and permutation tests for participants in the 10th percentile of poor scores in HRQoL, physical health, mental health and fatigue between cases and controls.

Results

Participants

Table 1. shows the descriptive characteristics at baseline. 5630 participants were included in the analyses of which 766 were cases i.e tested positive to SARS-CoV-2 in one of the rounds and 4864 were controls. The median age for controls was 54 years and 49 years for cases. 59.5% of the cases and 56.4% of controls identified as female. Majority of the participants are of moderate- high education and are of Dutch ethnicity. Median health related quality life is 0.86 in both cases and controls and most of the participants are in good physical health (cases, controls). Majority of the participants controls (49.8%), cases (53.4%), do not and have never smoked. However less people do not have comorbidities in both controls(35.6%) and cases(36%). The majority of both cases and controls reported corona related symptoms.

The baseline characteristics of controls vs cases (Table 1) are comparable to those of acute cases vs LongCovid cases (appendix 1) when it comes to ethnicity, presence of corona symptoms, presence of comorbidities and moderate to high levels of educations. Further demographic characteristics are summarized in Table 1 (cases vs controls) and in Appendix 1 (acute cases vs long COVID cases). Higher fatigue scores are observed in the acute cases (45,4%) compared to the LongCovid cases (34,5%).

Health related quality of life

Descriptive statistics for HRQoL measures for cases are shown in Table 2 and those for controls in Table 3 . The percentage of the study sample with missing HRQL data ranged from 0.3% (n=2) to 1% (n=8) for cases and 0.08% (n=4) to 0.49%(n=24) in controls. HRQOL utility scores range from 0.4 to 1 in both cases and controls. The mean and median scores are similar for both health cases and controls. No significant difference in health related quality of life was observed between cases and controls ($p = 0.22$). The weighted mean for controls was 0.810 (95%CI 0.806 to 0.814) and the weighted mean for cases was 0.804 (95%CI 0.796 to 0.813)Sensitivity analyses with alternative resampling (10000) and alternative analysis showed similar results.

Physical health

The mean physical health score were comparable between cases (mean- 54.1; SD-7.7) and controls 54.4 (SD 7.6) in controls. After controlling for confounders (age, sex, number of comorbidities, vaccination status and education level) the permutation test showed that there was a significant difference between cases and controls(p=0.04). The weighted mean for controls was 54.7(95% CI 54.4 to 54.9), and the weighted mean for cases was 54.1 (95%CI 53.6 to 54.7) .

Mental health

55% of controls compared to 52% of cases reported having normal/good mental health. No significant difference mental health was observed between cases and controls (p = 0.43). The weighted mean for controls was 47.125 (95%CI 46.799 to 47.451) and the weighted mean for cases was 46.741 (95%CI 45.976 to 47.506). Sensitivity analyses with alternative resampling (10000) showed similar results.

Fatigue

No significant difference in fatigue was observed between cases and controls (p = 0.09). The weighted mean for controls was 22.455 (95%CI 22.076 to 22.834) and the weighted mean for cases was 23.102 (95%CI 22.249 to 23.954). Sensitivity analyses with alternative resampling (10000) and showed similar results. (**sensitivity analyses for LC vs acute cases still to be performed and that of participants in the tails of the distribution).

Table 1: Baseline characteristics

	Controls	**Cases**
n	4,864	766
Sex = Female % (freq)	56.4 (2743)	59.5 (456)
Province % (freq)		
North (Groningen, Friesland, Drenthe, Overrijssel)	19.3 (938)	13.3 (102)
Midwest (Noord-Holland, Flevoland)	16.8 (818)	15.1 (116)
Mideast (Utrecht, Gelderland)	20.0 (973)	18.7 (143)
Southwest (Zuid-Holland, Zeeland)	17.6 (856)	14.0 (107)
Southeast (Noord-Brabant, Limburg)	19.7 (960)	28.6 (219)
LVC (low vaccination coverage of migrant sample)	6.6 (319)	10.3 (79)
Ethnicity % (freq)		
Dutch	88.9 (4325)	91.6 (702)
Western	7.7 (373)	6.0 (46)
Non-Western	3.4 (166)	2.3 (18)
Religious beliefs % (freq)		

None	54.1 (2518)	48.8 (356)
Roman Catholic	22.8 (1061)	27.2 (198)
Other	4.0 (187)	2.7 (20)
Regular Protestant	17.2 (799)	17.1 (125)
High refusing Protestant	1.9 (89)	4.1 (30)
Education level % (freq)		
High	47.2 (2248)	39.7 (296)
Moderate	32.1 (1528)	40.4 (301)
Low	20.7 (987)	19.9 (148)
Number of other household occupants (excluding you) % (freq)		
0	12.5 (605)	6.7 (51)
1	45.9 (2231)	42.8 (328)
2	13.9 (675)	15.0 (115)
3	19.3 (940)	22.2 (170)
4	6.3 (307)	9.0 (69)
5	1.1 (52)	2.6 (20)
6	0.5 (23)	0.8 (6)
7	0.1 (5)	0.8 (6)
8	0.1 (3)	0.1 (1)
9	0.1 (5)	0.0 (0)
10	0.1 (3)	0.0 (0)
11	0.1 (3)	0.0 (0)
12	0.1 (6)	0.0 (0)
Smoking % (freq)		
Yes (I smoke or someone else smokes in the house)	11.0 (521)	7.8 (56)
No (smoked in the past)	39.2 (1846)	38.8 (280)
No (never smoked and no one smokes in the house)	49.8 (2348)	53.4 (385)
Cormobidities= No % (freq)	35.6 (1704)	36.0 (270)
Corona Symptoms = No % (freq)	36.5 (1775)	24.8 (190)
BMI % (freq)		
Underweight	1.2 (58)	1.3 (9)
Normal weight	49.2 (2317)	49.0 (352)
Overweight	35.2 (1659)	36.2 (260)
Obese	14.4 (677)	13.6 (98)
Pregnant % (freq)		
Yes	1.1 (51)	1.6 (12)
No	61.1 (2959)	66.6 (508)
Not applicable	37.8 (1829)	31.8 (243)
Age (median [IQR])	54.00 [38.00, 66.25]	49.00 [32.00, 61.75]
Health related quality of life (utility) (SF6D) (median [IQR])	0.86 [0.76, 0.86]	0.86 [0.72, 0.87]
Physical Health (Rand-12) (median [IQR])	56.79 [52.34, 58.75]	56.59 [51.66, 58.75]
Mental Health (Rand-12) (median [IQR])	50.67 [43.85, 55.15]	50.31 [42.07, 55.10]
Fatigue (CIS)(median [IQR])	19.00 [12.00, 30.00]	21.00 [13.00, 32.00]
Vaccinated = Yes % (freq)	4.9 (230)	7.6 (56)

Fatigue cut off % (freq)		
normal	68.7 (3325)	63.4 (483)
severe	14.6 (708)	18.2 (139)
verhooged	16.7 (807)	18.4 (140)
Physical health cut off = physical condition % (freq)	18.0 (870)	19.8 (150)
Mental health cut off= normal % (freq)	55.0 (2664)	51.5 (390)

Table 2: Descriptive statistics for HRQoL measures (cases)

	N	Missing	Percentage missing	Mean	SD	Median	P25	P75	Minimum	Maximum
General Health	766	2	0,3	2,4	0,9	3	2	3	1	5
Physical Functioning (PF2)	766	4	0,5	2,8	0,4	3	3	3	1	3
Physical Functioning (PF4) (	766	5	0,7	2,8	0,5	3	3	3	1	3
Role-Physical(RP2)	766	6	0,8	1,8	0,4	2	2	2	1	2
Role-Emotional(RE2)	766	6	0,8	1,8	0,4	2	2	2	1	2
Role-Physical(RP3)	766	6	0,8	1,8	0,4	2	2	2	1	2
Role -Emotional	766	6	0,8	1,8	0,4	2	2	2	1	2
Bodily pain (BP2)	766	4	0,5	1,5	0,9	1	1	2	1	5
Mental Health (MH3)	766	4	0,5	2,4	1	2	2	3	1	6
Energy/Fatigue (VT2)	766	4	0,5	2,8	1,1	3	2	4	1	6
Mental Health (MH4)	766	4	0,5	4,8	1	5	4	6	1	6
Social Functioning(SF2)	766	4	0,5	4,2	1,1	5	4	5	1	5
Rand- 12 PCS	766	8	1	54,1	7,7	56,6	51,7	58,8	17, 9	70
Rand-12 MCS	766	8	1	46,8	11,1	50,3	42,1	55,1	7, 9	66
HRQoL utility (SF-6D)	766	7	0,9	0,8	0,1	0,9	0,7	0,9	0,4	1

Table 3: Descriptive statistics for HRQoL measures (controls)

n	n	Missing	Percentage missing	Mean	SD	Median	P25	P75	Minimum	Maximum
General Health	4864	4	0,08	2,5	0,8	3	2	3	1	5
Physical Functioning (PF2)	4864	9	0,19	2,8	0,4	3	3	3	1	3
Physical Functioning (PF4)	4864	10	0,21	2,8	0,5	3	3	3	1	3
Role-Physical(RP2)	4864	10	0,21	1,9	0,3	2	2	2	1	2

Role-Emotional(RE2)	4864	9	0,19	1,8	0,4	2	2	2	1	2
Role-Physical(RP3)	4864	10	0,21	1,9	0,3	2	2	2	1	2
Role -Emotional (RE3)	4864	13	0,27	1,8	0,4	2	2	2	1	2
Bodily pain (BP2)	4864	10	0,21	1,4	0,8	1	1	2	1	5
Mental Health (MH3)	4864	9	0,19	2,3	1	2	2	3	1	6
Energy/Fatigue (VT2)	4864	8	0,16	2,7	1,1	3	2	4	1	6
Mental Health (MH4)	4864	9	0,19	4,8	1	5	4	6	1	6
Social Functioning(SF2)	4864	11	0,23	4,3	1	5	4	5	1	5
Rand- 12 PCS	4864	24	0,49	54,4	7,6	56,8	52,3	58,8	10,3	72
Rand-12 MCS	4864	24	0,49	47,8	10,3	50,7	43,9	55,1	6,4	67
HRQoL utility (SF-6D)	4864	19	0,39	0,8	0,1	0,9	0,8	0,9	0,4	1

Table 4: Descriptive statistics for HRQoL measures (controls)

	Controls	**Cases**
n	4,864	766
General Health (median [IQR])	3.00 [2.00, 3.00]	3.00 [2.00, 3.00]
Physical Functioning (PF2) (median [IQR])	3.00 [3.00, 3.00]	3.00 [3.00, 3.00]
Physical Functioning (PF4) (median [IQR])	3.00 [3.00, 3.00]	3.00 [3.00, 3.00]
Role-Physical(RP2) (median [IQR])	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]
Role-Emotional(RE2) (median [IQR])	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]
Role-Physical(RP3) (median [IQR])	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]
Role -Emotional (RE3) (median [IQR])	2.00 [2.00, 2.00]	2.00 [2.00, 2.00]
Bodily pain (BP2) (median [IQR])	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]
Mental Health (MH3) (median [IQR])	2.00 [2.00, 3.00]	2.00 [2.00, 3.00]
Energy/Fatigue (VT2)(median [IQR])	3.00 [2.00, 4.00]	3.00 [2.00, 4.00]
Mental Health (MH4) (median [IQR])	5.00 [4.00, 6.00]	5.00 [4.00, 6.00]
Social Functioning(SF2) (median [IQR])	5.00 [4.00, 5.00]	5.00 [4.00, 5.00]
Rand- 12 PCS (median [IQR])	56.79 [52.34, 58.75]	56.59 [51.66, 58.75]
Rand-12 MCS (median [IQR])	50.67 [43.85, 55.15]	50.31 [42.07, 55.10]
HRQoL utility (SF-6D) (median [IQR])	0.86 [0.76, 0.86]	0.86 [0.72, 0.87]

Discussion

(discuss results, strengths and limitations of the study, application of results, future study, conclusion)

Conclusion

References

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Appendix 1: Baseline table Acute vs Long Covid cases

	Controls	Acute cases	LongCOVID cases
n	4,984	165	481
Sex = Female % (freq)	56.4 (2809)	66.7 (110)	58.2 (280)
Province % (freq)			
North (Groningen, Friesland, Drenthe, Overrijssel)	19.3 (962)	18.8 (31)	9.8 (47)
Midwest (Noord-Holland, Flevoland)	16.8 (835)	15.8 (26)	15.2 (73)
Mideast (Utrecht, Gelderland)	20.0 (997)	13.3 (22)	20.2 (97)
Southwest (Zuid-Holland, Zeeland)	17.5 (873)	13.3 (22)	14.1 (68)
Southeast (Noord-Brabant, Limburg)	19.8 (988)	26.1 (43)	30.8 (148)
LVC (low vaccination coverage of migrant sample)	6.6 (329)	12.7 (21)	10.0 (48)
Ethnicity % (freq)			
Dutch	88.9 (4429)	92.1 (152)	92.7 (446)
Western	7.7 (383)	6.1 (10)	5.4 (26)
Non-Western	3.5 (172)	1.8 (3)	1.9 (9)
Religious beliefs % (freq)			
None	54.0 (2577)	48.7 (77)	48.0 (220)
Roman Catholic	22.8 (1087)	24.1 (38)	29.9 (137)
Other	4.0 (192)	2.5 (4)	2.4 (11)
Regular Protestant	17.2 (820)	20.3 (32)	15.7 (72)
High refusing Protestant	2.0 (94)	4.4 (7)	3.9 (18)
Education level % (freq)			
High	46.8 (2284)	40.4 (65)	41.7 (195)
Moderate	32.4 (1581)	36.6 (59)	40.4 (189)
Low	20.8 (1014)	23.0 (37)	17.9 (84)
Number of other household occupants (excluding you) % (freq)			
0	12.2 (609)	8.5 (14)	6.9 (33)
1	45.8 (2279)	39.4 (65)	44.7 (215)

2	13.9 (694)	17.0 (28)	14.1 (68)
3	19.4 (967)	22.4 (37)	22.0 (106)
4	6.5 (324)	7.9 (13)	8.1 (39)
5	1.1 (56)	3.6 (6)	2.1 (10)
6	0.5 (24)	0.0 (0)	1.0 (5)
7	0.1 (5)	0.6 (1)	1.0 (5)
8	0.1 (3)	0.6 (1)	0.0 (0)
9	0.1 (5)	0.0 (0)	0.0 (0)
10	0.1 (3)	0.0 (0)	0.0 (0)
11	0.1 (3)	0.0 (0)	0.0 (0)
12	0.1 (6)	0.0 (0)	0.0 (0)
Smoking % (freq)			
Yes (I smoke or someone else smokes in the house)	11.1 (534)	6.2 (10)	7.4 (33)
No (smoked in the past)	39.0 (1883)	41.0 (66)	39.6 (177)
No (never smoked nad no one smokes in the house)	49.9 (2411)	52.8 (85)	53.0 (237)
Cormobidities= No % (freq)	35.5 (1742)	38.7 (63)	36.0 (169)
Corona Symptoms = No % (freq)	36.3 (1806)	36.4 (60)	20.6 (99)
BMI % (freq)			
Underweight	1.2 (59)	1.2 (2)	1.3 (6)
Normal weight	49.1 (2370)	47.2 (76)	50.0 (223)
Overweight	35.2 (1700)	37.9 (61)	35.4 (158)
Obese	14.4 (694)	13.7 (22)	13.2 (59)
Pregnant % (freq)			
Yes	1.0 (52)	1.2 (2)	1.9 (9)
No	61.1 (3029)	70.3 (116)	67.2 (322)
Not applicable	37.9 (1877)	28.5 (47)	30.9 (148)
Age (median [IQR])	54.00 [38.00, 66.00]	49.00 [34.00, 59.00]	50.00 [32.00, 63.00]
Health related quality of life (SF6D) (median [IQR])	0.86 [0.76, 0.86]	0.80 [0.70, 0.86]	0.86 [0.76, 0.92]
Physical Health (Rand-12) (median [IQR])	56.79 [52.34, 58.75]	56.16 [49.89, 59.14]	56.77 [52.10, 58.75]
Mental Health (Rand-12) (median [IQR])	50.67 [43.67, 55.15]	48.26 [38.68, 54.54]	50.67 [43.27, 54.97]
Fatigue (CIS)(median [IQR])	19.00 [12.00, 30.00]	25.00 [14.00, 35.00]	21.00 [12.00, 31.00]
Vaccinated = Yes % (freq)	5.0 (241)	5.7 (9)	7.7 (36)
Fatigue cut off % (freq)			
normal	68.7 (3405)	54.5 (90)	65.5 (313)
severe	14.7 (728)	24.2 (40)	16.5 (79)
verhooged	16.7 (826)	21.2 (35)	18.0 (86)
Physical health cut off = physical condition % (freq)	18.0 (894)	25.8 (42)	17.6 (84)
Mental health cut off= normal % (freq)	55.0 (2726)	42.3 (69)	54.4 (259)