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## Mental health up to 12 months following SARS-CoV-2 infection: A prospective cohort study

Anouk Verveen<sup>a,b,\*</sup>, Elke Wynberg<sup>c,d,e,1</sup>, Hugo D.G. van Willigen<sup>d,e,f,1</sup>, Udi Davidovich<sup>c,g</sup>, Anja Lok<sup>b,h,i</sup>, Eric P. Moll van Charante<sup>b,j,k</sup>, Menno D. de Jong<sup>e,f</sup>, Godelieve de Bree<sup>d,e</sup>, Maria Prins<sup>c,d,e</sup>, Hans Knoop<sup>a,b</sup>, Pythia T. Nieuwkerk<sup>a,b,e</sup>

<sup>a</sup> Amsterdam UMC location University of Amsterdam, Department of Medical Psychology, Meibergdreef 9, Amsterdam, the Netherlands

<sup>b</sup> Amsterdam Public Health, Amsterdam, the Netherlands

<sup>c</sup> Department of Infectious Diseases, Public Health Service of Amsterdam, Amsterdam, the Netherlands

<sup>d</sup> Amsterdam UMC location University of Amsterdam, Department of Infectious Diseases, Meibergdreef 9, Amsterdam, the Netherlands

<sup>e</sup> Amsterdam Institute for Infection and Immunity, Infectious Diseases, Amsterdam, the Netherlands

<sup>f</sup> Amsterdam UMC location University of Amsterdam, Department of Medical Microbiology & Infection Prevention, Meibergdreef 9, Amsterdam, the Netherlands

<sup>g</sup> Department of Social Psychology, University of Amsterdam, Amsterdam, the Netherlands

<sup>h</sup> Amsterdam UMC location University of Amsterdam, Department of Psychiatry, Meibergdreef 9, Amsterdam, the Netherlands

<sup>i</sup> Center for Urban Mental Health, University of Amsterdam, the Netherlands

<sup>j</sup> Amsterdam UMC location University of Amsterdam, Department of Public & Occupational Health, Meibergdreef 9, Amsterdam, the Netherlands

<sup>k</sup> Amsterdam UMC location University of Amsterdam, Department of General Practice, Meibergdreef 9, Amsterdam, the Netherlands

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### ABSTRACT

**Objective:** To investigate to what extent individuals report clinically relevant levels of depression, anxiety, post-traumatic stress disorder (PTSD) symptoms and concentration problems up to 12 months following COVID-19 symptom onset, using validated questionnaires.

**Methods:** RECOVERED, a prospective cohort study in Amsterdam, the Netherlands, enrolled both hospitalized and community-dwelling adult participants diagnosed with SARS-CoV-2. Symptoms of depression and anxiety were assessed with the Patient Health Questionnaire-9 and Generalized Anxiety Disorder-7 1, 3, 6 and 12 months following illness onset. The DSM-V PTSD checklist was administered at month 3 and 9. Concentration problems were assessed using the Checklist Individual Strength concentration subscale at month 1 and 12. Generalized Estimating Equations were used to determine factors related with clinically relevant levels of depression-, anxiety- and PTSD-symptoms and concentration problems over time.

**Results:** In 303 individuals, the prevalence of clinically relevant symptoms of depression, anxiety and concentration problems was 10.6% (95%CI = 7.2–15.4), 7.0% (95%CI = 4.4–11.2) and 33.6% (95%CI = 27.7–40.1), respectively, twelve months after infection. Nine months after illness onset, 4.2% (95%CI = 2.3–7.7) scored within the clinical range of PTSD. Risk factors for an increased likelihood of reporting mental health problems during follow up included initial severe/critical COVID-19, non-Dutch origin, psychological problems prior to COVID-19 and being infected during the first COVID-19 wave.

**Conclusion:** Our findings highlight that a minority of patients with COVID-19 face clinically relevant symptoms of depression, anxiety or PTSD up to 12 months after infection. The prevalence of concentration problems was high. This study contributes to the identification of specific groups for which support after initial illness is indicated.

### 1. Introduction

Since the beginning of the COVID-19 pandemic, concerns have been

raised regarding the mental health sequelae among COVID-19 patients [1]. Problems with concentration have been reported up to twelve months after illness onset [2] and several studies conducted during the

\* Corresponding author at: Department of Medical Psychology, Amsterdam UMC location AMC, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands.

E-mail address: [a.verveen@amsterdamumc.nl](mailto:a.verveen@amsterdamumc.nl) (A. Verveen).

<sup>1</sup> Contributed equally

beginning of the pandemic indeed have shown increased symptom levels of depression, anxiety and post-traumatic stress (PTSD) among survivors [3–5].

During previous outbreaks of infectious diseases such as SARS, MERS, Q-fever and West Nile virus, infected individuals had an increased risk of developing cognitive and psychiatric symptoms such as PTSD, depression and anxiety in the acute phase of infection and these symptoms could persist years after illness onset [5–10]. Proximity to or experience with life-threatening illness is a known risk factor for the development of clinical PTSD [11,12]. Additionally, experiencing critical illness is a known risk factor for developing symptoms of depression and anxiety [12]. Moreover, it is known that people who previously had psychiatric or psychological problems are at increased risk for clinical mental health problems following an infection [11]. These observations suggest that factors existing both prior to disease and those arising as a consequence of the physical manifestation of infection itself may play a role in the development of post-infectious mental health sequelae.

Factors related to the COVID-19 pandemic can also be expected to impact on the mental health of infected individuals. We expect that the psychological threat of COVID-19 might have been higher during the first wave of the pandemic compared to later waves as prognosis of infected individuals was poor, treatment options were limited, and there was intense pressure on the medical system. Consequently, individuals diagnosed with COVID-19 experienced more isolation, fear and stigmatization than those diagnosed in later waves [13]. Furthermore, COVID-19 lockdown and restrictions may negatively impact mental health, regardless of being infected with the virus [14–16].

Fatigue, concentration- and sleep- problems are not only frequently reported symptoms in survivors of COVID-19 [18,19], but also common symptoms of depression, anxiety and PTSD [17–19]. The extent to which symptoms of fatigue, concentration- and sleep- problems contribute to depression, anxiety and PTSD scores in COVID-19 is not well documented. To date, only a limited number of studies have investigated symptoms of PTSD, depression and anxiety among individuals with COVID-19 showing a wide variation in prevalence (range 6–53%). At least one study has shown that severity of COVID-19 disease is associated with increased symptom levels of depression and anxiety [20]. These studies were predominantly conducted among patients previously hospitalized for COVID-19 with follow-up periods up to 6 months after infection [3,20,21]. Since the vast majority of individuals infected with SARS-CoV-2 are not hospitalized this presents a gap in our knowledge of the impact of COVID-19 disease on mental health. As a result, the proportion of patients reporting clinically relevant levels of mental health symptoms, e.g. warranting treatment, following illness onset and the characteristics of individuals who are most vulnerable for developing severe or long-term mental health symptoms are currently not well documented.

This study aims to investigate the prevalence of depression-, anxiety-, and PTSD-symptoms and concentration problems up to 12 months following COVID-19 illness onset among patients at all levels of COVID-19 disease severity. In addition, we investigate whether socio-demographics, somatic comorbidities, history of psychiatric or psychological problems, initial disease severity of COVID-19 and infection during the first wave vs later waves of the pandemic are associated with an increased risk of mental health or concentration problems over time.

## 2. Methods

### 2.1. Study design

RECOVERED is an ongoing cohort study of individuals with laboratory-confirmed SARS-CoV-2 infection in the municipal region of Amsterdam, the Netherlands [22]. All included participants needed to have a PCR test or serological-confirmed positive SARS-CoV-2 diagnosis at the moment of enrolment. Further inclusion criteria comprised being aged between 16 and 85 years and having sufficient understanding of

Dutch or English. Exclusion criteria were having a severe mental disorder that would interfere with adherence to study procedures or the decision to participate in the study, such as dementia, or currently living in a long term care facility. Inclusion started in May 2020 and continued until July 2021. Up to 30 June 2020, a limited number of hospitalized patients were included retrospectively within 3 months following SARS-CoV-2 diagnosis.

Study visits at enrolment (D0) and day 7 of follow-up (D7) took place at the participant's home (if non-hospitalized) or on the hospital ward (if hospitalized) whilst subsequent visits at months 1, 3, 6, 9 and 12 took place at one of two study sites. All visits were performed by trained medical study staff. Participants completed online questionnaires at months 1, 3, 6, 9 and 12. Past medical history and socio-demographic data were collected during the first month of follow-up by means of patient interview and checking of medical records.

Loss to follow-up (LTFU) was defined as active withdrawal from the study or two consecutive no-show appointments despite 3 attempts to establish contact. Date of LTFU was defined as the date of last contact with the participant.

RECOVERED was approved by the medical ethical review board of the Amsterdam University Medical Centre (NL73759.018.20). All participants provided written informed consent.

#### 2.1.1. Measurements of depression, anxiety and PTSD symptoms and concentration problems

Symptoms of depression were measured using the Patient Health Questionnaire-9 (PHQ-9) [23]. The PHQ-9 scores the nine DSM criteria of depression on a scale from 0 (never present) to 3 (present nearly every day), where higher scores indicate higher levels of depressive symptoms. The PHQ-9 contains three items asking about fatigue, sleep problems and concentration problems. The Generalized Anxiety Disorder-7 (GAD-7) was used for assessing anxiety symptoms [24]. The GAD-7 consists of seven items, each of which is scored 0 (not at all) to 3 (nearly every day), providing a 0 to 21 severity score of anxiety symptoms. The GAD-7 does not include items on fatigue/sleep problems/concentration problems. A cut-off point of 10 indicates the presence of clinically relevant levels of anxiety or depression. Validity of the measures has been established [25]. Both measures were completed at 1, 3, 6 and 12 months after illness onset.

The DSM-V PTSD checklist (PCL-5) was used to assess PTSD symptoms 3 and 9 months after onset of COVID-19 [26]. The PCL-5 is a 20-item self-report measure of DSM-V PTSD symptoms. Items are scored on a scale from 0 (not at all) to 4 (extremely), where higher PCL-5 scores indicate greater PTSD symptom severity. A cut-off threshold of at least 30 was used to define clinically relevant symptoms of PTSD. The measure has strong reliability and validity [26]. The PCL-5 contains two items on sleep problems and concentration problems.

Concentration problems were assessed using the subscale concentration problems from the Checklist Individual Strength (CIS) at 1 and 12 months after onset of COVID-19 [27]. The subscale consists of 5 items, scored on a 7-point scale. In this paper, a cut-off threshold of  $\geq 18$  defines the presence of notable concentration problems. This cut-off is based on data from Worm-Smeitink et al. in which 1923 healthy subjects completed the CIS and corresponds with 85% of healthy subject scoring below this threshold [28]. Previously, a cut-off of 15 has also been used [28]. Therefore, the number of participants scoring between 15 and 18 is presented separately.

#### 2.1.2. Definitions

We defined history of psychiatric or psychological problems as either having psychiatric comorbidity at illness onset, which was extracted from the patients' medical files, or a confirmative response to a self-report question asking whether someone had previously received professional help for psychological problems. Migration background was categorized as Dutch and non-Dutch based on the country of birth of the participant and their parents [29,30]. Those of non-Dutch background

were further classified as originating from a OECD high-income (HIC) or low-/middle-income country (LMIC) [31]. Educational level was categorized as low (none, primary or secondary school), medium (vocational training) or high (university-level). BMI was coded in kg/m<sup>2</sup> as: <25, underweight or normal weight; 25–30, overweight; >30, obese. High-risk comorbidities were those identified by the WHO as being associated with severe COVID-19: cardiovascular disease (CVD), diabetes mellitus (DM), chronic lung disease (CLD), cancer and immunodeficiency [32].

Severity of initial COVID-19 was defined based on WHO COVID-19 disease severity criteria [32]. Mild disease was defined as having a RR < 20/min and SpO<sub>2</sub> > 94% on room air at both enrolment and day 7 study visits; moderate disease as having a RR 20–30/min and SpO<sub>2</sub> 90–94% or receiving oxygen therapy at enrolment or day 7 study visits; severe disease as having a RR > 30/min and SpO<sub>2</sub> < 90% or receiving oxygen therapy at enrolment or day 7 study visits; critical disease as requiring ICU admission as a result of COVID-19 at any point.

Individuals were categorized as being infected during the first COVID-19 wave in the Netherlands, which was from February 2020 until 31 May 2020, or being infected at a later time point (i.e. between 1 June 2020 and June 2021).

The Checklist Individual Strength (CIS) subscale fatigue is used to determine the presence of severe fatigue at 1 and 12 months after onset of COVID-19 [27,28]. A cut-off threshold of ≥35 determines severe fatigue.

## 2.2. Statistical analysis

Sociodemographic and clinical factors, and levels of anxiety, depression, PTSD and concentration problems are presented for the total group as well as by clinical severity. Using Chi-square, Mann-Whitney and Kruskal-Wallis tests, differences in the outcome measures were evaluated between severity groups.

To explore overlap of symptoms that can be both a symptom of COVID-19 as well as a symptom of a mental health condition, we compared the prevalence of severe fatigue and concentration problems between participants scoring above and below the cut-off of clinically relevant depressive symptoms and PTSD symptoms using chi-squared tests.

Generalized Estimating Equations (GEE) were used to analyse dichotomous outcomes for the anxiety, depression, PTSD and concentration scores as the dependent variables. Months since illness onset (month 1, 3, 6, 9, 12), age and sex were included as fixed covariates, regardless of statistical significance. Additionally, migration background, education, number of COVID-19 high-risk comorbidities, previous psychiatric or psychological problems, severity of initial COVID-19, and timing of infection (first wave vs. later) were added to the model. The method for purposeful selection of covariates by Hosmer and Lemeshow was used to reach the final multivariable model [33]. The final model includes all variables that were significant at the 0.05 level or were a confounder, meaning there was a change in any remaining parameter estimate >15% when adding or removing the variable. Two-sided *P*-values <0.05 were considered statistically significant. Statistical analyses were performed using Stata (v.15.1, College Station, TX, USA) and IBM SPSS statistics (v.28).

## 3. Results

### 3.1. Study sample

Between May 2020 and March 2022, 303 of 349 participants (86.8%), of whom 57% (*N* = 172) were male, and with a median age of 51.0 years [IQR 36.0–62.0], had completed at least one study questionnaire and were included in the current analysis. The participants who did not complete any surveys (*n* = 46 [13.2%]) and were excluded from the current analysis did not differ significantly in age, sex, BMI,

migration background, comorbidities or initial COVID-19 severity from included participants. Excluded individuals less often had psychiatric or psychological problems before COVID-19 (2%), than included individuals (22%, *p* = 0.004).

Participants with severe/critical initial disease were significantly older (mdn = 60 years) than those with moderate (mdn = 49 years) or mild (mdn = 40 years) disease (*H*(2) = 36.57, *p* < 0.001), had significantly higher BMI (mdn = 27.3, 26.2 and 24.6, respectively; *H*(2) = 15.91, *p* < 0.001), originated more often from a LMIC (36%, 25%, 11%, respectively; Fisher's exact test, *p* = 0.001). Individuals with severe initial illness had a lower level of education (*X*<sup>2</sup>(4) = 24.87, *p* < 0.001) as 46% had a university education compared to 55% of those with moderate and 79% of those with mild disease. Participants with initial severe disease more often had multiple comorbidities prior to COVID-19, 38% had 2 or more comorbidities compared to 20 or 9% of those with moderate or mild disease, respectively (Fisher's exact test, *p* < 0.001)(Table 1). Sixty-five participants (22%) had previous psychiatric or psychological problems; there was no difference in the percentage with previous psychiatric or psychological problems across initial COVID-19 severity groups (*X*<sup>2</sup>(2) = 0.50, *p* = 0.78). The majority of study participants enrolled following a SARS-CoV-2 infection during the first wave in the Netherlands, had initially severe/critical COVID-19 (*X*<sup>2</sup>(2) = 13.54, *p* = 0.001).

### 3.2. Depression

The prevalence of clinically relevant levels of depressive symptoms in participants with mild (*N* = 72), moderate (*N* = 102) and severe/critical (*N* = 37) disease one month after illness onset was 16.7% [95% CI = 9.7–27.2], 26.5% [95%CI = 18.8–35.9] and 22.2% [95%CI = 11.5–38.6], respectively (Table 2). The prevalence at month 1 did not differ significantly for initial COVID-19 severity, however, one year after illness onset it did (*X*<sup>2</sup>(2) = 6.9075, *p* = 0.032): 2.9% [95%CI = 0.7–10.9] of individuals with initial mild disease (*N* = 69) experienced clinically relevant depressive symptoms, compared to 11.8% [95%CI = 6.8–19.6] of those with initial moderate disease (*N* = 102) and 18.2% [95%CI = 10.0–30.7] of those with initial severe/critical disease (*N* = 53) (Table 2).

Multivariate Generalized Estimating Equations (GEE), adjusted for age, showed that the following factors were associated with clinically relevant levels of depressive symptoms over time: being female (OR = 2.21, 95%CI = 1.28–3.81); history of psychiatric or psychological problems (OR = 2.38, 95%CI = 1.41–4.01); being overweight (OR = 2.43, 95%CI = 1.28–4.60); being non-Dutch originating from a HIC (OR = 5.31, 95%CI = 2.61–10.81); and initial moderate (OR = 2.31, 95%CI = 1.11–4.79) or severe/critical COVID-19 disease (OR = 4.00, 95%CI = 1.79–8.94)(Table 3).

Mean item scores of the items regarding fatigue and sleep problems on the PHQ were highest at every time point (Supplementary Table A). The prevalence of severe fatigue (*X*<sup>2</sup>(2) = 20.43, *p* < 0.001) and concentration problems (*X*<sup>2</sup>(2) = 34.71, *p* < 0.001) at month 12 was significantly higher for individuals scoring above the cut-off for depressive symptoms (Supplementary table B).

### 3.3. Anxiety

One month after illness onset, the prevalence of clinically relevant levels of anxiety in survey responders with mild (*N* = 72), moderate (*N* = 102) and severe/critical (*N* = 37) disease was 6.9% [95%CI = 2.9–15.7], 9.8% [95%CI = 5.3–17.3] and 8.1% [95%CI = 2.6–22.4], respectively (Table 2). One year after illness onset, 7.2% [95%CI = 3.0–16.3] of participants with initial mild disease (*N* = 69), 5.8% [95%CI = 2.6–12.4] of those with initial moderate disease (*N* = 103) and 9.1% [95%CI = 3.8–20.1] of those with initial severe/critical disease (*N* = 53) reported above the cut-off for anxiety symptoms (Table 2). At both time points the likelihood of clinically relevant levels of anxiety was not

**Table 1**  
Socio-demographic, clinical (baseline and COVID-19-related) characteristics of RECoVERED study participants.

	Total N = 303	Initial mild COVID-19 N = 87	Initial moderate COVID-19 N = 136	Initial severe/critical COVID-19 N = 80	p-value
Sex					0.21
Male	172 (57%)	43 (49%)	79 (58%)	50 (63%)	
Female	131 (43%)	44 (51%)	57 (42%)	30 (38%)	
Age, years	51.0 (36.0–62.0)	40.0 (28.0–55.0)	49.0 (34.0–60.5)	60.0 (50.5–65.5)	<0.001
BMI, kg/m <sup>2</sup>	26.1 (23.4–29.4)	24.6 (22.8–27.7)	26.2 (23.5–29.4)	27.3 (25.6–32.9)	<0.001
BMI category					<0.001
Normal weight	123 (41%)	49 (56%)	56 (41%)	18 (23%)	
Overweight	106 (35%)	24 (28%)	48 (35%)	34 (43%)	
Obese	69 (23%)	13 (15%)	32 (24%)	24 (30%)	
Missing	5 (2%)	1 (1%)	0 (0%)	4 (5%)	
Migration background <sup>a</sup>					0.001
Dutch	187 (62%)	63 (72%)	78 (57%)	46 (57%)	
Non-Dutch, OECD high-income	37 (12%)	12 (14%)	21 (15%)	4 (5%)	
Non-Dutch, OECD low/middle income	73 (24%)	10 (11%)	34 (25%)	29 (36%)	
Missing	6 (2%)	2 (2%)	3 (2%)	1 (1%)	
Highest level of education					<0.001
None, primary or secondary education	42 (14%)	7 (8%)	24 (18%)	11 (14%)	
Vocational training	73 (24%)	9 (10%)	34 (25%)	30 (38%)	
University education	181 (60%)	69 (79%)	75 (55%)	37 (46%)	
Missing	7 (2%)	2 (2%)	3 (2%)	2 (3%)	
Number of COVID-19 high-risk comorbidities <sup>b</sup>					<0.001
0	168 (55%)	62 (71%)	81 (60%)	25 (31%)	
1	71 (23%)	17 (20%)	29 (21%)	25 (31%)	
2	38 (13%)	5 (6%)	17 (13%)	16 (20%)	
3 or more	26 (9%)	3 (3%)	9 (7%)	14 (18%)	
Previous psychiatric or psychological problems					0.78
No	237 (78%)	70 (80%)	107 (79%)	60 (75%)	
Yes	65 (21%)	17 (20%)	29 (21%)	19 (24%)	
Missing	1 (0%)	0 (0%)	0 (0%)	1 (1%)	
Infected during the first COVID wave <sup>c</sup>					0.001
No	198 (65%)	64 (74%)	96 (71%)	38 (48%)	
Yes	101 (33%)	22 (25%)	40 (29%)	39 (49%)	
Missing	4 (1%)	1 (1%)	0 (0%)	3 (4%)	
Lost to follow-up <sup>d</sup>	40 (13%)	12 (14%)	20 (15%)	8 (10%)	0.61

Abbreviations: BMI, Body Mass Index; COVID-19, coronavirus disease 2019; OECD, Organisation for Economic Co-operation and Development.

Continuous variables presented as median (IQR) and compared using the Kruskal-Wallis test; categorical and binary variables presented as n(%) and compared using the Pearson  $\chi^2$  test (or Fisher exact test if  $n < 5$ ).

COVID-19 clinical severity groups defined as: mild as having a respiratory rate (RR) <20/min and oxygen saturation (SpO<sub>2</sub>) on room air >94% at both day 0 and 7; moderate disease as having a RR 20–30/min, SpO<sub>2</sub> 90–94% and/or receiving oxygen therapy at day 0 or 7; severe disease as having a RR > 30/min or SpO<sub>2</sub> < 90% at day 0 or 7; critical disease as requiring intensive care unit admission.

<sup>a</sup> Migration background was based on country of birth of participant and that of their parents and included first and second generation migrants.

<sup>b</sup> COVID-related comorbidities are based on World Health Organisation Clinical Management Guidelines[16] and include: cardiovascular disease (including hypertension), chronic pulmonary disease (excluding asthma), renal disease, liver disease, cancer, immunosuppression (excluding HIV, including previous organ transplantation), previous psychiatric illness and dementia.

<sup>c</sup> First COVID-19 wave in the Netherlands: February 2020 until 31 May 2020.

<sup>d</sup> Lost to follow-up defined as active withdrawal from the study or two consecutive no-show appointments despite three attempts to establish contact.

significantly related with initial COVID-19 severity.

Multivariate Generalized Estimating Equations (GEE), adjusted for age and sex, showed that the following factors were associated with clinically relevant symptoms of anxiety over time: previous psychiatric or psychological problems (OR = 2.92, 95%CI = 1.58–5.39); non-Dutch originating from a HIC (OR = 4.90, 95%CI = 2.13–11.27) and severe initial COVID-19 (OR = 3.16, 95%CI = 1.32–7.55) (Table 3).

### 3.4. PTSD

Using the PCL-5 at month 3, 1.4% [95%CI = 0.2–9.3] of participants with initial mild disease ( $N = 72$ ), 4.9% [95%CI = 2.2–10.5] of participants with initial moderate disease ( $N = 123$ ) and 14.3% [95%CI = 7.6–25.3] with initial severe/critical disease ( $N = 63$ ) had scores above the cut-off for PTSD (Table 2), which differed significantly between the three groups ( $\chi^2(2) = 10.32, p = 0.006$ ). At month 9 none of the participants with initial mild COVID-19 scored above the cut-off ( $N = 72$ ), compared to 4.7% [95%CI = 2.0–11.0] and 8.5% [95%CI = 3.6–18.9] of the participants with initial moderate ( $N = 105$ ) or severe disease ( $N = 59$ ), respectively, although the effect of disease severity was not

statically significant.

Multivariate Generalized Estimating Equations (GEE), adjusted for age and sex, showed that the following factors were associated with clinically relevant symptoms of PTSD over time: non-Dutch originating from a HIC (OR = 6.00, 95%CI = 1.67–21.52) or LMIC (OR = 3.36, 95%CI = 1.09–10.31), infected during the first COVID-19 wave (OR = 5.19, 95%CI = 1.58–17.04) and having initial severe COVID-19 (OR = 31.00, 95%CI = 1.70–99.75) (Table 3).

The prevalence of severe fatigue ( $\chi^2(2) = 4.53, p = 0.03$ ) and concentration problems ( $\chi^2(2) = 13.78, p < 0.001$ ) at month 12 was significantly higher for individuals scoring above the cut-off for clinically relevant symptoms of PTSD (Supplementary table B).

### 3.5. Concentration

Mean scores on the concentration subscale of the CIS were 16.73 (SD = 8.72), and 14.52 (SD = 7.81) at month 1 and 12, respectively (Table 4). Individuals with initial severe COVID-19 scored significantly higher on the subscale, indicating more problems with concentration than those with mild or moderate COVID-19 at month 1 ( $H(2) = 7.84, p$



**Table 2**

Prevalence of clinically relevant PTSD, depression and anxiety among participants with initial mild, moderate and severe COVID-19.

	Month 1	Month 3	Month 6	Month 9	Month 12
	N = 212 n (%)	N = 259 n (%)	N = 240 n (%)	N = 236 n (%)	N = 227 n (%)
<b>PTSD (PCL-5)</b>					
Initial mild COVID-19		1 (1,4%)		0 (0,0%)	
Initial moderate COVID-19		6 (4,9%)		5 (4,7%)	
Initial severe/critical COVID-19		9 (14,3%)		5 (8,5%)	
<b>Depression (PHQ-9)</b>					
Initial mild COVID-19	12 (16,7%)	5 (6,9%)	6 (8,3%)		2 (2,9%)
Initial moderate COVID-19	27 (26,5%)	18 (14,6%)	18 (16,4%)		12 (11,8%)
Initial severe/critical COVID-19	8 (22,2%)	16 (25,4%)	11 (19,0%)		10 (18,2%)
<b>Anxiety (GAD-7)</b>					
Initial mild COVID-19	5 (6,9%)	3 (4,2%)	4 (5,6%)		5 (7,2%)
Initial moderate COVID-19	10 (9,8%)	14 (11,4%)	11 (10,0%)		6 (5,8%)
Initial severe/critical COVID-19	3 (8,1%)	12 (18,8%)	6 (10,3%)		5 (9,1%)

Abbreviations: COVID-19, coronavirus disease 2019; PTSD, post-traumatic stress disorder; PCL-5, The PTSD checklist for the DSM-5; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7.

= 0.02) and month 12 ( $H(2) = 12.95, p = 0.002$ ). Twelve months after illness onset, 20.3% [95%CI = 12.4–31.5] of patients with mild ( $N = 69$ ), 38.2% [95%CI = 29.3–48.0] with moderate ( $N = 102$ ) and 42.3% [95%CI = 29.7–56.1] with severe COVID-19 ( $N = 52$ ) had scores above the cut-off ( $\geq 18$ ) for concentration problems. These differences between the three groups were statistically significant ( $\chi^2(2) = 8.23, p = 0.02$ ).

Generalized Estimating Equations (GEE), adjusted for age and sex, showed that initial moderate COVID-19 compared to mild COVID-19 was associated with clinically relevant scores on concentration problems over time (OR = 2.52, 95%CI = 1.38–4.60)(Table 3). Furthermore, individuals were more likely to report clinically relevant levels of concentration problems over time if they were overweight (OR = 1.95, 95%CI = 1.08–3.50), originated from a HIC (OR = 2.29, 95%CI = 1.04–5.03), had vocational education (OR = 3.98, 95%CI = 1.44–11.03), one comorbidity (OR = 1.93, 95%CI = 1.01–3.67) or a history of psychiatric or psychological problems (OR = 2.26, 95%CI = 1.23–4.16).

#### 4. Discussion

In this well characterized cohort among hospitalized and community-dwelling COVID-19 patients, a minority of participants had clinically relevant symptom levels of depression, anxiety or PTSD up to 12 months after illness onset. Remarkably, more than half of the participants reported concentration problems 12 months after illness onset. This is substantially more than the percentage of patients reporting clinically relevant levels of depressive, anxiety or PTSD symptoms.

Reporting clinically relevant levels of depression, anxiety or PTSD was associated with initial severe/critical COVID-19 symptomology, being a migrant, previous psychiatric or psychological problems, and being infected during the first COVID-19 wave. Some of these predictors are generic predictors of mental health problems and not COVID-19

specific, such as female sex and previous psychological problems [34,35]. The finding that migrants from HIC more often had clinically relevant symptoms of depression, anxiety and PTSD was striking. Some studies on predictors of mental health problems have also found this relation [36], whereas others have not [37].

To date, only few studies have reported on mental health after COVID-19 disease with follow-up periods of one year. Our findings on symptoms of depression are in line with two studies from Europe among COVID-19 patients who were admitted to an intensive care unit. They found a prevalence of 18% clinically relevant symptoms of depression at 12 months after illness onset [38,39], which is similar to the prevalence among patients with initial severe/critical COVID-19 in our study. In contrast, a study from China among previously hospitalized patients found a lower depressive symptoms prevalence of around 10% one year after infection [40]. This difference might be due to cultural factors, as China generally has a lower population reported prevalence of depression than the Netherlands and other European countries [41]. Studies about long-term mental health among patients with initial mild and moderate COVID-19 are currently lacking. In a previous study from the Netherlands, describing mental health up to 6 months after infection, much higher percentages of PTSD, anxiety and depressive symptoms were reported [42]. However, this finding might be due to selection bias as the study only recruited patients with persistent complaints after COVID-19.

The overall prevalence of depression symptoms one year after illness onset ranged between 2.9 and 18.2%, with the highest prevalence among those with initial severe/critical illness. It seems that COVID-19 has a short-term impact on all infected individuals, but the impact is greater for individuals with a more severe initial illness, which can lead to depressive symptoms on the long-term. Using the clinical range of the PHQ-9, depressed mood is present in 5.8–18.8% of the Dutch general population, depending on the ethnic group to which someone belongs [43]. So, in the general population a higher overall prevalence of clinically relevant symptoms of depression can be found than in the participants of this study. Although the prevalence of depressive symptoms in the present study was already low, it might even be overestimated. The most frequently endorsed items of our depression questionnaire asked about fatigue and problems falling asleep. Post-hoc analysis showed that somatic symptoms of fatigue and concentration problems are more prevalent among individuals who score above the cut-off for depressive symptoms. Given that fatigue and concentration problems are both symptoms of depression as well as physical sequela of COVID-19, it is impossible to infer whether these symptoms are indicative of depression, reflect disease burden of COVID-19, or both [44].

While some participants reported clinically relevant symptoms of anxiety, the overall prevalence one year after illness onset was low and ranged between 7.2 and 9.1%. Previously, a higher pre-COVID-19-pandemic prevalence of anxiety (19%) was found in the Dutch population when using the GAD-7 [45].

Individuals with initial severe/critical disease had more often clinically relevant symptoms of anxiety, depression and PTSD, a finding which was in line with expectations and findings from previous studies [20,46]. None of the patients with initial mild disease reported clinically relevant symptoms of PTSD at month 12. This is in accordance with a previous study that described that for PTSD to be diagnosed after COVID-19, the event must have been acute, life-threatening, and/or catastrophic [47], which is more likely with severe or critical COVID-19. As expected, more individuals infected in the first COVID-wave reported symptoms of PTSD at 9 months of follow-up than those infected later, which could be due to the many uncertainties in the initial phase of the pandemic.

There are several strengths to our study. Our prospective cohort study followed individuals from disease onset, which minimized selection bias. In addition, we included both individuals with mild or moderate disease and hospitalized patients. The long and detailed follow-up of participants and use of validated measures further strengthen these

**Table 3**

Generalized Estimating Equations (GEE) of clinically relevant PTSD, depression, anxiety and concentration problems over time up to 12 months after illness onset.

	Depression (PHQ-9)		Anxiety (GAD-7)	
	Bivariate	Multivariate	Bivariate	Multivariate
Age		OR = 0.99 (0.97–1.01) p = 0.374		OR = 0.99 (0.97–1.01) p = 0.492
Sex (reference = male)	OR = 2.08 (1.27–3.41) p = 0.004	OR = 2.21 (1.28–3.81) p = 0.005	OR = 1.83 (1.00–3.34) p = 0.051	OR = 1.59 (0.85–2.98) p = 0.150
BMI (reference = normal weight)				Not in final model.
Overweight	OR = 1.81 (1.00–3.25) p = 0.048	OR = 2.43 (1.28–4.60) p = 0.006	OR = 1.45 (0.72–2.89) p = 0.297	
Obese	OR = 1.35 (0.72–2.56) p = 0.350	OR = 1.67 (0.84–3.32) p = 0.146	OR = 1.36 (0.64–2.90) p = 0.427	
Education (reference = none, primary or secondary education)		Not in final model		Not in final model
Vocational training	OR = 0.93 (0.40–2.14) p = 0.862		OR = 1.83 (0.61–5.50) p = 0.284	
University education	OR = 0.70 (0.32–1.52) p = 0.367		OR = 1.15 (0.40–3.29) p = 0.801	
Migration background (reference = Dutch)				
LMIC	OR = 2.16 (1.21–3.85) p = 0.010	OR = 1.60 (0.88–2.92) p = 0.124	OR = 2.20 (1.12–4.31) p = 0.022	OR = 1.91 (0.96–3.84) p = 0.066
HIC	OR = 4.69 (2.37–9.30) p < 0.001	OR = 5.31 (2.61–10.81) p < 0.001	OR = 5.09 (2.22–11.70) p < 0.001	OR = 4.90 (2.13–11.27) p < 0.001
Comorbidities (reference = none)		Not in final model		Not in final model
1 comorbidity	OR = 1.54 (0.86–2.75) p = 0.146		OR = 1.51 (0.76–3.03) p = 0.242	
2 comorbidities	OR = 1.05 (0.51–2.17) p = 0.903		OR = 0.87 (0.35–2.21) p = 0.773	
3 or more comorbidities	OR = 1.18 (0.48–2.89) p = 0.715		OR = 1.29 (0.44–3.82) p = 0.644	
Previous psychological or psychiatric problems	OR = 3.00 (1.80–5.01) p < 0.001	OR = 2.38 (1.41–4.01) p = 0.001	OR = 3.50 (1.91–6.44) p < 0.001	OR = 2.92 (1.58–5.39) p < 0.001
Initial COVID-19 severity (reference = mild)				Not in final model
Initial moderate COVID-19	OR = 1.82 (0.98–3.41) p = 0.059	OR = 2.31 (1.11–4.79) p = 0.025	OR = 1.33 (0.64–2.78) p = 0.444	OR = 1.56 (0.70–3.45) p = 0.274
Initial severe/critical COVID-19	OR = 2.65 (1.32–5.32) p = 0.006	OR = 4.00 (1.79–8.94) p = 0.001	OR = 2.65 (0.99–5.17) p = 0.053	OR = 3.16 (1.32–7.55) p = 0.010
Infected during first COVID-19 wave	OR = 0.68 (0.39–1.17) p = 0.165	Not in final model	OR = 1.18 (0.64–2.17) p = 0.606	Not in final model

  

	PTSD (PCL-5)		Concentration (CIS)	
	Bivariate	Multivariate	Bivariate	Multivariate
Age		OR = 1.01 (0.97–1.04) p = 0.787		OR = 1.00 (0.98–1.02) p = 0.853
Sex (reference = male)	OR = 1.84 (0.70–4.82) p = 0.215	OR = 2.83 (0.93–8.59) p = 0.066	OR = 1.58 (1.01–2.46) p = 0.043	OR = 1.61 (0.96–2.70) p = 0.069
BMI (reference = normal weight)		Not in final model.		
Overweight	OR = 1.97 (0.59–6.65) p = 0.272		OR = 1.71 (1.03–2.85) p = 0.039	OR = 1.95 (1.08–3.50) p = 0.026
Obese	OR = 2.09 (0.58–7.61) p = 0.262		OR = 1.03 (0.57–1.86) p = 0.930	OR = 1.12 (0.60–2.11) p = 0.72
Education (reference = none, primary or secondary education)		Not in final model		
Vocational training	OR = 2.25 (0.56–9.07) p = 0.255		OR = 2.61 (1.13–6.03) p = 0.024	OR = 3.98 (1.44–11.03) p = 0.008
University education	OR = 0.76 (0.18–3.10) p = 0.696		OR = 1.69 (0.80–3.57) p = 0.167	OR = 2.37 (0.86–6.51) p = 0.095
Migration background (reference = Dutch)				
LMIC	OR = 3.48 (1.11–10.90) p = 0.033	OR = 3.36 (1.09–10.31) p = 0.034	OR = 1.79 (0.93–3.44) p = 0.081	OR = 1.65 (0.89–3.06) p = 0.112
HIC	OR = 3.86 (1.00–15.00) p = 0.051	OR = 6.00 (1.67–21.52) p = 0.006	OR = 1.74 (1.02–2.97) p = 0.041	OR = 2.29 (1.04–5.03) p = 0.039
Comorbidities (reference = none)		Not in final model		
1 comorbidity	OR = 3.58 (1.19–10.77) p = 0.023		OR = 1.98 (1.17–3.37) p = 0.011	OR = 1.93 (1.01–3.67) p = 0.046
2 comorbidities	OR = 2.13 (0.49–9.23) p = 0.312		OR = 1.56 (0.77–3.19) p = 0.220	OR = 1.49 (0.63–3.54) p = 0.366
3 or more comorbidities	OR = 1.86 (0.21–16.11) p = 0.574		OR = 0.54 (0.18–1.58) p = 0.261	OR = 0.56 (0.18–1.72) p = 0.308
Previous psychological or psychiatric problems	OR = 3.35 (1.24–9.02) p = 0.017	OR = 3.72 (1.18–1.72) p = 0.025	OR = 2.92 (1.76–4.86) p < 0.001	OR = 2.26 (1.23–4.16) p = 0.009
Initial COVID-19 severity (reference = mild)				
Initial moderate COVID-19	OR = 7.20 (0.87–59.57) p = 0.067	OR = 5.15 (0.64–41.73) p = 0.125	OR = 2.26 (1.32–3.86) p = 0.003	OR = 2.52 (1.38–4.60) p = 0.003

(continued on next page)

Table 3 (continued)

	PTSD (PCL-5)		Concentration (CIS)	
	Bivariate	Multivariate	Bivariate	Multivariate
Initial severe/critical COVID-19	OR = 18.76 (2.32–151.64) p = 0.006	OR = 31.01 (1.70–99.75) p = 0.014	OR = 2.33 (1.32–3.86) p = 0.010	OR = 2.29 (0.98–5.33) p = 0.055
Infected during first COVID-19 wave	OR = 3.44 (1.27–9.30) p = 0.015	OR = 5.19 (1.58–17.04) p = 0.007	OR = 0.50 (0.30–0.85) p = 0.010	OR = 0.58 (0.31–1.06) p = 0.078

Abbreviations: BMI, Body Mass Index; COVID-19, coronavirus disease 2019; GEE, Generalized Estimating Equations; HIC, high-income country; LMIC, low-/middle-income country, PTSD, post-traumatic stress disorder; PCL-5, The PTSD checklist for the DSM-5; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7.

Table 4

Prevalence of concentration problems among participants with initial mild, moderate and severe COVID-19.

CIS concentration score	Month 1		Month 12	
	15–17 n (%)	≥18 n (%)	15–17 n (%)	≥18 n (%)
Initial mild COVID-19	3 (4,1%)	25 (34,2%)	2 (2,9%)	14 (20,3%)
Initial moderate COVID-19	10 (9,8%)	55 (53,9%)	13 (12,7%)	39 (38,2%)
Initial severe/critical COVID-19	2 (5,4%)	19 (51,4%)	4 (7,7%)	22 (42,3%)

Abbreviations: CIS, checklist individual strength, COVID-19, coronavirus disease 2019.

findings. Nevertheless, limitations need to be addressed. Findings from our cohort, based in Amsterdam, the Netherlands may not be representative for other geographical regions. The higher prevalence of prior psychiatric or psychological problems in included participants compared to excluded participants may have inflated our estimates of mental health problems. Furthermore, the use of the PHQ-9 as a measure of depression could have resulted in an overestimation of depressive symptoms as it includes symptoms of fatigue and concentration problems, which are prevalent in COVID-19 survivors. Additionally, concentration problems were solely measured using a subjective self-reported measure in this study. The association with objective measures of concentration, e.g., using neuropsychological tests, is recommended to be studied in further research.

Our findings highlight that a minority of patients infected with SARS-CoV-2 develop clinically relevant symptoms of depression, anxiety or PTSD. Migrants, individuals with initial severe/critical COVID-19, and those with previous psychiatric or psychological problems are at increased risk of reporting clinically relevant levels of depression, anxiety or PTSD. Future research should focus on these subgroups at risk of mental health problems after COVID-19. Concentration problems are common even 12 months after COVID-19 illness onset, especially in those who also experience mental health problems.

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## Declaration of Competing Interest

The authors declare no conflicts of interests.

## Data availability

Taking legal restrictions into account, the data collected for this study are available on request via the corresponding author up to 15 years after the end of the study.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychores.2023.111520>.

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