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Trajectories of depression and anxiety during the COVID-19 pandemic in a population-based sample of middle-aged and older adults

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ABSTRACT

The COVID-19 pandemic and the related governmental restrictions have greatly impacted the lives of people worldwide and have been suggested to negatively impact mental health. We describe the trajectories of depressive and anxiety symptoms during the pandemic and their determinants in a large population-based sample of middle-aged and older adults. From April to June 2020, participants of the Rotterdam Study were asked to complete questionnaires including questions on depressive symptoms (Center of Epidemiological Studies Depression Scale, 10 item version) and anxiety symptoms (Hospital Anxiety and Depression Scale, anxiety subscale). We compared depressive and anxiety symptom scores to those before the pandemic and described its trajectories during the pandemic by demographic variables, chronic disease status and pre-pandemic clinically relevant depressive or anxiety symptoms. In total, 6241 participants responded to the questionnaires (mean age [standard deviation] 70.1 years [11.6]; 58% women). Participants more often reported clinically relevant depressive symptoms during than before the pandemic (19% vs. 12%, $P < .001$), which was similar for clinically relevant anxiety symptoms (17% vs. 12%, $P < .001$). During the pandemic, depressive symptoms persisted over time while anxiety symptoms improved. Depressive and anxiety symptoms were more common among women, persons living alone, with chronic diseases and with pre-pandemic clinically relevant symptoms, although the trajectories of these symptoms over time were broadly similar for the subgroups. Together, these results suggest that it is important to be aware of long-term depressive symptoms following the COVID-19 pandemic in the general population.

1. Introduction

The COVID-19 pandemic has drastically changed the lives of people worldwide (Bedford et al., 2020). Aside from the direct health burden of contracting the virus, restrictions to prevent further spread of the virus have had a major impact on daily life. In the Netherlands, an "intelligent lockdown" was adopted to manage the outbreak; people were for example asked to limit social contacts, work from home, and keep at least 1.5 m distance to people outside their household (Rijksoverheid, 2020a).

Lockdown measures have affected engagement in social life and have been suggested to result in social isolation and feelings of loneliness (Brooks et al., 2020; Chiesa et al., 2021). Studies in selected groups, mainly consisting of adolescents (Loades et al., 2020), health care workers (Pappa et al., 2020), and respondents to online surveys (O'Connor et al., 2020), have underlined the psychosocial consequences of the pandemic. Fewer studies, however, have been able to compare mental health in the middle-aged and older general population during the pandemic to pre-pandemic data (Pierce et al., 2020; Röhr et al., 2020) and to study subgroup effects in the evolution of depressive and anxiety symptoms throughout the pandemic (Riehm et al., 2021; Saunders et al., 2021). Such studies in the general population are pivotal to identify people most vulnerable to persisting mental health complaints and related adverse outcomes.

Within the population-based Rotterdam Study, we sought to determine the effects of the COVID-19 pandemic on mental health in the general middle-aged and older Dutch population. In addition, we determined subgroup differences in the trajectories of depressive and anxiety symptoms during the pandemic.

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Table 1
Population characteristics.

Characteristic	N = 6187
Age, years	70.1 (11.6)
Women	3596 (58.1)
Cohort wave	
RS-I	621 (10.0)
RS-II	1150 (18.6)
RS-III	2505 (40.5)
RS-IV	1911 (30.9)
Education	
Lower	2468 (40.3)
Intermediate	1975 (32.2)
Higher	1686 (27.3)
Migration background	
No Dutch grandparents	382 (7.9)
One or two Dutch grandparents	209 (4.3)
Three or four Dutch grandparents	4275 (87.9)
Living situation	
Alone	1710 (29.4)
With house mates	4108 (70.6)
Working status	
Working	1620 (28.7)
Unemployed	169 (3.0)
Retired	3554 (63.0)
Other	297 (5.3)
Workless due to the pandemic	
No	1755 (94.9)
Yes	95 (5.1)
COVID-19[a]	
Definite COVID-19 case	14 (0.2)
Probable COVID-19 case	58 (1.0)
Possible COVID-19 case	255 (4.3)
Chronic diseases	
Yes	3240 (55.7)
No	2575 (44.3)
Pre-pandemic clinically relevant depressive symptoms[b]	
Yes	401 (12.0)
No	2931 (88.0)
Pre-pandemic clinically relevant anxiety symptoms[b]	
Yes	409 (12.3)
No	2913 (87.7)

Numbers are frequencies (percentages) or mean (standard deviation). Characteristics are derived from the first returned questionnaire (Q1 for 5800 persons, Q2 for 358, Q3 for 18, Q4 for 11). Missing values (N): Education (58), migration background (1321), living situation (369), working status (547), workless due to the pandemic (4,337), COVID-19 (420), chronic diseases (372), previous depressive symptoms (2,855), previous anxiety symptoms (2,865).

[a] As reported in the first three questionnaires.

[b] Based on data from the latest research round before the pandemic between 2015 and 2020 from 3332 persons.

2. Materials and methods

2.1. The Rotterdam Study

The Rotterdam Study is a long-standing population-based study that aims to investigate the frequency, risk factors and the natural course of diseases in middle-aged and older persons. The study started in 1990 with a first cohort of persons aged 55 and older (RS-I) and was extended in 2000–2001 (RS-II), in 2006–2008 (RS-III, aged 45 and older), and in 2016–2020 (RS-IV, aged 40 and older)(Ikram et al., 2020). Participants were invited for interviews and examinations every 3–6 years. The Rotterdam Study has been approved by the Medical Ethics Committee of the Erasmus MC University Medical Center and by the Dutch Ministry of Health, Welfare and Sport. All participants provided written informed consent to participate in the study and to have their information obtained from treating physicians.

2.2. COVID-19 sub-study

From April 2020, a series of questionnaires was distributed among participants of the Rotterdam Study that focused on various aspects of health, disease, comorbidities and impact of COVID-19. Details of this COVID-19 sub-study have been described previously (Licher et al., 2021). The first questionnaire was sent to all 8732 Rotterdam Study participants who were alive and not living in nursing homes on April 20th, 2020 (details in Supplementary Fig. 1). Follow-up questionnaires were initially sent with two-week intervals in April (infection peak), expanding to four-week and eight-week intervals by mid-May and August, respectively. The first two questionnaires were sent on paper to all participants. From the third questionnaire onwards, questionnaires were only sent to participants who agreed on further participation and participants could indicate their preference for paper or digital contacts. The current study is based on the first four questionnaires sent between April 2020 and July 2020. All participants who completed at least one questionnaire were included in this study. Of the 8732 participants who were sent the initial two questionnaires, 6241 responded (response rate 71%) to the first questionnaire and 5640 (65%) to the second. Of the participants who concurred with participation in the subsequent questionnaires, 4956 of the 5618 invited participants (88%) responded to the third questionnaire and 4745 of the 5979 invited participants (79%) responded to the fourth questionnaire.

Table 2
Population follow-up characteristics.

	Questionnaire			
	Q1 (N = 5800)	Q2 (N = 5228)	Q3 (N = 4774)	Q4 (N = 4627)
Response date, median	April 26	May 10	May 26	June 26
IQR	April 24 – May 1	May 8 – May 12	May 24 – May 28	June 25 – June 30
Minimum – maximum	April 22 – July 10	May 7 – July 25	May 22 – July 27	June 24 – July 30
Depressive symptoms				
CES-D-10 score, median [IQR]	4 [2–8]	4 [2–8]	4 [2–7]	4 [1–7]
Clinically relevant, N (%)	986 (17.0)	857 (16.4)	767 (16.1)	720 (15.6)
Anxiety symptoms				
HADS-A score, median [IQR]	3 [1–5]	2 [0–5]	2 [0–4]	2 [0–4]
Clinically relevant, N (%)	937 (16.2)	773 (14.8)	628 (13.2)	576 (12.4)

Follow-up characteristics shown for participants with at least one measurement of depressive and anxiety symptoms, assessed using the Center of Epidemiological Studies Depression Scale (10 item version; CES-D-10) and the Hospital Anxiety and Depression Scale A (HADS-A). Scores of 10 or higher on the CES-D-10 and 8 or higher on the HADS-A are considered clinically relevant. IQR, interquartile range; N, number; Q, questionnaire.

2.3. Measurement of mental health

In the pre-pandemic Rotterdam Study rounds, depressive symptoms were assessed with the Dutch version of the Center for Epidemiologic Studies Depression scale (CES-D)(Beekman et al., 1997; Radloff, 1977). A shorter, 10-item version of the CES-D (CES-D-10) was incorporated in the COVID-19 sub-study. All items were rated on a 0–3 scale, dependent upon the frequency of experienced symptoms. Participants could score from 0 to 30, with higher scores reflecting more symptoms. A score of 10 or higher on the CES-D-10 is suggestive of clinically relevant depressive symptoms (Andresen et al., 1994). Anxiety symptoms were assessed with the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A, 7 items) (Zigmond and Snaith, 1983) in both the pre-pandemic Rotterdam Study rounds and the COVID-19 sub-study. Again, participants rated the symptoms on a 0–3 scale and higher scores (range 0–21) reflect more symptoms. A HADS-A score of 8 or higher is considered positive for clinically relevant anxiety symptoms (Bjelland et al., 2002).

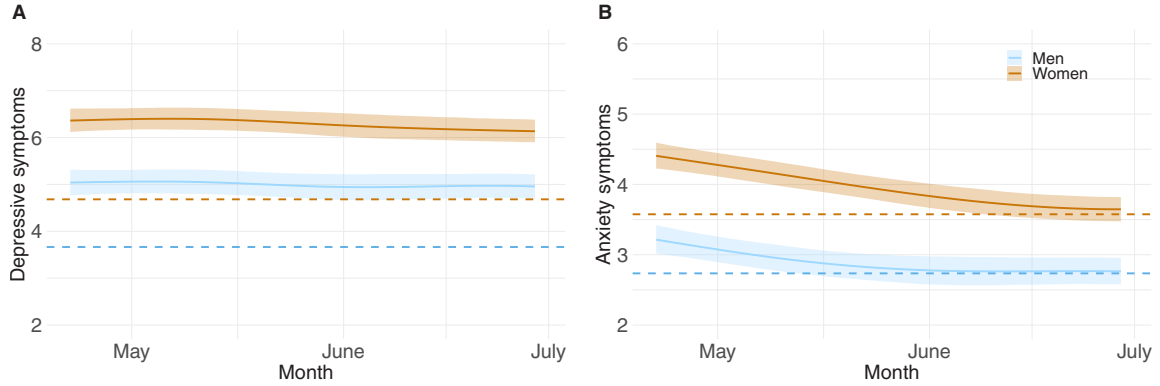

Fig. 1. Depressive symptoms (A) and anxiety symptoms (B) in the general population between April 20th, 2020 until June 30th, 2020
Trajectories are shown for men (blue) and women (orange) of mean age (70.1 years), with lower education, having a chronic disease and living together. The dashed lines are the average predicted scores for depressive and anxiety symptoms based on a pre-pandemic model and the participant characteristics at time of the first questionnaire.
Depressive symptoms are based on the Center of Epidemiological Studies Depression Scale (10 item version). Anxiety symptoms are based on the Hospital Anxiety and Depression Scale A.

Data from the latest pre-pandemic Rotterdam Study home interview were used to compare depressive and anxiety symptoms during the pandemic with the pre-pandemic situation. These data were collected between 2015 and 2020. Participants of RS-III (N = 2505), who took part in home interviews between 2012 and 2014, were excluded because of the large time gap between the pre-pandemic and the pandemic data collection. Pre-pandemic depressive and anxiety symptoms were determined by extracting the CES-D-10 items from the complete 20-item CES-D version and the HADS-A. Clinically relevant symptoms were determined using the cut-offs described above.

2.4. Other measurements

Education level and migration background were assessed at the baseline visit of the Rotterdam Study by interview. Education was categorized as lower, intermediate and higher education. Migration background was based on self-reported country of origin of participants' grandparents and was categorized as "no", "one or two" or "three or four" grandparents from the Netherlands. Information on migration background was not available for participants of RS-II (N = 1150). Information on living situation (alone/with housemates), and chronic disease (yes/no) was collected at the first questionnaire of the COVID-19 sub-study.

2.5. Statistical analysis

In order to determine the effects of the COVID-19 pandemic on mental health, we compared pre-pandemic CES-D-10 and HADS-A sum scores and the proportion of participants with clinically relevant symptoms to those at the first COVID-19 questionnaire. This comparison was made for participants of RS-I, RS-II and RS-IV with data available for the COVID-19 sub-study and the latest pre-pandemic round of the Rotterdam Study (3332 (90.5%) of the 3682 participants). Pre-pandemic questionnaires were completed on average 2.9 years before the date of sending the first questionnaire of the COVID-19 sub-study; 797 were completed in 2015, 623 in 2016, 598 in 2017, 644 in 2018, 585 in 2019 and 116 in 2020. Note that we did not include RS-III participants because their pre-pandemic assessment was more than 5 years ago.

To gain insight in the change of depressive and anxiety symptoms during follow-up, we presented the median and interquartile range (IQR) of the CES-D-10 and HADS-A and the proportion of individuals with clinically relevant symptoms for each COVID-19 sub-study questionnaire. Subsequently, we modelled the trajectories of depressive and anxiety symptoms over time using linear mixed models. Models with random intercepts were fitted, adjusted for sex, age, education, presence of chronic diseases and living situation and including interaction terms of age and sex with time. We used days since the date of sending the first questionnaire (April 20th, 2020) as the time scale and included splines for time with knots at May 11, June 1 and July 1 to allow nonlinearity of the model at the moment of relaxation of governmental restrictions (Rijksoverheid, 2020b). We modelled the expected level of depressive and anxiety symptoms based on the pre-pandemic questionnaires and the COVID-19 sub-study population characteristics, in order to compare expected depressive and anxiety symptoms with the evolution of symptoms during the pandemic. Hereto, we used data of the latest pre-pandemic round of the Rotterdam Study (RS-III excluded) to fit a linear regression model for the CES-D-10 and HADS-A using age, sex, education, living situation and the presence of chronic diseases as the predictors. Subsequently, we used this model to predict the CES-D-10 and HADS-A based on the population characteristics of the COVID-19 sub-study sample. We presented these analyses separately for men and women because sex importantly influenced depressive and anxiety symptoms.

In addition to sex, several other potential determinants of the evolution of depressive and anxiety symptoms over time were assessed, including age, education, migration background, living situation, presence of chronic disease, and pre-pandemic clinically relevant depressive or anxiety symptoms. For the stratification by age, we dichotomized age at 70 years because people above 70 years were considered a risk group according to the Dutch government. We generated separate trajectories for each subgroup and adjusted the linear mixed models for all other determinants except for migration background, because of limited predictive value in our dataset, and pre-pandemic clinically relevant depressive or anxiety symptoms. To allow non-parallel trajectories over time for the subgroups, we additionally included an interaction term of the determinant of interest with time. The trajectories were visualized for a person of mean age with all other characteristics set to the most common level.

We performed a sensitivity analysis by setting the knots of the splines for follow-up time at the tertiles of follow-up time.

All analyses were conducted in R version 4.0.3. Estimation of linear mixed models and imputation of missing covariates were performed using the JointAI package (Erler et al., 2019).

3. Results

Participants had a mean age of 70.1 years (standard deviation (SD) 11.6) at the time of the first questionnaire, 58% were women and the

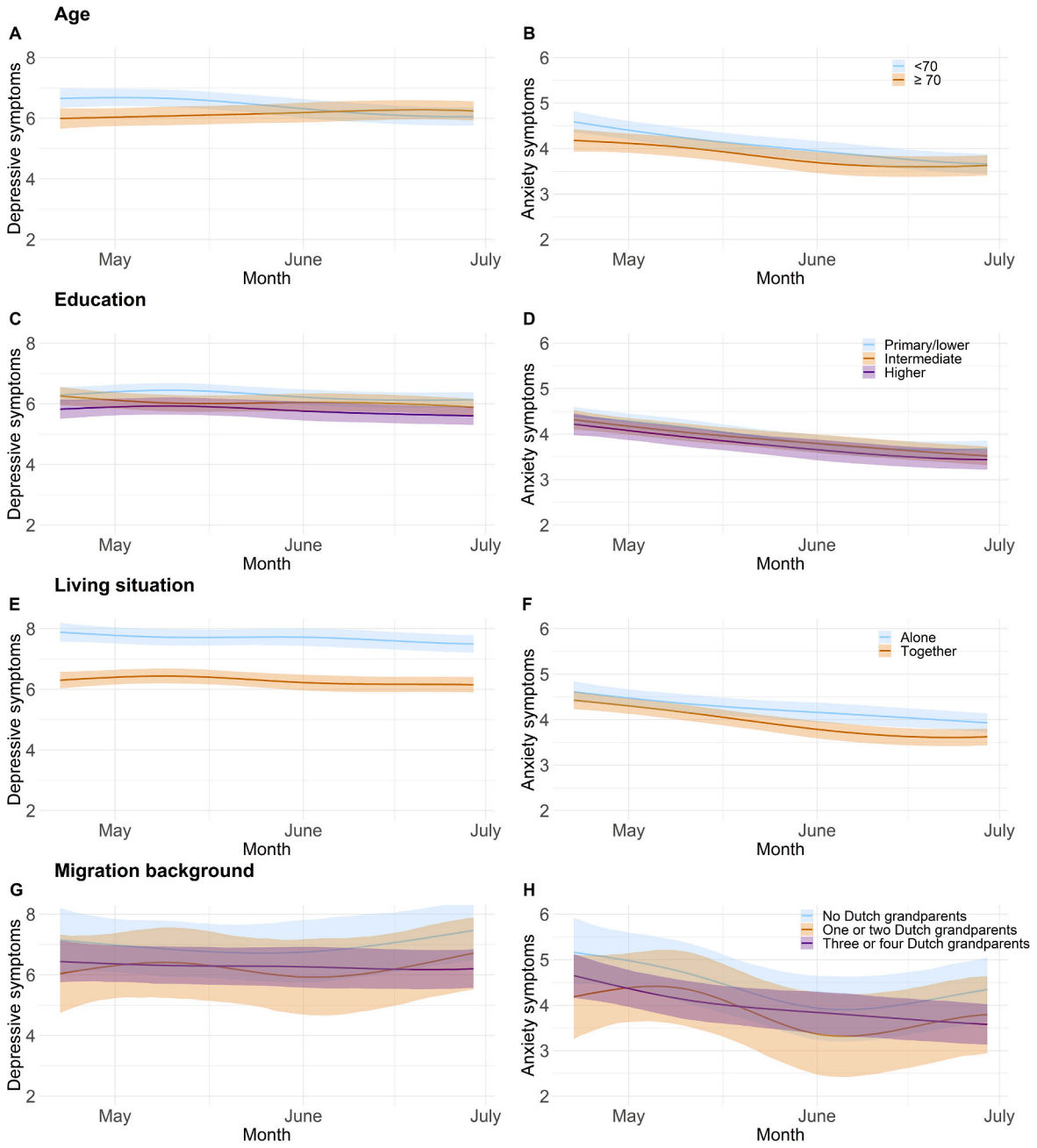

Fig. 2. Depressive and anxiety symptoms in demographic subgroups of the general population
Trajectories of depressive symptoms (left) and anxiety symptoms (right) in subgroups based on: age (panel A and B), education (C and D), living situation (E and F), and migration background (I and J). Trajectories are shown for women of mean age (70.1 years), with lower education, having a chronic disease and living together, unless one of these variables was the determinant of interest. For example, panel C and D show the trajectories for three different levels of education for women of 70.1 years old, having a chronic disease and living together.
Depressive symptoms are based on the Center of Epidemiological Studies Depression Scale (10 item version). Anxiety symptoms are based on the Hospital Anxiety and Depression Scale A.

majority (62%) were retired. Further characteristics are shown in Table 1.

Among participants who responded to the first questionnaire and also had data available from before the pandemic (N = 3300), 19% scored above the cut-off for clinically relevant depressive symptoms, compared to 12% before the pandemic (P < .001). Depressive symptoms on average increased with 1.7 points (SD 4.6). Similarly, 17% scored above the cut-off for clinically relevant anxiety symptoms, compared to 12% before the pandemic (P < .001), and anxiety symptoms on averaged increased with 0.9 (SD 3.4) points.

3.1. Change of depressive and anxiety symptoms during the pandemic

Participants responded to a median of 4 [IQR 3–4] questionnaires. Symptoms of depression and anxiety were scored highest in the first questionnaire and decreased during follow-up (Table 2), as did the percentages of participants meeting the cut-off for clinically relevant symptoms. Trajectories of depressive and anxiety symptoms from April 20th until June 30th stratified by sex are presented in Fig. 1. Both depressive and anxiety symptoms were initially increased compared to expected levels of depressive and anxiety symptoms based on pre-pandemic data. While anxiety symptoms gradually returned to

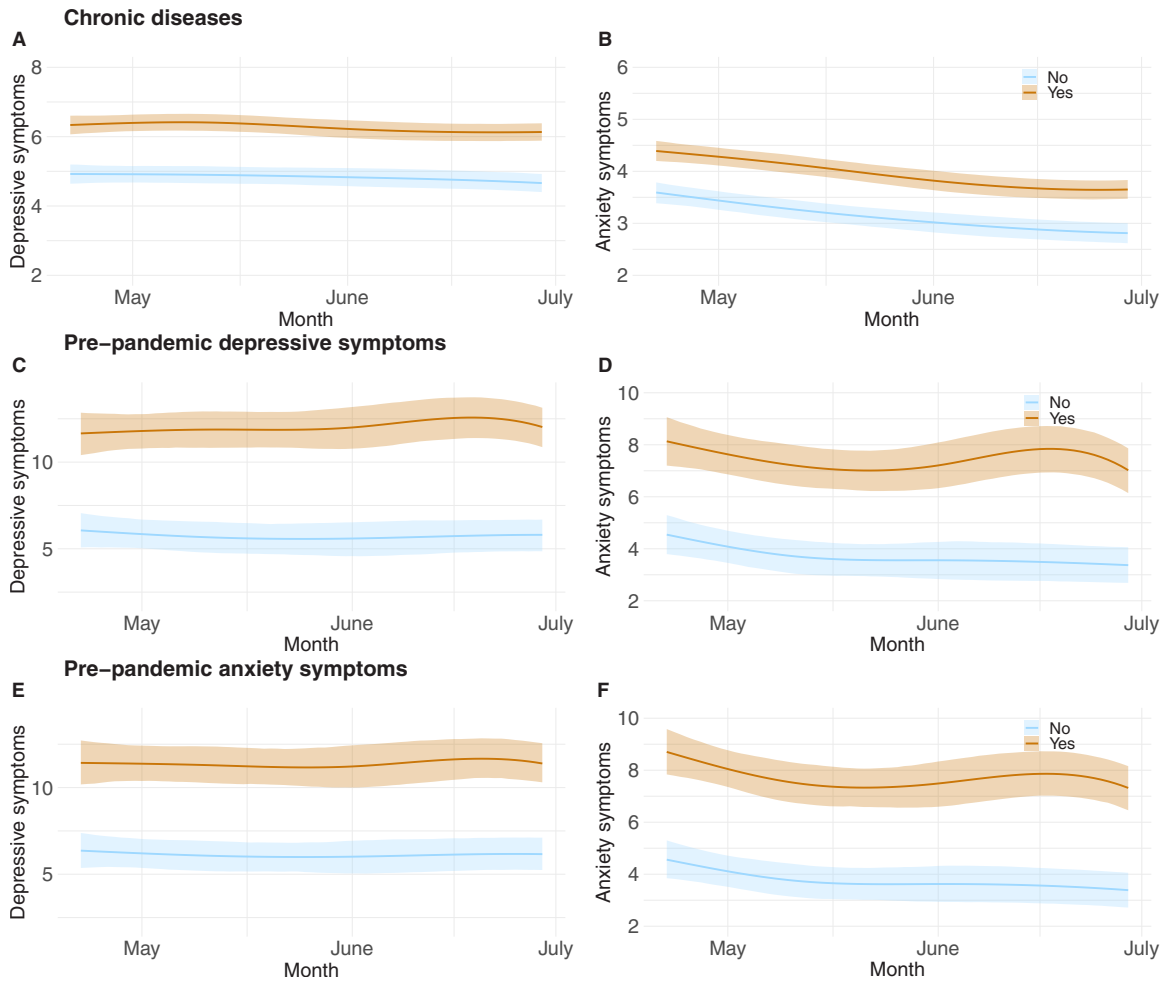

Fig. 3. Depressive and anxiety symptoms in the general population by presence of chronic diseases and pre-pandemic depressive or anxiety symptoms.
Trajectories of depressive symptoms (left) and anxiety symptoms (right) in individuals with and without self-reported presence of chronic diseases (A and B), persons with and without pre-pandemic clinically relevant depressive symptoms (C and D) and persons with and without pre-pandemic clinically relevant anxiety symptoms (E and F). Trajectories are shown for women of mean age (70.1 years), with lower education, having a chronic disease and living together, unless one of these variables was the determinant of interest. For example, panel C and D show the trajectories for women both with and without pre-pandemic depressive symptoms of 70.1 years old, having a chronic disease and living together.
Depressive symptoms are based on the Center of Epidemiological Studies Depression Scale (10 item version). Anxiety symptoms are based on the Hospital Anxiety and Depression Scale A.

predicted levels over the course of the first wave of the pandemic, depressive symptoms persisted at a higher level throughout May and June 2020.

Stratified analyses suggested higher scores of depressive and anxiety symptoms among persons with lower education, persons who were living alone and persons with chronic diseases or pre-pandemic clinically relevant depressive or anxiety symptoms, although these differences were stable over time (Figs. 2 and 3). In contrast, stratification by age suggested that initially participants aged 70 years and older reported slightly less depressive symptoms than participants below 70 years of age, while this difference disappeared in later months (Fig. 2). Confidence intervals were wide and largely overlapped for trajectories of persons with a migration background.

4. Discussion

We examined trajectories of depressive and anxiety symptoms during the first COVID-19 outbreak in the general population in the Netherlands. In April 2020, both depressive and anxiety symptoms were elevated in comparison to pre-pandemic levels. While symptoms of anxiety returned to the expected levels in case of no pandemic, between May and June 2020, depressive symptoms remained elevated. More symptoms were reported by women, persons who were living alone and persons with chronic diseases or pre-pandemic clinically relevant depressive or anxiety symptoms. These differences were generally stable over time.

In line with our results, several other studies showed that depressive and anxiety symptoms were more frequent during the pandemic compared to before the pandemic (van Tilburg et al., 2020). In addition, improvement of mental health over time during the first COVID-19 outbreak was also reported by previous studies (Mata et al., 2021; Picó-Pérez et al., 2021; Pierce et al., 2021; Varga et al., 2021). Regarding the trajectories of anxiety symptoms, the improvement over time may mainly be a consequence of a reduction in COVID-19-specific fear, as was also suggested previously (Bendau et al., 2021a). On the other hand, depressive symptoms remained increased over time in our study, presumably because these symptoms are merely related to the burden due to lockdown measures (Bendau et al., 2021a,b). Indeed, during the previous SARS pandemic, depressive symptoms persisted when the infection was under control while anxiety was most common in the initial phase (Chong et al., 2004).

It has been suggested that the COVID-19 pandemic has impacted

mental health particularly in persons more vulnerable to COVID-19 (e.g., older persons and persons with chronic diseases) and those who were highly affected by the lockdown measures (adolescents and persons with a history of mental health problems) (Pfefferbaum and North, 2021). Although we indeed found more depressive and anxiety symptoms in women, persons living alone, with chronic diseases and persons with previous depressive or anxiety symptoms, the trajectories of depressive and anxiety symptoms over time were broadly similar for these subgroups. Thus, our results suggest that these traditional risk factors did not substantially affect the trajectories of symptoms during the pandemic. An exception is seen with age: persons aged 70 years and older initially reported less depressive symptoms than younger persons, but the confidence intervals overlapped from the course of May 2020. This may be the result of the first relaxations of lockdown measures in the Netherlands in June and financial support that mainly applied to middle-aged adults rather than older adults.

Important strengths of the current study include the use of validated questionnaires for depressive and anxiety symptoms and the embedment in an existing population-based cohort, which allows comparison with examinations before the pandemic. Additionally, repeated measurements over the course of the first COVID-19 outbreak were available and a broad group of participants could be reached by sending questionnaires both on paper and online.

A limitation of this study includes the limited time period which was studied: the trajectories described a period from April 20th until July 2020 and we have no information on the first weeks of the pandemic, as well as the second and subsequent waves of infections. Second, the pre-pandemic data that were used for comparison were acquired between 2015 and 2020 and may not reflect mental health directly before the start of the pandemic. Third, our results described the average trajectory over time, but may fail to identify patterns in small subgroups of the study population. Fourth, we might have missed relevant factors to identify groups vulnerable for depression and anxiety, other than the set of sociodemographic and health-related characteristics we assessed. Finally, we defined the subgroups based on self-reported information of the first questionnaire. Changing situations during the COVID-19 pandemic were thus not taken into account.

5. Conclusion

Our results suggest that depressive and anxiety symptoms were initially increased during the COVID-19 pandemic. In May and June 2020, anxiety symptoms returned to pre-COVID-19 levels, whereas depressive symptoms remained increased. It is thus important to be aware of long-term depressive symptoms following the COVID-19 pandemic in the general population, and particularly in women, persons living alone, with chronic diseases and with a history of depressive or anxiety symptoms.

Author contributions

Lisanne Dommershuijsen and Annemarie Luik contributed to the conception and design of the study. Sanne Mooldijk and Lisanne Dommershuijsen performed the analyses. Sanne Mooldijk wrote the first draft of the paper. Sanne Mooldijk, Lisanne Dommershuijsen, Maud de Feijter and Annemarie Luik contributed to the interpretation of the results and critically revised the manuscript for intellectual content. All authors have read and approved the final manuscript.

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Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2022.03.002.

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