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Heterogeneity in depressive and anxiety symptoms and loneliness during the COVID-19 pandemic: Results from three Dutch psychiatric case-control cohorts from April 2020 to February 2022

Silvia S. Klokgieters [a,*], Brenda W.J.H. Penninx [a,b], Nathaly Rius Ottenheim [c], Erik J. Giltay [c], Didi Rhebergen [a,d], Almar A.L. Kok [a,b]

[a] Amsterdam UMC location Vrije Universiteit Amsterdam, Department of Psychiatry, Boelelaan 1117, Amsterdam, The Netherlands
[b] Amsterdam Public Health, Mental Health programme, Amsterdam, The Netherlands
[c] Department of Psychiatry, Leiden University Medical Center, Leiden, the Netherlands
[d] Mental Health Institute GGz Centraal, Amersfoort, the Netherlands

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ABSTRACT

Objective: While research found heterogeneous changes in mental health during the COVID-19 pandemic, less is known about the long-term changes in mental health in psychiatric groups. Therefore, we applied a data-driven method to detect sub-groups with distinct trajectories across two years into the pandemic in psychiatric groups, and described their differences in socio-demographic and clinical characteristics.
Method: We conducted sixteen rounds of questionnaires between April 2020 and February 2022 among participants ($n = 1722$) of three psychiatric case–control cohorts that started in the 2000's. We used Growth Mixture Modelling and (multinomial) logistic regression to identify characteristics associated with trajectory membership.
Results: We found low decreasing (1228 [72%] participants), intermediate ($n = 348$ [22%] participants) and high stable (106 [6%] participants) trajectories of depressive symptoms; decreasing low/intermediate (1507 [90%] participants) and high stable (161 [10%] participants) trajectories of anxiety symptoms; and stable low (1109 [61%] participants), stable high (315 [17%] participants), temporary lowered (123 [9%]) and temporary heightened (175 [13%] participants) trajectories of loneliness. Chronicity and severity of pre-pandemic mental disorders predicted unfavourable sub-group membership for all outcomes. Being female, having a low education and income level were associated with unfavourable trajectories of depression, being younger with unfavourable trajectories of anxiety and being female and living alone with unfavourable trajectories of loneliness.
Conclusion: We found relatively stable trajectories of depression and anxiety symptoms over two years, suggesting low heterogeneity in outcomes during the pandemic. For loneliness, we found two specific sub-groups with temporary increase and decrease in loneliness during the pandemic.

1. Introduction

Lockdowns implemented to reduce the spread of coronavirus disease 2019 (COVID-19) expected to large impact on people's mental health, particularly in people with pre-existing psychiatric disorders. However, studies hitherto yielded different findings concerning changes in mental health symptoms over the course of the pandemic. Some found a substantial increase in depressive and anxiety symptoms [1–3], while others found surprisingly small increases among young and older adults [4–8] during the first months of the pandemic. Longitudinal studies did observe an initial upsurge of mental health symptoms during the first lockdown, yet this was followed by a gradual decline afterwards [9–14]. Findings for loneliness showed larger, though still modest, average increases [15]. Similarly, in a previous study by our group, we found that depressive and anxiety symptoms were surprisingly stable across the COVID-19 pandemic's first year, yet loneliness levels substantially increased compared to pre-pandemic levels in groups with and without depressive, anxiety and obsessive-compulsive disorders (OCD) [16].

However, such conclusions are often based on *average* changes in mental health, sometimes stratified for a priori defined demographic or

* Corresponding author at: Room H3.05, Oldenaller 1, Amsterdam 1081 HJ, the Netherlands.
E-mail address: s.klokgieters@amsterdamumc.nl (S.S. Klokgieters).

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clinical characteristics. For instance, some studies found that lower socioeconomic position, female sex, younger age were associated with worse mental health trajectories [9,10,17,18]. Despite the merits of these studies, it has been suggested that the predominant focus on existing socio-demographic predictors is too deterministic and hides subpopulations with distinctive worsening, improving or stabilizing trajectories [17]. Therefore, applying a data-driven approach to detect sub-groups with distinct trajectories of mental health, and broadly explore characteristics of these sub-groups may be a valuable complementary approach to previous research.

Various studies have used such a data-driven, mixture modelling approach to capture mental health trajectories during the pandemic [11,17,19–23]. For example, two UK-based studies found five and four sub-groups with distinct trajectories of mental distress, with 53–76% of the population experiencing persistently low and very low distress levels, 11–15% experiencing continuously elevated distress levels and 8–12% experiencing recovery or only temporary elevated distress levels [11,17]. Another UK-based study [22] observed patterns that were more or less similar for anxiety and depression with about 73% experiencing stable low trajectories, about 6% stable high trajectories and about 4% experiencing recovering and about 15% experiencing stable medium trajectories of depressive and anxiety symptoms. Finally, for loneliness, another UK-based study found four sub-groups. Loneliness levels increased slightly in the highest loneliness group (14%), decreased slightly in the lowest loneliness group (48%), and stayed relatively constant in the middle two groups (23% and 14%) [19]. Overall, findings suggest that there was significant heterogeneity in mental health trajectories during the pandemic, but that the majority of the population experienced relatively favourable mental health trajectories.

Nevertheless, knowledge on the impact of the pandemic on mental health can be expanded in three important ways. First, so far, the majority of data-driven studies covered only the year 2020 [11,19–24] with a few exceptions lasting until mid-May 2021 [17] and December 2021 [25]. Therefore, knowledge on long-term mental health trajectories is limited. Specifically unknown are the changes since the upsurge of the Omicron variant of COVID-19, which was detected in Europe in December 2021 and evoked re-instalment of lockdown measures in many countries. Second, the majority of data-driven studies have been conducted in the UK [11,17,19,21,22], with some exceptions in Canada [24] Australia [20] and Israel [26]. As country-level contextual factors may affect mental health consequences [27], studies in other countries are warranted. Third, most data-driven studies were conducted in the general population [11,17,19–22,24,25] and found that pre-pandemic mental health status is strongly associated with unfavourable (i.e. consistently high level of symptoms) mental health trajectories [5,10,12,13]. Nevertheless, specific studies in psychiatric cohorts that have more detailed pre-pandemic information on this high-risk population are lacking. In sum, there is a need for in-depth research on long-term mental health trajectories among psychiatric groups during the COVID-19 pandemic that can reveal the role of pre-pandemic mental health history (e.g. chronicity of disorders) and examine heterogeneity in trajectories within this specific population.

In the Netherlands, the setting of the current study, the first national lockdown began in February 2020 and lasted until June 2020, after which the COVID-19 infections eased over the summer. In the fall of 2020 there was a new surge in COVID-19 infections, resulting first in a partial lockdown starting in October 2020 followed by a hard lockdown in December 2020, including a night-time curfew and complete closure of non-essential stores. COVID-19 infections eased over the summer of 2021 but cases started to rise again in October 2021, after which a last partial lockdown was implemented from November 2021 until January 2022, when due to the Omicron-variant the daily number of known infections peaked at >80,000 on a total of 17 m inhabitants.

Based on data spanning this entire period, in the present study we take a data-driven mixture modelling approach, similar to previous studies, but focusing specifically on persons with psychiatric disorders in the Netherlands. We investigate whether mental health trajectories are associated with chronicity of pre-pandemic mental health disorders and demographic characteristics.

2. Materials and methods

2.1. Study sample and design

We used data from three Dutch prospective cohort studies with largely identical methods for collecting pre-pandemic data: the Netherlands Study of Depression and Anxiety (NESDA) [28], the Netherlands Study of Depression in Older Persons (NESDO) [29], and Netherlands OCD Association Study (NOCDA, baseline: 2004) [30].

For NESDA, participants with a depressive or anxiety disorder (n = 2329), their biological siblings (n = 367), and controls without mental disorder (n = 652) were recruited from specialized mental health care, primary care and the community. When the baseline measurement took place in 2004–2007, participants were aged between 18 and 35 years. Follow-up measurements were conducted in 2008–11, 2010–13, and 2014–16.

For NESDO, participants with a primary diagnosis of depressive disorder (n = 378) and controls without lifetime diagnoses of mental health disorders (n = 132) were recruited from specialized mental health care and primary care. Participants were aged between 60 and 93 years at baseline in 2007–2010 and follow-up measurements took place in 2008–12, and 2012–16.

For NOCDA, participants with a lifetime diagnosis of obsessive-compulsive disorder (n = 419) were recruited from mental health-care institutions. Participants were aged 18–65 years at baseline in 2004–2009 and follow-up measurements took place in 2006–11, 2008–13, and 2012–16.

Participants who gave permission to be re-contacted, were invited to partake in the "COVID-19 questionnaire" via e-mail (n = 2748). Between April 1, 2020 until February 2022, participants partook in sixteen online measurements, which were held two to eight weeks apart. An exception was the last measurement in February 2022, which was held 7 months after the prior measurement in July 2021.

In the present analyses we included participants, both cases and controls, who had data on each mental health outcome during at least one COVID-19 measurement wave (depressive symptoms: n = 1681, anxiety symptoms: n = 1722 and loneliness: n = 1667). For all pre-COVID-19 measurements written consent was obtained and for during-COVID-19 measurements consent was obtained in electronic form. All study procedures were approved by the Institutional Review Board of the Vrije Universiteit Medical Center, Amsterdam (reference number 2020.166).

2.2. Mental health outcomes

Depressive symptoms were assessed using the 16-item Quick Inventory of Depressive Symptoms (QIDS) [31]. Items assessed symptoms of depressive disorder according to DSM-IV criteria, for instance depressed mood. Each item was scored on a scale of 0–3, with higher scores denoting greater symptom severity. The total score ranged from 0 to 27.

Anxiety symptoms were assessed using the Beck Anxiety Inventory (BAI) [32]. Participants were asked to what extent 21 anxiety symptoms (e.g. scared and fear of losing control) bothered them in the past week, with answer categories ranging from 0 (not at all) to 3 (severely) and with a total score ranging from 0 to 63.

Loneliness, both social and emotional, was obtained using the 6-item De Jong Gierveld Loneliness Scale [33]. An example item includes "I miss having people around". Answer categories ranged from 0 (no) to 2 (yes) and categories 1 (more or less) and 2 (yes) were collapsed, resulting in a total score ranging from 0 to 6.

2.3. Socio-demographic and mental health characteristics

In line with previous work [34], chronicity of mental disorders reflected the percentage of waves since 2006 in which the participants had any 1-year diagnosis of depressive disorder, anxiety disorder or OCD. This was categorized into No lifetime disorder (i.e. 'healthy controls'); Remitted Disorder (NOCDA and NESDA participants who only had lifetime disorders but no waves with 1-year disorders); Low-medium Chronicity (1–50% of previous measurements with disorders); and High Chronicity (51–100% of previous measurements with disorders). Included disorders were major depressive disorder, dysthymia, general anxiety disorder, panic disorder, social phobia, and agoraphobia for all three cohorts, and additionally obsessive-compulsive disorder in NOCDA. In NESDA and NESDO, diagnoses were based on the Composite Interview Diagnostic Interview (CIDI [35]), using DSM-IV criteria. In NOCDA, diagnoses were based on the Structured Clinical Interview for DSM-IV axis-I disorders (SCID [36]).

Pre-pandemic socio-demographic and health characteristics included sex (female and male), education level (low [elementary school to general secondary education] and high [college or university]), income (monthly household income in euros), living alone (no and yes), number of chronic diseases (self-reported). In line with previous work [34], pre-pandemic depressive and anxiety symptoms and loneliness levels were based on the mean number of symptoms from all available waves between 2006 and 2016, except for the baseline.

COVID-19-related characteristics included perceived mental health impact (based on nine items; observed range: 1.0–4.7), fear of COVID-19 (six items; observed range: 1.4–5.0) and positive coping (five items; observed range: 1.7–5.0) see also: [34] and Table S1). Furthermore, we included COVID-19 infection (no and yes), received treatment during (no and yes), and psychotropic medication use (no and yes) both during the COVID-19 pandemic.

2.4. Procedure

We generated descriptive statistics of socio-demographic, clinical (chronicity and severity of pre-pandemic mental health disorders) and COVID-19 related characteristics and investigated differences across chronicity groups using F-tests (ANOVA) and χ^2 tests, as appropriate (Table S2).

To identify sub-groups with distinct trajectories of depressive and anxiety symptoms and loneliness during COVID-19, we conducted Growth Mixture Modelling (GMM) [37] for each mental health outcome separately. The goal of this analysis was to identify sub-groups with distinct type of trajectories of depressive and anxiety symptoms and loneliness during the COVID-pandemic, based on a data-driven method.

GMM followed two subsequent steps [37,38]. First, we established baseline latent growth model comparing linear, quadratic, and cubic single-class models in order to find the best single-class representation of change. Second, we estimated a series of models with an increasing number of classes (a 'class' is a sub-group with a distinct type of trajectory). We used a combination of model fit criteria to determine the best fitting models: lower Bayesian and adjusted Bayesian information criteria (BIC and aBIC [39]), higher entropy and posterior class membership probabilities [40], adjusted Lo-Mendell-Rubin likelihood ratio test comparing the fit of the k-class model with the fit of the k-1 class [41,42], class size reflecting at least 5% of the total sample, and interpretability of emerging classes based on theory and distinctiveness [38]. This process was repeated until we found a class solution that exhibited both reasonable fit statistics and made theoretical sense.

To estimate associations between pre-pandemic chronicity of psychiatric disorders and other characteristics and most likely class membership, we used multinomial logistic regression. Because of missingness in the covariates (e.g. income (21%), number of chronic diseases (19%), and living alone (9%)) we could not account for classification uncertainty in these analyses by for example using the R3STEP-method, as this altered the sample size and assignment to latent classes. However, because entropy values, which denote the quality of class separation, were high, bias due to misspecification is likely limited [40,43]. The multinomial logistic regression Model 1 included chronicity of pre-pandemic mental health disorders, Model 2 additionally included socio-demographic characteristics, and Model 3 additionally included pre-pandemic depressive and anxiety symptoms and loneliness. All analysis we performed in Mplus Version 8.5 and SPSS version 26. In Mplus, we used maximum likelihood estimation under the missing at random (MAR) to handle missing data. In SPSS, we used multiple imputation for the predictors, with 21 imputed datasets, in line with the % of participants with at least one missing value.

3. Results

3.1. Depressive symptoms

The 3-class model had optimal fit. Comparison of BIC and aBIC indices of the linear and quadratic models indicated a model with a quadratic slope had the best fit (Table 1). A series of GMMs was performed with up to 5 classes. The BIC indicated improvement for each model and aBIC indicated improvement up to the 5 class model. However, class solutions above 3-classes yielded sub-group sizes of below 5% of the sample. In addition, The aLMR-LRT was nonsignificant in the 4-class solution, suggesting no significant improvement beyond the 3-class model.

In the 3-class model, a majority (C#1: $n = 1228$; 72%) experienced a low decreasing level of depressive symptoms. 22% (C#2: $N = 348$) had an intermediate trajectory and 6% (C#3: $n = 106$) experienced a stable high level of depressive symptoms (Fig. 1). The negative linear slope of class #1 was statistically significant ($S = -1.07$, $p = 0.048$; Table S3). Descriptive statistics of chronicity of pre-pandemic mental health disorders, socio-demographic and pre-pandemic mental health characteristics across classes are depicted in Table S4.

Multinominal logistic regression was performed to determine which socio-demographic and mental health characteristics were associated with trajectory membership (Table 2). Model 1 included chronicity of pre-pandemic psychiatric disorders and revealed that individuals with higher chronicity (i.e. medium and high) were more likely to experience stable high and intermediate compared to low and decreasing trajectories. The association remained statistically significant in model 2 where socio-demographic characteristics (i.e. age, sex, education level, living alone, number of chronic diseases) were added and in model 3 where pre-pandemic mental health symptoms were added. Model 2 also showed that individuals with a high education level were less likely to experience an intermediate and stable high trajectories, and individuals with higher income and living alone were more likely to experience an intermediate trajectory all compared the likelihood of experiencing a low and decreasing trajectory. When additionally adjusting for pre-pandemic mental health (model 3),the association with pre-pandemic mental health symptoms was no longer significant, while females were more likely to experience an intermediate trajectory.

3.2. Anxiety symptoms

For anxiety symptoms we selected the 2-class model. Differences in BIC and aBIC indices suggested optimal fit of a model with a quadratic slope (Table 1). Although the BIC, aBIC kept indicating model improvement, the aLMR-LRT indicated no significant improvement of the 3-class compared to the 2-class model. In addition, in the 3-class model, the smallest sub-group included <5% of the sample, which further disqualified this solution.

The majority of the sample experienced decreasing low/intermediate trajectory of anxiety symptoms (C#1: $n = 1507$; 90%) and a small portion experienced a high stable trajectory of anxiety symptoms (C#2: $n = 161$; 10%). Only the negative linear ($S = -1.373$, $p = 0.001$) and the

Table 1
fit indices for GMM outcomes depressive symptoms. Anxiety symptoms and loneliness.

Depressive symptoms	Class size	BIC	aBIC	aLMR-LRT	*p*	Entropy	PMP
Baseline model with a single class							
Linear	1682	59,508	59,441				
Quadratic	1682	59,363	59,283				
Cubic*	1682	–	–				
GMM 2–5 classes (Quadratic)							
2-class	1389; 293	58,988	58,896	391	0.003	0.833	0.85–0.97
3-class	106; 348; 1228	58,858	58,753	155	0.007	0.827	0.80–0.85
4-class	302; 1220; 109; 51	58,760	58,642	124	0.21	0.806	0.42–0.97
5-class	98; 35; 37; 294; 1218	58,714	58,584	72	0.18	0.806	0.35–0.98
Anxiety							
Baseline model with a single class							
Linear	1668	72,005	71,938				
Quadratic	1668	71,917	71,837				
Cubic	1668	71,917	71,837				
GMM 2–5 classes (quadratic)							
2-class	1507; 161	71,412	71,320	518	<0.001	0.919	0.86–0.99
3-class	48; 286; 1334	71,178	71,073	255	0.10	0.909	0.87–0.98
4-class	1332; 197; 94; 45	70,987	70,869	212	0.52	0.888	0.62–0.98
5-class	1306; 210; 86; 51; 15	70,905	70,774	108	0.75	0.897	0.63–0.98

Loneliness		BIC	aBIC	aLMR-LRT	*p*	Entropy	PMP
Baseline model with a single class							
Linear	1723	41,466	41,399				
Quadratic	1723	41,393	41,314				
Cubic*	1723	–	–				
GMM 2–5 classes (Quadratic) Note: model where variation around the quadratic slope is set to 0							
2-class	1258; 465	41,015	40,933	453	<0.001	0.835	0.93–0.97
3-class	390; 1238; 95	40,885	40,790	155	<0.001	0.796	0.47–0.98
4-class	124; 175; 1109; 315	40,789	40,681	121	0.31	0.767	0.56–0.97
5-class	151; 1089; 29; 325; 129	40,732	40,611	84	0.14	0.770	0.51–0.97

Note: model where variation around the quadratic slope is set to 0, BIC = Bayesian information criteria. aBIC = adjusted Bayesian information criteria, aLMR-LRT = adjusted Lo-Mendell-Rubin likelihood ratio test. and PMP = posterior class membership probabilities *the cubic model was not specified due to the fact that the cubic slope was nearly zero in these models.

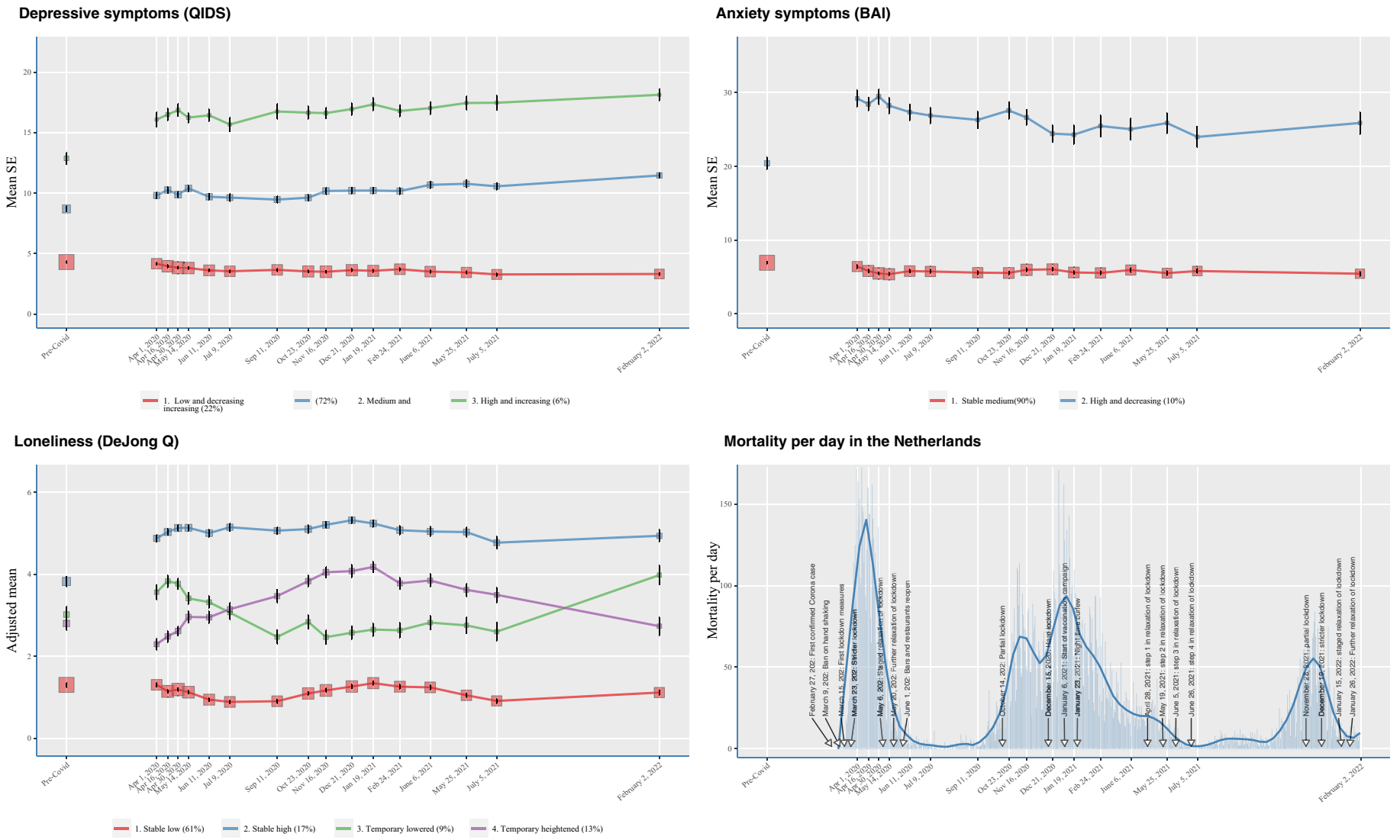

Fig. 1. Change trajectory profiles of depressive and anxiety symptoms and loneliness compared to pre-Covid-19 levels.Upper left panel: Average and standard error of the number of depressive symptoms per class across 16 COVID-19 measurements (n = 1682). Upper right panel: Average and standard error of anxiety symptoms per class across 16 COVID-19 measurements (n = 1668). Lower right panel: Average and standard error of loneliness per class across 16 COVID-19 measurements (n = 1723). Lower right panel: daily number of COVID-19 deaths during the pandemic in the Netherlands, with a sliding mean in dark blue. Key dates with regard to COVID-19 and its Dutch (lockdown) measures are given. Source: https://data.rivm.nl/meta/srv/dut/catalog.search#/metadata/2c4357c8-76e4-4662-9574-1deb8a73f724

Table 2
association between pre-pandemic demographic and health characteristics and class membership for depressive symptoms.

Intermediate (vs. low decreasing)	Model 1					Model 2					Model 3				
	OR	SE	95% CI		P	OR	SE	95% CI		P	OR	SE	95% CI		P
			lower	upper				lower	upper				lower	upper	
Remitted disorder (vs. healthy controls)	2.73	1.32	1.58	4.73	<0.001	2.80	1.33	1.61	4.86	<0.001	1.76	1.34	0.99	3.14	0.06
Low medium chronicity (vs. healthy controls)	6.24	1.30	3.73	10.43	<0.001	6.35	1.31	3.77	10.71	<0.001	1.98	1.34	1.12	3.49	0.02
High chronicity (vs. healthy controls)	16.09	1.29	9.71	26.68	<0.001	16.33	1.30	9.73	27.43	<0.001	2.38	1.36	1.29	4.37	0.005
Age						1.00	1.01	0.99	1.01	0.55	0.99	1.01	0.98	1.00	0.19
Sex: women (vs. men)						1.21	1.15	0.92	1.61	0.18	1.61	1.18	1.17	2.23	0.003
education: high (vs. Low)						0.79	1.15	0.60	1.04	0.09	0.91	1.17	0.67	1.24	0.55
Income						1.01	1.01	1.00	1.03	0.05	1.03	1.01	1.02	1.05	<0.001
Living alone: yes (vs no)						1.92	1.19	1.36	2.72	<0.001	2.16	1.21	1.48	3.17	<0.001
Number of chronic diseases						1.08	1.08	0.93	1.26	0.31	0.91	1.09	0.77	1.09	0.31
Average pre-COVID depressive symptom											1.30	1.03	1.22	1.38	<0.001
Average pre-COVID anxiety symptoms											1.04	1.01	1.01	1.07	0.004
Average pre-COVID loneliness											1.11	1.04	1.02	1.20	0.02
High stable (vs. low decreasing)															
Remitted disorder (vs. healthy controls)	2.02	1.85	0.60	6.77	0.25	1.76	1.86	0.52	5.98	0.36	0.77	1.86	0.20	3.01	0.71
Low medium chronicity (vs. healthy controls)	4.56	1.76	1.51	13.78	0.007	3.75	1.77	1.22	11.51	0.02	0.56	1.77	0.16	1.96	0.36
High chronicity (vs. healthy controls)	34.69	1.68	12.53	96.07	<0.001	25.76	1.71	9.04	73.38	<0.001	0.85	1.71	0.24	3.02	0.80
Age						0.99	1.01	0.97	1.01	0.21	0.98	1.01	0.96	1.00	0.08
Sex: women (vs. men)						1.02	1.27	0.64	1.62	0.94	1.87	1.27	1.06	3.27	0.03
education: high (vs. Low)						0.56	1.29	0.34	0.94	0.03	0.66	1.29	0.37	1.18	0.03
Income						0.98	1.02	0.95	1.02	0.33	1.02	1.02	0.99	1.06	0.17
Living alone: yes (vs no)						1.82	1.40	0.93	3.56	0.08	2.54	1.40	1.21	5.33	0.19
Number of chronic diseases						1.17	1.14	0.91	1.51	0.21	0.86	1.14	0.62	1.18	0.34
Average pre-COVID Depressive symptom											1.67	1.00	1.50	1.85	<0.001
Average pre-COVID anxiety symptoms											1.04	1.00	1.00	1.08	0.08
Average pre-COVID loneliness											1.11	1.00	0.96	1.29	0.15

Table 3
association between pre-pandemic demographic and health characteristics and class membership for anxiety symptoms.

High stable (vs. decreasing low/ intermediate)	Model 1					Model 2					Model 3				
	OR	SE	95% CI		P	OR	SE	95% CI		P	OR	SE	95% CI		P
			lower	upper				lower	upper				upper	lower	
Remitted disorder (vs. healthy controls)	3.52	1.76	1.16	10.71	0.03	2.89	1.77	0.94	8.85	0.06	1.76	1.81	0.55	5.63	0.34
Low medium chronicity (vs. healthy controls)	8.95	1.70	3.16	25.34	<0.001	7.01	1.71	2.46	20.02	<0.001	2.37	1.76	0.78	7.15	0.13
High chronicity (vs. healthy controls)	29.32	1.67	10.68	80.45	<0.001	20.68	1.68	7.44	57.49	<0.001	1.96	1.80	0.62	6.21	0.25
Age						0.98	1.01	0.97	1.00	0.03	0.98	1.01	0.96	1.00	0.03
Sex: women (vs. men)						1.19	1.22	0.81	1.75	0.38	1.42	1.26	0.90	2.23	0.13
Education: high (vs. Low)						0.67	1.23	0.45	1.00	0.048	0.85	1.26	0.54	1.33	0.48
Income						0.97	1.01	0.95	1.00	0.03	0.99	1.01	0.96	1.01	0.28
Living alone: yes (vs no)						1.15	1.28	0.70	1.87	0.58	1.19	1.33	0.68	2.07	0.54
Number of chronic diseases						1.14	1.10	0.94	1.39	0.18	0.92	1.13	0.73	1.17	0.50
Average pre-COVID depressive symptom											1.03	1.04	0.96	1.12	0.39
average pre-COVID anxiety symptoms											1.17	1.02	1.13	1.22	<0.001
Average pre-COVID loneliness											1.03	1.06	0.91	1.16	0.65

positive quadratic (S = 0.118, $p = 0.09$) slope of decreasing low/intermediate trajectory was statistically significant. Descriptive statistics of characteristics across classes are depicted in Table S5.

Results of the association between socio-demographic and health characteristics and latent class trajectory obtained with a logistic regression are depicted in Table 3. Compared to healthy controls, all chronicity levels (i.e. remittent, medium and high) were positively associated with experiencing a high stable as opposed a decreasing low/intermediate trajectory. After adjusting for socio-demographic characteristics in model 2, only the positive association between medium and high chronicity and high stable trajectory remained. Older and individuals with a high education level were less, and individuals with a

Table 4
association between pre-pandemic demographic and health characteristics and class membership for loneliness.

Stable high (vs. stable low)	Model 1					Model 2					Model 3				
	OR	SE	95% CI		P	OR	SE	95% CI		P	OR	SE	95% CI		P
			lower	upper				lower	upper				lower	upper	
Remitted disorder (vs. healthy controls)	2.24	1.30	1.35	3.73	<0.001	2.07	1.30	1.23	3.48	0.006	1.32	1.33	0.76	2.30	0.33
Low medium chronicity (vs. healthy controls)	4.30	1.28	2.66	6.97	0.002	3.71	1.29	2.26	6.10	<0.001	1.29	1.33	0.74	2.25	0.37
High chronicity (vs. healthy controls)	9.72	1.27	6.11	15.45	<0.001	7.64	1.28	4.71	12.40	<0.001	1.23	1.37	0.67	2.26	0.51
Age						1.00	1.01	0.99	1.01	0.99	0.99	1.01	0.98	1.01	0.35
Sex: women (vs. men)						1.00	1.16	0.75	1.34	0.99	1.43	1.18	1.03	1.99	0.03
Education: high (vs. Low)						0.73	1.16	0.54	0.99	0.04	0.93	1.18	0.67	1.29	0.67
Income						0.98	1.01	0.97	1.00	0.06	1.00	1.01	0.98	1.02	0.99
Living alone: yes (vs no)						1.98	1.21	1.36	2.88	<0.001	2.05	1.22	1.38	3.03	<0.001
Number of chronic diseases						1.19	1.09	1.00	1.42	0.05	1.04	1.10	0.86	1.25	0.71
Average pre-COVID depressive symptom											1.13	1.03	1.07	1.21	<0.001
Average pre-COVID anxiety symptoms											1.01	1.01	0.98	1.04	0.49
Average pre-COVID loneliness											1.69	1.05	1.54	1.85	<0.001
Temporary lowered (vs. stable low)															
Remitted disorder (vs. healthy controls)	1.94	1.38	1.04	3.63	0.04	2.03	1.38	1.08	3.84	0.03	1.46	1.40	0.76	2.82	0.26
Low medium chronicity (vs. healthy controls)	3.00	1.36	1.64	5.48	<0.001	3.07	1.37	1.66	5.70	<0.001	1.45	1.41	0.74	2.84	0.28
high chronicity (vs. healthy controls)	3.67	1.36	2.00	6.73	<0.001	3.66	1.38	1.95	6.86	<0.001	1.01	1.49	0.46	2.22	0.97
Age						1.01	1.01	0.99	1.02	0.40	1.00	1.01	0.99	1.02	0.79
Sex: women (vs. men)						0.85	1.22	0.57	1.26	0.41	1.08	1.24	0.72	1.64	0.71
Education: high (vs. Low)						1.04	1.23	0.69	1.55	0.86	1.25	1.24	0.83	1.90	0.29
Income						1.00	1.01	0.98	1.02	0.996	1.01	1.01	0.99	1.03	0.33
Living alone: yes (vs no)						1.39	1.28	0.86	2.25	0.18	1.41	1.29	0.85	2.32	0.18
number of chronic Diseases						1.15	1.12	0.93	1.42	0.20	1.04	1.12	0.83	1.30	0.76
Average pre-COVID depressive symptom											1.07	1.04	0.98	1.16	0.14
Average pre-COVID anxiety symptoms											1.01	1.02	0.98	1.06	0.46
Average pre-COVID loneliness											1.56	1.06	1.38	1.76	<0.001
Temporary heightened (vs. stable low)															
Remitted disorder (vs. healthy controls)	1.39	1.31	0.82	2.37	0.22	1.40	1.32	0.81	2.40	0.23	1.06	1.33	0.61	2.30	0.83
Low medium chronicity (vs. healthy controls)	2.79	1.28	1.71	4.55	<0.001	2.75	1.29	1.66	4.56	<0.001	1.48	1.33	0.85	2.25	0.17
High chronicity (vs. healthy controls)	3.18	1.29	1.94	5.23	<0.001	3.06	1.30	1.82	5.16	<0.001	1.05	1.40	0.54	2.26	0.88
Age						1.02	1.01	1.00	1.03	0.01	1.01	1.01	1.00	1.01	0.05
Sex: women (vs. men)						0.60	1.19	0.43	0.84	0.003	0.73	1.19	0.51	1.99	0.07
Education: high (vs. Low)						0.94	1.20	0.66	1.34	0.73	1.06	1.21	0.73	1.29	0.76
Income						0.98	1.01	0.96	1.00	0.04	0.99	1.01	0.97	1.02	0.21
Living alone: yes (vs no)						1.01	1.25	0.65	1.58	0.95	1.02	1.26	0.65	3.03	0.93
Number of chronic diseases						0.98	1.11	0.80	1.19	0.82	0.90	1.11	0.74	1.25	0.34
Average pre-COVID depressive symptom											1.11	1.04	1.03	1.21	0.005
Average pre-COVID anxiety symptoms											0.99	1.02	0.96	1.04	0.63
Average pre-COVID loneliness											1.37	1.06	1.23	1.85	<0.001

higher income more likely to experience a high stable trajectory compared a decreasing low/intermediate trajectory. In model 3, which included pre-pandemic mental health symptoms, all positive associations between chronicity and trajectory membership disappeared but the negative association with age remained statistically significant.

3.3. Loneliness

3.3.1. In contrast in depression and anxiety

For loneliness we selected a 4-class model. The model with a quadratic slope fitted the data best (Table 1). While the aLMR-LRT indicated no significant improvement in models with more than three classes, the BIC and aBIC still suggested a substantially improved model fit, and all class sizes remained >5%. Moreover, the smallest class-size remained above the cut-off of 5% and the intercepts, slopes and quadratic slopes were statistically significant in most classes of the 4-class model (Table S2).

The two largest sub-groups experienced stable low (C#1: $n = 1109$; 61%) and stable high (C#2: $n = 315$; 17%) trajectories of loneliness, respectively. A third sub-group experienced a temporary lowered level followed by a gradual return to their initial (high) level (C#3: $n = 123$; 9%). A fourth sub-group experienced a temporary heightened level followed by a recovery in 2022 (C#4: $n = 175$; 13%). Descriptive statistics of chronicity, socio-demographic and pre-pandemic mental health

characteristics are depicted in Table S6.

Multinomial regression (Table 4) showed that compared to individuals experiencing a stable low trajectory, higher pre-pandemic chronicity of mental health disorders was associated with higher odds of experiencing stable high, temporary lowered and temporary heightened trajectories. After adjusting for demographic characteristics, in model 2, associations between pre-pandemic chronicity of mental health disorders remained. Individuals with a low education level and living alone were more likely to be categorized in stable high trajectories. Older men and individuals with a lower income were more likely to be categorized in temporary heightened trajectories. After adjusting for pre-pandemic mental health symptoms, the association between chronicity of mental health disorders and trajectory membership became non-significant. In addition, only in the final model, women and individuals living alone were more likely to be classified in stable high compared to stable low.

4. Discussion

In the current paper, we extended our previous analyses of mental health trajectories during the COVID-19 pandemic [16,34] by using a GMM approach and a long follow-up of almost two years. In addition, we focused on persons with psychiatric disorders and a comparison group of healthy controls. Even with the explicit aim to detect heterogeneity in mental health trajectories, we found that trajectories mainly differed in level but not the type of change; the majority of the sample had relatively stable trajectories of mental health symptoms. For depressive symptoms we found that 72% was classified in a low/intermediate decreasing trajectory and for anxiety symptoms 90% was classified in a stable low trajectory. Heterogeneity in loneliness trajectories was larger: 61% of the participants were classified in a stable low trajectory, and we found sub-groups with substantial increases and decreases, yet these groups returned to the initial loneliness level by February 2022.

Relative stability in depression and anxiety symptoms is largely in line with other studies [9–11,44,45] and our previous analysis of the first month and year of the pandemic [16,34]. One explanation could be that newly available resources, for instance social cohesion, cushioned against the negative consequences of the pandemic [46]. Another explanation might be that lockdown measures have slowed down daily life and therefore have reduced time pressure and mental distress offsetting most pandemic related stressors [18]. In contrast to other studies [11,17,22], we did not find a clear recovering or temporarily elevated sub-group with depressive or anxiety symptoms. This might be because persons with chronic psychiatric disorders on average have a higher and more stable severity of symptoms than persons in the general population. Also possible is that sub-groups with substantial changes in mental health may be small and our sample size was insufficient to detect such groups.

In line with other studies [10,16,34,47], loneliness was more dynamic than depressive and anxiety symptoms. An explanation may be that many measures implemented have had a direct and profound impact on face-to-face contact, which conceptually links most closely to loneliness, i.e. the subjective experience of a lack of quantity and/or emotional depth of one's social contacts. In contrast to another study [19], we did not find that changes in loneliness trajectories occurred the higher and lower end of the loneliness continuum. Instead we found variations among those with intermediate levels of loneliness at the start of the pandemic, which included temporary heightened and temporary lowered trajectories. One explanation might be that our study had a longer follow-up time (February 2022 instead of May 2020). Large changes in the medium loneliness levels may have taken a longer time to become visible whereas fluctuations in lower and higher end of the continuum groups appear relatively stable by contrast. In addition the cushioning effect of newly available resources, for instance social cohesion, may have waned over time [46].

Consistent with others, we found that being younger [9,19,22,48], being female [9,11,19,22,48], individuals with a low education level [9] and income [9,19,22] and living alone [48] were associated having less favourable trajectories of depressive, anxiety symptoms or loneliness. We also found that chronicity of pre-pandemic mental disorders and pre-pandemic symptom severity were associated with unfavourable trajectory membership. For depressive symptoms, we found that those being female, having a low income and living alone were at risk of experiencing a stable intermediate instead of stable low trajectories of depressive symptoms. Arguably, females might have been more vulnerable than males during the pandemic because females carry more responsibility combining teleworking with family care and homeschooling duties [17]. Participants who were living alone might have been relatively more socially isolated [19] and participants who had a low income might have been more vulnerable adversities such as job losses or decreases in household income [9]. For anxiety specifically, we found that being younger related to more unfavourable trajectory. Younger compared to older individuals may have been more affected by job insecurity, balancing child care and teleworking, and by stronger disruptions in daily life because of social distancing and other preventive measures [47,48]. Lastly, for loneliness we found that being female and living alone were associated with unfavourable trajectories.

Strengths of the study are the use of multiple validated symptom severity scales and a well-phenotyped psychiatric status based on diagnostic interviews pre-pandemic. Limitations were selectivity of respondents; responders were less likely to report high chronicity. Therefore, the number of individuals reporting unfavourable trajectories may be underestimated, although stability of the trajectories would likely remain the same. The small sample size may have prohibited the detection of heterogeneity in mental health trajectories during the pandemic, especially for the outcomes of anxiety and depressive symptoms. For depression and anxiety we found that a 4-class and the 3-class solution, respectively, that contained one sub-group of 3%. Although some fit indices suggested an improvement of model fit over the 3 and 2-class models (i.e. lowered BIC), the slopes and quadratic slopes did not reach beyond the threshold of statistical significance, indicating a lack of statistical robustness. Moreover, accepting a model with a small latent class (i.e. $N = 51$ or $N = 48$) was not in line with recommendations in the literature [39]. Future studies may repeat this analysis using larger psychiatric samples. Lastly, the fact that this study was conducted among psychiatric cohorts makes generalizability to the general population limited, although this is not the goal of case-control studies.

Overall, we conclude that trajectories of depressive and anxiety symptoms during the pandemic were relatively stable among persons with psychiatric disorders in the Netherlands. For depressive and anxiety symptoms we nevertheless found small yet concerning groups with stable high levels of symptoms. Pre-pandemic mental health status formed a major risk factor for having such trajectories whereas being female, having a low income and living alone formed a risk for depression and being younger for anxiety. For loneliness a greater heterogeneity of trajectories emphasize that lockdown measures such as in the COVID-19 pandemic may have very different consequences for different population groups, although also here, the long-term consequences might be limited. We identified two risk groups of stable high (17%), and temporary heightened (13%)levels. The former was characterized by being female, living alone and having a more depressive symptoms and loneliness pre-pandemic while the latter was characterized by more depressive symptoms and loneliness pre-pandemic.

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Ethical considerations

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Institutional Review Board of the Vrije Universiteit Medical Center, Amsterdam, and adhered to the Declaration of Helsinki.

Declaration of Competing Interest

BWJHP reports grants from Janssen Research and Boehringer Ingelheim, outside of the submitted work. All other authors declare no competing interests.

Data availability

According to European law (General Data Protection Regulation), data containing potentially identifying or sensitive patients' information are restricted. However, for academic researchers, data can be made available on request via the NESDA (nesda@ggzingeest.nl), NESDO (d.rhebergen@ggzcentraal.nl), and NOCDA (p.vanoppen@ggzingeest.nl) data access committees.

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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.2022.111138.

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