



Psychological distress resulting from the COVID-19 confinement is associated with unhealthy dietary changes in two Italian population-based cohorts

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Abstract

Purpose To examine the relationship between psychological distress resulting from the COVID-19 lockdown and dietary changes.

Methods Cross-sectional analysis from 2 retrospective Italian cohorts recruited from May to September 2020: (1) The Moli-LOCK cohort consists of 1401 participants from the Moli-sani Study ($n=24,325$) who were administered a telephone-based questionnaire to assess lifestyles and psychological factors during confinement; (2) the ALT RISCOVID-19 is a web-based survey of 1340 individuals distributed throughout Italy who self-responded to the same questionnaire using Google® forms. Psychological distress was measured by assessments of depression (PHQ-9 and depressive items from the Screening Questionnaire for Disaster Mental Health- SQD-D), anxiety (GAD-7), stress (PSS-4), and post-traumatic stress disorder (SQD-P). Diet quality was assessed either as changes in consumption of ultra-processed foods (UPF) or adherence to Mediterranean diet (MD).

Results In ALT RISCOVID-19, increased UPF intake was directly associated with depression (both PHQ-9 and SQD-D; $p < 0.0001$), anxiety ($p < 0.0001$), stress ($p = 0.001$) and SQD-P ($p = 0.001$); similar results were obtained in the Moli-LOCK cohort except for perceived stress. When psychometric scales were analysed simultaneously, only depression (SQD-D) remained associated with UPF (both cohorts). In both cohorts, psychological distress poorly influenced changes toward an MD, except for depression (SQD-D) that resulted inversely associated in the ALT RISCOVID-19 participants ($\beta = -0.16$; 95% CI $-0.26, -0.06$).

Conclusions Psychological distress from the COVID-19 confinement is directly associated with unhealthy dietary modifications in two Italian cohorts. In view of possible future restrictive measures to contain pandemic, public health actions are warranted to mitigate the impact of psychological distress on diet quality.

Keywords Psychological distress · Depression · Anxiety · Stress · Post-traumatic stress disorder · Lockdown · COVID-19 · Mediterranean diet · Ultra-processed foods

Moli-LOCK Study Investigators are listed in the Supplementary Appendix.

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Introduction

The coronavirus disease 2019 (COVID-19) has aggressively spread across the globe since late 2019 and, as of September 10, 2021, more than 220 million confirmed cases and over 4 million deaths have been reported [1].

The COVID-19 pandemic led the Italian government to enact unprecedented restrictive measures nationwide between March 9 and May 3 2020, in order to limit the fast spread transmission of the disease and the subsequent overwhelming of hospitals and health care systems [2].

During the lockdown, Italian residents were required to stay at home and only essential needs/services were permitted, with huge limitations in terms of working activities that were converted into home working as far as possible. As a consequence, daily routine was dramatically disrupted with potential negative effects on mental health and dietary habits: the latter are highly susceptible to psychological well-being [3, 4] and vice versa [5, 6].

The negative effects of lockdown on psychological health were already documented by studies analysing the effect of confinement during the SARS and MERS outbreaks in 2003 and 2012 [7, 8], and there is evidence that the psychological impact of quarantine is wide-ranging, substantial, can be long lasting [9] and may translate to severe distress eventually leading to significant psychological disorders [7, 9].

The effect of lockdown due to COVID-19 outbreak on mental health has been analysed in a number of studies so far, all concordant in indicating an increase in the prevalence of post-traumatic stress disorder [10], depression [10–13], anxiety [12, 13], stress [12, 13] and insomnia [13].

More recently, a study on 6,882 individuals from 59 Countries found that the COVID-19 pandemic has affected global mental health with increased prevalence of depression and anxiety [14]. Consistently, findings from a national Irish cohort indicated that the COVID-19 quarantine was associated with stress and significant increase in symptoms of depression and anxiety [15].

However, the impact of psychological distress induced by COVID-19 lockdown on dietary changes during confinement has been poorly investigated. Available data from a national French survey indicated that depression and anxiety clustered with unfavourable nutritional changes or behaviours during the lockdown period [16]. Similarly, data from a web-based survey in France revealed that a negative change in mental health was strongly associated with adverse changes in nutrition [17].

We therefore aimed at examining the association between psychological distress induced by the confinement with concurrent changes in diet quality, by using data on 2,741 Italian men and women from two population-based cohorts recruited from May 2020 to September 2020.

The rationale of our study relies on the well-established association between mental health and diet quality reported in a number of epidemiological settings [18–20].

Methods

Study design and participants

The Moli-LOCK Study The Moli-LOCK Study was designed as an observational cohort study aiming to retrospectively investigate dietary, lifestyle and psychosocial

changes that possibly occurred after Italy's lockdown resulting from the COVID-19 pandemic, that is in the period of time between March 9 2020 and May 3 2020. The population of the Moli-LOCK Study consists of a subgroup of men and women who had first been recruited in the larger Moli-sani Study cohort [21] in 2005–2010 ($n = 24,325$) and then re-examined in 2017–2020 ($n = 2572$). From May 2020 to September 2020, subjects were contacted by telephone by trained researchers to assess lifestyle, dietary and psychosocial changes during the confinement resulting from the COVID-19 pandemic. A total of 1,563 completed the questionnaire. As compared to the eligible sample who did not participate ($n = 1009$), individuals included in the study were slightly younger (66.4 ± 8.6 vs 67.5 ± 9.3 ; p value < 0.001 for analysed vs excluded) and had higher education (upper secondary school or higher = 66.2% vs 61.5%, respectively, $p = 0.015$) while no differences were found for sex (men = 43.7% vs 47.1%, respectively, $p = 0.09$) and presence of chronic diseases (cardiovascular disease = 7.4% vs 9.3%, $p = 0.08$; cancer = 9.4% vs 9.2%, $p = 0.72$, respectively). The Moli-LOCK study complies with the Declaration of Helsinki and was granted the approval of the Ethics Committee of the IRCCS Neuromed, Pozzilli (IS), Italy. Verbal informed consent during the telephone interview was obtained from all participants. After exclusion of participants with missing information on one or more psychometric scales and dietary data, we finally analysed 1401 subjects (Supplementary Fig. 1).

The ALT RISCOVID-19 Study ALT RISCOVID-19 is a cross-sectional web-based survey carried out among Italian adults aged ≥ 18 years, resident in Italy during the confinement.

Data were collected through a structured self-administered questionnaire created in Google® Forms (Google LLC, Menlo Park, CA, USA). All subjects aged ≥ 18 from the general population, residing in Italy during the Italian lockdown, with access to electronic devices and the Internet (e.g. personal computer, smartphone) and fluent in Italian were eligible.

Individuals were invited to participate in the survey via social media (Facebook® and Whatsapp®) and e-mail contacts and the data collection occurred between June and September 2020. A total of 2060 subjects throughout Italy completed the survey.

Before starting the questionnaire, participants were informed about the aims of the study and were ensured that all data would be used for research purposes only; participants were required to accept the data sharing and privacy policy before taking part in the study. To protect the confidentiality of the participants, their personal information and data were anonymous, according to the provisions of the General Data Protection Regulation (GDPR 679/2016).

The study was granted the approval of the Ethics Committee of the IRCCS Neuromed, Pozzilli (IS), Italy.

Participants with missing data on one or more psychometric scales and diet were excluded and the analytic sample consisted of 1340 subjects (Supplementary Fig. 1).

The ALT RISCOVD-19 survey and the Moli-LOCK study were registered on clinicaltrials.gov (NCT04422262).

Data collection

The ALT RISCOVD-19/Moli-LOCK questionnaire was constructed by the Department of Epidemiology and Prevention at the IRCCS Neuromed. The questionnaire was divided into modules including questions on sociodemographic characteristics, medical history, COVID-19 related aspects, dietary and lifestyle practices, psychological assessment and sources of information (Supplementary Appendix 1).

Psychological distress included assessment of depression, anxiety, stress and post-traumatic stress disorder (PTSD) that were respectively assessed by administration of validated versions of the Patients' Health Questionnaire (PHQ-9) [22], the General Anxiety Disorder (GAD-7) [23], the 4-item Perceived Stress Scale (PSS-4) [24] and the Italian version of the Screening Questionnaire for Disaster Mental Health (SQD) [25] that includes nine items to assess PTSD (SQD-P) and six items to screen for depression at the same time (SQD-D).

Dietary changes were evaluated through a 41-food-item questionnaire asking participants to indicate whether during lockdown their consumption of each food was increased, decreased or unchanged as compared to their usual intake just before the confinement (Supplementary Appendix 1).

Modifications in adherence to the MD were evaluated by computing a score (MD score) which scored foods according to their position in the Mediterranean diet pyramid: we assigned 1 point to increased consumption of highly recommended foods (e.g. fresh fruits, nuts and seeds, fresh vegetables) and minus 1 point if that consumption was decreased; conversely, decreased consumption of foods less frequent in the Mediterranean diet and for which it is recommended from low to moderate intake was given 1 point (e.g. red meat, white meat, milk and yogurt) and minus 1 point was assigned to increased intake. Unchanged intakes received 0 point (Supplementary Table 1). The MD score potentially ranged from -18 to 18 with higher values reflecting maximal switching to an MD.

Changes in UPF consumption was assessed through questions aimed at evaluating modifications possibly occurred during lockdown in the intake of 19 food items grouped according to the NOVA classification system based on the degree of food processing (Supplementary Table 2). Briefly, we categorized each food item into one of the following categories according to the extent and purpose of food

processing: (1) unprocessed or minimally processed foods (e.g. fruits and vegetables, meat and fish); (2) processed culinary ingredients (e.g. butter, oils); (3) processed foods with salt, sugar, or oil (e.g. canned or bottled vegetables and legumes, canned fish); (4) UPF containing predominantly industrial substances and little or no whole food (e.g. carbonated drinks, processed meat, packaged snacks). For the purpose of the present analyses we used the fourth NOVA category.

We then computed an UPF score by assigning 1 point to increased intake, - 1 point to decreased intake while unchanged intakes received 0 points (Supplementary Table 3). The score potentially ranges from -19 to 19 with higher values indicating an increase in UPF consumption during confinement.

Statistical analyses

Data are represented as number and percentage in parentheses (%) for categorical variables, or mean and standard deviation (\pm SD) for continuous variables.

We tested the association of psychological distress (used as the exposure variable) with MD and UPF (dependent variables) by using multivariable linear regression analysis. Each psychometric score was scaled by its standard deviation so that regression coefficients indicate the variation in diet quality for 1 standard deviation change (cohort specific) for each measure of psychological distress. Associations were obtained by using the following models: Model 1 (adjusted for age and sex); multivariable Model 2 that was further controlled for main sociodemographic factors, namely geographical area (for ALT RISCOVD-19 only), living area, educational level, household income, marital status, number of cohabitants, occupational class, history of chronic diseases, diagnosis of ≥ 1 diseases during confinement, use of psychoactive drugs before and during lockdown; multivariable Model 3 as in Model 2 and including all the psychometric scales simultaneously.

Missing data on covariates (educational level = 7; household income = 381; marital status = 23; occupational class = 32; number of cohabitants = 22; living areas = 45; history of chronic disease = 21; diagnosis of disease during lockdown = 14; use of psychoactive drugs during lockdown = 79) were handled using multiple imputation (SAS PROC MI, followed by PROC MIANALYZE) to maximize data availability for all variables, avoid bias introduced by not-at-random missing (MNAR) data patterns and achieve robust results over different simulations ($n = 10$ imputed datasets).

Statistical tests were two-sided, and Bonferroni correction for multiple comparisons was applied to each analysis according to the number of independent tests carried out (see

Tables). Data analysis was generated using SAS/STAT software, version 9.4 of the SAS System for Windows©2009.

Results

The pooled sample of 2741 subjects had a mean age of 58.1 years (± 15.3) and included 40.8% men. The largest proportion lived in Southern Italy (75.0%), was well-educated (postgraduate education 45%), had high occupational class (43.2% professional/managerial) and prevalently lived in pairs (73.1%) (Table 1). MD score and UPF were inversely correlated (spearman correlation coefficient = -0.11 ; $p < 0.0001$, data not shown), and correlations among psychometric scales were also moderate to high (Supplementary Table 4).

Overall, we found a slight increase in consumption of MD (0.4 ± 2.2) and a mild decrease in UPF intake (-0.3 ± 4.0) experienced during the lockdown (Table 1).

During confinement, in the ALT RISCOVID-19 cohort, all measures of psychological distress were consistently associated with an increase in UPF intake (PHQ-9: $\beta = 0.16$, 95% CI 0.10, 0.22; GAD-7: $\beta = 0.14$, 95% CI 0.08, 0.20; PSS-4: $\beta = 0.10$, 95% CI 0.04, 0.16; SQD-P: $\beta = 0.10$, 95% CI 0.04, 0.16 and SQD-D: $\beta = 0.17$, 95% CI 0.11, 0.23; Table 2, models 2 and Supplementary Fig. 2B).

On the contrary, psychological distress was unlikely to be relevant to changes in MD, with the exception of depressive symptoms as assessed by the SQD-D that resulted inversely associated with modifications toward an MD ($\beta = -0.09$, 95% CI -0.15 , -0.03 ; Table 2, models 2 and Supplementary Fig. 2A). Results from multivariable-adjusted model 3, including all the psychometric scales simultaneously, showed that only depression as measured by the SQD-D was independently associated both with reduced adherence to an MD ($\beta = -0.16$, 95% CI -0.26 , -0.06) and an increase in the intake of UPF ($\beta = 0.14$, 95% CI 0.05, 0.24) (Table 2, models 3).

Analyses on 1,401 participants from the Moli-LOCK cohort revealed that perceived stress only predicted unfavourable dietary changes as reflected by a decrease of MD ($\beta = -0.07$; 95% CI -0.13 , -0.02 ; Table 3, models 2 and Supplementary Fig. 3A), although the statistical significance was not retained in model 3; all measures of psychological distress but perceived stress were associated with an increase in UPF intake (PHQ-9: $\beta = 0.07$, 95% CI 0.02, 0.13; GAD-7: $\beta = 0.08$, 95% CI 0.02, 0.13; SQD-P: $\beta = 0.09$, 95% CI 0.03, 0.14 and SQD-D: $\beta = 0.13$, 95% CI 0.08, 0.18; Table 3, models 2 and Supplementary Fig. 3B). Analyses from multivariable-adjusted model 3, where all psychometric scales were considered simultaneously, showed that only the SQD-D remained significantly associated with UPF intake ($\beta = 0.15$,

95% CI 0.07, 0.23). Also, an inverse association of PSS-4 with UPF consumption was observed (Table 3, Models 3).

A number of diet-related factors resulted associated with psychological distress as well (Tables 4 and 5). Analyses on the ALT RISCOVID-19 sample showed major behavioural changes associated with depressive symptoms (SQD-D) while other indicators of psychological distress did not independently correlate with changes in eating behaviours during lockdown. In particular, depressive symptoms resulting from a traumatic life event were positively associated with higher body weight during confinement, an increase in the number of daily meals and reduced water intake (Table 4). Analyses from the Moli-LOCK cohort provided similar results, with the SQD-D being more strongly associated with changes in eating behaviours, as reflected by increased body weight, lower consumption of local food and more frequent food supplement use (Table 5). In this Moli-LOCK cohort we also observed some behavioural changes associated with PSS-4 (Table 5).

Discussion

We analysed the association between psychological distress and diet quality during the Italian nationwide confinement imposed from March 9 to May 3 2020 to contain the spread of the SARS-CoV-2 virus. Our findings from two Italian population-based cohorts indicated that higher levels of psychological distress experienced during lockdown were directly associated with unhealthy dietary changes in the same timeframe.

Diet quality was measured by an assessment of the consumption of either Mediterranean diet or UPF; in the ALT-RISCOVID-19 web survey, participants with higher psychological distress reported an increase in highly processed foods, which are usually rich in sugar, saturated fats and dietary cholesterol, and a concurrent lower adherence to an MD. Similarly, in the Moli-LOCK cohort, psychological distress was linked to an increased consumption of UPF.

When psychometric scales were analysed simultaneously, only current depressive symptoms, as measured by the SQD-D, remained associated with unfavourable dietary changes in both cohorts.

This may be explained by the fact that, differently from the PHQ-9, the SQD-D is conceived to detect depressive symptoms immediately after the occurrence of a traumatic life event which is the case of the confinement resulting from the COVID-19 pandemic, and thus reinforcing the hypothesis that lockdown-induced depression could have had an impact on dietary changes.

Our findings align with those from a large study on UK individuals indicating that depressive symptoms during the COVID-19 lockdown were associated with an increased risk

Table 1 Sociodemographic characteristics of the two cohorts analysed in this study

	Both cohorts (<i>n</i> =2741)	ALT RISCOVID-19 (<i>n</i> =1340)	Moli- LOCK (<i>n</i> =1401)	<i>p</i> for difference
Age (y; means ± SD)	58.0 ± 15.3	47.8 ± 14.0	67.8 ± 8.6	<0.0001
Sex (men)	40.8	37.2	44.2	0.0002
Geographical areas				<0.0001
Northern	17.1	34.9	0.0	
Central	6.3	12.7	0.1	
Southern and Islands	75.0	49.0	99.9	
Missing data	1.6	3.4	0.0	
Living area				<0.0001
>200,000 inhabitants	11.3	23.0	0.1	
<200,000 inhabitants	12.0	24.3	0.1	
<50,000 inhabitants	54.6	23.6	84.4	
Villages/rural areas	22.1	29.1	15.4	
Educational level				<0.0001
Lower secondary school or less	18.4	4.1	32.0	
Upper secondary school	36.5	26.1	46.5	
Postgraduate education	44.8	69.6	21.2	
Missing data	0.3	0.2	0.3	
Household income (EUR/y)				<0.0001
≤10,000	5	5.1	5.4	
>10,000 ≤25,000	27.4	22.2	32.4	
>25,000 ≤40,000	29.4	22.0	36.6	
>40,000 ≤60,000	12.7	14.0	11.5	
>60,000	11.3	19.9	3.0	
Missing data	13.9	16.8	11.1	
Marital status				<0.0001
Married/in couple	72.3	61.8	82.3	
Single	15.5	27.7	3.8	
Divorced	5.5	7.4	3.6	
Widower	5.9	2.0	9.7	
Missing data	0.8	1.1	0.6	
Number of cohabitants				<0.0001
None	10.4	10.7	10.1	
1	38.4	28.8	47.5	
2	23.9	25.5	22.4	
>2	26.5	34.0	19.4	
Missing data	0.8	1.0	0.6	
Occupational class				<0.0001
Professional/managerial	42.3	57.4	27.9	
Skilled non-manual	31.1	22.9	39.0	
Skilled manual	4.9	3.0	6.6	
Partly skilled/unskilled	6.2	1.9	10.3	
Unemployed/unclassified	14.4	13.1	15.6	
Missing data	1.2	1.8	0.6	
History of chronic disease				<0.0001
No	89.6	85.4	93.6	
Yes	9.7	13.4	6.1	
Missing data	0.7	1.2	0.3	
Diagnosis of ≥1 diseases during lockdown				<0.0001
No	95.4	92.2	98.6	

Table 1 (continued)

	Both cohorts (<i>n</i> = 2741)	ALT RISCOVID-19 (<i>n</i> = 1340)	Moli- LOCK (<i>n</i> = 1401)	<i>p</i> for difference
Yes	4.1	6.9	1.3	
Missing data	0.5	0.9	0.1	
Use of psychoactive drugs before lockdown				0.011
No	95.4	95.4	95.3	
Yes	4.6	4.6	4.7	
Use of psychoactive drugs during lockdown				< 0.0001
No	93.8	90.5	97.0	
Yes	3.3	5.5	1.1	
Missing data	2.9	4.0	1.9	
PHQ-9 (means ± SD)	3.2 ± 4.2	4.6 ± 4.8	1.8 ± 3.0	< 0.0001
GAD-7 (means ± SD)	4.2 ± 4.1	5.4 ± 4.4	3.1 ± 3.3	< 0.0001
PSS-4 (means ± SD)	4.1 ± 3.1	5.2 ± 3.1	3.1 ± 2.7	< 0.0001
SQD-Post traumatic subscale (means ± SD)	1.5 ± 1.9	1.9 ± 2.1	1.1 ± 1.6	< 0.0001
SQD-Depression subscale (means ± SD)	1.2 ± 1.5	1.7 ± 1.7	0.6 ± 1.1	< 0.0001
Change in MD (means ± SD)	0.4 ± 2.2	0.6 ± 2.6	0.2 ± 1.6	< 0.0001
Change in UPF (means ± SD)	− 0.3 ± 4.0	− 0.9 ± 5.5	0.3 ± 1.6	< 0.0001

Values are presented as percentages unless otherwise stated

P values are adjusted for age and sex

PHQ-9 Patients' Health questionnaire, *GAD-7* General anxiety disorder scale, *PSS-4* Perceived stress scale, *SQD* Screening Questionnaire for Disaster Mental Health, *SQD-P* Post-traumatic Stress Disorder, *SQD-D* Depressive symptoms, *MD* Mediterranean diet (score − 18 to 18), *UPF* Ultra-processed food (score − 19 to 19)

of experiencing any changes in eating behaviours possibly through emotional eating, even though this potential link could not be directly assessed [26].

Our a priori research hypothesis was that psychological distress during confinement, possibly resulting from disruption of daily life and social isolation, would negatively impact diet quality and not vice versa, due to the relatively short timeframe in which such association has been analysed. Mental health can be influenced by diet through several mechanisms, including chronic inflammation as follows: healthy diets are usually associated with lower inflammation [27, 28] while raised inflammation has been associated with a broad range of psychiatric disorders [29]; thus, positive health-related behaviours might reduce the risk of adverse mental health also by a favourable modulation of the inflammatory pathway. Therefore, it is likely that mental health and dietary habits show a bidirectional relationship, especially over long time ranges. However, in our study the association of psychological distress and modification of diet quality has been investigated within a two-month period, which is a relatively short period of time for the inflammatory process possibly caused by unhealthy diets to have an effect on mental health.

The association between psychological health and diet is largely supported by previous investigations conducted not in a context of pandemics [4–6, 18, 19], but only a few

studies to date have analysed the association of psychological distress resulting from COVID-19 lockdown with diet quality during the same timeframe.

An early investigation on 5545 Spanish adults conducted 2 weeks after the nationwide lockdown highlighted that a healthy and balanced diet was predictive of reduced levels of anxiety symptoms and depression [30]. A national survey on 42,000 Brazilian adults found that people with previous diagnosis of depression were at higher risk of unhealthy behaviours during the COVID-19 pandemic quarantine, including low frequency of fruit or vegetable consumption and elevated frequency of UPF intake [31].

A small-sized web-based survey on French adults highlighted that the lockdown led to a decrease in nutritional quality of diet on average, which could be partly explained by an increase of mood as a food choice motive [32]. In the NutriNet-Santé cohort study including nearly 40,000 French adults [16], higher scores for depression and anxiety clustered with unfavourable nutritional changes or behaviours during the lockdown period. More recent studies are concordant in showing that psychological distress experienced during the lockdown and dietary changes are highly correlated; indeed, a community-based cross-sectional study on Portuguese adults indicated that there was a significant indirect effect of the experienced psychosocial impact of

Table 2 Association of psychological factors with changes in adherence to Mediterranean diet (MD) and consumption of ultra-processed foods (UPF) during the Italian lockdown resulting from the COVID-19 pandemic (March 9–May 3, 2020) in the ALT RISCOVID-19 web-based survey ($n = 1340$) using data obtained from multiple imputation

	Change in MD				Change in UPF			
	Regression coefficient β	Lower 95% CI	Upper 95% CI	p value	Regression coefficient β	Lower 95% CI	Upper 95% CI	p value
PHQ-9								
Model 1	– 0.04	– 0.10	0.01	0.12	0.15	0.09	0.20	< .0001
Model 2	– 0.05	– 0.11	0.02	0.15	0.16	0.10	0.22	< .0001
Model 3	– 0.02	– 0.12	0.08	0.67	0.07	– 0.03	0.17	0.15
GAD-7								
Model 1	– 0.03	– 0.09	0.02	0.23	0.14	0.08	0.19	< .0001
Model 2	– 0.03	– 0.09	0.03	0.38	0.14	0.08	0.20	< .0001
Model 3	– 0.01	– 0.10	0.09	0.87	0.06	– 0.03	0.16	0.20
PSS-4								
Model 1	– 0.01	– 0.06	0.05	0.84	0.10	0.05	0.16	0.0004
Model 2	0.01	– 0.05	0.07	0.75	0.10	0.04	0.16	0.001
Model 3	0.08	0.00	0.16	0.06	– 0.02	– 0.10	0.06	0.60
SQD-P								
Model 1	– 0.03	– 0.09	0.02	0.28	0.10	0.05	0.16	0.0002
Model 2	– 0.03	– 0.09	0.03	0.32	0.10	0.04	0.16	0.001
Model 3	0.07	– 0.03	0.16	0.16	– 0.06	– 0.15	0.03	0.18
SQD-D								
Model 1	– 0.08	– 0.14	– 0.03	0.004	0.16	0.11	0.22	< .0001
Model 2	– 0.09	– 0.15	– 0.03	0.003	0.17	0.11	0.23	< .0001
Model 3	– 0.16	– 0.26	– 0.06	0.001	0.14	0.05	0.24	0.004

Model 1 obtained from multivariable-adjusted linear regression including age and sex

Model 2 obtained from multivariable-adjusted linear regression including age, sex, geographical area, living area, educational level, household income, marital status, number of cohabitants, occupational class, history of chronic diseases, diagnosis of ≥ 1 diseases during lockdown and use of psychoactive drugs before or during lockdown

Model 3 as in model 2 and including all psychometric scales simultaneously. Significant associations surviving Bonferroni correction for multiple testing ($\alpha = 0.01$) are highlighted in bold

PHQ-9 Patients' Health questionnaire, *GAD-7* General anxiety disorder scale, *PSS-4* Perceived stress scale, *SQD* Screening Questionnaire for Disaster Mental Health, *SQD-P* Post-traumatic Stress Disorder, *SQD-D* Depressive symptoms

COVID-19 pandemic on disordered eating behaviours mediated through psychological distress [33].

An online survey on a small sample of Italians provided evidence of the negative effects of isolation and lockdown on emotional wellbeing, and, relatedly, on eating behaviours [34]. Perceived worsened diet quality during the COVID-19 pandemic possibly led to higher odds for clustered mental ill-health, including anxiety and depressive symptoms in a large cohort of Swedish people [35].

A favourable association between psychological health and an MD has been previously reported in numerous cross-sectional [36–38] and longitudinal analyses [39, 40] from population studies; consistently, a diet rich in UPF was unfavourably associated with mental health rather being associated with increased risk of incident depression [41, 42], while the association with other psychological disorders, such as stress or anxiety, has not been extensively addressed,

with few exceptions [43]. Our study is one of the first to provide evidence of an association between anxiety, stress and PTSD symptoms with a diet rich in UPF.

The role of psychological distress, including depression and anxiety, in the development and progression of cardiovascular disease is well established [44, 45] as well as that of unhealthy and unbalanced diets which are associated with a variety of negative health outcomes [46, 47].

Strength and limitations

A major strength of this study is the use of two population-based cohorts to examine the impact of psychological stress resulting from the lockdown on diet quality modifications. Also, the study relies on the use of a number of covariates which limit at least in part confounding, and data were collected shortly after the end of the Italian lockdown.

Table 3 Association of psychological factors with changes in adherence to Mediterranean diet (MD) and consumption of ultra-processed foods (UPF) during the Italian lockdown resulting from the COVID-19 pandemic (March 9–May 3, 2020) in the Moli-LOCK cohort ($n = 1401$) using data obtained from multiple imputation

	Change in MD				Change in UPF			
	Regression coefficient β	Lower 95% CI	Upper 95% CI	p value	Regression coefficient β	Lower 95% CI	Upper 95% CI	p value
PHQ-9								
Model 1	- 0.05	- 0.10	0.01	0.09	0.09	0.03	0.14	0.001
Model 2	- 0.06	- 0.11	- 0.0003	0.05	0.07	0.02	0.13	0.01
Model 3	- 0.01	- 0.09	0.07	0.79	0.04	- 0.04	0.11	0.38
GAD-7								
Model 1	- 0.05	- 0.10	0.003	0.07	0.09	0.04	0.14	0.001
Model 2	- 0.06	- 0.11	- 0.002	0.04	0.08	0.02	0.13	0.01
Model 3	- 0.01	- 0.10	0.07	0.75	0.05	- 0.04	0.13	0.29
PSS-4								
Model 1	- 0.06	- 0.12	- 0.01	0.02	- 0.05	- 0.11	0.00	0.04
Model 2	- 0.07	- 0.13	- 0.02	0.01	- 0.04	- 0.09	0.01	0.15
Model 3	- 0.05	- 0.12	0.01	0.11	- 0.14	- 0.20	- 0.07	< . 0001
SQD-P								
Model 1	- 0.05	- 0.10	0.005	0.07	0.11	0.06	0.16	< . 0001
Model 2	- 0.05	- 0.11	0.004	0.07	0.09	0.03	0.14	0.001
Model 3	0.02	- 0.07	0.12	0.65	0.00	- 0.09	0.09	0.93
SQD-D								
Model 1	- 0.05	- 0.10	0.004	0.07	0.14	0.09	0.19	< . 0001
Model 2	- 0.06	- 0.12	- 0.01	0.03	0.13	0.08	0.18	< . 0001
Model 3	- 0.04	- 0.13	0.04	0.33	0.15	0.07	0.23	0.0004

Model 1 obtained from multivariable-adjusted linear regression including age and sex

Model 2 obtained from multivariable-adjusted linear regression including age, sex, living area, educational level, household income, marital status, number of cohabitants, occupational class, history of chronic diseases, diagnosis of ≥ 1 diseases during lockdown and use of psychoactive drugs before or during lockdown

Model 3 as in model 2 and including all psychometric scales simultaneously. Significant associations surviving Bonferroni correction for multiple testing ($\alpha = 0.01$) are highlighted in bold

PHQ-9 Patients' Health questionnaire, *GAD-7* General anxiety disorder scale, *PSS-4* Perceived stress scale, *SQD* Screening Questionnaire for Disaster Mental Health, *SQD-P* Post-traumatic Stress Disorder, *SQD-D* Depressive symptoms

However, our results should be interpreted in light of some limitations. First, the ALT RISCOVID-19 is a web-based survey with potential selection bias and self-reported information that may lead to misreporting. However, our analyses also rely on data collected within the Moli-LOCK study which includes participants from a well-established population-based prospective cohort who were telephone-interviewed and this limits misreporting. Both cohorts used retrospective data; thus recall bias cannot be excluded and changes in dietary intakes were self-reported rather than assessed objectively through administration of dietary questionnaires before and after lockdown. Another limitation is the lack of assessment of some personality variables of the participants, such as psychological resilience, which has a clear influence on the psychological distress that a person can present in a situation like this of confinement.

Finally, this study was conceived to test the hypothesis that lockdown-induced psychological distress could be unfavourably associated with changes in diet quality during confinement; however the direction of the association cannot be derived, due to our cross-sectional design.

It might be possible that mental distress could result in dietary changes [48]; however, robust longitudinal data in recent years have strengthened the evidence that healthy diets may reduce the risk of depressive symptoms [49], while Western-like diets and processed foods are independent predictors of depression and anxiety [47, 50].

Whatever the cause-effect relation, the present findings show that during confinement resulting from the COVID-19 outbreak psychological distress and diet quality were closely related.

Table 4 Psychological factors associated with diet-related factors during the Italian lockdown resulting from the COVID-19 pandemic (March 9–May 3, 2020) in the ALT RISCOVID-19 web-based survey (n = 1340) using data obtained from multiple imputation

	PHQ-9			GAD-7			PSS-4			SQD-P			SQD-D		
	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI
Body change during lockdown															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.06	-0.01	0.13	-0.01	-0.08	0.06	0.04	-0.04	0.12	-0.09	-0.16	-0.01	0.21	-0.04	0.14
Decreased	0.02	-0.09	0.12	0.05	-0.05	0.16	0.02	-0.10	0.15	-0.03	-0.14	0.08	0.15	0.05	0.25
Take away food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.05	-0.04	0.13	-0.001	-0.08	0.08	-0.04	-0.14	0.06	0.08	-0.01	0.17	-0.04	-0.12	0.05
Reduced	-0.03	-0.11	0.05	0.01	-0.07	0.09	0.01	-0.09	0.11	0.01	-0.08	0.10	0.04	-0.04	0.12
Time spent on home food preparation															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.04	-0.03	0.10	0.06	-0.01	0.12	0.02	-0.06	0.09	0.05	-0.02	0.12	-0.07	-0.13	-0.001
Reduced	0.12	-0.10	0.35	-0.03	-0.26	0.19	-0.004	-0.27	0.26	0.04	-0.19	0.28	-0.01	-0.23	0.22
Number of daily meals															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.08	0.01	0.16	0.11	0.03	0.18	-0.10	-0.19	-0.01	-0.13	-0.21	-0.05	0.20	0.13	0.28
Reduced	0.08	-0.12	0.28	0.08	-0.12	0.28	0.05	-0.19	0.29	-0.01	-0.23	0.20	0.10	-0.10	0.29
Food supplements use															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	-0.001	-0.10	0.10	0.12	0.02	0.22	0.06	-0.06	0.18	0.14	0.03	0.24	-0.16	-0.26	-0.06
Reduced	0.25	0.05	0.46	0.06	-0.14	0.27	-0.05	-0.30	0.20	0.21	-0.01	0.43	-0.29	-0.49	-0.08
Water intake															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.005	-0.07	0.08	0.05	-0.02	0.12	0.002	-0.08	0.09	0.01	-0.07	0.09	0.04	-0.03	0.11
Reduced	0.07	-0.10	0.23	-0.10	-0.27	0.07	-0.11	-0.31	0.09	0.0003	-0.18	0.18	0.30	0.14	0.47
Food budget															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.03	-0.04	0.10	0.04	-0.03	0.11	-0.02	-0.10	0.06	-0.01	-0.08	0.07	0.06	-0.01	0.13
Reduced	0.08	-0.03	0.19	0.07	-0.04	0.18	-0.08	-0.21	0.05	-0.03	-0.15	0.09	0.03	-0.08	0.14
Short food supply chain															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.01	-0.06	0.08	0.03	-0.03	0.10	0.01	-0.07	0.09	0.06	-0.01	0.13	-0.07	-0.14	-0.003
Reduced	-0.02	-0.13	0.08	0.05	-0.06	0.15	0.05	-0.07	0.18	0.07	-0.05	0.18	-0.02	-0.13	0.08

Table 4 (continued)

	PHQ-9			GAD-7			PSS-4			SQD-P			SQD-D		
	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI
Long food supply chain															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.04	-0.04	0.12	0.03	-0.04	0.11	0.03	-0.06	0.12	0.04	-0.04	0.13	0.01	-0.06	0.09
Reduced	0.03	-0.05	0.10	0.06	-0.02	0.14	-0.05	-0.15	0.04	0.05	-0.03	0.13	-0.03	-0.10	0.05
Local food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	-0.01	-0.08	0.07	0.03	-0.05	0.11	-0.03	-0.12	0.07	0.09	0.01	0.17	-0.03	-0.10	0.05
Reduced	-0.02	-0.16	0.12	0.08	-0.07	0.22	0.08	-0.09	0.24	-0.11	-0.26	0.04	0.0001	-0.14	0.14
Organic food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.09	-0.02	0.20	0.03	-0.08	0.15	-0.04	-0.17	0.09	0.07	-0.05	0.19	-0.03	-0.14	0.08
Reduced	0.17	-0.02	0.36	-0.07	-0.26	0.12	0.16	-0.07	0.38	-0.05	-0.25	0.16	-0.05	-0.24	0.14
Pre-prepared meals															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.09	-0.03	0.21	0.05	-0.07	0.17	0.01	-0.13	0.16	0.07	-0.06	0.20	-0.05	-0.17	0.07
Reduced	0.0001	-0.08	0.08	-0.04	-0.12	0.04	0.04	-0.05	0.13	0.05	-0.03	0.13	-0.02	-0.09	0.06
Long shelf life food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.01	-0.06	0.09	0.02	-0.06	0.10	0.01	-0.08	0.11	0.09	0.001	0.17	0.02	-0.06	0.10
Reduced	0.03	-0.07	0.13	-0.08	-0.18	0.02	0.02	-0.10	0.14	0.08	-0.02	0.19	-0.05	-0.15	0.05

Regression coefficient β with 95% confidence interval (95% CI) obtained from multivariable-adjusted linear regression model 3 including age, sex, geographical area, living area, educational level, household income, marital status, number of cohabitants, occupational class, history of chronic diseases, diagnosis of ≥ 1 diseases during lockdown and use of psychoactive drugs before or during lockdown, and including all the psychometric scales simultaneously

Significant associations surviving Bonferroni correction for multiple testing ($\alpha = 0.0008$) are highlighted in bold

PHQ-9 Patients' Health questionnaire, GAD-7 General anxiety disorder scale, PSS-4 Perceived stress scale, SQD Screening Questionnaire for Disaster Mental Health, SQD-P Post-traumatic Stress Disorder, SQD-D Depressive symptoms

Table 5 Psychological factors associated with diet-related factors during the Italian lockdown resulting from the COVID-19 pandemic (March 9–May 3, 2020) in the Moli-LOCK cohort (*n* = 1401) using data obtained from multiple imputation

	PHQ-9			GAD-7			PSS-4			SQD-P			SQD-D		
	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI
Body change during lockdown															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.05	-0.03	0.13	0.06	-0.01	0.13	-0.05	-0.15	0.04	-0.10	-0.16	-0.03	0.14	0.06	0.21
Decreased	0.09	-0.03	0.21	0.17	0.06	0.28	-0.14	-0.28	0.01	-0.05	-0.15	0.05	0.09	-0.02	0.21
Take away food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	-0.05	-0.23	0.13	0.12	-0.05	0.29	-0.01	-0.23	0.22	-0.04	-0.19	0.12	0.17	-0.005	0.34
Reduced	0.10	-0.15	0.35	0.07	-0.16	0.29	0.07	-0.23	0.37	0.15	-0.07	0.36	0.09	-0.15	0.32
Time spent on home food preparation															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.01	-0.06	0.09	0.10	0.03	0.17	-0.20	-0.30	-0.11	0.03	-0.03	0.10	0.04	-0.03	0.11
Reduced	0.27	-0.07	0.61	0.16	-0.16	0.48	0.05	-0.36	0.47	-0.36	-0.65	-0.07	0.52	0.20	0.84
Number of daily meals															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.04	-0.07	0.15	-0.01	-0.11	0.09	-0.05	-0.18	0.08	-0.01	-0.10	0.08	0.16	0.06	0.26
Reduced	0.67	0.39	0.94	-0.16	-0.42	0.10	-0.07	-0.41	0.27	0.05	-0.19	0.29	0.25	-0.01	0.51
Food supplements use															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.19	-0.11	0.48	0.03	-0.24	0.31	0.09	-0.27	0.45	-0.25	-0.50	0.01	0.53	0.25	0.80
Reduced	-0.18	-0.76	0.40	0.23	-0.31	0.78	-0.12	-0.83	0.59	-0.13	-0.63	0.37	0.32	-0.23	0.87
Water intake															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.16	0.02	0.30	0.02	-0.10	0.15	-0.19	-0.35	-0.02	0.16	0.04	0.28	-0.08	-0.21	0.05
Reduced	0.09	-0.21	0.38	-0.26	-0.54	0.01	-0.13	-0.49	0.23	0.17	-0.09	0.42	0.08	-0.20	0.36
Food budget															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.14	0.04	0.23	0.19	0.10	0.28	-0.31	-0.42	-0.19	0.01	-0.07	0.09	-0.02	-0.11	0.07
Reduced	0.06	-0.04	0.17	0.12	0.03	0.22	-0.23	-0.35	-0.10	0.05	-0.03	0.14	-0.08	-0.17	0.02
Short food supply chain															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.06	-0.03	0.14	0.13	0.05	0.21	-0.23	-0.34	-0.13	0.04	-0.03	0.12	-0.09	-0.18	-0.01

Table 5 (continued)

	PHQ-9			GAD-7			PSS-4			SQD-P			SQD-D		
	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI	β	Lower 95% CI	Upper 95% CI
Reduced	0.03	-0.10	0.17	0.07	-0.05	0.20	-0.06	-0.22	0.11	0.07	-0.05	0.18	-0.05	-0.17	0.08
Long food supply chain															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.11	-0.02	0.25	0.02	-0.10	0.15	0.04	-0.12	0.20	0.04	-0.07	0.16	-0.16	-0.29	-0.03
Reduced	0.05	-0.03	0.14	0.09	0.01	0.17	-0.26	-0.36	-0.15	0.04	-0.03	0.11	0.00	-0.08	0.08
Local food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	-0.004	-0.14	0.13	0.10	-0.03	0.22	-0.40	-0.57	-0.24	-0.01	-0.12	0.11	0.09	-0.03	0.22
Reduced	0.14	-0.02	0.30	0.06	-0.09	0.21	-0.03	-0.23	0.16	-0.23	-0.37	-0.09	0.29	0.14	0.44
Organic food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.24	-0.10	0.59	-0.15	-0.48	0.18	0.02	-0.41	0.45	0.29	-0.01	0.59	-0.21	-0.54	0.12
Reduced	1.62	1.10	2.15	-0.30	-0.81	0.20	0.65	-0.01	1.31	0.14	-0.32	0.61	-0.88	-1.39	-0.37
Pre-prepared meals															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	-0.14	-0.34	0.07	-0.11	-0.30	0.09	0.12	-0.14	0.37	0.02	-0.16	0.20	0.29	0.10	0.48
Reduced	0.18	-0.21	0.58	0.16	-0.21	0.53	-0.07	-0.55	0.41	-0.25	-0.59	0.09	0.19	-0.18	0.57
Long shelf life food															
Unchanged	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Increased	0.15	0.01	0.28	0.09	-0.03	0.22	-0.06	-0.23	0.10	0.04	-0.08	0.16	0.01	-0.12	0.14
Reduced	0.20	-0.17	0.57	0.27	-0.07	0.62	-0.41	-0.86	0.03	-0.10	-0.42	0.21	0.16	-0.19	0.50

Regression coefficient β with 95% confidence interval (95% CI) obtained from multivariable-adjusted linear regression model 3 including age, sex, living area, educational level, household income, marital status, number of cohabitants, occupational class, history of chronic diseases, diagnosis of ≥ 1 diseases during lockdown and use of psychoactive drugs before or during lockdown, and including all the psychometric scales simultaneously

Significant associations surviving Bonferroni correction for multiple testing ($\alpha=0.0008$) are highlighted in bold

PHQ-9 Patients' Health questionnaire, GAD-7 General anxiety disorder scale, PSS-4 Perceived stress scale, SQD Screening Questionnaire for Disaster Mental Health, SQD-P Post-traumatic Stress Disorder, SQD-D Depressive symptoms

Conclusions

Psychological distress resulting from confinement due to the COVID-19 pandemic is directly associated with unhealthy dietary modifications among Italians, as reflected by a decrease in MD and an increase of UPF. A major role was found for depressive symptoms that may occur after a traumatic life event which seems to drive much of the observed association between psychological distress and changes towards unhealthy eating.

In view of possible future restrictive measures to contain the pandemic spread, which is far from being presently tamed, public health actions are warranted to mitigate the potential impact of psychological distress on diet quality. Indeed, psychological distress has direct and indirect effects on health and part of its harmful impact may also be mediated by unhealthy behaviours, such as an unfavourable diet which is a major modifiable risk factor of death globally [50].

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00394-021-02752-4>.

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Author contribution LI, MB and AG conceived and designed the study. FB, ER, MP, SE acquired the data. SC and MO managed the data. MB and ADC analysed the data. MB drafted the manuscript. SC, CC, MBD, GdG and LI critically revised the questionnaire and this manuscript. All authors gave final approval and agree to be accountable for all aspects of the work ensuring integrity and accuracy.

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Availability of data The data underlying this article will be shared on reasonable request to the corresponding author. The data are stored in an institutional repository (<https://repository.neuromed.it>) and access is restricted by the ethical approvals and the legislation of the European Union.

Declarations

Conflict of interest The authors declare that they have no competing interests.

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