

GOPEN ACCESS

Citation: Fornili M, Petri D, Berrocal C, Fiorentino G, Ricceri F, Macciotta A, et al. (2021)
Psychological distress in the academic population and its association with socio-demographic and lifestyle characteristics during COVID-19 pandemic lockdown: Results from a large multicenter Italian study. PLoS ONE 16(3): e0248370. https://doi.org/10.1371/journal.pone.0248370

Editor: Francesco Di Gennaro, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, ITALY

Received: October 19, 2020

Accepted: February 25, 2021

Published: March 10, 2021

Copyright: © 2021 Fornili et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Data cannot be shared publicly. Data are available from Bioethics Committees of the University of Pisa, Florence, Turin, Genoa and Messina (contact via the corresponding author and the Bioethics Committee of the University of Pisa comitatobioetico@unipi.it) for researchers who meet the criteria for access to confidential data.

RESEARCH ARTICLE

Psychological distress in the academic population and its association with sociodemographic and lifestyle characteristics during COVID-19 pandemic lockdown: Results from a large multicenter Italian study

Marco Fornili¹, Davide Petri¹, Carmen Berrocal², Giuseppe Fiorentino³, Fulvio Ricceri⁴, Alessandra Macciotta⁴, Andreina Bruno⁵, Domenica Farinella⁶, Michela Baccini⁷, Gianluca Severi^{7,8,9©}, Laura Baglietto^{1©}*

- 1 Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, 2 Department of Surgical, Medical and Molecular Pathology, and Critical Care Medicine, University of Pisa, Pisa, Italy, 3 Italian Naval Academy, Livorno, Italy, 4 Department of Clinical and Biological Science, University of Turin, Turin, Italy, 5 Department of Education Science, University of Genoa, Genoa, Italy, 6 Department of Political Science and Law, University of Messina, Messina, Italy, 7 Department of Statistics, Informatics, Applications "Giuseppe Parenti", University of Florence, Florence, Italy, 8 CESP, Fac. de Médecine—Univ. Paris-Sud, Fac. de Médecine—UVSQ, INSERM, Université Paris-Saclay, Villejuif, France, 9 Gustave Roussy, Villejuif, France
- These authors contributed equally to this work.
- * laura.baglietto@unipi.it

Abstract

Measures implemented in many countries to contain the COVID-19 pandemic resulted in a change in lifestyle with unpredictable consequences on physical and mental health. We aimed at identifying the variables associated with psychological distress during the lockdown between April and May 2020 in the Italian academic population. We conducted a multicenter cross-sectional online survey (IO CONTO 2020) within five Italian universities. Among about 240,000 individuals invited to participate through institutional communications, 18 120 filled the questionnaire. Psychological distress was measured by the selfadministered Hospital Anxiety and Depression Scale (HADS). The covariates collected included demographic and lifestyle characteristics, trust in government, doctors and scientists. Associations of covariates with influenza-like symptoms or positive COVID-19 test and with psychological distress were assessed by multiple regression models at the local level; a meta-analysis of the results was then performed. Severe levels of anxiety or depression were reported by 20% of the sample and were associated with being a student or having a lower income, irrespective of their health condition and worries about contracting the virus. The probability of being severely anxious or depressed also depended on physical activity: compared to those never exercising, the highest OR being for those who stopped during lockdown (1.53; 95% CI, 1.28 to 1.84) and the lowest for those who continued (0.78; 95% CI, 0.64 to 0.95). Up to 21% of severe cases of anxiety or depression might have been avoided if during lockdown participants had continued to exercise as before. Socioeconomic insecurity contributes to increase mental problems related to the COVID-19 pandemic and

Funding: The author(s) received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

to the measures to contain it. Maintaining or introducing an adequate level of physical activity is likely to mitigate such detrimental effects. Promoting safe practice of physical activity should remain a public health priority to reduce health risks during the pandemic.

Introduction

In March 2020 in Italy, a nationwide quarantine was introduced as a measure to contain the transmission of the COVID-19 pandemic. The measure caused a radical change in the lifestyle of individuals, with unpredictable consequences on their mental and physical health. The impact that isolation and social distancing can have on lifestyle habits and their consequences on the levels of anxiety and depression has been studied in very specific contexts [1]. During the lockdown periods, stress, forced physical inactivity and lifestyle changes can produce changes in metabolic parameters and obesity, leading to an increase in risk of cardiovascular events [2], post-traumatic stress disorder and depressive symptomatology [3–5]. Little is known about the effect of quarantine on the academic community, including students and employees, that in the context of the COVID-19 pandemic did not represent a group at high risk of severe health consequences. However, given the high incidence of emotional disorders among university students, the impact of lockdown measures on their mental health can be particularly relevant [6, 7]. A few studies investigated the effect of COVID-19 pandemic on mental health of student during confinement [8–11]. A nationwide survey conducted in France among more than 69,000 university students reported prevalences of 27% and 16% for anxiety and depression respectively [12]. A study conducted during the COVID-19 lockdown on 2,530 students and workers of a Spanish university found that 21%, 34% and 28% of the participants suffered from anxiety, depression and stress, respectively [13]. Fear of becoming infected, worries for friends and relatives, economic uncertainty, loneliness can all be determinants of increased anxiety and depression during lockdown [5]. Other factors that can contribute to increase emotional distress are prolonged physical inactivity and other changes in lifestyle and working routine [14, 15]; the effects of physical activity on stress and anxiety during the COVID-19 pandemic have already been discussed in literature [16].

The aim of our study was to measure the level of psychological distress during the lockdown period in response to the COVID-19 pandemic and investigate its association with sociodemographic characteristics and lifestyle in a large sample of the Italian academic population.

Methods

Study design

A large cross-sectional online survey was conducted in five Italian universities between April and May 2020. The study was approved by the Committee on Bioethics of the University of Pisa (Review No. 10/2020, 3rd of April 2020). Participants provided informed consent before completing the questionnaire. The survey included sections designed to assess socio-demographic characteristics, health status, psychological distress and changes related to work and lifestyle in the academic population during the nationwide COVID-19 lockdown that started on the 10th of March 2020. Data were collected through the Moodle learning platform of each university, anonymized and analyzed at the local level. Then the results from each participating center were sent to the Unit of Medical Statistics of the University of Pisa where a meta-analysis was conducted.

Study population

Among about 220,000 students and 20,000 employees of the Italian universities of Turin and Genoa (Northern Italy), Florence and Pisa (Central Italy) and Messina (Southern Italy) invited to participate in the online survey, 6% of the students and 19% of the employees filled the questionnaire. After excluding 1,046 participants who did not fill the section on psychological distress, 17,074 were left for the analysis.

Measurements and covariates

Students and employees of the participating universities have been invited to fill the question-naire through institutional communications. The survey took 20 to 30 minutes to be completed. The structured online survey included questions about socio-demographic characteristics of participants, housing, habits and symptoms related to COVID-19 and lifestyle during quarantine. Information about general health status of participants was collected (questions about 12 chronic conditions were asked) together with their influenza-like symptoms (temperature, cough or respiratory problems) or diagnosis of COVID-19 during quarantine. Psychological distress, one of the main indicators of mental health, was assessed through the Italian version of the Hospital Anxiety and Depression Scale (HADS) [17–19], a validated instrument composed by 7 items related to anxiety and 7 items related to depression. Each item is rated on a 4-score Likert scale ranging from 0 to 3, resulting in a total score ranging from 0 to 21 in each of the two components. On both subscales of anxiety and depression, subjects with scores \leq 7, 8–10 and \geq 11 were classified as normal, borderline cases or severe cases, respectively [20].

Statistical analysis

Data collected at each participating center were anonymized for statistical analysis. Categorical variables were described as absolute frequencies and percentages. The heterogeneity of the distribution of each variable across universities was assessed by Fisher's exact test. The associations of covariates with influenza-like symptoms or positive COVID-19 test and HADS scores were assessed by logistic and linear regression models, respectively. For both analyses two models were fitted: one including each covariate at a time together with age and sex (Model 1); the other including all covariates, except education level in the family and cohabitants (Model 2). Multinomial logistic regressions were fitted to estimate the odds ratios (ORs) of borderline versus normal and severe versus normal levels of anxiety and depression for categories of physical activity; logistic regressions were fitted to estimate the ORs of either severe level of anxiety or depression versus normal level of anxiety and depression; regression models were adjusted for all covariates. The number of severe cases of anxiety and depression predicted by the logistic models were calculated under the observed distribution of physical activity during lockdown and under the hypothetical scenario where the level of physical activity during lockdown were the same as before; then the percentage of severe cases that would have been avoided by continuing to exercise were calculated. The corresponding standard errors were estimated through a non-parametric bootstrap.

First, we fitted separate models for each participating center; then, we combined the parameters estimated from the models—i.e. linear coefficients and estimated marginal means (EMMs) from the linear models; ORs and percent reduction of the number of severe cases from the logistic regression models—through a random effect meta-analysis.

All statistical analyses were conducted with the R statistical software, version 4.0.2, and all tests were two-sided at the 0.05 significance level.

Results

Among the 18,120 participants 9,062 (50%) were from universities in Northern Italy, 8,264 (46%) from Central Italy and 794 (4%) from Southern Italy. Socio-demographic and lifestyle characteristics of participants are reported in <u>Table 1</u>. Sixty-seven percent of the participants, 67% were females and 78% were students. Overall, 23% of participants reported having suffered influenza-like symptoms (temperature, cough, breathing problems).

The odds of having suffered from influenza-like symptoms were higher in younger subjects (OR for 10-year increase of age, 0.87; 95% CI, 0.80 to 0.95), in males than in females (OR, 1.19; 95% CI, 1.02 to 1.38), in individuals with comorbidities (OR for 1 versus no comorbidities, 1.71; 95% CI, 1.54 to 1.91; OR for 2 or more versus no comorbidities, 2.19; 95% CI, 1.73 to 2.77), in those worried to contract the virus (OR, 1.23; 95% CI, 1.06 to 1.42), in those judging the measures by the government not adequate (OR for insufficient versus adequate measures, 1.31; 95% CI, 1.11 to 1.53) and in individuals with lower levels of physical activity during lockdown (OR for >4 versus <1 hours per week, 0.71; 95% CI, 0.62 to 0.81; S1 Table).

The HADS questionnaire was filled by 17, 074 (94%) participants; for anxiety, borderline and severe levels were reported by 16% and 15% of respondents; for depression, 14% and 8%; these figures resulted in 20% of participants being either severely anxious or severely depressed. The results of the linear association between overall psychological distress and socio-demographic and lifestyle variables are reported in Table 2. All variables, with the exception of the presence of cohabitants, were significantly associated with the psychological distress both in the univariate and in the multiple model. Younger individuals, females and students had higher levels of psychological distress. Having a low income or low level of education in the family, both proxies of the socio-economic status, were related to higher levels of psychological distress; similar results were observed for sharing the house with old or disabled people. Working in contact with the public was associated with lower HADS levels, whereas having cohabitants working with the public was associated with higher levels. Also, higher HADS levels were associated with having a frail health, having experienced COVID-like symptoms, and being worried to become infected; on the contrary, lower HADS levels were associated with the belief that the measures adopted were adequate and with trust in doctors and institutions.

HADS scores significantly decreased with levels of physical activity during quarantine and the association was not confounded by any of the variables we were able to adjust for. In particular, compared with those who did not exercised during quarantine, those reporting the highest level of physical activity had on average a HADS score 2.46 points lower (95% CI, 2.07 to 2.85; Table 2). In order to account for the effect of physical activity before quarantine, we fitted a model with both variables and their interaction. According to this model, those who performed physical activity before quarantine and then stopped to exercise had higher HADS scores than those who never exercised (EMM, 14.5; 95% CI, 14.2 to 14.8, versus 13.0; 95% CI, 12.6 to 13.4). Physical activity during quarantine was inversely associated with HADS scores (p < 0.001) irrespective of the physical activity status before quarantine, but its effects were more pronounced among those who exercised before quarantine than among those who did not: the estimated differences of the HADS score between those with the highest versus lowest level of physical activity were -1.8 (95% CI, -2.8 to -0.8) and -3.0% (95% CI, -3.4 to -2.5) in the group who did not exercised before lockdown and in those who did, respectively. As a result, HADS scores in those with the highest level of physical activity were very similar in the two groups (Table 3).

<u>Table 4</u> reports the association between anxiety and depression status and physical activity before and during quarantine in terms of OR of being borderline or being a severe case: compared to those who never exercised neither before nor during lockdown, the highest OR of

Table 1. General characteristics of participants.

	All		Turin	Genoa	Florence	Pisa	Messina	P-value
Variable	N	%	%	%	%	%	%	
Age categories (years)								< 0.001
<30	13,043	72.4	76.9	71.2	70.7	74.5	45.6	
30–39	1,413	7.8	7.3	8.3	7.8	7.7	9.5	
40+	3,555	19.7	15.7	20.5	21.4	17.8	44.9	
Gender								
Female	11,980	67.2	73.6	66.8	68.0	62.5	63.3	< 0.001
Male	5,849	32.8	26.4	33.2	32.0	37.5	36.7	
Position								
Student	14,028	78.3	80.4	78.1	77.8	80.3	54.1	< 0.001
Technical/administrative staff	1,810	10.1	8.8	9.8	11.1	8.8	24.7	
Teaching/research staff	2,088	11.6	10.8	12.1	11.0	10.9	21.1	
Household monthly income	2,000	1110	10.0	12.1	11.0	10.5	21.1	
Low (<1500 euros)	3,619	24.7	24.5	24.5	22.7	25.6	28.1	0.003
Medium (between 1501 and 3000 euros)	6,342	43.3	43.4	43.9	43.2	43.8	36.8	
High (>3000 euros)	4,684	32.0	32.1	31.5	34.1	30.6	35.1	
Education family (Which is the highest level of				31.3	31.1	30.0	33.1	
Primary Primary	453	2.6	2.8	2.2	2.9	2.4	3.1	< 0.001
Secondary	5,734	32.3	34.4	33.0	31.6	31.2	27.0	₹0.001
University degree	7,362	41.5	42.5	41.7	41.2	41.4	36.8	
Master degree	1,048	5.9	5.9	6.0	4.9	6.6	4.4	
PhD or equivalent	3,138	17.7	14.4	17.1	19.4	18.4	28.7	
House with a garden or balcony	3,136	17.7	14.4	17.1	19.4	10.4	26.7	
No	2,125	11.9	8.7	15.7	10.8	12.6	7.8	< 0.001
Yes	15,664	88.1	91.3	84.3	89.2	87.4	92.2	<0.001
Cohabitants	13,004	00.1	91.3	04.3	69.2	07.4	92.2	
	076		F 4	5.4	4.0	5 0	<i>C</i> 4	0.25
No V.	976	5.5	5.4	5.4	4.8	5.8	6.4	0.35
Yes	16,871	94.5	94.6	94.6	95.2	94.2	93.6	
Old or disabled (Do you live with old or disable		0.4.7	05.4	04.2	05.0	05.2	70.2	.0.001
No	14,138	84.7	85.4	84.2	85.0	85.3	78.3	< 0.001
Yes	2,555	15.3	14.6	15.8	15.0	14.7	21.7	
Currently working with the public (Are you cu								
No	17,254	95.5	95.1	94.8	95.5	96.7	94.1	< 0.001
Yes	805	4.5	4.9	5.2	4.5	3.3	5.9	
Cohabitants currently working with the public								
No	10,154	58.0	51.3	56.4	56.1	64.7	64.6	< 0.001
Yes	7,345	42.0	48.7	43.6	43.9	35.3	35.4	
General health (number of reported existing h	1	T						
0	12,538	69.2	68.8	69.0	69.4	70.9	60.1	< 0.001
1	3,838	21.2	22.1	21.1	20.8	20.6	22.3	
2+	1,744	9.6	9.1	10.0	9.7	8.6	17.6	
Symptoms (Since the beginning of the quarant respiratory problems)	ine have you bee	n diagnosed	with COVID	-19 or did you	suffer of any of t	the following	g symptoms: feve	er, cough,
No	13,499	77.3	75.1	75.9	79.6	78.2	84.9	< 0.001
Yes	3,954	22.7	24.9	24.1	20.4	21.8	15.1	
Worries (Are you worried to contract the virus		1		I			1	
No	12,238	78.8	78.9	75.2	81.5	79.7	83.6	< 0.001

(Continued)

Table 1. (Continued)

	All		Turin	Genoa	Florence	Pisa	Messina	P-value
Variable	N	%	%	%	%	%	%	
Yes	3,291	21.2	21.1	24.8	18.5	20.3	16.4	
Adequacy of the measures (How do you judg	ge the measures ad	opted by the	government	to contain the	spreading of the	infection?)		
Adequate	7,351	42.4	36.5	39.2	46.2	45.8	56.3	< 0.001
Insufficient	8,971	51.7	57.4	54.5	46.4	49.2	39.3	
Excessive	1,035	6.0	6.1	6.3	7.4	5.1	4.5	
Trust in doctors (Do you trust medical doct	ors?)							
No	778	4.4	3.3	4.6	4.8	3.8	11.1	< 0.001
Yes	17,100	95.6	96.7	95.4	95.2	96.2	88.9	
Trust in scientists (Do you trust scientists?)								
No	742	4.2	3.0	4.8	4.8	3.3	11.3	< 0.001
Yes	17,077	95.8	97.0	95.2	95.2	96.7	88.7	
Trust in the government (Do you trust the g	governments?)							
No	5,791	32.5	30.6	36.4	31.4	29.4	46.1	< 0.001
Yes	12,011	67.5	69.4	63.6	68.6	70.6	53.9	
Physical activity during lockdown (hours pe	er week)							
<1h	6,914	38.5	38.1	36.6	36.5	39.0	56.4	< 0.001
1-2h	3,991	22.2	21.6	21.1	22.6	23.3	23.7	
3-4h	3,777	21.0	21.2	21.9	21.4	21.4	11.6	
>4h	3,266	18.2	19.2	20.4	19.4	16.3	8.3	
HADS-anxiety categories								
Normal	11,301	68.6	65	70.4	69.1	70.2	65.4	< 0.001
Borderline	2,675	16.2	17.2	15.3	16.7	15.8	17.4	
Severe	2,501	15.2	17.8	14.3	14.3	13.9	17.1	
HADS-depression categories								
Normal	11,989	78.6	78.4	78.9	77.4	79.4	75.8	0.33
Borderline	2,099	13.8	14.1	13.2	14.3	13.3	16.1	
Severe	1,168	7.7	7.5	7.9	8.3	7.2	8.1	
HADS categories			·	·				
Normal	11,997	80.3	78.6	80.6	81.2	81.4	77.5	0.006
Severe anxiety or severe depression	2,945	19.7	21.4	19.4	18.8	18.6	22.5	

https://doi.org/10.1371/journal.pone.0248370.t001

being severely anxious or severely depressed was observed in those who stopped exercising (OR, 1.53; 95% CI, 1.28 to 1.84). Performing physical activity during lockdown was associated with a lower risk of being severely anxious or severely depressed in both groups: compared to those who never exercised, the odds for those who exercised during quarantine were 11% lower, although not statistically significant, if they were not physically active before quarantine, (OR, 0.89; 95% CI, 0.71 to 1.13) and 22% if they were physically active also before quarantine (OR, 0.78; 95% CI, 0.64 to 0.95). If during quarantine all individuals could continue to perform physical activity with the same frequency as before, the number of severe cases in the study population would have been 14% lower for anxiety (95% CI, 7 to 21%) and 21% lower for depression (95% CI, 10 to 32%). Similar results have been obtained for the two HADS subscales anxiety and depression separately (S2–S5 Tables).

Discussion and conclusions

The results of this large cross-sectional study highlight the implications of quarantine on psychological distress in the adult population. Twenty percent of the participants reported severe

Table 2. Linear regression of HADS.

		Model 1	Model 2			
Variable	Categorical Pseudocontinuo		ous	Categorical	Pseudocontinuous	
	Coefficient (95% CI)	Coefficient (95% CI)	P-value	Coefficient (95% CI)	Coefficient (95% CI)	P-value
Age (10-year increase)	-0.90 (-1.00 to -0.80)		< 0.001	-1.18 (-1.37 to -0.98)		< 0.001
Gender						
Female	Ref		< 0.001	Ref		< 0.001
Male	-2.66 (-2.91 to -2.42)			-2.42 (-2.71 to -2.12)		
Position						
Student	Ref	-0.79 (-1.04 to -0.54)	< 0.001	Ref	-0.32 (-0.61 to -0.03)	0.03
Technical/administrative staff	-0.91 (-1.53 to -0.29)			-0.53 (-1.21 to 0.15)		
Teaching/research staff	-1.61 (-2.12 to -1.09)			-0.70 (-1.29 to -0.11)		
Income						
Low	Ref	-0.74 (-0.91 to -0.57)	< 0.001	Ref	-0.28 (-0.47 to -0.09)	0.004
Medium	-0.92 (-1.23 to -0.60)			-0.22 (-0.57 to 0.12)		
High	-1.50 (-1.84 to -1.16)			-0.55 (-0.93 to -0.17)		
Education level in the family						
Primary	Ref	-0.31 (-0.45 to -0.18)	< 0.001			
Secondary	-0.69 (-1.76 to 0.38)					
University degree	-1.16 (-2.20 to -0.12)					
Master degree	-0.79 (-2.12 to 0.55)					
PhD or equivalent	-1.67 (-2.96 to -0.38)					
House with a garden or balcony						
No	Ref		< 0.001	Ref		< 0.001
Yes	-1.63 (-2.12 to -1.14)			-1.34 (-1.77 to -0.90)		
Cohabitants						
No	Ref		0.80			
Yes	-0.12 (-1.08 to 0.84)					
Old or disabled cohabitants						
No	Ref		< 0.001	Ref		0.009
Yes	0.91 (0.54 to 1.29)			0.50 (0.12 to 0.87)		
Currently working with the public	:					
No	Ref		< 0.001	Ref		0.004
Yes	-1.03 (-1.57 to -0.48)			-1.25 (-2.12 to -0.39)		
Cohabitants currently working wi	th the public					
No	Ref		0.004	Ref		< 0.001
Yes	0.35 (0.11 to 0.59)			0.51 (0.23 to 0.80)		
General health (number of comor	bidities)					
0	Ref	2.26 (1.84 to 2.69)	< 0.001	Ref	1.82 (1.34 to 2.30)	< 0.001
1	2.14 (1.62 to 2.66)			1.91 (1.24 to 2.59)		
2+	4.62 (3.78 to 5.47)			3.55 (2.74 to 4.37)		
Symptoms	,			, , , , , , , , , , , , , , , , , , , ,		
No	Ref		< 0.001	Ref		< 0.001
Yes	1.95 (1.64 to 2.25)			1.25 (0.88 to 1.63)		
Worries	,	ı		,		
No	Ref		< 0.001	Ref		< 0.001
Yes	2.80 (2.50 to 3.10)			2.35 (2.02 to 2.69)		
Adequacy of the measures	(1		, (1	1
Adequate	Ref	1.64 (1.43 to 1.85)	< 0.001	Ref	1.14 (0.90 to 1.37)	< 0.001
	1					(Continue

(Continued)

Table 2. (Continued)

		Model 1	Model 2			
Variable	Categorical Pseudocontinuous		ous	Categorical	Pseudocontinuous	
	Coefficient (95% CI)	Coefficient (95% CI)	P-value	Coefficient (95% CI)	Coefficient (95% CI)	P-value
Insufficient	1.64 (1.41 to 1.88)			1.05 (0.76 to 1.34)		
Excessive	3.22 (2.52 to 3.92)			2.42 (1.59 to 3.25)		
Trust in doctors						
No	Ref		< 0.001			
Yes	-3.38 (-4.11 to -2.64)					
Trust in scientists						
No	Ref		< 0.001			
Yes	-2.65 (-3.49 to -1.82)					
Trust in the government						
No	Ref		< 0.001			
Yes	-1.85 (-2.18 to -1.53)					
Trust in doctors, scientists and the	ne government					
No	Ref		< 0.001	Ref		< 0.001
Yes	-1.89 (-2.23 to -1.54)			-1.32 (-1.73 to -0.92)		
Physical activity during quaranti	ne					
<1h	Ref	-0.93 (-1.03 to -0.83)	< 0.001	Ref	-0.86 (-0.98 to -0.74)	< 0.001
1-2h	-1.49 (-1.80 to -1.19)			-1.30 (-1.66 to -0.94)		
3-4h	-2.43 (-2.74 to -2.12)			-2.09 (-2.46 to -1.71)		
>4h	-2.60 (-2.93 to -2.26)			-2.46 (-2.85 to -2.07)		

Model 1: linear regression adjusted for age and sex; Model 2: linear regression adjusted for age and sex and all variables in the table. Model 2 is based on the subsample of 9,091 participants with no missing value in any of the variables in the table.

https://doi.org/10.1371/journal.pone.0248370.t002

levels of anxiety or depression. The factors associated with a higher level of psychological distress were being a student, having a low income or a low educational level within the family, having suffered of influenza-like symptoms or having a frail health, living with older or disabled people; all the observed associations were independent of the fear of being infected by the virus. Psychological distress was associated with distrust of the government and medical and scientific community; individuals reporting the higher level of distress were also those who believed that the measures implemented to contain the spreading of the virus were inadequate, either insufficient or too strict. With regard to physical activity, those who stopped exercising during quarantine had higher HADS scores. On the contrary, being able to perform some level of physical activity during quarantine was associated with lower HADS scores, irrespective of previous level of physical activity.

Table 3. HADS estimated marginal means (EMMs) by levels of physical activity.

	Physical activity before lockdown				
	Less than one hour per week	At least one our per week			
	EMM (95% CI)	EMM (95% CI)			
Physical activity during lockdown					
Less than 1 hour per week	13.0 (12.6 to 13.4)	14.5 (14.2 to 14.8)			
1–2 hours per week	12.4 (11.9 to 13.0)	12.6 (12.2 to 13.0)			
3–4 hours per week	11.6 (11.0 to 12.2)	11.8 (11.5 to 12.2)			
More than 4 hours per week	11.2 (10.1 to 12.4)	11.5 (11.1 to 11.8)			

https://doi.org/10.1371/journal.pone.0248370.t003

Table 4. Effect of physical activity on psychological distress: Odds ratio of being borderline versus normal and severe versus normal.

	Level of Physical activity <u>before</u> lockdown						
	Less than one hour per week	More than one hour per wee					
	OR (95% CI)	OR (95% CI)					
Level of Physical activity during	Level of Physical activity during lockdown						
Anxiety							
Borderline versus normal							
Less than 1 hour per week	Ref	1.20 (0.92 to 1.56)					
More than 1 hours per week	0.81 (0.66 to 1.00)	0.82 (0.69 to 0.97)					
Severe versus normal							
Less than 1 hour per week	Ref	1.52 (1.25 to 1.86)					
More than 1 hours per week	0.95 (0.74 to 1.23)	0.85 (0.71 to 1.03)					
Depression							
Borderline versus normal							
Less than 1 hour per week	Ref	1.39 (1.15 to 1.68)					
More than 1 hours per week	0.72 (0.53 to 0.97)	0.68 (0.57 to 0.81)					
Severe versus normal							
Less than 1 hour per week	Ref	1.71 (1.34 to 2.17)					
More than 1 hours per week	0.56 (0.41 to 0.75)	0.51 (0.40 to 0.65)					
Anxiety or depression							
Severe anxiety or severe depression versu	is normal						
Less than 1 hour per week	Ref	1.53 (1.28 to 1.84)					
More than 1 hours per week	0.89 (0.71 to 1.13)	0.78 (0.64 to 0.95)					

https://doi.org/10.1371/journal.pone.0248370.t004

The proportion of participants in our survey reporting severe levels of anxiety or depression is similar to the proportions observed in other studies targeting European university communities: in a French and in a Spanish study, anxiety amounted to 27% and 21% and depression to 16% and 34%, respectively [12, 13].

In our population, those mostly affected by psychological distress were students and individuals with lower income, representing two groups of individuals highly suffering the occupational and economic uncertainty associated to the pandemic. Depression is known to be associated with the socio-economic status [21] and others reported that, during the COVID-19 pandemic as well as during other disasters, mental disorders were not evenly distributed in the population, being their incidence higher among disadvantaged groups of the population [22, 23].

The observed association between psychological distress and distrust of institutions, including government and medical staff, could be explained by the fact that people with an external locus of control—that is individuals believing that outcomes in their lives are determined by external factors—tend to cope worse with negative changes than those with an internal locus of control—that is individuals believing that outcomes in their lives depend largely on their own actions [24–29].

Stratifying our sample by level of physical activity before the lockdown period, we observed that subjects able to exercise during quarantine reported lower psychological distress irrespective of their previous level of physical activity. The association between level of physical activity during the lockdown period and more severe levels of anxiety and depression has been reported by others [16, 30–34]. One large cross-sectional study among French university students found association of low levels of physical activity with anxiety and depression [12]; one

longitudinal study in the United Kingdom before and after lockdown showed positive association between change in perceived stress and change in sedentary behavior [10]. The evidence that mental health is associated with levels of physical activity independently of age and socio-economic status mainly comes from observational studies [15, 35] and clinical trials on the effect of exercise as treatment for depressions and anxiety [36–38]. Results from studies in animals and humans indicate that the effect of physical activity on depressive symptoms might be mediated through factors associated to monoamine metabolism and immune and neurogenic markers [39]. Not surprisingly, the cessation of physical activity has a negative impact on mental health [39, 40]. Accordingly, our data showed that those who stopped to exercise due to home confinement and closure of sport facilities experienced the most severe psychological distress. Although our results are in line with the literature supporting the hypothesis that reducing physical activity increases psychological distress, we cannot rule out a mechanism of reverse causality, resulting from a reduction of physical activity in the individuals more anxious or depressed.

The main strength of our study is its large sample size and the wide range of variables assessed, allowing to investigate the role of many potential determinants of psychological distress and to control for potential confounding. We targeted the entire university community, including students as well as the teaching, technical and administrative staff, in order to have access to a wide range of exposures and to be able to compare the conditions of students with those of the working individuals. The instrument used to assess the level of psychological distress was developed for hospitalized patients but is able to capture anxiety and depression symptoms in other contexts and samples. Indeed, the HADS proved to have good construct validity and other psychometric properties not only in clinical but also in general population samples [19, 20].

The representativeness of our sample at the level of the nationwide academic population is supported by the multicenter study design that we have adopted. However, because the survey has been completed on voluntary basis, we cannot exclude that a selection bias of participants based on their psychological distress levels might have occurred. However, there is no reason to believe that the potential selection might have affected the association between psychological distress and the predictors. Moreover, the large number of variables collected allowed to adjust the analyses for a wide range of potential confounders.

The negative impact of the COVID-19 pandemic on mental health is a matter of concern and experts urge for action to monitor and control its negative effects especially among most vulnerable individuals [41]. The knowledge accumulated from large epidemiological studies conducted during the first wave of COVID-19 can contribute to face future waves of infection or epidemic by identifying highly susceptible groups and possible intervention approaches. The study IO CONTO 2020, investigating the factors associated with anxiety and depression in a large sample of individuals, is placed in this perspective of action. Identifying economic instability among the factors associated to the increased risk of psychological impairment, we addressed once more the well-known consequences of social impairment on the health of a population. In the light of the finding that physical activity could at least partially relieve the psychological burden of a health crisis, we might suggest that future measures adopted to contain the spreading of a disease guarantee the access to outdoor spaces or safe indoor environment where citizens can perform their exercise. Further investigations are needed to quantify the long-term impact that COVID-19 quarantine had on the population.

Supporting information

S1 Table. Logistic regression of influenza-like symptoms during quarantine (temperature, cough or respiratory problems) or diagnosis of COVID-19.

(DOCX)

S2 Table. Linear regression of HADS-anxiety. (DOCX)

S3 Table. Linear regression of HADS-depression.

(DOCX)

S4 Table. HADS-anxiety estimated marginal means (EMMs) by levels of physical activity. (DOCX)

S5 Table. HADS-depression estimated marginal means (EMMs) by levels of physical activity.

(DOCX)

Acknowledgments

We thank the universities of Pisa, Florence, Genoa, Turin and Messina for their administrative and technical support to the study IO CONTO 2020 and all participants for their time.

Author Contributions

Conceptualization: Carmen Berrocal, Giuseppe Fiorentino, Andreina Bruno, Gianluca Severi, Laura Baglietto.

Data curation: Marco Fornili, Davide Petri, Giuseppe Fiorentino.

Formal analysis: Marco Fornili, Davide Petri, Gianluca Severi, Laura Baglietto.

Investigation: Davide Petri, Giuseppe Fiorentino, Fulvio Ricceri, Alessandra Macciotta, Andreina Bruno, Domenica Farinella, Michela Baccini, Gianluca Severi, Laura Baglietto.

Methodology: Marco Fornili, Davide Petri, Carmen Berrocal, Giuseppe Fiorentino, Fulvio Ricceri, Alessandra Macciotta, Andreina Bruno, Domenica Farinella, Michela Baccini, Gianluca Severi, Laura Baglietto.

Writing - original draft: Marco Fornili, Gianluca Severi, Laura Baglietto.

Writing – review & editing: Marco Fornili, Davide Petri, Carmen Berrocal, Giuseppe Fiorentino, Fulvio Ricceri, Alessandra Macciotta, Andreina Bruno, Domenica Farinella, Michela Baccini, Gianluca Severi, Laura Baglietto.

References

- Barbisch D, Koenig KL, Shih FY. Is There a Case for Quarantine? Perspectives from SARS to Ebola. Disaster Med Public Health Prep [Internet]. 2015 Feb 18 [cited 2020 Sep 22]; 9(5):547–53. Available from: https://pubmed.ncbi.nlm.nih.gov/25797363/ https://doi.org/10.1017/dmp.2015.38 PMID: 25797363
- Mattioli AV, Ballerini Puviani M, Nasi M, Farinetti A. COVID-19 pandemic: the effects of quarantine on cardiovascular risk [Internet]. Vol. 74, European Journal of Clinical Nutrition. Springer Nature; 2020 [cited 2020 Sep 22]. p. 852–5. Available from: https://pubmed.ncbi.nlm.nih.gov/32371988/ https://doi. org/10.1038/s41430-020-0646-z PMID: 32371988
- Hawryluck L, Gold WL, Robinson S, Pogorski S, Galea S, Styra R. SARS control and psychological effects of quarantine, Toronto, Canada. Emerg Infect Dis [Internet]. 2004 [cited 2020 Sep 22]; 10 (7):1206–12. Available from: https://pubmed.ncbi.nlm.nih.gov/15324539/ https://doi.org/10.3201/ eid1007.030703 PMID: 15324539
- Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence [Internet]. Vol. 395, The Lancet. Lancet Publishing Group; 2020 [cited 2020 Sep 22]. p. 912–20. Available from: https://pubmed.ncbi. nlm.nih.gov/32112714/

- Shi L, Lu ZA, Que JY, Huang XL, Liu L, Ran MS, et al. Prevalence of and Risk Factors Associated With Mental Health Symptoms Among the General Population in China During the Coronavirus Disease 2019 Pandemic. JAMA Netw open [Internet]. 2020 Jul 1 [cited 2020 Sep 22]; 3(7):e2014053. Available from: https://pubmed.ncbi.nlm.nih.gov/32609353/ https://doi.org/10.1001/jamanetworkopen.2020. 14053 PMID: 32609353
- Araújo FJ de O, de Lima LSA, Cidade PIM, Nobre CB, Neto MLR. Impact Of Sars-Cov-2 And Its Reverberation In Global Higher Education And Mental Health. Vol. 288, Psychiatry Research. Elsevier Ireland Ltd; 2020.
- Sahu P. Closure of Universities Due to Coronavirus Disease 2019 (COVID-19): Impact on Education and Mental Health of Students and Academic Staff. Cureus [Internet]. 2020 Apr 4 [cited 2020 Sep 22]; 12(4):e7541. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32377489 https://doi.org/10.7759/ cureus.7541 PMID: 32377489
- 8. Khan AH, Sultana MS, Hossain S, Hasan MT, Ahmed HU, Sikder MT. The impact of COVID-19 pandemic on mental health & wellbeing among home-quarantined Bangladeshi students: A cross-sectional pilot study. J Affect Disord. 2020 Dec 1; 277:121–8. https://doi.org/10.1016/j.jad.2020.07.135 PMID: 32818775
- Saravanan C, Mahmoud I, Elshami W, Taha MH. Knowledge, Anxiety, Fear, and Psychological Distress About COVID-19 Among University Students in the United Arab Emirates. Front Psychiatry [Internet]. 2020 Oct 22 [cited 2021 Feb 5]; 11:582189. Available from: /pmc/articles/PMC7642490/?report = abstract https://doi.org/10.3389/fpsyt.2020.582189 PMID: 33192728
- Savage MJ, James R, Magistro D, Donaldson J, Healy LC, Nevill M, et al. Mental health and movement behaviour during the COVID-19 pandemic in UK university students: Prospective cohort study. Ment Health Phys Act [Internet]. 2020; 19:100357. Available from: https://doi.org/10.1016/j.mhpa.2020.100357
- Faisal RA, Jobe MC, Ahmed O, Sharker T. Mental Health Status, Anxiety, and Depression Levels of Bangladeshi University Students During the COVID-19 Pandemic. Int J Ment Health Addict [Internet]. 2021 Jan 4 [cited 2021 Feb 5];1–16. Available from: https://doi.org/10.1007/s11469-020-00458-y
- 12. Wathelet M, Duhem S, Vaiva G, Baubet T, Habran E, Veerapa E, et al. Factors Associated With Mental Health Disorders Among University Students in France Confined During the COVID-19 Pandemic. JAMA Netw open [Internet]. 2020 Oct 1 [cited 2021 Feb 4]; 3(10):e2025591. Available from: https://pubmed.ncbi.nlm.nih.gov/33095252/ https://doi.org/10.1001/jamanetworkopen.2020.25591 PMID: 33095252
- Odriozola-González P, Planchuelo-Gómez Á, Irurtia MJ, de Luis-García R. Psychological effects of the COVID-19 outbreak and lockdown among students and workers of a Spanish university. Psychiatry Res. 2020 Aug 1;290. https://doi.org/10.1016/j.psychres.2020.113108 PMID: 32450409
- 14. Triguero-Mas M, Donaire-Gonzalez D, Seto E, Valentín A, Martínez D, Smith G, et al. Natural outdoor environments and mental health: Stress as a possible mechanism. Environ Res. 2017; 159:629–38. https://doi.org/10.1016/j.envres.2017.08.048 PMID: 28938204
- 15. Chekroud SR, Gueorguieva R, Zheutlin AB, Paulus M, Krumholz HM, Krystal JH, et al. Association between physical exercise and mental health in 1.2 million individuals in the USA between 2011 and 2015: a cross-sectional study. The Lancet Psychiatry. 2018 Sep 1; 5(9):739–46. https://doi.org/10.1016/S2215-0366(18)30227-X PMID: 30099000
- Dunca GE, Aver AR, Seto E, Tsang S. Perceived change in physical activity levels and mental health during COVID-19: Findings among adult twin pairs. PLoS One [Internet]. 2020 Aug 1 [cited 2020 Sep 22]; 15(8 August). Available from: https://pubmed.ncbi.nlm.nih.gov/32790745/
- 17. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand [Internet]. 1983 Jun 1 [cited 2021 Feb 9]; 67(6):361–70. Available from: http://doi.wiley.com/10.1111/j.1600-0447.1983.tb09716.x PMID: 6880820
- 18. Costantini M, Musso M, Viterbori P, Bonci F, Del Mastro L, Garrone O, et al. Detecting psychological distress in cancer patients: Validity of the Italian version of the Hospital Anxiety and Depression Scale. Support Care Cancer [Internet]. 1999 May [cited 2020 Sep 14]; 7(3):121–7. Available from: https://pubmed.ncbi.nlm.nih.gov/10335929/ https://doi.org/10.1007/s005200050241 PMID: 10335929
- Iani L, Lauriola M, Costantini M. A confirmatory bifactor analysis of the hospital anxiety and depression scale in an Italian community sample. Health Qual Life Outcomes [Internet]. 2014 Jun 5 [cited 2020 Oct 9]; 12(1). Available from: https://pubmed.ncbi.nlm.nih.gov/24902622/
- Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. J Psychosom Res. 2002 Feb 1; 52(2):69–77. https://doi.org/10. 1016/s0022-3999(01)00296-3 PMID: 11832252
- 21. Ettman CK, Cohen GH, Galea S. Is wealth associated with depressive symptoms in the United States? Ann Epidemiol [Internet]. 2020 Mar 1 [cited 2020 Sep 23]; 43:25-31.e1. Available from: https://pubmed.ncbi.nlm.nih.gov/32147320/ https://doi.org/10.1016/j.annepidem.2020.02.001 PMID: 32147320
- Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S. Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic. JAMA Netwopen [Internet]. 2020 Sep 1

- [cited 2020 Sep 23]; 3(9):e2019686. Available from: https://jamanetwork.com/ https://doi.org/10.1001/jamanetworkopen.2020.19686 PMID: 32876685
- 23. Goldmann E, Galea S. Mental health consequences of disasters. In: Annual Review of Public Health [Internet]. Annual Reviews Inc.; 2014 [cited 2020 Sep 23]. p. 169–83. Available from: https://pubmed.ncbi.nlm.nih.gov/24159920/
- Rotter JB. Generalized expectancies for internal versus external control of reinforcement. [Internet].
 Vol. 80, Psychological monographs. Psychol Monogr; 1966 [cited 2020 Sep 23]. p. 1–28. Available from: https://pubmed.ncbi.nlm.nih.gov/5340840/
- 25. Jain M, Singh S. Locus of Control and its Relationship with Mental Health and Adjustment among Adolescent Females. J Ment Heal Hum Behav. 2015; 20:16–21.
- 26. Benassi VA, Sweeney PD, Dufour CL. Is there a relation between locus of control orientation and depression? J Abnorm Psychol [Internet]. 1988 [cited 2020 Sep 23]; 97(3):357–67. Available from: https://pubmed.ncbi.nlm.nih.gov/3057032/ https://doi.org/10.1037//0021-843x.97.3.357 PMID: 3057032
- Presson P, Benassi V. Locus of control orientation and depressive symptomatology: A meta-analysis. J Soc Behav Pers. 1996; 11(1):201–12.
- Cheng C, Cheung SF, Chio JHM, Chan MPS. Cultural meaning of perceived control: A meta-analysis of locus of control and psychological symptoms across 18 cultural regions. Psychol Bull [Internet]. 2013 [cited 2020 Sep 23]; 139(1):152–88. Available from: https://pubmed.ncbi.nlm.nih.gov/22642229/
- 29. Khumalo T, Plattner IE. The relationship between locus of control and depression: A cross-sectional survey with university students in Botswana. South African J Psychiatry [Internet]. 2019 [cited 2020 Sep 17];25. Available from: /pmc/articles/PMC6424533/?report = abstract https://doi.org/10.4102/sajpsychiatry.v25i0.1221 PMID: 30899579
- Arora T, Grey I. Health behaviour changes during COVID-19 and the potential consequences: A minireview [Internet]. Vol. 25, Journal of Health Psychology. SAGE Publications Ltd; 2020 [cited 2020 Sep 17]. p. 1155–63. Available from: https://pubmed.ncbi.nlm.nih.gov/32551944/ https://doi.org/10.1177/ 1359105320937053 PMID: 32551944
- Maugeri G, Castrogiovanni P, Battaglia G, Pippi R, D'agata V, Palma A, et al. The impact of physical activity on psychological health during Covid-19 pandemic in Italy. 2017; Available from: https://doi.org/10.1016/j.heliyon.2020.e04315
- Jacob L, Tully MA, Barnett Y, Lopez-Sanchez GF, Butler L, Schuch F, et al. The relationship between
 physical activity and mental health in a sample of the UK public: A cross-sectional study during the
 implementation of COVID-19 social distancing measures. Ment Health Phys Act [Internet]. 2020 Oct 1
 [cited 2020 Sep 17];19. Available from: https://pubmed.ncbi.nlm.nih.gov/32834833/
- 33. Stanton R, To QG, Khalesi S, Williams SL, Alley SJ, Thwaite TL, et al. Depression, anxiety and stress during COVID-19: Associations with changes in physical activity, sleep, tobacco and alcohol use in Australian adults. Int J Environ Res Public Health [Internet]. 2020 Jun 1 [cited 2020 Sep 17]; 17(11):1–13. Available from: /pmc/articles/PMC7312903/?report = abstract
- Lesser IA, Nienhuis CP. The impact of COVID-19 on physical activity behavior and well-being of canadians. Int J Environ Res Public Health. 2020 Jun 1; 17(11). https://doi.org/10.3390/ijerph17113899 PMID: 32486380
- 35. Harvey SB, Overland S, Hatch SL, Wessely S, Mykletun A, Hotopf M. Exercise and the prevention of depression: Results of the HUNT cohort study. Am J Psychiatry [Internet]. 2018 Jan 1 [cited 2020 Sep 24]; 175(1):28–36. Available from: https://pubmed.ncbi.nlm.nih.gov/28969440/ https://doi.org/10.1176/appi.ajp.2017.16111223 PMID: 28969440
- Schuch FB, Vancampfort D, Richards J, Rosenbaum S, Ward PB, Stubbs B. Exercise as a treatment for depression: A meta-analysis adjusting for publication bias. J Psychiatr Res [Internet]. 2016 Jun 1 [cited 2020 Sep 17]; 77:42–51. Available from: https://pubmed.ncbi.nlm.nih.gov/26978184/ https://doi. org/10.1016/j.jpsychires.2016.02.023 PMID: 26978184
- Kvam S, Kleppe CL, Nordhus IH, Hovland A. Exercise as a treatment for depression: A meta-analysis [Internet]. Vol. 202, Journal of Affective Disorders. Elsevier B.V.; 2016 [cited 2020 Sep 17]. p. 67–86. Available from: https://pubmed.ncbi.nlm.nih.gov/27253219/ https://doi.org/10.1016/j.jad.2016.03.063 PMID: 27253219
- 38. Rebar AL, Stanton R, Geard D, Short C, Duncan MJ, Vandelanotte C. A meta-meta-analysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. Health Psychol Rev [Internet]. 2015 Aug 7 [cited 2020 Sep 25]; 9(3):366–78. Available from: https://pubmed.ncbi.nlm.nih.gov/25739893/https://doi.org/10.1080/17437199.2015.1022901 PMID: 25739893
- 39. Morgan JA, Olagunju AT, Corrigan F, Baune BT. Does ceasing exercise induce depressive symptoms? A systematic review of experimental trials including immunological and neurogenic markers [Internet]. Vol. 234, Journal of Affective Disorders. Elsevier B.V.; 2018 [cited 2020 Sep 24], p. 180–92. Available

- from: https://pubmed.ncbi.nlm.nih.gov/29529552/ https://doi.org/10.1016/j.jad.2018.02.058 PMID: 29529552
- 40. Weinstein AA, Koehmstedt C, Kop WJ. Mental health consequences of exercise withdrawal: A systematic review [Internet]. Vol. 49, General Hospital Psychiatry. Elsevier Inc.; 2017 [cited 2020 Sep 25]. p. 11–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28625704/ https://doi.org/10.1016/j.genhosppsych.2017.06.001 PMID: 28625704
- 41. Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science [Internet]. Vol. 7, The Lancet Psychiatry. Elsevier Ltd; 2020 [cited 2020 Sep 17]. p. 547–60. Available from: /pmc/articles/PMC7159850/?report = abstract