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Original Article

Psychological distress in adults with and without cystic fibrosis during the COVID-19 lockdown

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ABSTRACT

Background: Hundreds of papers have been published on the COVID-19 pandemic, and several of them on psychological themes connected with it, but very little is so far known on how adult patients with Cystic Fibrosis (pwCFs) are coping with this dramatic event.

Methods: An online questionnaire was developed according to the Italian validated COVID-19 Peritraumatic Distress Index (CPDI) and addressed to the general population (GP). A similar questionnaire, augmented with CF specific questions, targeted pwCFs. The two web-based surveys were accessible for some weeks during the lockdown mandated by the Italian government.

Results: The CF questionnaire was completed by 712 adult pwCFs (422 females), matched for sex and age with a 1/5 ratio to GP questionnaire respondents. Mild or medium distress affected 40.2% of pwCFs and 43.9% of GP controls, severe distress 5.3% of pwCFs and 6.2% of GP controls. The level of psychological distress was not correlated with the degree of pulmonary function impairment. When symptoms of anxiety and depression, and physical manifestations were independently analyzed, the control group featured a 55% higher level of mild-moderate anxiety symptoms. Signs of psychological distress, symptoms of anxiety and depression, and physical manifestations were significantly more frequent in female pwCFs compared to males, similarly to GP.

Conclusion: Adult pwCFs seem to have equal, and in some domains, lower levels of psychological distress than GP controls. This might be sustained by lifelong experiences in coping with the demands of their chronic disease. These results may orient future psychological interventions.

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1. Background

The COVID-19 pandemic deeply and quickly changed people's life, disrupting behaviors and habits of individuals and families. The impact of restrictive measures adopted in many countries to contain the outbreak was not limited to everyday life routine, but had psychological and psycho-social implications [1,2,3]. Fear of the disease and uncertainty have become new "feelings" to reckon with.

Psychological distress and disorders during COVID-19 quarantine have been reported to include emotional disturbance, depression, stress, low mood, irritability, insomnia, anger, emotional exhaustion and, occasionally, adjustment disorders and post-traumatic stress disorders [1,2,3,4].

In Italy, a study conducted during the initial phase of COVID-19 pandemic [5] reported high and very high levels of psychological distress compared to European epidemiological standards [6,7]. Again in Italy, a survey showed that although the vast majority of participants (99.09%) did not contract COVID-19, one third of them experienced symptoms of mild/moderate and severe peritraumatic distress [8].

Since the first appearance of COVID-19, it has been evident, and widely reported by the media, that individuals with concomitant diseases had higher mortality rates [9]. The worse survival rates in those with chronic conditions have been cause for concern in the Cystic Fibrosis (CF) community, who perceived the chronic lung infection peculiar to CF as a significant risk factor for poor COVID-19 outcomes. The higher vulnerability was apparently not confirmed by following reports [10,11,12,13], but these reassuring data were not available in the first months of the viral outbreak, when previous experiences referring to H1N1 influenza pointed instead to a risk of poor outcomes for people with Cystic Fibrosis (pwCFs)

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and SARS-CoV2 infection [14]. Such alarming scenario made pwCFs a group particularly at risk for feelings of uncertainty and fear of suffering a negative psychological impact, possibly higher than in the general population.

Italy has been affected by the COVID-19 outbreak earlier and more extensively than several other European countries [15,10] and lockdown measures were ordered by the government since early March. The population was asked to stay at home except for necessity, work, and health circumstances. In the following weeks daily cases and deaths related to COVID-19 kept increasing, with a peak of almost 8,000 deaths per week in early April. This dramatic progression put a strain on the whole society, but even more on pwCFs, who, besides insecurities about their vulnerability to COVID-19, suffered the interruption of scheduled clinical appointments at CF Centers [15].

The concomitance of all these circumstances called for an investigation on how pwCFs were coping with the unsettling events taking place during the period of maximal diffusion of the SARS-CoV2 infection and with the enforcement of quarantine. This case-control study used a web-based questionnaire to assess the impact of the COVID-19 pandemic and lockdown on mental and physical health in Italian adult pwCFs, and to compare them with a large sample from the general population.

2. Methods

2.1. The questionnaires

Two similar web-based questionnaires were used, the first addressing the Italian general population, named GP questionnaire, the second the Italian adult CF population, named CF questionnaire.

The GP questionnaire was developed by the Public Health Department of the Research Institute Mario Negri according to the COVID-19 Peritraumatic Distress Index (CPDI). The CPDI is an online compilation tool developed in China during the Wuhan COVID-19 epidemic [16].

The questionnaire was addressed to the general population and incorporated relevant diagnostic guidelines for specific stress disorders specified in the International Classification of Diseases, 11th Revision and expert psychiatric opinions. In addition to demographic data (i.e. gender, age, education and occupation), the CPDI inquired about the frequency of anxiety, depression, specific phobias, cognitive change, avoidance and compulsive behavior, physical symptoms and loss of social functioning in the previous two weeks.

CPDI has been translated into Italian using a standard forward-backward-translation procedure and offered online to 329 people (191 females and 137 males, aged 46.49 ± 13.58 years). The CPDI showed an internal-consistency of Cronbach's $\alpha = 0.916$. Content validity was judged satisfactory by two psychologists experienced in stress and trauma. The construct validity is given by the high correlation with the dimensions of Intrusion, Avoidance and Hyperarousal as measured by the Impact of Event Scale-Revised ($r = 0.63$, $r = 0.57$, $r = 0.71$, respectively) [8].

A 5-point Likert-type scale was employed, with higher scores indicating higher distress: 0 "never", 1 "occasionally", 2 "sometimes", 3 "often", 4 "most of the time". The score ranges from 0 to 100. A score between 28 and 52 indicates mild to moderate distress. A score ≥ 52 indicates severe distress. The 3 subscales cut-offs were for the 12 anxiety questions normal 0–24, mild/moderate 24–34, severe > 34 ; for the 8 depression questions normal 0–16, mild/moderate 17–23, severe > 23 ; for the 4 symptoms questions, normal 0–8, mild/moderate 9–12, severe > 12 .

The same cut-off points as in the original Chinese version were used to analyze psychological distress [16].

The CF questionnaire was an expanded version of the GP one. Authors RC, RP and CC included CF specific questions, for a total of 47 items, divided into three sections. The first section (items 1–14) interrogated about basic demographic data and health conditions during lockdown. The second section (items 15–38) focused on the development of emotional symptoms, such as irritability, anxiety, depression, sleep disturbances, somatization and mood changes. The third section (items 39–47) was not included in the GP questionnaire and investigated subjective ratings of level of anxiety / concern, health literacy CF related, and repercussion on the psychological dimension. In this section a 10-point Likert scale explored how pwCFs knowledge and personal experiences influenced reactions to the COVID-19 pandemic. Perception of future needs of psychological support and of issues in social interactions were investigated as well. The CF questionnaire is reported in the supplementary material, Table 1.

2.2. The recruitment

Two groups were investigated, adult pwCFs by means of the CF questionnaire (CF group), and adults from the general population using the GP questionnaire (GP group).

The survey was conducted through a SurveyMonkey platform. The GP survey was open from April 6th 2020 to April 20th 2020 and the CF survey from April 14th 2020 to May 3rd 2020. In Italy, the population was asked to stay at home from March 9th 2020 to May 18th 2020. The adult CF population was made aware of the initiative through their regional CF Centers and the Italian Patient Association, CF Research Foundation and CF Scientific Society. The general population was reached through a snowballing sampling technique.

Information about the initiative and request to consent to the initiative were included at the beginning of the survey. The rigorously anonymous approach, in compliance with European privacy statements, required no formal approval from the local Ethical Committee.

2.3. The analysis

In Sections 1 and 2 a case-control analysis was used to compare pwCFs and individuals from the general population. The control group was a random sample of 3,560 responders (CF:GP ratio 1:5) extracted from the GP questionnaire dataset and matched with CF cases for age and sex.

Statistical analysis was performed using SAS version 9.4 (SAS, Institute Inc., Cary, NC, USA).

Categorical variables were summarized using proportions and associations tested using chi-square or Fisher's exact test where applicable. Continuous variables were summarized using means and standard deviations for normally distributed data, while skewed data were summarized using medians. One-way ANOVA (F-value) was used to test difference of means for normally distributed continuous variables and the Mann-Whitney U test for skewed continuous variables.

In the bivariable analyses, to identify risks for adult pwCFs and controls for Psychological Distress levels, we computed Odds Ratios (OR) considering the significance of the confidence intervals. Statistical significance was evaluated using 95% confidence interval and a two-tailed p -value of < 0.05 .

Section 3 was included only in the CF questionnaire and no comparison was possible with the GP data. Analysis was performed using descriptive statistics such as mean, median and range of values. A Kruskal-Wallis test was performed to look for differences in the score medians of the three FEV1 groups.

Table 1
Demographic and social data.

	pwCFs N = 712 N (%)	controls N = 3560 N (%)	total N = 4272 N (%)	χ^2	p-value
Gender					
Male	290 (40.7)	1450 (40.7)	1740 (40.7)	0.0000	1.0000
Female	422 (59.3)	2110 (59.3)	2532 (59.3)		
Age					
18–30 yrs	274 (38.5)	1370 (38.5)	1644 (38.5)	0.0005	0.9822
31–50 yrs	370 (52.0)	1850 (52.0)	2220 (52.0)		
51–65 yrs	62 (8.7)	310 (8.7)	372 (8.7)		
≥66 yrs	6 (0.8)	30 (0.8)	36 (0.8)		
Education					
Primary or junior high school	55 (7.7)	127 (3.6)	182 (4.3)	111.6129	0.0000
High school	396 (55.6)	1255 (35.3)	1651 (38.6)		
University	259 (36.4)	2036 (57.2)	2295 (53.7)		
Missing	2 (0.3)	142 (4.0)	144 (3.4)		
Occupation*					
Employee and Freelancer	450 (63.2)	2620 (73.6)	3070 (71.9)	94.0819	0.0000
Student	98 (13.8)	568 (16.0)	666 (15.6)		
Unemployed	56 (7.9)	167 (4.7)	223 (5.2)		
Housewife and Pensioner	106 (14.9)	168 (4.7)	274 (6.4)		
Habitation					
Alone	70 (9.8)	439 (12.3)	509 (11.9)	4.2325	0.0397
With others	642 (90.2)	3073 (86.3)	3715 (87.0)		
Missing	0	48 (1.3)	48 (1.1)		

• 46 pwCFs did not work for health reasons and were not considered in the table.

3. Results

In the period under study the CF questionnaire was completed by 712 adult pwCFs, that is, according to the latest available European CF Patient Registry data, 22.7% of the whole adult Italian population with CF [17]. The Mario Negri survey collected 35,011 replies, of which 20,518 provided sufficient data for analysis. Of these, 3,560 were matched for sex and age with the pwCFs, with a 1/5 ratio.

3.1. Section 1

Demographic and social data from Section 1 are shown in Table 1. Age and gender data confirm a successful case-matching and a homogeneous distribution of the two populations. Males and individuals above 50 years were less represented, 40.7% and 9.5% respectively. The educational course of CF respondents ended earlier than that of answerers from the general population, with 36.4% of the former group achieving a University degree as opposed to 57.2% of the latter. PwCFs belonged less frequently to the categories “employee and freelancer” and “student” and more frequently to “unemployed”, “housewife and pensioner”. Almost 30% of pwCFs declared that they did not work for health reasons as opposed to none in the control group. Responders in the GP group lived alone more frequently than those in the CF group.

The demographic and social description of the CF group was similar to the reports on occupation and education in the US Cystic Fibrosis Foundation Patient Registry [18] (53% of CF adults have full-time or part-time jobs; 39% have a college degree) and in the White Book on Adults with Cystic Fibrosis from the Italian Cystic Fibrosis Society (60% of CF adults have an occupation; 19% have a college degree) [35].

Information on health status of responders during lockdown are shown in Table 2. In the two weeks before answering the questionnaire, pwCFs reported recently developed health problems more frequently than the general population (34.6% vs 17.9%). More frequent in the CF group were also symptoms somehow evocative of COVID-19, swabs and quarantine for health obligations. Conversely, the GP cohort had more contacts with SARS-CoV2 positives and left the house more frequently.

Social media, family and friends were consulted more often by the GP group (65% vs 52.7%), whereas the CF cohort sought advice more frequently from family doctors or the CF center (52.2% vs 12.4%), the latter obviously being a resource not accessible to the general population.

3.2. Section 2

The analysis of answers in Section 2 showed that the cumulative levels of psychological distress were lower in pwCFs than in GP controls. Mild or medium distress affected 40.2% of pwCFs and 43.9% of GP controls, severe distress 5.3% of pwCFs and 6.2% of GP controls (Table 4). The level of psychological distress was not correlated with the degree of pulmonary function impairment expressed by ppFEV₁ (Table 3).

When symptoms of anxiety and depression symptoms and physical symptoms were independently analyzed, the control group featured a 55% higher level of mild-moderate anxiety symptoms compared to the CF group (OR 1.55 p 0.0325). No significant inter-groups differences in symptoms of depression and physical symptoms were recorded (Table 4).

Table 5 shows that signs of psychological distress, anxiety and depression symptoms, and physical symptoms were significantly more frequent in female than in male pwCFs, even taking into account the different gender distribution of respondents (females/males ratio 1.45). The females/males ratio among those who reported anxiety was 4, among those reporting depression 6.8 and among those reporting symptoms 11. Marginal gender differences were observed between the CF and the GP group.

3.3. Section 3

The scores of answers fractioned according to lung function values are reported in Table 6. The inter-ppFEV₁ groups median scores were statistically different for questions 44 and 46.

Males always scored less than females, except in question 44. Table 2 in supplementary material reports means, medians, minimum and maximum values, interquartile ranges and standard deviations in males and females.

Table 2
Information on health conditions during lockdown.

	pwCFs N = 712 N (%)	controls N = 3560 N (%)	total N = 4272 N (%)	χ^2	p-value
New health problems in the preceding two weeks					
No health problems	466(65.4)	2923(82.1)	3389(79.3)	33.5242	0.0000
Consultation to family doctor <i>and/or CF Center</i>	141(19.8)	182(5.1)	323(7.6)		
Go to hospital	0(0.0)	10(3.0)	10(2.4)		
Symptoms typical of COVID-19	0(0.0)	253(75.1)	253(60.8)		
Swab for COVID-19	79(100.0)	57(16.9)	136(32.7)		
Quarantine for health obligations	79(100.0)	83(24.6)	162(38.9)		
Missing	26(3.7)	118(3.3)	144(3.4)		
Contact with SARS-CoV2 positives					
Yes	24 (3.4)	387 (10.9)	411 (9.6)	40.1611	0.0000
No	688 (96.6)	3131 (87.9)	3819 (89.4)		
Missing	0	42 (1.2)	42 (1.0)		
Left house in the last week					
Yes	321 (45.1)	2136 (60.0)	2457 (57.5)	62.0424	0.0000
No	391 (54.9)	1358 (38.1)	1749 (40.9)		
Missing	0	66 (1.9)	66 (1.5)		
Contacts to get information about COVID-19					
Traditional media (press, TV, others)	564(79.2)	2818(79.2)	3382(79.2)	0.0011	0.9731
Social media, Internet, Messaging app	281(39.5)	1541(43.3)	1822(42.7)	3.5402	0.0598
Family doctor	102(14.3)	441(12.4)	543(12.7)	2.0089	0.1564
Family and/or friends	94(13.2)	771(21.7)	865(20.2)	26.2667	0.000
Cystic Fibrosis Center or other patients	270(37.9)	–	270		
Other	44(6.2)	311(8.7)	355(8.39)	5.0466	0.0247
Influenza Vaccinated					
No	148 (20.8)	3059 (85.9)	3207 (75.1)	1389.8080	0.0000
Yes	564 (79.2)	471 (13.2)	1035 (24.2)		
Missing	0	30 (0.8)	30 (0.7)		

Note: additions to the questionnaire for pwCFs are shown in italics.

Table 3
Psychological Distress in pwCFs by ppFEV1 value.

ppFEV ₁	Psychological Distress			Total N (%)	OR ¹	p
	Normal N (%)	Mild/Moderate N (%)	Severe N (%)			
≥80	152 (39.4)	115 (40.8)	21 (55.3)	288 (40.8)	Reference	
40–79	181 (46.9)	131 (46.5)	15 (39.5)	327 (46.3)	0.90 (0.66–1.24)	0.52
<40	53 (13.7)	36 (12.8)	2 (5.2)	91 (12.9)	0.80 (0.50–1.29)	0.36
Total	386 (100.0)	282 (100.0)	38 (100.0)	706 (100.0)		
Missing	2	4	0	6		

¹ OR¹Parameter Reference: Mild-Moderate/Severe vs Normal.

Table 4
Anxiety symptoms, depressive symptoms and physical symptoms domains in pwCFs and controls.

	pwCFs (N = 712) N (%)	controls (N = 3560) N (%)	Total (N = 4272) N (%)	OR ¹	CI 95%	p
PSYCHOLOGICAL DISTRESS						
Normal	388 (54.5)	1775 (49.9)	2163 (50.6)	Reference		
Mild/Moderate	286 (40.2)	1564 (43.9)	1850 (43.3)	1.20	(1.01–1.41)	0.0364
Severe	38 (5.3)	221(6.2)	259 (6.1)	1.27	(0.89–1.83)	0.1929
ANXIETY SYMPTOMS						
Normal	682 (95.8)	3344 (93.9)	4026 (94.2)	Reference		
Mild/Moderate	28 (3.9)	213 (6.0)	241(5.6)	1.55	1.04–2.32	0.0325
Severe	2 (0.3)	3 (0.1)	5 (0.1)	0.31	0.05–1.83	0.1949
DEPRESSIVE SYMPTOMS						
Normal	641 (90.0)	3127 (87.8)	3768 (88.2)	Reference		
Mild/Moderate	61 (8.6)	370 (10.4)	431 (10.1)	1.24	0.94–1.65	0.1327
Severe	10 (1.4)	63 (1.8)	73 (1.7)	1.29	0.66–2.53	0.4563
PHYSICAL SYMPTOMS						
Normal	688 (96.6)	3411 (95.8)	4099 (96.0)	Reference		
Mild/Moderate	21 (2.9)	133 (3.7)	154 (3.6)	1.28	0.80–2.04	0.3048
Severe	3 (0.4)	16 (0.4)	19 (0.4)	1.08	0.31–3.70	0.9078

¹ OR¹Parameter Reference: Mild/Moderate-Severe vs Normal.

4. Discussion

This study provides insights into behavioral and psychosocial reactions of adult pwCFs to the COVID-19 pandemic and to the consequent lockdown and compares them to those of the general population. In spite of more reasons for concern than controls, the survey results suggested that adult people with CF seem to have equal, and in some domains less psychological distress.

People with CF were scrupulous in following the isolation precautions suggested by the authorities: they stayed at home more frequently and had fewer contacts with SARS-CoV2 positives than controls. Such better adherence was possibly facilitated by the larger number of housewives, pensioners and individuals not working for health reasons in the CF cohort. The higher frequency of health problems reported by pwCFs in the two weeks before answering the questionnaire are possibly related to the respiratory

Table 5
Psychological distress, anxiety symptoms, depressive symptoms, physical symptoms in males and females.

PSYCHO-LOGICAL DISTRESS	pwCFs						Controls					
	Females N (%)	Males N (%)	Total N (%)	OR ₁	CI 95%	p	Females N (%)	Males N (%)	Total N (%)	OR ₁	CI 95%	p
Mild/Moderate/Severe	199 (51.3)	189 (48.7)	388 (100.0)	2.69	1.97–3.69		932 (52.5)	843 (47.5)	1775 (100.0)	2.70	2.35–3.10	
Normal	91 (28.1)	233 (71.9)	324 (100.0)				518 (29.0)	1267 (71.0)	1785 (100.0)			
ANXIETY SYMPTOMS												
Mild/Moderate-Severe	24 (5.7)	6 (2.1)	30 (4.2)	2.85	1.15–7.07	0.0182	160 (7.6)	56 (3.9)	216 (6.1)	2.04	1.49–2.79	0.0000
Normal	398 (94.3)	284 (97.9)	682 (95.8)				1950 (92.4)	1394 (96.1)	3344 (93.9)			
Total	422 (100.0)	290 (100.0)	712 (100.0)				2110 (100.0)	1450 (100.0)	3560 (100.0)			
DEPRESSIVE SYMPTOMS												
Mild/Moderate-Severe	62 (14.7)	9 (3.1)	71 (10.0)	5.38	2.63–11.01	0.0000	330 (15.6)	103 (7.1)	433 (12.2)	2.42	1.92–3.0	0.0000
Normal	360 (85.3)	281 (96.9)	641 (90.0)				1780 (84.4)	1347 (92.9)	3127 (87.8)			
Total	422 (100.0)	290 (100.0)	712 (100.0)				2110 (100.0)	1450 (100.0)	3560 (100.0)			
PHYSICAL SYMPTOMS												
Mild/Moderate-Severe	22 (5.2)	2 (0.7)	24 (3.4)	7.92	1.85–33.95	0.0010	115 (5.5)	34 (2.3)	149 (4.2)	2.40	1.63–3.54	0.0000
Normal	400 (94.8)	288 (99.3)	688 (96.6)				1995 (94.5)	1416 (97.7)	3411 (95.8)			
Total	422 (100.0)	290 (100.0)	712 (100.0)				2110 (100.0)	1450 (100.0)	3560 (100.0)			

OR₁=Mild/Moderate-Severe Psychological distress (or Anxiety symptoms or Depressive symptoms or Physical symptoms) vs Normal Psychological distress (or Anxiety symptoms or Depressive symptoms or Physical symptoms).

Table 6
Section 3 answers per lung function values.

Questions	Median	ppFEV1 >80	ppFEV1 40–79	ppFEV1 <40	Interquartile ranges	χ ²	p
39) Compared to your experience as a patient affected by Cystic Fibrosis, how much the current COVID-19 pandemic and the consequent restrictive measures affect your mental and physical health?	5	5	5	5	4	3.32	0.18
40) Do you think Cystic Fibrosis make you more susceptible to COVID-19?	8	7	8	8	5	2.86	0.23
41) The restrictive measures led to a temporary interruption of scheduled visits: how much this aspect has affected you in the management of Cystic Fibrosis?	3	4	4	3	5	0.72	0.69
42) Have you been feeling anxious lately?	4	4	4	3	6	2.72	0.25
43) Have you been feeling depressed lately?	2	2	2	2	5	2.16	0.33
44) How much do you think that the knowledge you have, because of the underlying pathology, such as the attention to hygiene rules (use of face masks, hand hygiene, etc.) has helped you in dealing with this pandemic?	9	8	9	9	3	10.12	0.0063
45) To what extent the attention paid to personal protection from COVID-19 (isolation, hygiene rules) is causing significant discomfort in your daily life?	5	5	5	5	6	2.41	0.29
46) When the pandemic is over do you think that, following this difficult situation, you will need a psychological support?	1	1	1	1	5	7.33	0.02
47) How much do you think this period of isolation can affect your social interaction in the future?	4	4	4	4	6	0.88	0.64

morbidity inherent in CF. They also referred less frequently to family or friends and to social media to collect information on COVID-19, which may reflect the attitude of many patients with chronic disease to turn to professionals for guidance. In fact, almost 40% of adult pwCFs sought advice from their multidisciplinary team, an option obviously not available to the GP group.

Approximately half of the control population gave answers consistent with psychological distress. This was in accordance with previous results from other researchers. In the Irish population generalized anxiety disorder and depression were common experiences, in Spain more than a quarter of the participants in a web survey reported symptoms of depression, anxiety and stress [19,20]. Similarly to the GP group, in our CF population about 1

person in 2 gave signs of psychological distress, although the cumulative assessment of the CPDI results indicated that pwCFs were faring marginally better than controls. The component of psychological distress that was significantly different in the CF and GP cohorts concerns the anxiety dimension, which was higher in the general population. This might be explained by the knowledge and abilities most pwCFs acquire in order to minimize the risk of cross-infections inherent in CF. The use of face masks and an adequate hand hygiene were already well known by pwCFs, although during the pandemic an even more rigorous compliance with these preventive measures was recommended. In fact, the question in section three that inquired whether expertise and health literacy had helped in dealing with the pandemic, produced a mean score close

to the highest end of the scale, indicating that pwCFs managed to integrate the knowledge and information acquired over time about their chronic disease and use it to face the COVID-19 emergency. Interestingly, the confidence in their skills was more pronounced in adults with more severe CF, perhaps because of a longer habit of using prevention measures.

Evidence in support of our results comes from a recently published Belgian paper showing that the impact of the pandemic on the emotional wellbeing is not higher in pwCFs than in the general population [21]. Among 80 adults, more than 30% reported more sadness and negative thoughts about the future and more than 40% experienced increased levels of stress compared to the pre-epidemic period. The study did not include a control group, but the authors found their results consistent with what had been previously reported by others in healthy people [1], and concluded that the psychological effects of the epidemic were not different and specific in pwCFs as compared to the general population.

Similar results emerged from a Turkish study [22]. The psychological impact of COVID-19 was assessed through interviews addressed to children with CF and their mothers, compared with age-matched healthy children and mothers. Healthy children aged 13 to 18 experienced higher states of anxiety than the CF counterparts, whereas mothers of children with CF reported higher scores of anxiety than mothers of healthy children. Although investigation tools were different in this and in our study, it seems that children with CF have coping skills greater than their healthy equivalents and highlight an analogy between CF children and CF adults in terms of psychological resources and related abilities to cope with difficult situations.

The notion that pwCFs do not fare worse than controls is indirectly corroborated also by a Greek paper on mental health during the COVID-19 quarantine, where anxiety and depression scores in chronic disease patients and in healthy individuals were similar [23]. The same result was confirmed by the authors in a subset of patients with respiratory disease [23].

The study investigated whether the clinical severity of CF affected the perceptions about COVID-19. No significant correlation was found between lung disease severity, represented by ppFEV1 levels, and psychological distress, suggesting that at least in our CF cohort the former is not a predictive factor for the latter. This was confirmed by the results of the third section of the questionnaire, where the scores of answers to questions investigating the impressions of pwCFs in relation to the COVID-19 scenario were substantially homogeneous in all the three ranges of ppFEV1. The only exception was found in the perception on the need of psychological support at the end of the pandemic, which was felt as unessential by all, but especially by the most severe pwCFs. The absence of correlation between CF severity and psychological distress appears to be in contradiction with previous reports based on CF Quality of Life (CFQoL) assessment. Low lung function has been associated with worse CFQoL measured by the CFQ-R questionnaire [24] and a progressive impairment of CFQoL (evaluated through CFQoL questionnaire and HADS - Hospital Anxiety and Depression Scale) [25,26] was shown to be concomitant with the increasing severity of the disease [27]. Our data need to be confirmed by further studies, but it may be that the exceptionality of the COVID-19 pandemic and the consequent lockdown make it hardly comparable with previous, more standard situations.

Most studies have so far reported that female gender is associated with higher rates of fear of COVID-19 [28], higher levels of mild or moderate stress [8] and in general stronger negative psychological symptoms than males [29]. Partially discordant conclusions emerged from a Spanish online survey, where men were found to have higher levels of depression than women, and similar levels of anxiety and stress [30]. In our experience female pwCFs

gave answers consistent with anxiety symptoms, depression symptoms and physical symptoms more frequently than males, and were in this regard similar to their counterparts from the general population.

The strengths of this study include its being the first to explore how adult pwCFs coped with the COVID-19 epidemic and the isolation measures implemented during the outbreak. Besides, we used a validated web-based questionnaire, that could be filled in less than 30 min and was disseminated through the main institutions operating in the CF field. This contributed to a high uptake, with more than 1 in 5 Italian adult pwCFs completing the questionnaire.

The study has some weaknesses as well. First, the size of the sample we wanted to achieve obliged us to use an online survey with closed-ended questions. This allowed us to reach a large number of pwCFs, but made it impossible to obtain a more granular description of individual characteristics. Respondents could not explain the reasons behind their answers or express concerns not investigated in the questionnaire. Second, some items in the validated anxiety and depression CPDI scales are part of CF disease (e.g. fatigue), which makes it difficult to differentiate what is CF and what is a mental health issue. Thus, we cannot exclude that the CPDI scale, either as a total distress scale or as separate subscales, perform differently in CF than in the general population. Third, the clinical data collected by the questionnaire were limited to a three-level ppFEV1 grading, which was used to classify respondents as affected by mild, moderate or severe CF. Other, not investigated, individual characteristics of the CF phenotype could have contributed to delineate a more complete picture of the actual burden of the disease. The very partial exploration of clinical parameters was motivated by the necessity to avoid overloading the survey and to limit the collection of sensitive data. Finally, the GP and CF questionnaires were open to the public in periods of time only partially coincident. That was because the GP survey was initially planned as an independent study, and only later the CF part was added to it. However, the basic conditions whose effect we wanted to investigate, that is high morbidity and mortality due to COVID-19 and concomitant lockdown, persisted during the whole study period. Finally, the data collection targeted a specific subset of pwCFs, that is adults of Italian nationality. Similar studies in different epidemic phases, countries or socio-cultural contexts could lead to different results.

At the time of writing this manuscript, the COVID-19 pandemic is subsiding in most of Europe, but still on the rise in other continents. It is unknown whether a second wave could in the near future hit again the regions that are presently registering a downward infection trend, but it seems reasonable to plan in advance the measures that should be implemented [31,32]. In case of an unfavorable unfolding, several countries are likely to resort again to strategies like lockdown or community-wide quarantine, which so far have proved effective in containing the diffusion of the infection.

In spite of these uncertainties, a confident attitude of pwCFs emerges from the answers to the question investigating opinions about prospective needs of psychological support. The mean score of 2, next to “not at all”, suggests a positive perception of the future impact of the pandemic. This is somehow reassuring, and so are the similar or even more positive reactions of adult pwCFs compared with the general population that emerged from this study. Nevertheless, a large subset of the pwCFs in this survey showed signs of psychological distress. Screening and support usually recommended in adult pwCFs [33,34] appear in the present scenario even more crucial in order to intercept specific conditions, control them, and monitor the risk of developing more severe psychopathological conditions or even Post-Traumatic Stress Disorder (PTSD). In the present epidemic context, resorting to traditional face to face psychological assessment and treatment may

prove challenging, and alternative approaches like tele-health technologies need to be considered [35,36].

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Riccardo Ciprandi: Conceptualization, Validation, Writing - original draft. **Maurizio Bonati:** Methodology, Software, Formal analysis, Data curation. **Rita Campi:** Methodology, Software, Formal analysis, Data curation. **Rita Pescini:** Investigation, Data curation, Writing - review & editing. **Carlo Castellani:** Conceptualization, Project administration, Supervision.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.jcf.2020.12.016](https://doi.org/10.1016/j.jcf.2020.12.016).

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