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Obsessive beliefs prospectively predict adherence to safety behaviours related to COVID-19 through obsessive-compulsive symptoms and COVID-19 distress: A serial multiple mediator analysis

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O bsessive-compulsive tendencies may render individuals vulnerable to elevated distress and over-adherence to safety behaviours during illness outbreaks. The present study investigated obsessive beliefs as a predictor of obsessive-compulsive symptoms, COVID-19 distress and the exercise of safety behaviours related to COVID-19 in a community sample. Four hundred seventy-nine participants responded to a questionnaire battery in March 2020 and 218 individuals participated in a follow-up assessment in September 2020. Results indicated that baseline obsessive beliefs predicted the exercise of baseline safety behaviours through obsessive-compulsive symptoms and COVID-19 distress. In addition, the relationship between baseline obsessive beliefs and safety behaviour adoption 6 months later was mediated by later obsessive-compulsive symptoms and COVID-19 distress. Findings extended prior research on the association between obsessive-compulsive phenomena and psychological changes related to illness outbreaks. The implications for prevention and treatment strategies are discussed.

Keywords: Obsessive beliefs; Obsessive-compulsive disorder; COVID-19 distress; Safety behaviours.

China reported the first cases of the coronavirus disease (COVID-19) to the World Health Organization (WHO) on 31 December 2019. Following its spread across multiple continents, the WHO declared COVID-19 a pandemic on 11 March 2020. The pandemic impacts mental health. Recent studies indicate that people experience increased depression, anxiety and stress in response to the COVID-19 pandemic (Aknin et al., 2022). The coronavirus pandemic also brought about behavioural changes. Since COVID-19 spreads via respiratory droplets generated by infected individuals and contaminated surfaces, public health authorities encourage people to wear masks, wash or disinfect their hands, maintain distances from others and avoid crowded places. Although a moderate level of anxiety and safety behaviour adoption are adaptive responses to the pandemic, they may impair psychological, social and occupational functioning if they become excessive (Taylor, 2019).

Cognitive-behavioural theories posit that cognitive biases may render individuals vulnerable to the development and maintenance of mental disorders (Clark & Beck, 2011). Obsessive beliefs that are associated with a predisposition to obsessive-compulsive disorder (OCD) include the overestimation of threat, the inflated responsibility for harm, perfectionism, the intolerance of uncertainty, the importance of thoughts and the need to control thoughts (Obsessive Compulsive Cognitions Working Group, 1997). It is important to note that, rather than being specific to OCD, obsessive beliefs are trans-diagnostic processes that contribute to the escalation of various mental disorders (e.g. Fergus & Wu, 2010; Tolin et al., 2006; Wheaton et al., 2010). Therefore, obsessive beliefs may also create vulnerability to distress or over-adherence to safety behaviours during the COVID-19 pandemic by increasing sensitivity to threats that would affect the well-being of oneself or loved ones, uncertainty related to the pandemic or responsibility for taking necessary precautions or transmitting the disease to others. Accordingly, prior research has shown that obsessive beliefs were associated with elevated H1N1

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Figure 1. Conceptual diagram of the serial mediation model.

anxiety (Brand et al., 2013). However, no study to date examined whether obsessive beliefs play a role in the occurrence of COVID-19 distress and adherence to safety behaviours related to COVID-19.

One of the ways in which obsessive beliefs create a susceptibility to pandemic distress and the exercise of COVID-19 related safety behaviours could be a correlated increase of OCD symptomatology. Studies indicate that the history or current existence of psychiatric disorders creates vulnerability, further escalating mental health issues (e.g. Asselmann et al., 2018). OCD is a heterogeneous disorder; nevertheless, one of the most common symptoms is the irrational fear of contamination (Abramowitz et al., 2010). Individuals with contamination fears may experience obsessional thoughts or images of germs or viruses, fear contracting illnesses and transmitting them to others, avoid items or situations in which viruses can be found (e.g. doorknobs, public transportation), and perform compulsions with the aim of preventing illnesses (e.g. excessive hand-washing, disinfecting surfaces). In addition, individuals with harm-related obsessions may be prone to developing fears of transmitting the disease to others. Consistently, emerging evidence suggests that individuals with mental health problems, especially anxiety disorders and OCD, may be more adversely affected by COVID-19 than healthy individuals (e.g. Asmundson et al., 2020; Khosravani et al., 2021). In a recent study, individuals with OCD reported to be more concerned about COVID-19 compared to the community control group and the worsening of OCD symptoms after the outbreak was more strongly linked to contamination and responsibility for harm symptoms than repugnant obsessions or symmetry symptoms (Wheaton et al., 2021). Moreover, in another study by Knowles and Olatunji (2021), pre-pandemic contamination fears predicted the frequency of safety behaviours during the COVID-19 pandemic. However, there was not a significant relationship between baseline contamination fear and later COVID-19 distress. These findings support the notion that OCD symptoms may create vulnerability to distress and over-adherence to safety behaviours during the pandemic.

Exploring the associations among obsessive beliefs, OCD symptoms, COVID-19 distress and safety behaviours related to COVID-19 may enhance our understanding of the predictors of COVID-19 related psychological changes and facilitate the anticipation of concerns among individuals with obsessive-compulsive tendencies during future illness outbreaks. Therefore, the current study investigated obsessive beliefs as a predictor of OCD symptoms, COVID-19 distress and safety behaviours related to COVID-19 in a community sample in Turkey. We hypothesised that baseline obsessive beliefs would predict adherence to baseline safety behaviours through OCD symptoms and COVID-19 distress. In addition, we hypothesised that baseline obsessive beliefs would predict adherence to safety behaviours 6 months later through the OCD symptoms and COVID-19 distress that followed (Figure 1). Turkey is the sixth-worst affected country in terms of the effects of COVID-19 around the world (Johns Hopkins University, 2021). Turkey confirmed the first COVID-19 case on 10 March, announced the closure of all schools and universities on 16 March, and declared a curfew that applied to all citizens on 11-12 April, 2020 (Turkish Medical Association, 2020a). Turkey's epidemic peaked after the sixth week and started to bend in the following weeks (Turkish Medical Association, 2020b). However, the "reopening" that began on 1 June, the end of the 12th week, led to an increase in the number of reported cases after the 14th week. During the summer of 2020, protection measures such as physical distancing were relaxed, and as a result, the number of daily patients, which has decreased to 786 on 2 June, started to show a fluctuating course and reached 1642 on 3 September 2020 (Turkish Medical Association, 2020b). As of 30 September 2020, Turkey ranked fifth in the European region with a total number of 312,966 patients and 7926 deaths (WHO, 2020), as reported by the Ministry of Health based on polymerase chain reaction-positive cases alone (Turkish Medical Association, 2020b). In the current study, the first assessment was conducted between 20-30 March, in the days following the confirmation of the first COVID-19 cases in the country, and the second assessment took place between 20 and 30 September, which corresponded to the days following the second peak in the number of new daily COVID-19 cases.

METHOD

Participants

Four hundred seventy-nine individuals (327 females, (68.3%) with a mean age of (33.75 years) = (5D) = 14.54, range 18-70) participated in the first assessment. Participants consisted of students (n = 113, 23.6%), employees (n = 330, 68.9%), retirees (n = 20, 4.2%) and unemployed individuals or housewives (n = 16, 3.3%). A small percentage of the participants lived alone (7.5%, n = 36), while the remaining lived with their partner, family or housemate (92.5%, n = 443). Some participants shared their house with individuals who might be more vulnerable to COVID-19: 6.7% shared their household with a baby under the age of 3 or a pregnant woman (n = 32), while 17.3% lived with an adult older than 65 (n = 83). A small number of participants reported having had COVID-19 before (0.6%, n = 3) and 1.5% had an infected family member (n = 7).

A subgroup of 218 participants (147 females, 67.4%) with a mean age of 32.95 (SD = 15.92, range 18–69) completed the follow-up assessment 6 months later. Participants included students (n = 81, 37.2%), employees (n = 127, 58.3%), retirees (n = 4, 1.8%) and unemployed individuals or housewives (n = 6, 2.8%); 4.6% stated that they live alone (n = 10), while others lived with their partners, family or housemates; 4.1% lived with a baby under three or a pregnant woman (n = 9), and 16.5% lived with an individual older than 65 (n = 36). Participants infected by the coronavirus made up 0.9% of the sample (n = 2) and 2.8% had an infected family member.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Hacettepe University Ethics Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual adult participants included in the study.

Materials

The Obsessive-Beliefs Questionnaire-20 (OBQ-TRIP; Moulding et al., 2011): The OBQ-20 is the 20-item short form of the OBQ-44 (Obsessive Compulsive Cognitions Working Group, 2001), a self-report inventory assessing dysfunctional beliefs related to OCD. The OBQ-20 has four subscales: overestimation of threat, inflated personal responsibility for harm, importance of and need to control thoughts, perfectionism/intolerance of uncertainty. The OBQ-20 and its Turkish adaptation demonstrated good psychometric properties (Moulding et al., 2011; Yorulmaz et al., 2019). The Cronbach's alpha values for the present study were .86 for the initial sample (N = 479) and .84 for the study sample at T1 (N = 218).

The Obsessive–Compulsive Inventory-Revised (OCI-R; Foa et al., 2002): The OCI-R is an 18-item self-report questionnaire of obsessive–compulsive symptoms. The OCI-R has six sub-scales measuring washing, checking, ordering, neutralising, hoarding and obsessing symptoms. Previous studies showed that the OCI-R has good reliability and validity (Foa et al., 2002). The psychometric properties of the Turkish version were excellent (Yorulmaz et al., 2015). The Cronbach's alpha values for the current study were .90 for the initial sample (N = 479) and .88 both for the study sample at T1 (N = 218) and T2 (N = 218).

COVID-19 Distress Scale (CDS; Trak et al., manuscript submitted for publication): The CDS is a 14-item self-report measure of COVID-19 distress. Items are rated on a Likert scale from 1 (not at all) to 5 (very much). Higher scores indicate higher levels of COVID-19 related distress. The CDS demonstrated robust psychometric properties in a community sample of Turkish adults. Exploratory factor analysis with 548 individuals suggested a three-factor structure: anxiety, threat perception and hopelessness related to COVID-19. The three-factor model obtained in the exploratory factor analysis was tested with confirmatory factor analysis in another sample consisting of 626 individuals and results confirmed the three-factor structure of the scale. The CDS had a Cronbach's alpha score of .87 and test-retest reliability of .79 over 2 weeks (N = 249). Items are provided in Appendix S1. In the present study, Cronbach's alpha values were .88 for the initial sample (N = 479), .85 for the study sample at T1 (N = 218) and .90 for the study sample at T2 (N = 218).

The COVID-19 Safety Behaviours Questionnaire (CSBQ): Based on the Safety Behaviour Checklist created by Deacon and Maack (2008) for contamination fear, we created the 27-item CSBQ, a self-report questionnaire assessing the frequency of changes in COVID-19-related safety behaviour. Participants were asked to rate the extent to which they typically exercise safety behaviours on a scale ranging from 1 (never) to 5 (always). If they did not have the opportunity to perform a particular behaviour, for instance, if they did not ride an elevator, go to the supermarket or encounter an animal, they marked, "Not applicable." We calculated a mean score for 27 items and used it as the measure of safety behaviour use. Items are presented in Appendix S1. Cronbach's alpha values were .89 for the initial sample (N = 479) and .88 for the study sample at T1 (N = 218) and T2 (N = 218).

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Procedure

The researchers announced the study to university students, employees and alumni via the university's mailing list and to community members through the university's social media accounts between 20 and 30 March 2020 (Time 1). Voluntary participants were directed to an online survey platform, where they first gave their informed consent and then completed the questionnaire battery that includes OBQ, OCI, CDS and CSBQ. Individuals who volunteer to participate in a follow-up survey 6 months later gave their e-mail addresses and received the link to a second assessment between 20 and 30 September 2020 (Time 2). The second assessment included OCI, CDS and CSBQ. Participants were not compensated for their participation. The study was approved by the Hacettepe University Ethics Committee.

Statistical analysis

We calculated means, standard deviations, internal consistencies and correlation coefficients of the questionnaires and performed a logistic regression to examine whether demographic and study variables predicted participation to assessment at T2 (Miller & Hollist, 2007) with SPSS 23.0 (IBM Corp., Armonk, NY). We conducted two serial mediation analysis with Model 6 of the PROCESS macro for SPSS 3.0 (Haves, 2018) to investigate the indirect effect of obsessive beliefs on safety behaviour adoption through OCD symptoms and COVID-19 distress. The PROCESS tests the statistical significance of indirect effects using bootstrapping (in the present study 5000 samples) and estimation of 95% confidence intervals (CIs). When bootstrapped confidence intervals does not include zero, indirect effects are considered statistically significant (Hayes, 2018).

RESULTS

Descriptive statistics and intercorrelations

Table 1 presents means, standard deviations and intercorrelations among study variables.

As expected, baseline obsessive beliefs level was positively correlated with obsessive–compulsive symptom severity and COVID-19 distress at Time 1 and Time 2. There was not a significant correlation between obsessive beliefs and COVID-19-related safety behaviour adoption at Time 1 and Time 2. OCD symptoms at Time 1 were positively associated with OCD symptoms at Time 2, COVID-19 distress at Time 1 and Time 2, and the frequency of safety behaviours at Time 1 and Time 2. Similarly, OCD symptoms at Time 2 were positively correlated with COVID-19 distress at two time points and safety behaviour adoption at Time 2. Baseline COVID-19 distress was significantly related to COVID-19 distress at Time 2 and safety behaviour frequency at two time points. Lastly, baseline COVID-19 related safety behaviours were positively associated with safety behaviour frequency at Time 2.

Logistic regression for differential attrition

We conducted a logistic regression to examine the differences in characteristics between participants who did and did not participate in the assessment at T2 (Miller & Hollist, 2007). With this aim, we created a dichotomous variable with 0 representing participants who dropped out of the study and 1 representing those who completed the second assessment. In the logistic regression, this dichotomous variable was the dependent variable and demographic variables (i.e. gender, age, years of education) as well as variables measured in the first assessment (i.e. obsessive beliefs, OCD symptoms, COVID-19 distress and safety behaviours related to COVID-19) were independent variables. Results revealed that none of the variables significantly predicted participation in a second assessment, thus suggesting that no attrition bias was detected (Table 2).

Serial multiple regression models

As seen in Table 3 and Figure 2, the results of the serial mediation analysis using the least square path analysis showed that obsessive beliefs were significantly associated with obsessive symptoms ($a_1: \beta = 0.44, p < .001$), obsessive symptom severity was significantly associated with COVID-19 distress ($d: \beta = 0.44, p < .001$) and COVID-19 distress levels were significantly related to the adoption of safety behaviours for COVID-19 ($b_2: \beta = 0.35, p < .001$). The 95% CIs created with 5000 bootstrap samples indicated that the indirect effect of obsessive beliefs on safety behaviour adoption through OCD symptoms and COVID-19 distress was significant ($a_1db_2 = 0.06, 95\%$ CI 0.025-0.106, SE = .02).

As presented in Table 4 and Figure 3, results of the serial mediation analyses using least squares path analysis indicated that baseline obsessive beliefs significantly predicted obsessive symptomatology six months later (a_1 : $\beta = 0.39$, p < .001), elevated OCD symptoms were associated with increased COVID-19 distress (d: $\beta = 0.44$, p < .001), and COVID-19 distress levels significantly predicted safety behaviour adoption (b_2 : $\beta = 0.35$, p < .001). 95% CIs created with 5000 bootstrap samples indicated that the indirect effect of obsessive beliefs on safety behaviour adoption through OCD symptoms and COVID-19 distress was significant ($a_1db_2 = 0.06$, 95% CI 0.025-0.106, SE = .02). We repeated the serial mediation analysis adding OCI scores at Time 1, CDS scores at Time 1 and CSBQ scores at Time 1 individually as covariates.

TABLE 1Summary of means, standard deviations and intercorrelations between study variables (N = 218)

	1	2	3	4	.5	6	М	SD
			-		-			
1. OBQ (Time 1)	_						3.64	.87
2. OCI (Time 1)	.55**	—					2.38	.70
3. OCI (Time 2)	.49**	.75**	—				2.36	.66
4. CDS (Time 1)	.35**	.43**	.39**	—			2.61	.67
5. CDS (Time 2)	.30**	.38**	.45**	.70**	—		2.85	.72
6. CSBQ (Time 1)	.07	.12**	.02	.23**	.16		4.12	.68
7. CSBQ (Time 2)	.07	.17*	.23**	.36**	.42**	.66**	3.98	.63

Note: CDS = COVID-19 Distress Scale; CSBQ = COVID-19 Safety Behaviours Questionnaire; OBQ = Obsessive Beliefs Questionnaire-20; OCI = Obsessive-Compulsive Inventory-Revised. *p < .05. *p < .01.

TABLE 2 Standardised regression coefficients for participation to second assessment regressed on demographic and study variables (N = 479) CDS scores at Time 2 R^2 β F df1, df2 t р 2.19 7,471 Step 1 .03 Gender .03 0.52 .60

.08

.28

.35

.30

.10

.3

-1.76

-0.94

-1.03

-1.66

0.85

1.09

Note: CDS = COVID-19 Distress Scale; CSBL = COVID-19 Safety Behaviours List; OBQ = Obsessive Beliefs Questionnaire-20; OCI = Obsessive – Compulsive Inventory-Revised.

TABLE 3

Regression coefficients, standard errors, and model summary information for the serial multiple mediation model with Time 1 variables

Predictors		Dependent variables												
	M ₁ (OCI)				M ₂ (CDS)					Y (CSBQ)				
		β	SE	р		β	SE	р		β	SE	р		
X (OBQ)	a_1	0.44	.03	.000	a_2	0.13	.04	.001	c'	-0.03	.04	.502		
M_1 (OCI)		_	_	_	d	0.32	.05	.000	b_1	0.05	.05	.371		
M_2 (CDS)		_		_		_		_	b_2	0.22	.05	.000		
Constant	i_{M1}	0.77	.12	.000	i_{M2}	1.37	.12	.000	i_Y	3.53	.15	.000		
	$R^2 = .30$					$R^2 = .20$					$R^2 = .05$			
F(1,477) = 204.54, p < .001					F(2,476) = 60.28, p < .001					F(3,475) = 9.01, p < .001				

Note: CDS = COVID-19 Distress Scale; CSBQ = COVID-19 Safety Behaviours Questionnaire; OBQ = Obsessive Beliefs Questionnaire-20; OCI = Obsessive-Compulsive Inventory-Revised.





-.09

-.05

-.06

-.09

.04

.06

Age Education

OBO

OCI

CDS

CSBL

Predictors	Dependent variables												
	M ₁ (OCI-R)			M ₂ (CDS)					Y(CSBQ)				
		β	SE	р		β	SE	р		β	SE	р	
X (OBQ)	a_1	0.39	.06	.000	a_2	0.09	.08	.258	c'	-0.07	.07	.299	
M_1 (OCI-R)	-	_	_	_	d	0.44	.10	.000	b_1	0.09	.09	.352	
M_2 (CDS)		_	_			_			b_2	0.35	.08	.000	
Constant	i_{M1}	1.02	.21	.000	i_{M2}	1.50	.26	.000	i_Y	3.02	.26	.000	
$R^2 = .24$						$R^2 = .21$					$R^2 = .18$		
	F(1,216) = 42.37, p < .001					F(2,	(215) = 17.9	98, <i>p</i> < .001	F(3,214) = 9.90, p < .001				

 TABLE 4

 Regression coefficients, standard errors and model summary information for the serial multiple mediation model with Time 2 variables

Note: CDS = COVID-19 Distress Scale; CSBQ = COVID-19 Safety Behaviours Questionnaire; OBQ = Obsessive Beliefs Questionnaire-20; OCI = Obsessive-Compulsive Inventory-Revised.



Figure 3. Statistical diagram of the serial mediation model with Time 2 variables.

The significance and the direction of the results remained the same.

DISCUSSION

The present study investigated the relationship between obsessive beliefs and COVID-19-related safety behaviour adherence through obsessive–compulsive symptoms and COVID-19 distress. Consistent with our hypothesis, the relationship between baseline obsessive beliefs and baseline adherence to safety behaviours were mediated by OCD symptoms and COVID-19 distress. In addition, OCD symptoms and COVID-19 distress 6 months later serially mediated the relationship between baseline obsessive beliefs and later adherence to safety behaviours related to COVID-19.

Cognitive models of OCD suggest that dysfunctional beliefs and maladaptive appraisals contribute to the misinterpretation of intrusive thoughts, and consequently, to the development and maintenance of OCD (Clark & Beck, 2011). Our findings indicated that the level of baseline obsessive beliefs was a significant predictor of OCD symptoms both at the baseline and 6 months later. In addition, the level of baseline obsessive beliefs was significantly associated with COVID-19-related safety behaviour adherence both at the baseline and 6 months later in terms of OCD symptoms and COVID-19 distress.

OCD is characterised by high levels of anxiety and proneness to disgust. Moreover, the themes of common symptoms include contamination and harm-related obsessions. The COVID-19 outbreak can be particularly anxiety-provoking for individuals with OCD (Asmundson et al., 2020; Fineberg et al., 2020; Khosravani et al., 2021; Wheaton et al., 2021). The COVID-19 pandemic has created an increased threat of contagion and an ongoing exposure in media and daily life to topics related to viruses and illnesses. Consequently, individuals with pre-existing OCD symptoms may worry more about loved ones or themselves getting sick or transmitting the disease to other people. They may also experience conflict with family, partners or roommates over their cleaning rituals or because others do not take the risk of contamination seriously enough (Brewer et al., 2021). These features might render individuals with pre-existing OCD symptoms vulnerable to COVID-19-related distress, and COVID-19 distress might be associated with a high level of adherence to safety behaviours.

Our study extended the previous literature on obsessive beliefs and OCD symptoms as predictors of changes in COVID-19 distress and safety behaviours related to COVID-19 by assessing a community sample of adults at two different time points. However, it has several limitations that need to be considered. First, our findings are only a snapshot of the situation in Turkey between March

and September 2020. This period could be too short for producing significant levels of negative affect and stress, particularly for individuals without mental distress. Therefore, our results have to be considered preliminary, and studies from other countries and with more extended periods are necessary to establish the generalisability of the findings. Second, we have assessed COVID-19 related safety behaviours with a modified version of the Safety Behaviours Checklist (Deacon & Maack, 2008). The Safety Behaviour Checklist was created to assess safety behaviours related to contamination fear. The scale has been adapted to COVID-19 for study purposes and its psychometric properties have not been comprehensively evaluated before the study. Future studies may explore similar research questions using scales whose validity and reliability have been examined in more detail. Future studies can also consider using methods other than self-report measures that have higher degrees of confidence. Our study has limitations regarding its sample as well. The mostly female, on average rather young composition of the sample limits the generalisability of our findings. In addition, our sample consisted of 23% college students. Thus, our results should be replicated with larger and balanced samples. Another limitation was the lack of compensation for participation in the study. Although advantages and disadvantages of the use of reimbursement in scientific research is a subject of ongoing debate (e.g. Largent & Lynch, 2017), concerns about COVID-19 may have driven some individuals to participate in the study, resulting in a possible selection bias in the study sample. Another limitation related to the sample was the high attrition rate of the study. Although we conducted a hierarchical regression to address this issue and the results of the hierarchical regression analysis suggested that no attrition bias was detected, future longitudinal studies should consider using methods such as reimbursement to obtain better attrition rates. Finally, while the present study focused on a community sample, future studies could focus on individuals with elevated obsessive beliefs or a clinically significant severity of OCD symptoms who might be at an increased risk for distress related to the COVID-19 outbreak and excessive adherence to safety behaviours.

As the pandemic continues, individuals are likely to experience varying amounts of distress and rely on safety behaviours for protection. Although moderate pandemic distress and the appropriate use of safety behaviours related to COVID-19 are adaptive, excessive distress and safety behaviour adherence can result in psychological, social and occupational dysfunction. Clinicians might consider cognitive vulnerability factors such as obsessive belief domains and pre-existing obsessive symptoms as potential risk factors for excessive distress and over-adherence to safety behaviours during the current and future pandemics. Furthermore, interventions targeting obsessive beliefs and OCD-related complaints can also help reduce COVID-19 distress.

CONCLUSION

To conclude, the current study investigated obsessive beliefs as a prospective predictor of the adherence to safety behaviours through OCD symptoms and COVID-19 distress after a period of 6 months. Results indicated that OCD symptoms and COVID-19 distress serially mediated the association between obsessive beliefs and safety behaviour adherence. These results point out that cognitive bias may play a role not only in future OCD symptoms but also in pandemic-related psychological changes. Future studies are needed to establish the generalisability of the findings to larger populations and the pandemic's later course.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1: Supporting information.

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