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The associations among the stress symptoms, depressive symptoms, anxiety symptoms and insomnia symptoms in depressed patients after the first COVID-19 outbreak was initially controlled in China: A prospective cohort study

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ABSTRACT

Background: Depressed patients suffered from severe psychological distress even after the first COVID-19 outbreak was initially controlled. The longitudinal changes and associations among stress and other psychological problems during this period remained unknown. In this study we investigated stress symptoms and the longitudinal impact of stress symptoms on other psychological symptoms in depressed patients after the first COVID-19 outbreak was initially controlled.

Methods: A total of 5241 depressed patients at the outpatients of 56 hospitals across mainland China were recruited from May 18 to June 18, 2020. Five months later, 2113 of them responded again. Demographic characteristics were collected and psychological symptoms were evaluated at baseline and the follow-up. The longitudinal associations between stress symptoms at baseline and the changes of other psychological problems were assessed using Poisson regression.

Results: The prevalence of stress symptoms, depressive symptoms, anxiety symptoms and insomnia symptoms declined over time. Having stress symptoms at baseline was positively associated with the new occurrences of depressive symptoms, anxiety symptoms and insomnia symptoms (range, adjusted RRs 1.69–1.81).

Limitations: The sampling method and the high dropout rate are the major limitations. Additionally, the mental conditions of the participants were not obtained, which may lead to unavoidable bias.

Conclusions: The prevalence of stress symptoms declined over time after the first COVID-19 outbreak was initially controlled. We found that having stress symptoms at baseline was a predictor for the new occurrences of depressive symptoms, anxiety symptoms and insomnia symptoms.

1. Introduction

The coronavirus disease (COVID-19) pandemic has resulted in great public health emergency globally. The first COVID-19 outbreak had lasted for several months in the mainland of China until the containment measures were brought into effect. Since April 29, 2020, only sporadic

cases have been reported in the mainland of China, while the inbound cases were also under control (State Council Information Office of the People's Republic of China, 2020). Therefore, it was stated that the first COVID-19 outbreak in the mainland of China was initially controlled and the mainland of China entered the 'regular ongoing prevention and control stage' (State Council Information Office of the People's Republic

Abbreviation: COVID-19, The coronavirus disease 2019; PRC, The People's Republic of China; WHO, World Health Organization; MDD, major depression disorder; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5); PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder Screener-7; ISI, Insomnia Severity Index; IES-R, Impact of Events Scale-Revised.

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of China, 2020). The Chinese government made vigorous efforts to resume work and hospitals could resume in-person outpatient visits.

The COVID-19 pandemic has raised great public concerns on psychological problems. Psychological distress, such as depression, anxiety, insomnia and acute stress symptoms, were all found to be more prevalent during the COVID-19 pandemic (Luo et al., 2020; Shi et al., 2020). Factors such as gender, age and living area, were found to be associated with the psychological distress (Özdin and Bayrak, 2020; Shi et al., 2020). Notably, having a history of psychiatric illness was found to be positively associated with post-traumatic stress disorders (Bromet et al., 2017), anxiety symptoms, depression symptoms, insomnia and acute stress (Özdin and Bayrak, 2020; Shi et al., 2020). A case-controlled study confirmed that the severity of negative psychological impact was greater in psychiatric patients during the COVID-19 pandemic compared to healthy controls (Hao et al., 2020). A systematic review showed worsening of preexisting psychiatric disorders in patients during the COVID-19 pandemic (Vindegaard and Benros, 2020). The World Health Organization (WHO) ranked major depression the third cause of burden of diseases worldwide in 2008 (World Health Organization, 2008). Psychological distress commonly occurs among depressed individuals across their lifespan (Ekholm et al., 2020; Saade et al., 2019). The biological mechanisms of psychological distress mainly involved genetic variation, changes of neural circuitry and neurotransmitters and neuroendocrine dysregulation in depressed patients (Chiriță et al., 2015). For example, the imbalance of serotonin (5-HT) was found to be involved in both depression and anxiety (Graeff et al., 1996). In addition, the abnormality of glucocorticoid was found to be involved in depression and acute or chronic stress (Villas et al., 2019). Due to the vulnerability of depressed patients for developing psychological distress, more attention need to be paid to depressed patients, especially during the pandemic time.

Stress symptoms, depressive symptoms, anxiety symptoms and insomnia symptoms are usually considered related to each other. Stressful life events, including daily hassles and some rare life-threatening situations, evoke behavioral and physiological stress responses and even lead to chronic stress (McEwen, 2006). Being “stressed out” may cause people to be anxious or depressed and to lose sleep at night (McEwen, 2006). The COVID-19 pandemic is certainly a great stressor to the public especially to the depressed patients, resulting in multiple psychological distress. However, the longitudinal impact of the stress from the COVID-19 pandemic on depressed patients has not been investigated, especially after the first COVID-19 outbreak was initially controlled.

Although plenty of studies have investigated different psychological problems during the COVID-19 pandemic, few studies focused on depressed patients; most of them only measured depressive symptoms or anxiety symptoms rather than stress symptoms. In addition, most of the previous studies were cross-sectional and were done during the COVID-19 outbreak. The causal links between stress symptoms and the changes of other psychological problems during the COVID-19 pandemic have not been explored. Furthermore, many of the studies were done online due to the restriction policy during the COVID-19 pandemic, resulting in reduced reliability in their findings. In this study, we conducted an offline prospective cohort study at outpatients to assess stress symptoms and the longitudinal impact of stress symptoms on other psychological symptoms in depressed patients after the first COVID-19 outbreak was initially controlled.

2. Method

2.1. Study design and samples

The study was conducted in 56 hospitals in 31 provincial-grade areas in the mainland of China. All the patients with a history of depression disorder at outpatients of these hospitals were invited to participate in the baseline survey from May 18 to June 18, 2020. These patients were

invited again to participate in the follow-up survey at the outpatients from October 18 to November 18, 2020. The data were collected and stored on a platform designed specially for the study. Prior to starting the study, the aim and significance of the survey were fully introduced to all participants, and the informed consent was obtained from all participants. The questionnaire was submitted only if the participant answered all questions. Participants who met the following criteria were included: (1) the participant was previously diagnosed with major depression disorder (MDD) according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), (2) the participant was able to read and understand a questionnaire, (3) the participant was an outpatient, and (4) the individuals volunteered to participate in the survey. Exclusion criteria were as follows: the participant was under 18 years old. The study was approved by the Ethics Committee of Nanfang Hospital, Southern Medical University.

2.2. Measures

For the depressed patients at outpatient in participating hospitals, we introduced the study and invited them to participate in the survey. All participants attended the study voluntarily. They were invited to complete the questionnaires using their mobile phones. The questionnaire consisted of demographic data, information related to COVID-19 pandemic and psychological symptoms. At the beginning of the study, demographic data (including age, gender, ethnicity, levels of education, marital status, living status and employment status) and information related to the COVID-19 pandemic (including personal infection status and surrounding people's infection status) were collected. Psychological symptoms, including depressive symptoms, anxiety symptoms, insomnia symptoms and stress symptoms, were evaluated at both baseline and follow-up.

The Patient Health Questionnaire-9 (PHQ-9) was used to assess depressive symptoms (Kroenke et al., 2001). Previous study showed a good reliability and validity of PHQ-9 among the general Chinese population (Wang et al., 2014). The cutoff score of 5 for PHQ-9 was adopted in this study (Shi et al., 2020).

The Generalized Anxiety Disorder Screener-7 (GAD-7) was used to evaluate the anxiety symptoms (Lowe et al., 2008). The Chinese version GAD-7 was proved to have good reliability and validity in general outpatients (He et al., 2010). The cutoff score was set at 5 for GAD-7 in our study (Zhang et al., 2020).

The Insomnia Severity Index (ISI) was used to evaluate insomnia symptoms (Bastien et al., 2001). The Chinese version of ISI had acceptable reliability and good sensitivity for assessing the severity of insomnia (Baghyahi et al., 2013). A total score of ≥ 8 was considered having symptoms of insomnia (Morin et al., 2011).

The Impact of Events Scale-Revised (IES-R) was used to evaluate the psychological distress (Wu and Chan, 2003). The IES-R used in the study was modified based on the COVID-19 pandemic. A total score of ≥ 9 was considered having stress symptoms (Guo et al., 2021).

2.3. Statistical analysis

All analyses were conducted using SPSS (IBM Corp., version 22.0). Descriptive statistics are presented as mean \pm standard deviation (SD) and percentage for continuous variables and discrete variables, respectively. In the cross-sectional analysis, a *t*-test or chi-square test was conducted to determine the associated factors of stress symptoms at baseline. Logistic regression analyses were performed to determine the association between stress symptoms and other psychological symptoms at baseline.

Participants without a certain kind of psychological symptoms (stress symptoms, depressive symptoms, anxiety symptoms or insomnia symptoms) at baseline were further classified into the new occurrence group and the persistently asymptomatic group. Participants with a certain kind of problem (stress symptoms, depressive symptoms, anxiety

symptoms or insomnia symptoms) at baseline were further classified into the persistence group and the remission group. McNemar's test was conducted to compare the prevalence between the baseline and the follow-up. Logistic regression analyses and Poisson regression analyses were performed to determine the association between stress symptoms at baseline and the outcomes of other psychological symptoms (new occurrence and persistence). The conditions of stress symptoms at baseline (with or without) were defined as independent variables, while the outcomes of depressive symptoms, anxiety symptoms and insomnia symptoms were defined as dependent variables in the regression models. The adjusted regression models were controlled for age, gender and other socio-demographics factors significantly correlated to stress symptoms at baseline. All analyses in the study were two-tailed with alpha level set at $p < 0.05$.

3. Result

3.1. Cross-sectional analyses

A total of 5241 participants participated in the survey at baseline, and 5047 of the received questionnaires were valid (validity rate: 96.30 %). Among the valid participants, 3195 (63.3 %) were female. The average age of participants was 36.70 ± 12.16 years. The percentage of participants with stress symptoms was 68.5 %. The prevalence of depressive symptoms, anxiety symptoms and insomnia symptoms at baseline was 62.8 %, 52.5 % and 52.8 %, respectively.

Table 1 shows the sample characteristics and the differences between the participants with and without stress symptoms at baseline. The age was significantly higher in the stress symptoms group compared to the non-stress symptoms group at baseline (36.94 ± 12.49 years vs. 36.20 ± 11.40 years). Higher percentage of females and higher percentage of minority ethnicities were found in the stress symptoms group. Higher levels of education and higher percentage of retired people or student were found in the stress symptoms group. Higher percentage in the stress symptoms group reported that they had been around with someone infected with COVID-19. There were no significant differences in other socio-demographics between the stress symptoms group and the non-stress symptoms group at baseline.

Table 2 presents the cross-sectional associations of stress symptoms with other psychological symptoms including depressive symptoms, anxiety symptoms and insomnia symptoms at baseline. The regression models revealed that depressive symptoms, anxiety symptoms and insomnia symptoms at baseline were all positively associated with the baseline stress symptoms (range, adjusted ORs 18.61–42.08).

3.2. Prospective analyses

At the follow-up, 2113 participants responded. The sample characteristics between respondents and non-respondents at the follow-up are delineated in eTable 1 in Appendix A Supplementary data. Significant differences were found in age, marital status, living status and having insomnia at the baseline between the respondents and non-respondents. Analyses of other socio-demographics and the COVID-19 related or psychological factors showed no significant differences between the respondents and the non-respondents. The percentage of participants with stress symptoms at follow-up was 51.1 %. The prevalence of depressive symptoms, anxiety symptoms and insomnia symptoms at follow-up was 45.8 %, 35.8 % and 32.2 %, respectively. The results of McNemar's test showed that the prevalence of stress symptoms, depressive symptoms, anxiety symptoms and insomnia symptoms declined over time. (Shown in eTable 4 in Appendix A Supplementary data).

Table 3 shows the prospective associations of stress symptoms at baseline with the new occurrences of other psychological outcomes. Both the univariate analyses and the adjusted models revealed that having stress symptoms at baseline was positively associated with the

Table 1

Comparisons in sample characteristics between participants with and without stress symptoms at baseline.

	Total sample (N = 5047)	Non stress symptoms (n = 1588)	Stress symptoms (n = 3459)	t/ χ^2
Age (years), mean \pm SD	36.70 \pm 12.16	36.20 \pm 11.40	36.94 \pm 12.49	-2.069*
Gender (female), n (%)	3195 (63.3)	945 (59.5)	2250 (65.0)	14.374**
Ethnicity				5.883*
Han, n (%)	4859 (96.3)	1544 (97.2)	3315 (95.8)	
Minority, n (%)	188 (3.7)	44 (2.8)	144 (4.2)	
Level of education (Bachelor or above), n (%)	3354 (66.5)	1101 (69.3)	2253 (65.1)	8.604*
Marital status				4.970
Married, n (%)	3410 (67.6)	1107 (69.7)	2303 (66.6)	
Unmarried, n (%)	1473 (29.2)	431 (27.1)	1042 (30.1)	
Divorced, n (%)	164 (3.2)	50 (3.1)	114 (3.3)	
Employment status				27.173**
Employed, n (%)	3779 (74.9)	1263 (79.5)	2516 (72.7)	
Unemployed, n (%)	505 (10.0)	124 (7.8)	381 (11.0)	
Retired or student, n (%)	763 (15.1)	201 (12.7)	562 (16.2)	
Living status				0.128
With others (parents, friends, etc.), n (%)	3619 (71.7)	1144 (72.0)	2475 (71.6)	
Alone, n (%)	1428 (28.3)	444 (28.0)	984 (28.4)	
Anyone around confirmed infected with COVID-19 (Yes), n (%)	131 (2.6)	29 (1.8)	102 (2.9)	5.425*
Infected with COVID-19 (Yes), n (%)	30 (0.6)	6 (0.4)	24 (0.7)	1.839

Abbreviation: SD, standard deviation.

* $p < 0.05$.

** $p < 0.001$.

new occurrences of depressive symptoms, anxiety symptoms and insomnia symptoms (range, adjusted RRs 1.69–1.81).

Table 4 presents the long-term associations between stress symptoms at baseline and the persistence of other psychological problems. Compared to the participants without stress symptoms at baseline, participants with stress symptoms at baseline had a higher risk of having persistent depressive symptoms and anxiety symptoms. However, the associations were not statistically significant.

3.3. Additional analyses

eTable 2 and eTable 3 in Appendix A Supplementary data present the longitudinal associations between stress symptoms situations (persistently asymptomatic, new occurrence, remission, and persistence) and the outcomes of depressive symptoms, anxiety symptoms and insomnia symptoms (new occurrence or persistence). New occurrences or persistence of stress symptoms was found to be positively associated with new occurrences or persistence of depressive symptoms, anxiety symptoms and insomnia symptoms (range, adjusted ORs 3.43–53.16). The remission of stress symptoms was found to be negatively associated with the persistence of depressive symptoms, anxiety symptoms and insomnia symptoms (range, adjusted ORs 0.06–0.55).

Table 2
Associations of stress symptoms with psychological symptoms at baseline.

	Total sample (n = 5047)	Prevalence of mental distress at baseline		Crude OR (95%CI) ^a	Adjusted OR (95%CI) ^{a,b}
		Non stress symptoms	Stress symptoms		
Depressive symptoms (Yes), n (%)	3168 (62.8)	318 (20.0)	2850 (82.4)	18.69(16.07–21.73)**	19.21 (16.48–22.40)**
Anxiety symptoms (Yes), n (%)	2648 (52.5)	100 (6.3)	2548 (73.7)	41.62(33.53–51.66)**	42.08 (33.86–52.29)**
Insomnia symptoms (Yes), n (%)	2666 (52.8)	194 (12.2)	2472 (71.5)	18.00(15.22–21.28)**	18.61 (15.69–22.06)**

Abbreviation: OR, odds ratio; CI, confidence interval.

^a The Reference in Logistic regression models were the non-stress symptoms group.

^b Logistic regression models were controlled for age, gender and other socio-demographics significantly correlated with stress symptoms at baseline (enter method).

** p < 0.001.

Table 3
Long-term associations between stress symptoms at baseline and the new occurrences of psychological distress symptoms at follow-up.

	New occurrence of psychological distress symptoms at follow-up		Crude RR (95%CI) ^a	Adjusted RR (95%CI) ^{a, b}
	Non stress symptoms	Stress symptoms		
Depressive symptoms (168/801)	16.8 %	29.8 %	1.78 (1.32–2.41)**	1.81 (1.33–2.46)**
Anxiety symptoms (167/1004)	13.3 %	22.2 %	1.68 (1.24–2.27)*	1.69 (1.24–2.30)*
Insomnia symptoms (141/960)	11.7 %	19.4 %	1.66 (1.19–2.31)*	1.71 (1.23–2.39)*

Abbreviation: RR, risks ratio; CI, confidence interval.

^a The Reference in Poisson regression models were the non-stress symptoms group.

^b Regression model were controlled for age, gender and other socio-demographics significantly correlated with stress symptoms at baseline.

* p < 0.01.

** p < 0.001.

Table 4
Long-term associations between stress symptoms at baseline and the persistence of psychological distress symptoms at follow-up.

	Persistence of psychological distress symptoms at follow-up		Crude RR (95%CI) ^a	Adjusted RR (95%CI)
	Non stress symptoms	Stress symptoms		
Depressive symptoms (799/1312)	50.0 %	62.0 %	1.24 (0.95–1.62)	–
Anxiety symptoms (589/1109)	51.4 %	53.2 %	1.03 (0.65–1.65)	–
Insomnia symptoms (539/1153)	48.7 %	46.6 %	0.96 (0.68–1.33)	–

Abbreviation: RR, risks ratio; CI, confidence interval.

^a The Reference in Poisson regression models were the non-stress symptoms group.

4. Discussion

In this study, we found that the prevalence of stress symptoms among depressed patients was 68.5 % at baseline; it declined to 51.1 % at follow-up. We also found that having stress symptoms at baseline was a predictor for the new occurrences of depressive symptoms, anxiety symptoms and insomnia symptoms.

The prevalence of stress symptoms in depressed patients in our study

was higher than that of general population during the COVID-19 pandemic period (Mazza et al., 2020; Shi et al., 2020; Tee et al., 2020) or after the COVID-19 outbreak was initially controlled (Guo et al., 2021). Firstly, it is because we used different scales or different cut-offs compared to these previous studies. We used a cut-off of ≥ 9 in IES-R, which may be more sensitive to detect stress symptoms. Secondly, another notable reason for the higher prevalence in depressed patients was the greater sensitivity and awareness of sensations in depressed patients' own bodies (Özdin and Bayrak, 2020). Apart from the higher vulnerability for developing psychological distress, depressed patients are more susceptible to psychiatric symptoms during the COVID-19 pandemic due to the reduction in mental health services (Hao et al., 2020). Because of suspended hospital visits during the COVID-19 pandemic, 24.5 % of new patients could not receive timely diagnoses and treatment, while 22.0 % of existing patients with diagnosed mental disorders were unable to receive routine psychiatric care (Zhou et al., 2020). One possible reason for the decline in prevalence from the baseline to the follow-up was the containment measures during the COVID-19 pandemic in mainland China. Our baseline investigation was done when the first COVID-19 outbreak had just been initially controlled, while the follow-up survey was completed five months later. The effective containment measures during the COVID-19 pandemic may reduce the patients' stress responses over time. Another possible reason was that the gradual return to normal life and restart of the routine medical care in the regular ongoing prevention and control stage may reduce the stress responses in the depressed patients.

We found that having stress symptoms at baseline was a predictor for the new occurrences of depressive symptoms, anxiety symptoms and insomnia symptoms. Multiple studies have confirmed the associations between stress and other mental health problems such as depression, anxiety and insomnia (Kalmbach et al., 2018; Seib et al., 2018; Yang et al., 2015). Stressful life events produce acute stress reactions or even chronic stress, making people be anxious or depressed and lose sleep at night (McEwen, 2006).

Previous studies also demonstrated the longitudinal relationships among stress and other psychological problems. A cohort study suggested that both prenatal stress and the pattern of postnatal stress exposure can indicate adult depressive or anxiety symptoms, depending on gender and timing of exposure (Herbison et al., 2017). A study using animal models suggested that acute and chronic stress exposures induced maladaptive encoding of emotional memories, which might lastly become a source of chronic anxiety (Roozendaal et al., 2009). Stress also plays an important role in developing insomnia. A retrospective study demonstrated an increase of negative life events before the outbreak of insomnia (Åkerstedt, 2006). The perceived impact of daily minor stressors and the intensity of major negative life events were rated higher for insomniacs than for good sleepers (Morin et al., 2003). For the pathophysiology mechanisms in the longitudinal relationships between stress and other psychological problems, the abnormality of hypothalamic-pituitary-adrenal (HPA) axis function is a fundamental factor (Hori et al., 2010). The stress-induced dysregulation in prefrontal cortex and amygdala and the enhancement of immune system are playing important roles in developing depression, anxiety and insomnia

(Gold et al., 2015; Jaremka et al., 2013; Pike and Irwin, 2006; Ray et al., 2017).

Although a large amount of resources have been allocated to fighting against COVID-19 during the pandemic, necessary attention should be paid to the vulnerable people who previously had psychiatric disorders, such as depressed patients. Clinical services are recommended to be redistributed to ensure that the psychiatric patients can receive timely diagnoses, treatment or routine psychiatric care. Considering the inconvenience of traffic controls and quarantine measures in many areas, online mental health services such as hot-lines and mobile application platforms are recommended to be adopted more widely (Li et al., 2020). The government and authorities should also timely release the COVID-19-related information and enhance the education on knowledge of the pandemic to reduce the psychological stress in the public.

5. Strengths and limitations

One of the strengths of this study is its wide coverage among the Chinese depressed patients. The participants were recruited nationwide from multiple centers and provincial-grade areas. All subjects were recruited by professionals at the outpatients. Therefore, the data were more credible and representative. Additionally, we were able to conduct the survey offline at the outpatients, making our surveys more reliable compared to the online surveys. Moreover, this is a longitudinal study, which enables us to understand the changes of psychological symptoms and the role of stress symptoms in these changes after the first COVID-19 outbreak was initially controlled. Furthermore, our study focused on depressed patients, who were vulnerable and in need of attention during the COVID-19 pandemic.

Our study has several limitations. First, the participants were recruited by using a convenience sampling method. Only the outpatients from the hospitals were obtained in the study. Therefore, the representativeness and the generalizability of the findings might be limited. In addition, we could not calculate the participation rate because we did not record the total number of the patients we invited. Second, there were 5047 valid participants attending the survey at baseline, but only 2113 of them were investigated at follow-up. The high dropout rate may undermine the validity of our results. Third, all the mental health symptoms in the survey were self-reported rather than evaluated by the professionals, which might lead to some biases. Finally, the current mental conditions of the participants and the duration of their depression disorders were not recorded in the study, which might affect the results and lead to unavoidable bias when evaluating their psychological symptoms.

6. Conclusion

In this study, a high prevalence of stress symptoms was found among the depressed patients after the first COVID-19 outbreak was initially controlled in China. The prevalence declined five months later. We found that having stress symptoms at baseline was a predictor for the new occurrences of psychological symptoms.

Ethical statement

On behalf of all authors, I certify that the manuscript is original, which has not been published before and is not being considered for publication elsewhere. All authors have contributed to the creation of this manuscript for important intellectual content and read and approved the final manuscript. We declare there is no conflict of interest.

The study procedures were approved by the Ethics Committee of Nanfang Hospital, Southern Medical University. Informed consent was given and confidentiality was guaranteed. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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Conflict of interest

We declared no conflict of interest.

CRediT authorship contribution statement

Dr. B. Zhang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: B. Zhang.

Acquisition, analysis, or interpretation of data: J.L. Guo, Y.H. Zhao, L.Q. Fang, Y. Xu, B. Zhang.

Drafting of the manuscript: J.L. Guo, Y.H. Zhao.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: J.L. Guo, Y.H. Zhao, J.J. Wang, Z.H. Lv.

Obtained funding: B. Zhang, S. Liu, X. Luo.

Administrative, technical, or material support: C. Tang, E.Z. Li, X. Luo, J.H. Zhang, B. Zhang.

Supervision: J.L. Guo, Y.H. Zhao, S. Liu, J.H. Zhang, B. Zhang.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2022.05.001>.

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