The impact of COVID-19 on subthreshold depressive symptoms: a longitudinal study

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Abstract

Aims
The COVID-19 pandemic represents an unprecedented threat to mental health. Herein, we assessed the impact of COVID-19 on subthreshold depressive symptoms and identified potential mitigating factors.

Methods
Participants were from Depression Cohort in China (ChiCTR registry number 1900022145). Adults (n=1722) with subthreshold depressive symptoms were enrolled between March and October 2019 in a 6-month, community-based interventional study that aimed to prevent clinical depression using psychoeducation. A total of 1506 participants completed the study in Shenzhen, China: 726 participants, who completed the study between March 2019 and January 2020 (i.e., before COVID-19), comprised the “wave 1” group; 780 participants, who were enrolled before COVID-19 and completed the 6-month endpoint assessment during COVID-19, comprised “wave 2.” Symptoms of depression, anxiety and insomnia were assessed at baseline and endpoint (i.e., 6-month follow-up) using the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7) and Insomnia Severity Index (ISI), respectively. Measures of resilience and regular exercise were assessed at baseline. We compared the mental health outcomes between wave 1 and wave 2 groups. We additionally investigated how mental health outcomes changed across disparate stages of the COVID-19 pandemic in China, i.e., peak (Feb. 7-13), post-peak (Feb. 14-27), remission plateau (Feb. 28-present).

Results
COVID-19 increased the risk for three mental outcomes: 1) depression (odds ratio \( OR = 1.30, 95\% \ CI: 1.04-1.62 \); 2) anxiety (\( OR = 1.47, 95\% \ CI: 1.16-1.88 \)); and 3) insomnia (\( OR = 1.37, 95\% \ CI: 1.07-1.77 \)). The highest proportion of probable depression and anxiety was observed post-peak, with 52.9% and 41.4%, respectively. Greater baseline resilience scores had a protective effect on the three main outcomes (depression: \( OR = 0.26, 95\% \ CI: 0.19-0.37 \); anxiety: \( OR = 1.22, 95\% \ CI: 0.14-0.33 \); and insomnia: \( OR = 0.18, 95\% \ CI: 0.11-0.28 \)). Furthermore, regular physical
activity mitigated the risk for depression ($OR=0.79$, 95% CI: 0.79-0.99).

**Conclusions**

The COVID-19 pandemic exerted a highly significant and negative impact on symptoms of depression, anxiety and insomnia. Mental health outcomes fluctuated as a function of the duration of the pandemic and were alleviated to some extent with the observed decline in community-based transmission. Augmenting resiliency and regular exercise provide an opportunity to mitigate the risk for mental health symptoms during this severe public health crisis.
Introduction

The COVID-19 pandemic poses an unprecedented mental health threat globally as a consequence of the fear of contraction, as well as government reaction to containing community spread (e.g., economic shut down, unemployment). Replicated studies from around the world have reported on the increased prevalence of mental disorders as a result of COVID-19, including depression, anxiety and insomnia (i.e., prevalence of 10.6% to 50.7%, 10.4% to 44.7% and 33.9% to 36.1%, respectively) (Zhang et al., 2020; Lai et al., 2020; Wang et al., 2020b; Liu et al., 2020; Potloc Study, 2020). Furthermore, as a consequence of heightened anxiety due to the pandemic, along with the economic shock and stress related to quarantine, an increase in suicide is expected in Canada, the United States, and possibly other countries (McIntyre and Lee, 2020a; 2020b).

Subthreshold depressive symptoms (i.e., not meeting minimum diagnostic threshold for a major depressive episode) are an important risk indicator for incident major depressive disorder (MDD). Persons with subthreshold depressive symptoms are approximately twice as likely to be diagnosed with MDD relative to those without (Lee et al., 2019; Rodriguez et al., 2012). In the general population, the absolute risk of conversion to MDD from subthreshold depressive symptoms (excluded lifetime MDD) ranged from 0.012 to 0.096 per 100 person years (Cuijpers and Smit, 2004). A 13-year prospective study in communities indicated the mean age of first depressive episode in people with subthreshold depressive symptoms was 34 years, which was similar with the age onset in MDD (Chen et al., 2000). It has been estimated that approximately 2.9% to 9.9% of adults in primary care and 1.4% to 17.2% of adults in community settings manifest subthreshold depressive symptoms (Lee et al., 2019).

Recent studies have raised concerns about populations that are more vulnerable to the detrimental mental health effects of the COVID-19 pandemic. For example, people with mental health conditions may be more substantially influenced by the emotional distress brought on by the COVID-19 pandemic, resulting in relapses or worsening of pre-existing mental health condition(s) compared with the general population. 

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population (Yao et al., 2020). In addition, psychological response may change with fluctuations in the epidemic and clinical knowledge improvement. For example, a related longitudinal study investigating psychological adaptions during the severe acute respiratory syndrome (SARS) outbreak suggested that increasing knowledge and understanding of SARS could improve mental health outcomes (Su et al., 2007).

The primary aim of this longitudinal study is to evaluate the impact of COVID-19 in a subthreshold depressive symptom population. The secondary aim of this study is to explore potential predictors of mental health improvement to recommend feasible intervention under acute stress.

Methods

Study design and participants

Data in this study were derived from an ongoing longitudinal, population-based study for the early identification, treatment, prevention, and management of depression and subthreshold depression (Depression Cohort in China [DCC] study, ChiCTR registry number 1900022145). Individuals were identified via a standardized community-based screening protocol for the detection of depression in 2 communities, 21 primary care centers, 1 general hospital and 1 specialized mental health hospital in Shenzhen, China. Participants aged 18-64 years meeting criteria for subthreshold depressive symptoms were enrolled between March 2019 and October 2019. Subthreshold depressive symptoms were operationalized as having a Patient Health Questionnaire-9 (PHQ-9) total score of ≥ 5 without current or history of MDD. The follow-up period was 6 months. Exclusion criteria were: (1) a diagnosis of MDD, severe psychiatric disorders (i.e. schizophrenia, bipolar disorder, schizoaffective mental disorder, paranoid mental disorder, mental disorder caused by epilepsy, mental retardation) and/or alcohol or drug addiction disorder, (2) pregnant or perinatal women, (3) not being fluent in mandarin, and (4) not having a plan to leave Shenzhen within 6 months. Psychiatric diagnoses were confirmed by trained psychiatrists using the Mini International Neuropsychiatric Interview (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria). The study protocol was approved by the Ethical
Review Boards of all the participating centers, and all the participants gave written informed consent.

A total of 3,715 people were screened, of which 2,645 (71.2%) were from 21 primary care centers, 468 (12.6%) were from 2 communities, 368 (9.9%) were from a general hospital and 234 (6.3%) people were from a specialized mental health hospital. A total of 1,722 participants were enrolled in the study between March 2019 and October 2019. Of the 1,722 participants, 1,506 (87.5%) participants completed the 6-month study; 216 participants were lost during follow-up (i.e., withdrew from study, n=71; did not complete questionnaires, n=29; unable to contact, n=116). Of the 1,506 participants with endpoint data, participants who completed the baseline and 6-month follow-up before the COVID-19 outbreak were classified into the “wave 1” group (i.e., from March 2019 to January 2020) and participants who completed baseline before the COVID-19 outbreak but completed the 6-month follow-up during the COVID-19 outbreak were classified into “wave 2” group (i.e., from August 2019 to April 2020).

**BRIDGES integrate care**

The DCC study used a Building Bridges to Integrate Care (BRIDGES) model, which used the Toronto-based BRIDGES model as a reference (Bhattacharyya et al., 2016), and linked primary care centers, specialist hospitals and community care in accordance to the health system in Shenzhen. In this healthcare model, psychiatrists from specialist hospitals trained general practitioners (GPs) in primary care centers to identify, and provided treatment and education programs for participants with subthreshold depressive symptoms. Project managers, who were public health doctors, from specialist hospitals supervised and ensured the quality administration of the intervention provided by the GPs. Both wave 1 cohort and wave 2 cohort received the same usual care, including 1) delivering project introduction brochures; 2) sending a short message service (SMS) monthly that provide mental health education (i.e., mental health stereotypes, depression treatments and stress arrangement); 3) telephone-based mental health consult every 6 months (i.e., mental health condition communication and updated information of psychiatric evaluation in study); 4)
referral and face-to-face psychiatric evaluation for participants with PHQ-9 >9 or for those with an active request to see a doctor.

**Outcome and covariates**

Depression and anxiety symptoms in the past 2 weeks were assessed using the Patient Health Questionnaire-9 (PHQ-9, Cronbach’s α=0.89) and Generalized Anxiety Disorder-7 (GAD-7, Cronbach’s α=0.89), respectively (Kurt Kroenke et al., 2001; Löwe et al., 2008). The severity of depression and anxiety was divided into minimal, mild, moderate, and severe based on a score of 0-4, 5-9, 10-15 and above 15, respectively (Kurt Kroenke et al., 2001; Löwe et al., 2008). Participants with a score of PHQ-9 or GAD-7 ≥ 5 were considered as probable depression or anxiety, respectively. Insomnia symptoms were assessed using the Insomnia Severity Index (ISI, Cronbach’s α=0.92), where participants were classified based on their score (i.e., group of none, subthreshold, moderate and severe of score 0-7, 8-14, 15-21 and 22-28, respectively) (Bastien et al., 2001; Gagnon et al., 2013). Participants with ISI>7 was considered to have suspected insomnia.

To explore the fluctuations of the three main outcomes, as well as the COVID-19 related behaviors and perceived impacts during the outbreak, we separated wave 2 follow-up time into three intervals, which included the height of the pandemic (i.e., February 7 to February 13, 2020 when the daily incidence of new COVID-19 cases climb to the peak and rigorous lockdown measures were implemented), the peak of the COVID-19 crisis (i.e., February 14 to 27), and the remission plateau (i.e., February 28 April 23). These three time intervals were defined as peak, post-peak and remission plateau, respectively. Before the COVID-19 outbreak, the questionnaires were conducted face-to-face or online. During the COVID-19 outbreak, all of our questionnaires were conducted online.

We also assessed somatic symptoms, resilience and demographic characteristics (only at baseline) to explore the risk factors related to the main outcomes. The mean score for the seven pain-related items (items 2,3,9,14,19,27 and 28) in the 28-item Somatic Symptoms Inventory (SSI, Cronbach’s α=0.80) was used to assess painful and non-painful somatic symptoms. Participants with mean scores for each item <2.2
in SSI were considered to be without pain (Goldstein et al., 2004). Resilience was assessed using the Connor-Davidson Resilience Scale (CD-RISC, Cronbach’s $\alpha=0.91$)(Yu and Zhang, 2007). As the cut-point score in the general population, we considered the mean score of CD-RISC below 80 as poor resilience (Connor and Davidson, 2003).

Demographic characteristics were measured using self-report questionnaires, which included basic information, health status and behaviors. COVID-19 related behaviors and perceived impacts were also measured in wave 2 at the 6-month follow-up during the outbreak, including the number of days worrying about COVID-19 in the past week (i.e., 0-2 days, 3 days and above), perceived COVID-19 influence on current life (i.e., none or mild, moderate or severe), perceived COVID-19 influence on future life (i.e., none or mild, moderate or severe) and perceived risk of infection COVID-19 (i.e., none or low, moderate or high).

**Statistical analysis**

We estimated the proportion of depression, anxiety and insomnia symptoms at baseline and 6-month follow-up using the longitudinal surveys. For interpretative purposes, all outcomes and baseline characteristics were measured as categorical variables. In the univariate analysis, we identified the change between baseline and 6-month follow-up of severity in three main outcomes using the chi-squared test, as well as comparing the difference between wave 1 and 2 at baseline and follow-up. To explore the impact of COVID-19 and other potential factors on outcomes, we included all participants ($n=1506$) in the binary logistic regression analysis to estimate their associations with probable depression, anxiety and suspected insomnia during the 6-month follow-up by adjusting for baseline severity of depression, anxiety and insomnia categories, respectively, presenting results as odds ratios. To examine the relationship between main outcomes in different time intervals of the COVID-19 outbreak and COVID-19-related behaviors, we selected participants in wave 2 and applied the chi-square trend test. All tests were two-tailed, with a significance level of $P$-values$<0.05$. Statistical analysis was performed on SPSS Statistic 25.0 (Property of IBM Corp.).
Results

1. Baseline characteristics

In our recruitment process, there were 36 people were excluded due to the presence of a severe psychiatric illness in two waves (14 and 22 in wave 1 and 2, respectively). Of the 1506 participants, 726 participants completed the study in wave 1 and 780 participants completed the study in wave 2 (table 1). Differences in baseline characteristics between participants who completed versus those who did not complete the study were not significant. Participants in wave 1 were older and more likely to be married when compared to participants in wave 2. Other baseline demographic characteristics were well balanced and similar between participants within the two waves. Furthermore, wave 2 participants had higher rates of chronic disease and smoking behavior, as well as lower rate of exercise habit at baseline when compared to wave 1. There were no statistically significant differences in measures of depression, anxiety and insomnia at baseline between wave 1 and 2 (Table 2).

2. Comparison of main outcomes between baseline and 6-month follow-up

The unadjusted percentages of depression severity, anxiety and insomnia at baseline and 6-month follow-up were compared across all and separated waves in Table 2. There was 56% of participants with probable depression at baseline improved into the minimal group at 6-months. The prevalence rate of probable anxiety and suspected insomnia also increased by approximately 20% in both the minimal and none group, respectively. Additionally, the mean (s.d.) score of depression, anxiety and insomnia at the 6-month follow-up had a significant decrease compared with baseline, which were 4.7 (4.2) vs 8.1 (4.0), 3.5 (3.6) vs 5.6 (4.4) and 5.9 (5.5) vs 8.6 (6.2), respectively. However, in terms of the magnitude of remission, wave 2 showed a dramatic magnitude of remission compared to wave 1. Focusing on the severe group, depression accounted for the highest proportion among three main outcomes with 4.7% in wave 2 follow-up, compared with 2.6% in wave 1, followed by insomnia (2.8% and 1.2%, respectively). However, anxiety had a lower prevalence rate in the severe group of wave 2, as it accounted for a higher rate of 6.0% in the moderate group, compared with 3.3% in wave 1. The severity of the mild group took up largest
proportion in depression, anxiety and insomnia in wave 2, which were 33.1%, 28.3% and 24.1%, respectively.

3. **COVID-19 and other indicators related to the main outcomes in 6-month follow-up**

According to the severity change of mood scales, we examined whether the baseline characteristics had a favorable or unfavorable effect on depression, anxiety and insomnia. We defined 6-month outcomes into probable depression, probable anxiety and suspected insomnia. In table 3, after adjusting for all indicators, participants who completed 6-month follow-up during COVID-19 outbreak was a risk factor for probable depression ($OR= 1.30$, 95% CI: 1.04, 1.62), anxiety ($OR=1.47$, 95% CI: 1.16, 1.88) and suspected insomnia ($OR=1.37$, 95% CI: 1.07, 1.77). Baseline severity of depression, anxiety and insomnia also showed a strong dose-response gradient with probable depression, anxiety and suspected insomnia, respectively. For somatic symptoms and mood resilience, SSI was not associated with all three main outcomes, whereas participants with better resilience (CD-RISC score >80) had a stronger beneficial effect on them.

In terms of the demographic indicators, being married contributed a beneficial effect to all of depression, anxiety and insomnia. Participants with alcohol consumption (i.e., 3 days and above in a month) were more vulnerable to probable depression ($OR= 1.43$, 95% CI: 1.05, 1.95) and anxiety ($OR=1.39$, 95% CI: 1.01, 1.94), whereas the association with suspected insomnia was not detected. In particular, exercising once per week and living with a non-relative were protective factors against depression. Having lived in Shenzhen for more than 10 years was associated with a greater risk for insomnia, whereas being overweight was protective against insomnia. Unadjusted and adjusted pooled estimates of probable depression, anxiety and suspected insomnia are available in the supplementary materials.

4. **Time-dependent change of main outcomes and behaviors during COVID-19 outbreak**

To characterize the effects of the COVID-19 pandemic on depression, anxiety, and insomnia, we compared the proportion of participants meeting criteria for probable
depression, anxiety, and suspected insomnia at endpoint at the three different time intervals. Of the 780 participants who completed the study during the COVID-19 pandemic, 161 (20.6%), 367 (47.1%), and 252 (32.3%) were included in the peak, post-peak and remission plateau subgroups, respectively.

Baseline symptom severity did not differ between the three COVID-19-related subgroups (i.e., probable depression, \( \chi^2=3.86, P=0.43 \); probable anxiety, \( \chi^2=2.01, P=0.92 \); suspected insomnia, \( \chi^2=7.29, P=0.30 \)). Figure 1 showed that probable depression and anxiety significantly changed across the follow-up time intervals. The highest rates of probable depression and anxiety were detected between February 14, 2020 and February 27, 2020, which was after the peak of the newly diagnosed cases per day. From February 28, 2020 and onwards, the rate of probable depression and anxiety dropped to the lowest rate at 43% and 29%, respectively. However, the rate of suspected insomnia was not significantly different across the time process of COVID-19.

Individuals reporting greater symptoms of COVID-19-related distress, as operationalized by the number of days worried about COVID-19 in the past week (i.e., more than 3 days), perceived influence of COVID-19 on current and future life (i.e., moderate to severe), and perceived risk of infection (i.e., moderate to high), were significantly more likely, than those reporting fewer symptoms of distress, to have probable depression, anxiety and/or insomnia. Focusing on the COVID-19 related behaviors (Figure 2), all four items demonstrated an inverse linear relationship with time process, with the Pearson correlation coefficient of -0.163 (\( P<0.001 \)), -0.154 (\( P<0.001 \)), -0.136 (\( P<0.001 \)) and -0.155 (\( P<0.001 \)) in days focus on COVID-19, perceived influence on current life, perceived influence on future life and perceived risk of COVID-19 infection, respectively. Different from the main outcomes change, the highest rate of behaviors was detected in the first time period of February 13, 2020 and before. Participants who perceived moderate or severe influence on current life accounted for the highest rate among all behaviors items.

**Discussion**
Our prospective longitudinal study described the psychological impact of the COVID-19 pandemic on subthreshold depressive symptoms. The general remission of depression, anxiety and insomnia had been detected from baseline to 6-month follow-up, whereas wave 2 participants who completed the follow-up during the COVID-19 pandemic had significantly higher rates of probable depression, anxiety and insomnia relative to wave 1, after controlling for the sociodemographic characteristics, health status and behaviors, and severity of baseline mental health outcomes. With the time process of COVID-19 outbreak in China, the highest rate of probable depression and anxiety had been found after the peak of newly diagnosed cases, and further decreased with the remission plateau. Similarly, the frequency and degree of COVID-19 related behaviors were also improving as the severity of the COVID-19 pandemic subsided.

**COVID-19 and subthreshold depressive symptoms**

The COVID-19 pandemic is having a profound effect on all aspects of society. We found that participants in our study had a relative higher proportion (47.8%) of probable depression during COVID-19 outbreak (wave 2), when compared to the general population in a previous study (30.3%) (Wang et al., 2020a). A survey conducted in southwestern China, near Wuhan, also demonstrated a relative low prevalence of depression and anxiety with 8.3% and 14.6%, respectively (Lei et al., 2020). Nevertheless, health care workers shared similar rates of probable depression, anxiety and suspected insomnia with our study, which were 50.4%, 44.6% and 34.0%, respectively (Lai et al., 2020). It could be hypothesized that the significant workload, as well as close contact with people who potentially have been infected by the virus, were also considered a susceptible population during the COVID-19 outbreak.

**COVID-19 and stress**

Epidemics act as a stressor during an outbreak and never affect all populations equally. For example, the individual effects of mental health stressors are moderated by personality and cognitive constructs. In our study, we found that resilience may play a more important protective role on depression, anxiety and insomnia. For example, it has been reported that the association between adverse childhood experiences and depression was stronger among individuals with low resilience.
compared to those with high resilience (Poole et al., 2017). Psychological models suggest that individual differences in the strength of the personality or schema features determine how stressors will be interpreted. Stress appraisals that represent threats or depletion in the core areas of self-worth may portend depressive symptoms (Hammen, 2005). A separate study also demonstrated that the SL genotype in serotonin transporter (5-HTTLPR) gene appeared resilient to depression in terms of cortisol and recent stress (Ancelin et al., 2017).

With respect to this large-scale pandemic and similar disasters, improving coping methods and mood resilience were an effective way to prevent mental health disorders. A randomized controlled trial demonstrated that interventions targeting stress management, goal setting, cognitive reframing, and meaning making significantly improved resilience and marginal effect to avoid depression in patients with cancer (Rosenberg et al., 2018). Second, stressor content can lead to various mental health outcomes. Chronic and unpredictable stress (defined as stress for more than 12 months) is a stronger predictor of depressive symptoms than acute stressors. Interpersonal “loss” event was unique significance for depression, which included bereavement, separations, endings or threats of separation (Hammen, 2005). To explore the psychological impact of COVID-19, we not only needed to consider the susceptible population, but also consider the different interpretations of stress in varying populations.

The temporality of the epidemic may lead to various outcomes vis-a-vis mental health conditions. In our study, probable depression and anxiety fluctuated with the COVID-19 outbreak curve, but, overall, the increasing rate of mental health outcomes were consistent with a study that showed higher average levels of symptoms (stress, anxiety, and depression) after the nationwide state of alert and stay-at-home order (Ozamiz-Etxebarria et al., 2020). The study suggested that individuals have difficulty assimilating and processing the current crisis. The late stage reduction trend was similar to a meta-analysis which showed that depression, anxiety and insomnia symptoms in post-illness stage were lower than acute stage in SARS and Middle East respiratory syndrome (MERS) epidemic among the population (Rogers et al., 2020).
This study suggested that if a COVID-19 infection follows a similar course to that of SARS or MERS, most patients should recover without experiencing mental illness. In general, an increasing trend of depression and anxiety may only be specific to a time interval of an acute stimulation. Some positive effects in terms of psychological regulation and personal coping styles were worth noting for mental health improvement. In addition, these mental health symptoms levels can be expected to increase further as confinement and isolation are extended, in addition to the adverse events induced by epidemic. Hence, it would be useful to further evaluate mental health conditions over time (Brooks et al., 2020).

Target interventions

In our study, there were other factors that drew our attention to their effects on the mental health condition in the 6-month follow-up. Regular exercise may attenuate the probability of developing depression compared with people with non-regular exercise habits (adjusted OR=0.79, 95% CI=0.63-0.99). The result was consistent with a meta-analysis which indicated that higher levels of physical activity were related to lower odds of developing depression (adjusted OR =0.83, 95% CI=0.79-0.88) (Schuch et al., 2018). A randomized controlled trial also demonstrated that the intervention of yoga plus regular care could significantly improve depression symptoms and score on CD-RISC, but not anxiety (Michael de Manincor et al., 2016). We also found that high frequency of alcohol consumption was harmful on probable depression and anxiety compared to low frequency.

The foregoing finding was in accordance with a study that indicated that hazardous drinking (a score≥8 of Alcohol Use Disorder Identification Test) was associated with a higher risk of depression than non-hazardous alcohol consumption (risk ratio= 1.8, 95% CI= 1.4, 2.4) (Gemes et al., 2019). However, depending on the various definitions of alcohol consumption, depression is primarily related to drinking larger quantities per occasion and less related to volume, and unrelated to drinking frequency; this effect is stronger for women than for men (Graham et al., 2007). Further studies need to identify the dose-response relationship between behaviors and mental health outcomes. Recommending a healthy lifestyle may afford a positive
attitude to coping with adverse events.

**Further research**

Taken together, we draw the following views and provide some directions for the further research: 1) more attention (e.g., resource allocation) could be paid to vulnerable and susceptible populations when an adverse event occurs. For example, expert resources including psychiatrists, psychologists and mental health hospital may target the people at severe risk actively (i.e., bereavement, COVID-19 infected/suspected cases and severe mental health symptoms). People with mild mental health symptoms could be monitored by social workers and receive psychoeducation from public medias and service. It may be more cost-effective to allocate mental health resources in a reasonable way; 2) finding an appropriate way to improve mood resilience and coping methods under the stress may afford protections to prevent mental health disorders; 3) medical health workers may need to invest resources to mitigate the effects of a mental health outbreak during an epidemic and provided intervention promptly, as well as the further attentions on the following adverse events induced by epidemic; 4) mental health education may need to be provided, and may not only convey general information about mental health, but also recommend and conduct behaviors- and life-style-related intervention to prevent mental health problems.

**Strengths and limitations**

Major strengths of this study are its prospective design, the large representative community-based sample and the use of a clinically validated diagnostic interview to establish a wide range of mental disorders (Mini International Neuropsychiatric Interview). However, our study also has several methodological limitations that affect the inferences and interpretations of our data. First, we did not compare participants with mental health disorders to the general population in our study, wherein individuals without mental health disorders may have different reactions to mental health conditions on COVID-19. Second, our study only estimated the mental health impact until April 2020. Consequently, the effect of an economic recession, unemployment and concern about epidemic relapse after the epidemic may have a
greater mental health impact on the general population and should be taken into consideration in future research.

In conclusion, COVID-19 plays an essential role to worsen mental health conditions, including depression, anxiety and insomnia. During the COVID-19 outbreak, mental health conditions and behaviors fluctuated with the epidemic time process, which may provide insight to mental health workers to conduct interventions to alleviate stress and anxiety. Furthermore, regular exercise and ways to improve resilience may be a feasible recommendation as a mental health prevention, whether or not an adverse event occurs.

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Conflict of interest
All other authors declare no competing interests.

Ethical standards
The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Availability of data and materials
Data for the Depression Cohort in China are available through the Sun Yat-Sen University. Contact Prof. Lu for access approval.
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**Figure 1** Time-dependent change of probable depression, anxiety and suspected insomnia during COVID-19 outbreak

*P-values<0.05

**P-values<0.01
Figure 2 Time-dependent change of behaviors during COVID-19 outbreak

*P-values<0.05

**P-values<0.01

***P-values<0.001
Table 1 Baseline demographic information. All participants were enrolled in the 6-month study between March and October 2019.

| Baseline characteristics | All participants N=1506 | Wave 1 group N=726 | Wave 2 group N=780 | P-values |
|--------------------------|-------------------------|--------------------|--------------------|----------|
| **Baseline characteristics** |                         |                    |                    |          |
| Age group, N (%)         |                         |                    |                    |          |
| 18-39                    | 897 (59.6)              | 408 (56.2)         | 489 (62.7)         | 0.008    |
| 40-59                    | 540 (35.9)              | 275 (37.9)         | 265 (34.0)         |          |
| ≥60                      | 69 (4.6)                | 43 (5.9)           | 26 (3.3)           |          |
| **Gender, N (%)**        |                         |                    |                    | 0.089    |
| Male                     | 560 (37.2)              | 254 (35.0)         | 306 (39.2)         |          |
| Female                   | 946 (62.8)              | 472 (65.0)         | 474 (60.8)         |          |
| **Education, N (%)**     |                         |                    |                    | 0.900    |
| Below undergraduate      | 442 (61.7)              | 451 (62.1)         | 487 (62.4)         |          |
| Undergraduate and above  | 274 (38.3)              | 275 (37.5)         | 293 (37.6)         |          |
| **Occupation, N (%)**    |                         |                    |                    | 0.055    |
| Unemployed               | 133 (18.9)              | 162 (22.3)         | 143 (18.3)         |          |
| employed                 | 583 (81.4)              | 564 (77.7)         | 637 (81.7)         |          |
| **Marital status, N (%)**|                         |                    |                    | 0.025    |
| Unmarried                | 370 (24.6)              | 156 (21.5)         | 214 (27.4)         |          |
| Married                  | 1085 (72.0)             | 546 (75.2)         | 539 (69.1)         |          |
| Divorced or widowed      | 51 (3.4)                | 24 (3.3)           | 27 (3.5)           |          |
| **Birth place, N (%)**   |                         |                    |                    | 0.204    |
| Hubei                    | 159 (10.6)              | 79 (10.9)          | 80 (10.3)          |          |
| Local                    | 121 (8.0)               | 49 (6.7)           | 72 (9.2)           |          |
| Non-local                | 1226 (81.4)             | 598 (82.4)         | 628 (80.5)         |          |
| **Years live in Shenzhen, N (%)** |             |                    |                    | 0.709    |
| 5 years and below        | 440 (29.2)              | 205 (28.2)         | 235 (30.1)         |          |
| 5-10 years               | 251 (16.7)              | 124 (17.1)         | 127 (16.3)         |          |
| 10 years and above       | 815 (54.1)              | 397 (54.7)         | 418 (53.6)         |          |
| **Living status, N (%)** |                         |                    |                    | 0.292    |
| Single                   | 154 (10.2)              | 75 (10.3)          | 79 (10.1)          |          |
Abbreviation: wave 1: participants completed the baseline and 6-month follow-up before the COVID-19 outbreak (i.e., from March 2019 to January 2020); wave 2: participants completed the baseline before COVID-19 outbreak but 6-month follow-up during the COVID-19 outbreak (i.e., from August 2019 to April 2020).

|                          | Wave 1 | Wave 2 | Wave 3 |
|--------------------------|--------|--------|--------|
| With relatives           | 1174(78.0) | 575 (79.2) | 599 (76.8) |
| With non-relatives       | 178 (11.8) | 76 (10.5) | 102 (13.1) |

**Health status and behaviors**

**Chronic diseases, N (%)**

|                    | Wave 1 | Wave 2 | Wave 3 |
|--------------------|--------|--------|--------|
| No                 | 521 (72.8) | 579 (79.8) | 540 (69.2) |
| Yes                | 195 (27.2) | 147 (20.2) | 240 (30.8) |

**Insomnia drug, N (%)**

|                | Wave 1 | Wave 2 | Wave 3 |
|----------------|--------|--------|--------|
| No             | 646 (90.2) | 652 (89.8) | 702 (90.0) |
| Yes            | 70 (9.8) | 74 (10.2) | 78 (10.0) |

**Referral and see psychologist, N (%)**

|                | Wave 1 | Wave 2 | Wave 3 |
|----------------|--------|--------|--------|
| No             | 1306 (86.7) | 626 (86.2) | 680 (87.2) |
| Yes            | 200 (13.3) | 100 (13.8) | 100 (12.8) |

**Exercise habit per week (at least 1 time and ≥30 mins), N (%)**

|                    | Wave 1 | Wave 2 | Wave 3 |
|--------------------|--------|--------|--------|
| No                 | 854 (56.7) | 391 (53.9) | 463 (59.4) |
| Yes                | 652 (43.3) | 335 (46.1) | 317 (40.6) |

**Frequency for smoke in a month, N (%)**

|                     | Wave 1 | Wave 2 | Wave 3 |
|---------------------|--------|--------|--------|
| 2 days and below    | 1322 (87.8) | 652 (89.8) | 670 (85.9) |
| 3 days and above    | 184 (12.2) | 74 (10.2) | 110 (14.1) |

**Frequency for alcohol consumption in a month, N (%)**

|                     | Wave 1 | Wave 2 | Wave 3 |
|---------------------|--------|--------|--------|
| 2 days and below    | 1254 (83.3) | 692 (82.9) | 652 (83.6) |
| 3 days and above    | 252 (16.7) | 124 (17.1) | 128 (16.4) |

**Body-mass Index, N (%)**

|               | Wave 1 | Wave 2 | Wave 3 |
|---------------|--------|--------|--------|
| Normal (18.5-23.9) | 945 (62.7) | 463 (63.8) | 482 (61.8) |
| Underweight   | 153 (10.2) | 76 (10.5) | 77 (9.9) |
| Overweight    | 408 (27.1) | 187 (25.8) | 221 (28.3) |
Table 2 Changes in depression, anxiety, and insomnia symptom severity scores from baseline to endpoint. Outcomes were additionally compared between participants who completed the study before the COVID-19 pandemic (i.e., March 2019 to January 2020) and during the COVID-19 pandemic (i.e., August 2019 to April 2020).

|                  | Baseline, N (%) | 6-month follow-up, N (%) |
|------------------|-----------------|--------------------------|
|                  | All N=1506      | Wave 1 group N=726       | Wave 2 group N=780 | P-values * | All N=1506 | Wave 1 group N=726 | Wave 2 group N=780 | P-values # |
| **PHQ-9**        |                 |                          |                        |            |            |                 |                          |            |
| Minimal          | NA              | NA                       | NA                     | 0.101      | 843 (56.0) | 436 (60.1)       | 407 (52.2)             | <0.001    |
| Mild             | 1094 (72.6)     | 543 (74.8)               | 551 (70.6)             |            | 491 (32.6) | 233 (32.1)       | 258 (33.1)             |           |
| Moderate         | 299 (19.9)      | 138 (19.0)               | 161 (20.6)             |            | 116 (7.7)  | 38 (5.2)        | 78 (10.0)              |           |
| Severe           | 113 (7.5)       | 45 (6.2)                 | 68 (8.7)               |            | 56 (3.7)   | 19 (2.6)        | 37 (4.7)               |           |
| **GAD-7**        |                 |                          |                        | 0.199      | 1023 (67.9)| 523 (72.0)       | 500 (64.1)             | 0.003     |
| Minimal          | 744 (49.4)      | 347 (47.8)               | 397 (50.9)             |            | 1037 (68.9)| 523 (72.0)       | 514 (65.9)             |           |
| Mild             | 524 (34.8)      | 271 (37.3)               | 253 (32.4)             |            | 387 (25.7) | 166 (22.9)       | 221 (28.3)             |           |
| Moderate         | 157 (10.4)      | 74 (10.2)                | 83 (10.6)              |            | 71 (4.7)   | 24 (3.3)        | 47 (6.0)               |           |
| Severe           | 81 (5.4)        | 34 (4.7)                 | 47 (6.0)               |            | 25 (1.7)   | 13 (1.8)        | 12 (1.5)               |           |
| **ISI**          |                 |                          |                        | 0.981      | 1037 (68.9)| 523 (72.0)       | 514 (65.9)             | 0.022     |
| None             | 756 (50.2)      | 362 (49.9)               | 394 (50.5)             |            | 1037 (68.9)| 523 (72.0)       | 514 (65.9)             |           |
|                  | Baseline, N (%) | 6-month follow-up, N (%) | P-values | P-values |
|------------------|-----------------|--------------------------|----------|----------|
|                  | All N=1506      | Wave 1 group N=726       | Wave 2 group N=780 | All N=1506 | Wave 1 group N=726 | Wave 2 group N=780 |
| Subthreshold     |                 |                          |          |          |                      |                      |
|                  | N=726           | N=780                    |          |          |
|                  | 495 (32.9)      | 241 (33.2)               | 254 (32.6) | 342 (22.7) | 154 (21.2)           | 188 (24.1)            |
|                  |                 |                          |          |          |                      |                      |
| Moderate         |                 |                          |          |          |                      |                      |
|                  | N=726           | N=780                    |          |          |
|                  | 193 (12.8)      | 92 (12.7)                | 101 (12.9) | 96 (6.4) | 40 (5.5)             | 56 (7.2)              |
|                  |                 |                          |          |          |                      |                      |
| Severe           |                 |                          |          |          |                      |                      |
|                  | N=726           | N=780                    |          |          |
|                  | 62 (4.1)        | 31 (4.3)                 | 31 (4.0) | 31 (2.1) | 9 (1.2)               | 22 (2.8)              |
|                  |                 |                          |          |          |                      |                      |
| **SSI pain-related items** | |                          |          |          |                      |                      |
|                  |                 |                          |          |          |                      |                      |
| Without pain     | 1351 (89.7)     | 647 (89.1)               | 704 (90.3) | 1386 (92.0) | 675 (93.0) | 711 (91.2) |
| mean <2.2        |                 |                          |          |          |                      |                      |
| With pain, N (%) | 155 (10.3)      | 79 (10.9)                | 76 (9.7) | 120 (8.0) | 51 (7.0)             | 69 (8.8)              |
|                  |                 |                          |          |          |                      |                      |
| **CD-RISC group** |                 |                          |          |          |                      |                      |
| Weak resilience  | 1253 (83.2)     | 595 (82.0)               | 658 (84.4) | NA | NA | NA | - |
| ≤80              |                 |                          |          |          |                      |                      |
| Better resilience| 253 (16.8)      | 131 (18.0)               | 122 (15.6) | NA | NA | NA | - |

* Baseline comparison of wave 1 and 2  
# 6-month follow-up comparison of wave 1 and 2

Abbreviations: PHQ-9: Patient Health Questionnaire-9; GAD-7: Generalized Anxiety Disorder-7; ISI: Insomnia Severity Index; SSI: Somatic Symptoms Inventory; CD-RISC: Connor-Davidson Resilience Scale. Wave 1: participants completed the baseline and 6-month follow-up before the COVID-19 outbreak (i.e., from March 2019 to January 2020); Wave 2: participants completed the baseline before COVID-19 outbreak but 6-month follow-up during the COVID-19 outbreak (i.e., from August 2019 to April 2020).
Table 3 Moderators of probable depression, anxiety and insomnia

|                      | PHQ-9                  | GAD-7                      | ISI                      |
|----------------------|------------------------|----------------------------|--------------------------|
| **Follow-up time point** |                        |                            |                          |
| Before outbreak (wave 1 group) | Ref.                  | Ref.                      | Ref.                     |
| During outbreak (wave 2 group) | 1.30 (1.04, 1.62) * | 1.47 (1.16, 1.88) ** | 1.37 (1.07, 1.77) * |
| **Age**              |                        |                            |                          |
| 18-39                | Ref.                   | Ref.                      | Ref.                     |
| 40-59                | 0.85 (0.63, 1.13)      | 0.86 (0.63, 1.18)         | 1.19 (0.86, 1.67)        |
| ≥60                  | 1.02 (0.56, 1.86)      | 1.24 (0.65, 2.37)         | 1.60 (0.82, 3.11)        |
| **Gender**           |                        |                            |                          |
| Male                 | Ref.                   | Ref.                      | Ref.                     |
| Female               | 1.25 (0.96, 1.64)      | 1.30 (0.97, 1.75)         | 0.92 (0.68, 1.25)        |
| **Education**        |                        |                            |                          |
| Below undergraduate  | Ref.                   | Ref.                      | Ref.                     |
| Undergraduate and above | 1.06 (0.83, 1.35) | 0.87 (0.67, 1.14)         | 1.28 (0.97, 1.69)        |
| **Occupation**       |                        |                            |                          |
| Unemployed           | Ref.                   | Ref.                      | Ref.                     |
| employed             | 1.08 (0.79, 1.48)      | 1.20 (0.85, 1.68)         | 0.90 (0.64, 1.27)        |
|                                | PHQ-9          | GAD-7          | ISI            |
|--------------------------------|----------------|----------------|----------------|
| **OR (95% CI)**                |                |                |                |
| Marital status                |                |                |                |
| Unmarried                      | Ref.           | Ref.           | Ref.           |
| Married                        | 0.61 (0.43,0.87)** | 0.57 (0.40,0.84)** | 0.57 (0.39,0.85)** |
| Divorced or widowed            | 1.13 (0.58,2.22) | 1.26 (0.63,2.51) | 1.05 (0.51,2.16) |
| **Years live in Shenzhen**     |                |                |                |
| 5 years and below              | Ref.           | Ref.           | Ref.           |
| 5-10 years                     | 0.97 (0.68,1.38) | 1.33 (0.91,1.94) | 1.25 (0.84,1.87) |
| 10 years and above             | 1.11 (0.83,1.49) | 1.30 (0.94,1.78) | 1.42 (1.02,1.99) * |
| **Living status**              |                |                |                |
| Single                         | Ref.           | Ref.           | Ref.           |
| With relatives                 | 0.85 (0.56,1.28) | 1.17 (0.75,1.83) | 1.08 (0.68,1.72) |
| With non-relatives             | 0.56 (0.35,0.90) * | 0.60 (0.36,1.00) | 0.81 (0.48,1.37) |
| **Chronic disease**            |                |                |                |
| No                             | Ref.           | Ref.           | Ref.           |
| Yes                            | 1.06 (0.81,1.39) | 1.00 (0.75,1.33) | 1.14 (0.85,1.54) |
| **Insomnia drugs**             |                |                |                |
| No                             | Ref.           | Ref.           | Ref.           |
|                          | OR (95% CI) |
|--------------------------|-------------|
|                          | PHQ-9       | GAD-7       | ISI          |
| **Referral and see psychologist** |             |             |              |
| No                       | Ref.        | Ref.        | Ref.         |
| Yes                      | 1.32 (0.92,1.89) | 1.02 (0.72,1.46) | 1.42 (1.00,2.04) |
| **Exercise habit per week** |             |             |              |
| (at least 1 time and ≥30 mins) |             |             |              |
| No                       | Ref.        | Ref.        | Ref.         |
| Yes                      | 0.79 (0.63,0.99) * | 0.81 (0.63,1.03) | 0.97 (0.75,1.26) |
| **Frequency for alcohol consumption in a month** | | | |
| 2 days and below         | Ref.        | Ref.        | Ref.         |
| 3 days and above         | 1.43 (1.05,1.95) * | 1.39 (1.01,1.94) * | 0.93 (0.66,1.33) |
| **Frequency for smoke in a month** | | | |
| 2 days and below         | Ref.        | Ref.        | Ref.         |
| 3 days and above         | 1.15 (0.78,1.68) | 1.09 (0.71,1.65) | 1.35 (0.88,2.07) |
| **Body-mass Index**      |             |             |              |
| Normal (18.5-23.9)       | Ref.        | Ref.        | Ref.         |
|                        | OR (95% CI) |          |          |
|------------------------|-------------|----------|----------|
|                        | PHQ-9       | GAD-7    | ISI      |
| Underweight            | 0.93 (0.64, 1.35) | 1.06 (0.71, 1.58) | 0.91 (0.60, 1.40) |
| Overweight             | 1.07 (0.82, 1.40) | 0.99 (0.74, 1.32) | 0.70 (0.52, 0.95) * |
| **SSI pain related items** |            |          |          |
| Without pain           | Ref.        | Ref.     | Ref.     |
| With pain              | 1.07 (0.73, 1.58) | 1.13 (0.76, 1.68) | 1.15 (0.76, 1.73) |
| **CD-RISC**            |            |          |          |
| Weak resilience (≤80)  | Ref.        | Ref.     | Ref.     |
| Greater resilience     | 0.26 (0.19, 0.37) *** | 0.21 (0.14, 0.33) *** | 0.18 (0.11, 0.29) *** |
| **Severity**           |            |          |          |
| Minimal (None)         | NA          | Ref.     | Ref.     |
| Mild (Subthreshold)    | Ref.        | 2.15 (1.65, 2.81) *** | 2.98 (2.24, 3.97) *** |
| Moderate               | 1.76 (1.31, 2.37) *** | 4.19 (2.80, 6.27) *** | 7.68 (5.11, 11.55) *** |
| Moderately severe and above | 2.98 (1.85, 4.79) *** | 7.62 (4.33, 13.40) | 10.71 (5.28, 21.73) *** |

*P-values<0.05

**P-values<0.01
***P-values<0.001

Abbreviations: PHQ-9: Patient Health Questionnaire-9; GAD-7: Generalized Anxiety Disorder-7; ISI: Insomnia Severity Index; SSI: Somatic Symptoms Inventory; CD-RISC: Connor-Davidson Resilience Scale