



The impact of acute COVID-19 symptoms on insomnia: A longitudinal study among medical students

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ABSTRACT

Objective: The COVID-19 pandemic has profoundly disrupted global mental health. Medical students, already vulnerable to high stress, experience heightened psychological distress. This study aimed to investigate the association between acute COVID-19 infection and the development of psychological symptoms in medical students, exploring the role of specific COVID-19 symptoms and lifestyle factors.

Methods: A longitudinal study of 2359 medical students assessed psychological symptoms (depression, anxiety, insomnia) before and after COVID-19 infection. Logistic regression models, adjusted for confounders, examined the relationship between COVID-19 status (with or without infection), and the onset of psychological symptoms. The study also explored acute COVID-19 symptoms and lifestyle factors associated with psychological symptoms in the COVID-19 infected (COVID+) group.

Findings: The COVID + group exhibited significantly greater increases in depression and insomnia compared to non-infected group. COVID-19 infection was significantly associated with the onset of insomnia post-infection (OR [95 % CI] 1.83 [1.05–3.21]). Moderate to severe acute symptoms, including sleep disturbances (2.20 [1.17–4.14]), decreased attention/memory (2.47 [1.02–6.00]), and breathlessness (2.05 [1.08–3.85]), were identified as risk factors for onset of insomnia. Regular exercise was found to be negatively associated with the onset of insomnia (0.54 [0.33–0.88]).

Conclusion: Early intervention targeting these acute-phase risk symptoms is crucial for preventing long-term insomnia. Regular exercise is effective in preventing the development of insomnia in medical students following COVID-19 infection. These findings will assist in formulating targeted interventions to address recurrent infections in the post-pandemic era.

1. Introduction

As a major global public health crisis of the 21st century, COVID-19 pandemic not only threatens human lives but also has a profound and unparalleled impact on mental health (Alwan, 2020; Weich, 2022).

Following the outbreak of COVID-19, college students have faced a surge in the prevalence of depression, anxiety, and insomnia (Liu et al., 2022; Chen and Lucock, 2022). Especially medical students, given their occupational duties and academic obligations, exhibit heightened susceptibility to virus exposure, thereby experiencing increased depression,

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anxiety, and insomnia (Obradovic et al., 2024; Li et al., 2022). These mental health challenges also significantly affect academic performance, well-being, and future career prospects, and future career prospects (Barbosa-Camacho et al., 2022; Perotta et al., 2021), making it necessary to monitor changes in psychological symptoms among this vulnerable population.

Given the unique trajectory of the pandemic in China, the prolonged restrictions and life disruption were followed by a surge in infections after the nationwide lockdown was lifted in December 2022 (Liang et al., 2023; Fu et al., 2023). The pandemic represents a substantial biopsychosocial stressor, which makes it an ideal context for investigating the psychological impact of COVID-19. COVID-19 is a multisystem disease that, in addition to respiratory symptoms, often presents with neurological manifestations in acute patients, with headache and fatigue being commonly reported (Wesselingh, 2023). The neurological syndromes observed in COVID-19 survivors may stem from the immune response elicited by the body against the virus (Radke et al., 2024). This neuroinflammatory response contributes to neurological syndromes; furthermore, these neurological sequelae are expected to persist for two years (Bowe et al., 2023). COVID-19 survivors face long-term post-acute neuropsychiatric symptoms (Awadalla et al., 2022), with insomnia being one of the most common complications among long-term COVID-19 patients (Akbarialiabad et al., 2021; Alkodaymi et al., 2022). The emergence of post-COVID neuropsychiatric sequelae underscores the need to investigate the relationship between acute COVID-19 symptoms and subsequent mental health outcomes.

COVID-19 survivors who experienced more acute physical symptoms during hospitalization are more likely to develop more severe emotional symptoms and sleep disturbances three months after discharge (Tracy et al., 2024). Furthermore, cognitive impairment and shortness of breath during the acute phase in children and adolescents with pre-existing insomnia predict worsening symptoms after the infection (Zhu et al., 2024). However, there is insufficient awareness of the impact of acute-phase symptoms on the neuropsychiatric sequelae of COVID-19 among medical students. Medical students faced significant academic and psychosocial stressors during COVID-19, including campus closures and career uncertainty, while some also served on pandemic frontlines, raising their infection risk. This dual burden of academic pressures and frontline exposures may render them particularly susceptible to long-term psychiatric sequelae of COVID-19^{19–21}. Investigating how acute symptoms affect the risk of long-term psychiatric sequelae can inform targeted interventions for this vulnerable population, especially in the context of recurrent infections in the post-pandemic era.

This longitudinal study involved two assessments of depression, anxiety, and insomnia among medical students, conducted before and after restrictions were lifted. The objectives of this study are, first, to determine whether COVID-19 infection is a risk factor for the onset of depression, anxiety, and insomnia after balancing for confounding factors such as lifestyle behaviors; and second, to identify the risk factors of acute COVID-19 symptoms and lifestyle behaviors for post-acute psychiatric sequelae in the infected students. In the post-pandemic era, especially medical students who are prone to recurrent COVID-19 infections, identifying the risk of acute-phase symptoms is crucial for preventing long-term psychiatric sequelae.

2. Material and methods

2.1. Study design and participants

This study is part of a mixed longitudinal cohort at Xinxiang Medical University, with six psychological screenings at different time points, including five screenings under COVID-19 restrictions (March 2020 [*n* = 28584], October 2020 [*n* = 18545], March 2021 [*n* = 23019], October 2021 [*n* = 6829], and February 2022 [*n* = 4995]), and one screening after the lifting of restrictions in August 2023 (*n* = 5885). This study included participants from the sixth psychological screening who

had completed at least one screening before the lifting of restrictions. The most recent screening record before the sixth screening was used as T1 in this study. Therefore, a total of 2359 medical students aged 18–24 years from Xinxiang Medical University were finally included in this study, covering T1 (between March 2020 and February 2022) and T2 (August 2023). All participants completed the questionnaires using the WeChat official account platform and provided informed consent before participation. The study was approved by the Biomedical Ethics Committee of Xinxiang Medical University (XYLL-2020235).

2.2. Study measures

2.2.1. The characterization of demographic and lifestyle factors

The participants' age, sex, ethnicity, and educational levels were collected in the study. The lifestyle behaviors consisted of cigarette consumption over the week (yes/no); alcohol consumption over the past week (yes/no), and physical exercise before the outbreak of the pandemic [frequency (infrequent, 1–3 days per week, or 4–7 days per week); intensity of exercise (no exercise, mild (e.g., walking), moderate (e.g., cycling, tai chi, table tennis, and badminton), or vigorous (e.g., running, swimming, soccer, basketball, and jumping rope); duration of exercise (<30 min, 30–60 min, or > 60 min)].

2.2.2. Measurements of psychological symptoms

The severity of psychological symptoms was assessed using the Patient Health Questionnaire-9 (PHQ-9), the Generalized Anxiety Disorder Questionnaire-7 (GAD-7), and the Insomnia Severity Index (ISI). PHQ-9 measures depressive over the past 2 weeks, total score greater than 5 defined as the presence of depression. The GAD-7 assesses anxiety symptoms over the past two weeks, with a total score greater than 5 defining the presence of anxiety disorder. ISI measures sleep problems over the past 2 weeks, and total score greater than 7 defined as the presence of insomnia. Depression, anxiety, and insomnia symptoms were used in subsequent analyses.

2.2.3. COVID-19 infection

Prior COVID-19 infection was confirmed and characterized using self-report questionnaires. Questions included: 1) Was COVID-19 infection confirmed through the polymerase chain reaction (PCR), antibody, or lateral flow test, or the presence of COVID-19 positive symptoms? 2) Have there been two or more times of COVID-19 infection till the completion of the questionnaire? 3) Did you experience any of the acute-phase symptoms of COVID-19 infection and their severity? We assessed for 13 acute-phase symptoms (fatigue, sleep disturbances, decreased attention/memory, difficulty thinking, pharyngeal symptoms, nasal congestion, breathlessness, fever, cough/phlegm, olfactory impairment, gastrointestinal symptoms, headache, fear of COVID-19 virus)? 4) What is the overall severity of acute COVID-19 infection symptoms? 5) What is the cumulative extent of psychological distress experienced during the COVID-19 epidemic? 6) What is the level of concern about the virus before COVID-19 infection? (Appendix p1).

This scale rates the severity of 13 acute-phase symptoms as none, mild, moderate, or severe, and assesses the overall severity of symptoms, the extent of psychological distress during the pandemic, and the level of concern about the virus before infection on a scale from 0 to 10, where 0 represents no symptoms and 10 represents extreme severity.

2.2.4. Patient and public involvement

All participants were recruited through notifications issued by the School of Psychology of Xinxiang Medical University via academic counselors, and the participants voluntarily participated in and completed the psychological assessments.

2.3. Statistical analysis

All statistical analyses were performed using R Studio software

(4.3.1). All statistical significance was defined as a two-sided P-value <0.05 level.

2.3.1. Changes (Δ) in symptom scores between COVID + group and COVID-group

The changes (Δ) of PHQ-9, GAD-7, and ISI scores from T1 to T2 were calculated and compared between participants with (COVID+) and without (COVID-) COVID-19 infection using T-tests.

2.3.2. Effects of COVID-19 infection on psychological symptoms

To further investigate the impact of COVID-19 infection on the onset of psychological symptoms, participants were stratified into two groups based on their psychological status change from T1 to T2: healthy controls (HC; asymptomatic at T1 and T2) and symptom onset group (ONS; asymptomatic at T1 and symptomatic at T2). The HC group consisted of those who were asymptomatic at T1 and T2 for twice psychological surveys. Sample sizes for the HC and ONS groups for each psychological symptom are listed in [Appendix p2](#).

Propensity score-based weighting was used to control for demographic and lifestyle factors, including age, gender, ethnic group, education levels, cigarette consumption, alcohol consumption, physical exercise, and the intervals between survey response periods. We constructed separate logistic regression models for depression, anxiety, and insomnia symptoms to estimate the propensity scores for group membership after considering the covariates. We then computed the inverse probability weights for each participant and employed logistic regression models to assess whether COVID-19 infection posed a risk for changes in the mental well-being of medical students.

2.3.3. Risk and protective factors for psychological symptoms in COVID + group

To address collinearity and overfitting, we employed lasso techniques for symptom selection during the acute phase. Logistic regression models were performed to evaluate the effects of acute COVID-19 symptoms, and lifestyle factors associated with ONS of psychological symptoms, in terms of the odds ratio (OR) and 95 % confidence interval

(CI).

3. Results

The study flowchart is shown in [Fig. 1](#). The COVID+ and COVID-groups consisted of 2021 (85.67 %) and 338 (14.33 %) medical students, respectively ([Table 1](#)).

3.1. Changes (Δ) in psychological symptoms with COVID-19 infection

The Δ psychological symptoms were significantly different between COVID+ and COVID-groups for depression and insomnia scores ([Fig. 2](#)). Participants in the COVID + group demonstrated greater increases in depression ($T = 2.07$; $P = .038$) and insomnia ($T = 2.89$; $P = .004$) than those in the COVID-group.

3.2. Onset of psychological symptom associated with COVID-19 infection

After inverse probability weighting, the confounding factors (including demographic and lifestyle factors) were well balanced between COVID+ and COVID-groups at T1 (see [Appendix p6](#)). [Fig. 3](#) depicts the odds ratios of ONS of psychological symptoms between the COVID+ and COVID-groups. Compared to the COVID-group, COVID + group had increased risk of insomnia ONS (OR [95 % CI] 1.83 [1.05–3.21]).

3.3. Effects of acute COVID-19 symptoms and lifestyle factors on insomnia status in COVID + group

Severity levels for all acute COVID-19 are presented in [Appendix p5](#). After conducting lasso regressions, sleep disturbances, decreased attention/memory, difficulty thinking, breathlessness, olfactory impairment, gastrointestinal symptoms, headache, fear of COVID-19 virus during acute-phase, overall severity of acute COVID-19 infection symptoms, cumulative extent of psychological distress during the COVID-19 pandemic, and level of concern regarding COVID-19 infection

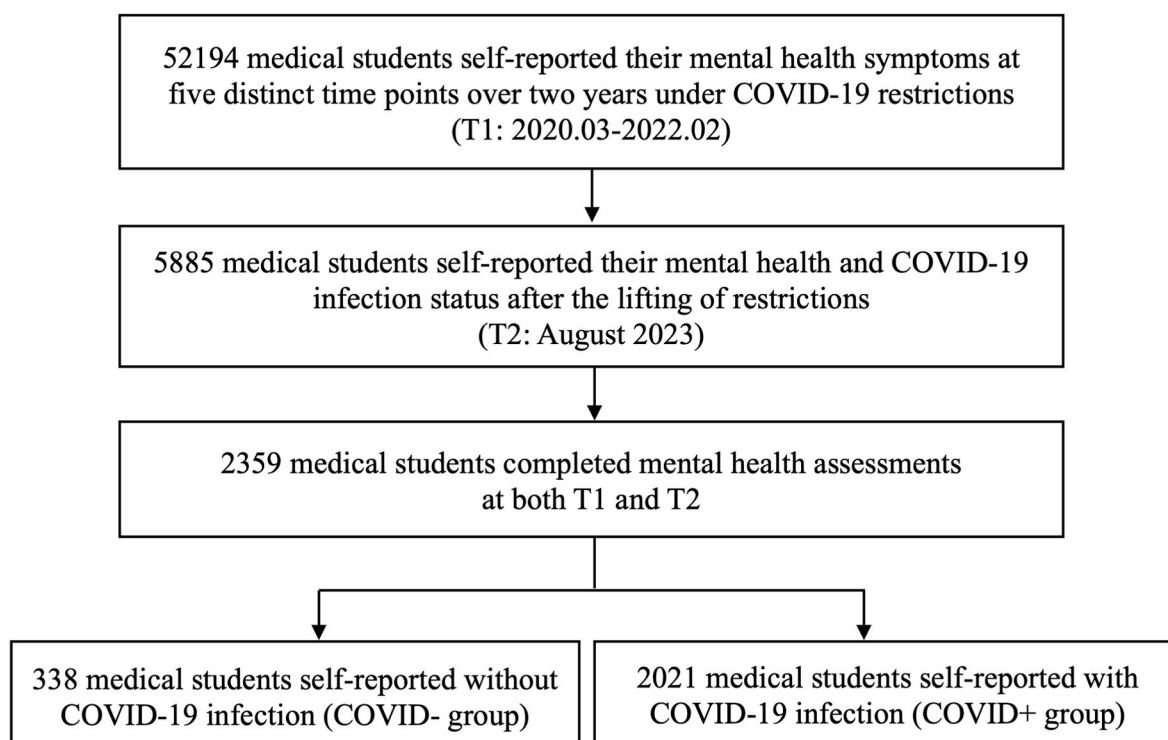


Fig. 1. Study flowchart.

Table 1
Demographic characteristics of participants.

| Characteristics | All participants (N = 2359) | COVID-group (N = 338) | COVID + group (N = 2021) | T/ χ^2 value ^a | P value ^a |
|---|-----------------------------|-----------------------|--------------------------|--------------------------------|----------------------|
| Age (Mean, SD) | 22.23 (2.49) | 21.72 (2.69) | 22.32 (2.45) | -4.09 | <0.001 |
| Sex (n, %) | | | | 12.26 | 0.001 |
| Female | 1485 (62.95) | 184 (54.44) | 1301 (64.37) | | |
| Male | 874 (37.05) | 154 (45.56) | 720 (35.63) | | |
| Ethnic (n, %) | | | | | |
| Han | 2320 (98.35) | 331 (97.93) | 1989 (98.42) | 0.42 | 0.674 |
| Minority | 39 (1.65) | 7 (2.07) | 32 (1.58) | | |
| Educational level (n, %) | | | | | |
| Bachelor degree | 1871 (79.31) | 276 (81.66) | 1595 (78.92) | 1.32 | 0.282 |
| Master degree | 488 (20.69) | 62 (18.34) | 426 (21.08) | | |
| Cigarette consumption (n, %) | | | | | |
| No | 2233 (94.66) | 315 (93.20) | 1918 (94.90) | 1.67 | 0.245 |
| Yes | 126 (5.34) | 23 (6.80) | 103 (5.10) | | |
| Alcohol consumption (n, %) | | | | | |
| No | 1587 (67.27) | 248 (73.37) | 1339 (66.25) | 6.67 | 0.012 |
| Yes | 772 (32.73) | 90 (26.63) | 682 (33.75) | | |
| Physical exercise (n, %) | | | | | |
| No | 118 (5.00) | 16 (4.73) | 102 (5.05) | 0.60 | 0.807 |
| Yes | 2241 (95.00) | 322 (95.27) | 1919 (94.95) | | |
| Survey response periods at T1 ^b (n, %) | | | | | |
| March 2020 to October 2021 | 601 (25.48) | 97 (28.70) | 504 (24.94) | 2.16 | 0.161 |
| February 2022 | 1758 (74.52) | 241 (71.30) | 1517 (75.06) | | |

NOTE.

^a the T test and χ^2 test were preformed between COVID-group and COVID + group.

^b according to the psychological survey at T2, the most recent historical psychological survey records of the participants before the lifting of restrictions were selected for analysis.

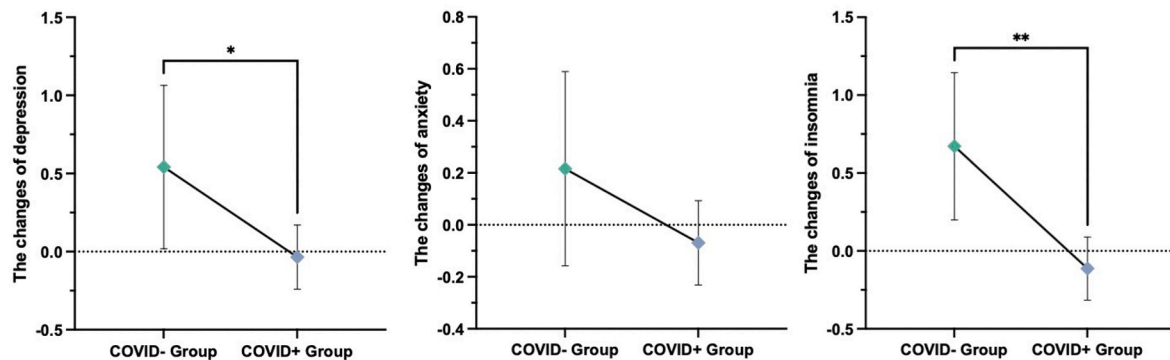


Fig. 2. The differences in symptom changes (T1-T2) between the COVID-group and COVID + group.

NOTE: * indicates significance at $p < .05$; ** indicates significance at $p < .01$; COVID-group: participants who self-reported COVID-19 infection; COVID + group: participants who self-reported no COVID-19 infection.

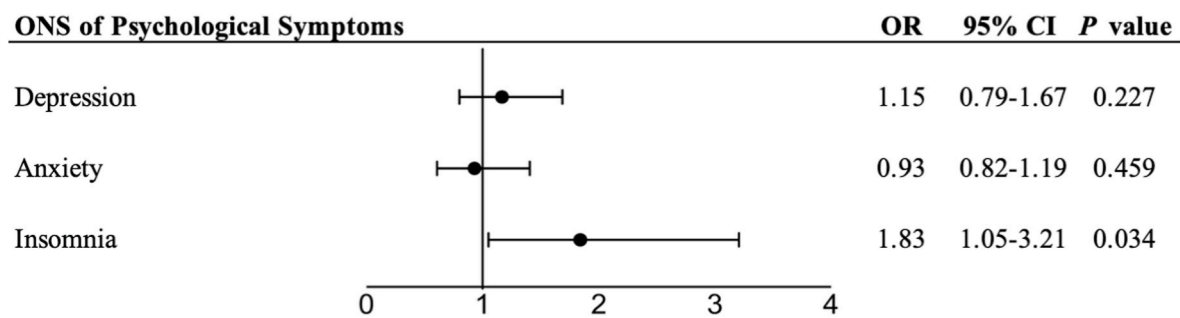


Fig. 3. The odds ratio (OR) of onset of psychological symptoms in COVID + group compared to COVID-group.

NOTE: ONS: asymptomatic at T1 and symptomatic at T2.

were included for subsequent logistic regression analyses assessing the effect of acute COVID-19 symptoms on onset of insomnia.

Mild and moderate to severe sleep disturbances (1.85 [1.09–3.16], 2.20 [1.17–4.14], respectively), moderate to severe decreased

attention/memory (2.47 [1.02–6.00]), moderate to severe breathlessness (2.05 [1.08–3.85]), moderate to severe fear of COVID-19 virus (2.23 [1.11–4.48]), and mild level of concern regarding COVID-19 infection (1.85 [1.14–3.00]) was positively associated with insomnia

ONS in COVID + group (Fig. 4). Alcohol consumption was positively associated with insomnia ONS (1.67 [1.10–2.52]) in COVID + group. Physical activity, whether 1–3 days/week (0.60 [0.38–0.95]) or 4–7 days/week (0.54 [0.33–0.88]), was negatively correlated with insomnia ONS in COVID + group (Fig. 4).

4. Discussion

To our knowledge, this is the first longitudinal study to examine how COVID-19 infection affects the onset of psychological symptoms in medical students and to identify specific acute COVID-19 symptoms that pose a risk for these psychological outcomes. Depression and insomnia worsened significantly more in the COVID + group compared to the COVID-group. However, following the lifting of COVID-19 restrictions, the COVID-group exhibited improvements in depression, anxiety, and

insomnia. Additionally, compared to the COVID-group, the COVID + group was positively associated with the onset of insomnia, indicating that COVID-19 infection poses a higher risk of insomnia. Persistence of sleep problems have been observed even two years post-COVID-19 infection in general population (Fernandez-de-Las-Peñas et al., 2024). Moreover, individuals with pre-existing insomnia symptoms are more prone to experiencing prolonged COVID-19 symptoms (Vargas et al., 2023). To minimize confounding effects of pre-existing insomnia symptoms on post-COVID-19 infection outcomes, this study only included participants without insomnia pre-infection. At the same time, this study found that the onset of insomnia was associated with COVID-19 infection, even after balancing of lifestyle factors. In individuals without pre-existing insomnia symptoms before infection, the incidence of long-COVID insomnia post-infection was 60.6 % (Chen et al., 2023). Therefore, COVID-19 as a risk factor for long-term

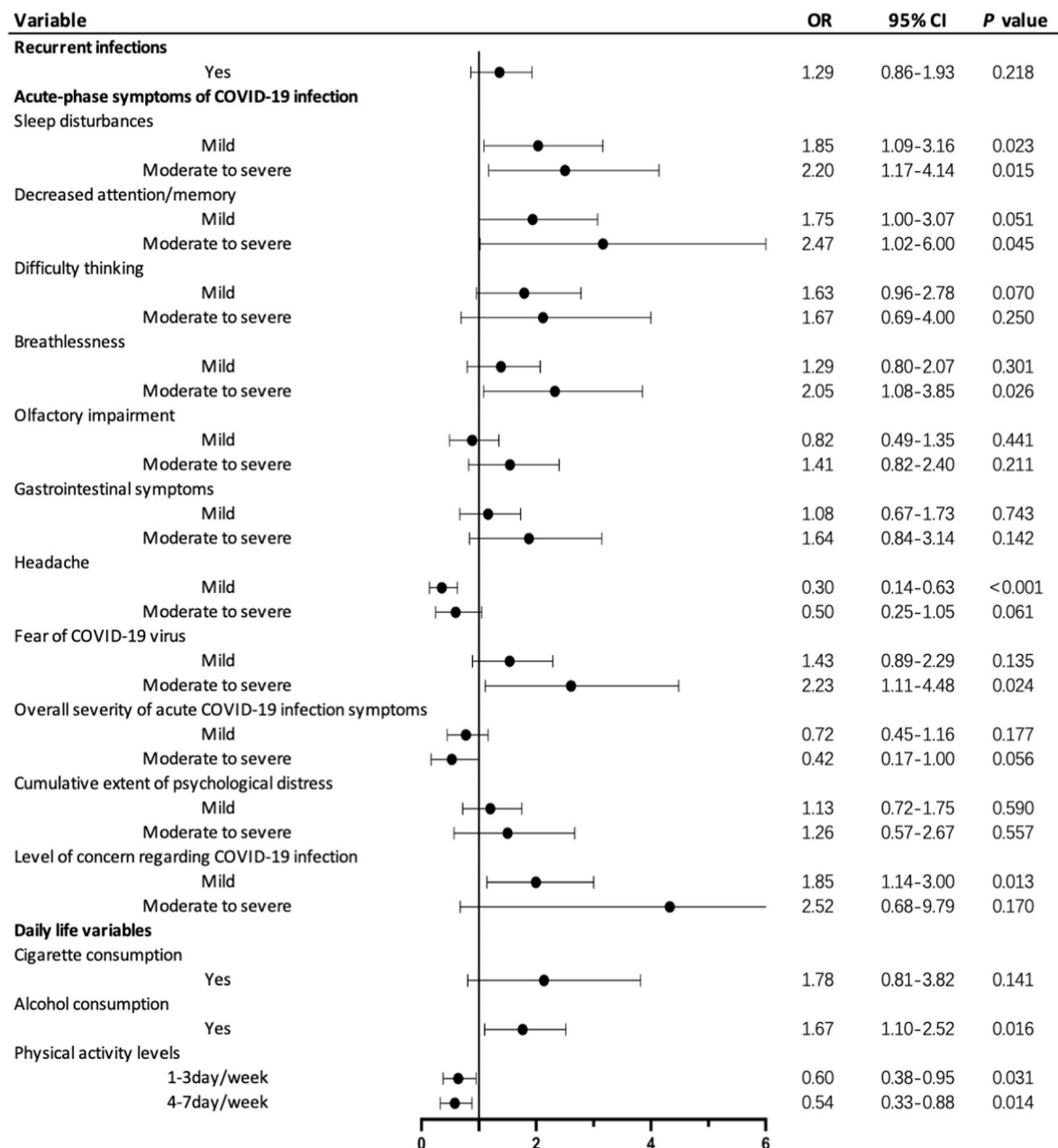


Fig. 4. The risk and protective factors related to acute COVID-19 symptoms and daily lifestyle for insomnia in the COVID + group.

NOTE: The healthy controls as reference. Recurrent infections: not recurrent infection as reference; acute-phase symptoms of COVID-19 infection: no acute symptom as reference; physical activity levels: infrequent exercise as reference.

insomnia underscores the critical need for early intervention for insomnia following infection.

Our study also indicates that in the COVID + group, acute symptoms such as moderate to severe decreased attention/memory, breathlessness, and mild to severe sleep disturbances were associated with the onset of insomnia post-COVID-19 infection. Cognitive dysfunction, such as brain fog, memory deterioration, and attention decline, appears to be key features of post-COVID-19 syndrome (Premraj et al., 2022). There is a significant correlation between continuous attention dysfunction and C-reactive protein levels at admission in COVID-19 patients, with the inflammatory process contributing to long-term cognitive impairment (Zhou et al., 2020). Despite the lack of persistent virus in the central nervous system, ongoing peripheral inflammation contributes to neurological sequelae of COVID-19. This study finds that reduced attention/memory during the acute stage predicts long-term insomnia, suggesting that cognitive impairment and sustained inflammation increase the risk of long-COVID insomnia.

Another interesting finding of the study is the significant correlation between acute-phase insomnia and long-term insomnia post-acute. Among adolescents with long COVID-19, 32.1 % reported insomnia as the primary reason for their school absences (Sakurada et al., 2023). Long-term COVID-19 insomnia is highly prevalent and significantly impacts academic performance, yet most affected individuals in China do not receive treatment. (Lu et al., 2024). Digital sleep interventions have been confirmed as effective tools for improving sleep quality and addressing insomnia during the COVID-19 pandemic (Zhang et al., 2023). Insomnia, as an undeniable mental health challenge impacting both physical and mental well-being, as well as academic performance, of students. This issue is particularly critical among medical students, given the demanding nature of their academic pursuits; therefore, timely intervention following infection is imperative.

Maintaining regular exercise habits before COVID-19 infection was found as a protective factor against developing insomnia post-infection in the study. In the post-pandemic era, recurrent infections are unavoidable, and promoting regular exercise may be an effective measure for preventing and treating long-COVID insomnia. Various intensities and types of exercise have been shown to significantly enhance sleep duration and quality, and mitigate the severity of insomnia (Tian et al., 2024; Riedel et al., 2024). Increased exercise frequency can alleviate insomnia in individuals concerned about COVID-19, potentially due to the anxiety-reducing effects of physical activity (Yu et al., 2024). Exercise offers a cost-effective, safe, and easily accessible strategy for the prevention and treatment of insomnia. Therefore, in the post-pandemic era, college administrators are advocating for increased physical activity among students as a potential measure to mitigate long-COVID insomnia.

The strengths of our study include that the participants comprised students from a single medical school, providing a relatively homogeneous living environment that effectively controls for potential confounding factors. As future healthcare professionals, these medical students represent a critical reserve force for the healthcare system. Therefore, it is important to investigate the impact of COVID-19 on their mental health, which not only pertains to their academic performance but also has significant implications for the entire healthcare system. The study has several limitations, as detailed below. Firstly, the COVID-19 infection status among students was determined through self-reports without validation by laboratory results, which could lead to misclassification bias due to underreporting of asymptomatic infections, thereby weakening group differences. Although this study focuses on the impact of acute COVID-19 symptoms on long-term mental health, this bias may still underestimate the true psychological impact of COVID-19 infection. Secondly, there was variability in the response periods of individuals prior to their COVID-19 infection (T1). More than 25 % of participants responded between March 2020 to October 2021. In the study, the intervals between survey response periods were used in propensity score-based weighting to balance their confounding effects.

Thirdly, to control for the influence of prior mental health conditions, we included only students without a history of mental health problems in the logistic regression analyses assessing the impact of COVID-19 infection. However, we did not account for participants' pre-existing physical health conditions, which could potentially amplify their physiological stress responses, leading to an overestimation of the severity of acute COVID-19 symptoms and, consequently, an exaggeration of the psychological impact of COVID-19 infection.

5. Conclusion

Medical students infected with COVID-19 experienced more severe depression and insomnia symptoms post-infection. COVID-19 infection is a risk factor for the onset of insomnia. Furthermore, acute symptoms such as sleep disturbances, decreased attention/memory, and breathlessness are also risk factors for insomnia. In the post-pandemic era, recurrent and persistent COVID-19 infections are inevitable. Early intervention targeting these risk acute-phase symptoms is essential for preventing long-term insomnia. Additionally, college administrators should advocate for and encourage students to develop regular exercise habits, as this is an effective method for preventing insomnia.

CRediT authorship contribution statement

Yue Zhu: Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Xiaoyang Qin:** Writing – original draft, Visualization, Methodology. **Yuhong Lu:** Writing – original draft. **Yuenan Yu:** Visualization, Software, Methodology. **Rongxun Liu:** Resources, Project administration, Data curation. **Rongxin Zhu:** Resources, Project administration. **Kuan-Pin Su:** Resources, Project administration. **Fei Wang:** Supervision, Resources, Project administration, Data curation, Conceptualization.

Data availability statement

Data are available upon reasonable request. Deidentified original transcript data will be available exclusively for academic purposes. For reasonable data requests, please contact the corresponding author (fei.wang@yale.edu).

Ethics statements

All participants completed the questionnaires using the WeChat official account platform and provided informed consent before participation. The study was approved by the Biomedical Ethics Committee of Xinxiang Medical University (XYLL-2020235).

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Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bbih.2025.101067>.

Data availability

Data will be made available on request.

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