The Prevalence of Insomnia Symptoms and Its Association With Quality of Life Among Clinically Stable Older Patients With Psychiatric Disorders in China During the COVID-19 Outbreak

Xiuying Xu  
Xiamen Xianyue Hospital

Wen Li  
University of Macau  https://orcid.org/0000-0002-6722-0804

Siyun Zou  
Guangji Hospital Affiliated to Soochow University

Yulong Li  
Lanzhou University Second Hospital

Huan Wang  
Lanzhou University Second Hospital

Xiaona Yan  
Xiamen Xianyue Hospital

Xiang-Dong Du  
Guangji Hospital Affiliated to Soochow University

Lan Zhang  
Lanzhou University Second Hospital

Qinge Zhang  
Beijing Anding Hospital

Teris Cheung  
Hong Kong Polytechnic University

Gabor S. Ungvari  
University of Notre Dame Australia

Yu-Tao Xiang (xyutly@gmail.com)  
Building E12, Faculty of Health Sciences, University of Macau, Avenida da Universidade, Taipa, Macau SAR, China

Research

Keywords: Older patients, psychiatric disorder, insomnia symptoms, quality of life, COVID-19

DOI: https://doi.org/10.21203/rs.3.rs-95735/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Aims: The negative impact of the COVID-19 outbreak on sleep quality of clinically stable psychiatric patients is unknown. This study examined the prevalence of insomnia symptoms and its association with quality of life (QOL) in clinically stable older psychiatric patients during the COVID-19 outbreak.

Methods: This multicenter, cross-sectional study involved older patients attending maintenance-treatment at the outpatient departments of four major psychiatric hospitals in China. Patients’ basic socio-demographic and clinical characteristics were collected. Insomnia symptoms, depressive symptoms, and QOL were assessed with the Insomnia Severity Index (ISI), Patient Health Questionnaire (PHQ-9), and two items of the World Health Organization Quality of Life-brief version (WHOQOL-BREF), respectively. Binary logistic regression analysis was conducted to examine the independent associations of socio-demographic and clinical variables with insomnia symptoms, while the association between insomnia symptoms and QOL was examined with analysis of covariance.

Results: A total of 941 patients were recruited. The prevalence of insomnia symptoms was 57.1% (95% CI: 53.9-60.2%). Analysis of covariance revealed that QOL was significantly lower in patients with insomnia symptoms compared to those without them ($P<0.01$). Multivariate logistic regression analysis showed that insomnia symptoms were positively and independently associated with more severe depressive symptoms ($P<0.01$, OR=1.31, 95%CI: 1.26-1.37). Compared to patients with major depressive disorder, those with other psychiatric diagnoses had significantly higher prevalence of insomnia symptoms ($P=0.03$, OR=1.47, 95%CI: 1.02-2.12).

Conclusions: Insomnia symptoms were common among clinically stable older psychiatric patients during the COVID-19 outbreak. Considering their negative impact on QOL, regular assessment and treatment of insomnia symptoms need to be addressed in this population.

1. Introduction

The Coronavirus Disease 2019 (COVID-19) was first reported in Wuhan, China at the end of 2019, and subsequently was found in over 200 countries (1). Compared to the general population, psychiatric patients are arguably one of the most vulnerable subpopulations affected by the COVID-19 outbreak. Psychiatric patients have a higher risk of contagion due to their sedentary lifestyle, limited awareness of self-protection, and non-adherence to preventive public health measures (2). In addition, psychiatric patients, such as major depressive disorder (MDD), schizophrenia, and bipolar disorder, require long-term treatment. Due to the under-developed community mental health services in China, clinically stable patients need to regularly visit psychiatric outpatient departments located in urban hospitals for maintenance treatment (3, 4). Travelling during the outbreak of any infectious disease inevitably increases the risk of infection. A significant proportion of patients have difficulties to attend their psychiatric outpatient appointments due to quarantine and traffic restrictions for prevention and control of the COVID-19 outbreak (5). These public health preventive measures interrupt treatment leading to relapse and undesirable behaviors including self-harm and aggression.

Among those individuals affected by the COVID-19 outbreak, special attention should be given to older psychiatric patients. Compared with other age groups, older adults infected with COVID-19 have poor treatment outcomes and higher mortality rates (6, 7). Older adults are scared about COVID-19, which could worsen their pre-existing mental health problems (8). Patients with MDD and anxiety disorder, in particular, are exceptionally vulnerable (9). Besides, most mental health services and education related to the COVID-19 (e.g., psycho-education and psychological counseling) are primarily delivered online (10). Many older psychiatric patients could not benefit from these online services due to their limited access to smartphones and broadband internet, and poor digital health literacy (8).
Insomnia symptoms are a major health problem worldwide (11). During the COVID-19 outbreak, insomnia symptoms were found to be very common in the general population (12) and subpopulations, such as frontline clinicians (13) and patients with COVID-19 (14). However, to the best of our knowledge, no study has focused on older adults, especially those with psychiatric disorders. Insomnia symptoms are associated with treatment with psychotropic medications (15), impaired cognitive function (16), increased risk of psychiatric disorders (17) and cardiovascular and metabolic diseases (18), poor quality of life (QOL) (19), increased consumption of health care services and economic burden (20). Insomnia symptoms are also risk factor for deterioration and relapse of psychiatric disorders (17). In order to reduce the negative impact of insomnia symptoms on health outcomes and daily life, it is important to understand their patterns and associated factors.

QOL is a widely used health outcome, which reflects individuals' general perception over their physical and mental health (21, 22). The impact of insomnia symptoms on QOL in older psychiatric patients during the COVID-19 outbreak has not been explored. Thus, the aim of this study was to examine the prevalence of insomnia symptoms and its association with QOL in a sizeable cohort of clinically stable older psychiatric patients.

2. Methods

2.1. Participants

This was a cross-sectional study conducted between May 22 and June 23, 2020 in four major tertiary psychiatric hospitals located in the northern (Beijing), southern (Fujian province), eastern (Jiangsu province), and western parts (Gansu province) of China that represent a range of clinical settings. Older patients attending outpatient departments of the four psychiatric hospitals for maintenance treatment were consecutively invited to participate in this study. To be eligible, participants should be: 1) aged 50 years and above; 2) had a principal diagnosis of any types of psychiatric disorders diagnosed according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) and confirmed by their treating psychiatrists; 3) were clinically stable judged by their treating psychiatrists. Following previous studies (23, 24), those with changes in doses of psychotropic medications of less than 50% in the past three months were considered “clinically stable patients”. This criterion has been used in clinical practice in the participating hospitals; and 4) they were able to give written informed consent. The study protocol was approved by the Ethical Committees of the respective hospitals.

2.2 Measurements

Patients' basic socio-demographic and clinical data were collected including age, gender, education, marital status, current severe medical conditions affecting the cardiovascular, respiratory, digestive, hematological, endocrine, urinary, connective tissue, and nervous systems (25). One additional COVID-19 related question was also asked, namely, whether they were concerned about the COVID-19 outbreak during the past months.

The severity of depressive symptoms was evaluated with the Chinese version of the 9-item Patient Health Questionnaire (PHQ-9) (26, 27). Each item of the PHQ-9 is scored from 0 (not at all) to 3 (nearly every day). This psychometrically validated scale is widely used in Chinese populations (28). The total score of PHQ-9 that ranged between 0 and 27 was calculated by adding up all its item scores. The PHQ-9 total score of < 5, ≥ 5, and ≥ 10 indicated “no depressive symptoms”, “mild depressive symptoms”, and “moderate to severe depressive symptoms”, respectively (29). Severity of insomnia symptoms was assessed with the 7-item Insomnia Severity Index (ISI), a Likert scale with each item ranging from 0 to 4 (30). The ISI has satisfactory psychometric properties in China (31). The ISI total score ranges from 0 to 28, with higher total scores representing more severe insomnia symptoms. The cut-off value of ≥ 8 was considered as “having insomnia symptoms” (32). The total score of the two items on the overall QOL of the World Health Organization (WHO) SF-12 was elicited, which is a brief health status measure that provides two scores: Physical Component Summary (PCS) and Mental Component Summary (MCS).
Health Organization Quality of Life-brief version (WHOQOL-BREF) (33–35) were used to assess patients’ QOL. The QOL score ranged between 0 and 10, with a higher score representing higher QOL.

2.3 Data analysis

All data analyses were performed with the Statistic Package for Social Science (SPSS), Version 24.0. The normality of continuous variables was examined with the P-P Plot. Social-demographic (e.g., age, gender, marital status, education years) and clinical characteristics (e.g., severe medical diseases, concerns about the COVID-19 outbreak, principal psychiatric diagnoses, and severity of depressive symptoms) were compared between patients with and without insomnia symptoms. Normally distributed continuous variables were compared using the two independent samples t-tests, while those that did not follow normal distribution were compared using Mann-Whitney U tests. Categorical variables were compared using $\chi^2$ tests. Independent associations of socio-demographic and clinical variables with insomnia symptoms were examined applying binary logistic regression analysis with the “enter” method. All socio-demographic and clinical variables were entered as independent variables, and the presence of insomnia symptoms was the dependent variable. The QOL between patients with and without insomnia symptoms was compared using analysis of covariance (ANCOVA) after controlling for variables with significant group differences in univariate analyses. The level of significance was set at $P<0.05$ (two-tailed).

3. Results

A total of 946 patients were invited to participate in the study; 941 met the eligibility criteria, yielding a response rate of 99.5%. The mean age of participants was 62.89 (SD: 9.43) years and 32.4% (n = 305) were men. The prevalence of insomnia symptoms (ISI total score of $\geq 8$) was 57.1% (95% confidential interval (CI): 53.9%-60.2%) in the whole sample. The mean ISI total score was 8.94 (SD: 6.30). The prevalence of “no depressive” symptoms, mild, and moderate to severe depressive symptoms was 37.4% (95%CI: 34.3%-40.5%), 32.7% (95%CI: 29.7%-35.7%), and 29.8% (95%CI: 26.9%-32.7%), respectively in the whole sample.

Univariate analyses revealed that patients with insomnia symptoms were younger ($P=0.02$) and had shorter education ($P<0.01$) and higher PHQ-9 total scores ($P<0.01$). In addition, the prevalence of insomnia symptoms was significantly different across principal psychiatric diagnoses ($P<0.01$). There was no significant difference in the prevalence of insomnia symptoms between male and female patients (58.0% (95%CI: 52.4%-63.6%) vs. 56.6% (95%CI: 52.7%-60.4%), $\chi^2 = 0.17$, $P=0.68$). Binary logistic regression analysis found that the presence of insomnia symptoms was positively and independently associated with more severe depressive symptoms ($P<0.01$, OR = 1.31, 95%CI: 1.26–1.37). Compared to MDD patients, those with other psychiatric diagnoses were more likely to have insomnia symptoms ($P = 0.03$, OR = 1.47, 95%CI: 1.02–2.12) (Table 1). ANCOVA revealed that patients with insomnia symptoms had a significantly lower overall QOL compared to those without them ($F_{(1,941)} = 19.37$, $P<0.01$).
Table 1: Participants’ socio-demographic and clinical characteristics and their associates with insomnia symptoms

| Variable                                      | Total (N = 941) | No insomnia symptoms (N = 404) | Insomnia symptoms (N = 537) | Univariate analyses | Multivariate logistic regression# |
|-----------------------------------------------|-----------------|--------------------------------|-----------------------------|---------------------|----------------------------------|
|                                               | N    | %    | N    | %    | N    | %    | χ²  | df | P   | OR  | 95% CI | P    |
| Gender                                        |      |      |      |      |      |      |      |     |     |     |      |       |
| Female                                        | 636  | 67.6 | 276  | 68.3 | 360  | 67.0 | 0.17 | 1   | 0.68 |      | -      |       |
| Male                                          | 305  | 32.4 | 128  | 31.7 | 177  | 33.0 |      |     |     | 1.09 | 0.77–1.55 | 0.59   |
| Married                                       | 847  | 90.0 | 367  | 90.8 | 480  | 89.4 | 0.54 | 1   | 0.46 | 0.68 | 0.38–1.22 | 0.20   |
| Severe medical conditions¹                    | 172  | 18.3 | 73   | 18.1 | 99   | 18.4 | 0.21 | 1   | 0.89 | 1.14 | 0.71–1.84 | 0.56   |
| Concern about the COVID-19 outbreak           |      |      |      |      |      |      | 0.84 | 2   | 0.66 |      |        |       |
| None                                          | 405  | 43.0 | 170  | 42.1 | 235  | 43.8 |      |     |     |      |        |       |
| Sometimes                                     | 353  | 37.5 | 150  | 37.1 | 203  | 37.8 |      |     |     | 0.96 | 0.66–1.40 | 0.86   |
| Frequently                                    | 183  | 19.4 | 84   | 20.8 | 99   | 18.4 |      |     |     | 0.95 | 0.60–1.51 | 0.84   |
| Principal psychiatric diagnosis ²              |      |      |      |      |      |      | 14.13 | 3 | < 0.01 |      |        |       |
| Major depressive disorder                     | 433  | 46.0 | 179  | 44.3 | 254  | 47.3 |      |     |     |      |        |       |
| Schizophrenia                                 | 59   | 6.3  | 38   | 9.4  | 21   | 3.9  | 0.56 |     | 0.28–1.12 | 0.10 |
| Organic mental disorders                     | 57   | 6.1  | 29   | 7.2  | 28   | 5.2  | 1.26 |     | 0.60–2.61 | 0.53 |
| Other psychiatric diagnoses                   | 392  | 41.7 | 158  | 39.1 | 234  | 43.6 | 1.47 |     | 1.02–2.12 | 0.03 |
| Age (years)                                  | Mean | SD  | Mean | SD  | Mean | SD  | t/Z  | df | P   |      |        |       |
|                                               | 62.89| 9.43 | 63.71| 9.57 | 62.28| 9.29 | 2.31 | 939 | 0.02 | 0.99 | 0.97–1.01 | 0.87   |
| Education (years)                             | 7.90 | 4.01 | 8.36 | 3.96 | 7.56 | 4.01 | -4.21|     |      | 0.99 | 0.95–1.04 | 0.88   |
### Table

| Variable               | Total (N = 941) | No insomnia symptoms (N = 404) | Insomnia symptoms (N = 537) | Univariate analyses | Multivariate logistic regression# |
|------------------------|-----------------|-------------------------------|-----------------------------|---------------------|----------------------------------|
|                        | N               | %                             | N                           | %                   | χ²     | df | P      | OR     | 95% CI | P       |
| PHQ-9 total score      | 7.66            | 6.63                          | 3.82                        | 4.36                | -16.72 | -  | < 0.01 | 1.31   | 1.26–1.37 | < 0.01 |
| Quality of life        | 6.20            | 1.54                          | 6.82                        | 1.44                | 5.72   | 1.43 | 11.65  | 939    | < 0.01   |

1. Current severe medical disease affecting the cardiovascular, respiratory, digestive, hematological, endocrine, urinary, connective tissue, and nervous systems.

2. Only psychiatric diagnoses with the percentage > 5% are presented separately; those with percentage of < 5% were included in “others”.

#. The independent variables were all social-demographic and clinical variables: age, gender, marital status, education years, severe physical diseases suffering, concerns about the COVID-19 outbreak, principal psychiatric diagnoses, and PHQ-9 total score and study sites that were controlled, while the dependent variable was insomnia symptoms;

Bold values: <0.05;

Abbreviations: COVID-19 = Coronavirus Disease 2019; CI = Confident Interval; MDD = major depressive disorder; PHQ-9 = 9-item Patient Health Questionnaire; Ref = reference group; SD = standard deviation.

## 4. Discussion

This study investigated the prevalence of insomnia symptoms in clinically stable older psychiatric patients and their impact on QOL during the COVID-19 outbreak in China. Over half (57.1%, 95%CI: 53.9%-60.2%) of the patients suffered from insomnia symptoms, which is higher than the corresponding figures reported in other populations using the same measure and cutoff value during the COVID-19 outbreak, such as frontline clinicians (28.75%-38.4%) (36–38), inpatients with COVID-19 (42.8%) (14), breast cancer patients (36.2%) (39), and the general population (28.5%) (40). In addition, the prevalence of insomnia symptoms in this study was also much higher than the figures in both the general population (15.0%, 95%CI: 12.1%-18.5%) (41) and older psychiatric patients (27.0%, 95%CI: 24.5%-29.4%) (42) in China before the COVID-19 outbreak, although measures on insomnia symptoms were different.

The reasons for frequent insomnia symptoms in older psychiatric patients are complex. Psychiatric disorders and insomnia symptoms often co-exist, because sleep rhythm often changes in many psychiatric disorders as well as with the use of psychotropic medications (43, 44). Besides, age is a risk factor for insomnia (45). In older adults, sleep and circadian rhythm changes occur along with the physiologic changes, which presents as gradually decreased sleep efficiency and total sleep time. Unrealistic expectations about sleep duration and quality could elevate the risk of insomnia (46). Moreover, increased prevalence of medical problems (e.g., nocturia and physical disability) (47) and treatments (e.g., beta-blockers, glucocorticoids, and nonsteroidal anti-inflammatory drugs) (46) could contribute to the occurrence of insomnia. Aging women including those with psychiatric disorders are more likely to suffer from insomnia symptoms (44, 50) than men. However, no gender difference was found in the current study. This discrepancy between the current and previous studies may be due to the increased prevalence of insomnia symptoms in both genders during the COVID-19 outbreak, which may offset the gender difference found earlier.
The COVID-19 outbreak could further trigger insomnia symptoms and related problems in older psychiatric patients for a number of reasons. First, more severe consequences and higher mortality rates in older adults with COVID-19 could spread fear and mental distress. Second, mass quarantine measures lead to loneliness, fatigue, and daytime sleepiness (48, 49) and thus affect sleep and circadian rhythm. Third, older psychiatric patients have frequent comorbid chronic medical conditions and require long-term medication treatment. Difficulties in attending hospitals during the COVID-19 outbreak further aggravate patients’ distress about discontinuation of treatment contributing to the development of insomnia symptoms.

As expected, patients with insomnia symptoms reported more severe depressive symptoms in this study. The association between insomnia symptoms and depressive disorders is bidirectional. On one hand, insomnia symptoms are a risk factor of depressive disorders (50, 51); on the other hand, depressive disorders increase the likelihood of insomnia symptoms (52). In meta-analyses insomnia symptoms significantly predicted the onset of depressive episodes (51, 53, 54) with an overall odds ratio (OR) of up to 2.83 (95%CI: 1.55–5.17) (51). This could be partly explained by the impairment of emotional processing caused by insomnia, which could lead to depressive symptoms (55). Furthermore, the association between insomnia and depressive symptoms might be related to common pathomechanisms, e.g., similar alterations of arousal states (56–58) and level of inflammatory markers (59). In this study, patients with other psychiatric diagnoses, mainly schizophrenia and organic mental disorders, were more likely to suffer from insomnia symptoms than those with MDD. The diagnostic heterogeneity makes it difficult to interpret the reasons for the unexpectedly significant group difference. Head-to-head comparative studies between different psychiatric diagnoses are warranted to replicate or refute this finding.

Patients with insomnia symptoms had a lower overall QOL than those without, which is consistent with previous findings (60, 61). According to the distress/protection QOL model (62), QOL is determined by the interaction between protective (e.g., good social support and economic status) and distressing factors (e.g., poor health). Insomnia symptoms are associated with impaired daytime functioning (63), deficits of attention, working memory, and executive function (64), poor physical health (18), and psychiatric symptoms (65), all of which could lower QOL.

The strengths of this study include the multicenter study-design and the large sample size, which increase the overall representativeness of the study sample. However, several methodological limitations need to be addressed. First, the study only included clinically stable patients, which limits the generalizability of the findings to patients in different illness stage. Second, due to logistical reasons during the COVID-19 outbreak, clinical stability was judged by the treating psychiatrists, rather assessed by the aid of standardized rating instruments. Third, the causal relationships between demographic and clinical characteristics and insomnia symptoms could not be examined due to the cross-sectional study design. Fourth, factors potentially associated with insomnia symptoms (e.g., social support and economic status) were not examined in this study.

5. Conclusion

In conclusion, insomnia symptoms were common in clinically stable, older psychiatric patients during the COVID-19 outbreak. Given the negative impact of insomnia symptoms on QOL and daily functioning, regular assessment of sleep duration and quality should be included in the routine clinical care of this vulnerable population. and a variety of treatment modalities, such as cognitive-behavioral therapy (66), repetitive transcranial magnetic stimulation (67), neuro-feedback (68), and sleep medications (69), should be offered to patients presenting with insomnia symptoms.

Declarations
Ethical approval and consent to participate

All participants provided written informed consent. The study protocol was approved by the ethics committee of the University of Macau, China.

Consent for publication

Not applicable.

Availability of data and materials

The Clinical Research Ethics Committee of participating hospitals that approved the study prohibits the authors from making the research dataset of clinical studies publicly available. Readers and all interested researchers may contact Dr. YT Xiang (Email address: xytly@gmail.com) for details. Dr. Xiang could apply to the Clinical Research Ethics Committee of participating hospitals for the release of the data.

Conflict of Interest

The authors have no conflicts of interest to declare.

Funding

The study was supported by the National Science and Technology Major Project for investigational new drug (2018ZX09201-014), the Beijing Municipal Science & Technology Commission (No. Z181100001518005), the University of Macau (MYRG2019-00066-FHS), and the Suzhou Key Medical Center for Psychiatric Diseases (Szzx201509).

Authors’ contributions

Study design: Qinge Zhang, Yu-Tao Xiang. Data collection, analysis and interpretation: Xiuying Xu, Wen Li, Siyun Zou, Yulong Li, Huan Wang, Xiaona Yan, Xiang-Dong Du, Lan Zhang, Qinge Zhang. Drafting of the manuscript: Wen Li, Teris Cheung, Yu-Tao Xiang. Critical revision of the manuscript: Gabor S. Ungvari. Approval of the final version for publication: all co-authors.

Acknowledgements

The authors are grateful to all participants and clinicians involved in this study.

References

1. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard. https://covid19worldwide.org/ (access June 22, 2020). 2020.
2. Zhu Y, Chen L, Ji H, Xi M, Fang Y, Li Y. The risk and prevention of Novel Coronavirus pneumonia infections among inpatients in psychiatric hospitals. Neuroscience Bulletin. 2020;36(3):299-302.
3. Xiang YT, Ng CH, Yu X, Wang G. Rethinking progress and challenges of mental health care in China. World Psychiatry. 2018;17(2):231.
4. Xiang Y-T, Yu X, Sartorius N, Ungvari GS, Chiu HF. Mental health in China: challenges and progress. Lancet (London, England). 2012;380(9855):1715-6.

5. Li W, Yang Y, Liu Z-H, Zhao Y-J, Zhang Q, Zhang L, et al. Progression of mental health services during the COVID-19 outbreak in China. International Journal of Biological Sciences. 2020;16(10):1732.

6. Shahid Z, Kalayanamitra R, McClafferty B, Kepko D, Ramgobin D, Patel R, et al. COVID-19 and older adults: what we know. Journal of the American Geriatrics Society. 2020;68(5):926-9.

7. Du R-H, Liang L-R, Yang C-Q, Wang W, Cao T-Z, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J. 2020;55(5):2000524.

8. Yang Y, Li W, Zhang Q, Zhang L, Cheung T, Xiang YT. Mental health services for older adults in China during the COVID-19 outbreak. The Lancet Psychiatry. 2020;7(4):e19.

9. Hao F, Tan W, Jiang L, Zhang L, Zhao X, Zou Y, et al. Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and research implications for immunopsychiatry. Brain, behavior, and immunity. 2020;87:100-6.

10. Liu S, Yang L, Zhang C, Xiang Y-T, Liu Z, Hu S, et al. Online mental health services in China during the COVID-19 outbreak. The Lancet Psychiatry. 2020;7(4):e17-e8.

11. Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, et al. European guideline for the diagnosis and treatment of insomnia. Journal of Sleep Research. 2017;26(6):675-700.

12. Kokou-Kpolou CK, Megalakaki O, Laimou D, Kousouri M. Insomnia during COVID-19 pandemic and lockdown: prevalence, severity, and associated risk factors in French population. Psychiatry Research. 2020;290:113128.

13. Pappa S, Ntella V, Giannakas T, Giannakoulis VG, Papoutsi E, Katsaounou P. Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: a systematic review and meta-analysis. Brain, behavior, and immunity. 2020;88:901-7.

14. Wang Y, Zhu L-Y, Ma Y-F, Bo H-X, Deng H-B, Cao J, et al. Association of insomnia disorder with sociodemographic factors and poor mental health in COVID-19 inpatients in China. Sleep Medicine. 2020;75:282-6.

15. Bajaj V, Kalra I, Bajaj A, Sharma D, Kumar R. A case of zolpidem dependence with extremely high daily doses. Asia Pacific Psychiatry. 2019;11(4):e12356.

16. Koo DL, Shin J-H, Lim J-S, Seong J-K, Joo EY. Changes in subcortical shape and cognitive function in patients with chronic insomnia. Sleep Medicine. 2017;35:23-6.

17. Khurshid KA. Comorbid insomnia and psychiatric disorders: an update. Innov Clin Neurosci. 2018;15(3-4):28-32.

18. Khan S, Malik BH, Gupta D, Rutkofsky I. The role of circadian misalignment due to insomnia, lack of sleep, and shift work in increasing the risk of cardiac diseases: a systematic review. Cureus. 2020;12(1):e6616-e.

19. Kyle SD, Morgan K, Espie CA. Insomnia and health-related quality of life. Sleep Medicine Reviews. 2010;14(1):69-82.

20. Ozminkowski RJ, Wang S, Walsh JK. The direct and indirect costs of untreated insomnia in adults in the United States. Sleep. 2007;30(3):263-73.

21. Monson E, Caron J, McCloskey K, Brunet A. Longitudinal analysis of quality of life across the trauma spectrum. Psychological Trauma: Theory, Research, Practice, and Policy. 2017;9(5):605.

22. Gao K, Su M, Sweet J, Calabrese JR. Correlation between depression/anxiety symptom severity and quality of life in patients with major depressive disorder or bipolar disorder. Journal of Affective Disorders. 2019;244:9-15.

23. Xiang Y-T, Weng Y-Z, Leung C-M, Tang W-K, Ungvari GS, Gerevich J. Clinical and social determinants of psychotropic drug prescription for schizophrenia outpatients in China. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2007;31(3):756-60.
24. Lobana A, Mattoo SK, Basu D, Gupta N. Quality of life in schizophrenia in India: comparison of three approaches. Acta Psychiatrica Scandinavica. 2001;104(1):51-5.

25. Xiang YT, Ma X, Lu JY, Cai ZJ, Li SR, Xiang YQ, et al. Alcohol-related disorders in Beijing, China: prevalence, socio-demographic correlates, and unmet need for treatment. Alcoholism: Clinical and Experimental Research. 2009;33(6):1111-8.

26. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of General Internal Medicine. 2001;16(9):606-13.

27. Chen M, Sheng L, Qu s. Diagnostic test of screening depressive disorder in general hospital with the Patient Health Questionnaire (in Chinese). Chinese Mental Health. 2015;29(4):241-5.

28. Wang W, Bian Q, Zhao Y, Li X, Wang W, Du J, et al. Reliability and validity of the Chinese version of the Patient Health Questionnaire (PHQ-9) in the general population. General hospital psychiatry. 2014;36(5):539-44.

29. Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. General hospital psychiatry. 2010;32(4):345-59.

30. Morin CM. Insomnia: psychological assessment and management. New York, NY, US: Guilford Press; 1993. xvii, 238-xvii, p.

31. Bai C, Daihong J, Chen L, Liang L, Wang C. Reliability and validity of Insomnia Severity Index in clinical insomnia patients (in Chinese). Chinese Journal of Practical Nursing. 2018;34(28):2182-6.

32. Smith MT, Wegener ST. Measures of sleep: the Insomnia Severity Index, Medical Outcomes Study (MOS) Sleep Scale, Pittsburgh Sleep Diary (PSD), and Pittsburgh Sleep Quality Index (PSQI). Arthritis Care & Research. 2003;49(S5):S184-S96.

33. Harper A, Power M, Grp W. Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med. 1998;28(3):551-8.

34. Fang JQ, & Hao, Y. A. . Reliability and Validity for Chinese Version of WHO Quality of Life Scale (in Chinese). Chinese Mental Health Journal. 1999;13(4):203-9.

35. Xia P, Li N, Hau K-T, Liu C, Lu Y. Quality of life of Chinese urban community residents: a psychometric study of the mainland Chinese version of the WHOQOL-BREF. BMC Medical Research Methodology. 2012;12(1):37.

36. Que J, Shi L, Deng J, Liu J, Zhang L, Wu S, et al. Psychological impact of the COVID-19 pandemic on healthcare workers: a cross-sectional study in China. General Psychiatry. 2020;33(3):e100259.

37. Zhang W-r, Wang K, Yin L, Zhao W-f, Xue Q, Peng M, et al. Mental health and psychosocial problems of medical health workers during the COVID-19 epidemic in China. Psychotherapy and Psychosomatics. 2020;89(4):242-50.

38. Zhang C, Yang L, Liu S, Ma S, Wang Y, Cai Z, et al. Survey of insomnia and related social psychological factors among medical staff involved in the 2019 novel coronavirus disease outbreak. Frontiers in Psychiatry. 2020;11:306.

39. Li J, Augusto S-MC, Feng H, Wang L, Zhang P, Xu Y, et al. Patient reported outcomes of breast cancer patients during the COVID-19 outbreak in the epicenter of China: a cross sectional survey study. Clinical Breast Cancer. 2020;20(5):e651-e62.

40. Lin L-y, Wang J, Ou-yang X-y, Miao Q, Chen R, Liang F-x, et al. The immediate impact of the 2019 novel coronavirus (COVID-19) outbreak on subjective sleep status. Sleep Medicine. 2020.

41. Cao X-L, Wang S-B, Zhong B-L, Zhang L, Ungvari GS, Ng CH, et al. The prevalence of insomnia in the general population in China: a meta-analysis. PloS one. 2017;12(2):e0170772.

42. Zheng W, Luo X-N, Li H-Y, Ke X-Y, Dai Q, Zhang C-J, et al. Prevalence of insomnia symptoms and their associated factors in patients treated in outpatient clinics of four general hospitals in Guangzhou, China. BMC Psychiatry.
2018;18(1):232.

43. Krystal AD. Psychiatric disorders and sleep. Neurol Clin. 2012;30(4):1389-413.

44. Higuchi T, Ishigooka J, Iyo M, Hagi K. Safety and effectiveness of lurasidone for the treatment of schizophrenia in Asian patients: results of a 26-week open-label extension study. Asia Pacific Psychiatry. 2020;12(1):e12377.

45. Sonnega A, Leggett A, Pepin R, Assari S. Physical activity and insomnia symptoms over 10 years in a US national sample of late-middle-age and older adults: age matters. Journal of Aging and Physical Activity. 2020;1(aop):1-10.

46. Patel D, Steinberg J, Patel P. Insomnia in the elderly: a Review. J Clin Sleep Med. 2018;14(6):1017-24.

47. Foley DJ, Monjan A, Simonsick EM, Wallace RB, Blazer DG. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. Sleep: Journal of Sleep Research & Sleep Medicine. 1999;22:Suppl 2:S366-72.

48. Griffin SC, Williams AB, Mladen SN, Perrin PB, Dzierzewski JM, Rybarczyk BD. Reciprocal effects between loneliness and sleep disturbance in older Americans. Journal of Aging and Health. 2019:0898264319894486.

49. Um Min Allah N, Arshad S, Mahmood H, Abbas H. The psychological impact of coronavirus outbreak in Pakistan. Asia-Pacific psychiatry : official journal of the Pacific Rim College of Psychiatrists. 2020:e12409-e.

50. Jaussent I, Bouyer J, Ancelin ML, Akbaraly T, Pérès K, Ritchie K, et al. Insomnia and daytime sleepiness are risk factors for depressive symptoms in the elderly. Sleep. 2011;34(8):1103-10.

51. Hertenstein E, Feige B, Gmeiner T, Kienzler C, Spiegelhalder K, Johann A, et al. Insomnia as a predictor of mental disorders: a systematic review and meta-analysis. Sleep Medicine Reviews. 2019;43:96-105.

52. Sunderajan P, Gaynes BN, Wisniewski SR, Miyahara S, Fava M, Akingbala F, et al. Insomnia in patients with depression: a STARD report. CNS Spectrums. 2010;15(6):394-404.

53. Li L, Wu C, Gan Y, Qu X, Lu Z. Insomnia and the risk of depression: a meta-analysis of prospective cohort studies. BMC Psychiatry. 2016;16(1):375.

54. Baglioni C, Battagliese G, Feige B, Spiegelhalder K, Nissen C, Voderholzer U, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. Journal of Affective Disorders. 2011;135(1-3):10-9.

55. Yoo S-S, Gujar N, Hu P, Jolesz FA, Walker MP. The human emotional brain without sleep—a prefrontal amygdala disconnect. Current Biology. 2007;17(20):R877-R8.

56. Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. Sleep Medicine Reviews. 2010;14(1):19-31.

57. de Lecea L, Carter ME, Adamantidis A. Shining light on wakefulness and arousal. Biological Psychiatry. 2012;71(12):1046-52.

58. Hein M, Lanquart J-P, Loas G, Hubain P, Linkowski P. Similar polysomnographic pattern in primary insomnia and major depression with objective insomnia: a sign of common pathophysiology? BMC Psychiatry. 2017;17(1):273.

59. Krysta K, Krystanek M, Bratek A, Krupka-Matuszczyk I. Sleep and inflammatory markers in different psychiatric disorders. Journal of Neural Transmission. 2017;124(1):179-86.

60. Léger D, Scheuermaier K, Philip P, Paillard M, Guilleminault C. SF-36: evaluation of quality of life in severe and mild insomniacs compared with good sleepers. Psychosomatic Medicine. 2001;63(1):49-55.

61. Berkley AS, Carter PA, Yoder LH, Acton G, Holahan CK. The effects of insomnia on older adults’ quality of life and daily functioning: a mixed-methods study. Geriatric Nursing. 2020;S0197-4572.

62. Voruganti L, Heslegrave R, Awad AG, Seeman MV. Quality of life measurement in schizophrenia: reconciling the quest for subjectivity with the question of reliability. Psychol Med. 1998;28(1):165-72.
63. Hatoum HT, Kong SX, Kania CM, Wong JM, Mendelson WB. Insomnia, health-related quality of life and healthcare resource consumption. Pharmacoeconomics. 1998;14(6):629-37.

64. Fortier-Brochu E, Beaulieu-Bonneau S, Ivers H, MORIN C. Insomnia and daytime cognitive performance: a meta-analysis. Sleep Medicine Reviews. 2012;16(1):83-94.

65. Zhang J, Lam S-P, Li S, Tang N, Yu M, Li A, et al. Insomnia, sleep quality, pain, and somatic symptoms: sex differences and shared genetic components. Pain. 2012;153(3):666-73.

66. Carlbring P, Andersson G, Cuijpers P, Riper H, Hedman-Lagerlöf E. Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. Cognitive Behaviour Therapy. 2018;47(1):1-18.

67. Song P, Lin H, Li S, Wang L, Liu J, Li N, et al. Repetitive transcranial magnetic stimulation (rTMS) modulates time-varying electroencephalography (EEG) network in primary insomnia patients: a TMS-EEG study. Sleep Medicine. 2019;56:157-63.

68. Luctkar-Flude MF, Tyerman J, Groll D. Exploring the use of neurofeedback by cancer survivors: results of interviews with neurofeedback providers and clients. Asia-Pacific Journal of Oncology Nursing. 2019;6(1):35-42.

69. Myrto ST, Huhn M, Chiocchia V, Schneider-Thoma J, Wiegand M, Salanti G, et al. Efficacy, acceptability and tolerability of all available treatments for insomnia in the elderly: a systematic review and network meta-analysis. Acta Psychiatrica Scandinavica. 2020;142(1):6-17.