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Review article

The prevalence and risk factors of mental problems in medical students during COVID-19 pandemic: A systematic review and meta-analysis

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ABSTRACT

Background: This meta-analysis and systematic review aimed to evaluate the global prevalence and risk factors of mental problems (i.e., depression, anxiety, stress, sleep disorder, posttraumatic stress disorder (PTSD), burnout, psychological distress, and suicidal ideation) among medical students during the COVID-19 pandemic.

Method: We searched PubMed, Embase, Web of Science, psycARTICLES, PsycINFO, CNKI, and Wan Fang for studies on the prevalence of mental problems among medical students from January 1, 2020, to April 1, 2022. The pooled prevalence was calculated by random-effect models. We performed a narrative review to identify the risk factors.

Results: The meta-analysis included 201 studies ($N = 198,000$). The prevalence of depression (41 %, 95 % CI, 37–45 %), anxiety (38 %, 95 % CI, 34–42 %), stress (34 %, 95 % CI, 27–42 %), sleep disorder (52 %, 95 % CI, 44–60 %), psychological distress (58 %, 95 % CI, 51–65 %), PTSD (34 %, 95 % CI, 22–46 %), suicidal ideation (15 %, 95 % CI, 11–18 %) and burnout (38 %, 95 % CI, 25–50 %) was high. The major risk factors were being female, being junior or preclinical students, exposure to COVID-19, academic stress, psychiatric or physical disorders history, economic trouble, fear of education impairment, online learning trouble, fear of infection, loneliness, low physical activity, low social support, problematic internet or smartphone use, and young age.

Limitations: Most studies were cross-sectional. Few studies provided a reasonable response rate, suggesting potential selection bias.

Conclusions: The study demonstrated a high prevalence and risk factors for mental problems during COVID-19, calling for mental health services. Our findings are valuable for college and health authorities to identify high-risk students and provide targeted intervention.

1. Introduction

The outbreak of the coronavirus disease 2019 (COVID-19) has caused profound and long-lasting psychological harm (Kunzler et al., 2021; Prati and Mancini, 2021; Wu et al., 2021b). Medical students were found to be extremely vulnerable to the mental problems during the pandemic, which might result from the high risk of infection, significant lifestyle change, strict confinement, and disturbance in education

program (Eleftheriou et al., 2021). Studies demonstrated a high prevalence of depression, anxiety, and sleep disorder among medical students worldwide during the pandemic (Cao et al., 2020; Chandratre, 2020; Eleftheriou et al., 2021; Kuman Tunçel et al., 2021; Leroy et al., 2021; Yuan et al., 2021). In addition, the common mental problems might lead to their attrition from the medicine learning (Deng et al., 2021a; Khalafallah et al., 2021; Peng et al., 2022; Wang et al., 2020; Yang et al., 2022b), suggesting the urgent need to screen mental problems and

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explore their risk factors among medical students.

To date, most of the studies among medical students were limited by small sample size and reported varied prevalence and possible associated factors. So far, only a few reviews on the mental health of medical students during this pandemic were available (Chandratre, 2020; Lasheras et al., 2020; Mittal et al., 2021; Vythilingam and Atiomo, 2021). Nevertheless, those reviews focused on certain mental problems (depression or anxiety) and most of the included studies were from the very early phase of the pandemic. More importantly, the risk factors of those symptoms were rarely reviewed. A more comprehensive review which assesses a broader range of mental problems and their risk factors in medical students shall provide more valuable insights for university, hospital, and health policymakers to identify at-risk students and to provide timely mental intervention.

Hence, we conducted the present systemic review and meta-analysis of the prevalence and risk factors of mental problems among medical students. Our study aims to evaluate the global prevalence and risk factors of several mental problems (i.e., depression symptoms, anxiety symptoms, burnout, sleep disorder, high perceived stress, PTSD, psychological distress, burnout, and suicidal ideation) among medical students during the COVID-19 pandemic.

2. Method

The systematic review and meta-analysis was performed according to Preferred Reporting Items For Systematic Reviews and Meta-analyses (PRISMA) guidelines (Moher et al., 2009), and the checklist could be found in Table S1. The study was registered in PROSPERO (CRD42022306025).

2.1. Search strategy

Two independent researchers, Qiuxia Wu and Pu Peng, searched the following database: PubMed, Embase, Web of Science, psycARTICLES, PsycINFO, CNKI, and Wan Fang. All the publications from 01 January 2020 to 01 April 2022 will be researched without country and language restrictions. We did the first search in Feb 2022, and updated them on 01 April 2022. Reference lists of all selected articles will independently be screened to identify additional studies left out in the initial search. Detailed search strategies were provided in Supplementary materials Table S2.

2.2. Selection criteria

All abstracts and full-text were independently reviewed by two researchers: Pu Peng and Qiuxia Wu. Any disagreement will be dissolved by discussion until reaching consensus or by consulting Tieqiao Liu.

To be included in the meta-analysis, the studies should (i) assess a group of medical students (ii) provide the prevalence of mental problems or the prevalence could be calculated according to the article; (iii) determine the prevalence of that mental problem using validated instruments and questionnaires, and (iv) be carried out at least 1 week after the onset of COVID-19 in the specific country where the study was conducted. Studies that included medical students as a subgroup will also be included when detailed information on the prevalence of mental problems of medical students was provided. The exclusion criteria were: (i) failed to provide any aggregate prevalence of mental problems in the medical students group; (ii) had included nursing, dentistry, or pharmacy students as part of the medical student group and did not provide enough data to calculate the prevalence of mental problems in medical students (iii) were not accessible for full review; (iv) all interventional studies, editorials, case reports, case series, meeting abstracts and commentaries; (v) were carried out before the breakout of COVID-19 or failed to provide the study setting, and (vi) the number of participants was <50.

For the narrative review of associated factors of mental problems,

studies should meet the additional criteria that they performed appropriate statistical methods (i.e., multiple or single-factor regression model, chi-square test, Student's *t*-test, Pearson's/Spearman's correlation test, and Wilcoxon Rank-Sum test) to evaluate the possible associated factors. When the studies provided both multiple and single-factor regression, we only included the results of multiple regression.

2.3. Data extraction

Two authors (Pu Peng and Qiuxia Wu) did the literature search and quality assessment independently and completed a data extraction form: author, study design, geographic location; study time, sample characteristics (age, gender, size), study period (during the lockdown or out of the lockdown), measurement tools (the questionnaires and cutoff points, for example), reported prevalence estimates (the number of cases and the total participants), risk factors of that mental problems, and quality assessment. For studies assessing the prevalence of mental problems at multiple time points, only the latest data was extracted. When multiple studies were found reporting on the same population cohort, only the study reporting the most informative and complete data was chosen. We contacted the corresponding authors to gain the information when necessary.

2.4. Quality assessment

A modified version of the Newcastle-Ottawa Quality Assessment Scale (NOS) was used to evaluate the quality of literature (Rotenstein et al., 2016). Five dimensions include sample size, representativeness, response rate, valid assessment of mental problems, and strong statistic methods. Details of the scoring system could be found in Table S3. A score lower than three represented a high risk of bias.

2.5. Data synthesis and statistical analyses

We performed the statistical analyses on R foundation (Version 4.0.2). The main outcome was the pooled prevalence and 95 % confidence intervals (CI) of mental problems (depressive symptoms, anxiety symptoms, high stress, sleep disorder, burnout, psychological distress, suicidal ideation, and PTSD). Random effect models were performed due to the high heterogeneity between studies. The publication bias was evaluated by funnel plot and Egger's test, with a $p > 0.05$ showing low public bias. We assessed the heterogeneity by I^2 statistic, and an $I^2 > 75$ % indicated a high heterogeneity. Subgroup analysis and meta-regression were performed to identify the source of heterogeneity including study time, COVID-19 period, study location, measurement tools, and study quality. Subgroup analysis was conducted when $k \geq 10$ with a cell size of $k > 3$ for each categorical comparison.

3. Result

As illustrated in the flow diagram (Fig. 1), 6273 records were screened after removing duplicates. 1021 studies were read in full text to include studies that met the inclusion criteria. 201 studies were included in the meta-analysis. The study reference, geographic location, study time, sample characteristics (age, gender, size), study period (during the lockdown or out of the lockdown), measurement tools, and prevalence of mental problems were provided in Table S2.

3.1. Study characters

A total of 201 studies regarding 198,000 medical students were included in this study. Of them, the prevalence of a wide range of mental problems was assessed including depression (in 116 studies), anxiety (in 125 studies), high perceived stress (in 43 studies), sleep problems (in 34 studies), psychological distress (in 25 studies), PTSD (in 13 studies), suicidal ideation (in 13 studies) and burnout (in 13 studies).

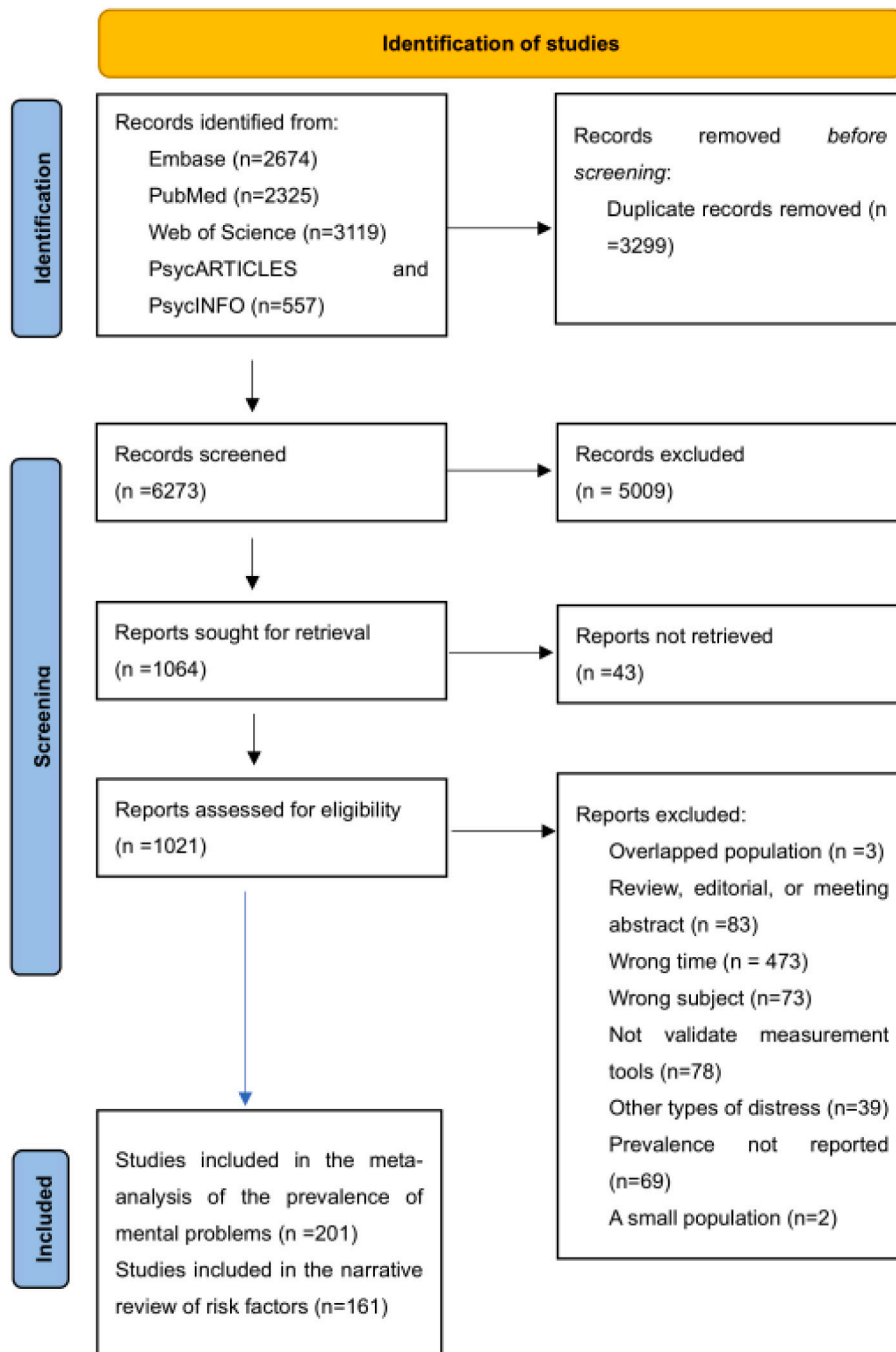


Fig. 1. PRISMA workflow of identification of studies.

Most of the studies were from Asia (72, 35.8 %) and East Asia (72, 35.8 %), followed by Europe (24, 11.9 %), South America (11, 5.4 %), North America (10, 5 %), and Africa (9, 4.4 %). Only one study was carried out in Australia and two studies recruited participants from diverse geographical regions. Nearly half of the studies were carried out during the nationwide COVID-19 lockdown, while 85 (42.3 %) studies were in the post-lockdown period. 24 studies were carried out before lockdown or did not report enough information to identify. 162 studies were carried out during 2020, and 24 studies were carried out in 2021. 15 studies did not report the exact time point. The majority of the studies (193 in 201) were cross-sectional, and 8 studies were longitudinal or repeat cross-sectional.

3.2. Pooled prevalence of mental health problems

The pooled prevalence of depression (41 %, 95 % CI, 37–45 %), anxiety (38 %, 95 % CI, 34–42 %), stress (34 %, 95 % CI, 27–42 %), sleep disorder (52 %, 95 % CI, 44–60 %), psychological distress (58 %, 95 % CI, 51–65 %), PTSD (34 %, 95 % CI, 22–46 %), suicidal ideation (15 %, 95 % CI, 11–18 %) and burnout (38 %, 95 % CI, 25–50 %) are summarized in Table 1. 81 studies investigated the moderate or severe depression, yielding a pooled prevalence of 27 % (95 % CI, 22–31 %). The pooled prevalence of moderate or severe anxiety was 24 % (95 % CI, 20–29 %). There was high heterogeneity between studies, with I^2 ranging from 98.5–100 %. The forest plot of each mental health problem was found in Figs. S1–8.

Table 1
Pooled prevalence, heterogeneity, and publication bias.

Distress	Studies	Cases	N	Prevalence	95 % CI	I ²	p-Value ¹
Depression							
Overall depression	116	43,557	126,044	41 %	37 %–45 %	99.9 %	0.052
Mild and above	89	33,264	93,310	43 %	39 %–48 %	99.8 %	
Moderate and severe	81	19,735	82,418	27 %	22 %–31 %	99.9 %	
Anxiety							
Overall anxiety	125	46,755	155,291	38 %	34 %–42 %	100 %	<0.001
Mild and above	103	38,819	122,966	39 %	34 %–43 %	100 %	
Moderate and severe	89	18,488	107,648	24 %	20 %–29 %	100 %	
Stress	43	9102	34,231	34 %	27 %–42 %	99.9 %	0.932
Sleep disorder	34	10,945	20,661	52 %	44 %–60 %	99.7 %	0.002
PTSD	13	3231	17,622	34 %	22 %–46 %	99.5 %	0.001
Distress	25	8146	15,195	58 %	51 %–65 %	99.2 %	0.178
Suicidal ideation	13	3857	26,708	15 %	11 %–18 %	98.7 %	0.219
Burnout	13	8089	17,577	38 %	25 %–50 %	99.8 %	0.928

¹ p-Value for egger's test, with a $p > 0.05$ suggested no publication bias.

3.3. Publication bias

Egger's test indicated that there was no publication bias in the prevalence of depression, stress, psychological distress, suicidal ideation, and burnout (All $p > 0.05$). However, egger's test suggested a significant publication bias in anxiety, sleep disorder, and PTSD. The funnel plot of each mental health problem was provided in Fig. S9.

3.4. Meta-regression

Meta-regression suggested a rising prevalence of depression and anxiety symptoms over time. For every 1-month increase, a 1.14 % increase in the prevalence of depression ($k = 108$; rate = 0.0142, 95 % CI: 0.0032, 0.0206; $p = 0.0071$) and a 1.17 % increase in anxiety ($k = 117$; rate = 0.0117, 95 % CI: 0.0020, 0.0214; $p = 0.018$). The regression model bubble plot was available in Fig. S9. No association of study time with other mental health problems was found.

3.5. Subgroup analysis

We performed a subgroup analysis of the prevalence of mental symptoms based on lockdown period, study quality, study location, and measurement tools (Table 2). Subgroup difference between groups was only conducted in subgroups with a cell size of $k > 3$, and the full results could be found in Table S5. We found no association between the lockdown period and the prevalence of all mental health problems. Studies with a high risk of bias demonstrated a significantly higher prevalence of anxiety symptoms (44 % vs 34 %, $p = 0.033$) than studies with a low risk of bias, while such association did not exist in other mental health problems. The subgroup analysis revealed that study location was the major resource of heterogeneity of depression ($p < 0.001$), anxiety ($p < 0.001$), and distress ($p = 0.041$), with studies from East Asia demonstrating a lower prevalence. Moreover, a similar trend was observed in sleep disorder ($p = 0.204$) and stress ($p = 0.102$). Measurement tools were the main moderators of the prevalence of depression ($p = 0.016$), anxiety ($p < 0.001$), sleep disorder ($p < 0.001$), and PTSD ($p = 0.009$). However, we found no such relationship in the prevalence of stress ($p = 0.913$), and psychological distress ($p = 0.488$). The forest plot of each subgroup for mental health symptoms was available in Figs. S10–18.

3.6. Factors associated with mental health symptoms

161 studies were included in the narrative review of factors associated with mental health symptoms. We categorized these factors in terms of “Sociodemographic factor” (such as gender, age, and “household income”) “Education factor” (such as education level, preclinical or clinical, academic performance, disruption of education, and online

education), “COVID-19 factor” (such as fear of COVID-19 infection, relatives infected COVID-19, and lived in a high-epidemic COVID-19 area), “Physiological factor” (such as a history of mental disorder), “Lifestyle factor” (such as physical activity, internet addiction, and diet.), “Physiological and health factor” (such as a history of disease or current health status), “Relational factor” (such as family relationship, friendship, and loneliness) and “Predictors of response to trauma” based on the Furber's theory with some modification (Furber et al., 2017).

Table 3 summarized the most frequently reported associated factors. The major risk factors for mental symptoms were being female (in 62 studies), being preclinical students (in 31 studies), being in a high-epidemic COVID-19 area or having relatives infected with COVID-19 (in 26 studies), having low academic performance or heavy academic burden (in 19 studies), with psychiatric disorders history (in 18 studies), economic instability (in 14 studies), fear of education or career impairment (in 12 studies), difficulties with online learning (in 14 studies), fear of COVID-19 infection (in 12 studies), with physical illness or bad somatic health (in 11 studies), living alone or loneliness (in 12 studies), low physical activity (in 10 studies), low social support (in 10 studies), smartphone addiction or extreme screen time (in 10 studies), and young age (in 11 studies). However, there were inconsistent results across the literature. Nine studies demonstrated that male was more prone to mental problems than female. Six studies reported a positive association between age and the incidence of mental problems. Moreover, for the study period, seven studies showed that clinical students had a higher mental health burden than preclinical students.

4. Discussion

The present meta-analysis is composed of 201 studies. It assesses the global prevalence and risk factors of various mental symptoms among medical students during the COVID-19 pandemic, including depression, anxiety, high perceived stress, sleep disorder, psychological distress, PTSD, burnout, and suicidal ideation. This is the largest meta-analysis on that topic. Our study demonstrates a heavy mental burden among medical students worldwide during this period and highlights risk factors for mental symptoms at a variety of levels. Our findings are valuable for university and health policy makers to early detect and provide targeted interventions for mental problems in medical students.

Our study demonstrated the profound and long-lasting psychological impact of COVID-19 on medical students. There was an extreme high prevalence of depression (41 %, 95 % CI, 37–45 %), anxiety (38 %, 95 % CI, 34 %–42 %), stress (34 %, 95 % CI, 27 %–42 %), sleep disorder (52 %, 95 % CI, 44 %–60 %), psychological distress (58 %, 95 % CI, 51 %–65 %), PTSD (34 %, 95 % CI, 22 %–46 %), suicidal ideation (15 %, 95 % CI, 11 %–18 %) and burnout (38 %, 95 % CI, 25 %–50 %) among medical students during the pandemic period. The prevalence of depression, anxiety, suicidal ideation, and psychological distress was higher than

Table 2
Subgroup analysis of mental health problems.

Symptom	Subgroup	k	Prevalence	LLCI	ULCI	I ²	p ¹
Depression	Lockdown						0.917
	After lockdown	47	0.41	0.35	0.47	1	
	Lockdown	59	0.41	0.35	0.47	1	
	Area						<0.001
	Africa	6	0.66	0.51	0.81	0.99	
	Asia	36	0.49	0.41	0.57	1	
	East Asia	47	0.29	0.24	0.33	1	
	Europe	12	0.43	0.31	0.54	1	
	North America	6	0.41	0.28	0.54	0.99	
	South America	7	0.54	0.4	0.68	0.99	
	Quality						0.511
	High risk of bias	34	0.39	0.32	0.46	1	
	Low risk of bias	82	0.42	0.37	0.47	1	
	Scale						0.016
	BDI or BDI-2	10	0.38	0.31	0.46	0.99	
	DASS-21	25	0.40	0.30	0.50	1	
	HADS	4	0.41	0.21	0.62	1	
	PHQ2	4	0.27	0.17	0.37	0.93	
	PHQ9 or PHQ8	55	0.46	0.40	0.52	1	
	SDS	13	0.32	0.22	0.41	0.99	
Anxiety	Lockdown						0.376
	After lockdown	44	0.39	0.33	0.46	1	
	Lockdown	71	0.36	0.30	0.41	1	
	Area						<0.001
	Africa	5	0.58	0.51	0.65	0.98	
	Asia	40	0.46	0.38	0.54	1	
	East Asia	53	0.23	0.19	0.27	0.99	
	Europe	11	0.42	0.30	0.55	0.99	
	North America	7	0.61	0.48	0.74	1	
	South America	8	0.54	0.45	0.63	0.94	
	Quality						0.033
	High risk of bias	42	0.44	0.36	0.52	1	
	Low risk of bias	83	0.34	0.30	0.39	1	
	Scale						<0.001
	BAI	4	0.40	0.27	0.53	0.98	
	DASS-21	26	0.39	0.30	0.48	1	
	GAD2	4	0.34	0.21	0.47	0.96	
	GAD7	64	0.42	0.36	0.48	1	
	HADS	5	0.50	0.34	0.65	0.99	
	SAS	16	0.16	0.10	0.22	0.99	
STAI	5	0.40	0.19	0.60	0.98		
Stress	Lockdown						0.265
	After lockdown	14	0.32	0.19	0.45	0.99	
	Lockdown	25	0.37	0.27	0.48	1	
	Area						0.102
	Asia	19	0.35	0.23	0.47	1	
	East Asia	15	0.23	0.16	0.31	1	
	Europe	4	0.49	0.18	0.80	0.99	
	Quality						0.216
	High risk of bias	14	0.42	0.26	0.59	1	
	Low risk of bias	29	0.31	0.23	0.38	1	
	Scales						0.792
	DASS-21	24	0.32	0.21	0.43	1	
PSS-10	13	0.38	0.23	0.52	0.99		
PSS-14	6	0.37	0.28	0.45	0.98		
Sleep disorder	Lockdown						0.602
	After lockdown	18	0.55	0.45	0.65	1	
	Lockdown	14	0.51	0.39	0.63	1	
	Area						0.204
	Asia	14	0.53	0.44	0.61	0.98	
	East Asia	12	0.41	0.26	0.56	1	
	Quality						0.345
	High risk of bias	12	0.58	0.41	0.75	1	
	Low risk of bias	22	0.49	0.42	0.56	0.99	
	Scale						0.029
ISI	5	0.38	0.24	0.52	0.99		
PSQI	21	0.57	0.47	0.67	1		
Distress	Lockdown						0.625
	After lockdown	12	0.58	0.48	0.69	0.99	
	Lockdown	9	0.54	0.42	0.68	0.99	
	Area						0.041
	Asia	11	0.64	0.53	0.74	0.99	
	East Asia	4	0.38	0.16	0.60	0.98	
Quality						0.849	

(continued on next page)

Table 2 (continued)

Symptom	Subgroup	k	Prevalence	LLCI	ULCI	I ²	p ¹
PTSD	High risk of bias	6	0.60	0.43	0.76	0.98	0.417
	Low risk of bias	19	0.58	0.50	0.66	0.99	
	Scale						
	GHQ12	7	0.62	0.53	0.72	0.97	
	K10	9	0.64	0.51	0.77	0.99	
	K6	5	0.51	0.32	0.70	0.99	
	SQR20	4	0.48	0.28	0.68	0.98	
	Lockdown						
	After lockdown	4	0.32	0.04	0.61	1	
	Lockdown	6	0.35	0.16	0.54	1	
	Quality						
	High risk of bias	3	0.33	0.06	0.60	1	
	Low risk of bias	10	0.35	0.21	0.49	1	
	Scale						
	IES-R	9	0.42	0.28	0.56	0.99	
PCL-5	4	0.18	0.05	0.30	0.99		
Quality							
High risk of bias	4	0.40	0.24	0.56	0.95		
Low risk of bias	9	0.36	0.20	0.53	1		
Area							
Asia	6	0.29	0.09	0.50	0.99		
Europe	6	0.51	0.42	0.60	0.99		
Suicidal ideation	Lockdown						
After lockdown	8	0.15	0.11	0.20	0.96		
Lockdown	4	0.14	0.06	0.21	0.99		
Area							
East Asia	4	0.12	0.06	0.19	0.99		
Europe	4	0.16	0.11	0.20	0.94		

Abbreviation: BAI Beck Anxiety Inventory, BDI Beck Depression Inventory, BDI(–II) Beck Depression Inventory(–II), DASS-21 Depression Anxiety Stress Scale-21, GAD-2(–7) Generalized Anxiety Disorder Scale-2(–7), HADS Hospital Anxiety and Depression Scale, IES-R Impact of Event Scale-Revised, ISI Insomnia Severity Index, K-6 (–10) Kessler Psychological Distress Scale-6(–10), NA not available, PCL-5 Post-traumatic Stress Disorder Checklist-5, PHQ-2(–8/–9) Patient Health Questionnaire-2(–8/–9/), PSQI Pittsburgh Sleep Quality Index, PSS-10(–14) Perceived Stress Scale-10(–14), SAS Self-Rating Anxiety Scale, SDS Self-Rating Depression Scale, SRQ-20 20-item Self-Report Questionnaire, STAI-Y State Trait Anxiety Inventory-Y, GHQ12 General health questionnaire-12.

¹ p<0.05 indicated significant difference between the subgroups.

that before the COVID-19 pandemic (Hope and Henderson, 2014; Quek et al., 2019; Rotenstein et al., 2016). However, the prevalence of sleep disorder or burnout was similar to that before the COVID-19 pandemic (Frajerman et al., 2019; Rao et al., 2020). Moreover, when compared with studies on the general public during the COVID-19 pandemic, our study demonstrated a much higher prevalence of depression, anxiety, distress, sleep disorder, and PTSD (de Sousa et al., 2021; Jahrami et al., 2022; Yunitri et al., 2022).

Based on the subgroup analysis and meta-regression, our study indicated a slight increase in the prevalence of all symptoms except stress and PTSD during the post-lockdown period. However, the changes were not significant. Besides, we found a positive association between the time of data collection and the prevalence of depression and anxiety. Those findings suggest that COVID-19 might be continuing to affect psychological health even long after the initial or peak point. This hypothesis was supported by numerous longitudinal studies which found increasing mental distress among the general population over time (Ausín et al., 2022; Kok et al., 2022; MacDonald et al., 2022). Taken together, our study suggested the mental problems might persist in the late stage of this pandemic. Therefore, it is critical that medical schools and hospitals screen medical students for common mental problems when medical students returned back.

In line with similar meta-analyses in other populations, our study found that studies in East Asia reported the lowest prevalence of mental symptoms (Deng et al., 2021b; Zhu et al., 2021), which might result from effective epidemic disease control. Various studies showed that the severity of the epidemic was positively associated with unhealthy mental status (Essangri et al., 2021; Lee et al., 2021; Lu et al., 2022). Most studies in East Asia were carried out in China, which was the very first country hit by COVID-19 but managed to control it in three months.

Our study has identified several high-risk groups that deserved more attention. Despite several inconsistent results, most studies found female medical students were at a higher risk for mental problems, which was in

line with previous studies in different populations (Balakrishnan et al., 2022; Kunzler et al., 2021; Sheldon et al., 2021). There might be several explanations. First, epidemiological studies demonstrated that females could be more susceptible to mental distress even before the pandemic (Lim et al., 2018). The gender difference in mental distress might be maintained during the pandemic. Second, studies suggested that females might have severer health anxiety, which might lead to worse mental health during the pandemic (Bleichhardt and Hiller, 2007; Solomou and Constantinidou, 2020). Another important risk factor for mental problems was being preclinical or junior students. Interestingly, studies on non-medical students reported similar results, finding junior students were more prone to mental distress (Wathelet et al., 2020). Junior or preclinical students were at the early stage of their medical education. They might have difficulties in adjusting to the stressful medicine learning and the new online learning mode during the pandemic (Çimen et al., 2021). Several studies also suggest junior students might experience more academic stress than senior students during the pandemic (Hakami et al., 2021), which might result in mental problems. Our study also demonstrated low social support and bad family relationship were positively associated with mental distress, which might be explained by the lockdown policy. During the home quarantine, medical students had to live with their family members for a long time. Hence, low social support and bad family relationship might lead to conflicts, which caused mental problems (Wu et al., 2021a). Other important risk factors included economic trouble, pre-existing mental or physical illness, and COVID-19 infection or exposure, which was consistent with studies in other populations (Yuan et al., 2022). Further qualitative interviews in those high-risk students are needed to determine how these factors impacted the mental health of the medical students.

Moreover, our study indicated many modifiable risk factors for mental symptoms, hence targeted intervention could be applied. For example, fear of COVID-19 infection (Bilgi et al., 2021; Gruba et al., 2021; Kuman Tunçel et al., 2021; Safa et al., 2021; Saraswathi et al.,

Table 3
Most frequently reported risk factors for mental health symptoms^a.

Type	Details	Studies	Numbers
Sociodemographic factor	Female	(Abdulghani et al., 2020; AbuDujain et al., 2021; Aftab et al., 2021; AlJhani et al., 2021; Alkhamees et al., 2020; Alkwai, 2021; Allah et al., 2021; Alotiby et al., 2021; Alrashed et al., 2021; Alshammari et al., 2021; Biswas et al., 2021; Capdevila-Gaudens et al., 2021; Çimen et al., 2021; Cockburn et al., 2022; Domínguez-González et al., 2022; Duan et al., 2022; Eleftheriou et al., 2021; Esmat et al., 2021; Essadek et al., 2022; Essangri et al., 2021; Goweda et al., 2020; Gupta et al., 2021; Halperin et al., 2021; Hassnain et al., 2021; Huarcaya-Victoria et al., 2021; Khurram et al., 2020; Kuman Tunçel et al., 2021; Lee et al., 2021; Lingyu et al., 2021; Menon et al., 2021; Muhammad Alfareed Zafar et al., 2020; Nakhostin-Ansari et al., 2020; Natalia and Syakurah, 2021; Ni et al., 2021; Nihmath Nisha et al., 2020; Nikas et al., 2022; Pedraz-Petrozzi et al., 2021; Pelaccia et al., 2021; Pelissier et al., 2021; Perissotto et al., 2021; Puranachaikere et al., 2021; Roka et al., 2020; Rolland et al., 2022a, 2022b; Safarini et al., 2021; Saravia-Bartra et al., 2020; Seetan et al., 2021; Shrestha et al., 2021; Simic et al., 2021; Soltan et al., 2021; Teixeira et al., 2021; Toubasi et al., 2021; Vala et al., 2020; Wang et al., 2021; Xiao et al., 2020; Xie et al., 2020; Yuan et al., 2021; Tian et al., 2021; Jiang et al., 2020; Xing et al., 2020; Zheng et al., 2021b; Zheng et al., 2021c)	62
	Male	(Chang et al., 2021; Gao et al., 2021; Kumar et al., 2021; Xie et al., 2020, 2021; Feng et al., 2021;	9

Table 3 (continued)

Type	Details	Studies	Numbers
Physiological factor	Be younger	Zhang et al., 2020b; Jin et al., 2021; Ma et al., 2021)	11
		(Abdulghani et al., 2020; AlJhani et al., 2021; Eid et al., 2021; Lee et al., 2021; Mishra et al., 2021; Muhammad Alfareed Zafar et al., 2020; Pedraz-Petrozzi et al., 2021; Rolland et al., 2022a; Seetan et al., 2021; Yang et al., 2021; Zhang et al., 2021c)	
	Be older	(Allah et al., 2021; Kumar et al., 2021; Periasamy et al., 2021; Risal et al., 2020; Xie et al., 2021; Zheng et al., 2021a)	6
		(Cao et al., 2020; Gao et al., 2021; Liu et al., 2021a; Meng et al., 2021; Xiao et al., 2021; Zheng et al., 2021a; Zhang et al., 2020c; Wang et al., 2022; Jin et al., 2021)	
	Living in rural	(Allah et al., 2021; Cao et al., 2020; Capdevila-Gaudens et al., 2021; Çimen et al., 2021; Huarcaya-Victoria et al., 2021; Khurram et al., 2020; Kumar et al., 2020; Nishimura et al., 2021; Puranachaikere et al., 2021; Rolland et al., 2022b; Simic et al., 2021; Xiao et al., 2021; Ye et al., 2020; Jiang et al., 2020)	14
(Dahanayake et al., 2021; Elhadi et al., 2020; Nikas et al., 2022; Teixeira et al., 2021)			
Not living home or housing stress	(Aftab et al., 2021; AlJhani et al., 2021; Chootong et al., 2022; Çimen et al., 2021; Crisol-Deza et al., 2022; Domínguez-González et al., 2022; Essangri et al., 2021; Forycka et al., 2022; Guo et al., 2021; Mishra et al., 2022; Nishimura et al., 2021; Pelissier et al., 2021; Puranachaikere et al., 2021; Risal et al., 2020; Soltan et al., 2021; Teixeira et al., 2021; Zhang et al., 2021c; Wang et al., 2022)	4	
	(Lu et al., 2022; Mishra et al., 2021; Saali et al., 2021; Yuan et al., 2021; Zhao et al., 2021; Xia et al.,		

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Table 3 (continued)

Type	Details	Studies	Numbers
Education factor	Low resilience	2022; Zheng et al., 2021b) (Forycka et al., 2022; Saali et al., 2021; Zhao et al., 2022, 2021; Xu et al., 2021)	5
	Junior student or preclinical students ^b	(Adhikari et al., 2021; Ali et al., 2020; AlJhani et al., 2021; Alshammari et al., 2021; Büssing et al., 2021; Capdevila-Gaudens et al., 2021; Chan et al., 2022; Chootong et al., 2022; Çimen et al., 2021; Essadek et al., 2022; Essangri et al., 2021; Goweda et al., 2020; Guse et al., 2021; Halperin et al., 2021; Huarcaya-Victoria et al., 2021; Ismail et al., 2021; Kolcu and Başer Kolcu, 2021; Kostina et al., 2021; Lee et al., 2021; Lingyu et al., 2021; Natalia and Syakurah, 2021; Perissotto et al., 2021; Romic et al., 2021; Saeed and Javed, 2021; Sandoval et al., 2021; Seetan et al., 2021; Shrestha et al., 2021; Simic et al., 2021; Teixeira et al., 2021; Zhao et al., 2021; Zhang et al., 2020c)	31
	Senior students or clinical students ^c	(Elhadi et al., 2020; Hassnain et al., 2021; Xiao et al., 2021; Xie et al., 2020; Zis et al., 2021; Xu et al., 2021; Jiang et al., 2020)	7
	3rd year student	(Abdulghani et al., 2020; Chang et al., 2021; Guo et al., 2021; Jin et al., 2021; Gao et al., 2020)	5
	Low academic performance or heavy academic burden	(AlJhani et al., 2021; Allah et al., 2021; Atta and Almilaibary, 2022; Bolatov et al., 2020; Capdevila-Gaudens et al., 2021; Cardoso et al., 2022; Chang et al., 2021; Esmat et al., 2021; Gao et al., 2021; Nakhostin-Ansari et al., 2020; Safa et al., 2021; Xiao et al., 2021; Yang et al., 2022a; Yuan et al., 2021; Zhong et al., 2021; Ren et al., 2021; Feng et al., 2021; Jiang et al., 2020; Chen et al., 2020)	19
Decreased willingness in medicine learning	(Deng et al., 2021a; Khalafallah et al., 2021; Peng et al., 2022; Wang et al., 2020; Yang et al.,	7	

Table 3 (continued)

Type	Details	Studies	Numbers
COVID-19 factor	Being postgraduate ^d	2022b; Tian et al., 2021; Zheng et al., 2021c) (Duan et al., 2022; Meng et al., 2021; Wang et al., 2020; Xiao et al., 2020; Zhan et al., 2020; Liu et al., 2021b)	7
	Fear of education or career impairment	(Bilgi et al., 2021; Cao et al., 2020; Gruba et al., 2021; Guse et al., 2021; Huarcaya-Victoria et al., 2021; Khalafallah et al., 2021; Kuman Tunçel et al., 2021; Kumar et al., 2020; Saali et al., 2021; Teixeira et al., 2021; Wang et al., 2020; Xie et al., 2020)	12
	Online learning trouble or dissatisfaction	(Abdulghani et al., 2020; AlJhani et al., 2021; Chang et al., 2021; Dwivedi et al., 2020; Ecker et al., 2022; Forycka et al., 2022; Nikas et al., 2022; Nishimura et al., 2021; Pelissier et al., 2021; Potapova et al., 2021; Teixeira et al., 2021; Wang et al., 2021; Zhao et al., 2021; Jin et al., 2021)	14
	Clinical duties	(Aftab et al., 2021; Alrashed et al., 2021; Wang et al., 2020)	3
	Infected with COVID-19 or symptoms of COVID-19	(Eleftheriou et al., 2021; Essadek et al., 2022; Kolcu and Başer Kolcu, 2021; Meng et al., 2021; Nakhostin-Ansari et al., 2020; Tahir et al., 2021; Wu et al., 2020; Zhang et al., 2020a)	8
Covid-19 related worry on daily life	Fear of infection with COVID-19 or health worry	(Bilgi et al., 2021; Gruba et al., 2021; Kuman Tunçel et al., 2021; Safa et al., 2021; Saraswathi et al., 2020; Simic et al., 2021; Teixeira et al., 2021; Wang et al., 2021, 2020; Wu et al., 2020; Zhang et al., 2020a; Ma et al., 2021)	12
	Covid-19 related worry on daily life	(Cuschieri and Calleja Agius, 2020; Guo et al., 2021; Safa et al., 2021; Simic et al., 2021; Ren et al., 2021)	5
	Negative perception of lockdown or COVID-19	(Abdulghani et al., 2020; Essadek et al., 2022; Kumar et al., 2020; Pelaccia et al., 2021; Saguem et al., 2021; Xiong et al., 2021)	6
	(Gao et al., 2021; Jindal et al., 2020;	7	

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Table 3 (continued)

Type	Details	Studies	Numbers
Health factor	Low health literacy or little knowledge of COVID-19	Muhammad Alfareed Zafar et al., 2020; Xie et al., 2021; Ye et al., 2020; Zhong et al., 2021; Gao et al., 2020)	6
	High degree of focusing on COVID-19	(Muhammad Alfareed Zafar et al., 2020; Meng et al., 2021; Xie et al., 2020; Wu et al., 2020; Gao et al., 2020; Yang et al., 2021)	
	Being in high-epidemic COVID-19 area or relatives infected with COVID-19	(Aftab et al., 2021; Bilgi et al., 2021; Cao et al., 2020; Çimen et al., 2021; Eleftheriou et al., 2021; Essangri et al., 2021; Halperin et al., 2021; Huarcaya-Victoria et al., 2021; Kolcu and Başer Kolcu, 2021; Kuman Tunçel et al., 2021; Lee et al., 2021; Lingyu et al., 2021; Lu et al., 2022; Meng et al., 2021; Moayed et al., 2021; Risal et al., 2020; Saraswathi et al., 2020; Tahir et al., 2021; Teixeira et al., 2021; Xiao et al., 2020; Xie et al., 2021; Zhang et al., 2021b; Zhang et al., 2021c; Zhang et al., 2020a; Zhang et al., 2020c; Ma et al., 2021)	26
	Current health status or physical distress history	(Capdevila-Gaudens et al., 2021; Çimen et al., 2021; Mishra et al., 2021; Natalia and Syakurah, 2021; Risal et al., 2020; Sandoval et al., 2021; Yang et al., 2021; Zhang et al., 2021b; Zhang et al., 2022; Feng et al., 2021; Wang et al., 2022)	
Lifestyle factor	Problematic smartphone/internet use or much screen time or smartphone/internet addiction	(Biswas et al., 2021; Dhamija et al., 2021; Goweda et al., 2020; Milasauskiene et al., 2021; Mishra et al., 2022, 2021; Tahir et al., 2021; Telgote et al., 2021; Xie et al., 2021; Zhang et al., 2021a)	10
	Smoking or other substance use	(Capdevila-Gaudens et al., 2021; Cardoso et al., 2022; Gao et al., 2021; Pelissier et al., 2021; Safarini et al., 2021; Saguem et al., 2021)	
	Unhealthy lifestyle (such as irregular diet, irregular sleep, and soft-drink consumption)	(Gao et al., 2021; Mishra et al., 2021; Shafique et al., 2021; Teixeira et al., 2021; Xiao et al., 2020, 2021; Zhang et al., 2021c; Miu and Y, 2021)	8
	Low physical activity	(Cardoso et al., 2022; Mendes et al., 2021;	

Table 3 (continued)

Type	Details	Studies	Numbers
Relational factor	Family relationship	Menon et al., 2021; Mishra et al., 2022; Saguem et al., 2021; Souza et al., 2021; Toubasi et al., 2021; Xiao et al., 2021; Zhang et al., 2021c; Chen et al., 2020; Lei et al., 2021)	9
		(Capdevila-Gaudens et al., 2021; Chang et al., 2021; Lingyu et al., 2021; Simic et al., 2021; Song et al., 2021; Ren et al., 2021; Wang et al., 2022; Jiang et al., 2020; Jin et al., 2021)	
	Living alone or loneliness	(Allah et al., 2021; Bolatov et al., 2020; Cao et al., 2020; Elhadi et al., 2020; Lee et al., 2021; Lu et al., 2022; Menon et al., 2021; Rolland et al., 2022a; Ren et al., 2021; Feng et al., 2021; Xia et al., 2022; Zhang et al., 2021d; Zheng et al., 2021c; Chen et al., 2020)	14
Low social support	(Al-Hasani et al., 2021; Cao et al., 2020; Capdevila-Gaudens et al., 2021; Lu et al., 2022; Pelissier et al., 2021; Puranachaikere et al., 2021; Saali et al., 2021; Zhong et al., 2021; Zhang et al., 2020c; Zheng et al., 2021b)		
Predictors of response to trauma	History of traumatic events (such as traffic accidents or sexual harassments)	(Pelissier et al., 2021; Rolland et al., 2022b; Saali et al., 2021; Soltan et al., 2021)	4

^a Factors which were reported as statistically significant associated factors in at least k = 3 studies were defined as frequently reported associated factors.
^b Junior students refer to 1st year or 2nd year medical students.
^c Senior students refer to 4th year or 5th year medical students.
^d Compared with undergraduate students.

2020; Simic et al., 2021; Teixeira et al., 2021; Wang et al., 2021, 2020; Wu et al., 2020) and little health literacy (Gao et al., 2021; Jindal et al., 2020; Muhammad Alfareed Zafar et al., 2020; Xie et al., 2021; Ye et al., 2020; Zhong et al., 2021) was found negatively associated with mental health. Therefore, more education on the knowledge of the prevention and control of COVID-19 might help reduce the mental burden. Dissatisfaction with online learning and fear of education impairment due to COVID-19 was other risk factor for mental symptoms (Abdulghani et al., 2020; AlJhani et al., 2021; Chang et al., 2021; Forycka et al., 2022; Nikas et al., 2022; Nishimura et al., 2021; Pelissier et al., 2021; Potapova et al., 2021; Teixeira et al., 2021; Wang et al., 2021; Zhao et al., 2021). Difficulties in following online learning, communicating with teachers, and developing practical skills are major concerns of medical students (Forycka et al., 2022; Pelissier et al., 2021; Jin et al., 2021). Those findings highlighted the need for medical colleges to gather students' opinions on the present online learning mode and made timely adjustments. Besides, growing studies showed unhealthy lifestyles (i.e., low physical activities (Cardoso et al., 2022; Mendes et al., 2021; Menon et al., 2021; Saguem et al., 2021; Souza et al., 2021; Toubasi et al., 2021;

Xiao et al., 2021; Zhang et al., 2021c)), increasing substance use (Capdevila-Gaudens et al., 2021; Cardoso et al., 2022; Gao et al., 2021; Pelissier et al., 2021; Safarini et al., 2021; Saguem et al., 2021), irregular diet and sleep (Gao et al., 2021; Mishra et al., 2021; Shafique et al., 2021; Teixeira et al., 2021; Xiao et al., 2020, 2021; Zhang et al., 2021c), and problematic smartphone and internet use (Biswas et al., 2021; Dhamija et al., 2021; Goweda et al., 2020; Milasauskiene et al., 2021; Mishra et al., 2021; Tahir et al., 2021; Telgote et al., 2021; Xie et al., 2021; Zhang et al., 2021a) was an emerging risk factor for mental problems, which were less frequently discussed among medical students before the pandemic. The rapid lifestyle change might result from the stay-at-home policy during this period (Colley et al., 2020; Li et al., 2021; Tison et al., 2020). Further studies are in need to determine whether lifestyle modification, such as exercise at home, will help protect students from mental symptoms.

5. Strength and limitation

The present study has several substantial strengths. First, to our knowledge, this study is the first meta-analysis and systemic review that assessed the prevalence and risk factors for mental problems in medical students in the context of the COVID-19 pandemic. By including a broader range of mental problems (depression, anxiety, stress, sleep problem, PTSD, burnout, psychological distress, burnout, and suicidal ideation), our study provided a more comprehensive description of mental problems in this population. Second, we applied the validated risk categorization scheme, which provided a detailed taxonomy of risk factors for mental problems. In addition to risk factors that were consistently reported in previous findings in the general population, our study also identified a unique set of risk factors, which was closely related to the medicine learning process such as being preclinical students, low academic performance, fear of education impairment, online learning trouble, and decreased willingness in medicine learning. In addition, most of the risk factors we identified were reversible, which could be promising targets for the prevention and intervention of psychological distress in medical students. Taken together, our findings could help hospitals, universities, and health policymakers to identify groups of medical students at risk of poor mental health and to make timely modifications.

Our results should be interpreted with the following limitation. First, there is a high heterogeneity between studies, which might come from the varied study design and measurement tools. The subgroup analysis and meta-regression didn't account for the total heterogeneity. Second, as most of the studies included were cross-sectional, we could not establish a causal relationship between mental symptoms and risk factors. Moreover, the inconsistency of those risk factors across literature might affect the accuracy of our results. Besides, the lack of longitudinal studies limited us to track the trajectory of these symptoms. Third, only one study adapted diagnosed interviews to identify major depression disorder (Rolland et al., 2022b). Most studies used a self-rating scale which might reduce the accuracy of the study. Fourth, there might be a large selection bias as only a few studies gave a reasonable response rate. Also, most of the studies were web-based and applied convenience sampling, which limited the representativeness of the participants. Fifth, although our meta-analysis included all available research up to date and provided the most comprehensive analysis of the prevalence and risk factors for mental problems during the COVID-19 period, most of those studies were carried out during the first year of COVID-19 and were limited to the first wave. More studies regarding the mental problems during the recurrent waves or remission period of the COVID-19 pandemic are in need. Taken together, more longitudinal, multi-center studies with large sample sizes and validated measurement tools are in need to track the dynamics of those mental symptoms.

6. Conclusion and relevance

Our study demonstrated an extremely high prevalence of mental symptoms during the COVID-19 pandemic and identified multiple risk factors. These findings call for timely mental screening and intervention for medical students. The revealed risk factors are valuable for schools, health systems, and policymakers to identify high-risk subgroups of medical students and provide targeted intervention, as most of the risk factors we found in this study are reversible.

CRedit authorship contribution statement

QX Wu, P Peng, TQ Liu contributed to study design, article search, review and quality assessment. Q Yang, MY Li, and X Wang reviewed the study protocol and contributed to the data collection. P Peng, HY He, YZ Hao, and QX Wu contributed to the drafting of the manuscript. SB Chen, YF Wang, and YH Liu designed the statistical analysis strategy and performed statistical analyses. All authors contributed to the critical revision of the paper and have agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2022.10.040>.

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