GLOBAL EXCELLENCE IN PUBLIC MENTAL HEALTH: ASIA AND AUSTRALASIA

EDITED BY: Liye Zou, Jing Sun and Liping Li
PUBLISHED IN: Frontiers in Psychiatry and Frontiers in Public Health







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ISSN 1664-8714 ISBN 978-2-83250-715-5 DOI 10.3389/978-2-83250-715-5

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GLOBAL EXCELLENCE IN PUBLIC MENTAL HEALTH: ASIA AND AUSTRALASIA

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Citation: Zou, L., Sun, J., Li, L., eds. (2022). Global Excellence in Public Mental

Health: Asia and Australasia. Lausanne: Frontiers Media SA.

doi: 10.3389/978-2-83250-715-5

Table of Contents

- 04 Relationship Between Childhood Left-Behind Experience and Quality of Life Among Chinese University Freshmen: Place of Origin Matters Hai-Mei Li, Yan-Min Xu and Bao-Liang Zhong
- 11 Efficacy of Face-to-Face Delivered Cognitive Behavioral Therapy in Improving Health Status of Patients With Insomnia: A Meta-Analysis

 Dawei Xu, Elizabeth Cardell, Simon A. Broadley and Jing Sun
- 33 Do Global Adolescents With Food Insecurity Feel Lonely?
 Haowen Wu, Zhijun Gu, Linmiao Zeng and Tianyou Guo
- 40 Possible Avoidant Personality Disorder Magnifies the Association Between Bullying Victimization and Depressive Symptoms Among Chinese University Freshmen
 - Yan-Min Xu, Shan-Shan Pu, Yi Li and Bao-Liang Zhong
- 46 Temporal Trends in the Incidence and Disability Adjusted Life Years of Schizophrenia in China Over 30 Years
 - Wanyue Dong, Yunning Liu, Jianzhong Sun, Yan Liu, Zhonghe Sun and Ruhai Bai
- 56 Network Analysis of Time Use and Depressive Symptoms Among Emerging Adults: Findings From the Guizhou Population Health Cohort Study
 - Zhihao Ma, Fouxi Zhao, Yiying Wang, Tao Liu and Naipeng Chao
- 67 Mental Health in Australia: Psychological Distress Reported in Six Consecutive Cross-Sectional National Surveys From 2001 to 2018

 Joanne Enticott, Shrinkhala Dawadi, Frances Shawyer, Brett Inder, Ellie Fossey, Helena Teede, Sebastian Rosenberg, Ingrid Ozols AM and Graham Meadows
- 81 Structure of Hypomanic Symptoms in Adolescents With Bipolar Disorders: A Network Approach
 - Yuan Yang, Wu-Yang Zhang, Yao Zhang, Shuying Li, Teris Cheung, Dexing Zhang, Todd Jackson, Fan He and Yu-Tao Xiang
- 92 The Association of Sports Participation With Depressive Symptoms and Anxiety Disorder in Adolescents
 - Guijun Chi and Lei Wang
- 99 Correlates of Suicidal Ideation in Rural Chinese Junior High School Left-Behind Children: A Socioecological Resilience Framework Yu-ming Zhou, Leona Mak, Chun-xia Zhao, Fan He, Xiao-na Huang,
 - Xiao-bo Tian, Yi-zheng and Jing Sun
- 112 Mental Health Research During the COVID-19 Pandemic: Focuses and Trends
 - Yaodong Liang, Li Sun and Xin Tan
- 124 Comparative Efficacy of Face-to-Face and Internet-Based Cognitive Behavior Therapy for Generalized Anxiety Disorder: A Meta-Analysis of Randomized Controlled Trial
 - Wenle Zhang, Yun Du, Xiangyun Yang, Encong Wang, Jiexin Fang, Ziqi Liu, Shanqian Wu, Qinqin Liu and Yongdong Hu





Relationship Between Childhood Left-Behind Experience and Quality of Life Among Chinese University Freshmen: Place of Origin Matters

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OPEN ACCESS

Edited by:

Jing Sun, Griffith University, Australia

Reviewed by:

Weimin Dang, Peking University Sixth Hospital, China Wenwang Rao, University of Macau, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 05 October 2021 Accepted: 25 October 2021 Published: 24 November 2021

Citation:

Li H-M, Xu Y-M and Zhong B-L (2021)
Relationship Between Childhood
Left-Behind Experience and Quality of
Life Among Chinese University
Freshmen: Place of Origin Matters.
Front. Psychiatry 12:789622.
doi: 10.3389/fpsyt.2021.789622

Background: Childhood left-behind experience (LBE) has a long-term detrimental effect on the mental health of Chinese University students, but it remains unclear whether childhood LBE negatively impacts the quality of life (QOL) of University students and whether the LBE–QOL association differs between students of rural origin and students of urban origin. This study examined the LBE–QOL relationship and the interactive effect between LBE and place of origin on QOL among Chinese University freshmen.

Methods: By using a two-stage random cluster sampling approach, a total of 5,033 freshmen were recruited from two comprehensive universities. The students completed an online, self-administered questionnaire that included sociodemographic variables, a 2-week physical morbidity assessment, and assessments of depressive symptoms, academic stress, and QOL. The Chinese six-item QOL scale was used to assess QOL. Multiple linear regression was used to test the independent LBE–QOL association and the interaction between LBE and place of origin.

Results: Students with childhood LBE had significantly lower QOL scores than those without LBE (60.1 \pm 13.1 vs. 64.3 \pm 11.7, p < 0.001). After adjusting for the potential confounding effects of other sociodemographic variables, 2-week physical morbidity, depressive symptoms, and academic stress, childhood LBE was significantly associated with a lower QOL score (β : -3.022, p < 0.001) and the LBE-place of origin interaction was still significantly associated with the QOL score (β : -2.413, p < 0.001). Overall, compared to non-LBE, LBE was associated with a QOL score decrease of 5.93 among freshmen of urban origin and of 3.01 among freshmen of rural origin.

Conclusion: In Chinese University freshmen, childhood LBE is independently associated with poor QOL, and the LBE-QOL association is greater among freshmen from urban backgrounds than among freshmen from rural backgrounds.

Keywords: freshmen, University, left-behind experience, quality of life, place of origin, China

INTRODUCTION

In China, the past four decades have witnessed the unprecedented migration of young laborers from impoverished rural villages to thriving coastal cities and concentrated industrial zones, seeking greater employment opportunities, and pursuing a better life for themselves and their families (1). In 2019, the total number of migrant workers reached 290.8 million, or 20.6% of the whole Chinese population (2). Because of the high cost of living, unstable employment, and difficulties in arranging child care and schooling in cities, many migrant parents have to leave their children behind, in the care of grandparents, other relatives, or friends who remain in their rural villages of origin (3). Despite the lack of official, up-to-date statistics, left-behind children have become a large segment of the population in China; for example, according to the All China Women's Federation, there were 61.0 million left-behind children in rural China in 2013 (4).

Early separation from parents, from either one or both parents, has a profound and long-lasting negative impact on both the physical and mental health of children. Accumulating evidence has shown a higher risk of wasting, stunning, slow physical development, poor nutritional status, obesity, depressive symptoms, anxiety symptoms, suicidal ideation, substance use, and poor health-related quality of life (QOL) among leftbehind children than among children from intact families (5-10). Importantly, the negative mental health effect of childhood left-behind experience (LBE) does not diminish over time but persists to late adolescence and young adulthood; for example, compared to University students without childhood LBE, those with LBE are at a significantly higher risk for developing depressive symptoms, anxiety symptoms, low selfesteem, suicidal and self-harm behaviors, and other mental health problems (11-15).

It is worth noting that being left behind is not a unique experience for rural Chinese children. In recent years, due to the rapid economic growth, increasing urban-to-urban migration, parental return to universities to pursue advanced degrees, and long-term parental business travel, there has been a substantial increase in the number of urban left-behind children in China (16) as well, 3.1 million in 2000 and 28.3 million in 2015 (17). Empirical studies have revealed that urban left-behind children have significantly more mental health and substance abuse problems than both rural left-behind children and urban non-left-behind children (18, 19), suggesting a potentially high risk of mental health problems in this emerging vulnerable population.

University students, in particular first-year students, are facing the transition period from late adolescence to young adulthood along with the difficulties of adjusting to college life, changing social identities, and forming new social relationships (20). Numerous studies have reported the high prevalence of mental health problems and poor self-rated health among Chinese University students (20–25). In addition to LBE, place of origin is one of the commonly reported factors associated with both physical and mental health in Chinese University students; for example, compared to University

students of urban origin, students of rural origin have more mental health problems and poorer mental and physical QOL (26-29). Accordingly, among University students with childhood LBE, it is reasonable to hypothesize that students from rural origins have poorer physical and mental health than students from urban origins. However, findings from two comparative studies do not support this hypothesis. One study reported a similar prevalence of psychological symptoms among rural and urban LBE University students, and the other study reported significantly better mental health among rural LBE students than among urban LBE students (12, 13). This suggests that the effect of LBE on the mental health may differ between University students of rural origin and urban origin. In other words, place of origin may moderate the detrimental effects of childhood LBE on the mental health of University students. Nevertheless, nearly all existing studies on the long-term impact of LBE on the health of University students either did not consider or ignored the differences in health effects of LBE between students of rural origin and those of urban origin (11, 15, 30, 31).

University is an important life phase, when the introduction of targeted health-related interventions has the potential to positively impact both short- and long-term health status and health-related QOL outcomes (32). By definition, QOL is broader than health, and refers to a sense of well-being that encompasses physical health, role functioning, social functioning, and mental health (33). To facilitate the campus-based health policymaking and planning, it is necessary to identify factors associated with QOL and contextual factors that may influence the factor-QOL associations in University students. The present study investigated the relationship between childhood LBE and QOL among Chinese University freshmen and examined whether the relationship varied between students of rural origin and students of urban origin. Based on the above literature review, we speculated that childhood LBE was significantly associated with poorer QOL and that there was a significant interactive effect between LBE and place of origin.

METHODS

Participants

This study was a cross-sectional survey, which was carried out to investigate QOL and mental health help-seeking behaviors among freshman students at two comprehensive universities, one in Fuzhou and the other in Wuhan, China, between November and December 2019. First-year students who were admitted in the fall of 2019 and of Chinese nationality were invited to join this study. Students who were repeating the academic year and international students were excluded. Participants were selected by using a two-stage random cluster sampling approach. By using a random number table, 22 schools were selected from a total of 42 schools at the two universities. These selected schools had 5,469 first-year students, and all the students were invited to participate in this study.

The survey protocol was approved by the Ethics Committee of Wuhan Mental Health Center. Participants electronically signed

the informed consent form first and then were automatically directed to the online survey page.

Assessments and Procedures

We used a self-administered questionnaire to collect data, and the questionnaire was distributed online *via* the "Questionnaire Star," a popular platform providing free online survey services in China.

Sociodemographic variables included study site, sex, age, status as an only child in the family, ethnic group, academic major (science vs. liberal arts) (34), marital status of parents, LBE, and place of origin. Students with childhood LBE were those who lived in their original domicile but who did not live together with their parents for a minimum of 6 months before being admitted to the universities because either one parent or both parents migrated elsewhere for work (14, 17). Place of origin referred to the students' household registration location as either a rural or an urban area (17).

We assessed the physical health of respondents by using the 2-week physical morbidity question from China's Multiwave National Health Services Surveys (35), which asked their experiences of any physical health problems during the past 2 weeks, including infectious diseases and chronic noncommunicable diseases.

The validated Chinese 9-item Patient Health Questionnaire (PHQ-9) was used to assess depressive symptoms over the past 2 weeks (36). All items of the PHQ-9 were answered on a four-point scale, from "0 = not at all" to "3 = nearly every day." The total scores on the PHQ-9 ranged between 0 and 27, with seven or higher denoting clinically significant depressive symptoms (37).

The level of perceived academic stress was assessed with a single question developed by the authors: "What is your level of academic stress?" (high, not high).

The validated Chinese six-item QOL scale was used to assess the QOL of students (33). The scale was developed by Phillips et al. and has been widely used to evaluate QOL in a variety of Chinese populations, including students (33, 38, 39). This scale assesses QOL in terms of six domains: physical health, psychological health, economic circumstances, study, family relationship, and relationship with non-family associates. Each item is rated on a five-point scale, from "1 = very poor" to "5 = very good." The crude total QOL score ranges from 6 to 30, with a higher score denoting better QOL. As recommended by Phillips et al. (38), the crude total QOL score was further rescaled on a "0–100" scale to obtain the total QOL score.

Statistical Analysis

The independent-samples *t*-test was used to compare QOL scores between groups according to sociodemographic characteristics. To examine the LBE-QOL association, a multiple linear regression analysis was performed that entered LBE as the main predictor; place of origin, other sociodemographic variables, 2-week physical morbidity, depressive symptoms, and academic stress as the covariates; and QOL score as the outcome variable ("main effect model"). To test whether the LBE-QOL association differed between places of origin, an interaction term, the production of LBE and place of origin, was

included as an additional independent variable in the above linear regression model ("interactive effect model"). Statistically significant regression coefficients of LBE in the main effect model and the interaction term in the interactive effect model suggested the presence of the impact of LBE on QOL and the moderating effect of place of origin on the LBE-QOL association. Finally, a graph was used to visualize the interactive effect of LBE and place of origin, where predicted QOL scores by LBE and place of origin from the interactive effect model are shown. Prior to the formal analysis, the assumption of the absence of multi-collinearity was tested. The results of collinearity diagnostics analysis showed that variance inflation factor values of all independent variables ranged between 1.001 and 1.149, much lower than the critical threshold of 10 (40); therefore, no significant multi-collinearity was present among the independent variables in our regression analysis. We performed all statistical analyses using SPSS 25.0, assuming a two-sided test at the 0.05 level of significance.

RESULTS

A total of 5,033 students completed the survey, for a response rate of 93.0%. The average age of the study sample was 18.5 years [standard deviation (SD): 0.9; range: 15–30 years]; 98.2% were 17–20 years, 54.1% were girls, 29.2% had childhood LBE, and 60.2% were from rural areas. The detailed sociodemographic characteristics, the 2-week physical morbidity, depressive symptoms, and academic stress of freshmen are shown in **Table 1**.

The mean QOL score was 63.1 (SD: 12.3, range: 0–100). As displayed in **Table 1**, students with childhood LBE had significantly lower QOL scores than those without LBE (60.1 \pm 13.1 vs. 64.3 \pm 11.7, p < 0.001), and rural students had significantly lower QOL scores than urban students (62.3 \pm 11.6 vs. 64.2 \pm 13.2, p < 0.001).

In the main effect model (**Table 2**), after adjusting for the confounding effects of sociodemographic variables, physical health, depressive symptoms, and academic stress, childhood LBE was still significantly associated with a lower QOL score [coefficient (β): -3.022, p < 0.001].

In the interactive effect model (**Table 3**), after adjusting for the confounding effects of sociodemographic variables, physical health, depressive symptoms, and academic stress, the interactive effect of childhood LBE and place of origin was still significantly associated with the QOL score (β : -2.413, p < 0.001). As shown in **Figure 1**, a one-unit increase in the LBE status, from non-LBE to LBE, was associated with a QOL score decrease of 5.93 among urban freshmen and 3.01 among rural freshmen.

DISCUSSION

To the best of our knowledge, this is the first large-scale study in China that examined both the negative impact of childhood LBE on QOL among University students and the interactive effect of childhood LBE and place of origin on the QOL of freshmen. In the Chinese general population, the normative QOL score, as measured by the Chinese six-item QOL scale, was 70.8

TABLE 1 | Characteristics of freshmen and quality of life (QOL) scores of different groups.

Characteristics		n (%)	QOL score	t	p
Site	Wuhan	2,193 (43.6)	63.26 ± 12.14		
	Fuzhou	2,840 (56.4)	62.95 ± 12.41	0.891	0.373
Sex	Male	2,311 (45.9)	63.01 ± 13.80		
	Female	2,722 (54.1)	63.15 ± 10.85	0.415	0.678
Age (years)	<18	260 (5.2)	62.96 ± 11.95		
	≥18	4,773 (94.8)	63.09 ± 12.31	0.163	0.870
The only child	Yes	1,708 (33.9)	64.08 ± 12.93		
	No	3,325 (66.1)	62.58 ± 11.93	3.995	< 0.001
Ethnic group	Han	4,698 (93.3)	63.17 ± 12.37		
	Minorities	335 (6.7)	61.92 ± 11.07	1.804	0.071
Academic major	Liberal arts	1,604 (31.9)	62.46 ± 12.76		
	Science	3,429 (68.1)	63.38 ± 12.06	2.479	0.013
Marital status of parents	Married	4,019 (79.9)	63.49 ± 12.26		
	Others*	1,014 (20.1)	61.47 ± 12.32	4.686	< 0.001
Childhood left-behind experience	Yes	1,471 (29.2)	60.13 ± 13.08		
	No	3,562 (70.8)	64.31 ± 11.74	10.611	< 0.001
Place of origin	Urban	2,004 (39.8)	64.22 ± 13.19		
	Rural	3,029 (60.2)	62.33 ± 11.61	5.217	< 0.001
Two-week morbidity	Yes	1,294 (25.7)	58.84 ± 11.47		
	No	3,739 (74.3)	64.55 ± 12.23	15.175	< 0.001
Depressive symptoms	Yes	1,497 (29.7)	57.04 ± 12.25		
	No	3,536 (70.3)	65.65 ± 11.39	23.266	< 0.001
Academic stress	High	1,417 (28.2)	59.22 ± 13.31		
	Not high	3,616 (60.8)	64.60 ± 11.53	13.364	< 0.001

^{*}Others included never-married, remarried, cohabiting, separated, divorced, and widowed.

TABLE 2 | Multiple linear regression on relationship between childhood left-behind experience (LBE) and quality of life (QOL) among freshmen, adjusting for the confounding effects of sociodemographic variables, physical health, depressive symptoms, and academic stress.

Charac	cteristics	Unstandardized coefficient	Standard error	t	р
Childhood LBE	Yes vs. no	-3.022	0.356	8.490	< 0.001
Place of origin	Rural vs. urban	-1.362	0.344	-3.958	< 0.001
Site	Fuzhou vs. Wuhan	-0.306	0.320	-0.955	0.340
Sex	Female vs. male	0.410	0.341	1.202	0.229
Age (years)	≥18 vs. <18	-0.464	0.719	-0.645	0.519
The only child	No vs. yes	-1.074	0.359	-2.992	0.003
Ethnic group	Minorities vs. Han	0.059	0.640	0.093	0.926
Academic major	Science vs. liberal arts	0.822	0.360	2.287	0.022
Marital status of parents	Others* vs. married	-1.295	0.398	-3.254	0.001
Two-week morbidity	No vs. yes	-3.607	0.375	-9.625	< 0.001
Depressive symptoms	No vs. yes	-7.031	0.361	-19.492	< 0.001
Academic stress	Not high vs. high	-3.679	0.360	-10.214	< 0.001

^{*}Others included never-married, remarried, cohabiting, separated, divorced, and widowed.

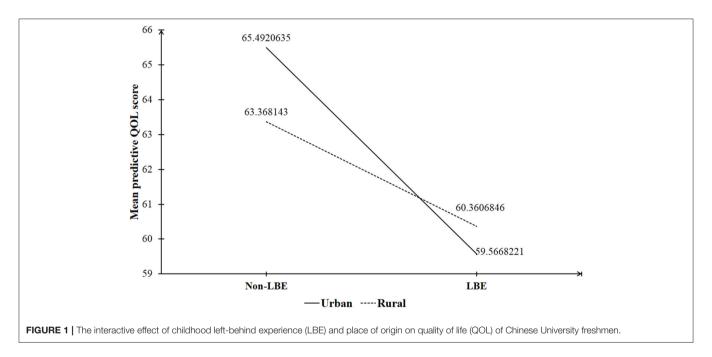
(41). Compared to the normative data, we found a significantly and substantially lower QOL score in University freshmen than in the general population (63.1 vs. 70.8, t=-44.705, p<0.001), suggesting the poor QOL of Chinese University freshmen and the urgent need to develop programs to improve QOL in this population.

As shown in Table 1, many factors other than LBE were also associated with QOL among freshmen; therefore, it is important to consider the possible confounding effects of these factors on the LBE-QOL association. In the main effect model, the significant LBE-QOL association suggests that LBE was independently associated with poor QOL among

TABLE 3 | Multiple linear regression on interactive effect of childhood left-behind experience (LBE) and place of origin on quality of life (QOL) among freshmen, adjusting for the confounding effects of sociodemographic variables, physical health, depressive symptoms, and academic stress.

Charac	cteristics	Unstandardized coefficient	Standard error	t	p
Childhood LBE × place of origin		-2.413	0.750	-3.218	0.001
Childhood LBE	Yes vs. No	-4.644	0.618	7.529	< 0.001
Place of origin	Rural vs. Urban	0.412	0.651	0.638	0.522
Site	Fuzhou vs. Wuhan	-0.308	0.320	-0.964	0.335
Sex	Female vs. male	0.397	0.341	1.165	0.244
Age (years)	≥18 vs. <18	-0.418	0.719	-0.581	0.561
The only child	No vs. yes	-1.012	0.359	-2.818	0.005
Ethnic group	Minorities vs. Han	0.049	0.639	0.077	0.939
Academic major	Science vs. liberal arts	0.833	0.359	2.319	0.020
Marital status of parents	Others* vs. married	-1.287	0.398	-3.238	0.001
Two-week morbidity	Yes vs. no	-3.588	0.374	-9.582	< 0.001
Depressive symptoms	Yes vs. no	-7.026	0.360	-19.495	< 0.001
Academic stress	High vs. not high	-3.663	0.360	-10.179	< 0.001

^{*}Others included never-married, remarried, cohabiting, separated, divorced, and widowed.



University freshmen. In previous University students-based studies, childhood LBE was reported to be significantly associated with mental health problems (11–15), but in the present study, we revealed the independent LBE–QOL association among University freshman students, extending the long-term health outcomes of childhood LBE from mental health problems to worsened QOL.

Parents' company and supervision play a vital role in the development and functioning of their children and in preparing them to manage the challenges they will confront in their academic, social, occupational, and cultural lives as adults (42). According to the attachment theory (43), the early absence of parents disrupts the development of secure attachment bonds between children and their parents, which has a long-term

negative effects on a child's psychological development in terms of personality, cognition, psychopathology, resilience, and coping style. Therefore, children with LBE are more likely to experience mental health problems, maladaptive behaviors, adjustment problems, poor coping skills, and interpersonal difficulties after they enter the universities. These findings may explain the association of childhood LBE with poor QOL among University freshmen.

The greater LBE-QOL association among urban freshmen than among rural freshmen observed in this study is similar to the greater negative effect of childhood LBE on mental health among urban freshmen than among rural college freshmen observed in a prior study (13). Because the interactive effect of LBE and place of origin was independent of sociodemographic variables, physical health, depressive symptoms, and academic stress, we speculated that some place-specific contextual factors may magnify or mitigate the detrimental effect of childhood LBE on OOL among University freshmen. First, in China, the urban community is a "stranger" society, but the rural community is an "acquaintance" or "relationship" society where the cultural value is still deeply influenced by Confucianism and the patriarchal clan system (44). Despite a lack of or insufficient parental care and company, urban left-behind children are less likely than rural left-behind children to obtain support and supervisions from relatives. Second, compared to rural children, urban children are more likely to be exposed to the internet, new types of drugs, and electronic games; therefore, urban left-behind children are at greater risk than rural leftbehind children for developing addictive behaviors. The effects of weaker care from relatives and a higher prevalence of addictive behaviors among urban left-behind children than among rural left-behind children may persist into young adulthood and result in the poorer QOL reported among urban than rural LBE University freshmen. Third, rural left-behind children who pass the National College Entrance Examination and become University students represent the most successful fraction of this vulnerable population. Because of difficulties experienced during childhood, these rural LBE students are more resilient, capable of living independently, and adaptive to new environments than urban LBE students. These straits may partly offset the negative effect of childhood LBE, possibly leading to the relative health disadvantages observed among urban but not among rural LBE students.

This study has two limitations. First, characteristics of childhood LBE were not assessed in detail. Since the relationship with the caregiver during the left-behind period, the age at onset of being left behind, and the length of the left-behind period are associated with depressive symptoms in Chinese LBE University students (45), it remains unclear whether the poorer QOL among urban LBE students was related to their characteristics of LBE or other factors. Second, childhood LBE was retrospectively assessed in this study; therefore, recall bias in the measurement of LBE may exist.

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In summary, in Chinese University freshmen, childhood LBE is significantly associated with poor QOL, and the LBE-QOL association is greater among freshmen of urban origin than among freshmen of rural origin. Freshmen with LBE, in particular freshmen of urban origin with LBE, could be considered as a target group of campus-based QOL promotion programs. Campus-based programs designed to improve QOL among Chinese University freshmen may include health education, psychosocial support, social skills training, and stressmanagement training.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of Wuhan Mental Health Center. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

H-ML: acquisition and analysis of data for the study, drafting the paper, and interpretation of data for the study. Y-MX: design and acquisition of data for the study. B-LZ: drafting the paper, revising the paper for important intellectual content, and interpretation of data for the study. All authors contributed to the article and approved the submitted version.

FUNDING

This work was supported by the National Natural Science Foundation of China (Grant Number: 71774060). The funding source listed had no role in study design, in the collection, analysis, and interpretation of data, in the writing of the report; and in the decision to submit the paper for publication.

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Efficacy of Face-to-Face Delivered Cognitive Behavioral Therapy in Improving Health Status of Patients With Insomnia: A Meta-Analysis

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Background: Face-to-face cognitive behavioral therapy (CBT) is one of the most widely used non-pharmacological treatment approaches for insomnia. The aim of this study is to assess the efficacy of face-to-face delivered CBT on health outcomes and to evaluate the effect of CBT components as subgroup variables to explain the efficacy of face-to-face delivered CBT on health outcomes in adults over 18 years old with insomnia.

Methods: Relevant randomized controlled trial studies published in the past 22 years were searched through the electronic databases. The Physiotherapy Evidence Database (PEDro) scale was used to assess the quality of the 31 included studies. The mean difference and standard deviation of outcome variables and subgroup variables were analyzed using random effect model, and the heterogeneity among the articles was assessed with the Q-test and I^2 . Egger regression analysis was used to assess publication bias.

Results: The meta-analysis showed a significant reduction in Insomnia Severity Index [standardized mean difference (SMD) = -2.56, 95% CI -3.81 to -1.30, p < 0.001], Pittsburgh Sleep Quality Index (SMD = -0.96, 95% CI -1.25 to -0.68, p < 0.001), sleep onset latency (SMD = -1.31, 95% CI -2.00 to -0.63, p < 0.001), wakening after sleep onset (SMD = -1.44, 95% CI -2.14 to -0.74, p < 0.001), number of awakenings (SMD = -1.18, 95% CI -2.10 to -0.26, p < 0.05), depression (SMD = -1.14, 95% CI -1.85 to -0.42, p < 0.01), and fatigue (SMD = -2.23, 95% CI -3.87 to -0.58, p < 0.01), and a significant increase in total sleep time (SMD = 0.63, 95% CI 0.28 to 0.98, p < 0.001), sleep efficiency (SMD = 1.61, 95% CI 0.92 to 0.29, p < 0.001), and physical health (SMD = 0.42, 95% CI 0.08 to 0.76, p < 0.05), in the CBT intervention group compared with the control group. There was no significant change in anxiety (SMD = -0.62, 95% CI -1.55 to 0.32, p > 0.05) and mental health (SMD = 1.09, 95% CI -0.59 to 0.277, p > 0.05) in CBT intervention group compared with control group. Group-delivered studies with larger number of intervention sessions and longer duration of single session provided a larger improvement in sleep quality.

Conclusion: Face-to-face delivered CBT is effective in increasing total sleep time, sleep efficiency, and physical health, and reducing Insomnia Severity Index scores, Pittsburgh Sleep Quality Index scores, sleep onset latency, wakening after sleep onset, number

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Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Sitong Chen, Victoria University, Australia Yu Qian, University of Macau, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 20 October 2021 Accepted: 17 November 2021 Published: 23 December 2021

Citation

Xu D, Cardell E, Broadley SA and Sun J (2021) Efficacy of Face-to-Face Delivered Cognitive Behavioral Therapy in Improving Health Status of Patients With Insomnia: A Meta-Analysis. Front. Psychiatry 12:798453. doi: 10.3389/fpsyt.2021.798453

of awakenings, depression, anxiety, and fatigue in patients with insomnia. Face-to-face delivered CBT is more effective when delivered through a larger number of sessions with longer duration of each session, and when delivered in groups. Face-to-face CBT is recommended to provide treatment to patients with insomnia in clinical settings.

Systematic Review Registration: www.crd.york.ac.uk/prospero/display_record.php ?ID=CRD42020200091, identifier: CRD4202020009.

Keywords: cognitive behavioral therapy (CBT), face-to-face, insomnia, quality of sleep, health outcomes

INTRODUCTION

Insomnia is one type of psychiatric disease that influences the quality, timing, and amount of sleep, resulting in fatigue and mental distress (1). Insomnia has a high prevalence across the world (2). It was reported that the global prevalence of insomnia was up to 30% (3). Mentally, insomnia can impair daytime concentration and generate anxious or depressed feels that may lead to or aggravate other psychiatric diseases such as depression and anxiety (4). Physically, a chronic condition of insomnia can increase the risks of a great amount of chronic diseases such as diabetes, cardiovascular diseases, and cancer (5).

Currently, insomnia is treated with pharmacological and nonpharmacological treatments. Cognitive behavioral therapy (CBT) is one of the widely studied non-pharmacological treatment option for insomnia, with marked long-term and short-term effects (6). It is currently the first-line therapy in managing all kinds of psychiatric diseases including depression, anxiety, and insomnia (7). The CBT approach perceives the psychiatric symptoms are underpinned by distorted cognition and related behaviors, and these symptoms could be reduced if the distorted cognition and behaviors are corrected (8). Based on the CBT principles, multiple CBT strategies were developed to change the thinking and behavioral patterns, and different strategies were involved in CBT treatments (9). For patients with insomnia, previous studies indicated that it was common for these patients to have dysfunctional understandings about sleep and worries about falling asleep (10). These thoughts may lead to behavioral changes such as spending more time in bed trying to fall asleep and irregular sleep times, which may make falling asleep more difficult, further providing reinforcement of the dysfunctional understandings and creating a vicious loop that exacerbates the existing insomnia symptoms (10). Applying CBT to these patients can break this loop from multiple directions. Cognitive behavioral therapy has been commonly delivered in a face-to face format, in which patients has face-to-face consultations with the therapists. The consultations can take place between one patient and a therapist individually (individual delivered) or one or more therapists and multiple patients (group delivered). The face-to-face delivery of CBT is commonly used to patients with insomnia because the components of CBT such as alliances building can be easily achieved in the face-to-face therapy mode. Previous studies have shown that CBT provided a similar efficacy in treating insomnia compared with pharmacological treatments (11). Furthermore, it has been found CBT treatment has fewer side effects than sleep medication intake (6).

Existing meta-analysis studies also found that CBT had a significant overall effect on sleep outcomes in patients with insomnia (12, 13), but these studies focused on sleep outcomes only, and subgroup analysis of CBT components was not included. In addition to sleep outcomes (Insomnia Severity Index, Pittsburgh Sleep Quality Index, total sleep time, sleep efficiency, sleep onset latency, wakening after sleep onset, and number of awakenings), health outcomes were considered in this study, including psychiatric diseases (scores of depression and anxiety scales), fatigue (scores of fatigue scales), and qualityof-life related physical and mental health (scores of qualityof-life surveys). By assessing the effect of face-to-face CBT on these outcomes, our study will provide a comprehensive overview of the effect of face-to-face CBT on the health status of insomnia patients from a different perspective. We also conducted subgroup analysis to assess the effects of different CBT treatment designs and components on the sleep and psychiatric disease outcomes and the overall efficacy of face-to-face CBT to help develop a reasonable CBT treatment plan.

METHODS

The procedure of this study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines (14). The protocol of this study was registered at the International Prospective Register of Systematic Reviews (PROSPERO Registration ID: CRD42020200091, https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020200091).

Search Strategy

The database search process was completed by two researchers (Xu and Sun) independently. Five electronic databases including PubMed, Scopus, EMBASE, Cochrane Library, and PsycINFO were searched for relevant studies by the two researchers. Gray literatures were acquired from ProQuest central: Dissertations and Thesis. The following Boolean approach for the keywords were used for the search: "insomnia" OR "sleep" AND "cognitive behavioral therapy" OR "cognitive behavior therapy" OR "CBT" AND "face-to-face delivered" OR "group delivered" OR "individual delivered" AND "randomized controlled trial" OR "RCT." The search results from the defined five electronic databases were exported into the EndNote X9 software, and duplicates across databases were removed. Two researchers then examined the titles and

abstracts of the articles and excluded articles that did not focus on insomnia or CBT. The full text of the rest of the articles were examined and selected based on the inclusion and exclusion criteria.

Study Selection

Full-text assessment of the articles was also completed by two researchers independently. In this study, PICO approach (15) was used to develop the inclusion and exclusion of articles. Only randomized controlled trial studies were included in this study. The studies must be published in English, and the publishing date should be from 1 January 1990 to 31 August 2021, with no restriction in sample size. Articles that were not peer reviewed or that scored 3 or less on the PEDro (16) scale were excluded from the study. If full text of the article was not available online, reasonable attempts were made, such as sending emails directly to the authors to request the full text of the articles.

Inclusion Criteria

P: The participants in the studies must be over 18 years in age and be self-reported or diagnosed with insomnia according to the International Classification of Sleep Disorders (ICSD), diagnostic and statistical manual of mental disorders fourth edition (DSM-IV) or fifth edition (DSM-V), or sleep questionnaires such as the Insomnia Severity Index (score > 7) (17), and Pittsburgh Sleep Quality Index (score > 4) (18). Participants should be randomly assigned to CBT intervention groups or control groups.

- I: The face-to-face delivered CBT should be applied to the participants as interventions of insomnia. The CBT intervention must utilize at least two of the core components, including sleep restriction, stimulus control, cognitive therapy, and sleep hygiene. The number of other components in the intervention plan is not limited.
- C: Participants in the control group in the studies received normal treatment, were placed in a waiting list (waiting list control, WLC), or received placebo treatments that did not provide significant effects on sleep.
- O: The studies must report at least one of the primary outcomes required in this meta-analysis study. The primary outcomes include Insomnia Severity Index, Pittsburgh Sleep Quality Index, total sleep time, sleep efficiency, sleep onset latency, wake after sleep onset, and number of awakenings.

Exclusion Criteria

- P. The participants in the study were diagnosed with other severe psychiatric diseases including schizophrenia, severe depression, and severe bipolar disorders.
- I. The intervention group received mindfulness-based intervention or remote-delivered CBT intervention.
- C. No proper control groups presented in the study or patients in the control groups received any forms of face-to-face delivered CBT intervention.
- O. The study did not provide complete data for the primary outcomes.

Quality Assessment

Studies passing the full-text assessment underwent a further quality assessment process conducted by two researchers independently using the Physiotherapy Evidence Database (PEDro) scale (16). The PEDro scale defines the quality of the articles by giving scores ranging from 0 to 10. The marking criteria include random allocation of participants, concealed allocation of participants, similar baseline characteristics between intervention and control groups, blinding to all participants, blinding to all therapists in the study, blinding to assessors who assessed the key outcomes of the study, enough outcome measures obtained, participants received intervention or control condition as study designed, presence of between-group comparison analysis, and presence of both point measures and measures of variability. For each of the criteria, 1 point would be given if the study completely met the criteria; otherwise, no point would be given. Articles scoring 3 or less were defined as poor quality articles (19). Scores 4–5 indicated moderate quality studies, scores 6-8 indicated good quality studies, and scores 9-10 indicated excellent quality studies (19).

Research Outcomes

The primary outcomes in this study were sleep outcomes, including severity of insomnia measured by the Insomnia Severity Index (17), sleep quality measured by the Pittsburgh Sleep Quality Index (18), total sleep time, sleep efficiency, sleep onset latency, wakening after sleep onset, and number of awakenings.

The secondary outcomes in this study included psychiatric disease outcomes, fatigue, and quality-of-life related physical and mental health. The psychiatric disease outcomes included scores of depression scales (20–24) and anxiety scales (25–27). The fatigue outcome was measured by the scores of various fatigue scales (28, 29). The quality-of-life related health outcomes were measured by the scores of the physical health section and mental health section in the short-form quality-of-life surveys (SF-12 and SF-36) (30).

Data Extraction

The extraction of data was completed by two researchers independently. The third researcher was invited to confirm the data if disagreement occurred between the two researchers. If the article provided results for both post intervention and follow-up, the results in the longer intervention time for follow-up were extracted. Reasonable attempts, such as direct email requests to the authors, were also made to acquire the full datasets of the studies, if possible, when the published articles did not provide enough data.

Characteristics of the included studies and the PEDro scores are summarized in **Table 1**. The study characteristics include the location where the study was conducted (country), sample size, gender distribution (percentage of females), average age, type of disorder including any comorbid diseases, diagnosis criteria, drugs used in the study, intervention format, presence of manuals, number of intervention sessions, duration of a single session, total treatment time, type of therapist, percentage of

December 2021 | Volume 12 | Article 798453

Efficacy of CBT on Insomnia

Xu et al.

TABLE 1 | Characteristics of included studies.

References	Location	N	Female, n (%)	Age	PEDro score	Disorder	Diagnosis	Drugs	Intervention	Delivery format
Arnedt et al. (34)	USA	17	6 (35%)	46	6	Insomnia, alcohol dependent	ISI ≥8, ICSD, DSM-IV	Not specified	CBT for insomnia for alcohol dependent	Individual
Ayabe et al. (35)	Japan	51	15 (30%)	60	8	Pharmacotherapy-resistant insomnia	ISI ≥8, ICSD, DSM-IV	Benzodiazepine	Add-on cognitive behavioral treatment for insomnia	Individual
Bothelius et al. (36)	Sweden	66	57 (86%)	51	8	Chronic insomnia	Self-report, daytime impairment	Hypnotics	Manual-guided CBT-I delivered by ordinary primary care personnel	Group
Carney et al. (37)	USA	107	68 (73%)	42	5	Insomnia, depression	ISI ≥15, SE, TWT, SCID, HAMD-17	Escitalopram	CBT for insomnia	Individual
Chen et al. (38)	Taiwan	72	42 (58%)	58	6	Sleep disturbance, renal disease	PSQI >5, self-report	Not specified	CBT for insomnia	Group
Currie et al. (39)	Canada	60	18 (30%)	43	5	Insomnia, alcohol dependent	Self-report, SCID	Hypnotics	Brief individual cognitive behavioral interventions for insomnia	Individual
Drake et al. (40)	USA	154	154 (100%)	56	5	Chronic insomnia	DSM-5, ICSD	Not specified	CBT for insomnia	Individual
Ellis et al. (41)	UK	40	Not reported	33	7	Acute insomnia	DSM-5	Not specified	"Single-shot" CBT for insomnia	Individual
Espie et al. (42)	UK	201	137 (68%)	54	7	Persistent insomnia	DSM-IV, ICSD	Not specified	Nurse-administered small-group CBT	Group
Garland et al. (43)	USA	45	43 (96%)	56	6	Insomnia	ICSD	Armodafinil	CBT for insomnia	Individual
Hou et al. (44)	China	98	56 (57%)	53	8	Insomnia, renal disease	PSQI >7, SCL-90	Not specified	Progressive muscle relaxation, sleep-related behavior modification	Group
Jacobs et al. (45)	USA	30	27 (70%)	47	6	Insomnia	ICSD	Hypnotics	CBT + 1 telephone treatment session	Individual
Jansson-Fröjmark et al. (46)	Sweden	32	20 (63%)	56	5	Insomnia, hearing impairment	ICSD	Not specified	CBT for insomnia	Individual
Jungquist et al. (47)	USA	28	24 (86%)	49	5	Insomnia, chronic pain	ICSD	Drugs for pain	CBT for insomnia	Individual
Lovato et al. (48)	Australia	118	63 (53%)	64	6	Insomnia	PSQI, self-report	Not specified	Brief 4-week group-administered CBT for insomnia	Group
Manber et al. (49)	USA	30	17 (61%)	35	7	Insomnia, major depression	DSM-IV, HRSD-17, ICSD	Escitalopram	CBT for insomnia	Individual
McCrae et al. (50)	USA	76	76 (100%)	53	8	Insomnia, chronic pain	ICSD	Antidepressants, drugs for pain	CBT for insomnia	Individual
Morin et al. (51)	USA	78	50 (64%)	65	5	Insomnia	ICSD	Temazepam	CBT (stimulus control, sleep restriction, sleep hygiene, cognitive therapy)	Group
Norell-Clarke et al. (52)	Sweden	64	25 (77%)	52	8	Insomnia, depressive symptom	DSISD, SCID, BDI	Not specified	Group CBT for insomnia	Group

(Continued)

TABLE 1 | Continued

References	Location	N	Female, <i>n</i> (%)	Age	PEDro score	Disorder		Diagnosis	Drugs		Interver		Deliv form	•
Pigeon et al. (53)	USA	21	14 (67%)	51	5	Insomnia, chronic p	pain	ICSD, apnea-hypopnea index <10	Not sp	ecified	CBT for insomnia, CBT for pain		Indivi	ridual
Sadler et al. (54)	Australia	72	40 (56%)	75	4	Insomnia, depressi	on	DSM-5	Not sp	ecified	CBT for	insomnia	Grou	qı
Savard et al. (55)	Canada	58	58 (100%)	54	8	Insomnia secondar cancer	y to	IIS, ICSD	Hypno	tics	Immedia	tely delivered CBT	Grou	qı
Schiller et al. (56)	Sweden	51	32 (63%)	42	7	Moderate insomnia	Moderate insomnia		Not sp	ecified	Workpla insomnia	0 1	Grou	qı
Sivertsen et al. (57)	Norway	30	16 (53%)	61	5	Chronic insomnia		DSM-IV	SM-IV Not sp		restrictio	ep hygiene, sleep on, stimulus control, e therapy, and relaxation)	Indivi	ridual
Smith et al. (58)	USA	100	79 (79%)	59	5	Insomnia, osteoarth	nritis	ICSD, self-report	Not sp	ecified	Standard	dized CBT for insomnia	Indivi	ridual
Soeffing et al. (59)	USA	47	Not reported	64	8	Insomnia, hypnotic dependent		SCID, ICSD	Hypno	tics	CBT for	insomnia	Indivi	ridual
Song et al. (60)	Korea	40	26 (65%)	56	6	Insomnia, restless I syndrome	eg	ICSD-3	Not sp	ecified	CBT for	insomnia	Grou	qı
Talbot et al. (61)	USA	45	31 (69%)	37	5	Insomnia, PTSD		DSM-IV	Not specified		CBT for	insomnia	Indivi	ridual
Taylor et al. (63)	USA	100	85 (85%)	32	5	Insomnia		DSM-5, SE <85%, self-report	Not sp	ecified	CBT for insomnia		Grou	qı
Taylor et al. (62)	USA	151	27 (18%)	32	8	Insomnia		DSM-5, SE <85%, self-report	Not sp	ecified	CBT for	insomnia	Grou	qı
Vitiello et al. (64)	USA	367	288 (79%)	73	8	Insomnia, osteoarth	nritis pain	Self-report	Not sp	ecified	CBT for	insomnia	Grou	qı
References	Manua		umber of essions (n)	Duration of se (min)	essions	Duration of treatment (weeks)	Therapi	st type	Compliance	Control		Outcome measuremen		Follow up
Arnedt et al. (34)	Yes		8	15–60		8 w	2 Author	s with certificate	59	Behavioral treatment	placebo	ISI, sleep diaries, BDI-II, STAI-T, MFI-20, SF-36		N/A
Ayabe et al. (35)	Yes		5	50		10 w	Trained o	clinical psychologists	96	Treatment	as usual	ISI, PSQI, sleep diaries, S	3DS	4 w
Bothelius et al. (36)	Yes		5	60–90		9 w	4 Primar 1 social	y health-care nurses and worker	85	Wait list co	ontrol	ISI, sleep diaries		18 m
Carney et al. (37)	Yes		4	60		8 w	Master's	-level students	63	Sleep hygi	ene	ISI, Sleep diaries, HAMD	-17	6 m
Chen et al. (38)	No		2	30		6 w	2 Psychi psycholo	atrists and 1 assistant	100	Sleep hygi	ene	PSQI, sleep diaries, BAI, BDI, FSS		N/A
Currie et al. (39)	Yes		5	60		7 w	3 Menta	health professionals	78%	Wait list co	ontrol	PSQI, sleep diaries, BDI		6 m
Drake et al. (40)	No		6	<60		6 w	1 Regist	ered nurse	97	Sleep hygi	ene	ISI, sleep diaries		6 m
Ellis et al. (41)	No		1	60–70		1 w 1 Pract		ing health psychologist nologist	100	Wait list co	ontrol	ISI, sleep diaries		1 m
Espie et al. (42)	No		5	60		5 w	7 Primar	y care nurses	89	Treatment	as usual	PSQI, sleep diaries, SF-3	36	6 m
Garland et al. (43)	No		7	15–60		7 w	Not repo	rted	83	Medication	only	Sleep diaries		N/A
Hou et al. (44)	No		36	20		3 m	Not repo	rted	100	Treatment	as usual	PSQI, SCL-90		N/A
Jacobs et al. (45)	No		4	30		6 w	Not repo		93	Placebo tr		Sleep diaries		12 m

Xu et al.

TABLE 1 | Continued

References	Manual	Number of sessions (n)	Duration of sessions (min)	Duration of treatment (weeks)	Therapist type	Compliance (%)	Control	Outcome measurements	Follow up
Jansson-Fröjmark et al. (46)	Yes	7	<60	7 w	3 Trained psychologists	94	Wait list control	ISI, sleep diaries, HADS	3 m
Jungquist et al. (47)	Yes	8	30–60	8 w	1 Masters prepared nurse therapist	75	Treatment as usual	ISI, sleep diaries, BDI	N/A
Lovato et al. (48)	No	4	60	4 w	5 Trainee psychologists	97	Wait list control	ISI, sleep diaries, flinders fatigue scale, sleep anticipatory anxiety	3 m
Manber et al. (49)	No	7	60	12 w	2 Licensed clinical psychologists	73	Sleep hygiene	ISI, sleep diaries, HRSD-17	N/A
McCrae et al. (50)	Yes	8	50	8 w	3 Predoctoral students in clinical psychology	72	Wait list control	Sleep diaries, BDI, STAI-T	6 m
Morin et al. (51)	No			95	Placebo treatment	Sleep diaries	24 m		
Norell-Clarke et al. (52)	Yes	4	120	8 w	1 Licensed psychologist	83	Relaxation training	ISI, sleep diaries, BDI-II	6 m
Pigeon et al. (53)	Yes	10	30–60	10 w	2 Experienced CBT psychologists	100	Wait list control	ISI, sleep diaries, CESD-R, MFI	N/A
Sadler et al. (54)	Yes	8	60–90	8 w	2 Therapists	96	Psychoeducation	ISI, sleep diaries, GDS	3 m
Savard et al. (55)	Yes	8	90	8 w	1 Master-level psychologist	93	Wait list control	ISI, sleep diaries	12 m
Schiller et al. (56)	No	5	120	3 m	1 Trained, certified clinical psychologist	100	Wait list control	ISI, sleep diaries, HADS	3 m
Sivertsen et al. (57)	Yes	6	50	6 w	2 Clinical psychologists	94	Placebo treatment	Sleep diaries	6 m
Smith et al. (58)	Yes	8	45	8 w	Postdoctoral clinical psychology fellows/faculty	91	Behavioral desensitization	ISI, sleep diaries	6 m
Soeffing et al. (59)	No	8	60	8 w	Doctoral students in clinical psychology	100	sham biofeedback treatment	Sleep diaries	N/A
Song et al. (60)	Yes	4	60	4 w	Not reported	63	Sleep hygiene	ISI, sleep diaries, BDI, BAI	3 m
Talbot et al. (61)	Yes	8	60	8 w	Licensed clinical psychologists, certified psychiatrist	93	Wait list control	ISI, PSQI, sleep diaries, BDI	6m
Taylor et al. (63)	No	6	60	6 w	Licensed clinical psychologists, clinical psychology postdoctoral fellows, licensed clinical social worker	86	Minimal contact	ISI, sleep diaries	6 m
Taylor et al. (62)	No	6	60	6 w	Licensed clinical psychologists, clinical psychology postdoctoral fellows, licensed clinical social worker	87	Minimal contact	ISI, sleep diaries, MFI, BDI, BAI	6 m
Vitiello et al. (64)	No	6	90	6 w	1 master's-level family counselor and 1 Ph.D. psychologist	93	Education only control	ISI, SE, GDS	9 m

BAI, Beck anxiety inventory; BDI, Beck depression inventory; CBT, cognitive behavioral therapy; CESD-R: Center for Epidemiologic Studies Depression Scale-revised; DSISD, Duke structured clinical interview for insomnia; DSM-IV, diagnostic and statistical manual of mental disorders fifth edition; FSS, fatigue severity scale; GDS, geriatric depression scale; HADS, hospital anxiety and depression scale; HAMD-17, Hamilton depression rating scale; HRSD-17, 17-item Hamilton rating scale for depression; ICSD, international classification of insomnia; IIS, insomnia interview schedule; ISI, insomnia severity index; MFI, multidimensional fatigue inventory; PSQI, Pittsburgh Sleep Quality Index; PTSD, posttraumatic stress disorder; PEDro, Physiotherapy Evidence Database; RT, relaxation training; SDS, self-rating depression scale; SCID, structured clinical interview for DSM-IV; SCL 90, symptom checklist 90; SE, sleep efficiency; SF-36: 36-item medical outcomes study short-form general health survey; SOL, sleep onset latency; STAI-T, state-trait anxiety inventory-trait subscale; TWT, total wake time; WASO, wake after sleep onset.

participants that completed the treatment, type of control group, outcome variable names, and length of follow-up period.

The mean and standard deviation for the primary and secondary outcomes were extracted directly from the results sections, tables, and figures in the studies for both the CBT intervention group and the control group before and after the intervention. The mean difference was calculated by subtracting the mean before intervention from the mean after intervention, and the total pooled mean difference was also calculated. The standardized mean difference (SMD) was calculated by dividing the mean difference by the pooled standard deviation (31).

Subgroup Data Extraction

The designs and groupings of the subgroup variables were based on the recommended CBT design from the CBT for insomnia guidelines (32) written by Perlis and colleagues. Subgroup information was collected mainly based on the characteristics of intervention delivery and CBT components in each study. The characteristics of intervention were collected from each study and coded into subgroup manually. The subgroups include participant dropout rate (0 for <20% drop out rate and 1 for ≥20% drop out rate), number of treatment sessions (0 for <6 sessions and 1 for \geq 6 sessions), duration of treatment sessions (0 for <1 h and 1 for >1 h), duration of treatment (0 for <6 weeks and 1 for \geq 6 weeks), form of delivery (0 for group-delivered and 1 for individual-delivered), drugs used in the study (0 for no drugs, 1 for hypnotics, and 2 for other drugs including antidepressants and pain drugs), and co-morbid diseases (0 for no co-morbid diseases, 1 for psychiatric diseases, and 2 for chronic diseases). The CBT module component subgroups included treatment rationale, sleep hygiene, relapse prevention, relaxation training, and basic sleep information. The presence of each component was coded as 1, and the absence of certain module was coded as 0.

Data Analysis

Because of expected heterogenicity, a random effects model, which provided a statistical parameter of the variations among the studies (33), was used to measure the mean difference and SMD of all outcome variables, and the results were presented as forest plots. A SMD between 0.2 and 0.5 indicated a small effect size, between 0.5 and 0.8 a medium effect size, and >0.8 a large effect size. In addition, the 95% confidence interval (CI) and p-value were determined for both mean difference and SMD. A p-value < 0.05 suggested that the result was statistically significant. The Q test and I^2 -values were used to assess the heterogenicity of the studies. The I^2 -value ranges from 0 to 100%. An I^2 -value larger than 50% indicates that the study has a high heterogenicity and a subgroup analysis is required to explore the possible causes. In addition, Egger regression analysis was used to assess the potential publication bias among the studies for each of the research outcomes, and the funnel plots were presented. A pvalue >0.05 indicated that the publication bias for the research outcome was not significant. At the study level, sensitivity analysis was conducted by removing one study at a time vs. all the studies together to identify whether the overall publication bias results for the research outcome were related to any particular study or studies. The software used for data analysis was STATA 17.0.

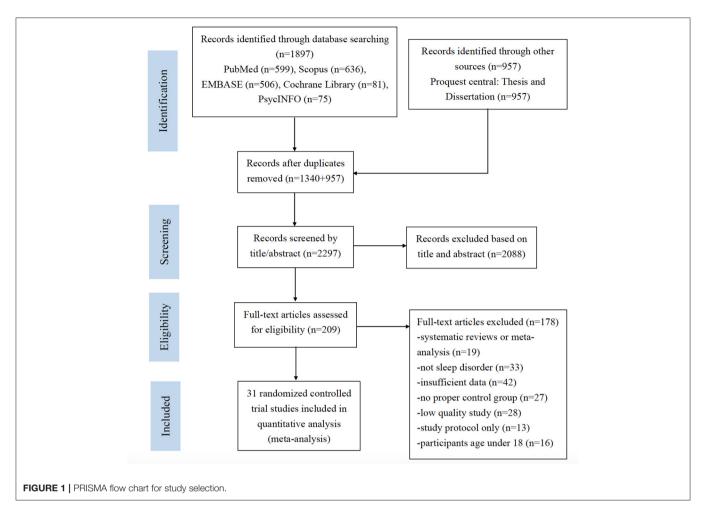
RESULTS

Study Selection

A total of 2,854 studies were identified through database search and other sources. After removing the duplicates, 2,297 studies were screened by titles and abstracts. After the screening of titles and abstracts, 2,088 studies were excluded, and the remaining 209 studies underwent full-text assessment. Another 178 studies were excluded after full-text assessment. Among the 178 excluded studies, 19 were meta-analysis or systematic reviews. Thirty-three studies were not related to insomnia. Fortytwo studies did not provide sufficient data for analysis. Twentyseven studies did not have control groups. Twenty-eight studies provided PEDro scores lower than 3 and were considered as low-quality studies. Thirteen studies were study protocols for clinical trials. Sixteen studies involved participants aged under 18, which did not meet the inclusion criteria. The final number of eligible studies included for meta-analysis was 31. The detailed process of study screening for meta-analysis was presented in Figure 1.

Study Characteristics

A total number of 2,449 patients were included in the 31 studies (34-64), with 1,107 of which in the intervention group and 1,342 of which in the control group. A total of 12 studies (37, 39, 40, 46, 47, 51, 53, 54, 57, 58, 61, 63) received PEDro scores of 4-5, suggesting that they had moderate quality. The remaining 19 studies (34-36, 38, 41-45, 48-50, 52, 55, 56, 59, 60, 62, 64) received PEDro scores of 6-8, suggesting that they had good quality. The studies were carried out in nine different countries including USA (34, 37, 40, 43, 45, 47, 49-51, 53, 58, 59, 61-64), UK (41, 42), Canada (37, 39, 55), Australia (48, 54), China (38, 44), Japan (35), Sweden (36, 46, 52, 56), Norway (57), and Korea (60). The percentage of female taking part in the studies was 66.9%, and the average age of the participants was 54.6 years. All of the studies included patients with insomnia. Among of which, some of the studies included patients with different co-morbid diseases including alcohol dependence (34, 39), chronic pain (47, 50, 53, 58, 64), renal diseases (38, 44), hearing impairment (46), depression (37, 49, 52, 54), and posttraumatic stress disorder (61). The percentage of patients that reported co-morbid depression was 30.7% (34, 37-39, 46, 47, 49, 50, 52–55, 60–62), and the percentage of patients that reported co-morbid anxiety was 20.1% (34, 38, 46, 50, 54, 55, 60, 62). Thirteen studies (32, 34, 35, 40, 42, 43, 45-47, 49-51, 53, 55) used the ICSD as diagnosis criteria. Six studies (34, 35, 42, 49, 57, 61) diagnosed insomnia using the DSM-IV, while five studies (40, 41, 54, 62, 63) used the DSM-V. All of the included studies used either group-delivered or individual-delivered CBT in the intervention group, with 16 out of 31 studies (34-37, 39, 46, 47, 50, 52-55, 57, 58, 60, 61) using intervention manuals. Moreover, the total number of intervention sessions ranged from 1 to 36 and the time of a single session ranged from 15 to 120 min. The duration of



the intervention ranged from 1 day (one single session) to 3 months. The CBT interventions were all delivered by trained professionals. In addition, an average of 88% of the patients completed the treatment across the 31 included studies. All of the included studies reported at least one of the sleep outcomes. The characteristics of studies included for meta-analysis were displayed in **Table 1**.

Overall Effect of Face-to-Face CBT on Sleep Outcomes

The results of meta-analysis were presented in **Table 2**. The forest plots were presented in **Figures 2**, 3.

Insomnia Severity Index was reported by 20 studies (34, 36, 37, 40, 41, 46–49, 52–56, 58, 60–64) as an outcome measurement. Patients in the CBT intervention group showed a significant reduction in insomnia severity as measured by Insomnia Severity Index (mean difference = -5.19, 95% CI -6.30 to -4.07, p < 0.001, $I^2 = 97.57$) compared with the control group, with large effect size (SMD = -2.56, 95% CI -3.81 to -1.30, p < 0.001). Subgroup analysis was conducted for Insomnia Severity Index, and the results are presented in **Table 3**. We found that the subgroup variable that provided greatest effect in improving reducing insomnia severity was relapse prevention. Studies that included relapse

prevention (mean difference = -6.765, 95% CI -8.117 to -5.413, p < 0.001, $I^2 = 84.05$) reported a significantly greater improvement in insomnia severity scores than studies that did not include relapse prevention (mean difference = -6.042, 95% CI -7.106 to -4.978, p < 0.001, $I^2 = 90.56$). Other effective subgroup variables included drop-out rate <20%, number of sessions ≥ 6 , duration of one session <1 h, sleep hygiene, and relaxation training.

Pittsburgh Sleep Quality Index was reported in only five studies (35, 38, 39, 42, 44), and there was an overall significant improvement in sleep quality measured by Pittsburgh Sleep Quality Index in the intervention group (mean difference = -3.13, 95% CI -3.71 to -2.56, p < 0.001, $I^2 = 0.00$) in comparison with the control group, with large effect size (SMD = -0.96, 95% CI -1.25 to -0.68, p < 0.001).

Among the sleep quality outcomes, the intervention group reported a significant increase in total sleep time (mean difference = 23.21, 95% CI 14.56 to 31.87, p < 0.001, $I^2 = 83.31$) compared with the control group, with medium effect size (SMD = 0.63, 95% CI 0.28 to 0.98, p < 0.001). The results of subgroup analysis for total sleep time are displayed in **Table 3**. The duration of intervention sessions showed greatest effect on total sleep time. In studies in which the duration of one session was longer than 60 min (mean difference = 27.18, 95% CI 14.27

TABLE 2 | Total effects of CBT on all outcomes.

Variables	Studies (n)	Participants (N)	Mean differ	ence		Effect si	ze		Publication bias
			Mean difference (95% CI)	Q-test	I ² (%)	Standardized mean difference (95% CI)	Q-test	I ² (%)	Egger's <i>t</i> (95% CI)
Insomnia Severity Index	20	1,398	-5.19*** (-6.30, -4.07)	1952.01***	97.57***	-2.56*** (-3.81, -1.30)	516.28***	98.89***	1.05 (-0.89, 2.69)
Pittsburgh Sleep Quality Index	5	462	-3.13*** (-3.71, -2.56)	2.93	0.00	-0.96*** (-1.25, -0.68)	7.43	47.62	0.20 (-3.99, 4.52)
Total sleep time	25	1,523	23.21*** (14.56, 31.87)	235.35***	83.31***	0.63*** (0.28, 0.98)	215.91***	91.20***	-0.18 (-1.19, 1.00)
Sleep efficiency	24	1,698	8.53*** (6.41, 10.65)	919.31***	96.67***	1.61*** (0.92, 2.29)	474.64***	97.26***	1.51(-0.36, 2.27)
Sleep onset latency	21	1,477	-16.43*** (-21.04, -11.81)	447.91***	93.75***	-1.31*** (-2.00, -0.63)	367.33***	97.09***	-0.87 (-2.02, 0.84)
Wake after sleep onset	20	1,387	-25.74*** (-32.46, -19.02)	217.21***	92.56***	-1.44*** (-2.14, -0.74)	360.23***	97.01***	-0.42 (-1.76, 1.18)
Number of awakenings	7	543	-0.69*** (-0.91, -0.46)	18.60**	72.02**	-1.18* (-2.10, -0.26)	142.09***	95.23***	0.98 (-1.22, 2.71)
Depression	15	753	-3.67*** (-5.66, -1.68)	294.27***	97.58***	-1.14** (-1.85, -0.42)	135.21***	95.20***	0.04 (-1.82, 1.89)
Anxiety	8	493	-0.66 (-1.53, 0.22)	73.20***	88.09***	-0.62 (-1.55, 0.32)	67.90***	95.83***	-0.86 (-1.89, 0.90)
Fatigue	6	426	-4.74* (-9.34, -0.14)	860.29***	99.94***	-2.23** (-3.87, -0.58)	183.37***	97.35***	-1.77 (-5.01, 1.43)
Physical health	3	369	1.90*** (1.02, 2.78)	1.01	0.00	0.42* (0.08, 0.76)	3.85	51.86	1.00 (-9.78, 11.45)
Mental health	3	369	4.95* (1.01, 8.90)	10.40**	80.07**	1.09 (-0.59, 2.77)	86.20***	97.34***	-3.18 (-14.87, 8.91

CI, confidence interval.

to 40.08, p<0.001, $I^2=91.65$), a greater effect of CBT was observed than in studies providing sessions shorter than 60 min (mean difference = 16.40, 95% CI 9.81 to 22.99, p<0.001, $I^2=0.00$). Other effective CBT characteristics included number of sessions \geq 6, group delivered, treatment with drugs, sleep hygiene, relaxation training, and relapse prevention.

We also found that there was a significant increase in sleep efficiency (mean difference = 8.53, 95% CI 6.41 to 10.65, p <0.001, $I^2 = 96.67$) in the CBT intervention group compared with the control group, with large effect size (SMD = 1.61, 95% CI 0.92 to 2.29, p < 0.001). Subgroup analysis was conducted for sleep efficiency, and the results are presented in Table 4. Both relapse prevention and relaxation training showed a significant effect in improving sleep efficiency. Studies that included relapse prevention (mean difference = 10.834, 95% CI 7.572 to 14.097, p < 0.001, $I^2 = 87.34$) had a greater effect on sleep efficiency than studies that did not include relapse prevention (mean difference = 7.476, 95% CI 4.920 to 10.031, p $< 0.001, I^2 = 97.01$). Likewise, studies that included relaxation training reported a more significant increase in sleep efficiency (mean difference = 9.779, 95% CI 7.087 to 12.472, p < 0.001, $I^2 = 93.96$) than studies that did not include relaxation training (mean difference = 6.787, 95% CI 3.737 to 9.837, p < 0.001, $I^2 = 95.83$). Sleep efficiency was also significantly improved when drop-out rate was <20%, number of sessions were ≥6, length of intervention was ≤ 6 weeks, and sessions were group delivered.

In addition, sleep onset latency time was significantly improved in the CBT intervention group (mean difference = -16.43, 95% CI -21.04 to -11.81, p < 0.001, $I^2 = 93.75$) in comparison with the control group, with large effect size (SMD = -1.31, 95% CI -2.00 to -0.63, p < 0.001).

Subgroup analysis was also conducted for sleep onset latency, and the results are presented in **Table 4**. We found that the subgroup variable that provided greatest effect in improving sleep onset latency was comorbid disease. There was a significantly greater improvement in sleep onset latency when patients had comorbid psychiatric diseases (mean difference = -21.382, 95% CI -25.870 to -16.895, p < 0.001, $I^2 = 87.73$) compared with patients who had comorbid chronic diseases (mean difference = -14.774, 95% CI -24.092 to -5.455, p < 0.01, $I^2 = 88.72$) and patients who had no comorbid diseases (mean difference = -12.726, 95% CI -21.113 to -4.338, p < 0.01, $I^2 = 77.14$). Other effective CBT characteristics and components included drop-out rate <20%, number of sessions <6, duration of one session ≥ 60 min, group delivered, relapse prevention, relaxation training, and basic sleep information.

Wake time after sleep onset was also significantly improved in the CBT intervention group (mean difference = -25.74, 95% CI -32.46 to -19.02, p < 0.001, $I^2 = 92.56$) compared with the control group, with large effect size (SMD = -1.44, 95% CI -2.14 to -0.74, p < 0.001). The results of subgroup analysis for wakening after sleep onset are displayed in Table 5. The subgroup variables that provided greatest effect in improving wake time after sleep onset were duration of intervention session and relaxation training. The subgroup analysis indicated that wakening after sleep onset was more significantly improved in studies providing intervention sessions longer than 1 h (mean difference = -30.149, 95% CI -39.022 to -21.296, p < 0.001, $I^2 = 94.17$) compared with studies providing sessions shorter than 1 h (mean difference = -17.375, 95% CI -20.768 to -13.987, p < 0.001, $I^2 = 0.00$). A greater improvement in wakening after sleep onset was observed in studies that included

p < 0.05, p < 0.01, p < 0.01, p < 0.001.

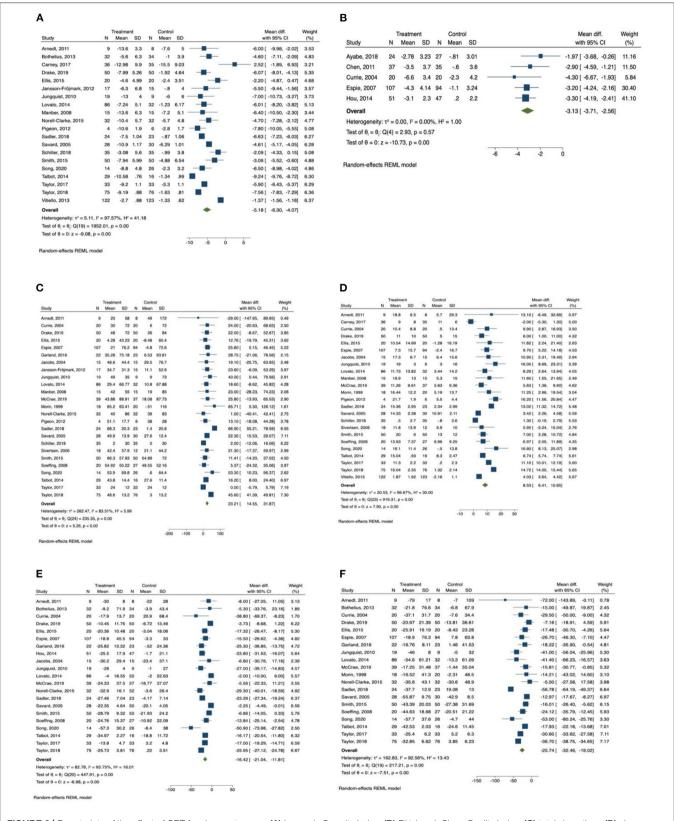
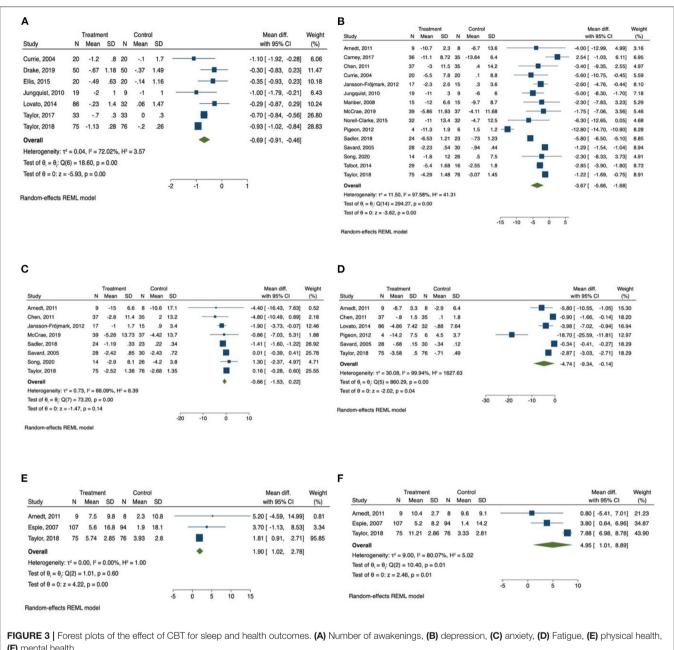


FIGURE 2 | Forest plots of the effect of CBT for sleep outcomes. (A) Insomnia Severity Index, (B) Pittsburgh Sleep Quality Index, (C) total sleep time, (D) sleep efficiency, (E) sleep onset latency, (F) wake after sleep onset.



(F) mental health.

relaxation training (mean difference = -30.034, 95% CI -40.118to -19.950, p < 0.001, $I^2 = 94.89$) compared with studies that did not include relaxation training (mean difference = -19.597, 95% CI -25.892 to -13.302, p < 0.001, $I^2 = 62.68$). Other effective CBT characteristics and components included group delivered, comorbid psychiatric diseases, sleep hygiene, and relapse prevention.

The meta-analysis also showed that there was a significant improvement in number of awakenings (mean difference = -0.686, 95% CI -0.91 to -0.46, p < 0.001, $I^2 =$ 72.02) in the CBT intervention group compared with the control group, with large effect size (SMD = -1.18, 95% CI -2.10 to -0.26, p < 0.05).

The O-test results were consistent with the I^2 results in all analyses, indicating the same levels of significance of heterogenicity. The p-values between groups were all smaller than 0.001, suggesting that there was a significant difference between groups for each of the subgroup variables.

Overall Effect of Face-to-Face CBT on **Psychiatric Diseases**

A total of 15 studies measured the effect of CBT on depression (31, 34-36, 43, 44, 46, 47, 49-52, 57-59) and the total number of participants in these studies was 753. We found that there was a significant improvement of depressive symptoms measured by depression scales (mean difference = -3.67, 95% CI -5.66

to -1.68, p < 0.001, $I^2 = 97.58$) in CBT intervention groups compared with the control group, and there was a large effect size (SMD = -1.14, 95% CI -1.85 to -0.42, p < 0.01).

Subgroup analysis was also conducted on depression. The results for subgroup analysis on depression were presented in **Table 5**. The subgroup analysis showed that relapse prevention had greatest effect on depression. Studies that included relapse prevention reported a significantly greater improvement on depressive conditions (mean difference = -5.120, 95% CI -7.856 to -2.384, p < 0.001, $I^2 = 93.81$) than studies that did not include relapse prevention (mean difference = -1.273, 95% CI -1.495 to -1.052, p < 0.001, $I^2 = 0.00$). Other characteristics of the studies including drop-out rate <20%, number of sessions >6 sessions, duration of 1 session <1 h, length of intervention >6 weeks, individual delivered, using sleep drugs, and patients with co-morbid chronical diseases had significant effect on the reduction of depression. CBT intervention components including sleep hygiene, relaxation training, and basic sleep information had significant effect on the improvement of depression. The Q-test results were consistent with the I^2 results, indicating the same levels of heterogenicity. The p between groups were all smaller than 0.001, suggesting that there was a significant difference between groups for each of the subgroup variables.

Anxiety was measured in eight studies (31, 35, 43, 47, 51, 52, 57, 59), and the total number of participants in these studies was 493. Compared with control groups, CBT intervention groups only reported a slight improvement in anxiety symptoms measured by anxiety scales (mean difference = -0.66, 95% CI -1.53 to 0.22, p > 0.05, $I^2 = 88.09$), with moderate effect size (SMD = -0.62, 95% CI -1.55 to 0.32, p > 0.05). The *Q*-test result was consistent with the I^2 result, indicating a high level of heterogenicity.

Overall Effect of Face-to-Face CBT on Fatigue

Fatigue was reported as outcome measurement in six studies (34, 38, 48, 53, 55, 62), and the total number of participants in these studies was 426. The meta-analysis found that there was a significant reduction of daytime fatigue measured by different fatigue scales (mean difference = -4.74, 95% CI -9.34 to -0.14, p < 0.05, $I^2 = 99.94$) in CBT intervention groups compared with the control group with a large effect size (SMD = -2.23, 95% CI -3.87 to -0.58, p < 0.01). The Q-test result was consistent with the I^2 result, indicating a high level of heterogenicity.

Overall Effect of Face-to-Face CBT on Quality of Life

The scores of SF 12 and SF 36 quality of life survey were reported in three studies (34, 42, 62). The scores of physical health section and mental health section were collected from all of the three studies. Patients in the CBT intervention groups showed a significant improvement in physical health measured by SF 12 and SF 36 survey (1.90, 95% CI 1.02 to 2.78, p < 0.001, $I^2 = 0.00$), with a medium effect size (SMD = 0.42, 95% CI 0.08 to 0.76, p < 0.05). Mental health measured by SF 12 and SF 36 survey was also

improved in CBT intervention group (4.95, 95% CI 1.01 to 8.90, p < 0.05, $I^2 = 80.07$) compared with control group, with a large but not statistically significant effect size (SMD = 1.09, 95% CI -0.59 to 2.77, p > 0.05). The Q-test results were consistent with the I^2 results, indicating the same levels of heterogenicity.

Publication Bias

The results of the Egger's regression test for all of the research outcomes were summarized in Table 2. The funnel plots of the outcome variables were provided in **Supplementary Figures 1**, **2**. A symmetric distribution of mean difference in all outcomes was observed upon the visual inspection of the funnel plots, indicating that there was no significant publication bias. The results of Egger's test of all variables had no significant results including Insomnia Severity Index (t = 1.05, 95% CI -0.89 to 2.69, p > 0.05), Pittsburgh Sleep Quality Index (t = 0.20, 95%CI -3.99 to 4.52, p > 0.05), total sleep time (t = -0.18, 95% CI -1.19 to 1.00, p > 0.05), sleep efficiency (t = 1.51, 95% CI -0.36to 2.27, p > 0.05), sleep onset latency (t = -0.87, 95% CI -2.02to 0.84, p > 0.05), wakening after sleep onset (t = -0.42, 95% CI -1.76 to 1.18, p > 0.05), number of awakenings (t = 0.98, 95% CI -1.22 to 2.71, p > 0.05), depression (t = 0.04, 95% CI -1.82 to 1.89, p > 0.05), anxiety (t = -0.86, 95% CI -1.89 to 0.90, p > 0.05), physical health (t = 1.00, 95% CI -9.78 to 11.45, p > 0.05), and mental health (t = -3.18, 95% CI -14.87 to 8.91, p > 0.05). These results suggested that there is no significant publication bias for these outcomes. The study by Pigeon et al. (53) was excluded in the analysis of fatigue because it provided a high publication bias for this outcome. The Egger's t-value for fatigue after excluding this study was -1.77 (95% CI -5.01to 1.43, p > 0.05), which suggested that there is no significant publication bias for fatigue in the rest of the studies. Removing any single study in other outcomes did not change the overall results. Therefore, all of the included studies contributed to the overall publication bias results in all outcomes except fatigue.

DISCUSSION

This study included 31 randomized controlled trial studies to assess the effect of face-to-face delivered CBT on different health outcomes in patients with insomnia. The results from this meta-analysis study showed that face-to-face delivered CBT had a significant positive effect in improving all of the sleep outcomes (Insomnia Severity Index, Pittsburgh Sleep Quality Index, total sleep time, sleep efficiency, sleep onset latency, wakening after sleep onset, and number of awakenings), one of the psychiatric disease outcomes (depression), fatigue, and quality-of-life related physical and mental health. Face-to-face delivered CBT did not show significant effects on the other psychiatric disease outcome (anxiety).

Efficacy of Face-to-Face CBT Intervention on Sleep Outcomes

The meta-analysis results were consistent with the findings from previous studies (12, 65), suggesting that face-to-face CBT had an overall significant effect in improving sleep quality and reducing insomnia symptoms. Previous studies (65, 66)

Xu et al.

TABLE 3 | Subgroup analysis for Insomnia Severity Index and total sleep time.

Subgroups			Insom	nia Severity Index				Total sleep time						
	Study (n)	Participan (n)	t MD (95% CI)	SMD (95% CI)	MD /² (%)	MD Q-test	<i>p</i> Between	Study (n)	Participant (n)	MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between
Dropout rate							<0.001							<0.001
<20%	15	1,194	-5.368*** (-6.608, -4.128)	-2.912*** (-4.529, -1.295)	97.93***	1937.33**	*	19	1,274	22.87*** (12.66, 33.08)	0.66** (0.23, 1.09)	86.26***	231.55***	
≥20%	5	204	-4.422** (-7.449, -1.369)	-1.535* (-2.956, -0.114)	79.81*	12.81*		6	249	22.76*** (16.31, 29.21)	0.55* (0.03, 1.07)	0.00	1.50	
Number of sessions							< 0.001							< 0.001
<6 sessions	7	469	-3.691***	-0.718**	73.67**	20.53**		8	603	15.77**	0.28**	23.97	7.97	10.00
3 0000.0110			(-5.616, -1.766)	(-1.152, -0.284)						(4.12, 27.43)	(0.11, 0.44)			
>6 sessions	13	929	-5.908***	-3.581***	98.20***	1931.33**	*	17	920	25.52***	0.80**	88.75***	217.84***	
_0 0000.0110			(-7.203, -4.612)	(-5.326, -1.836)						(14.51, 36.52)	(0.30, 1.30)			
Duration of one session				,			< 0.001			, ,	, , ,			< 0.001
<1h	6	304	-6.516***	-2.995	81.40**	36.34***	<0.001	11	532	16.40***	0.32***	0.00	2.16	<0.001
\ 111	-		(-8.456, -4.576)	(-6.007, 0.016)						(9.81, 22.99)	(0.15, 0.49)			
≥1 h	14	1,094	-4.668***	-2.399**	97.94***	1549.47**	*	14	991	27.18***	0.85**	91.65***	220.71***	
2111	• •	1,001	(-5.965, -3.372)	(-3.777, -1.021)	07.10	10 10111			00.	(14.27, 40.08)	(0.27, 1.44)	01.00		
Longth of intervention			(0.000, 0.0.2)	(0,			< 0.001			(* 1121) (0100)	(0.21,)			< 0.001
Length of intervention	7	760	-5.100***	-2.898*	98 80***	1443.20**		9	776	23.47**	0.67	85 62***	159.40***	
≤6 weeks	,		(-6.910, -3.290)	(-5.143, -0.654)	30.00	1440.20		9	770	(9.97, 36.96)	(-0.02, 1.37)	00.02	100.40	
0	13	638	-5.223***	-2.368**	02 47***	193.81***		16	747	22.99***	0.60**	76 02***	72.19***	
>6 weeks	10		(-6.712, -3.733)	(-3.937, -0.800)	90.47	190.01		10	747	(11.39, 34.59)	(0.22, 0.98)	10.90	12.19	
			(-0.712, -0.700)	(-0.907, -0.000)						(11.09, 04.09)	(0.22, 0.30)			0.004
Form of delivery	10	925	-5.021***	-3.094**	00 10***	1535.76**	× <0.001	10	853	28.04**	1.03*	95.15***	219.32***	<0.001
Group-delivered	10				90.10	1555.76		10	000			95.15	219.32	
	10	473	(-6.341, -3.702) -5.304***	(-4.856, -1.332) -2.009*	00 50***	00 10***		15	670	(12.02, 44.06) 17.10***	(0.23, 1.83) 0.33***	0.00	0.70	
Individual-delivered	10		-5.304 (-7.311, -3.297)	-2.009 (-3.826, -0.192)	86.56***	83.10***		15	670			0.00	3.70	
			(-1.311, -3.291)	(-3.826, -0.192)						(10.84, 23.37)	(0.18, 0.48)			
Drug treatment	4.0	4 000	E 00 4***	0.010***	07 00***	1000 74**	<0.001	47	1 100	00.00***	0.75**	00 50***	004 44**	<0.001
No drug used	16	1,203	-5.384***	-3.019***	97.88***	1939.74**	*	17	1,183	22.36***	0.75**	89.58***	231.11***	
			(-6.556, -4.212)	(-4.527, -1.510)				_	000	(11.95, 32.76)	(0.25, 1.25)			
Hypnotics	1	66	-4.600***	-0.874**	N/A	0.00		5	200	20.36*	0.34*	0.00	3.28	
			(-7.111, -2.089)	(-1.374, -0.374)	0.4.40**	10 10++				(1.50, 39.23)	(0.06, 0.61)			
Other	3	129	-3.707	-0.707	84.43**	12.18**		3	140	30.64*	0.38*	0.00	0.36	
			(-9.669, 2.254)	(-1.760, 0.346)						(6.05, 55.24)	(0.04, 0.73)			
Comorbid disease							< 0.001							< 0.001
None	6	434	-4.633***	-0.945***	64.06*	13.86*		10	714	17.44**	0.31***	22.46	10.90	
			(-6.215, -3.052)	(-1.277, -0.613)						(6.99, 27.90)	(0.17, 0.46)			
Psychiatric	9	736	-5.276***	-3.924**	99.32***	1922.02**	*	8	460	25.70*	1.03**	95.89***	207.94***	
			(-7.413, -3.139)	(-6.448, -1.399)						(5.37, 46.03)	(0.01, 2.05)			
Chronic	5	228	-5.410***	-2.082**	66.78*	10.65*		7	349	21.99***	0.59**	0.00	1.89	
			(-7.142, 3.679)	(-3.585, -0.579)						(15.92, 28.05)	(0.18, 1.01)			
Treatment rationale							< 0.001							< 0.001
No	17	1,231	-5.480***	-2.929***	97.69***	1942.46**	*	22	1,351	23.79***	0.68**	85.86***	233.72***	
			(-6.614, -4.345)	(-4.351, -1.507)						(14.41, 33.17)	(0.29, 1.07)			
Yes	3	167	-2.748	-0.497	80.93*	8.98*		3	172	18.59	0.23	0.00	0.93	
			(-7.507, 2.011)	(-1.286, 0.293)						(-2.04, 39.21)	(-0.07, 0.53)			

TABLE 3 | Continued

Efficacy
of CBT
9
Insomnia

Subgroups			Insom	nia Severity Index				Total sleep time						
	Study (n)	Participar	nt MD (95% CI)	SMD (95% CI)	MD /² (%)	MD Q-test	<i>p</i> Between	Study (n)	Participant (n)	MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between
Sleep hygiene							<0.001							<0.001
No	4	172	-3.498** (-5.521, -1.476)	-0.650*** (-0.957, -0.343)	41.70	5.12		8	325	15.66* (2.42, 28.90)	0.32** (0.10, 0.53)	18.16	6.55	
Yes	16	1,226	-5.477*** (-6.708, -4.245)	-3.030*** (-4.543, -1.517)	98.06***	1944.75**	*	17	1,198	24.37*** (13.82, 34.92)	0.77** (0.27, 1.27)	88.83***	219.76***	
Relapse prevention							< 0.001							< 0.001
No	12	1,076	-4.292*** (-5.751, -2.833)	-2.194** (-3.666, -0.722)	98.25***	1464.78**	*	16	990	19.75*** (9.68, 29.81)	0.56* (0.12, 1.00)	81.62*** 75.59***	181.15***	
Yes	8	322	-6,765*** (-8.117, -5.413)	-3.151** (-5.531, -0.771)	84.05***	57.67***		9	533	28.43*** (13.00, 43.87)	0.77* (0.161, 1.37)		52.82***	
Relaxation training							< 0.001							< 0.001
No	11	816	-4.472*** (-6.296, -2.647)	-1.997* (-3.623, -0.371)	97.50***	71.06 ***		11	583	19.70*** (14.87, 24.53)	0.49** (0.17, 0.81)	0.00	6.66	
Yes	9	582	-6.042*** (-7.106, -4.978)	-3.236** (-5.189, -1.282)	90.56***	58.29***		14	940	25.07*** (12.48, 37.65)	0.74* (0.17, 1.32)	88.72***	215.32***	
Basic sleep information							< 0.001							< 0.001
No	10	857	-5.732*** (-7.259, -4.205)	-4.080*** (-6.232, -1.928)	98.82***	1920.24**	*	13	764	24.91*** (12.01, 37.82)	0.89** (0.25, 1.54)	92.27***	215.45***	
Yes	10	541	-4.511*** (-6.153, -2.868)	-0.869*** (-1.267, -0.472)	71.68***	30.35***		12	759	17.93*** (8.12, 27.74)	0.31*** (0.17, 0.46)	18.20	11.44	

MD, mean difference; SMD, standardized mean difference; CI, confidence interval. $^*p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001.$

TABLE 4 | Subgroup analysis for sleep efficiency and sleep onset latency.

Subgroups			Sle	ep efficiency				Sleep onset latency						
	Study (n)	Participant (n)	t MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between	Study (n)	Participant (n)	MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between
Dropout rate							<0.001							<0.001
<20%	17	1,378	9.196*** (6.953, 11.438)	1.951*** (1.032, 2.871)	96.62***	850.68***		16	1,258	-17.288*** (-22.149, -12.428)	-1.509*** (-2.379, -0.640)	92.64***	177.91***	
≥20%	7	320	6.863** (1.908, 11.818)	0.787**	87.45***	29.50***		5	219	-13.494* (-25.890, -1.097)	-0.634** (-1.101, -0.166)	77.70***	20.90***	
Number of sessions			(,,	()			< 0.001			(==::::)	(,,			< 0.001
<6 sessions	8	610	7.431** (3.017, 11.845)	0.585*** (0.281, 0.889)	86.02***	45.70***	<0.001	8	599	-19.335*** (-30.200, -8.471)	-0.643*** (-1.023, -0.263)	78.26***	29.72***	<0.001
≥6 sessions	16	1,088	9.129***	2.128***	96.90***	830.25***		13	878	-15.535*** (-20.706, -10.365)	-1.721*** (-2.766, -0.676)	95.30***	415.05***	
D 11 ((6.820, 11.438)	(1.180, 3.075)			0.004			(-20.706, -10.365)	(-2.700, -0.070)			0.001
Duration of one session	9	455	8.072***	1.242**	63.33*	17.09*	< 0.001	9	558	-12.918***	-0.732***	73 25***	31.18***	< 0.001
<1 h	9		(5.567, 10.578)	(0.406, 2.079)	00.00	17.09		9	550	(-18.726, -7.109)	(-1.157, -0.307)	70.20	31.10	
	15	1,243	8.815***	1.794***	98.11***	901.29***		12	919	-19.410***	-1.750**	96.76***	384.18***	
≥1 h			(5.841, 11.789)	(0.831, 2.757)						(-26.392, -12.428)	(-2.869, -0.631)			
Length of intervention							< 0.001							< 0.001
≤6 weeks	10	1,021	9.701*** (6.909, 12.494)	1.878** (0.572, 3.183)	96.24***	729.98***		8	746	-15.975*** (-24.535, -7.414)	-1.747* (-3.406, -0.088)	96.63***	145.86***	
>6 weeks	14	677	7.792*** (4.770, 10.814)	1.384*** (0.664, 2.104)	94.48***	177.78***		13	731	-16.870*** (-22.591, -11.149)	-1.032*** (-1.500, -0.565)	86.39***	138.64***	
Form of delivery			((0.00 1, 21.0 1)			< 0.001			(22.00.,)	(1.000, 0.000)			< 0.001
Group-delivered	10	1,034	8.915*** (5.658, 12.172)	2.319**	98.53***	865.70***		10	909	-18.678*** (-26.363, -10.992)	-1.862** (-3.198, -0.526)	97.53***	382.00***	<0.001
Individual-delivered	14	664	8.185***	(0.995, 3.644)	80.33***	53.59***		11	568	-14.012***	-0.793***	68.15***	32.32***	
			(5.317, 11.053)	(0.484, 1.557)						(-19.398, -8.625)	(-1.173, -0.412)			
Drug treatment No drug used	16	1,338	8.801***	2.052***	97.60***	882.33***	<0.001	14	1,140	-16.076***	-1.634***	96.28***	438.32***	<0.001
Hypnotics	4	155	(6.334, 11.267) 8.920***	(1.085, 3.019) 0.844***	0.00	1.19		5	233	(-21.724, -10.427) -18.240***	(-2.610, -0.658) -0.588**	21.52	5.42	
Other	4	205	(5.581, 12.259) 7.139	(0.520, 1.167) 0.639	88.28***	25.25***		2	104	(-27.033, -9.447) -17.089	(-1.010, -0.167) -0.879	75.68*	4.11*	
			(-0.789, 15.066)	(-0.130, 1.409)						(-38.040, 3.862)	(-2.405, 0.648)			
Comorbid disease							< 0.001							< 0.001
None	10	714	7.901*** (4.943, 10.859)	0.631*** (0.478, 0.783)	66.28***	39.63***		8	642	-12.726** (-21.113, -4.338)	-0.482** (-0.781, -0.182)	77.14**	25.06**	
Psychiatric	9	712	8.639***	2.682**	98.86***	800.55***		7	430	-21.382***	-2.637**	87.73***	63.11***	
Chronic	5	272	(4.754, 12.524) 9.149** (3.953, 14.345)	(1.148, 4.215) 1.343*** (0.591, 2.095)	90.59***	39.13***		6	405	(-25.870, -16.895) -14.774** (-24.092, -5.455)	(-4.317, -0.958) -0.807***	88.72***	53.07***	
											(-1.267, -0.347)			
Treatment rationale	0-	. ==:	0.40	. =		000	< 0.001			40.4				<0.001
No	22		9.194*** (7.141, 11.247)	1.746*** (1.024, 2.468)		892.26***		19		-16.140*** (-20.911, -11.369)	-1.377*** (-2.124, -0.630)		442.00***	
Yes	2	147	1.690 (-5.784, 9.163)	0.155 (-0.694, 1.004)	86.99**	7.69**		2	140	-18.343 (-41.539, 4.853)	-0.726 (-1.878, 0.427)	81.70*	5.47*	

Xu et al.

TABLE 4 | Continued

Subgroups			Sle	ep efficiency				Sleep onset latency						
	Study (n)	Participant (n)	t MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between	Study (n)	Participant (n)	t MD (95% CI)	SMD (95% CI)	MD /² (%)	MD Q-test	p Between
Sleep hygiene							<0.001							<0.001
No	6	248	8.307*** (3.654, 12.960)	0.703*** (0.450, 0.955)	65.73**	21.48**		5	253	-21.756*** (-26.820, -16.693)	-0.957*** (-1.316, -0.597)	0.00	4.22	
Yes	18	1,450	8.590*** (6.156, 11.024)	1.910*** (1.022, 2.797)	97.47***	863.02***		16	1,224	-15.184*** (-20.628, -9.739)	-1.443** (-2.334, -0.552)	95.59***	442.81	
Relapse prevention							< 0.001							< 0.001
No	17	1,261	7.476***	1.386** (0.573, 2.198)	97.01***	837.06***		14	950	-15.303*** (-21.471, -9.135)	-1.337** (-2.290, -0.384)	95.89***	433.40***	
Yes	7	437	(4.920, 10.031) 10.834***	2.180**	87.34***	55.92***		7	527	-19.871*** (-24.995, -14.746)	-1.254** (-2.117, -0.391)	56.53*	14.13*	
			(7.572, 14.097)	(0.891, 3.469)										
Relaxation training							< 0.001							< 0.001
No	11	790	6.787***(3.737, 9.837)	1.228***(0.563, 1.893)	95.83***	62.51***		9	515	-14.383*** (-21.427, -7.340)	-0.963*** (-1.419, -0.507)	89.41***	77.27***	
Yes	13	908	9.779***(7.087, 12.472)	1.946**(0.805, 3.088)	93.96***	282.25***		12	962	-18.259*** (-24.314, -12.204)	-1.564** (-2.721, -0.406)	93.10***	127.32***	
Basic sleep information			,	,			< 0.001			,	,			< 0.001
·	13	964	8.744*** (6.270, 11.218)	2.244***	97.32***	813.36***		13	832	-15.742***	-1.727** (-2.771, -0.683)	95.25***	413.47***	
No	11	734	8.431***	(1.154, 3.334) 0.649***	85 66***	79.70***		8	645	(-20.939, -10.544) -18.835**	(-2.771, -0.663) -0.625**	79.58***	30.51***	
Yes			(4.691, 12.171)	(0.384, 0.914)	33.00	70.70		O	010	(-29.656, -8.014)	(-1.006, -0.244)	70.00	00.01	

MD, mean difference; SMD, standardized mean difference; CI, confidence interval. $^*p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001.$

TABLE 5 | Subgroup analysis for wake after sleep onset and depression.

Subgroups	Wake after sleep onset								Depression							
	Study (n)	Participan (n)	t MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between	Study (n)	Participant (n)	MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between		
Dropout rate							<0.001							<0.001		
<20%	15	1,168	-25.810*** (-33.770, -17.850)	-1.549** (-2.475, -0.623)	93.85***	152.11***		8	461	-4.725** (-7.598, -1.853)	-1.726* (-3.163, -0.289)	97.44***	221.19**	k		
≥20%	5	219	-25.133*** (-38.650, -11.615)	-1.086*** (-1.610, -0.562)	73.45**	16.20**		7	292	-2.087 (-4.313, 0.138)	-0.686 (-1.398, 0.026)	62.28	12.46			
Number of sessions							< 0.001							< 0.001		
<6 sessions	7	569	-25.781***	-0.545***	42.04	10.49	10.001	5	287	-2.571	-0.239	56.75*	10.00*			
	10	818	(-36.605, -14.956) -25.564***	(-0.806, -0.283) -1.909***	OF 61***	204.31***		10	466	(-6.156, 1.013) -4.055**	(-0.580, 0.102) -1.692**	00 50***	284.23***	k		
≥6 sessions	13	818	-25.564**** (-34.024, -17.104)		95.61	204.31		10	400	(-6.467, -1.643)	-1.692*** (-2.787, -0.598)	98.52	284.23			
Duration of one session							< 0.001							< 0.001		
Daration of one coccion	7	430	-17.375***	-0.880**	0.00	6.59	V0.001	6	252	-4.830*	-1.217	92.17***	86.79***	\0.001		
<1 h			(-20.762, -13.987)	(-1.414, -0.346)						(-8.699, -0.961)	(-2.545, 0.112)					
	13	957	-30.149***	-1.735**	94.17***	142.31***		9	501	-2.813**	-1.136*	96.80***	160.42**	k		
≥1 h			(-39.002, -21.296)	(-2.764, -0.705)						(-4.777, -0.850)	(-2.095, -0.178)					
Length of intervention							< 0.001							< 0.001		
<6 weeks	7	716	-28.502***	-1.956*	93.85***	40.32***	<0.001	3	263	-1.240***	-0.494*	0.00	0.63	<0.001		
ZO WEEKS			(-38.685, -18.318)	(-3.632, -0.280)						(-1.704, -0.775)	(-0.912, -0.077)					
>6 weeks	13	671	-23.996***	-1.147***	87.67***	115.79***		12	490	-4.031**	-1.374**	96.87***	284.44**	k		
			(-32.979, -15.012)	(-1.747, -0.546)						(-6.391, -1.671)	(-2.320, -0.429)					
Form of delivery			,	,			< 0.001			,	,			< 0.001		
Group-delivered	10	849	-30.329***	-1.887**	96.17***	135.77***		6	432	-3.047**	-1.468*	97.37***	149.21**	*		
aroup donvoiou			(-41.395, -19.263)	(-3.213, -0.560)						(-5.187, -0.908)	(-2.841, -0.095)					
Individual-delivered	10	538	-19.934***	-0.963***	47.72	16.72		9	321	-3.955*	-0.707**	90.25***	102.55**	k		
			(-25.494, -14.374)	(-1.386, -0.539)						(-7.009, -0.901)	(-1.231, -0.184)					
Drug treatment							< 0.001							< 0.001		
No drug used	13	1,047	-26.880***	-1.795**	96.23***	206.58***		10	508	-4.259**	-1.630**	98.55	282.91**			
			(-36.232, -17.529)	(-2.820, -0.771)						(-6.761, -1.757)	(-2.744, -0.516)					
Hypnotics	5	236	-22.412***	-0.607**	0.00	1.24		1	40	-5.600*	-0.660*	N/A	0.00			
Other			(-30.592, -14.233)	(-0.965, -0.249)		5.42*		4		(-10.754, -0.446)	(-1.285, -0.036)					
	2	104	-28.393*	-1.230	81.54*				205	-1.605	-0.248	63.86	9.32*			
			(-53.079, -3.708)	(-2.823, 0.363)						(-5.165, 1.955)	(-0.811, 0.315)					
Comorbid disease							< 0.001							< 0.001		
None	8	650	-22.820***	-0.565***	52.33*	14.37*		1	40	-2.300	-0.243	N/A	0.00			
			(-32.381, -13.258)	(-0.819, -0.311)						(-8.335, 3.735)	(-0.882, 0.396)					
Psychiatric	7	430	-31.968***	-2.736**	97.58***	109.84***		8	276	-2.922**	-1.036*	93.67***	125.19**	k		
			(-45.169, -18.766)	(-4.381, -1.090)						(-5.084, -0.759)	(-2.049, -0.023)					
Chronic	5	307	-19.743***	-0.949***	71.19*	12.26*		6	437	-4.623*	-1.627*	94.80***	144.30**	k		
			(-29.190, -10.295)	(-1.482, -0.415)						(-8.368, -0.877)	(-3.192, -0.061)					
Treatment rationale							< 0.001							< 0.001		
No	18	1,247	-27.238***	-1.574***	93.22***	208.59***		11	510	-4.341***	-1.532**	98.22	286.07**	k		
			(-34.324, -20.152)	(-2.334, -0.814)						(-6.656, -2.025)	(-2.525, -0.539)					
Yes	2	140	-12.513*	-0.300	0.00	0.61		4	243	-1.594	-0.238	63.66	8.11*			
			(-24.985, -0.041)	(-0.655, 0.056)						(-4.900, 1.712)	(-0.695, 0.220)					

TABLE 5 | Continued

Subgroups	Wake after sleep onset								Depression							
	Study (n)	Participan (n)	t MD (95% CI)	SMD (95% CI)	MD / ² (%)	MD Q-test	<i>p</i> Between	Study (n)	Participant (n)	MD (95% CI)	SMD (95% CI)	MD /² (%)	MD Q-test	<i>p</i> Between		
Sleep hygiene							< 0.001							<0.001		
No	4	163	-19.641***	-0.640***	0.00	1.15		3	102	-2.961**	-0.593**	0.00	1.17			
			(-28.584, -10.699)	(-0.950, -0.330)						(-4.834, -1.089)	(-0.982, -0.204)					
Yes	16	1,224	-27.058***	-1.647***	94.83***	210.35**	r	12	651	-3.726**	-1.337**	98.39	291.81			
			(-35.085, -19.031)	(-2.505, -0.790)						(-6.133, -1.319)	(-2.295, -0.380)					
Relapse prevention							< 0.001							< 0.001		
No	13	860	-24.200***	-1.469**	89.18***	123.21***	r	7	449	-1.273***	-0.654	0.00	8.12			
			(-31.025, -17.375)	(-2.387, -0.550)						(-1.495, -1.052)	(-1.329, 0.021)					
Yes	7	527	-27.126***	-1.391*	90.08***	89.22***		8	304	-5.120***	-1.765*	93.81***	91.71***			
			(-41.376, -12.876)	(-2.540, -0.241)						(-7.856, -2.384)	(-3.204, -0.327)					
Relaxation training							< 0.001							< 0.001		
No	10	553	-19.597***	-0.949***	62.68*	19.93*		7	313	-2.239*	-0.877*	83.57**	19.99**			
			(-25.892, -13.302)	(-1.404, -0.495)						(-4.182, -0.296)	(-1.616, -0.139)					
Yes	10	834	-30.034***	-1.912**	94.89***	79.11***		8	440	-4.651**	-1.569*	96.81***	221.23**	k		
			(-40.118, -19.950)	(-3.221, -0.604)						(-7.616, -1.686)	(-3.059, -0.080)					
Basic sleep information							< 0.001							< 0.001		
,	11	704	-27.019***	-2.192***	96.59***	199.25***		7	418	-3.103***	-1.613**	96.49***	155.60**	k		
No			(-36.458, -17.579)	(-3.312, -1.072)						(-4.804, -1.403)	(-2.716, -0.509)					
	9	683	-22.827***	-0.497***	25.36	11.78		8	335	-4.021*	-0.353*	86.04***	86.41***			
Yes			(-30.934, -14.721)	(-0.686, -0.308)						(-7.561, -0.480)	(-0.673, -0.032)					

MD, mean difference; SMD, standardized mean difference; CI, confidence interval. $^*p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001.$

mentioned that one of the major goals of CBT interventions on insomnia was to initially limit sleep opportunities at wrong time points in order to increase the pressure for sleep at right time points. Ultimately, the increased sleep drive would lead to an improvement of homeostatic regulation of sleep, and then right sleep opportunities at right time points. Variables such as sleep efficiency, sleep onset latency, and wake after sleep onset were related to homeostatic regulation of sleep, and these variables reported a relatively immediate improvement during the intervention, indicating an improvement of homeostatic regulation (65, 66). Other variables, including total sleep time and number of awakening, may show greater improvements over time as participants continue to practice the skills acquired during CBT intervention and gradually increase their opportunity for sleep (65, 66).

In randomized controlled trial studies, especially studies which were delivered in groups, frequent drop-out of participants may bring negative thoughts, such as untrust of the intervention and therapists, to other participants in the study. Participants would be less focused during the intervention sessions, and the overall effect of intervention would be reduced. Moreover, larger number of intervention sessions and longer duration of single sessions give the therapists a better chance to deliver the contents of the intervention in detail. Participants in these studies will get better understandings of the intervention contents and strategies and more likely to apply the strategies to their real life. We noticed that one of the included studies by Ellis (41) provided only one session of CBT intervention, but this study provided similar results on sleep outcomes compared with other studies which provided larger number of sessions. Considering this study was aimed to treat acute insomnia at early phase, further study was needed to confirm the effects of brief CBT on acute insomnia. In addition, longer intervention period could lead to the impatience of the participants and becoming unwilling to participate. Another important point is the form of delivery of the intervention. Patients in group-delivered CBT could discuss the contents of the interventions with peers, which promoted better understanding of the contents than patients who received CBT treatment alone. Also, the effect of face-to-face CBT was more significant when the patients had co-morbid psychiatric diseases or taking drugs such as hypnotics and antidepressants, which was consistent with the findings in previous study (67). A possible explanation for this result is that psychiatric diseases could be a main cause of insomnia. Although the studies included in this study all used CBT that was specially adapted for treating insomnia, some of the components such as cognitive therapy and relaxation training, still remained the functions of identifying and relieving anxious thoughts, which was effective in treating psychiatric disease symptoms. As a result, depressive or anxious symptoms were relieved due to CBT itself or other drug treatments. The relief of psychiatric disease symptoms led to a better mental health status, and therefore, insomnia was treated more effectively.

Sleep hygiene component was widely used as an individual treatment option in previous studies (68), which aimed to provide a better environment that is suitable for sleep. Although the effect of sleep hygiene alone on insomnia was very limited,

a well-established bedroom environment is still advantageous when patients attempted to make behavioral changes (68). Consistent with the findings from previous study (69), relaxation training component was found to be effective. Relaxation training component taught the patients how to fall asleep more easily, establishing a positive mental condition toward insomnia, and patients with positive mental status are more determined to make behavioral changes and change their old sleep habits in order to improve sleep quality (69). As insomnia was a chronic condition, sustaining improvement is required after CBT intervention is finished. Therefore, relapse prevention is very important in CBT intervention program because the presence of relapse prevention component ensured the long-term effect of the intervention. In contrast, the rarely used components such as treatment rationale and basic sleep information did not seem to have great effects on sleep. These components only provided background information of disease and intervention to the patients, with limited effect on thoughts or behavioral changes. As the number of studies utilizing these components was limited, the effect of these components on sleep outcomes was uncertain.

Efficacy of Face-to-Face CBT Intervention for Psychiatric Diseases

It has been reported in prior study that face-to-face CBT has a significant effect in improving depressive symptoms (65), which is similar to our findings. A possible explanation for the result would be face-to-face CBT intervention established a regularized sleep-wake cycle, and previous study mentioned that patients with a regularized sleep-wake cycle was more likely to experience a reduction in daytime symptoms, including depression and pain (65).

In previous studies, traditional cognitive behavioral showed an overall significant effect on anxiety (70, 71), which was quite different from our findings. However, all of the studies included in this study used CBT for insomnia (CBT-I), a specially adapted form of CBT targeting insomnia only. Different to the traditional CBT interventions, the contents in the CBT-I intervention focused on sleep problems and topics on anxiety were not discussed. On the other hand, only five studies reported anxiety in this study. Due to the limited number of studies, the results of meta-analysis on anxiety may not be representative.

Efficacy of Face-to-Face CBT Intervention on Fatigue

It is recognized that the most direct consequence of poor sleep quality caused by insomnia is fatigue during the day (72). Face-to-face CBT has already shown a significant effect in improving sleep quality. It is plausible that patients receiving CBT intervention have developed a more efficient rest in bed, which led to an apparent reduction in daytime fatigue.

Efficacy of Face-to-Face CBT Intervention on Quality of Life

The proposed mechanism for the improvement of physical and mental health is that face-to-face CBT intervention established a regularized sleep-wake cycle, which enabled the participants

to get enough rest across the night. The adequate rest of the body would be helpful in reducing daytime symptoms such as depression, fatigue, and pain, leading to an overall increase in physical health. In this context, negative thoughts were rectified, and patients would have a more positive attitude toward life after the treatment. The improvement of both physical health and mental health contributed to the overall improvement of quality of life

Strength, Limitations, and Implications of Study

This study included a large number of high quality randomized controlled trial studies on the effectiveness of face-to-face delivered CBT in treating insomnia published in the last 22 years since the first RCT study (51) was published, and the results from subgroup analysis explained the contribution of specific subgroup variables to the overall effects. However, there are a number of limitations for the study. First, articles published in languages other than English were not included in this study. Second, although some of the research outcomes including Pittsburgh Sleep Quality Index, anxiety, fatigue, and scores of SF-12 and SF-36 health surveys were good indicators for sleep quality and health, they were reported in a very limited number of studies, making it hard to conclude if face-to-face CBT had a significant effect on those outcomes. Third, the effect of some CBT components was hard to measure because those components were presented in only one or two of the included studies, and we were not able to measure the heterogenicity and p-value between groups for those components. Therefore, further studies that include more trials with larger sample sizes, published in different languages, are needed to confirm the results of this study.

The using of face-to-face CBT when treating insomnia was highly recommended. When designing the CBT treatment plans, it is recommended that an appropriate design can include more than six sessions, duration of one session >1 h, length of intervention shorter than 6 months, and group delivered intervention. The retention of participants should be encouraged in the program, and the inclusion of the following components was recommended: sleep restriction, stimulus control, cognitive therapy sleep hygiene, relapse prevention, and relaxation training. Treatment rationale and basic sleep information was not recommended, but the inclusion of these components could still be considered if the circumstances permitted.

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CONCLUSION

In conclusion, face-to-face delivered CBT is effective in improving the sleep-related outcomes, including Insomnia Severity Index, Pittsburgh Sleep Quality Index, total sleep time, sleep efficiency, sleep onset latency, and wake after sleep onset in patients with insomnia. It was also found that face-toface delivered CBT can improve other health outcomes in insomnia patients, including depression, fatigue, physical health, and mental health. Face-to-face delivered CBT is more effective when delivered through a larger number of sessions with longer duration of each session, and when delivered in groups. Apart from the most traditional components such as sleep restriction, stimulus control, and cognitive therapy, other components including sleep hygiene, relapse prevention, and relaxation training also showed promising effects and can be considered to add into study designs and treatment plans. More studies with larger sample sizes are required in further studies to confirm the findings.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

DX: data collection, data analysis, and writing of original draft. JS: conceptualization, methodology, data collection, and reviewing and editing of writing. EC and SB: critically reviewing and editing of writing. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt. 2021.798453/full#supplementary-material

Supplementary Figure 1 | Funnel plots for sleep outcomes. (A) Insomnia Severity Index, (B) Pittsburgh Sleep Quality Index, (C) total sleep time, (D) sleep efficiency, (E) sleep onset latency, (F) wake after sleep onset.

Supplementary Figure 2 | Funnel plots for sleep and health outcomes. (A) Number of awakenings, (B) depression, (C) anxiety, (D) fatigue, (E) Physical health, (F) mental health.

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Do Global Adolescents With Food Insecurity Feel Lonely?

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As a proxy measure of socioeconomic status, food insecurity is understudied in mental health-related research. This study aimed to explore the association between food insecurity and loneliness in adolescents. Using cross-sectional data from the Global Student Health Survey (GSHS), 164,993 adolescent participants were included in this study. Food insecurity, loneliness, and other covariates were assessed by self-reported questionnaire. Multivariable logistics regression considering complex survey was used to explore the association between food insecurity and loneliness. The prevalence of loneliness was 10.8% in adolescents. With higher levels of food insecurity, the prevalence of loneliness in general increased, but "most of the time" was the most frequently reported item in terms of food insecurity. Adolescents who reported severe food insecurity had significantly greater odds for loneliness: (1) being most of the time [odd ratio (OR) = 2.54, 95% CI = 2.13-3.02]; (2) always hungry (OR = 1.97, 95% CI = 1.55-2.51). Of all the 53 countries, adolescents from 39 countries reported significantly higher prevalence of loneliness when exposed to food insecurity. The pooled OR was 1.74 (1.60-1.89) with a negligible heterogeneity (higher I-squared was 34.2%). Adolescents with food insecurity were more likely to be exposed to be lonely. Eliminating socioeconomic disparities in adolescents might be a good approach to promote mental health in adolescents. Future studies are encouraged to utilize longitudinal studies to confirm or negate our study findings.

OPEN ACCESS

Edited by:

Jing Sun, Griffith University, Australia

Reviewed by:

Diyang Qu, City University of Hong Kong, Hong Kong SAR, China Yanjie Zhang, Seoul National University, South Korea

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Public Health

Received: 23 November 2021 Accepted: 14 January 2022 Published: 10 February 2022

Citation:

Wu H, Gu Z, Zeng L and Guo T (2022) Do Global Adolescents With Food Insecurity Feel Lonely? Front. Public Health 10:820444. doi: 10.3389/fpubh.2022.820444 Keywords: adolescent, food insecurity, socioeconomic status, loneliness, GSHS

INTRODUCTION

Loneliness is the unpleasant emotional state in response to social isolation and poor social connection (1, 2). Loneliness has become a public health concern, as the prevalence has reached approximately 11% in the general population in 2017 (3), resulting in both physical and mental illnesses (4). For example, several previous studies indicate loneliness-related adverse effects on elevating blood pressure, weakening the immune system as well as such mental problem was linked to the greater possibility of developing diabetes, dementia, and depressive and anxiety disorders. Of note, theses mental problems have been commonly reported among older individuals, immigrants, LGBT, and violence victims (5), for example, poor social relationship or social isolation (loneliness) of adults over 50 and older faced 50, 29 and 32% increased risk of dementia, heart disease and stroke respectively (6); even it can result in the greater possibility of premature death (5).

Wu et al. Food Insecurity and Loneliness

Researchers have also studied loneliness of adolescents as they are experiencing developmental transitions biologically and socially (7–10). Specifically, this age group has started to explore friendship and reduce the opportunity of communicating with their parents (11). Such transition from parents to friends may create a big challenge, resulting in an emotional distress (12, 13). In particular, such dis-comfortable or isolation feeling lasted throughout the entire lifespan. Loneliness is also accompanied with other negative emotion like depression and anxiety among adolescents–such co-existing mental health problems are associated with greater probability of committing suicide (14). Thus, the above-mentioned health problems (caused by loneliness) across different age groups could shorten the lifespan as well as bring financial burden to their family.

To this end, potential risk factors for loneliness have attracted great attention from researchers and clinicians. In particular, previous research findings have indicated the potential role of physical or mental illnesses, poor educational level, economically disadvantaged condition, and social isolation (single and living alone) (15). In addition, a study focused on school-aged adolescents, suggesting that parental divorce, family member with physical or mental illness, being bullied, poor student-teacher relationship, excessive use of social media were significantly predictive of being lonely (16). Except for the abovementioned risk factors, a recent seminal neurological study (14) found that loneliness and hunger (food insecurity refers to the persisting difficulty of accessing to food, leading to disrupted food intake or eating habits) share a home in the brain. Furthermore, previous studies confirmed associations of loneliness with stressrelated outcomes (depression, anxiety, and sleep disturbance) but was not linked to food insecurity. In this context, the question is whether loneliness is related to food insecurity. Thus, the aim of this study was to investigate association between food insecurity and loneliness among adolescents across globe.

METHODS

Study Survey

In this cross-sectional study, the publicly accessible data were retrieved from the GSHS (Details can be found via these Websites: http://www.cdc.gov/gshs; http://www.who.int/ chp/gshs) that aimed to identify the modifiable variables contributing to multiple non-infectious illnesses (also known as chronic diseases-including cancer, diabetic, Alzheimer's disease, and mental disorders) in adolescents. Its associated design and sampling procedure are detailed in previous studies (17, 18). In addition, the protocol of this research project was submitted to the National Government Authorities (e.g., the U.S. Department of Education) and their respective ethical review boards, followed by an evaluation process, generating official approval letters for participating researchers and institutions to start data collection. Specifically, participants were invited to complete the consent form before they volunteered to attend this study as well as they were informed that their private information would be kept confidential and anonymous; they were allowed to withdraw at any time if they feel uncomfortable about the question or item being asked in this survey. For data analysis, we selected the latest year/data from each country if they provided more than two datasets. As a result, 68 countries were finally included and they were nationally representative except for several countries where surveys were conducted in selected regions. Given the fact that economical level may be directly linked to food insecurity, income at country level was categorized as low-income, lower-and middle- income, upper-income and middle-income, and high-income, and this variable was controlled in the analysis. Of note, 53 countries were categorized into four groups (based on the World Back Classification) as follow: (1) low-income countries [n=4]; (2) lower- and middle-income countries [n=24]; (3) upper-and middle-income (n=13); (4) high-income countries (n=12). The characteristics of each country are presented in **Table S1** (see **Supplementary Materials**).

Loneliness (Dependent Variable)

Loneliness as the dependent variable was measured in this study and it involves a single-item question: "During the past 12 months, how often have you felt lonely?". Five independent options (representing experience of participants: 1 = never, rarely = 2, sometimes = 3, most of the time = 4, and 5 = always) were presented to participants for their selection. For data analysis, these responses were dichotomized into groups: (1) no loneliness [never, rarely and sometimes]; (2) affirmative loneliness [most of the time and always], based on previous studies (19).

Food Insecurity (Hunger) (Independent Variable)

Food insecurity (hunger) as a predictive variable was measured in this study and it involves a single-item question (2): "During the past 30 days, how often did you go hungry because there was not enough food in your home?" Five independent options (representing experience of participants: 1 = never, rarely = 2, sometimes = 3, most of the time = 4, and 5 = always) were presented to participants for their selection. These responses were in turn grouped into: (1) no food insecurity (never); (2) moderate food insecurity (rarely/sometimes); (3) severe food insecurity indicates compromised food consumption in terms of quality/quantity, while severe food insecurity represents reduced food intake and disrupted eating patterns.

Controlling Variables

Other variables contributing to loneliness were also extracted in this study in order for more reliable conclusion, including age, sex, physical activity, sedentary behaviors, fruit and vegetable consumption, physical attack, bullying victimization, number of close friends, peer support and parental understanding. These above-mentioned variables were considered as covariates during data analysis in this study.

Statistical Analysis

For both dependent and predictive variables, overall and countryspecific prevalence as descriptive information were computed. To substantiate the association between food insecurity and sleep disturbance (overall and by gender) among adolescents, multivariate logistic regression analyses were conducted while Wu et al. Food Insecurity and Loneliness

controlling for the above-mentioned variables (gender, age, physical activity, sedentary behavior, bullying victimization, and country). Of note, gender-stratified and country-wise analyses were not adjusted for gender and country, respectively. The value of Higgin's I² that represents the degree of heterogeneity across countries was computed (20) and its associated criteria are presented as follow: (1) <40% = negligible heterogeneity; (2) 40-60% = moderate heterogeneity (21). The pooled estimate was computed based on the random-effects model. A complete case analysis was performed for the cases of missing data. Taylor linearization method was applied to account for the sample weight and clustered study design. Results generating from Logistic regression analyses were presented as odds ratios (ORs) with 95% confidence intervals (CIs). The statistical significance level was set at p < 0.05. All statistical analyses were performed using Stata 16.1 (Corp Limited).

RESULT

Prevalence in terms of the degrees of food insecurity is reported in Supplementary data. Being most of time and always hungry were 3.3 and 2.3% of the global adolescents (n=164,993). In addition, the prevalence of complaining loneliness has reached 10.8% among these adolescents. The prevalence of loneliness across different severity levels of food insecurity is presented in (**Figure 1**). Specifically, adolescents with severe food insecurity were linked to greater possibility of reporting loneliness in the overall and gender-stratified samples, as compared with their peers with less severe food insecurity (never/rarely/sometimes).

In the fully adjusted model, **Table 1** has shown results on association between food insecurity and loneliness. Adolescents who complained "rarely, sometimes, most of the time, or always hungry" were linked to higher perception of loneliness, as compared to their peers who reported food insecurity. In particular, adolescents who reported severe food insecurity contributed to significantly greater odds for loneliness: (1) being most of the time [OR = 2.54, 95% CI = 2.13-3.02]; (2) always hungry [OR = 1.97, 95% CI = 1.55-2.51]. In addition, a similar result on significant relationship was observed in both boys and girls (**Table 1**).

Figure 2 shows results in terms of country-wise multivariate logistic regression analysis. adolescents who were always hungry or in most the time (representing severe food insecurity) were significantly linked to an increased risk of perceiving loneliness in 39 of the 53 included countries, as compared to less severe food insecurity (never/rarely/sometimes). The pooled OR is 1.74 (1.60–1.89), with the country-based I-square of 34.2% (negligible heterogeneity). Higher I-squared value ($I^2 = 59.5\%$, representing moderate heterogeneity) was observed in lower- and middle-income countries while investigating the association between food insecurity and loneliness.

DISCUSSION

Main Findings

With respect to the role of food insecurity in emotional regulation, to our knowledge, the current study is the first time to

investigate the association between food insecurity and loneliness among adolescents, especially in a global sample. Being most of time and always hungry were 3.3 and 2.3% of the global adolescents, while the prevalence of complaining loneliness was 10.8%. In addition, results indicated that 41.7% of adolescents with loneliness complained with severe food insecurity (reflected by most of time and always)-the number is relatively smaller in other three groups (never, rarely, and sometime). In other words, the prevalence of loneliness has become greater as the degree of food insecurity elevated. With the adjustment of covariates, being hungry in most of time has the greatest likelihood of complaining loneliness, followed by being always hungry, which is independent of sexes (boys and girls). Furthermore, serious food insecurity was observed to associate, of great significance, with a higher likelihood of complaining loneliness in 39 of 53 economies within the global studying sample, with overall OR being 1.74 (1.60-1.89, $I^2 = 34.2\%$, negligible heterogeneity). Taking closer into income-based sub-group analysis, significant association between food insecurity and loneliness was only observed in lower- and middle-income countries, with great degree of heterogeneity.

Interpretation of Findings

Approximately 46% of adolescents reported moderate food insecurity. Such number is relatively higher as compared to a previous study based on the Global School-based Student Health Survey, but the severe food insecurity is relatively smaller in the current study (22). Accumulating evidence indicate that the negative effects of food insecurity on both psychological and physical measures, which may be attributed to malnutrition (lack of nutrient intake). Such impairment has become more serious as adolescents experience developmental transition in a relatively rapid speed, which specifically resulted in short height (greater BMI–obesity), neuro-cognitive impairment, sleep disturbance (23), leading to poor academic performance at school and worse social relationship. Such public health issue requires greater attention.

Investigation on association between food insecurity and loneliness, based on this global sample, can be confirmed. Previous studies mainly focused on association of food insecurity with other mental health measures including stress, depression, anxiety, suicidal behaviors (24–26), and sleep condition. To this end, our results in the present study adds to existing literature. From the biological perspective, a previous study, especially those relating to brain science, have come up with the conclusion that the part of the brain lighting up in the condition of hungry shares the same part in active as that of the situation of feeling lonely, thus may, to a certain extent, imply the correlation between food insecurity and loneliness, somehow could as well be considered as supporting materials indicating the association between food insecurity and loneliness. If understanding the findings from the standpoint of contextual factors, when talking about food security and one direct consequence, hunger, lack of money may always be the first thought. Indeed, shortage of living resources caused by poverty may not directly lead to the condition of isolation and loneliness, yet bare livelihood would undoubtedly result in dilemma, especially when facing necessity in respect

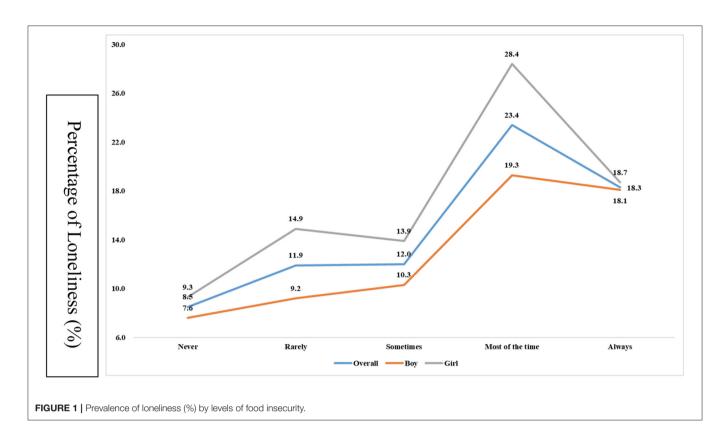


TABLE 1 | Association between food insecurity and loneliness based on logistic regression model.

		Overalla			Boy ^b			Girl ^b		
	OR	959	%CI	OR	959	%CI	OR	95%CI		
Never	Reference group									
Rarely	1.21	1.08	1.35	1.06	0.87	1.29	1.36	1.18	1.57	
Sometimes	1.40	1.22	1.61	1.32	1.04	1.67	1.49	1.32	1.68	
Most of the time	2.54	2.13	3.02	2.32	1.76	3.07	2.80	2.31	3.41	
Always	1.97	1.55	2.51	2.20	1.51	3.23	1.81	1.41	2.31	

a Model controlled for age, sex, fruit and vegetable consumption, physically attack, bullying victimization, number of close friends, peer support and parental understanding.

of various kinds of expenditure, such as housing loan, rent, children's education fee and health care fee. It is not difficult to foresee that such difficulties may, of great possibility, aggravate the feeling of helplessness, which may probably lead to and increase the degree of loneliness.

Overall speaking, the heterogeneity of the correlation between food insecurity and loneliness was negligible, indicating that the correlation between food insecurity and loneliness was not something rare in individual cases, it, instead, was common among adolescents within the sample of selected economies (different levels of income). Yet, large difference concerning the association between food insecurity and loneliness was found especially in the category of lower- and middle-income economies, which could be understood from such perspective that even falling into the same scope, social determinants

influencing the degree of food insecurity, including but not limited to economy, culture, environment and related policies, would vary, probably to a large extent, the relationship among these factors and food insecurity may still need to be further clarified so as to accordingly look deeper into the association between food insecurity and loneliness.

Implications for Practice

In addition to the results, corresponding analysis indeed implied the prevalence of food insecurity (27) and loneliness (28) among adolescents, thus it would be helpful in providing one perspective to understand the correlation between such two issues and to accordingly put forward targeted plans and strategies plus carrying out effective measures, including but not limited to the increase of continuous capital investment and the establishment

^bModel controlled for age, sex, fruit and vegetable consumption, physically attack, bullying victimization, number of close friends, peer support and parental understanding except for sex.

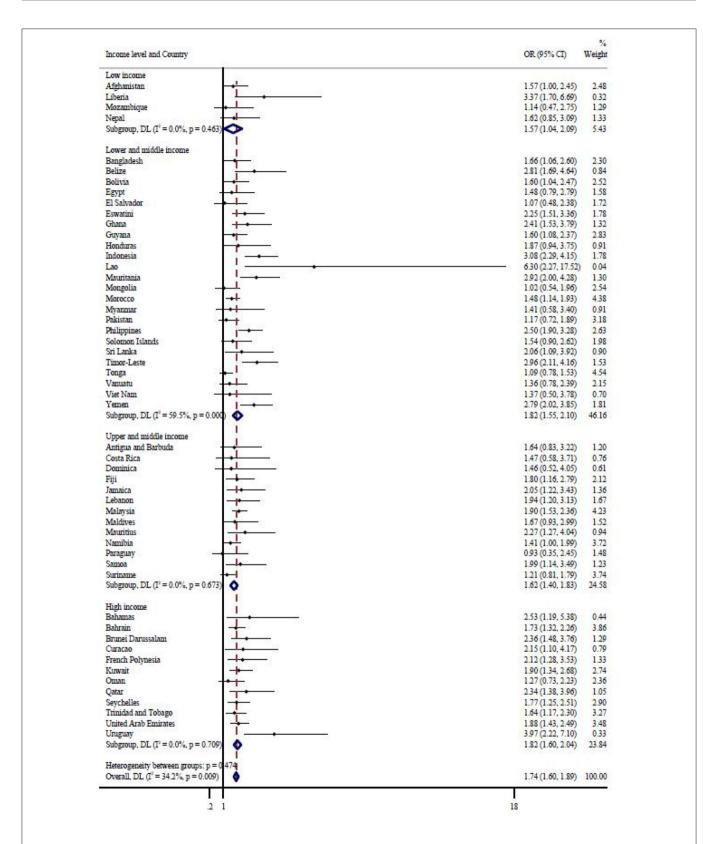


FIGURE 2 | Country-wise association between severe food insecurity (most of the time/always hungry) and loneliness estimated by multivariable logistic regression. OR, Odds ratio; CI, Confidence interval. Reference category is no food insecurity (never, rarely, sometimes). Models are adjusted for age, sex, fruit and vegetable consumption, physically attack, bullying victimization, number of close friends, peer support and parental understanding. Overall estimates were obtained by meta-analysis with random effects.

of proper coordination mechanisms concerning food supplies to students, especially to those from families that are shortage of most basic food security. The findings of the possible role of food insecurity in forming loneliness as well-indicates the necessity of more detailed researches on hunger-caused loneliness and mental health protection and intervention. Specifically, together with persistent researches concerning brain science and respective working mechanisms, especially those relating to neuroscience, well-directed analysis and assessment need to be carried out, with the inclusion of more factors such as eating habits.

Limitations and Strength

Indeed, compared with existing observations (26, 29), this study, instead of only focusing on one or few economies with a relatively small sample, paid attention to a larger sample of adolescents from 53 economies of various income levels so as to look into the relationship between food insecurity and loneliness, providing a relatively wider perspective of understanding in respect of influence factors of loneliness. Despite such advantage, some limitations of this study need to be admitted. Firstly, the data from GSHS was collected based on self-reporting, which means that recall bias and desirability bias would be possible to some extent. Secondly, as the data adopted were cross-sectional, longitudinal study, in addition to current research perspective, might still be conducted in case the association between food insecurity and loneliness was uneasy to clearly establish. Thirdly, as previously noted, the level of food loneliness was decided by the frequency of hunger, yet such aspect may not be sufficient to come up with a comprehensive picture of food loneliness. Fourth, loneliness in this study mainly refers to the kind probably caused by hunger, thus the finding applicable to other kinds of loneliness should be made with caution.

CONCLUSION

Food insecurity has found to be prevalent among adolescents and to be positive correlation with the level of loneliness within the economies of this study. As food insecurity, especially with the continuous epidemic globally, tends to be more severe, it

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is not difficult to foresee that loneliness would become one of the global mental problem, which urgently require effective and promptly resolutions, including but not limited to targeted policies and measures with official and unofficial efforts plus international cooperation and coordination among developed and developing countries.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

HW: manuscript writing-original draft preparation, methodology, and analysis. TG: supervision and validation. ZG and LZ: editing. All authors: review and editing. All authors contributed to the article and approved the submitted version.

FUNDING

This work was supported by grant of National Natural Science Foundation of China (No. 31871115).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh. 2022.820444/full#supplementary-material

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Possible Avoidant Personality Disorder Magnifies the Association Between Bullying Victimization and Depressive Symptoms Among Chinese University Freshmen

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OPEN ACCESS

Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Lan Xiao Cao, Shenzhen Children's Hospital, China Chuanjun Zhuo, Tianjin Anding Hospital, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 02 December 2021 Accepted: 24 January 2022 Published: 17 February 2022

Citation:

Xu Y-M, Pu S-S, Li Y and Zhong B-L (2022) Possible Avoidant Personality Disorder Magnifies the Association Between Bullying Victimization and Depressive Symptoms Among Chinese University Freshmen. Front. Psychiatry 13:822185. doi: 10.3389/fpsyt.2022.822185 ¹ Wuhan Mental Health Center, School of Mental Health and Psychological Sciences, Anhui Medical University, Wuhan, China, ² Department of Psychiatry, Wuhan Mental Health Center, Wuhan, China

Background: Bullying victimization has been associated with depressive symptoms in Chinese university students. This study examined the moderating effect of possible avoidant personality disorder (APD) on association between bullying victimization and depressive symptoms in university freshmen.

Methods: A total of 1,453 freshmen were recruited from a comprehensive university in Wuhan, China, and administered a self-report questionnaire. The APD subscale of Personality Diagnostic Questionnaire–Version 4 and Beck Depression Inventory were used to measure the presence of possible APD and depressive symptoms, respectively. The moderating effect of possible APD was examined by testing the statistical significance of the interaction between victimization and possible APD in multiple logistic regression analysis.

Results: The prevalence of depressive symptoms was 24.8%. In multiple logistic regression analysis, the interaction between bullying victimization and possible APD was significantly associated with depressive symptoms (OR: 1.80, P=0.029). Subsequent subgroup analyses according to the status of possible APD showed that, the victimization-depression association was stronger among freshmen with possible APD (OR: 3.23, P<0.001) than those without possible APD (OR: 1.82, P=0.001).

Conclusion: In Chinese university freshmen, bullying victimization is significantly associated with depressive symptoms, and possible APD magnifies the victimization-depression association. Bullied freshmen, particularly freshmen with possible APD, could be considered as the target group of campus-based depression intervention programs.

Keywords: bullying victimization, depressive symptoms, avoidant personality, freshmen, China

INTRODUCTION

The transitioning from junior middle schools to universities is challenging for most university freshmen because of difficulties in adjusting to new surroundings, forming new self-identities, forging friendships, gaining independence, and overcoming academic pressure (1, 2). Accordingly, studies have shown the high risk of mental health problems in first-year university students, in particular depression; for example, as high as 35.4–41.4% of the Chinese university freshmen suffer from depressive symptoms (3, 4).

The etiology of depression is complex and multifactorial, and, in the population of university students, commonly reported factors associated with depressive symptoms were female sex, rural origin, low family income, inadequate social support, loneliness, negative life events, academic stress, and certain personality features such as high neuroticism (3–6). Despite extensive research on the epidemiology of depressive symptoms in university students, few studies have examined mechanisms linking these factors and depressive symptoms.

Bullying victimization refers to exposure to aggressive behavior repeatedly and over time from one or more perpetrators who have greater physical or social power than their victims (7). Convincing evidence has shown the causal association between being bullied and mental health problems in children and adolescents including anxiety, depression, non-suicidal self-injury, and suicidal behaviors (8). Although traditional bullying such as verbal and physical bullying is primarily recognized as a public health problem in primary and middle school students, bullying victimization is also prevalent among university students (9). For example, as high as 88.2% of the Chinese university freshmen experienced verbal bullying in the past 12 months and Chinese university students who are bullied are two times more likely than those who are not bullied to have depressive symptoms (9, 10).

The vulnerability–stress model of depression argues that personality interacts with stressors to influence the development of depressive symptoms (11–13). Several subtypes of personality psychopathology have been associated with the increased risk of major depression such as depressive, borderline, and avoidant personality disorders (14–17). In the literature, the mechanisms underlying associations between depressive and borderline personality disorders and depressive disorders have been extensively examined, but the way in which avoidant personality disorder (APD) increases the risk of depression remains poorly understood (18–20).

Persons with APD avoid intimate and social contact with others, are sensitive to negative criticism and rejection, and have a high level of fear of being ridiculed by others (20). Findings from a comparative study have shown that compared to university students without APD, those with APD have significantly lower levels of self-esteem and, therefore, are more likely to experience negative affect (21).

In Chinese universities, although only 0.54–0.66% of the students meet the DSM-IV diagnostic criteria for APD (22, 23), 30.4–33.4% of the students have possible APD, as defined by the APD subscale of Personality Diagnostic Questionnaire–Version

4 (PDQ-4), a widely used screener of personality disorders (24-26). Despite not a clinical diagnosis of APD, possible APD has been found to be a stable personality trait in Chinese university students and the severity of depressive symptoms is significantly associated with the APD subscale score of PDQ-4 in this population (26, 27). Because of the vulnerability of persons with APD, we speculated that Chinese university students with possible APD would experience more depressive symptoms if they were bullied. Since understanding the contextual roles of APD and other personality disorders on the relationship between bullying victimization and depressive symptoms would facilitate the development of campus-based depression prevention programs in Chinese universities, this study examined the moderating role of possible APD on the bullying-depression association in Chinese university freshmen, that is, whether the negative effect of bullying victimization on depressive symptoms differed between students with and without possible APD.

MATERIALS AND METHODS

Participants

This study was part of a large-scale survey, which investigated mental health, quality of life, and personality among fresh students of a comprehensive university in Wuhan, China, between November and December 2019. Eligible respondents were first-year undergraduates who were of Chinese nationality and voluntary to join the study. We randomly selected seven schools from a total of 19 schools of the university and invited all the freshmen to participate in the survey.

The Ethics Committee of Wuhan Mental Health Center approved the study protocol. All respondents signed the informed consent before the formal survey.

Procedures and Instruments

We used a standardized self-administered questionnaire to gather data on sociodemographics, lifestyle, experience of being bullied, and depressive symptoms.

Sociodemographic factors included sex, age, ethnic group, place of origin (urban vs. rural), living arrangement (with roommates vs. with family members), self-rated family financial status (good, moderate, poor), the only-child status, and marital status of parents (married vs. others).

Lifestyle factors included current drinking and current smoking. According to the official manual of the Chinese Adolescent Health-Related/Risk Behavior Surveillance, current drinkers and smokers were defined as individuals who consumed any alcoholic beverage and smoked at least once in the past month, respectively (28).

Questions for assessing bullying victimization were adapted from previous school bullying studies in China (29–31), which asked respondents about the presence of any one of the seven subtypes of traditional bullying victimization at universities during any time of the past 12 months: "been teased in a mean or hurtful way," "been asked for money or other possessions in a mean or hurtful way," "been left out of a group or ignored on purpose in a mean or hurtful way", "been threatened or

intimidated in a mean or hurtful way," "been hit, kicked, pushed, squeezed, or locked in a mean or hurtful way," "had sexual jokes or gestures made to you in a mean or hurtful way," and "had your things stolen or damaged in a mean or hurtful way".

We used the APD subscale of the validated Chinese PDQ-4 to identify the possible presence of APD among respondents (32). The subscale has seven self-report questions and responses are in a true/false (1/0) format. According to previous studies (24, 33), a total score of four or higher was used to denote possible APD in Chinese university students.

Depressive symptoms were measured with the validated Chinese 21-item Beck Depression Inventory, the Second Edition (BDI-II), which is one of the most widely used scales for assessing the severity of depressive symptoms in both clinical and non-clinical populations in China, including university students (34–36). All BDI-II items use a 0–3 scale to rate the magnitude to which a persons has experienced each depressive symptom during the past 2 weeks. The total score ranges between zero and 63 with a cut-off score of 14 or more denoting the presence of depressive symptoms.

Statistical Analysis

Rates of depressive symptoms were calculated and comparisons between/across subgroups according to sociodemographics were made using the univariate logistic regression analysis. To examine the independent victimization-depression association, a multiple logistic regression analysis was performed, which entered bullying victimization as the main predictor; possible APD, sociodemographic factors, and lifestyle factors as the covariates; and depressive symptoms as the outcome variable ("main effect model"). To test whether the victimizationdepression association differed between students with and without possible APD, an interaction term, the production of victimization and possible APD, was included as an additional independent variable in the main effect model ("interactive effect model"). A statistically significant interaction term suggested the presence of the moderating effect of possible APD on the victimization-depression association. Finally, we repeated the above multiple logistic regression analyses within samples with and without possible APD to estimate the adjusted victimizationdepression associations in the contexts of the presence and absence of possible APD, respectively. We quantified the factoroutcome association by using odds ratio (OR) and its 95% confidence interval (CI). All statistical analyses were performed by using SPSS 25.0, assuming a two-sided test at the 0.05 level of statistical significance.

RESULTS

Altogether, 1,557 freshmen were invited and 1,453 completed the survey questionnaire (response rate: 93.3%). Among the completers, 868 (59.7%) were boys and the mean age was 20.3 years (standard deviation: 0.9, range: 16–26). The prevalence rates of bullying victimization, possible APD, and depressive symptoms were 39.2, 31.7, and 24.8%, respectively. Other detailed sociodemographic and lifestyle characteristics of the study sample are displayed in **Table 1**.

In both the univariate analysis and the main effect model, both bullying victimization and possible APD were significantly associated with depressive symptoms (OR: 2.50 and 4.39, P < 0.001; OR: 2.39 and 4.20, P < 0.001). In the interactive effect model, the interaction between bullying victimization and possible APD was significantly associated with depressive symptoms (OR: 1.80, P = 0.029). In the subsequent subgroup analyses according to the status of possible APD, the victimization-depression association was stronger among freshmen with possible APD (OR: 3.23, P < 0.001) than those without possible APD (OR: 1.82, P = 0.001) (Table 1).

DISCUSSION

To the best of our knowledge, this is the first study in China that examined both the victimization-depression association and the moderating effect of possible APD on the victimization-depression association among university freshmen. Compared to the 8.0% 12-month prevalence of bullying victimization in college students in Changsha, China (9), we found a much higher 12-month prevalence of bullying victimization in university freshmen (39.2%). However, due to the heterogeneity in definitions and timeframes of depressive symptoms, prevalence rate of depressive symptoms in our study are lower than those reported in prior studies (24.8% vs. 35.4-41.4%) (3, 4). Nevertheless, the figure, nearly one-fourth of the freshmen were depressed, still indicates that depressive symptoms are a substantial mental health problem in Chinese university freshmen and there is an urgent need for developing intervention programs to prevent or reduce depression in this population.

In the sample of Chinese university freshmen, we observed significant and independent associations of depressive symptoms with bullying victimization and possible APD, which are consistent with findings from studies with middle school students and other populations (8, 26). The significant victimization-APD interactive effect on depression and greater victimizationdepression association in freshmen with than those without possible APD suggest that possible APD magnifies the negative effect of bullying victimization on emotional health in university freshmen. Since the interactive effect was independent from sociodemographic and lifestyle factors, we speculated that some core features of APD may explain the moderating role of possible APD on victimization-depression association. First, social support can buffer the negative effect of a stressful event on the mental health of individuals (37). Because persons with APD avoid social contact with others and are more likely to have insufficient social support to cope with stressful situations, freshmen with possible APD would be more likely to be depressed if they were bullied. Second, persons with APD are overly concerned with "looking foolish" and tend to adopt avoidance coping strategies to deal with stressful situations, so bullied students are more likely to be stressed and depressed if they had possible APD.

This stud has two limitations. First, our assessment of bullying victimization did not include cyberbullying victimization, which

Bullying, Avoidant Personality, and Depression

February 2022 | Volume 13 | Article 822185

TABLE 1 | Relationships across bullying victimization, possible avoidant personality disorder (APD), and depressive symptoms among Chinese university freshmen.

Variables		n	Number of Univariate logistic regression analysis students (%)			Multiple logistic regression analysis		Multiple logistic regression analysis with the interaction term		Multiple logistic regression analysis in sample without possible APD		Multiple logistic regression analysis in sample with possible APD	
				Odds ratio (95% CI)	P	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Bullying victimization >	< Possible AF	D						1.80 (1.06, 3.04)	0.029				
Sex	Male	868	200 (23.0)	1		1		1		1		1	
	Female	585	161 (27.5)	1.27 (0.99, 1.61)	0.053	1.54 (1.17, 2.04)	0.002	1.55 (1.17, 2.06)	0.002	1.55 (1.17, 2.06)	0.039	1.56 (1.02, 2.39)	0.040
Age-group (years)	≤20	861	216 (25.1)	1		1		1		1		1	
	>20	592	145 (24.5)	0.97 (0.76, 1.24)	0.797	0.98 (0.75, 1.28)	0.877	0.98 (0.75, 1.28)	0.871	0.83 (0.58, 1.20)	0.316	1.18 (0.79, 1.77)	0.417
Ethnic group	Han	1,339	330 (24.6)	1		1		1		1		1	
	Minority	114	31 (27.2)	1.14 (0.74, 1.76)	0.546	1.25 (0.78, 2.00)	0.346	1.28 (0.80, 2.04)	0.306	1.64 (0.93, 2.92)	0.089	0.83 (0.38, 1.80)	0.636
Place of origin	Urban	1,050	246 (23.4)	1		1				1		1	
	Rural	403	115 (28.5)	1.31 (1.01, 1.69)	0.044	1.22 (0.88, 1.68)	0.238	1.22 (0.88, 1.70)	0.229	1.22 (0.79, 1.90)	0.375	1.29 (0.79, 2.11)	0.313
Living arrangement	With roommates		3 349 (24.6)	1		1		1		1		1	
	With family members	35	12 (34.3)	1.60 (0.79, 3.25)	0.195	1.68 (0.76, 3.71)	0.201	1.67 (0.76, 3.68)	0.202	2.42 (0.93, 6.29)	0.070	0.88 (0.25, 3.11)	0.843
Self-rated family financial status	Good	299	75 (24.1)	1		1		1		1		1	
	Moderate	1,027	242 (23.6)	0.92 (0.68, 1.24)	0.588	1.12 (0.80, 1.55)	0.518	1.11 (0.80, 1.55)	0.422	1.12 (0.70, 1.78)	0.642	1.11 (0.69, 1.80)	0.671
	Poor	127	44 (34.6)	1.58 (1.01, 2.48)	0.045	1.64 (0.94, 2.85)	0.083	1.60 (0.91, 2.80)	0.101	1.31 (0.59, 2.92)	0.513	1.98 (0.87, 4.50)	0.104
The only child	No	373	92 (24.7)	1		1		1		1		1	
	Yes	1,080	269 (24.9)	1.01 (0.77, 1.33)	0.926	1.32 (0.93, 1.87)	0.119	1.35 (0.95, 1.91)	0.094	1.30 (0.89, 2.06)	0.275	1.55 (0.90, 2.66)	0.113
Marital status of parents	Married	1,363	3 326 (23.9)	1		1		1				1	
	Others*	90	35 (38.9)	2.02 (1.30, 3.15)	0.002	1.83 (1.12, 2.99)	0.016	1.87 (1.15, 3.06)	0.012	1.97 (1.04, 3.74)	0.038	1.87 (0.87, 4.02)	0.108
Current drinking	No	884	210 (23.8)	1		1		1				1	
	Yes	569	151 (26.5)	1.16 (0.91, 1.48)	0.231	1.28 (0.97, 1.68)	0.085	1.28 (0.97, 1.69)	0.08	1.36 (0.94, 1.98)	0.105	1.18 (0.78, 1.80)	0.436
Current smoking	No	1,379	339 (24.6)	1		1		1				1	
	Yes	73	22 (30.1)	1.33 (0.79, 2.22)	0.286	1.19 (0.67, 2.11)	0.550	1.21 (0.68, 2.16)	0.512	1.44 (0.69, 3.01)	0.327	0.95 (0.39, 2.29)	0.901
Bullying victimization	No	883	159 (18.0)	1		1		1				1	
	Yes	570	202 (35.4)	2.50 (1.96, 3.19)	< 0.001	2.39 (1.84, 3.10)	< 0.001	1.84 (1.29, 2.61)	0.001	1.82 (1.28, 2.59)	0.001	3.23 (2.17, 4.82)	< 0.001
Possible APD	No	993	155 (15.6)	1		1							
	Yes	460	206 (44.8)	4.39 (3.41, 5.64)	< 0.001	4.20 (3.24, 5.44)	< 0.001	3.17 (2.21, 4.54)	< 0.001				

^{*}Others included never-married, remarried, cohabiting, separated, divorced, and widowed.

is also prevalent and associated with depression in university students (38). So the current study can not examine the moderating effect of possible APD on association between cyberbullying victimization and depression. Second, the sample was selected from a comprehensive university in Wuhan, China, and fresh students from universities of other cities and other categories (i.e., medical) were not included, so there might be selection bias in the study sample. Third, some psychosocial factors associated with depressive symptoms such as social support and possible dependent personality were not measured and included in the adjustment analysis. Further studies are needed to exclude the confounding effects of these unmeasured psychosocial factors.

In summary, in Chinese university freshmen, bullying victimization is significantly associated with depressive symptoms, and possible APD magnifies the victimization-depression association. Bullied freshmen, particularly freshmen with possible APD, could be considered as the target group of campus-based depression prevention programs. In addition, campus-based programs designed to prevent depression in freshmen may include bullying intervention program, psychosocial support, social skills training, and stress management training.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of Wuhan Mental Health Center. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

Y-MX: acquisition and analysis of data for the study, drafting the paper, and interpretation of data for the study. Y-MX and S-SP: design and acquisition of data for the study. YL and B-LZ: drafting the paper, revising the paper for important intellectual content, and interpretation of data for the study. All authors contributed to the article and approved the submitted version.

FUNDING

This work was supported by National Natural Science Foundation of China (Grant Number: 71774060). The funding source listed had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

ACKNOWLEDGMENTS

The authors thank all the research staff for their team collaboration work and all the students involved in this study for their cooperation and support.

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Temporal Trends in the Incidence and Disability Adjusted Life Years of Schizophrenia in China Over 30 Years

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Background: Schizophrenia is an important public health problem in China. This study aims to assess the long-term trends in the incidence and disability-adjusted life years (DALYs) rate of schizophrenia in China between 1990 and 2019.

Methods: The incidence and DALYs data were drawn from the Global Burden of Disease Study 2019, and an age-period-cohort model was used in the analysis.

Results: The age-standardized incidence rate (ASIR) and age-standardized DALYs rate (ASDR) of schizophrenia increased by 0.3 and 3.7% for both sexes between 1990 and 2019. For males, the local drift for incidence was higher than 0 (P < 0.05) in those aged 10 to 29 years (local drifts, 0.01 to 0.26%) and lower than 0 (P < 0.05) in those aged 35 to 74 years (local drifts, -1.01 to -0.06%). For females, the local drift was higher than 0 (P < 0.05) in those aged 10 to 34 years (local drifts, 0.05 to 0.26%) and lower than 0 (P < 0.05) in those aged 40 to 74 years (local drifts, -0.86 to -0.11%). The local drift for DALYs rate was higher than 0 (P < 0.05) in the age group from 10 to 69 years (local drifts, 0.06 to 0.26% for males and 0.06 to 0.28% for females). The estimated period and cohort relative risks (RR) for DALYs rate of schizophrenia were found in monotonic upward patterns, and the cohort RR for the incidence increased as the birth cohort moved forward starting with those born in 1972.

Conclusion: Although the crude incidence of schizophrenia has decreased in China, the ASIR, ASDR, and crude DALYs rate all showed a general increasing trend over the last three decades. The DALYs rate continue to increase as the birth cohort moved forward, and the increasing trend of incidence was also found in individuals born after 1972. More efforts are needed to promote mental health in China.

Keywords: age-period-cohort analysis, schizophrenia, incidence, trends, China, disability adjusted life years (DALYs)

OPEN ACCESS

Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Jiayuan Wu, Affiliated Hospital of Guangdong Medical University, China Sumaira Mubarik, Wuhan University, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 08 December 2021 Accepted: 14 February 2022 Published: 09 March 2022

Citation:

Dong W, Liu Y, Sun J, Liu Y, Sun Z and Bai R (2022) Temporal Trends in the Incidence and Disability Adjusted Life Years of Schizophrenia in China Over 30 Years. Front. Psychiatry 13:831188. doi: 10.3389/fpsyt.2022.83118

INTRODUCTION

Schizophrenia is a chronic and serious mental disease characterized by distortions in language, perception, emotions, thinking, behavior and sense of self (1). Patients with schizophrenia are more likely to suffer from HIV infection, obstetric complications, cardiovascular disease, obesity and other physical diseases than the general population (2). Compared with the general population, the

life expectancy of patients with schizophrenia is shortened by 10 to 25 years (3–5). Schizophrenia not only seriously affects the patients themselves and their families but also brings a heavy burden to society (6). In 2017, there were 19.78 million schizophrenic patients worldwide, an increase of 62.74% over 1990 (7), and this number may continue to rise in the future (8).

Globally, schizophrenia is more common in East Asia and South Asia, especially in China and India (7). In 2017, disability-adjusted life years (DALYs) in China and India accounted for 35% of the total DALYs of schizophrenia, with new cases accounting for 45% (7). China had the largest absolute number of newly diagnosed schizophrenia cases among the 20 most populous countries in the world in 2017 (0.29 million, 95% UI = 0.26 to 0.33 million), and it is also the country with the highest DALYs (3.67 million, 95% UI = 2.75 to 4.5 million) (7). Schizophrenia has become an important public health problem in China (9).

In 2008, China enacted the "National Guiding Outline for the Development of the Mental Health Service System (2008-2015), followed by regulations and laws including "Regulations on the Management of Severe Mental Diseases (2012 Edition)" and "Mental Health Law." These efforts all contributed to promoting the development of mental health in China (10). From 2005 to 2015, the number of specialist psychiatric hospitals nationwide was 557 in 2005, 874 in 2010, and 1235 in 2015. Meanwhile, the total number of psychiatric beds increased from 109,000 in 2005 to 433,100 in 2015. In 2015, the number of psychiatric beds per 10,000 populations nationwide was 3.15, and the number of psychiatric professionals per 10,000 populations was 4.16 (10). However, there is still gap when compared with the average number of psychiatric beds and psychiatric professionals in middle and high-income countries (10). Moreover, 29% of registered psychiatrists in China only had a junior college diploma, and 14% had not received any training (10).

Previous studies have shown the trend in the prevalence of schizophrenia in China over time (11). However, few studies have explored changes in the incidence and DALYs rates of schizophrenia in different age groups in China. Furthermore, the potential effects underlying the temporal trends are still unknown. Statistical methods used commonly to assess the trends of disease in populations are descriptive, agnostic, and nonparametric (12), which may miss some important information. Parametric statistical models would play a more prominent role, especially the age-period-cohort (APC) frameworks, which would discern three types of time-varying phenomena from the temporal trends: Age, period, and cohort effects. In this study, we used APC frameworks to investigate the long-term trend in the incidence and DALYs rates of schizophrenia in China and explored the potential effect of age, period, and cohort on the incidence and DALYs rates of schizophrenia, which would provide more information to help us understand the temporal trends of schizophrenia in China. The results are a necessary supplement to the existing research on the burden of schizophrenia in China and provide a scientific basis for evidence-based public health policies and the optimal allocation of health resources.

MATERIALS AND METHODS

Data Sources

The data were extracted from the Global Burden of Disease (GBD) 2019 database. GBD 2019 provided a standardized, replicable approach and comprehensive estimation of incidence, prevalence, and years lived with disability for a total of 369 diseases and injuries for 204 countries and territories (13). In the GBD, the incidence data of schizophrenia in China was systematically reviewed from community representative epidemiological studies (14). Studies found were evaluated against a series of inclusion criteria, including cross-sectional or longitudinal design, reported estimates of incidence, utilized the International Classification of Diseases (ICD) or Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria, reported estimates of incidence in the form of hazard rates, representative study design, etc. More information on the inclusion criteria is available elsewhere (8). Reported estimates of incidence were entered in DisMod-MR. DisMod-MR is a Bayesian meta-regression instrument, which can compute the age-specific and sex-specific estimates from the available data (14). DALYs is a summary measure of population health, which was composed of years lived with disability and years of life lost due to premature mortality. In GBD 2019, disability weight (0.778 for acute state, and 0.588 for residual state) was used to estimate the DALYs of schizophrenia. More information on the calculation of DALYs is available elsewhere (13). The GBD world population standard was used for the calculation of agestandardized rate of schizophrenia (13).

In this study, schizophrenia was confirmed based on DSM or ICD diagnostic criteria (DSM-IV-TR: 295.10-295.30, 295.60, 295.90; ICD 10: F20) (13).

Data Analysis

This study used the APC framework to assess the incidence and DALYs rates of schizophrenia in China and to assess the potential impact of age, period, and cohort effects on these trends. The APC model was developed based on Poisson distribution, and can be generally expressed as follows (15):

$$Y = log(M) = \mu + \alpha Age_i + \beta Period_j + \gamma Cohort_k + \varepsilon$$
 (1)

Where, M for the incidence/DALYs rate of the corresponding age group, μ for the intercept item, α , β , and γ for the age, period and cohort effect, and ϵ for random error. To address the problem of identification of the model parameters (perfect collinearity of the age, period, and cohort variables), weighted least squares regression was used to partition the effects of age, period, and cohort effect (12, 16).

By using the APC framework, the following parameters were evaluated: local drifts, represents annual percentage change of the expected age-specific rates over time. The longitudinal age curve represents the age effect, which indicates the risk of incidence/DALYs of schizophrenia in different age groups in the reference cohort adjusted for period effects. Period rate ratios (RR) represent period effects, indicates the risk of incidence/DALYs of schizophrenia over the years belonging

to different periods. Cohort RR represent cohort effects, indicate the risks of incidence/DALYs of schizophrenia in different birth cohorts.

To conduct APC analysis, we divided the population, incidence, and DALYs data into 6 periods from 1990–1994 (median 1992) to 2015–2019 (median 2017) at 5-year intervals. We also divided the age data into 13 consecutive age groups (10–14 years old to 70–74 years old at five-year intervals). The birth cohort was divided into 18 birth cohorts from 1918–1922 to 2003–2007 at intervals of 5 years.

Estimable parameters were estimated using the American National Cancer Institute's APC web tool (Biostatistics Branch, National Cancer Institute, Bethesda, MD, United States) (12). By default, the average age, period, and birth cohort were set as the reference group. In this study, the central age group (40–44 years), period group (2000–2004), and birth cohort (cohort 1958–1962) were set as references.

Wald chi-square tests were used to estimate the significance of estimable functions. All statistical tests were two-sided, and a *P-value* less than 0.05 was considered statistically significant.

RESULTS

Trends in the Incidence and Disability-Adjusted Life Years Rate of Schizophrenia in China for the Period From 1990 to 2019

Figure 1A shows the age-standardized incidence rate (ASIR) and crude incidence rate (CIR) of schizophrenia in China from 1990 to 2019 in both sexes. In 1990, the ASIR of schizophrenia was 18.41/100,000, and it increased to 18.47/100,000 in 2019 (increased by of 0.3%). The CIR in 1990 was 21.40/100,000, and it decreased to 18.14/100,000 in 2019 (decreased by 15.2%).

Figure 1B shows the trends in CIR and ASIR of schizophrenia by sex from 1990 to 2019 in China. For males, the CIR decreased from 22.23/100,000 in 1990 to 19.28/100,000 in 2019 (decreased by 13.3%), and the ASIR decreased from 19.28/100,000 in 1990 to 19.26/100,000 in 2019 (decreased by 0.1%). For females, the CIR decreased from 20.51/100,000 in 1990 to 16.96/100,000 in 2019 (decreased by 17.3%), and the ASIR increased from 17.47/100,000 in 1990 to 17.66/100,000 in 2019 (increased by 1.1%).

In 1990, the age-standardized DALYs rate (ASDR) of schizophrenia was 195.04/100,000, and it increased to 202.42/100,000 in 2019 (increased by 3.8%). The crude DALYs of schizophrenia was 195.98/100,000, and it increased to 250.99/100,000 in 2019 (increased by 28.1%) (**Figure 2A**).

For males, the crude DALYs rate increased from 202.85/100,000 in 1990 to 258.54/100,000 in 2019 (increased by 27.4%), and the ASDR increased from 201.90/100,000 in 1990 to 209.30/100,000 in 2019 (increased by 3.7%). For females, the crude DALYs rate increased from 188.66/100,000 in 1990 to 243.15/100,000 in 2019 (increased by 28.9%), and the ASDR increased from 187.62/100,000 in 1990 to 195.36/100,000 in 2019 (increased by 4.1%) (**Figure 2B**).

Local Drift Values for the Incidence and Disability-Adjusted Life Years Rate of Schizophrenia in China

Figure 3 shows the annual percentage change of the expected age-specific rates (local drifts) over the last three decades. As **Figure 3A** shows, for males, the local drift for incidence was higher than 0 (significance with P < 0.05) in the age group from 10 to 29 years (local drifts, 0.01 to 0.26%), and lower than 0 (significance with P < 0.05) in the age group from 35 to 74 years (local drifts, -1.01 to -0.06%). For females, the local drift was higher than 0 (significance with P < 0.05) in the age group from 10 to 34 years (local drifts, 0.05 to 0.26%), and lower than 0 (significance with P < 0.05) in the age group from 40 to 74 years (local drifts, -0.86 to -0.11%). The greatest increasing of schizophrenia incidence were found in females aged 30 to 34 years (local drifts = 0.26%, 95% confidence interval [CI] = 0.13 to 0.40%). The greatest improvements was found in males aged 70-74 years (local drifts = -1.01%, 95%CI = -1.42 to -0.61%).

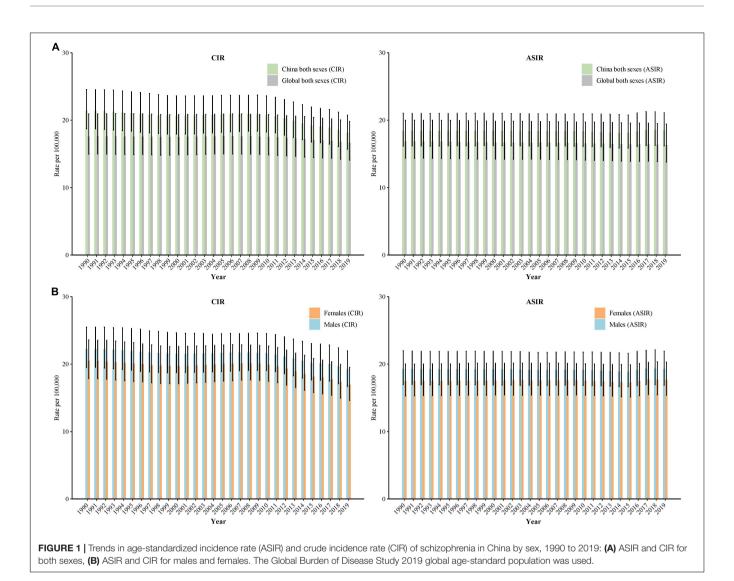
As **Figure 3B** shows, for both males and females, the local drift for DALYs was higher than 0 (significance with P < 0.05) in the age group from 10 to 69 years (local drifts, 0.06 to 0.26% for males and 0.06 to 0.28% for females). The greatest increasing of DALYs were found in both males and females aged 10 to 14 years, local drifts = 0.26% (95%CI: 0.13%, 0.39%) for males and 0.28% (95%CI: 0.15%, 0.40%) for females.

Longitudinal Age Curves of the Incidence and Disability-Adjusted Life Years Rate of Schizophrenia in China

Figure 4 shows the longitudinal age curve of the incidence and DALYs rate of schizophrenia. After adjusting for period effects, in the reference cohort, the incidence and DALYs rate of schizophrenia all showed a general V-shape reversal with aging, which increased firstly, then decreased. For both males and females, individuals aged 20–24 years old had the highest incidence of schizophrenia (53.48/100,000 person years for males, 54.97/100,000 person years for females), and individuals aged 35–39 years had the highest DALYs rate of schizophrenia (409.70/100,000 person years for males, 382.24/100,000 person years for females).

Period Rate Ratios of Schizophrenia Incidence and Disability-Adjusted Life Years Rate in China

Based on the Wald tests (**Table 1**), the period effects were statistically significant for both sexes (P < 0.05 for all). **Figure 5** shows the estimated period effects by sex during the whole study period. For the incidence, the period effects showed a decreasing tendency during the period from 1990–1994 to 2010–2014 for both males and females, with the period RR decreased from 1.02 to 0.96 (decreased by 5.7%), and 1.01 to 0.97 (decreased by 4.1%), respectively. However, this decreasing tendency slowed down in males (0.96 to 0.956) and stopped in females (0.97 to 0.97) in the period from 2015 to 2019. For the DALYs rate, the period



RR showed similar monotonic increased patterns for both sexes (increased by 3.9% for males, and 4.0% for females).

Cohort Rate Ratios of Schizophrenia Incidence and Disability-Adjusted Life Years Rate in China

Based on the Wald tests, the cohort effects were statistically significant for both sexes (P < 0.05 for all) (**Table 1**). **Figure 6** shows the estimated cohort effects by sex. For the incidence, the cohort RR showed a decreasing trend for the cohort individuals born before 1972 (birth cohort 1918–1922 to 1968–1972), with cohort RR decreased from 1.37 to 0.99 (decreased by 27.9%) in males, and 1.27 to 0.99 (decreased by 22.4%) in females; however, this decreasing tendency was reversed afterward and increased sharply in the recent birth cohort (birth cohort 1968–1972 to 2003–2007), with cohort RR increased from 0.99 to 1.08 (increased by 8.9%) in males, and 0.99 to 1.08 (increased by 10.6%) in females. For the DALYs rate, the cohort RR showed general increased

patterns for both sexes (increased by 14.7% for males, and 17.1% for females).

DISCUSSION

Our research illustrates the long-term trend in the incidence and DALYs rate of schizophrenia in China and detected the potential effects of age, period, and birth cohort. To our knowledge, this is the first study that used the APC framework to explore the trend in the incidence and DALYs rate of schizophrenia in China. Our research showed that compared with the decreased CIR, the ASIR of schizophrenia increased in China from 1990 to 2019. Although the incidence of schizophrenia decreased in the elderly population, it increased in the young population. The risk of schizophrenia incidence continued to increase in people born after 1972. For DALYs, both crude DALYs rate and ASDR increased over the past three decades, this increasing trend was found in almost all age groups, and the period and cohort effects all showed an overall increasing trend.

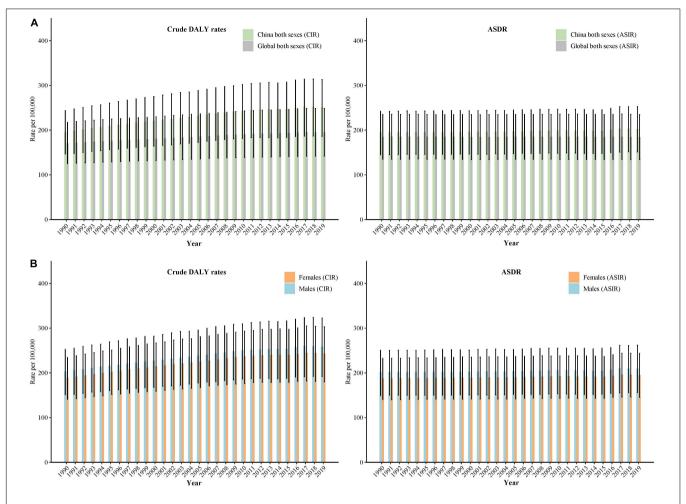


FIGURE 2 | Trends in crude disability adjusted life years (DALYs) rate and age-standardized DALYs rate (ASDR) of schizophrenia in China by sex, 1990 to 2019: (A) ASDR and crude DALYs rate for both sexes, (B) ASDR and crude DALYs rate for males and females. The Global Burden of Disease Study 2019 global age-standard population was used.

In our study, we found a slight increase in the ASIR of schizophrenia in China, which was not consistent with the decreasing tendency globally (7). Rapid urbanization may be the possible reason for the increase in age-standardized incidence of schizophrenia in China. Since the initiation of the reform and opening policy in 1978, China has experienced an unprecedented scale of urbanization - a nearly fivefold increase in the urban population in the past four decades (17). Urbanization creates opportunities for improved health conditions and high-quality health care, but it also brings huge health risk factors associated with schizophrenia (18), e.g., migration, crowded living conditions, stress in the working environment, and disparities in health care delivery (19), which may lead to a high risk of mental health problems for urban residents (17). In a previous study, a 10% increase in the degree of urbanicity was associated with an increased risk of schizophrenia in China (OR = 1.44) (17). Drug abuse may be another reason for the increased age-standardized incidence of schizophrenia in China. In the late 1980s, the drug problem reappeared in China, and spread quickly in the early 1990s (20).

Previous evidence has illustrated associations between drug abuse and an increased risk of developing schizophrenia later in life (21). In addition, more willingness to admit symptoms than before (22), may also contribute to the increase of schizophrenia incidence. In this study, the crude DALYs rate and ASDR of schizophrenia in China all showed an increasing tendency. Besides the possible reason described above, increasing life expectancy in China may also play a role in increasing the burden of DALYs.

In our study, for the different sexes, females showed a slightly increasing trend of ASIR in schizophrenia. This may be related to females being more likely to be affected by the urbanization process (23). During the process of urbanization, a mass of populations leave rural areas and live and work in cities. As mentioned above, urbanization arose problems such as lack of contact with nature, social insecurity, pollution, and social disparities, which have been shown to be particularly associated with mental health among females with lower socio-economic status (24). In addition, females were more vulnerable to repeated stress exposures than males (25).

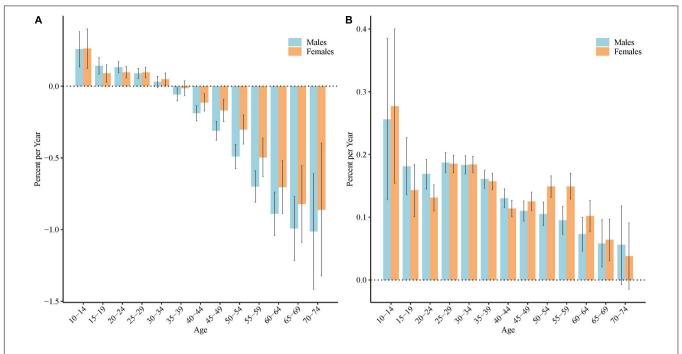


FIGURE 3 | Local drift values for the incidence and disability adjusted life years (DALYs) rate of schizophrenia in China. Age group-specific annual percent change (local drift) in the incidence (A) and DALYs rate (B) of schizophrenia and corresponding 95% confidence intervals.

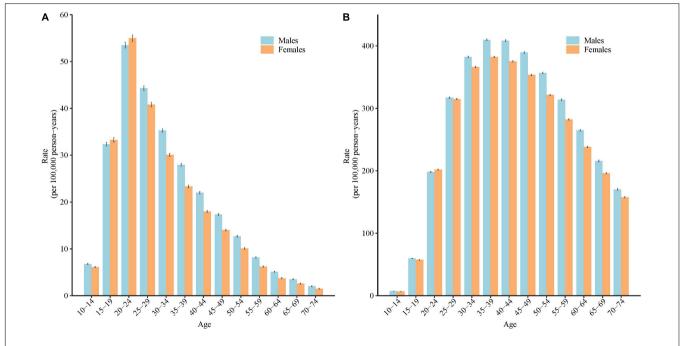


FIGURE 4 | Longitudinal age curves of the incidence and disability adjusted life years (DALYs) rate of schizophrenia in China: (A) incidence, (B) DALYs rate. Fitted longitudinal age-specific rates of the incidence/DALYs rate of schizophrenia (per 100,000 person-years) and the corresponding 95% confidence intervals (some of them were too narrow to show in the figure).

In our study, the CIR, ASIR, ASDR, and crude DALYs rate were higher in males than in females during the study period. Previous studies have reported that the incidence of schizophrenia in men is usually slightly higher than that in

women, with a risk ratio of 1.4 (26). These sex differences in schizophrenia can be interpreted by different hypotheses. Hormone hypotheses emphasize that gonadal hormones played an important role in the sex differences in schizophrenia.

TABLE 1 | Wald Chi-Square tests for estimable functions in the APC model

Null hypothesis		Incid	lence			DALYs	rates			
	Male	es	Fema	les	Male	es	Females			
	Chi-square	P-Value	Chi-square	P-Value	Chi-square	P-Value	Chi-square	P-Value		
All period RR = 1	178.9	<0.001	67.8	<0.001	789.2	<0.001	929.7	<0.001		
All cohort RR = 1	334.9	< 0.001	151.0	< 0.001	1070.7	< 0.001	1535.2	< 0.001		
All local Drifts = Net Drift	334.1	< 0.001	143.3	< 0.001	115.8	< 0.001	275.1	< 0.001		

DALYs, disability-adjusted life years. RR, Rate Ratio. Net Drift, annual percentage change of the expected age-adjusted rates over time. Local Drift, annual percentage change of the expected age-specific rates over time.

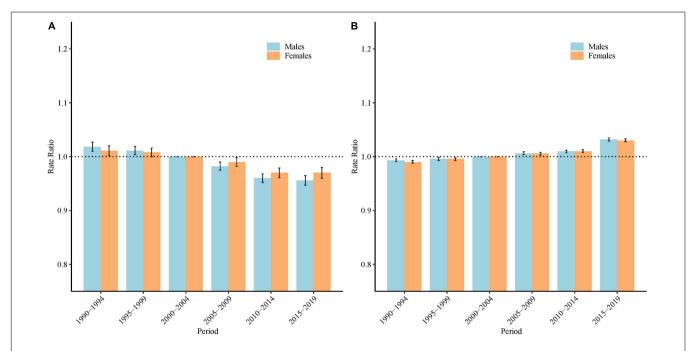


FIGURE 5 | Period rate ratios (RR) of the incidence and disability adjusted life years (DALYs) rate of schizophrenia by sex in China: (A) incidence, (B) DALYs rate. The RR of each period compared with the reference period (2000 to 2004) adjusted for age and nonlinear cohort effects and the corresponding 95% confidence intervals. The black dash lines indicates an RR = 1.

Estrogen may play neuroprotective roles in females against schizophrenia (27). Sex chromosome hypotheses emphasize that sex chromosomes may roles in neurodevelopment and sexspecific patterns of transmission in schizophrenia patients (27). In addition, differences in brain maturity and morphology, and differences in behavior patterns for specific ages and sex may also contribute to the sex differences of schizophrenia burden (28).

In this study, we found a certain difference between the CIR (crude DALYs rate) and ASIR (ASDR) of schizophrenia for both sexes. This may be related to changes in the age structure of China. Over the past more than half a century, the proportion of young people in China has decreased, while the proportion of elderly people has increased (29). Meanwhile, schizophrenia is common among younger adults (7). Crude rates were calculated based on the whole population, which was vulnerable by the age distribution of the population. With the decline in the cases of schizophrenia, the crude incidence rate of schizophrenia has decreased. A previous study predicted

that China will continue to age (30), and the reduction in the proportion of young people may further decrease the CIR of the incidence of schizophrenia. While this seems to be a good expectation in terms of the CIR of schizophrenia in China, our study also indicated that unlike the decreasing trends among the elderly, the incidence of schizophrenia in young people in China has increased in the past 30 years. It seems that the increase in the incidence of schizophrenia in young people has not reversed the downward trend in the CIR in schizophrenia in the past 30 years, but it still reminds us that more attention should be given to the problem of schizophrenia among young people in China.

Age is an important demographic risk factor that affects the incidence and DALYs of schizophrenia. In our study, we found that both the incidence and DALYs rate of schizophrenia showed a V-shape reversal with aging, which was consistent with previous studies (7). Schizophrenia nearly always occurs in late adolescence or early adulthood, when the prefrontal cortex is

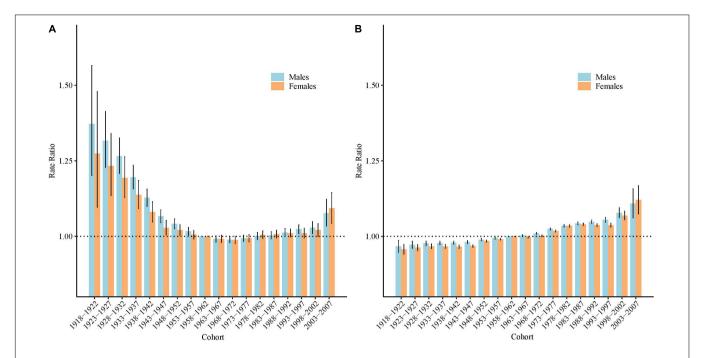


FIGURE 6 | Cohort rate ratios (RR) of the incidence and disability adjusted life years (DALYs) rate of schizophrenia by sex in China: (A) incidence, (B) DALYs rate. The RR of each cohort compared with the reference cohort (1958 to 1962) adjusted for age and nonlinear period effects and the corresponding 95% confidence intervals. The black dash lines indicates an RR = 1.

still developing (31). Previous longitudinal neuroimaging studies have demonstrated that the prefrontal cortex is the last to mature (32). Some researchers believe that a variety of outside factors can cause the prefrontal cortex to finish developing differently than it would have, which would cause the development of schizophrenia in young people (33). From a psychology point of view, the late-adolescent onset of schizophrenia is a consequence of blocked psychological maturation during adolescence (34), and the troubled teenage state, such like stress, depress, and limited understanding of other people's minds, fails to be solved with normal maturation, and this state deteriorates into the appearance of schizophrenia symptoms (34).

The period effect reflects variations in the outcome over time that influence all age groups simultaneously, and the cohort effect reflects the changes in outcome across groups of individuals with the same birth year (35). Although under certain restrictions, the period effect and cohort effect can be estimated separately by the period RR and cohort RR, respectively, it is not easy to interpret them in practice (36). When the period effect influences all age groups, certain age groups would be affected simultaneously, which leads to the cohort effect to some extent. Different birth cohorts are often born in different periods, inevitably having an impact on the period effect (35). Therefore, in this study, we comprehensibly discussed the possible reasons for the trends in the period and cohort effects.

In this study, both the period effect and cohort effect for the incidence of schizophrenia show a decreasing trend in the earlier period (before 2015) and older birth cohort (those born before the year 1972). This may be related to one or more of China's achievements in mental health. Since 1949, psychiatric hospitals

have been gradually established in different provinces. Since 1958, mental health facilities were established in some provinces to train professionals and to develop work plans (early detection and treatment and relapse prevention of psychoses). Health, civil affairs, and public security departments have established a three-level network, including cities, districts/counties, and streets/towns, to prevent and treat psychoses since 1980, and successful experiences with treatment models were extended to other places. Although the demands of the economic reform that emerged over the 1990s rendered some models unviable, by the late 1990s, the Ministry of Health of China began to reconsider the principles of and approaches to mental health care. In 2002, an 8-year mental health plan was signed to build an effective mental health system, thus accelerating mental health legislation, increasing citizen awareness, strengthening mental health services, and developing mental health human resources (37). In 2004, China launched a mental health reform plan to incorporate mental health into the scope of public health (37). By 2009, the plan covered 96.88 million people in 112 cities and had trained nearly 30,000 professional and technical personnel, including psychiatrists, psychiatric nurses, community physicians, case managers, community workers, public safety personnel, and family members (38). In 2013, China's "Mental Health Law" went into effect, which was the first national law on mental health. The government's continued attention and investment partially explained the continued decrease in period and cohort risk of schizophrenia incidence. However, although the period effect and cohort effect show a decreasing trend in the earlier period and birth cohort, as mentioned before, the burden of schizophrenia risk factors,

including urbanization, is increasing in China. The period and cohort effect already showed the potential unfavorable trends - the decreasing trend of period RR slowed down and stalled in the recent period year, and the decreasing trend of cohort RR was reversed with people born after 1972. In addition, period and cohort effects for the DALYs rate of schizophrenia all showed an unfavorable trend. As the incidence risk increases in newly born young people, schizophrenia may bring a huge burden to population health in China, which calls for more effective efforts.

For the potential increased risk of schizophrenia, more prevention and management measures are needed. The government is suggested to allocate sufficient human and facilities resources, strengthen the ability of the general practitioners to identify high-risk populations, and take early intervention to prevent high-risk individuals from developing schizophrenia (39). In addition, social support is also important for individuals to manage stressful life events and prevent triggers for schizophrenia.

Although this study used the APC framework to illustrate the long-term trend in the incidence and DALYs rate of schizophrenia in China and detect the underlying effect of this trend, which may provide supplementary information for understanding the burden of schizophrenia in China, there are still some limitations that should be noted. First, this is an ecological study; ecological studies examine the characteristics of population groups rather than individuals, and further individual-based studies are needed to confirm the results. Second, because GBD data do not distinguish the incidence/DALYs rate of schizophrenia in urban and rural areas, this study does not analyze the long-term trend of schizophrenia incidence and DALYs rate in urban and rural areas in China. Considering the difference between the prevalence of schizophrenia in this region (11), future analyses of the incidence and DALYs of schizophrenia in rural and urban areas in China are needed.

CONCLUSION

In conclusion, our research shows that although the CIR of schizophrenia generally decreased in China over the last

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30 years, the ASIR, ASDR, and crude DALYs rate increased. By using the APC framework, we affirmed that the incidence of schizophrenia decreased in the elderly population, but it has increased among young people, and the DALYs rate increased in almost all age groups. In the same birth cohort, the incidence and DALYs rate of schizophrenia all showed a V-shape reversal with aging, individuals aged 20-24 years old had the highest incidence of schizophrenia, and individuals aged 35-39 years old had the highest DALYs rate of schizophrenia. The estimated period and cohort RR for DALYs rate all showed potential unfavorable trends. For incidence, the decreasing trend of period RR slowed down and stalled in the recent period year, and the cohort RR increased as the birth cohort moved forward starting with those born in 1972. These potential trends all play a warning call for more effective efforts. Considering that there is no evidence that China's urbanization process will stop soon, it is necessary to pay attention to vulnerable populations, and policies also need to be formulated to promote mental health.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: http://ghdx.healthdata.org/gbd-2019.

AUTHOR CONTRIBUTIONS

WD and RB initially conceived the research idea, designed the study, performed data collection, management, and analysis. ZS provided administrative support. WD and RB drafted the original manuscript. YuL, JS, YaL, and ZS critically revised the manuscript. All co-authors have read and approved the final manuscript.

ACKNOWLEDGMENTS

We are grateful to individuals who participated in the study.

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Network Analysis of Time Use and Depressive Symptoms Among Emerging Adults: Findings From the Guizhou Population Health Cohort Study

OPEN ACCESS

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Edited by: Liye Zou, Shenzhen University, China

Reviewed by:

Sitong Chen, Victoria University, Australia Filipa Isabel Ferreira, Instituto Universitário da Maia (ISMAI), Portugal

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 05 November 2021 Accepted: 09 March 2022 Published: 01 April 2022

Citation:

Ma Z, Zhao F, Wang Y, Liu T and Chao N (2022) Network Analysis of Time Use and Depressive Symptoms Among Emerging Adults: Findings From the Guizhou Population Health Cohort Study. Front. Psychiatry 13:809745. doi: 10.3389/fpsyt.2022.809745 ¹ Computational Communication Collaboratory, School of Journalism and Communication, Nanjing University, Nanjing, China, ² Prevention and Control Institute for Chronic Non-communicable Diseases, Guizhou Provincial Center for Disease Control and Prevention, Guiyang, China, ³ School of Media and Communications, Shenzhen University, Shenzhen, China

Background: To date, the relationship between diverse time use behaviors and depression status among emerging adults have not been disentangled in the literature. Therefore, if and how the time displacement mechanism activates depressive symptoms among emerging adults remains unclear.

Methods: To fill this gap in the literature, we employed a network analysis to make estimations. The emerging adult sample (N = 1,811) was collected by the Guizhou Population Health Cohort Study. Time use behaviors were measured by an adaption of the self-administered International Physical Activity Questionnaire, and depressive symptoms were assessed using the 9-item Patient Health Questionnaire (PHQ-9).

Results: The results revealed that the time displacement mechanism of emerging adults differed from that of adolescents. Sleep duration was not crowded out by other activities, while the time spent on computer use was found to be negatively related to time spent on heavy work activities. Moreover, computer use behavior triggered three depressive symptoms ("Anhedonia," "Guilt," and "Motor"), but inhibited "Suicide." The results of the directed acyclic graph revealed that females and heavy drinkers were at risk of depression.

Limitations: The study sample was confined to only one province, which may limit its generalizability. The cross-sectional design impeded the ability to draw causal inferences.

Conclusion: Our results enhance the current understanding of the internal mechanism of how time use behaviors influence depressive symptoms among emerging adults.

Keywords: time use, screen time, time displacement, depression, emerging adult, network analysis

INTRODUCTION

Existing literature have established the effects of physical activity (1, 2), screen time (3, 4), and sleep duration (5, 6) on the depression status of both, adolescent and adult populations. Moreover, previous studies revealed that unhealthy time use activities (e.g., excessive sedentary time, inadequate sleep duration) were risk predictors of physiological diseases, including cardiovascular diseases (7-9), hypertension (10, 11), and cancers (12-14). Based on plentiful existing evidence, the World Health Organization (WHO) and other health institutes proposed updated time use guidelines to direct people's daily activities for substantial health benefits (15-18). For example, WHO recommended that adults (aged 18-64 years) should do at least 150-300 min of moderate-intensity aerobic physical activities; or at least 75-150 min of vigorous-intensity aerobic physical activities; or an equivalent combination of moderateand vigorous-intensity activities throughout the week (15). The Canadian Society for Exercise Physiology recommended that adults (aged 18-64 years) should do at least 150 min of moderate to vigorous aerobic physical activities per week, and get 7-9 h of good-quality sleep (17).

However, the existing research pool still has two significant gaps. First, the number of studies focusing on emerging adults, who are undergoing a unique stage of psychological development, and present different mental health features than adolescents and adults older than thirty, are relatively few. Second, previous studies that adopted a regression analysis approach were unable to disentangle the underlying linkages among diverse time use behaviors and depressive symptoms.

Emerging adults are those individuals who are leaving adolescence behind to experience young adulthood, a definition originally proposed by Arnett (19). The concept of emerging adulthood describes a period of development during which an individual has already passed through adolescence, but has not entirely taken on adult responsibility and independent decision making (19, 20). The emerging adulthood stage was initially defined as the age group 18-25 years (19); this was later revised to the age group 18-29 (20). During emerging adulthood, individuals are already biologically mature, but most have not yet established a stable structure in diverse domains of life (e.g., intimate relationships, work, and fertility). These individuals are not identified as socially mature, and thus, they present different behaviors and psychological patterns than either adolescents or adults in their thirties. Previous studies have expounded on the unique patterns observed in emerging adults in several areas, such as substance use (21), Internet addition (22), technology adoption (23), and social integration (24). Previous research revealed that peak alcohol consumption and drug abuse occur during emerging adulthood (25, 26), and some instances of excessive substance use appear to be normative behavior for emerging adults (25, 27). Moreover, one recent study reported that emerging adults present the highest online social network usage among all age groups (28). They have a significantly higher likelihood of adopting pathological social network use behaviors, which further decreases self-regulation, escalates the depression status, and magnifies the likelihood of involvement

in cyberbullying (29, 30). However, it remains unclear as to how diverse time use behaviors affect depressive symptoms among emerging adults.

Studies focusing on adolescents provide potential theoretical mechanisms to understand the relationship between time use and depressive symptoms in emerging adults. Previous research has identified that screen time is a crucial predictor of depression (4, 31, 32). Based on this point, Boers et al. (33) put forth three explanations: time displacement, social comparison, and reinforcing spiral. Time displacement refers to the time required for healthy activities (e.g., physical activity and sleep) that may be displaced by excessive sedentary activities, such as screen time (34), causing potential depressive reactions (31, 35). Social comparison states that one's self-esteem may be damaged by focusing on favorable objects (e.g., having an "ideal body shape" or a "luxury lifestyle"), which triggers relative deprivation, a significant predictor of individual psychological wellbeing (36, 37). A reinforcing spiral implies a selective exposure scenario that is reinforced by both individual intention and algorithmic recommendation of specific media content. Individuals are thereby repeatedly exposed to certain types of content, and depressive reactions might be triggered if individuals view excessive volumes of content that may lead to depression (33). Among these three theories, the social comparison and reinforcing spiral mechanisms were mostly used to understand the negative effects of media on children and adolescents (38-41). Given that emerging adults present a more mature decisionmaking pattern during daily activities (19), they are relatively less sensitive toward media contents compared with children and adolescents. Thus, we believe that time displacement mechanism is an optimal approach for interpreting the relationship between time use and depression in emerging adults.

Moreover, life course theorists have indicated that behaviors or experiences during one's early adult life may have potential effects on one's later life, and such effects tend to accumulate (42, 43). For example, adverse experiences during childhood were found to be crucial risk factors in experiencing psychotic symptoms and health burden (44, 45). However, one recent study demonstrated that individuals who experienced traumatic events during emerging adulthood reported worse health status compared with individuals who only experienced traumatic events during adolescence (46). Such cumulatively disadvantageous phenomena were reported in diverse age groups (47–49). But the cause of the disadvantages was rarely discussed. Therefore, understanding the time displacement mechanism in terms of diverse time use behaviors, and its impact on depressive symptoms during emerging adulthood also has enormous potential for predicting long-term health outcomes.

Existing studies also have several limitations as they have been unable to clarify the detailed patterns of relationship between diverse time use behaviors and depressive symptoms. First, both psychiatric and psychological studies usually presuppose one specific disorder as a latent structure model, with several symptoms as observed variables (50). The latent structure model implies that related symptoms are mutually independent; however, this approach ignores the inter-trigger mechanism among these symptoms (51, 52). Moreover, studies that adopt

the traditional regression approach often use the sum score or mean score of a group of symptoms to represent a certain disorder (50). Although this operation is effective in screening for the prevalence of a certain disorder, it neglects the occurrence of specific symptoms in non-disordered individuals. Additionally, most time use studies that adopt a regression approach can only consider one dependent variable in one model, which also presents limitations in simultaneously revealing the interrelationships among diverse time use behaviors.

The network analysis approach was employed in this study to address the methodological gap described above. This approach presupposes that a mental disorder is a complex system, in which the relationships and network properties of different symptoms are identified in detail (51, 53). Both the inter-trigger mechanisms among different symptoms, and the relationships between external shocks and psychiatric reactions can be modeled when using the network analysis approach (54-56). Recent studies have also adopted network analyses to identify the central domains of a specific psychological construct (57), and the central symptoms within a certain mental disorder (58, 59). Moreover, the network analysis approach provides novel insights in understanding the predictability of a certain symptom within a complex network (60, 61), and further identifying the potential interventions of clinical practices (60). Additionally, the network analysis approach was also employed to investigate the issue of comorbidity among different disorders (62). It has the methodological advantage of distinguishing between the bridge symptom and shared symptom among diverse mental disorders (63).

In the current study, both time use behavior and depressive symptoms were complex systems. We employed the network approach in three ways: First, it was difficult to highlight the intercorrelation pattern of diverse time use behavior—namely, the time displacement, using the traditional linear regression approach. Whereas, network analysis has the merit to illustrate the intercorrelation pattern. Second, diverse time use behaviors were conceptually external shocks that may trigger depressive symptoms via different paths which should be calculated via the network analysis. Third, one type of network method—the Bayesian network, provides a novel approach to algorithmically characterize cross-sectional data as a causal system (64). We thus used the Bayesian network to present the potential causal predictors of depression among emerging adults.

Considering the two literature gaps described, the current study employed network analysis to answer the following two questions: (1) Does the time displacement mechanism explain the inter-correlations among diverse time use behaviors in emerging adults? (2) Does the time displacement mechanism explain the connections between time use behaviors and depressive symptoms in emerging adults?

MATERIALS AND METHODS

Participants

The data used in this study were obtained from the Guizhou Population Health Cohort Study, a prospective

community-based cohort in Guizhou Province, China. Based on a multistage proportional stratified cluster sampling method, a total of 9,280 adult residents of 48 townships in 12 districts in Guizhou Province were included. The original study took place from 2010 to 2012. The inclusion criteria were: (1) age 18 years or above; (2) living in the study region, and having no plan to move; (3) completing the survey questionnaire and blood sampling; and (4) providing written informed consent. For the current study, we exclude 7,408 participants who were 30 years old or older. Further 38 participants with missing depressive symptom variables, 21 participants with outlier responses on time use variables, and two participants with missing height or weight information were excluded. Finally, the remaining 1,811 participants were eligible for our analysis.

This study was carried out in accordance with the stipulations of the Declaration of Helsinki and approved by the Institutional Review Board of Guizhou Provincial Center for Disease Control and Prevention (No. S2017-02). All participants provided written informed consent at enrollment. The information was collected by trained investigators using a structured questionnaire via faceto-face interviews.

Assessment Measures

Depressive Symptoms

We used the 9-item Patient Health Questionnaire (PHQ-9) to measure participants' depressive symptoms (65). Participants were asked to rate how frequently they experienced nine specific depressive symptoms during the previous 2 weeks on a 4-point Likert scale, ranging from 0 = not at all to 3 = nearly every day. A higher score for a certain item indicates that participants were experiencing severe symptoms, while a higher total score indicates that participants overall had a severe depressive status. The PHQ-9 used in the current study presented excellent reliability (Cronbach's alpha = 0.828). The one-factor construct was also supported by the confirmatory factor analyses (CFI = 0.980, TLI = 0.964, RMSEA = 0.057, SRMR = 0.030).

Time Use

We measured nine time use behaviors in participants across three domains: physical activities (five items), screen activities (three items), and sleep duration (one item). Time use behaviors were measured by adapting the long version of the self-administered International Physical Activity Questionnaire (IPAQ-L) (66). Measures of time use on physical activities included weekly minutes spent on heavy work activities (vigorous-intensity physical activities during work, farming, and housework), moderate work activities (moderate-intensity physical activities during work, farming, and housework), traffic time (walking or cycling for transport), heavy leisure activities (vigorous-intensity leisure activities such as long-distance running, swimming, and playing football), and moderate leisure activities (moderateintensity leisure activities such as quick walking and performing Tai Chi). Measures of time use for screen activities included weekly minutes spent on watching TV, using computer, and playing video games. Sleep duration was measured in weekly minutes. We employed confirmatory factor analyses to assess the psychometric properties of the measurement. Results

revealed that the one-factor construct had adequate fit indices (CFI = 0.955, TLI = 0.919, RMSEA = 0.035, SRMR = 0.027).

Control Variables

We took sex, age, body mass index (BMI), drinking behavior, and smoking behavior as control variables. Age and BMI were treated as continuous variables. Sex, drinking behavior, and smoking behavior were treated as binary variables. Sex was coded as female or not, drinking behavior was coded as heavy drinker (drinking frequency of 3–4 days a week or more) or not, and smoking behavior was coded as daily smoker (who reported smoking every day) or not.

Statistical Analysis

Descriptive Analysis

We first used a descriptive analysis to present the outline of the participants' data. We employed a cutoff point of five to calculate the prevalence of mild depression among the current study sample (65). Moreover, we conducted a correlation matrix among nine items of time use behavior and the PHQ-9 score to present the basic patterns of potential time displacements, and possible correlations between diverse time use behaviors and depressive status.

Network Estimation

When using a network analysis approach, all variables are treated as nodes, and edges among the nodes can be interpreted as partial correlation coefficients among these variables (67). Given that we included both continuous and binary variables in the analysis, we employed a mixed graphic model approach via R package mgm software (an algorithm of regularized generalized regression) to estimate the networks (68), and we used the extended Bayesian information criterion with tuning parameter $\gamma = 0.5$ to make the estimates.

We first estimated a network that only includes time use and symptom items to present the inter-correlations among the diverse items. The second network included time use items, symptom items, and all control variables; which were estimated to verify if the findings in the first network were stable. Networks were visualized using the *R* package *qgraph* software (69). Additionally, to assess the accuracy of the edges in the two networks, we constructed a 95% bootstrapped confidence interval around the edges (67). The accuracy estimation was conducted using the *R* package *bootnet*, and 1,000 resamples were used for the bootstrapping technique. Moreover, the correlation stability coefficient (CS-coefficient) was used to assess the edge stabilities of two estimated networks.

Directed Acyclic Graph

To identify potential causal directions among the diverse time use behaviors, depression status, and controlling variables, we adopted the Incremental Association Markov Blanket (IAMB) algorithm, a constraint-based structure Bayesian network learning algorithm implemented in the *R* package *bnlearn* (70), to estimate the directed acyclic graph (DAG).

Following suggestions from an existing study (71), the total score of the PHQ-9 was included in the DAG estimation. We set

no whitelist to elaborate on the efficacy of the IAMB algorithm to calculate the edges within the network. Meanwhile, as sex and age were not influenced by other variables, and we also assumed that depression status cannot influence time use behaviors, the following edges were blacklisted: (1) all edges toward sex and age; (2) edges from the total score of PHQ-9 toward nine time use behaviors. Moreover, we performed 1,000 non-parametric bootstraps to check the stability of the DAG results. Based on the bootstrapping results, edges (both directed and undirected) related to the total score of PHQ-9 and crucial time use behavior were re-calculated via *t*-test or correlation test to reveal the causal triggers of depression. All *R* packages were carried out using version 4.1.2 of *R* software.

RESULTS

Descriptive Results

Table 1 provides a description of all the variables used in the current study. Of the sample, 49.70% (n = 900) participants were female, 22.25% (n = 403) were daily smokers, and 5.52% (n = 100) were heavy drinkers. The mean age of participants was 24 years (mean = 23.88, SD = 2.309). Participants reported an average healthy BMI (mean = 21.905; SD = ± 3.038). The total PHQ-9 score for the sample was fairly low (mean = 0.701; SD = ± 1.856), and the percentage of participants with mild depression was 5.02% (n = 91). These results indicate that the participants in the current study did not experience significant depressive symptoms. The participants' mean weekly sleep duration was 3,415.71 min, which meets the recommended sleep time for adults as suggested in previous studies (72). However, the time spent on both heavy leisure activities (mean = 18.771, $SD = \pm 92.525$) and moderate leisure activities (mean = 21.526, $SD = \pm 111.559$) was significantly lower than the WHO's recommendations, which states that adults should get 150-300 min of physical activity per week (15). The mean weekly duration of participants' heavy and moderate work activities were 270 and 444 min, respectively. On average, they spent 227 min in traffic per week. Their mean weekly duration of watching TV was 883 min, using computer was 347 min, and playing video games was 43 min.

Table 2 presents the correlation matrix of relationship between time use and the total score of the PHQ-9. To present comparable results, all time use behaviors were standardized. The results revealed that participants who spent more time on moderate work activities reported a lower PHQ-9 score, while participants who spent more time using computer reported a higher PHQ-9 score. The positive relationship between computer usage and PHQ-9 score implies that computer use may function as a direct trigger of depression, and therefore, we should focus on the time displacement mechanism around computer use. Computer use time was negatively correlated with both heavy work activities and moderate work activities; however, it was positively correlated with heavy leisure activities and moderate leisure activities. Additionally, the results revealed that sleep duration was negatively correlated with traffic time and duration of playing video games.

TABLE 1 Descriptive statistics (N = 1.811).

Variables	Mean (Std. dev.)	N (%)	Min	Max
Depression status				
Sum score of PHQ-9	0.701 (1.856)	_	0	23
Mild depression (1 = yes)	-	91 (5.02%)	0	1
Time use behaviors (minutes per week)				
Heavy work activities	270.413 (574.878)	_	0	3360
Moderate work activities	444.445 (630.311)	_	0	3570
Traffic time	226.596 (326.428)	_	0	2400
Heavy leisure activities	18.771 (92.525)	_	0	1200
Moderate leisure activities	21.526 (111.559)	_	0	1800
TV watching	882.808 (576.518)	_	0	5040
Computer use	347.368 (666.677)	-	0	5040
Video game	42.591 (195.817)	_	0	3360
Sleep duration	3415.71 (452.301)	_	0	5040
Control variables				
Female (1 = yes)	-	900 (49.70%)	0	1
Age	23.88 (3.309)	_	18	29.98
BMI	21.905 (3.038)	_	14.479	37.188
Smoking (1 = daily smoker)	-	403 (22.25%)	0	1
Drinker (1 = heavy drinker)	-	100 (5.52%)	0	1

TABLE 2 | Correlation matrix of relationships among time use and the total score of PHQ-9.

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
(1) Heavy work activities	1.000									
(2) Moderate work activities	0.099 (0.000)	1.000								
(3) Traffic time	0.145 (0.000)	0.203 (0.000)	1.000							
(4) Heavy leisure activities	-0.005 (0.824)	-0.039 (0.098)	0.162 (0.000)	1.000						
(5) Moderate leisure activities	-0.041 (0.084)	-0.021 (0.378)	0.076 (0.001)	0.462 (0.000)	1.000					
(6) TV watching	-0.026 (0.276)	0.045 (0.054)	0.016 (0.500)	-0.042 (0.075)	-0.009 (0.700)	1.000				
(7) Computer use	-0.170 (0.000)	-0.161 (0.000)	-0.036 (0.127)	0.176 (0.000)	0.091 (0.000)	-0.044 (0.061)	1.000			
(8) Video game	-0.036 (0.128)	-0.063 (0.008)	0.025 (0.288)	0.165 (0.000)	0.088 (0.000)	0.072 (0.002)	0.319 (0.000)	1.000		
(9) Sleep duration	-0.038 (0.101)	0.001 (0.952)	-0.049 (0.037)	-0.037 (0.118)	0.030 (0.203)	0.017 (0.460)	-0.028 (0.230)	-0.059 (0.011)	1.000	
(10) Sum score of PHQ-9	0.025 (0.283)	-0.065 (0.005)	-0.013 (0.595)	-0.017 (0.469)	-0.007 (0.766)	0.023 (0.321)	0.086 (0.000)	0.010 (0.657)	-0.017 (0.460)	1.000

All time use behaviors were standardized; P-values were presented in parentheses.

Results of the Network Estimation

The estimated network results are shown in Figure 1. Figure 1A displays the internal linkages among diverse time use behaviors and the nine depressive symptoms. Figure 1B displays the results of the network with the control variables. The reference names of items used for the assessment of time use and depressive symptoms are listed in **Supplementary Table 1**. Detailed edge weights are listed in **Supplementary Tables 2**, 3, and the bootstrapped accuracy plots are displayed in **Supplementary Figures 1**, 2. Moreover, two networks have high edge stabilities (all CS-coefficients = 0.75).

After controlling for all time use behaviors and depressive symptoms, Figure 1A shows that the negative relationships

between sleep duration and traffic time, and between sleep duration and video games time were not significant. Computer use time is positively correlated with time spent on video games and heavy leisure activities, but negatively correlated with TV watching time, heavy work activities, and moderate work activities. The direct linkages between leisure activities (both heavy and moderate) and work activities (both heavy and moderate) were not significant; however, Figure 1A reveals that negative relationships between leisure activities and work activities were mediated by computer use. Figure 1B presents consistent results after controlling for age, sex, BMI, smoking behavior, and drinking behavior.

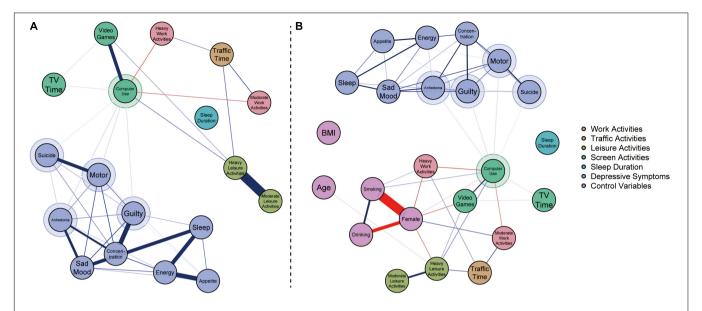


FIGURE 1 Results of kestimated network models. The blue edges denote the positive relationships, and the red edges denote the negative relationships. The direct linked nodes among time use behaviors and depressive symptoms were highlighted with larger circles. **(A)** Results of the estimated network without control variables. **(B)** Results of the estimated network with control variables.

According to Figure 1A, computer use was the only trigger for depressive symptoms. Computer use significantly triggered three depressive symptoms: "Anhedonia," "Guilt," and "Motor." These results imply that participants who spend more time using computers will have little interest or pleasure in doing other things in their daily life, may feel bad about themselves, and may have slow behavioral reactions. However, computer use was found to be an inhibitor of "Suicide." The linkages between computer use and these four depressive symptoms were found to be robust when controlling for age, sex, BMI, and smoking and drinking behaviors (see Figure 1B).

Results of the Directed Acyclic Graph

Figure 2 presents the results of the DAG. **Figure 2A** presents the initial estimated DAG results, where computer use has direct effects on heavy work activities, heavy leisure activities, video games time, and the total score of PHQ-9. The total score of PHQ-9 was directly affected by computer use, sex, and drinking behavior.

Figure 2B presents the bootstrapped inclusion proportions of each directed and undirected linkage among the variables. Compared with the results in **Figure 2A**, predictors of the total score of the PHQ-9 were consistent: female sex (diff = 0.267, t = 3.067, p < 0.01), being a heavy drinker (diff = 0.242, t = 1.268, p = 0.205), and computer use (r = 0.086, p < 0.001) were predictors for the risk of depression.

The direct linkages related to computer use that are presented in **Figure 2B** were slightly different from the results in **Figure 2A**: first, the linkage between computer use and heavy work activities was undirected in **Figure 2B**; second, the linkage between computer use and moderate work activities was directed from computer use to moderate work activities in **Figure 2B**; third, age was found to directly affect computer use (**Figure 2B**). Using

a t-test and correlation test, the DAG results in **Figure 2B** revealed that older participants reported decreased time spent on computer use (r = -0.085, p < 0.001). The time spent on computer use was negatively correlated with the time spent on heavy work activities (r = -0.170, p < 0.001). Moreover, computer use was found to directly decrease the time spent on moderate leisure activities (r = -0.161, p < 0.001) and increase the time spent on both heavy leisure activities (r = 0.176, p < 0.001), and on video games (r = 0.319, p < 0.001).

DISCUSSION

To the best of our knowledge, this is the first study to adopt a network analysis to disentangle the underlying linkages among diverse time use behaviors and depressive symptoms in emerging adults. While the prevalence of mild depression among emerging adults in the Guizhou Population Health Cohort Study was quite low, this study contributes novel insights to understanding the potential mechanism of triggering depressive symptoms.

First, the time displacement mechanism explains the underlying connections among diverse time use behaviors among emerging adults. Previous studies focusing on adolescents' time use behaviors revealed a pattern in which higher screen time led to a decreased sleep duration (32, 73). However, our results demonstrated that emerging adults maintain adequate sleep duration, and that it is not influenced by other time use behaviors when controlling for all concerned variables. Poor sleep quality usually leads to significant psychiatric reactions, including inattention and fatigue (74–77). The different patterns of the time displacement mechanism regarding sleep between adolescents and emerging adults could be explained in two ways: First, the crucial stressors that lead to unhealthy sleep

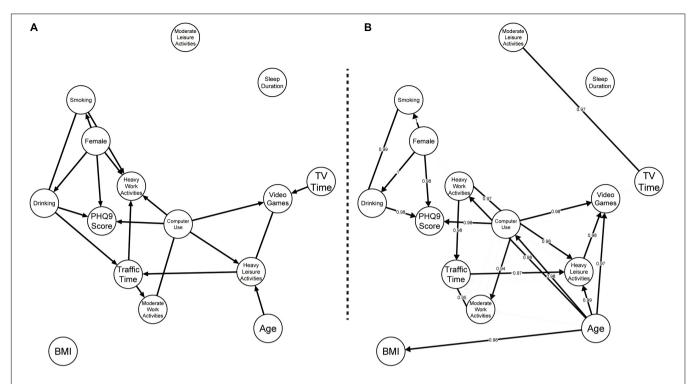


FIGURE 2 | Results of directed acyclic graph (DAG). (A) The initial estimated results of the DAG. (B) The results based on 1,000 bootstrap replications. Numbers on each edge indicate the non-zero proportions.

among adolescents and emerging adults were different. In China, stressors related to academic work served as crucial risk factors in determining adolescents' sleep quality (78, 79), while the work environment stressors were key predictors of emerging adults' sleep quality (80-82). For adolescents, screen time significantly replaces sleep duration (83). However, emerging adult participants in the current study were living in Guizhou—a developing province during the survey time, and they may not have faced significant stressors from the work environment. Second, emerging adults present more mature social interactions and activities compared with adolescents. The time spent on certain behaviors was not compulsory. Thus, as the results revealed that, time spent on computer use was found to be negatively associated with the time spent on work activities. These results indicate that individuals who were undergoing emerging adulthood—a unique developmental stage with initial social independence-replaced their working time with time spent on computer use. The decreased work time is the behavior compensation for excessive screen time.

Second, the time displacement mechanism also explains the connections between time use behaviors and depressive symptoms. The time spent on using computer was significantly correlated with four depressive symptoms. It triggered "Anhedonia," "Guilt," and "Motor;" but inhibited "Suicide." As the connections between time spent on using computers, playing video games, and leisure activities were positive, the negative connection between time spent on computer use and "Suicide" could be explained by the fact that emerging adults usually use computers for recreational purposes, which

distracts them from depressive and suicidal content. Given that participants who spent more time on computer use usually spent less time on working activities, the positive connections between computer use and the symptoms "Anhedonia," "Guilt," and "Motor" could be because computer use is a potential disengagement coping strategy for emerging adults, to distract them when they have to take on social responsibilities in scenarios they never experienced during their adolescence (84). The disengagement coping strategy granted emerging adults an escape from dealing with the stressors they faced, thus leading to worse depressive status. "Anhedonia" was triggered since emerging adults who used computers excessively may have an inadequate locus of control toward the rewards from the work-related activities, spend more time in online activity (85), and have a high possibility of problematic Internet use (86, 87). Moreover, the activated symptom—"Guilt" could be explained as excessive computer use worsens emerging adults' social connections (88), and decreased social provisions are typically related to low self-esteem and severe depression status (89). Additionally, the activated "Motor" implies that excessive time spent on computers has potentially negative effects on emerging adults' physical and cognitive development (90, 91).

Third, the results from the DAG revealed that depression was also linked to two other factors. Sex (specifically, being female) and drinking behavior were risk predictors of depression. While the t-test result was insignificant (diff = 0.242, t = 1.268, p = 0.205), the DAG indicated that being a heavy drinker increases emerging adults' depression, which is consistent with most previous studies (92–94). This result could be explained

by shared genetic and environmental determinant theories (95, 96). Previous twin and adoption studies revealed the presence of genetic influence on alcohol dependence, depression, and the comorbidity of alcohol dependence and depression (95, 97-99). Moreover, such effects were also moderated by social environments, including peer effect (100, 101), living regions (102), and marital status (103, 104). Given that most of the emerging adults have not yet assumed full family responsibilities, the genetic association between heavy drinking behavior and depression status among emerging adults may be intensified by their drinking peers and unmarried status. Additionally, females reported more severe depressive status (diff = 0.267, t = 3.067, p < 0.01). One previous study indicated that stressors related to pregnancy and postpartum experiences increased the incidence of depression in the female population (105). While not all emerging adult females had experienced pregnancy, fertilityrelated issues in traditional Chinese family situations may affect females persistently, and lead to further depressive episodes.

Fourth, our results also provide beneficial practical implications to cope with the COVID-19 pandemic. Given the lockdown measure and social distancing recommendations were most adopted policies during the repeated outbreak periods, most of the offline activities have to be taken online. Several depression risk factors, including problematic Internet use (86, 106) and cyberbullying involvement (30, 107, 108) were intensified. Governments and public institutes should promote timely psychological support campaigns to guide individuals' online behavior, and relieve the stress generated via intensified online activities.

This study has several limitations. First, while the DAG approach provides potential causal directions among the variables, the causal mechanism is obtained by the algorithm, rather than the longitudinal design. The data that were analyzed were cross-sectional, which leads to limitations in causal inference. Second, it remains unknown if the time displacement mechanism has long-term effects on individuals' depression status. Further studies should collect longitudinal data to address these issues. Third, the sample was recruited from only one province in China. Therefore, caution should be exercised when generalizing the findings to other populations. We hope that scholars, in future, will employ network analysis to test the linkages between time use behaviors and depressive symptoms for other populations. Further meta-analyses of these potential

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network studies are required. Finally, we only verified the effect of the time displacement mechanism in depression. If and how the other two mechanisms, namely social comparison and reinforcing spiral (33), could explain the depression pathogenesis among emerging adults remains unclear. Further studies are needed to verify how these potential mechanisms influence emerging adults' mental outcomes.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Institutional Review Board of Guizhou Provincial Center for Disease Control and Prevention. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

ZM and FZ wrote the first draft of the manuscript. YW revised the first draft of the manuscript. TL and NC made the design. All authors approved the final manuscript.

FUNDING

This study was supported by Major Project of the National Social Science Fund of China (Grant No. 19ZDA324) and Guizhou Province Science and Technology Support Program (Qiankehe [2018]2819).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt. 2022.809745/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The handling editor LZ declared a shared affiliation, with one of the author NC, at the time of the review.

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Mental Health in Australia: Psychological Distress Reported in Six Consecutive Cross-Sectional National Surveys From 2001 to 2018

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OPEN ACCESS

Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Gaia Sampogna, University of Campania "L. Vanvitelli", Italy Gerard Hutchinson, University of the West Indies, Trinidad and Tobago

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 16 November 2021 Accepted: 25 February 2022 Published: 01 April 2022

Citation:

Enticott J, Dawadi S, Shawyer F,
Inder B, Fossey E, Teede H,
Rosenberg S, Ozols AM I and
Meadows G (2022) Mental Health in
Australia: Psychological Distress
Reported in Six Consecutive
Cross-Sectional National Surveys
From 2001 to 2018.
Front. Psychiatry 13:815904.
doi: 10.3389/fpsyt.2022.815904

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Purpose: To examine Australian psychological distress trends from 2001 to 2017/18, including analysis by age, sex, location, and household income.

Methods: Secondary analysis of the working age population (18–64 years) in six successive representative national health surveys. Measures were prevalence of psychological distress at very-high symptom level (defined by a Kessler Psychological Distress Scale (K10) score of 30 or more) and combined high/very-high level (K10 score of 22 or more). Very-high K10 scores are associated with mental health problems meeting diagnostic thresholds in past year.

Results: From 2001 to 2017/18 Australian rates of K10 very-high distress rose significantly from 3.8 to 5.1% and combined high/very-high from 13.2 to 14.8%. In women aged 55–64, very-high distress rose significantly and substantially from 3.5 to 7.2% and high/very-high distress from 12.4 to 18.7%. In men aged 25–34, very-high distress increased from 2.1 to 4.0% and high/very-high from 10.6 to 11.5%. Income was strongly and inversely associated with distress (lowest vs. highest quintile adjusted OR 11.4). An apparent association of increased distress with regional location disappeared with adjustment for income.

Conclusion: Australia's population level of psychological distress increased significantly from 2001–2017/18, with levels highest in women and with rates inversely associated with income. This is likely to be indicative of increased community rates of mental disorders. Given that this has occurred whilst mental healthcare expenditure has increased, there is an urgent need to reconsider how best to respond to mental illness, including targeting the most vulnerable based on social determinants such as age, gender, and lower incomes.

Keywords: psychological distress, mental health services, prevalence, population measures, mental health

INTRODUCTION

Monitoring Australia's Mental Health

Australia has had two instances of a National Survey of Mental Health and Wellbeing (NSMHWB); one in 1997 (n=10,641, response rate 78%) and another in 2007 (n=8,841, response rate 60%) (1, 2) while a further survey with some similarities is underway (3). These provide valuable in-depth cross-sectional information including administration of lengthy symptom-based interviews designed to elicit Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD) diagnoses. However, the relative infrequency and irregularity of these surveys, changes in instrumentation, and variability in response rates mean that, for valuable surveillance information on trends in psychological distress and mental disorders in Australia, we need to look elsewhere.

The Australian National Health Survey (ANHS) is an important source of data on health and social determinants (4) which through this century has usually been conducted every 3 years. Typically ANHS sample sizes exceed 20,000 with response rates around 80%. The ANHS includes the Kessler-10 (K10) questionnaire (5). The K10, commonly described as measuring psychological distress, is a ten-item Likert scale, items having a timeframe of 4 weeks and asking how often symptoms occurred in that time. Scoring points range from "all of the time" (5) through "most of the time" (4), "some of the time" (3), "a little of the time" (2), and "none of the time" (1). Total scores range from 10 to 50. Buoyed by the World Health Organization's World Mental Health Survey Initiative that began in the early 2000s, there is K10 stratum data from over 40 countries, which has enabled estimations of population mental health and comparisons (5-11).

The construction of psychological distress as measured by the K10 includes symptoms commonly associated with common mental disorders, particularly when these are endorsed at higher frequency levels. There are content similarities with symptoms in diagnostic criteria for anxiety and affective disorders but also with responses to other disorder states. Examples here would be K10 items 2, 3, 7 and 9 with specific wordings being of feeling: "nervous"; so nervous that nothing could calm you down"; "depressed"; and "so sad that nothing could cheer you up." The timeframe of 4 weeks prior where items are scored 4 or 5 involves persistence of symptoms for longer than required to meet diagnostic criteria for an episode of depression (12, 13). Therefore, it appears reasonable that high scores on the K10 would correlate with active common mental disorders. In fact, elevated K10 scores correlating with common mental disorders are reported from the 2007 NSMHWB across Australia (5, 7). In this survey, 79.6% of people with a K10 score in the veryhigh distress range (scores of 30 and above) had a 12-month CIDI assessed mental disorder (Positive Predictive Value or PPV) and the Stratum-Specific Likelihood ratio (SSLR: probability of a person who has the disease testing positive divided by the probability of a person who does not have the disease testing positive) for any mental disorder was 15.6. High K10 scores (scores of 22-29) had a lower PPV for any mental disorder of 57.1%, with a lower SSLR of 5.3 (7). Therefore, ANHS-based population rates of very-high K10 score represent a reasonable regular survey proxy for recently active mental health problems and our best available measure of this collected regularly in representative surveys in Australia. Combined high/very-high scores provide a measure more broadly of psychological distress rates. This regular ANHS collection of K10 data is currently Australia's best source for surveillance of mental disorder trends along with those of a broader construct of psychological distress in the Australian population.

Previous Work on Time Trends

Previous published work examined trends in psychological distress as measured by the K10 in the adult Australian population from the ANHS between 2001 and 2014 and reported stable rates (14). Headline ANHS rates of very-high K10 as reported by the Australian Bureau of Statistics until 2017/18, so with a further survey data point than in previous reporting, do seem to have increased (up from 2014/15 by 1.3%: from 11.7 to 13.0% for combined high/very-high K10 scores) (15); however comparisons of rates were not standardized for demographic changes. So time trends found in simple rate comparisons could reflect altered population structure rather than valid secular trend findings. Examination focusing primarily on a large Australian nationally representative household panel study with a focus on workforce issues (16) - and with a timespan extending to 2017/18 - did indicate an increase in elevated K10 scores, also commenting on some increase in the ANHS findings for elevated K10. But these comparisons did not apply standardization to the ANHS data for demographic changes.

International Comparisons

In a review of major surveys conducted in Australia, Canada, the United Kingdom, and the United States, and in the context of appreciable funding increases for mental health services during recent times particularly in Australia (17, 18), again no improvements in population health were observed (19). We note a possible different picture across some of Europe, as recent analysis of the European Social Health Survey show that in most countries of Europe between 2006 and 2014 the population rates of symptoms associated with depressive disorders seem to have declined (20). The recent comprehensive review of the national burden of 12 mental disorders in 204 countries has examined up-to-date information on the prevalence and burden of mental disorders across the world between 1990 and 2019. No marked changes were found in age-standardized prevalence of any mental disorder (including anxiety and depressive disorders) in any country between 1990 and 2019 (21). However, a limitation of its Australian finding applies as the most recent input data meeting the inclusion criteria (of providing mental disorder prevalence from probability sampling to capture a representative sample of the general population) was obtained in 2007.

Timing of This Work

The COVID-19 pandemic represents an adventitious event without parallel during the period of history of modern survey

methodologies in mental health. Considerable volumes of work have gone on in the context of this pandemic to assess its impact on aspects of mental health; this is critically important, and also important is to understand the trends underway in the mental health of a nation before the pandemic took hold and create an evidence baseline for ongoing population mental health surveillance.

During the previous two decades before the COVID-19 pandemic, Federal and state governments in Australia had increased constant-dollar per-capita mental health services expenditure by 50% (22). Reducing population rates of mental illness featured as an aspiration in key Australian Federal and State policy mental health policy documents [e.g., (23, 24)]. Reducing psychological distress in the population as measured with the K10 was also documented as an intention for the State of Victoria's 10-year Mental Health Plan (24). Therefore, it is important to report K10 band score population rates regularly. By this, the trends hoped for in policy may be identified and acknowledged if policy implementation is successful, while there can be holding of governments to account if progress is not achieved.

Given that mental health services were accessed by an estimated 12% of Australian adults prior to the pandemic (25), there is appreciable opportunity for treatment services to influence the course of mental health problems and impact population mental health outcomes in Australia. Treatment services may not prevent case onsets, but where a mental disorder within the last year has been detected and effectively treated, we might expect that K10 scores will reduce over time from the higher ranges more rapidly than they would have done without this treatment. Inadequate treatment of an established disorder may be associated with persistent symptoms apparent as elevated K10 scores. Therefore, improved case ascertainment and treatment might reasonably be expected to reduce surveyed rates of very-high K10 scores. If effective treatment rates increase, then more people with the identified problems will have, with support by treatment and care, transitioned from the higher to lower rates of symptomatology reflected in K10 scores. Noting here that the K10 is one of the instruments advised for use as an outcome measure in Australian primary mental health care, (26) we might hope to find population mental health improvement in the previous two decades when funding for treatment services increased substantially. Given that further increases in mental health services spending are now occurring as part of the response to the mental health impacts arising from the COVID-19 pandemic, it is critical to explore and understand what impact previous increases in mental health expenditure had on population measures if any. This can help to inform future services spending and support the implementation of evidence based initiatives to support improvements population mental health.

Regular Population Mental Health Surveillance in Australia and the Aims of This Work

Previous work has reported overall ANHS rates of K10 score bands up to 2014 (14, 27) - this work adds by inclusion of a

further national survey data point and, like that reporting, applies standardization for population changes. Also, adding to previous work (14, 28, 29), we examine prevalence of psychological distress in Australia between 2001 and 2018, exploring subgroups by age, gender, household income and location. In order for the relationships with income to be coherently examined and consistent with other data presented we restrict analyses to the working age population.

MATERIALS AND METHODS

Design

This study was a large-scale secondary analysis (n = 78, 204) of K10 data collected by the Australian Bureau of Statistics (ABS) from working-age Australian adults across six National Health Surveys (ANHS) (2001-02, 2004-05, 2007-08, 2011-12, 2014-15, and 2017-18). We analyzed responses from adults aged 18–64 years in each survey, except for the 2004-05 ANHS as data was only available for adults aged 20–64 years. We standardized all surveys to the 2001 Australian census population based on the strata of sex and age (30). Elevated psychological distress rates were calculated and compared across sex as available in the ANHS.

National Health Surveys

These ANHS cross-sectional household-based surveys are undertaken at 3-year intervals to monitor health trends over time with detailed methods described elsewhere (4). Trained ABS interviewers conducted face-to-face interviews in each survey. Household and person weights are assigned by the ABS to adjust for the probability of sample selection, seasonality and non-response, and the data are then calibrated to the population benchmarks. This ensures that the estimates are representative of population distributions and compensates for any over- or underrepresentation of particular categories of persons or households.

Psychological Distress Measure

The K10, a self-administered 10-item Likert scale tool, measures current psychological distress, particularly symptoms of anxiety and depressive disorders (5). Used in ordinal form, band scores are closely associated with mental health disorders (5). K10 scores range between 10 and 50, and score bands are: low (10–15), moderate (16–21), high (22–29), and very-high (30–50). Here we also generated an overlapping and combined high/very-high category, which consisted of scores 22 and higher.

Geographic Location

A residential location variable for each survey participant is available and based on the Accessibility and Remoteness Index of Australia (ARIA+) (4). It describes the residential location as Major cities of Australia, Inner Regional Australia or Other.

Data Analysis

All statistical analyses were performed in Stata 16.0 (StataCorp, College Station, TX, United States). When not stratified by age, data were directly age-standardized against the estimated resident

population of Australia as at 30 June 2001. Using this direct age-adjustment approach, the 2001 age-structured population is used as the reference and each survey round is weighted to match this (30). Effect size estimates for dichotomous outcomes of combined high/very-high and very-high psychological distress are presented as odds ratios calculated using logistic regression on the K10 data from the Australian working age population. Independent variables examined first in a univariate regression with the outcome, then in a multivariable regression, were: year, sex, age-group, household income, and location. All independent variables were specified as categorical, including the "year" variable because prevalence changes over time was not linear. For time trend examinations the reference year was 2001. The overall time trend examinations done using the regression analyses had a level of significance set at an alpha of 0.05. Subsequent sub-group pairwise comparisons using 2001 and 2017-18 data employed tests for two proportions. Given that twelve sub-group pairwise comparisons were planned (see the section "Results"), to minimize the occurrences of spurious positives a Bonferroni correction was applied with the alpha value was set at 0.0042 (i.e., approx. 0.05/12).

Ethics Approval

As is common practice for the ABS, data collection occurred under the auspices of the Census and Statistics Act 1905. Per the ABS and Universities Australia Agreement (31), students, staff, and researchers affiliated with participating universities have access to the basic, anonymized, microdata for the 2001-02, 2004-05, 2007-08, 2011-12, 2014-15, and 2017-18 cycles of the ANHS. Therefore, ethics approval was not required for these analyses.

RESULTS

Overall Results and Time Trends

In the six national surveys between 2001 and 2017-18 there were n=78,204 surveys completed by working-age adults producing K10 distress data, see **Table 1**. **Figure 1** shows that the greatest distress occurred in the latest survey at 2017-18: for combined high/very-high level distress the 14.8% rate was significantly greater than all previous years (p<0.001); for very-high level distress the 5.1% rate was significantly greater than 2001, 2004, 2007, and 2011 (p<0.01).

For very-high distress, multivariable regression identified similar rates of very-high distress across 2001, 2004, and 2007, see **Table 2**. Then compared to 2001, greater rates were evident in 2011, 2014 and 2017-18 with odds ratios (OR) of 1.15 (95% CI: 1.001–1.33), 1.21 (1.06–1.39) and 1.40 (1.23–1.59), respectively.

For combined high/very-high distress, multivariable regression identified that compared to 2001, the 2011 rate was significantly lower with OR of 0.91 (0.84–0.99), whilst in 2017-18 rate was greater with OR of 1.18 (1.09–1.27), see **Table 2**.

Age and Gender

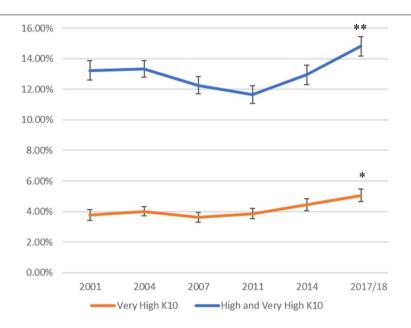
Figure 2 shows the K10 distress data broken down by age and gender over time. In analysis by gender, very-high distress was more prevalent in women at 5.2% (95% CI: 5.0–5.4) compared to

men at 3.3% (95% CI: 3.1–3.5), see **Table 1**. Combined high/very-high distress was also more prevalent in women at 16.1% (95% CI: 15.7–16.4) compared to men at 10.9% (95% CI: 10.6–13.9). Multivariable regression confirmed that women had greater odds

TABLE 1 Age-standardized prevalence of psychological distress in the Australian working age population, 2001–2017/18.

		K10 ve	ry-high	K10 combined high/ very-high				
	ns	Ratea	95%	CI	Ratea	95%	CI	
Age Group								
18 – 24	7846	4.05%	3.62%	4.49%	15.75%	14.95%	16.56%	
25 – 34	17292	3.55%	3.27%	3.82%	12.78%	12.28%	13.28%	
35 – 44	19874	3.97%	3.69%	4.24%	12.99%	12.52%	13.46%	
45 – 54	17742	5.39%	5.05%	5.72%	14.00%	13.49%	14.51%	
55 – 64	15470	4.53%	4.20%	4.85%	12.96%	12.43%	13.49%	
Location ^a								
Major cities	51289	4.09%	3.92%	4.27%	13.13%	12.83%	13.43%	
Inner regional	15073	4.75%	4.40%	5.10%	14.42%	13.83%	15.00%	
Other	11862	4.24%	3.87%	4.61%	13.66%	13.01%	14.30%	
Sexr ^a								
Male	36809	3.30%	3.12%	3.49%	10.90%	10.57%	11.22%	
Female	41415	5.18%	4.96%	5.41%	16.05%	15.68%	16.42%	
Male and Yea	ır ^a							
2001	6797	3.01%	2.60%	3.41%	10.86%	10.11%	11.61%	
2004	7135	3.27%	2.86%	3.69%	11.33%	10.57%	12.08%	
2007	6095	2.87%	2.46%	3.28%	10.29%	9.52%	11.06%	
2011	5871	3.08%	2.63%	3.52%	9.54%	8.77%	10.31%	
2014	5197	3.43%	2.92%	3.93%	10.35%	9.50%	11.19%	
2017/18	5714	4.19%	3.66%	4.72%	12.57%	11.68%	13.46%	
Female and Y	'ear ^a							
2001	7844	5.19%	4.69%	5.69%	17.00%	16.15%	17.84%	
2004	8033	5.02%	4.54%	5.50%	16.73%	15.89%	17.58%	
2007	6509	4.59%	4.08%	5.11%	15.33%	14.44%	16.23%	
2011	6461	4.61%	4.09%	5.13%	13.72%	12.85%	14.58%	
2014	6099	5.43%	4.85%	6.02%	15.50%	14.55%	16.44%	
2017/18	6469	5.90%	5.31%	6.50%	16.97%	16.03%	17.92%	
Household in	come qu	iintiles						
(poor) 1	10031	10.88%	9.25%	12.51%	24.56%	22.36%	26.76%	
2	10050	6.06%	4.78%	7.35%	20.11%	17.95%	22.26%	
3	13307	1.98%	1.41%	2.56%	11.82%	10.27%	13.37%	
4	15601	2.14%	1.47%	2.81%	9.12%	7.82%	10.43%	
(rich) 5	16897	1.01%	0.58%	1.45%	5.76%	4.82%	6.70%	
Female and F	louseho	ld income	quintile	s				
(poor) 1	5915	11.91%	9.78%	14.03%	26.94%	24.06%	29.82%	
2	6005	6.80%	5.07%	8.52%	23.31%	20.37%	26.24%	
3	7078	2.53%	1.59%	3.46%	14.99%	12.55%	17.43%	
4	7840	2.75%	1.66%	3.84%	11.44%	9.38%	13.49%	
(rich) 5	7736	1.75%	0.92%	2.58%	7.79%	6.16%	9.42%	
Male and Hou								
(poor) 1	4120	9.64%	7.13%	12.15%	21.72%	18.35%	25.08%	
2	4050	5.12%	3.22%	7.03%	15.99%	12.86%	19.11%	
3	6229	1.45%	0.77%	2.13%	8.70%	6.83%	10.58%	
4	7761	1.54%	0.75%	2.33%	6.88%	5.29%	8.47%	
(rich) 5	9161	0.43%	0.01%	0.85%	4.16%	3.09%	5.24%	

^aStandardized to 2001 Australian Census. Derived from a total of n=78,204 survey participants aged 18–64 years. ^SNumber of survey respondents.



		K10			K10		
	n	very-	95%	CI	high/very-	95%	CI
Year		high			high		
2001	14641	3.78%	3.42%	4.13%	13.24%	12.60%	13.89%
2004	15168	4.02%	3.72%	4.33%	13.34%	12.81%	13.87%
2007	12604	3.62%	3.30%	3.94%	12.27%	11.71%	12.83%
2011	12332	3.86%	3.52%	4.20%	11.65%	11.07%	12.23%
2014	11296	4.44%	4.05%	4.83%	12.95%	12.31%	13.58%
2017/18	12183	5.06%	4.66%	5.46%	14.81%	14.16%	15.46%

FIGURE 1 Age-standardized prevalence of psychological distress in the Australian working age population, 2001–2017. ^aStandardized to 2001 Australian Census. Derived from a total of n = 78,204 survey participants aged 18–64 years. **Rate at 2017 significantly greater than all previous years (p < 0.001). * Rate in 2017 significantly greater than 2001, 2004, 2007, and 2011 (p < 0.001).

for very-high distress (OR 1.39, 95% CI: 1.28 to 1.50) and for combined high/very-high distress (OR 1.39, 95% CI: 1.33 to 1.46), as compared to men, see **Table 2**.

In analysis by age groups, very-high distress rates ranged between 3.6% (95% CI: 3.3–3.8) in those aged 25–34 years to 5.4% (95% CI: 5.1–5.7) in those aged 45–54 years, see Table 1. Multivariable regression showed that only the 45–54 age group [5.4% (95% CI: 5.1–5.7)] had significantly greater odds for very-high distress (OR 1.48, 95% CI: 1.27 to 1.72) compared to the youngest group at 4.1% (95% CI: 3.6–4.5), see Table 2. Prevalence of combined high/very-high distress was greatest in those aged 18–24 years at 15.8% (95% CI: 15.0–16.6). Multivariable regression confirmed that most other age-groups had significantly lower rates than those aged 18–24 years with an OR of 0.86 (95% CI: 0.79–0.94), 0.86 (95% CI: 0.79–0.94), and 0.72 (95% CI: 0.66–0.79) for 25–34, 35–44, and 55–64 years, respectively, see Table 2.

The results of the pre-specified two-sample comparisons of the first and the last surveys (2001 and 2017/19) are shown in **Table 3**. Positive differences indicate an increase in prevalence in 2017/18 compared to 2001. Given that twelve sub-group comparisons

were planned, to minimize the occurrences of spurious positives, the alpha value was set at 0.0042. The most marked increase in psychological distress between 2001 and 2017/18 is seen in women aged 55-64 years old, with very-high distress in 2001 at 3.5% (95% CI: 2.5-4.56) up to 7.2% (95% CI: 5.9-8.5%) in 2017 (Figure 2 and Supplementary Table 2). This doubling of prevalence was highly significant with a difference of 3.7% (z = 4.10, p < 0.0001). Combined high/very-high distress also significantly increased from 12.4% (95% CI: 10.5-14.2%) in 2001 to 18.7 (95% CI: 16.7–20.7%) in 2017. This increase of prevalence was highly significant with a difference of 6.4% (z = 4.51, p < 0.0001). Another almost doubling of combined high/veryhigh distress between 2001 and 2017 is seen in men aged 25-34 years old, with very-high distress in 2001 at 2.1% (95% CI: 1.4-2.8) up to 4.0% (95% CI: 2.9-5.1%) in 2017, which was also significant with a difference of 1.9% (z = 2.87, p = 0.002).

Income

In terms of household income, very-high distress was significantly more prevalent in those in the poorest quintile at 10.9% (95% CI: 9.3–12.5) compared to all other quintile

groups, see **Table 1**. The richest quintile had the least prevalent rate of combined very-high distress at 1.0% (95% CI: 0.6–1.5). Combined high/very-high distress was also significantly more prevalent in the poorest quintile at 24.6% (95% CI: 22.4–26.8) compared to all other quintiles. The richest quintile had the least prevalent rate of combined high/very-high distress at 5.8% (95% CI: 4.8–6.7). Multivariable regression (**Table 2**) found those in the poorest household income quintile to have the greatest odds for very-high distress (OR 11.54, 95% CI: 9.94–13.39) compared to the richest quintile; and greatest odds for combined high/very-high distress (OR 6.22, 95% CI: 5.76–6.72) compared to the richest quintile.

Location

In terms of geographical location, very-high distress was more prevalent in those residing in inner regional areas at 4.8% (95% CI: 4.4–5.1) compared to major cities at 4.1% (95% CI: 3.9–4.3), see **Table 1**. Combined high/very-high distress was also more prevalent in inner regional areas at 14.4% (95% CI: 13.8–15.0) compared to major cities at 13.1% (95% CI: 12.8–13.4). Multivariable regression (**Supplementary Table 1**) adjusting by age and sex found those in inner regional areas to have greater odds for very-high distress (OR 1.16, 95% CI: 1.06–1.26) compared to capital cities; and greater odds for combined high/very-high distress (OR 1.11, 95% CI: 1.05–1.17) compared to capital cities. When income is added into the regression (**Table 2**), however, this association disappears (OR 0.98, 95% CI 0.89–1.08). For combined high/very-distress, the OR then

reverses is in favor of lower distress in inner regional (OR 0.93, 05% CI: 0.88-0.99), and other regions (OR 0.90, 95% CI: 0.84-0.96).

DISCUSSION

Key Trend Findings

In Australia from 2001 to 2018, levels of very-high psychological distress significantly rose from 3.8% at the start of this period to 5.1% at the end. Combined high/very-high distress increased from 13.2 to 14.8%. A modest rate of decline in distress during the late 2000s was unsustained. After adjusting for age, sex, location and income, very-high distress was significantly more prevalent in 2011, 2014 and 2017/18 as compared to 2001; and high/very-high distress was significantly greater at 2017/18 as compared to 2001.

Changes Vary Between Subgroups

Very-high distress in women aged 55–64 has doubled this century (from 3.5 to 7.2%) and combined high/very-high distress has increased by 50% (12.4–18.7%), both of which are highly significant findings. Very-high distress also increased in males, significantly in those aged 25–34 years, but this is a more tentative finding since a significant increase did not extend to the combined high/very high distressmetric (10.6–11.5%). Overall, distress was greatest in women aged 18–24 years during all years; 8.0% for very-high levels and 22.1% for combined high/very-high

TABLE 2 | Odds ratio of psychological distress adjusted for year, sex, age, residential location, and household income.

		K1	10 very-high			K	10 combined	high/very-high	
		Odds Ratio	p-value	[95% Conf.	Interval]	Odds Ratio	p-value	[95% Conf.	Interval]
Year	2001	(Ref)	_	_		(Ref)	-	-	
	2004	1.06	0.366	0.93	1.20	1.05	0.165	0.98	1.13
	2007	1.01	0.871	0.88	1.16	0.99	0.723	0.91	1.07
	2011	1.15	0.048*	1.00	1.32	0.91	0.025*	0.84	0.99
	2014	1.21	0.006**	1.06	1.39	1.00	0.998	0.92	1.09
	2017/18	1.40	<0.001***	1.23	1.59	1.18	<0.001***	1.09	1.27
Sex	Males	(Ref)	-	_		(Ref)	-	_	
	Females	1.39	<0.001***	1.28	1.50	1.39	<0.001***	1.33	1.46
Age	18 – 24	(Ref)	-	-		(Ref)	-	_	
(years)	25 – 34	0.97	0.712	0.83	1.14	0.86	0.001**	0.79	0.94
	35 – 44	1.06	0.440	0.91	1.24	0.86	0.001**	0.79	0.94
	45 – 54	1.48	<0.001***	1.27	1.72	0.97	0.517	0.89	1.06
	55 – 64	0.95	0.550	0.82	1.11	0.72	<0.001***	0.66	0.79
Location	Major cities	(Ref)	-	-		(Ref)	-	_	
	Inner regional	0.98	0.733	0.89	1.08	0.93	0.024*	0.88	0.99
	Other	0.86	0.007**	0.77	0.96	0.90	0.001**	0.84	0.96
Household income quintile	Richest	(Ref)	-	_		(Ref)	-	_	
	4	1.52	<0.001***	1.27	1.81	1.52	<0.001***	1.39	1.65
	3	2.47	<0.001***	2.09	2.92	2.03	<0.001***	1.87	2.20
	2	5.54	<0.001***	4.73	6.48	3.53	<0.001***	3.25	3.82
	Poorest	11.54	<0.001***	9.94	13.39	6.22	<0.001***	5.76	6.72

^{*** &}lt; 0.001, ** < 0.01, and * < 0.05. Income quintile 1 are lowest incomes, and quintile 5 are highest.



FIGURE 2 | By age-groups and sex, shown are the age-standardized prevalence of psychological distress (solid lines are the Very-high K10; and broken lines are the combined High/very-high K10). Standardized to 2001 Australian Census. Derived from a total of n = 78,204 survey participants aged 18–64 years. The 95% confidence intervals are given in **Supplementary Table 2**.

in 2017/18 (2.1-4.0%). Although this study examined successive cross-sectional national surveys, the individuals in whom the distress has increased would have been younger versions of themselves at the times of the initial comparison survey so the increase in distress should be assessed with this context. At

face value, and as much as can be inferred from this data set, these increases do not appear to be due to a birth cohort effect. For women, the 55–64 age group had the lowest prevalence of very-high psychological distress in 2007 (then aged 45–54 years) compared with females of the same age bracket in other years.

TABLE 3 | Two-sample comparisons of psychological distress rates between the first and the last surveys in 2001 and 2017/19.

		K10 very-h	nigh		K10 combined high/very-high						
	Difference	p-value	95%	CI	Difference	p-value	95%	CI			
Male	1.09	0.001*	0.43	1.75	1.71	0.004*	0.55	2.87			
Female	0.71	0.067	-0.05	1.47	0.03	0.963	-1.23	1.29			
Male											
18 – 24	1.27	0.045	0.03	2.51	4.23	0.023	0.57	7.89			
25 – 34	1.86	0.003*	0.62	3.10	0.84	0.925	-16.59	18.27			
35 – 44	0.40	0.505	-0.77	1.58	0.21	0.957	-26.59	28.27			
45 – 54	1.09	0.160	-0.43	2.61	1.15	0.179	-0.72	3.81			
55 – 64	1.42	0.090	-0.22	3.06	3.14	0.022	0.449	5.83			
Female											
18 – 24	2.37	0.252	-1.70	6.44	-0.96	0.655	-5.06	3.14			
25 – 34	-1.05	0.149	-2.48	0.379	-1.98	0.133	-4.57	0.61			
35 – 44	-0.16	0.826	-1.59	1.27	-2.32	0.047	-4.61	-0.03			
45 – 54	0.51	0.995	-183.5	183.4	0.95	0.462	-1.59	3.49			
55 – 64	3.63	<0.0001*	1.94	5.32	6.35	<0.0001*	3.45	9.33			

Positive differences indicate an increase in prevalence in 2017-18 compared to 2001. Given that twelve sub-group comparisons were planned (see **Table 2**), to minimize the occurrences of spurious positives, the alpha value was set at 0.0042. *indicates $p \le 0.0042$.

A decade earlier, the male 25–34 age group (approximated in the 18–24 years age group) also had the lowest prevalence of very-high psychological distress compared with men of the same age bracket in other years. Rather than birth cohort effects, the findings of an increasing rate of psychological distress (and rapidly increasing in women in the 55–64 age subgroup) is concerning and is looking more like arising from adventitious cause(s), which are discussed more further below.

Income was strongly associated with distress, with the largest subgroup prevalence differences seen between the lowest and highest income quintiles. Income is important to examine in analyses of populations as it can be a proxy for many factors, including education, economic environment, and employment. These in turn may also affect access and utilization of mental health services. Without considering income in the analyses, we found significantly greater psychological distress among Australians residing outside of major cities; however this result reverses when income is included. This demonstrates the evident protective effect of higher incomes for mental health, and the fact that people living outside of major cities generally have lower incomes and higher costs than their major city neighbors (32, 33). Across the timespan of the study, distress was very much greater in the context of lower income levels. Indeed, when the effects of population demographics and income are controlled for, a small protective effect of living in inner and outer regional and remote Australia was found.

Possible Causality and Remedies: Policy Implications

Social Policy Implications

The World Health Organization (WHO) has noted that "Mental health and many common mental disorders are shaped to a great extent by the social, economic, and physical environments in which people live" and that social inequalities increase risk of many common disorders (34). Social determinants link with gender, biological and environmental factors, health and other policies to influence incidence of mental health problems, their persistence or otherwise, and related outcomes across the lifespan (34, 35). Possible contemporary negative influences of social determinants on population mental health include: increased job insecurity and casualization of the workforce; financial stress associated with housing affordability (36); increased working hours and disruptions to work life balance; continuing unaddressed intergenerational disadvantage applying to indigenous peoples and other minority and diverse groups; and the pervasive existential threat posed by climate change (34, 37). There is reason to believe that inequalities in society may be associated with worse mental health and wellbeing outcomes across populations for many problems with social gradients (38, 39); cross-nationally, rates of mental illness symptoms are positively associated with income inequality as measured with the Gini index (40). We note that in Australia, income inequity as measured by the Gini index and calculated for weekly income, increased appreciably from 0.304 in 2001-02 to 0.313 in 2017-18 (41). Wealth inequity also increased in Australia between 2003 and 2016, with the most affluent financial quintile experiencing a 53% increase in wealth, and the poorest, a 9% decline (42).

In calling for action to address social determinants of mental health issues, the WHO has argued that action needs to be universal, across the whole of society and proportionate to need, seeking to level the social gradient in health outcomes. Proposed strategies included environmental, structural and local interventions (34). The finding that Australia's mental health, based on best available national data, has been worsening as the 21st century has unfolded so far, has implications far beyond what is usually regarded as mental health policy. Rather, it should prompt consideration as to changes to wider policy settings across ranges of: taxation, housing, educational, employment, social benefits, and anti-discrimination and reconciliation

actions, and even climate policy. There is no simple prescription here, but there is guidance. For example, current fiscal policy has contributed to greatly increasing house prices in Australia and decreasing home-ownership for young people and those with lower incomes (whereas 35 years ago home-ownership rates were high for Australians in all income levels and in younger people too) (36). Those on low incomes - increasingly renters – are experiencing more financial stress by spending more of their income on housing, and intergenerational inequity is being propagated as home ownership for young people is now becoming associated with the wealth of the parents (36). The WHO social determinants framework (34) would suggest that addressing factors such as financial stress and intergenerational inequity could make an important contribution to improving mental health in young adults. Contributing to the finding of increasing psychological distress in women aged 55-64 will be contemporary structural and occupational factors affecting women in this age group such as the impacts of divorce, gender pay gap, carer responsibilities, and insecure work (43-45). Women in this age group are more likely to be at risk of poverty and homelessness in Australia (46), while greater socioeconomic disadvantage of geographical areas where such women may need to live (17, 47) and lower personal income (48) are associated with 2-3 fold increased prevalence of mental health issues. These influences may be contributing to these findings regarding increasing psychological distress in this demographic group (47). Income stress may further compromise access to healthcare services that require co-payments.

Recognition of the fundamental inter-relationship between mental health and the social determinants of health has led several governments both in Australia (49) and elsewhere (50) to develop wellbeing frameworks. These frameworks are designed to use social and environmental indicators, along with economic and fiscal ones, to prioritize mental health and guide Government investment and funding decisions beyond the health system, and into key relevant areas such as employment, housing, education and social inclusion. While proof of the impact of such frameworks is yet to emerge, they demonstrate increased appreciation of the need to promote holistic policy and planning, beyond the confines of the health system.

Health Policy Implications

From the perspective of healthcare, advocacy can include broad modifiable societal and social determinants: however, addressing many of these social determinants lies outside the direct influence of healthcare providers, policymakers, or those concerned with institutional care quality. The importance of broader societal changes notwithstanding, given the intent to influence population mental health expressed in national and state policy documents, these findings raise questions about Australian mental health policy and its implementation.

Increasing Service Volumes

Service and funding innovations in the first two decades of the 21st century in Australia have led to substantial increases in items of mental health care delivered (28, 51), with an estimated 12%

of the population accessing mental health care prior to the start of the pandemic in 2020 (25). In a major expansion of Australia's national Medicare health insurance scheme from November 2006 onward, the Better Access initiative (28) has enabled a range of non-medical service providers including psychologists, social workers, and occupational therapists, to access rebates through the Medicare scheme. Through the Better Access initiative among others, much of the increased investment in mental health care in Australia has been targeted at care for higher prevalence mental health problems and has led to a very considerable increase in delivery of focused psychological strategies. Success in lifting the rate of access to care for higher prevalence problems is in contrast to state and territory care, principally provided to people with lower prevalence disorders, for which access to care has remained static over the past two decades (52).

Mental Health Care Can Be Effective

Contemporary mental health care has a large body of evidence supporting its efficacy and effectiveness. For instance, a range of antidepressant medications can be found to consistently improve outcomes of depression (53), while the same can be said for many forms of psychotherapy in treatment of anxiety, depression, and other common mental health problems (54). Increasing public awareness of mental health and reducing stigma has occurred in Australia (55, 56). So there is a rational causal pathway between scaling up of such interventions to population health delivery and the attainment of positive change in mental health indices in the population. These clinical interventions, if applied, will not necessarily avert new episodes of poor mental health but they can lead to earlier resolution of active symptom status and prevent relapse or recurrence (57-60), which will be reflected in lower overall K-10 psychological distress when measured crosssectionally in surveys.

So why are things getting worse? It could be argued that recent service changes in Australia might be expected to have had some impact on rates of psychological distress as measured with the K10. Instead, these years (in the 21st century to date before the COVID-19 pandemic) have seen the mental health of Australians worsen appreciably, as measured using psychological distress in national surveys. The likely potent role of changing social determinants in worsening mental health has been discussed above, so now we turn to considering the ways in which the mental health care system may be not functioning well in ameliorating the effect of these determinants, or even possibly contributing to mental ill health.

Navigation and Access to Effective Care

Repeated inquiries have found that Australia's mental health system is hard to navigate (61) and concern has been raised about the likely scale of a quality gap in some mental health service delivery as well as important gaps in access (28). Poor articulation of responsibilities between different levels of government have permitted the evolution of a proliferation of service structures (61, 62). Comprehensive, recovery-oriented and person-centered care is rare (63). Navigation could be assisted by better coordinated services including around collaborative care models

(64). The need to develop collaborative approaches to the training of mental health professionals has also been noted as a key to creating the multidisciplinary teams required to respond, particularly to more complex mental health needs (65). Australia is yet to develop such training approaches. There is also a need to promote collaborative mental health research, such as in the evolving field of research and practice that is global mental health (66) which "prioritizes equity, and is informed by many disciplines, including neuroscience, genomics, social sciences (especially psychology, medical anthropology and sociology), epidemiology, health services research, and implementation science." There have been examples of successful innovations in primary care collaboration in Australia (67) but the division of healthcare responsibility in this country between the federal responsibility for ambulant care through the Medicare insurance system and the state administered hospital and community mental health care systems presents obstacles to making such innovations seamless and sustainable.

Targeting Specific Demographics

Specific demographic groups identified here as having rapidly high rates of problems are those aged less than 34 years and females 55-64. There is a longstanding focus in Australia on services for youth mental health and these findings confirm that this phase of life is associated with high levels of mental health problems. We have already introduced some of the social and economic drivers that may be affecting younger people, and it might be speculated that the observed high distress levels could reflect disproportionate impacts of various social factors, such as personal income and relationship stressors, and worsening housing affordability across Australia (36) at a stage of life where young people are often establishing long-term co-habiting relationships and starting families and careers (68-72). This emphasizes that, with services focusing on youth often defined as up to 25, the needs of people who may just miss out on these more intensive services should not be neglected, and furthermore that social, education, employment and mental health programs need better integration to address these needs.

For women aged 55–64, multiple social and economic causes may also converge, given aforementioned increased risks of poverty, homelessness as well as impacts of family violence in this group (44, 47). Therefore, services may need to find ways to better reach out to these women; to integrate practical help around issues, such as homelessness risk and income security, with mental health responses; and to attend to workforce development in areas that may be particularly deficient in response to key influences on mental health in this group of women, including screening for and supporting those experiencing family violence (73).

Funding Models and Access

While the Australian health care system is commonly described as universal in nature, the public health insurer Medicare permits providers to charge co-payments, creating manifestly substantial inequities in the delivery of psychological services (51). The Commonwealth Fund recently reported on the health care system

from Australia and other high-income OECD countries (74) – the source data was a questionnaire assessment of cost-related access problem to medical care. Australia together with Norway and the Netherlands were the top three overall for health care system performance (74). However, while the gap between higher and lower income groups on a binary split was small, overall the 21% of Australians who identified cost-related access problem to medical care actually ranked third of eleven countries, behind only the United States and Switzerland. Data presented here confirms that those with lower household income have much greater psychological distress, and those on especially low incomes are most likely logically to have income stress associated with their health and mental health care. They also will have other possible barriers to access and participation in care so the approach to evening out these inequities will likely be complex.

Clinical mental health services may well be useful, though only to those who receive them. The challenge for policy and service planning is to encourage access that is proportional and equitable. There is considerable evidence of widespread failure in this regard. Increased care volume in Australia has been demonstrated as misaligned with community needs and not necessarily providing care at consistent quality (17, 18, 28, 33).

Inequity, Ineffectiveness, and latrogenesis

In turn, these problems may have compromised effectiveness of Australia's mental health service delivery system quality (28, 29), impacted by inequity in service delivery and forms of iatrogenesis (17, 75). A lack of data precludes the analysis of service quality across much of the service system and this itself is a problem (62). However, greater attention to consistent attainment and assurance of quality care is important going forward. Addressing disparities in mental healthcare outside major cities should be a continuing priority. While the finding from this work was that the increased rate of psychological distress found in regional areas was not retained in analyses when income was controlled for, nevertheless it showed increased distress in the lowest income areas which are often located in regional areas. Service delivery needs to be structured with these needs in mind.

Perhaps inequitable and lower quality treatment for mental health problems may actually do some harm as well as good. It has been suggested that iatrogenic influences based on a loss of agency arising from medicalization might perhaps negate the relatively modest effect of antidepressant monotherapy (17, 75, 76). It also has been proposed that antidepressants themselves may have a significant property of oppositional perturbation, so increasing the rates of depression among those who have been prescribed them above the rates that would have been observed had they never been exposed to this therapy (75). Between them, these two explanations constitute a possible route for understanding why undoubted therapeutic benefits that may flow to some individuals fortunate enough to get access to comprehensive and appropriate care, may be offset by what can be seen as iatrogenic harms for those receiving more limited forms of care, and so constituting a failure of quaternary prevention (77, 78). Is it also worth noting that despite significant new public funding for talk therapies under the Better Access

program, the rate of prescribing of antidepressants has increased: it was 11.4/100 persons in 2013-14 and 13/100 in 2019-20 (79).

Complexity and New Modeling Approaches

Past planning approaches have failed to reflect the array of influences on population mental health. Newer and more sophisticated approaches are required (80, 81), and a paradigm shift in mental health research is required to achieve further progress (76). Simulation modeling has become a topic of regular household discussion during the pandemic yet is rarely employed in directing mental health planning with the same kind of sophistication with which it has been applied to COVID-19. Such modeling must, and has the capacity to, reflect the range of social determinants we have identified. It can demonstrate how mental health services may be adapted to achieve better outcomes for more people and influence prevalence even in such adverse conditions.

Limitations

A limitation was our data structure, since age was provided in 5-year bands and the survey was conducted every 3 years, a cohort variable could not be determined. To fully examine cohort effects, an alternative analytic approach would be a full ageperiod-cohort (APC) analysis. Our analysis plan did follow APC guidance (82), and assumed that the cohort dimension was nonoperative (83) based on the above observations of no evidence of birth cohort effects.

We note that further subgroup examination may add to our understanding of the operation of other social determinants, but that is beyond the scope of this paper. We included income and geographical location in our analyses because of the widely known effects between mental health and these variables (48). Although income can be a proxy for many things (education, economic environment, employment and service access, and utilization) further research using these variables as available in the ANHS could expand knowledge in these areas. Additionally, for the ANHS undertaken to date, very remote areas are out of scope. Forthcoming detailed mental health surveys will apply more specifically valid diagnostic instruments (84) but will be smaller and so less able to examine subgroups as here.

Another limitation is the increasing public awareness of mental health and reducing stigma has occurred over this period in Australia (55, 56), which may have contributed to an increased reporting of psychological distress. The argument for use of veryhigh K10 as a proxy for common mental disorder rates rests partly on content but also on findings from the PPV in the 2007 NSMHW (7). The PPV of the very-high K10 scores may change as the prevalence of ICD-diagnosed mental health disorders in the population changes and the provision by Slade et al. (7) of SSLRS enables us to estimate the possible impact of this. For example, if the prevalence of affective disorders has doubled from Slade et al's estimation of 6.2% to 12.4%, the PPV of the K10 would increase to an estimated 72%. So an increase in population prevalence of mental disorder would lead to an expected increase in the PPV for very-high K10 rather than a decrease.

We note here that these data sources pre-date the COVID-19 pandemic. The impacts of COVID-19 are

significant and mental health impacts including increased psychological distress have been reported to be greater in women (85); however, this will be reported separately in other publications with a focus on the unique set of determinants arising from the "one in one hundred years pandemic" crisis.

CONCLUSION

As we aspire to improve mental health services, and improve population mental health in an equitable way (86), we need population level surveillance to understand and address root causes. If inequity or other social or economic conditions are driving prevalence up, then we need models that quantify this. Perhaps these conditions are so powerful that mental health services cannot reasonably be expected alone to influence national prevalence. But services also have a part to play in the aspiration toward improving population mental health. At the very least, they should not make the situation worse. Recent interest in mental health and new funding may go some way toward bridging the gap between the level of funding and the burden of disease for which mental illness is responsible (24). In this context, resources for mental health care are precious and cannot be wasted. They should be carefully directed to where they are needed most, and to whom, including with attention to equity in service provision, then to delivery of acceptable and effective kinds of help. Effective actions must also model broader cooperation across a mental health "ecosystem" (87), and attend to social determinants of mental health in economic, housing, educational, employment and other policy spheres across government portfolios and with the community. This is perhaps Australia's greatest challenge in mental health reform now, beyond the usual calls for political will and more funding. Informed by contemporary modeling and paying particular attention to equitable implementation of evidence-based care, treatment and recovery support, we should be seeking to set and implement a broad and bold agenda for planning and reform, one that could provide all Australians with enjoyment of the greatest attainable standard of mental health.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**. The original data can be obtained by contacting the Australian Bureau of Statistics.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for

participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

JE and GM were responsible for the conception and design of the study. JE and SD were responsible for the acquisition of data and analysis. All authors made contributions to the interpretation of data, drafting the article or revising it critically for important intellectual content, and approval of the version to be submitted.

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FUNDING

This study was made possible by the high-quality data collection conducted by the Australian Bureau of Statistics. HT was funded by a National Health and Medical Research Council fellowship.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt. 2022.815904/full#supplementary-material

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Structure of Hypomanic Symptoms in Adolescents With Bipolar Disorders: A Network Approach

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OPEN ACCESS

Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Bao-Liang Zhong, Wuhan Mental Health Center, China Bing Xiang Yang, Wuhan University, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

Received: 28 December 2021 Accepted: 24 February 2022 Published: 18 April 2022

Citation:

Yang Y, Zhang W-Y, Zhang Y, Li S, Cheung T, Zhang D, Jackson T, He F and Xiang Y-T (2022) Structure of Hypomanic Symptoms in Adolescents With Bipolar Disorders: A Network Approach. Front. Psychiatry 13:844699. doi: 10.3389/fpsyt.2022.844699 **Background:** Bipolar disorders (BD) are severe mental illnesses that are often misdiagnosed or under-diagnosed. The self-report 33-item Hypomania Checklist (HCL-33) and the 33-item Hypomania Checklist – external assessment (HCL-33-EA) are well-validated scales for BD symptom detection. This study compared the network structure, central symptoms, and network stability of hypomanic symptoms measured by the HCL-33 vs. the HCL-33-EA.

Methods: This cross-sectional study was conducted from January to December 2019. Adolescents (aged between 12 and 18 years) with BD were recruited from the outpatient department of Child Psychiatry, First Affiliated Hospital of Zhengzhou University. All participants were asked to complete the HCL-33, and their caregivers completed the HCL-33-EA. Network analyses were conducted.

Results: A total of 215 adolescents with BD and their family caregivers were recruited. Node HCL17 ("talk more," node strength = 4.044) was the most central symptom in the HCL-33 network, followed by node HCL2 ("more energetic," node strength = 3.822), and HCL18 ("think faster," node strength = 3.801). For the HCL-33-EA network model, node HCL27 ("more optimistic," node strength = 3.867) was the most central node, followed by node HCL18 ("think faster," node strength = 3.077), and HCL17 ("talk more," node strength = 2.998). In the network comparison test, there was no significant difference at the levels of network structure (M = 0.946, P = 0.931), global strength (S: 5.174, P = 0.274), or each specific edge (all P's > 0.05 after Holm–Bonferroni corrections) between HCL-33 and HCL-33-EA items. Network stabilities for both models were acceptable.

Conclusion: The nodes "talk more" and "think faster" acted as central symptoms in BD symptom network models based on the HCL-33 and HCL-33-EA. Although the most prominent central symptom differed between the two models ("talk more" in HCL-33 vs. "more optimistic" in HCL-33-EA model), networks based on each measure were highly similar and underscored similarities in BD symptom relations perceived by adolescents and their caregivers. This research provides foundations for future studies with larger sample sizes toward improving the accuracy and robustness of observed network structures.

Keywords: HCL-33, HCL-33-EA, network, adolescents, Chinese, bipolar, hypomanic

INTRODUCTION

Bipolar disorders (BD) are a category of major mental illnesses that are often misdiagnosed as major depressive disorder (MDD) or under-diagnosed in clinical practice (1–3). According to a recent meta-analysis, there are an estimated 1.54 million people with BD in China (4). A previous study revealed that about 21% of BD patients in China report having been misdiagnosed in clinical practice (5). Consequently, it can take up to 10 years before the appropriate diagnosis is made, with consequences that include lowered treatment efficacy, and increased suicide risk (6, 7).

To reduce the likelihood of BD misdiagnosis, several diagnostic instruments have been developed including the clinician-rated Mini-International Neuropsychiatric Interview (M.I.N.I) (8), and the lay interviewer-rated Composite International Diagnostic Interview (CIDI) (9). However, these diagnostic tools are both time-consuming and expensive. Therefore, a number of brief, cost-saving self-report scales that assess clinical features of BD have also been developed, including the Hypomania Checklist (HCL) (10). The HCL is specifically designed to detect subtle BD symptoms in the domains of emotion, thinking, and behavior typically observed in hypomanic states (10). The HCL has been well-validated in various countries, with good psychometric properties (11).

The 33-item Hypomania Checklist (HCL-33) is a patientrated screening instrument for hypomanic symptoms in past and/or current episodes and has been validated in various populations including Chinese adolescents and older adults (12, 13). Conversely, the 33-item Hypomania Checklist external assessment (HCL-33-EA) is an observer-rated version of the HCL-33 that was designed to assess patients' hypomanic symptoms based on ratings of their caregivers (14). The HCL-33 and HCL-33-EA are significantly and positively correlated with one another (15), though the HCL-33-EA is more sensitive in correctly distinguishing BD patients from MDD patients compared to the HCL-33 (16). To date, no study has examined the network structure of the HCL-33 or the HCL-33-EA. Previous studies typically focused singularly on HCL-33 total or mean scores without any attention to the relative importance and interrelations of specific symptoms. Consequently, investigating HCL scales at a symptom level using network analysis might provide new insights into the importance of different individual symptoms in relation to BD as a whole (17). Network analysis is a novel approach to examining the structure of psychopathology.

Recently, several network analyses have been conducted on different psychiatric disorder categories including depression, anxiety, obsessive compulsive disorder, and eating disorders (18–20). For example, one study found that "self-hatred," "loneliness," "sadness," and "pessimism" were the most central (influential) depressive symptoms in adolescents (17), while another study found death wishes were a key symptom that sustains depression (21). It has also been found that patients who endorse more central symptoms of depression at baseline have a greater chance of experiencing MDD in their later life compared to those who endorse more peripheral symptoms of depression at baseline (22).

In network analysis, higher centrality indicates greater importance (23). Analyzing the structure of symptoms measured by HCL scales from the perspective of network analysis would enable us to understand which symptoms might be particularly important in triggering and maintaining a broader range of hypomanic symptoms. The identification of central symptoms would also be potentially useful from the perspective of developing targeted interventions that address critical hypomania symptoms.

Hence, this study examined the structure of BD symptoms measured by the HCL-33, and the HCL-33-EA using a network approach. In addition, we compared the network structure, central symptoms, and network stability of network models generated on the basis of each HCL version.

MATERIALS AND METHODS

Study Participants

This cross-sectional study was conducted from January to December 2019. All participants were consecutively recruited from the outpatient department of Child Psychiatry of a tertiary hospital, the First Affiliated Hospital of Zhengzhou University. To be eligible, all participants were: (1) aged between 12 and 18 years; (2) diagnosed with a BD according to the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (24); and (3) able to understand Chinese and the contents of the assessments. Patients with acute manic episodes and those with severe medical or neurological conditions were excluded. Participants' diagnosis, clinical status, and eligibility were confirmed by their treating psychiatrist. Additionally, participants' caregivers (e.g., mother,

father, sibling, or close friends) were invited to complete the HCL-33-EA. All participants provided verbal informed consent while their legal guardians provided written informed consent. The study protocol was approved by the Medical Ethics Committee of the First Affiliated Hospital of Zhengzhou University.

Measurements

Participants' and caregivers' basic demographic data were collected. Chinese versions of the validated self-report HCL-33 (12, 13) and caregiver-rated HCL-33-EA (14, 15) were administered to assess the patient's hypomanic symptoms. Both the HCL-33 and the HCL-33-EA consist of 33 symptom items with dichotomous response options to assess presence of a symptom (Yes/No). Total scores on these scales range from 0 to 33, with higher scores indicating more severe hypomanic symptoms. A previous comparative study found that the HCL-33-EA was more sensitive than the HCL-33 in distinguishing BD patients from MDD patients (0.83 vs. 0.59) while the HCL-33 presented better specificity than the HCL-33-EA did (0.82 vs. 0.68) (16).

Network Estimation

All network analyses were conducted using R program (25). To estimate the network structure of hypomanic symptoms measured by the HCL-33 and HCL-33-EA, an Ising model was applied since all scale items (nodes) were dichotomous (26). In network analysis, each symptom is defined as a "node," and the pairwise association between symptoms is defined as an "edge." Nodes that are stronger or more connected with other nodes are located in the central area of the model. A thicker edge indicates a stronger correlation. Green edges indicate positive correlations while red edges indicate negative correlations (23). Following previous studies (18, 27), the "estimateNetwork" function was adopted to establish the network model, with 0.5 as the default tuning parameter (28).

Network Centrality

As recommended previously (17, 29), in the subsequent network analysis we focused on the centrality index of strength (17) which is the total sum of absolute weights of the edge connecting a node to all other nodes (30). In addition, predictability, which qualifies how well a specific node is predicted by all its neighboring nodes, was estimated using R-package "mgm" (Version 1.2-11) (31).

Network Stability and Accuracy

The stability and accuracy of each network model were assessed using R-package "bootnet" (28). First, a case-dropping bootstrap procedure was performed to compute correlation stability coefficients (CS-C) (1,000 replications). A CS-C is required to be above 0.25, and preferably 0.50 (28). Second, non-parametric bootstrapping was used to estimate the accuracy of edge-weights by computing confidence intervals (CIs). Larger CIs indicated poorer precision in the estimation of edges while narrower CIs indicated a more precise edge-weight network (17). Finally, differences in network properties (i.e., edge weights and node strengths) were evaluated via bootstrapped difference tests (28).

Network Comparison

To compare the network characteristics of hypomanic symptom communities measured by the HCL-33 and the HCL-33-EA, respectively, we used the "NetworkComparisonTest" package. These analyses investigated possible differences between the two BD measures at the levels of network structure (i.e., edge weight distributions), global strength (i.e., overall absolute connectivity among the symptoms), and each specific edge (28). The package is a permutation-based test that randomly regroups participants from each network repeatedly (1,000 replications) and then examines the differences between networks (32). The general network structure invariance test explores differences in the network structure as a whole. In instances of significant differences observed between the two network structures, we tested for specific edges that displayed significant differences.

RESULTS

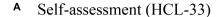
Participant Characteristics

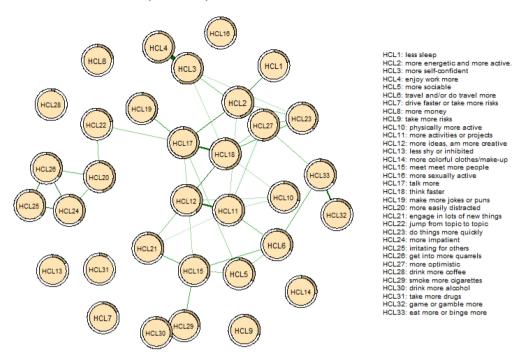
In total, 215 patients with BD (46 males and 169 females) and 215 caregivers (56 males and 159 females) participated in the study and completed all assessments. The mean age of patients was 15.43 years (SD = 1.61); their mean age of onset was 14.05 years (SD = 1.92), and their mean length of education was 9.65 years (SD = 1.77). More than half of the patients were suffering from their first episode (n = 115, 53.5%) at the time of the assessment and most did not report a family history of psychiatric disorders (n = 203, 94.4%). For caregivers, the mean length of education was 12.32 years (SD = 3.40). Descriptive statistics of the HCL-33 and the HCL-33-EA are presented in **Supplementary Table 1**.

Network Model of the 33-Item Hypomania Checklist

Figure 1A shows the network structure of hypomanic symptoms measured by the HCL-33. The edge HCL29-HCL30 ("smoke more cigarettes" – "drink more alcohol," edge weight = 2.172) showed the strongest positive connection in the model, followed by the edges HCL3-HCL4 ("more self-confident" – "enjoy work more," edge weight = 1.848), and HCL11-HCL12 ("more activities" – "more ideas," edge weight = 1.184).

The centrality plot indicated node HCL17 ("talk more," node strength = 4.044) was the most central symptom in the HCL-33 symptom model, followed by nodes HCL2 ("more energetic," node strength = 3.822), and HCL18 ("think faster," node strength = 3.801). In contrast, nodes HCL7 ("drive faster"), HCL8 ("spend more money"), HCL9 ("take more risks"), HCL13 ("less shy"), HCL14 ("more colorful clothes/makeup"), HCL16 ("more sexually active"), HCL28 ("drink more coffee"), and HCL31 ("take more drugs") were the least central responses in the symptom network (all node strength = 0). In addition, the predictability index showed that HCL3 ("more self-confident," 59.1%), HCL4 ("enjoy work more," 54.2%), and HCL17 ("talk more," 51.0%) had the highest predictability in the network (Figure 2A and Table 1).





B External-assessment (HCL-33-EA)

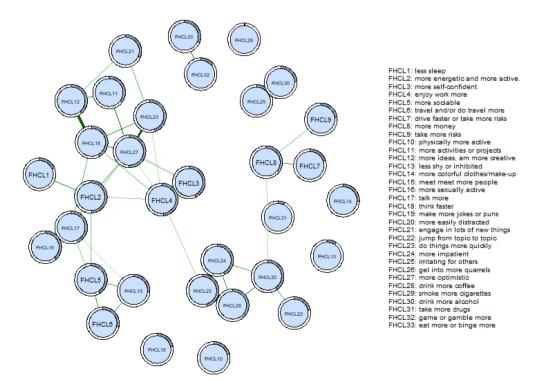
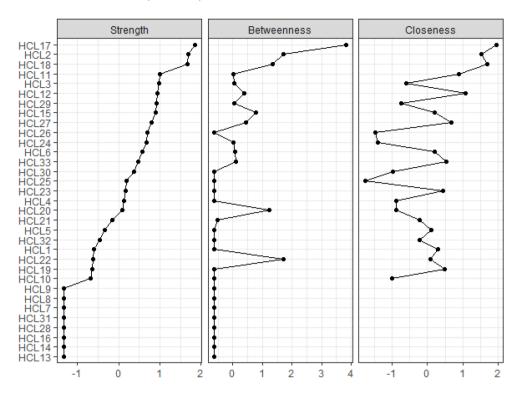


FIGURE 1 Comparison of network structure between HCL-33 **(A)** and HCL-33-EA **(B)**. In this diagram, nodes with stronger correlations are closer to each other. The thickness of an edge indicates the strength of the correlation. Green lines indicate positive associations. Red line indicates negative association. HCL-33, the 33-item Hypomania Checklist (self-assessment version); HCL-33-EA, the 33-item Hypomania Checklist (external assessment version).

A Self-assessment (HCL-33)



B External-assessment (HCL-33-EA)

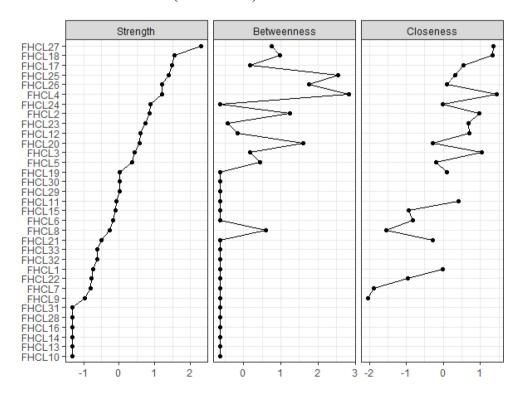


FIGURE 2 | Comparison of the centrality indices between HCL-33 (A) and HCL-33-EA (B). HCL-33, the 33-item Hypomania Checklist (self-assessment version); HCL-33-EA, the 33-item Hypomania Checklist (external assessment version).

TABLE 1 | Centrality of hypomania checklist items.

		HCL-33 (self-as	sessment version)	HCL-33-EA (external assessment version)					
	Strength	Betweenness	Closeness	Predictability	Strength	Betweenness	Closeness	Predictability		
HCL1	0.934	0	0.008	0.218	0.627	0	0.005	0.188		
HCL2	3.822	80	0.011	0.472	2.314	63	0.007	0.491		
HCL3	2.927	23	0.007	0.591	1.884	27	0.007	0.432		
HCL4	1.848	0	0.006	0.542	2.684	116	0.007	0.483		
HCL5	1.270	0	0.008	0.338	1.800	36	0.005	0.406		
HCL6	2.406	24	0.008	0.306	1.226	0	0.004	0.282		
HCL7	0	0	NA	0.196	0.561	0	0.003	0.198		
HCL8	0	0	NA	0.231	1.133	41	0.004	0.355		
HCL9	0	0	NA	0.292	0.369	0	0.003	0.231		
HCL10	0.835	0	0.006	0.291	0	0	NA	0.209		
HCL11	2.947	22	0.010	0.381	1.316	0	0.006	0.359		
HCL12	2.891	34	0.010	0.384	2.058	16	0.006	0.394		
HCL13	0	0	NA	0.157	0	0	NA	0.091		
HCL14	0	0	NA	0.232	0	0	NA	0.257		
HCL15	2.829	48	0.008	0.337	1.302	0	0.004	0.265		
HCL16	0	0	NA	0.273	0	0	NA	0.219		
HCL17	4.044	152	0.012	0.510	2.998	27	0.006	0.434		
HCL18	3.801	67	0.011	0.494	3.077	54	0.007	0.420		
HCL19	0.864	0	0.009	0.390	1.430	0	0.006	0.386		
HCL20	1.802	63	0.006	0.440	2.018	75	0.005	0.407		
HCL21	1.481	3	0.008	0.324	0.866	0	0.005	0.313		
HCL22	0.895	80	0.008	0.224	0.565	0	0.004	0.219		
HCL23	1.915	0	0.009	0.378	2.185	7	0.006	0.447		
HCL24	2.542	22	0.005	0.362	2.356	0	0.005	0.427		
HCL25	1.939	0	0.005	0.444	2.881	106	0.006	0.447		
HCL26	2.572	0	0.005	0.353	2.691	80	0.006	0.387		
HCL27	2.709	36	0.009	0.509	3.867	46	0.007	0.507		
HCL28	0	0	NA	0.029	0	0	NA	0.008		
HCL29	2.847	23	0.007	0.253	1.425	0	NA	0.201		
HCL30	2.172	0	0.006	0.289	1.425	0	NA	0.240		
HCL31	0	0	NA	0.088	0	0	NA	0.067		
HCL32	1.113	0	0.008	0.187	0.754	0	NA	0.143		
HCL33	2.298	25	0.009	0.328	0.754	0	NA	0.310		

HCL-33, the 33-item Hypomania Checklist (self-assessment version); HCL-33-EA, the 33-item Hypomania Checklist (external assessment version).

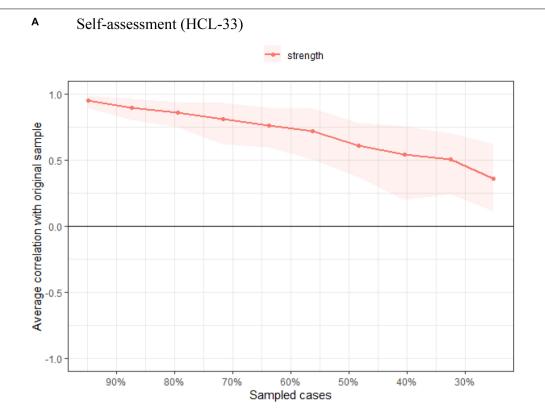
For stability of the HCL-33 network model, the case-dropping test showed that the CS coefficient for strength (0.284), exceeded the recommended threshold of 0.25, but was lower than 0.50 (Figure 3A). This indicated that the network model should be interpreted with caution as results might not be robust. Additionally, bootstrapped 95% CIs for estimated edge weights were relatively wide, suggesting comparatively low accuracy of edge strengths in the network (Supplementary Figure 1A). Plots of bootstrapped differences tests for HCL-33 edge weights and node strengths are presented in Supplementary Figures 2A, 3A.

Network Model of the 33-Item Hypomania Checklist – External Assessment

Figure 1B shows the network structure of the HCL-33-EA. Similar to the HCL-33 model, the edge HCL3-HCL4 ("more

self-confident" – "enjoy work more," edge weight = 1.439) showed the strongest positive connection in the model, followed by edges HCL29-HCL30 ("smoke more cigarettes" – "drink more alcohol," weight = 1.425), and HCL25-HCL26 ("irritating for others" – "get into more quarrels," edge weight = 1.373). The only negative edge in the network was HCL4-HCL25 ("enjoy work more" – "irritating for others," edge weight = -0.213).

The centrality plot showed that node HCL27 ("more optimistic," node strength = 3.867) was the most central symptom in the HCL-33-EA network, followed by nodes HCL18 ("think faster," node strength = 3.077), and HCL17 ("talk more," node strength = 2.998). In contrast, nodes HCL10 ("physically more active"), HCL13 ("less shy"), HCL14 ("more colorful clothes/makeup"), HCL16 ("more sexually active"), HCL28 ("drink more coffee"), and HCL31 ("take more drugs") were the least central symptoms in the network (all node strength = 0). In addition, the predictability index showed that HCL27 ("more



B External-assessment (HCL-33-EA)

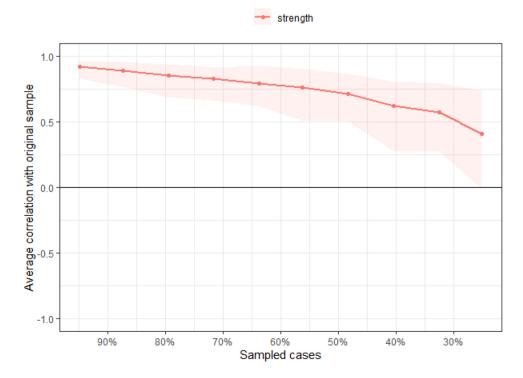


FIGURE 3 | Comparison of stability of centrality indices between HCL-33 **(A)** and HCL-33-EA **(B)**. The *x*-axis represents the percentage of cases in the original sample used at each step. The *y*-axis represents the average of correlations between the centrality indices in the original network and the centrality indices in the networks that were re-estimated after dropping increasing percentages of cases. Color areas indicate 95% confidential intervals.

optimistic," 50.7%), HCL2 ("more energetic," 49.1%), and HCL4 ("enjoy work more," 48.3%) had the highest predictability in the network (**Figure 2B** and **Table 1**).

Similar to the HCL-33 model, the CS coefficient for strength in the HCL-33-EA network was also 0.284 (Figure 3B). Bootstrapped 95% CIs for estimated edge weights were relatively wide, suggesting low stability of the model and low accuracy of the edge weights (Supplementary Figure 1B). Plots of bootstrapped difference tests for HCL-33-EA edge weights and node strengths are presented in Supplementary Figures 2B, 3B.

Network Comparison Between 33-Item Hypomania Checklist and 33-Item Hypomania Checklist – External Assessment Communities

The network comparison test showed that there were no significant differences in network structures of HCL-33 vs. HCL-33-EA symptom communities (M=0.946, P=0.931, Supplementary Figure 4A). Results of the global strength invariance test also indicated that the difference was not significant between the two network models generated from the HCL-33 and HCL-33-EA (HCL-33: 24.165 vs. HCL-33-EA: 18.991; S: 5.174, P=0.274); as such, the total absolute connectivity among symptoms was similar for HCL-33 vs. HCL-33-EA communities (Supplementary Figure 4B). Tests of individual edge weights did not find significant differences between the two models (P=0.005, using Holm-Bonferroni corrections for multiple comparisons).

DISCUSSION

This is the first study to examine the structure of hypomanic symptoms using network analysis and the first to consider hypomania symptom communities, not only from the perspective of adolescent patients but also from the perspective of their caregivers (typically their parents). We found that "talk more" and "think faster" acted as central symptoms in network models of both the HCL-33 and HCL-33-EA but the most influential central symptom differed between these models ("talk more" in the HCL-33 model vs. "more optimistic" in the HCL-33-EA model). According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (33), unusual talkativeness, overall increases in energy, abnormally upbeat/inflated self-esteem, and racing thoughts are among the key characteristic behaviors of individuals with hypomania, in line with our findings. Conversely, "less shy," "wear more colorful clothes/makeup," "more sexually active," "drink more coffee" and "take more drugs" were the least central nodes in networks of both the HCL-33 and HCL-33-EA. The reduced importance of these later symptoms and "driving faster" in networks of our sample was likely due to the reduced access adolescents have to alcohol/caffeine and drugs, sex with others, money for colorful clothes/makeup and a driver's license/car compared to their adult counterparts.

Central symptoms may play critical roles in triggering the occurrence of a psychiatric disorder, maintaining the disorder, and predicting its course and clinical outcome (23). As such, central symptoms are potentially important as targets for treatment and prevention of psychiatric disorders (17, 23, 28). Our findings indicated that "talk more," "more energetic," "more optimistic," and "think faster" were more influential than other hypomanic symptoms and had more connections with other symptoms in networks of both participants and caregivers. Therefore, it is possible that calculating a weighted total score of these central nodes or prioritizing these symptoms in clinical assessments (rather than total scores from entire hypomania symptom scales) may have utility in effectively capturing those hypomanic symptoms that are most crucial for understanding the severity of a BD (17, 23).

In this study, the edges "smoke more cigarettes" - "drink more alcohol," and "more self-confident" - "enjoy work more" showed strong positive connections in network models of both the HCL-33 and HCL-33-EA. As such, these two edges were stable, strong, and tended to occur spontaneously. Significant links between alcohol use and smoking behaviors have been consistently reported in previous studies (34, 35). For example, heavy alcohol users smoke more frequently than do nonusers, people tend to smoke more in settings where alcohol is served, and smokers are more likely than non-smokers to be binge drinkers (36). One reason for the strong smokingalcohol use association is that alcohol and nicotine both increase dopaminergic activity levels in the human brain; therefore, coadministration of nicotine and alcohol may increase feelings of pleasure more than using either one of them alone (35). Furthermore, alcohol could enhance rewarding effects or calming effects of nicotine on frequent users (34). Finally, the current sample comprised Chinese adolescents often undergoing their initial episode of BPD. Hence, the link between smoking and alcohol use in this group may reflect low use levels of both substances compared to older BPD samples with chronic illness courses.

Regarding the link between self-confidence and work enjoyment, previous studies found that self-esteem was positively associated with job satisfaction (37–39). When an individual feels valued and fulfilled at work, he/she is more able to go above and beyond what is asked of him/her, which contributes to feelings of increased accomplishment and confidence (37, 38, 40).

The only negative edge found in the two networks was the connection between "irritating for others" and "work enjoyment" in the HCL-33-EA model; this association indicated that these two symptoms were not likely to occur simultaneously in patients from the perspective of their caregivers. Previous studies found that both positive and negative emotions are significantly associated with job satisfaction and performance (41). For example, anger emotions in the workplace could lead to aggressive and risky behaviors against colleagues, while sadness is related to elevations in job dissatisfaction. Job satisfaction has

been defined as a positive emotional state resulting from an individual's subjective experience with his/her job (42). When one enjoys his/her work, positive affect is more likely to be fostered, interpersonal relationships are less likely to be conflicted or irritating, and social support may help to increase enjoyment of one's own work (43).

Previous research (44) has also found that when assessing health/disease status, external examiners (e.g., physicians, or caregivers) are more likely to focus on patients' objective symptoms and diagnoses, whereas patients tend to focus more on their subjective symptoms, functional limitations, and quality of life. Therefore, there tends to be some discordance between patient self-assessments and external examiners' assessments. Notably, the network comparison test in this study did not find significant differences at levels of network structure, global strength, or each specific edge between the patient HCL-33 and caregiver HCL-33-EA models. Hence, results provided preliminary evidence suggesting that HCL versions (self-report and external assessment) may not produce significantly different network model structures. Perhaps characteristics of adolescentcaregiver relationships (e.g., living together, a long-shared history, and often prolonged current contact) contributed to the lack of overall lack of disparity in observed network models but replications are needed to confirm the robustness of these assessment results.

A notable strength of the current study compared to a vast majority of network studies based exclusively on patient selfreports was its inclusion of a caregiver's assessment of hypomania symptoms in each adolescent patient. Despite this strength and potential implications the research has for elucidating the structure of hypomania symptoms among adolescents diagnosed with BP, several limitations should also be noted. First, although network stabilities for both network models were acceptable, adolescent-caregiver sample sizes were relatively small as suggested by less-than-optimal CS-C results. Second, because data were drawn from a single China-based study-site, generalizability of findings to adolescent-caregiver dyads in other regions of China and other countries is unknown. Third, due to the cross-sectional study design, the evolution of hypomania symptom networks over time could not be determined from the present data. Fourth, BD subtypes were not diagnosed in this hospital; therefore, subtypes were not included for analyses in this study.

CONCLUSION

In conclusion, the patient-assessed HCL-33 and caregiver-assessed HCL-33-EA generated similar hypomania symptom network structures and global strengths. The most and least

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influential hypomania symptoms in each of these network models were also somewhat similar: "talk more" and "think faster" emerged as important central symptoms in both HCL-33 and HCL-33-EA network models, though the single most influential symptom differed between the two models (i.e., "talk more" in the HCL-33, vs. "more optimistic" in the HCL-33-EA). Future studies with larger, more varied samples are warranted to confirm the accuracy and robustness of the hypomania symptom networks observed in this study.

DATA AVAILABILITY STATEMENT

The Medical Ethics Committee of the First Affiliated Hospital of Zhengzhou University that approved the study prohibits the authors from making the research dataset of clinical studies publicly available. Readers and all interested researchers may contact Y-TX (xyutly@gmail.com) for details. Y-TX will apply to the Medical Ethics Committee of the First Affiliated Hospital of Zhengzhou University for the release of the data.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Medical Ethics Committee of the First Affiliated Hospital of Zhengzhou University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

SL and Y-TX: study design. YY, W-YZ, YZ, FH, TC, and DZ: data collection, analysis, and interpretation. YY and Y-TX: drafting of the manuscript. TJ: critical revision of the manuscript. All co-authors contributed to the approval of the final version for publication.

FUNDING

Beijing Hospitals Authority Clinical Medicine Development of Special Funding Support (No. ZYLX202128).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt. 2022.844699/full#supplementary-material

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The Association of Sports Participation With Depressive Symptoms and Anxiety Disorder in Adolescents

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Aim: An increasing body of evidence has evidenced that physical activity is negatively associated with depression and anxiety in adolescents, although the associations between various modalities of PA with depression and anxiety have yet to be effectively explored. This study aimed to investigate the associations between sports participation and depression and anxiety among a sample of Chinese adolescents.

Methods: 2,374 adolescents from eight schools were invited to participate in this survey, of whom 1,714 adolescents from grades 7, 8, 10 and 11 were included for final analysis. Depressive symptoms and anxiety disorder were assessed using the Patient Health Questionnaire—9 (PHQ-9), as well as the Generalized Anxiety Disorder—7 (GAD-7), respectively. Sport participation was assessed using a single question. Additionally, sociodemographic factors were assessed using a self-reported questionnaire. Ordinal logistic regression was used to estimate sport participation's associations with depressive symptoms and anxiety disorders separately, having controlled for all sociodemographic covariates.

Results: Among all study participants, those with less participation in sport-related activities had a greater likelihood of reporting depressive symptoms (Odd ratio [OR] for never = 2.07; OR for 1–3 times per month = 1.77; OR for 1–2 times per week = 1.77), as well as anxiety disorders (OR for never = 1.61; OR for 1–3 times per month = 1.69; OR for 1–2 times per week = 1.38).

Conclusion: Encouraging adolescents to engage in more sports participation would provide an effective and feasible approach for mental health promotion. Despite this study having found promising evidence, the research findings should be replicated using more improved research with an enhanced study design. Future researchers are encouraged to design and implement sports participation interventions aimed at promoting mental health among adolescents, while future China-based studies are encouraged to replicate or negate our study findings.

Keywords: depression, anxiety, adolescents, sport participation, sport team

OPEN ACCESS

Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Cheng Chen, Karlsruhe Institute of Technology (KIT), Germany Fan Huiying, Shanghai Normal University, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Public Health

Received: 24 January 2022 Accepted: 14 February 2022 Published: 03 June 2022

Citation:

Chi G and Wang L (2022) The Association of Sports Participation With Depressive Symptoms and Anxiety Disorder in Adolescents. Front. Public Health 10:860994. doi: 10.3389/fpubh.2022.860994

INTRODUCTION

Physical activity (PA) is defined as any bodily movement that increases energy expenditure (1-3). Substantial evidence has indicated that regular PA participation is linked with numerous health benefits, for example healthy weight, improved cognitive function, in addition to enhanced cardiorespiratory fitness (4, 5). Across the literature, the associations between PA and mental health or disorder outcomes have been investigated and effectively established (6), suggesting that PA results in improved mental health status or may hinder the development of mental disorder across a spectrum of the population. In Biddle et al.'s (7) review, the authors summarized the evidence regarding the associations between PA and mental health or disorder outcomes among adolescents, while also recommending that researchers should unravel the association between various types of PA and health outcomes. Such evidence may assist with designing and implementing efficient and specific interventions aimed at promoting mental health in adolescents, because mental health problems have been a priority internationally (7). In this regard, recent studies have focused on specific modes of PA and their association with mental health or disorder outcomes (8, 9).

As an umbrella concept, an array of PA modes exist in the real world. For adolescents, sports participation is deemed a notable opportunity to promote healthy behaviors and overall development among children and youth, while also providing a way of increasing PA levels. It may be straightforwardly achieved in various settings (10), including school- or community-based contexts (11). An expanding body of evidence has suggested that sports participation is linked to numerous health benefits (12), among which mental health or disorder outcomes have been strongly focused on by researchers. Certain previous studies have investigated the relationship between sports participation and mental disorder outcomes among adolescents (13). For example, a recent systematic review identified the negative association of a higher frequency of sports participation with depressive symptoms and anxiety disorders among adolescents (14).

Despite evidence having convincingly demonstrated the significance of sports participation for preventing risks of depressive symptoms and anxiety disorders among adolescents (15), to date, no study has yet used a China-based data set, In turn, this has made researchers uncertain about the association between sports participation and mental disorders among Chinese adolescents. China is undergoing a period of rapid development, economic growth and societal transformation (16), thus making adolescents more exposed to health risks. Mental health problems are highly prevalent among Chinese adolescents, thus exerting health burdens on the family, community and entire society (17). In this regard, it is urgently necessary to identify effective approaches for preventing mental health problems. From the perspective of PA promotion, increasing PA levels would provide a feasible approach. Nevertheless, this assumption lacks China-based evidence. Moreover, little knowledge exists concerning the role of sports participation in relation to commonly occurring mental disorder outcomes among Chinese adolescents, for example depressive symptoms and anxiety disorder. Sports participation may be straightforwardly organized in different settings in China (18), including schools, as well as community and commercial sports organizations, which may provide an effective means of combatting increasingly pervasive mental health problems among Chinese adolescents. This calls for evidence-based findings to guide the action plans if possible. Nevertheless, such China-based data or evidence is extremely rare, meaning that it must be accumulated through relevant studies. This evidence accumulation can assist policymakers, researchers and practitioners to implement feasible and relevant mental health promotion actions.

To assist with resolving the literature gaps, this study aimed to analyse the associations of sports participation with depressive symptoms and anxiety disorders among a sample of Chinese adolescents.

METHODS

Study Design and Participants

This cross-sectional study was conducted between March and October 2021 in various cities in South-eastern China. Adopting a convenience sampling method, school-aged adolescents at public middle and high schools were invited to participate in a paper-based survey. Five middle schools and three high schools agreed to join this survey. For each participating school, adolescents from grades 7-8 in middle school and grades 10-11 in high schools were targeted as study participants, because adolescents in the 9th and 12th grades were immersed in academic activities relating to the college entrance examination. These were excluded from our study due to time allocation considerations. All students in one to three classes that had been randomly selected per participating school were included (this selection was conducted by contacting the teacher). In total, 2,374 participants consented to complete the questionnaire (with permission from their parents or guardians), with the assistance of the participating schools' teachers and principals. Data were collected and analyzed anonymously. All invited participating adolescents were informed of the research aim and provided with instructions prior to signing their consent form. Participants received detailed instructions explaining how to answer the survey. For this study, after removing cases with incomplete questionnaires and abnormal answers or completion time, 1,714 participants who had provided valid information relating to the variables were included for the final data analysis. The study was approved by the university ethics committee (102772021RT071). All participants agreed to participate in the study with parents giving their written, informed consent.

Measures

Sport Participation [Independent Variable]

Sport participation was analyzed using a single item, which stated: 'over the past 12 months, did you participate in a sports team, sports club or sport-related activity?' The possible responses to this question were: never; 1–3 times per month; 1–2 times per week, as well as 3 times or more per week. This measurement question has been confirmed as a reliable and valid item for assessing young people's sports participation (10).

Depressive Symptoms and Anxiety [Dependent Variables]

Depressive symptoms were analyzed using the Chinese version of the 9-item Patient Health Questionnaire (PHQ-9). This instrument consists of nine items concerning experiences of depressive symptoms within the last 2 weeks. Each item is rated on a four-point Likert scale, ranging from 0 (not at all) to 3 (nearly every day). Total scores range between 0 and 27, with higher scores indicating more severe depressive symptoms. Depressive symptoms' severity may be classified based on PHQ-9 scores: 0-4 (minimal), 5-9 (mild), 10-14 (moderate), 15-19 (moderately severe), as well as 20-27 (severe) (19). PHQ-9's psychometric properties have been tested with Chinese children and provide adequate reliability and validity (20).

Anxiety disorders were assessed using the 7-item Generalized Anxiety Disorder Scale (GAD-7). This scale comprises seven items, with each item response having a four-point Likert scale (from 0 to 3). The total scores for GAD-7 are between 0 and 21, with a higher score indicating a greater severity of anxiety disorders. Anxiety disorders' severity may be classified as minimal (0–4), mild (5–9), moderate (10–14) or severe (15–21) (21). The translated GAD-7 has been pervasively adopted in relation to Chinese children and adolescents, having shown acceptable reliability and validity (20).

Covariates

The following variables were treated as covariates in the further analysis, including sex, grade, age, residence, family affluence, as well as living with a parent or not.

Statistical Analysis

All statistical analysis was performed using SPSS 26.0. Descriptive statistics (percentage for the categorical variable; mean with standard deviation for the continuous variable) were applied to report the sample characteristics. To estimate the associations of sport participation with depressive symptoms and anxiety disorder, the odds ratio (OR) was calculated using Generalized Linear Models with Ordinal Logistic Regression, having controlled all the covariates noted above.

RESULTS

Data from 1,714 study participants were available for this research. Of the 1,714 study participants, males accounted for 53.4% (see **Table 1**). Study participants aged 16 were the highest proportion of participants, with adolescents in 10th grades also being the largest proportion. Over 70% of study participants lived in urban areas. 83.8% of study participants resided with their parents. Concerning sports participation, 64.7% of study participants reported that they never engage in sports participation. 52.5% and 64.8% of study participants reported normal severity of depressive symptoms and anxiety disorder, respectively.

Figure 1 presents the results regarding the correlation between sports participation and depressive symptoms among the study participants. Compared with study participants engaging in sports participation three or more times per week,

TABLE 1 | Sample characteristics of this study.

		n	%
Gender			
	Boys	915	53.4
	Girls	799	46.6
Age			
	12 years old	110	6.4
	13 years old	340	19.8
	14 years old	290	16.9
	15 years old	184	10.7
	16 years old	608	35.5
	17 years old	182	10.6
Grade			
	7th	350	20.4
	8th	415	24.2
	10th	517	30.2
	11th	432	25.2
Residence			
	Rural	158	9.2
	Suburban	342	20.0
	Urban	1,214	70.8
Live with parent			
	Yes	1,437	83.8
	No	277	16.2
Family affluence			
		5.05 ± 1.54	
Sport participation			
	Never	1,109	64.7
	1-3 times per month	265	15.5
	1-2 times per week	236	13.8
	3 or more times per week	104	6.1
Depressive symptoms			
	Normal	900	52.5
	Mild	520	30.3
	Moderate	162	9.5
	Moderately severe	62	3.6
	Severe	70	4.1
Anxiety disorder			
	Normal	1,111	64.8
	Mild	390	22.8
	Moderate	119	6.9
	Severe	94	5.5

those with a lower frequency of sport participation had a greater likelihood of reporting higher depressive symptoms (OR for never = 2.07; OR for 1–3 times per month = 1.77; OR for 1–2 times per week = 1.77).

Figure 2 shows the results for the correlation between sports participation and anxiety disorder among the study participants. Compared with those study participants engaging in sports participation three or more times per week, those with a lower frequency of sports participation had a greater likelihood of reporting higher anxiety disorder (OR for never = 1.61; OR for 1-3 times per month = 1.69; OR for 1-2 times per week = 1.38).

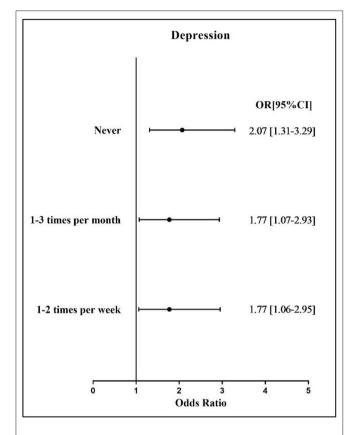


FIGURE 1 Association between sport participation and depressive symptoms severity. OR, odds ratio; CI, confidence interval. Reference group: 3 or more times per week.

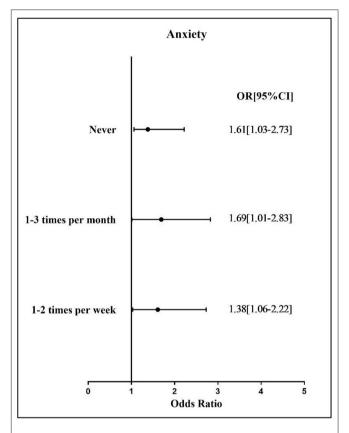


FIGURE 2 | Association between sport participation and anxiety disorder severity. OR, odds ratio; CI, confidence interval. Reference group: 3 or more times per week.

DISCUSSION

This study aimed to analyse the association of sports participation with depressive symptoms and anxiety disorders among adolescents, given that they are at higher risk of depression and anxiety. Our results primarily evidenced that in contrast with no sports participation, participating in more sport-related activities (for example, team or club activities) made the individual less likely to be identified with depressive symptoms. Significantly, we determined that adolescents engaging in greater sports participation (apart from three or more times per week) had lower odds of reporting anxiety disorders, compared with adolescents who never engaged in sports participation. In-depth analysis is presented below.

Our results indicated that sports participation among adolescents could be perceived as a potential means of combatting depressive symptoms. This research finding concerning the negative relationship between sports participation and depressive symptoms established in our research is supported by extant studies (14). For example, a recently published systematic review including meta-analysis revealed a small negative mean correlation between the frequency of sport participation and depression symptoms ($\rho=-0.09$, 95% CI: -0.11, -0.06) among adolescents (14). A prospective

study using cross-lagged analysis identified that greater sports participation predicted subsequent fewer depressive symptoms in adolescents (22). Furthermore, a substantial body of evidencebased cross-sectional studies is consistent with our research findings, thus collectively emphasizing the significance of sports participation for preventing depression (23, 24). Certain potential underpinning mechanisms have been proposed to explain the association between sports participation and depressive symptoms. One possible explanation is that sports participation is enhancing, which partially protect adolescents from depressive symptoms via neurobiological pathways (25). A further potential explanation is that participating in sportsrelated activities may enable engagement in positive social interactions that reduce individuals' negative emotions, which in turn diminishes depressive symptoms among adolescents (26). However, our study was a cross-sectional survey, which does not allow an exploration of the mechanisms connecting sport participation and depressive symptoms, although answers may be identified from the literature. Notably, in our study we did not observe a dose-dependent association between sport participation and depressive symptoms. Such a dose-dependent association should be expected, because it has been assumed that greater engagement in physical activity has a linear and negative correlation with fewer symptoms of depression, with this assumption being observed in previous studies. Our study identified that the odds of having fewer depressive symptoms when engaging in sport three or more times per week were higher than when participating in sport 1–2 times per week. This indicated that more sport participation may not have a stronger role in preventing depression compared with lower sport participation among adolescents. This significant finding has not been observed in prior studies, because they have suggested that greater sport participation is linked with consecutively decreased odds of depressive symptoms among adolescents. Our study has been unable to explain this interesting finding, therefore it should be addressed in future studies.

Our study results further suggested that sports participation among adolescents is negatively correlated with anxiety disorders. This research finding was consistent with previous studies (27–29). Sports participation may provide opportunities for engagement in physical activity and social interactions that can reduce symptoms of anxiety among adolescents. For example, a recent systematic review suggested that sports participation in adolescents was conversely related to anxiety symptoms (30). Additionally, some single empirical research has offered consistent evidence of this (31, 32).

Regardless of our research findings, certain previous studies have suggested that sports participation leads to detrimental mental health effects due to certain adverse social interactions and experiences (33–35). This point is rational, given that there is much evidence to support it. Studies have proposed that the relationship between sport participation and mental health outcomes among adolescents is affected by the types of sport, the volume of sport, duration of sport, the context of sport and some further factors (for example, measures to improve mental health outcomes, or the operationalisation of sport participation). Therefore, it is suggested that determining the association between sports participation and mental health outcomes is a complex research topic, calling for greater research interests and efforts.

Although the current study identified consistent evidence of the association between sports participation and depressive symptoms and anxiety disorders among adolescents, the research limitations should be mentioned to reach an improved understanding of the research findings. The study limitations include: (1) the cross-sectional design that cannot infer any conclusive evidence; (2) the nonprobability sampling method that generated a sample with lower representation; (3) self-reporting measures for collecting data on independent outcomes. To acquire more convincing evidence concerning the association between sports participation and mental health among adolescents, studies with a more optimal design are required that will enable a determination of whether sports participation can be an efficient method for fighting depression and anxiety.

Practical Implications

In accordance with our research findings, some practical implications may be proposed:

- (1) To reduce or prevent depressive symptoms and anxiety among adolescents, encouraging adolescents to participate in more sport-related activities (for example, joining a club or team) is a potentially feasible approach.
- (2) Because there are relatively low levels of sport participation among adolescents, efficient intervention should aim at improving sport participation.
- (3) Sport participation promotion among adolescents should be integrated into policy design and implementation, to enable young people's overall healthy growth and development.

CONCLUSION

Drawing on cross-sectional data for adolescents (high school students) in an economically developed city, this study has provided evidence that an appropriate frequency of engagement in sports may provide a protective measure against depression and anxiety among adolescents, thereby promoting mental health. Although the current study has provided promising evidence, the research findings require replication through enhanced research with an improved study design. Therefore, future researchers are encouraged to design and implement sports participation interventions aimed at promoting mental health among adolescents.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/supplementary material.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University Ethics Committee (102772021RT071). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

GC and LW: conceptualization, writing, investigation, data curation, and resources. LW: methodology, formal analysis, writing—review and editing, and visualization. GC: original draft preparation. Both authors have read and agreed to the published version of the manuscript.

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OPEN ACCESS

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SPECIALTY SECTION

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

RECEIVED 22 March 2022 ACCEPTED 28 June 2022 PUBLISHED 22 July 2022

CITATION

Zhou Y-m, Mak L, Zhao C-x, He F, Huang X-n, Tian X-b, Yi-zheng and Sun J (2022) Correlates of suicidal ideation in rural Chinese junior high school left-behind children: A socioecological resilience framework. *Front. Psychiatry* 13:901627. doi: 10.3389/fpsyt.2022.901627

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Correlates of suicidal ideation in rural Chinese junior high school left-behind children: A socioecological resilience framework

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Introduction: Suicide is one of the top five causes of adolescent mortality around the world. The socioecological resilience framework in explaining the risk factors and protective factors for suicidal ideation in left-behind children (LBC) has not been well explored. The current study aims to compare the prevalence of suicidal ideation in LBC and non-LBC, and explore its correlations with resilience factors among LBC.

Methodology: This study was part of an epidemiological survey conducted by UNICEF exploring mental health outcomes in left-behind children. We implemented a cross-sectional study collecting data from 11 provinces and 1 municipal, with 5,026 participants (3,359 LBC, 1,667 controls) in year one junior high school living in impoverished areas of rural China. Data on suicidal ideation, self-harm, resilience factors including health-risk behaviors, psychological wellbeing as it was measured by the Strengths and Difficulties Questionnaire, peer relationship within the school environment, and family support were collected.

Results: Overall prevalence of suicidal ideation among LBC was 7.2% which is significantly different from 5.5% reported by NLBC ($\chi^2=4.854$, p=0.028). LBC reported a higher prevalence of self-harm (16.4%) than NLBC (13.0%; $\chi^2=10.232$, p=0.001), but there was no difference in the prevalence of suicide plan, suicide attempt or help-seeking. LBC had significantly poorer psychological feeling, and greater emotional and behavioral difficulties peer relationship in the school environment than controls. In the multiple logistic regression, history of self-harm was the greatest predictor for suicidal ideation among LBC (OR = 2.078, 95% CI: 1.394–3.100, p<0.001). Health risk behavior including previous smoking attempt, poor psychological feeling, and emotional and behavior difficulties, and poor peer relationship within school environment, were also significant risk factors for suicidal ideation among LBC.

Conclusion: The prevalence of suicidal ideation and self-harm was greater among left-behind than non-left-behind children. Our results show resilience factors including previous self-harm, emotional and behavioral problems, smoking, and poor peer relationship are significantly associated with suicidal ideation in left-behind adolescents.

KEYWORDS

suicide, left-behind children, resilience, emotional and behavioral problems, self-harm

Introduction

Left-behind children are a unique group of children who have been subject to separation from one or both parents who have migrated for at least 6 months (1). Labor migration describes the migration of parents living in low-income areas to regions of higher income in search for better employment, opportunity, and lifestyle. Their children usually remain in the hometown and are cared for by their grandparents, other relatives, or the wider community. According to UNICEF China 2015 Reports, there are currently 69 million children who identify as being "left-behind" which estimates to every four out of ten Chinese children being directly affected by parental migration (2).

Childhood and adolescence are a crucial period in a person's life where an individual develops a sense of self and the world they live in (3). Parents influence the development of externalizing behaviors and internalizing behaviors in children and these foundations continue to affect behaviors in adulthood (4). The absence of a parental figure can present significant problems. As such, the vast majority of literature suggests that stark differences exist among left-behind children and nonleft-behind children in terms of physical health and mental health outcomes. An extensive meta-analysis which aimed to analyse the effect of parental migration on the health of LBC in adolescents from low- and middle-income countries analyzed global data from more than 250,000 left-behind children (LBC) from 111 studies (1). They found that compared to nonleft-behind children (NLBC), LBC had significantly increased risks for wasting, stunting, substance use, poorer psychological wellbeing, greater symptoms of depression, anxiety, suicidal ideation and conduct disorder (1). Of note, children exposed to parental migration had 1.7 times higher risk of experiencing suicidal ideation compared to controls (1).

Consistently ranked among the top five leading causes of death in children and adolescents, the World Health Organization describes suicide as a global health priority (5). Suicide is defined as a fatal self-injurious act with some evidence of intent to die (6). While preventable in its definition, annually, there are more than 700,000 reported

cases of suicide around the world (7). Self-harm is defined as "an expression of personal distress by an individual who hurts him or herself" (8). An overlap between suicide and self-harm exists. Self-harm can be separated into two broad categories—non-suicidal self-injury, and self-injury with suicidal intent. According to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders, non-suicidal self-injury is defined as 'self-injury directed to the surface of the body undertaken to induce relief from a negative feeling, and or cognitive state, or to achieve a positive mood state' (9). This article explores the broad term self-harm and does not distinguish between non-suicidal self-injury and self-injury with suicidal intent.

Regardless of whether self-harm is with or without suicidal ideation, self-harm may escalate into suicidal behaviors when it becomes insufficient as a coping strategy against trauma or stress (10), and individuals who self-harm may perceive a suicide attempt to be less frightening upon desensitization to pain (11). A recently published meta-analysis exploring prevalence of suicidal behaviors among LBC, found the prevalence of suicidal ideation was 18.7, 6.4% for suicide plan, and 3.1% for suicide attempt (12). LBC had 26% greater risk of having suicidal ideation than NLBC, and this was statistically significant (12).

Suicide behaviors among children are predictive for suicide behaviors in adulthood. One longitudinal study that prospectively traced the development of children from ages 5-30, examined whether suicidal ideation in community adolescents represents normative adolescent angst or is predictive of psychopathology, suicidal behaviors, and/or compromised functioning 15 years after onset (13). They found the risk of suicide attempts was increased by almost 12 folds in adolescents who described suicidal ideation at age 15, compared to those who denied of having suicidal ideations (13). Another study that aimed to investigate psychopathological consequences of University students who were LBC found the effects of parental migration perpetuate into adulthood as more of these University students reported suicide attempts (OR 1.67; 95%CI: 1.57-1.77, p < 0.001) and self-harm (OR 1.65; 95% CI: 1.53-1.79) than University students who were never 'leftbehind' (14).

Resilience is a multidimensional construct that can be explained as both a personality trait and a process (15). It is described as a characteristic relating to an adaptive stress resistant personal quality leading to healthier outcomes (16). Resilience is also defined as the dynamic process of overcoming the negative effects and trajectories associated with risk exposure and coping successfully with traumatic experiences (17). In addition to neural and psychological self-organizations, the transaction between the ecological context and the developing organism influences the resilience process (18).

The socioecological resilience framework proposes that the degree of positive emotional and behavioral development is determined by the child's interaction with their distal and proximal support systems including caregivers, family, school, peers, and the broader community (19). Successful support systems can promote positive feelings of security in individuals and their environment; whereas the availability of a child's primary caregiver in conjunction with their peers, school and broader community supports may promote healthy emotional and behavioral development in the context of parental absence as seen in LBC (1, 20). The socioecological resilience framework can also explain the significance of negative social factors, individual character, and negative psychological factors on unhealthy outcomes such as suicide (21, 22). Smoking and drinking alcohol have been described as negative coping of stressful life events when other supports are not available (23). A meta-analysis found smoking and alcohol use were risk factors for suicide ideation among mainland Chinese youth (24). Ultimately, the socioecological resilience framework emphasizes that individual traits, family aspects, and the social environment have a pivotal role in resilience (25).

Left-behind children are a unique population exposed to a lack of parental support and are thus at risk of development self-harm and suicidal ideation. No studies to date have used the socioecological resilience framework to describe correlates of suicidal ideation among left-behind children as important protective factors for healthy emotional and behavior development. Our research aims to fill in this gap by examining correlates of suicide among LBC including individual factors (negative coping, emotional and behavioral problems), duration of parental migration and negative school environment.

This project aims to (1) compare the prevalence of self-harm, suicidal ideation and psychological wellbeing among LBC and NLBC, and (2) to identify factors relating to suicidal ideation among LBC. We hypothesized that emotional and behavioral problems, negative coping behavior including smoking and drinking alcohol, poor school environment, were associated with suicidal ideation in left-behind children.

Methodology

Study design

This cross-sectional study collected data between November 2016 to January 2017 using purposive sampling. The reporting of the study followed the STROBE statement for observational study and had a rigorous quality control process. Firstly, all participating health professionals in the rural health centers were trained by United Nation's Child Fund assigned project experts. These trained health professionals went to each school, explained the study aim to each participating school teachers. All teachers contacted parents or caregivers of each student and obtained consent form from main caregivers. Students were also asked to provide consent before they understood the survey study. Schools were randomly selected to participate in the study. There is <2% missing data in this study as a result of the quality of training of people who conducted the data collection. Counties were recruited based on classification as "povertystricken area" defined as having two percent of the population living below the poverty line (per capita annual income of 2,300 Chinese Yuan ~360USD http://www.xinhuanet.com/english/ 2018-10/17/c_137538566.html). A total of 27 poverty-stricken counties were identified from 11 provinces and 1 municipality located in rural areas across China. In this study, left-behind children were defined as children registered in rural areas in Grade 1 of Junior school who had been exposed to at least 6 months of parental migration by either one parent or both parents. Non-left behind children were defined as children registered under a rural household who had not been exposed to parental migration. Grade 1 junior high school students were selected for two reasons—researchers were interested in exploring the students in their year of transition from primary schooler to high schooler, and grade 1 students would be most practical for follow-up if the study design was changed from cross-sectional to a longitudinal study.

Participants

The sample size was calculated using the formula $N=(D_deffxZ^2P(1-P)/d^2)$, with a confidence interval of 95% and z-value of 1.96. Probability p demonstrated the low prevalence of emotional and behavioral problems for LBC over 15.0%, and the design effect D_{deff} was 3 with a relative error of 15%; thus $d=15\times15.0\%$. Based on these calculations, the corresponding sample size was estimated to be \sim 2,900 with no <200 people from each province. The National Health and Family Planning Commission of PRC states research related to LBC should have a 2:1 ratio of LBC to NLBC (26). As per these recommendations, the study recruited 3,359 left-behind children and 1,667 non-left-behind children. The total sample size of 5,026 participants included is adequate for data analysis.

Procedure

To ensure the population was adequately represented using post-weight adjustment, quota sampling was chosen to recruit participants. Grouping was performed based on reported number of LBC from each county. Further information was collected from each county including: (i) total number of children and their age, (ii) total number of LBC, (iii) ratio of boys to girls. Eleven provinces (Anhui, Guangxi, Guizhou, Hebei, Henan, Hubei, Hunan, Jiangxi, Shaanxi, Shanxi, Sichuan) and 1 municipality (Chongqing) which were identified to have a high proportion of left-behind children were selected. This study was part of an epidemiological survey on mental health of left-behind children. Its design was approved by local health administration bureaus, participating schools, and the Ethics Committee of Beijing Anding Hospital affiliated with Capital Medical University under ethical approval number of 2013 (06). The surveys on LBC and NLBC were collected from the same schools. Participation was voluntary and informed consent was obtained from both students and their caregivers. Students completed the survey in class under supervision from teachers who were briefed earlier by trained local health workers.

Measures

Outcome measures: Self-harm and suicidality indicators

Self-harm

Assessment of self-harm was assessed based on the question—"In the past 6 months, have you intentionally hurt yourself (such as burn with a cigarette butt, cut with a blade, hit a wall with your head)?" The response was "yes" or "no".

A self-assessment questionnaire asked students about markers of suicidality including suicidal ideation, suicide plan, previous suicide attempt and whether help was sought upon experiencing suicidal thoughts in the past 6 months. These were dichotomous variables responded with "yes" or "no".

Risk factors for suicidality

According to resilience framework, risk factors were measured as individual level factors including emotional and behavior problems, socio-ecological factors including lack of caregiver support, peer bullying and negative school environment. Data in individual left-behind experience, and demographic characteristics were also collected.

Emotional and behavioral problem was measured by strengths and difficulties questionnaire

The Strengths and Difficulties questionnaire initially designed by Goodman (1997) is a globally used measurement tool for child and adolescent mental health and assessment

of emotional and behavioral problems. The Chinese version of the SDQ is a reliable and valid instrument for measuring psychopathology in children and adolescents, as demonstrated by its satisfactory test-retest reliability, internal consistency, concurrent validity and discriminant validity (27, 28). The SDQ student edition contains 25 items assessing five subscales: (1) emotional symptoms; (2) conduct problem; (3) hyperactivityinattention; (4) peer problems; and (5) prosocial behavior. Each item has three response options: "not true", "somewhat true", and "certainly true", weighted with different scores of 0, 1 and 2 respectively; and reverse scoring for five items. The total scores for items under subscale 1 to 4 were combined to provide a total emotional and behavioral problem score, and subscale remained as an independent factor as prosocial behavior. The reliability for SDQ was 0.70 Cronbach's alpha and had reasonable level of reliability when it was applied to this new and unique population. Higher emotional and behavioral problems were associated with greater severity of psychological behavioral problems of the child.

School environment

The negative school environment score was derived from the combined score of 6 questions: (1) maliciously teased, (2) asked for property, (3) exclusion, (4) threatened, intimated, (5) physically harmed (hit, kicked), (6) teased due to appearance or other defect. Three response options were given: "never", "occasionally", "often", weighted 0, 1, and 2 respectively. A high school environment score reflected poor school environment.

Negative psychological feeling of adolescents

Psychological feeling was attributed to the combined scores of 5 items: (1) unhappy because of stress or academic problems, (2) insomnia due to fear, (3) feelings of loneliness in past 6 months; (4) considered leaving home in past 6 months, (5) intentionally hurt yourself (burn with cigarette, cut blade). Those who described low psychological feeling were further asked if those feelings impacted: (1) family life, (2) relationship with friends, (3) study in class, (4) extracurricular activities, (5) burden others (family, friends, teachers). The difficulties impact score was calculated from the sum of these five items.

Demographic characteristics

Information of demographic characteristics were collected: gender, boarding status, frequency of outdoor activity, primary guardian, education of main guardian, history of engaging with cigarette smoking, history of engaging in drinking alcohol, duration of most recent paternal migration, duration of most recent maternal migration.

Statistical analysis

Data was retrieved, coded and entered into Epidata 3.1 (Odense, Denmark). Categorical data such as demographic

variables and self-harm were analyzed using chi-squared testing to identify potential confounding factors which may confound the relationship between suicidal ideation and independent variables. Independent samples t-test was used to compare continuous variables (emotional and behavioral problems, school environment, parenting questions, psychological characteristics) based on left-behind status and suicidality. Demographic variables found to significantly differ between adolescents who reported high suicidality and low suicidality were included in the subsequent multivariate analysis. Multiple logistic regression analysis assessed the association between school environment, adolescent psychological characteristics, emotional behavioral problems, self-harm with suicidality indicators in left-behind children. All statistical analyses were conducted by SPSS for Windows 28.0 (IBM, Chicago, IL) with statistical significance level defined as p < 0.05, two-tailed.

Results

A total of 5,026 first year junior high school students--3,359 (66.8%) LBC and 1667 (33.2%) NLBC—were included in the data analysis. All students who were invited to the study when data collection was conducted answered the survey. When 55 invalid surveys with more than 50% of questions were not answers and were excluded, this yielded high valid survey response rate of 98.9%. Table 1 illustrates a greater proportion of LBC stayed in dormitories (70.6%) compared to NLBC (62.6%; $\chi^2 = 33.396$, p < 0.001). The majority of LBC identified the primary caregiver to be their grandparents (88.9%), whereas among NLBC 94.1% reported their parents as the primary caregiver. More LBC (37.9%) reported having tried alcohol than NLBC (34.7%; $\chi^2 = 8.045$, p = 0.018). Significant differences were also found in the frequency of outdoor activity among LBC and NLBC (χ^2 = 14.390, p = 0.002). There was no significant difference in gender $(\chi^2 = 0.322, p = 0.570)$, previous smoking attempt $(\chi^2 =$ 1.573, p = 0.210) or highest educational attainment of the primary caregiver ($\chi^2 = 2.128$, p = 0.712) based on parental migration experience.

As shown in Table 2, the overall prevalence of suicidal ideation among LBC was 7.2% which is significantly >5.5% reported by NLBC ($\chi^2=4.854,\ p=0.028$). The prevalence of self-harm in the past 6 months was also significantly greater among LBC (16.4%) than NLBC (13.0%; $\chi^2=10.232,\ p=0.001$).

Table 3 reports LBC experienced significantly poorer school environment (M=8.812, SD = 1.927) than NLBC (M=8.638, SD = 1.838; t-ratio=3.108, p<0.001), lower psychological feeling (M=9.427, SD = 2.911) than NLBC (M=8.925, SD = 2.818; t-ratio=5.795, p<0.001), and more emotional and behavioral problems (M=13.089, SD = 5.303) than NLBC (M=12.477, SD = 5.363, t-ratio=3.846, p<0.001). There

was no significant difference among LBC and NLBC based on prosocial behavior or how bothered the children were about their difficulties.

Table 4 suggests students who report suicidal ideation experienced more negative school environment, negative psychological wellbeing, more emotional and behavioral problems, and are more bothered by these difficulties compared to students who did not report suicidal ideation, and these all reached statistical significance of p < 0.001 among LBC and NLBC. For these four determinants, the magnitude of the t-value was consistently greater among LBC than NLBC. Only prosocial behavior was found not to have no relationship with suicidal ideation of students.

According to Table 5, the greatest statistical difference observed among LBC who had suicidal ideation and those who denied of suicidal ideation was based on self-harm in the past 6 months. Among the LBC who had admitted to suicidal ideation, approximately half (55.0%) had performed self-harm in the past 6 months, while in those who denied of suicidal ideation only 13.4% had a history of self-harm ($\chi^2 = 280.489$, p < 0.001). A greater proportion of LBC who reported suicidal ideation had smoked in the past (29.2%) than those who denied of suicidal ideation (13.2%; $\chi^2 = 46.413$, p < 0.001). Likewise, 61.9% of LBC with suicidal ideation reported having drunken alcohol before, compared to 37.3% who had drunken alcohol but never considered suicide ($\chi^2 = 52.586$, p < 0.001). In terms of demographic variables, suicidal ideation differed based on the highest educational attainment of the primary caregiver (χ^2 = 22.478, p < 0.001). There was no significant difference in the distribution of student's gender, boarding status, frequency of outdoor activity, or the identify of primary caregiver based on suicidal ideation. Regarding NLBC, similar to LBC, there was significant difference (p < 0.001) in the proportion of students who had smoked or drunk alcohol in the past or performed selfharm in the past 6 months based on suicidal ideation. However, on the contrary, the proportion of NLBC who described suicidal ideation also differed based on student gender. NLBC of the female gender were more likely to report suicidal ideation than boys ($\chi^2 = 7.032, p = 0.008$).

Table 6 provides statistical evidence suggesting the relationship between negative school environment, negative psychological feeling, emotional and behavioral difficulties, self-harm, and past smoking attempt are significantly associated with suicidal ideation among LBC. The Nagelkerke variance of 30.2% indicates 30.2% of the variance in suicidal ideation can be explained by the psychosocial wellbeing markers, self-harm and the listed confounders.

History of self-harm was the single greatest predictor for suicidal ideation among LBC. LBC who reported having performed self-harm in the past 6 months were 2.078 times more likely to report having suicidal ideation compared to those who had not self-harmed in the past 6 months (95% CI: 1.394–3.100, p < 0.001). Previous smoking attempt was the next significant

TABLE 1 Comparison of demographic characteristics, smoking attempt, previous alcohol use in LBC (n = 3359) and NLBC (n = 1667).

Variables	LBC n(%)	NLBC n(%)	χ^2	p	Total n(%)
Sex					
Male	1574 (46.9)	767 (46.0)	0.322	0.57	2341 (46.6)
Female	1785 (53.1)	900 (54.0)			2685 (53.4)
Boarding status					
In boarding school	2373 (70.6)	1043 (62.6)	33.396	< 0.001	3416 (68.0)
Not in boarding school	986 (29.4)	624 (37.4)			1610 (32.0)
Smoking attempt					
Yes	483 (14.4)	218 (13.1)	1.573	0.21	701 (13.9)
Never smoked	2876 (85.6)	1449 (86.9)			4325 (86.1)
Drinking attempt					
Yes	1274 (37.9)	579 (34.7)	8.045	0.018	1853 (36.9)
Never drank alcohol	1993 (59.3)	1054 (63.2)			3047 (60.6)
Outdoor activity					
Everyday	1057 (31.5)	523 (31.5)	14.39	0.002	1580 (31.4)
Every week	926 (27.6)	527 (31.7)			1453 (28.9)
Every month	160 (4.8)	89 (5.4)			249 (5.0)
Rarely	1214 (36.2)	523 (31.5)			1737 (34.6)
Identity of main caregiver					
Father / Mother	47 (1.4)	1568 (94.1)	4389.89	< 0.001	1615 (32.1)
Grandma/Grandpa	2987 (88.9)	84 (5.0)			3071 (61.1)
Other relatives (adults)	245 (7.3)	11 (4.3)			256 (5.1)
Non-adult relatives	80 (2.4)	3 (0.2)			83 (1.7)
Caregiver highest education					
Never went to school	808 (24.5)	25 (26.9)	2.128	0.712	34 (1.0)
Primary school	1564 (47.5)	45 (48.4)			169 (5.0)
Junior high school	724 (22.0)	17 (18.3)			741 (21.9)
Senior high school	165 (5.0)	4 (4.3)			1609 (47.5)
University	32 (1.0)	2 (2.2)			833 (24.6)
Duration of previous father mi	gration				
<6 months	503 (15.0)				
6 months-1 year	1865 (55.7)				
1 year—2 year	762 (22.7)				
>2 years	213 (6.4)				
Duration of previous mother n	nigration				
<6 months	643 (19.2)				
6 months-1 year	1980 (59.2)				
1 year-2 years	447 (13.4)				
>2 years	275 (8.2)				

risk factor; those who had smoked were 1.613 times more likely to report suicidal ideation (95% CI: 1.053–2.473, p=0.028). Three out of the five psychosocial wellbeing determinants were found to be risk factors for suicidal ideation. One unit increase in psychological feeling score increased the chance that LBC experienced suicidal ideation by 24.2% (95% CI: 1.162–1.328, p<0.001). Suicidal ideation was increased by 10.9% per unit

for poor school environment (95% CI: 1.020–1.206, p=0.015), and 6.8% for total difficulties (95% CI: 1.031–1.108, p<0.001). In comparison, feeling bothered by difficulties (OR=1.067, p=0.077), prosocial behavior (OR=1.000, p=0.997), and past alcohol drinking attempt (OR=1.311, p=0.163), and length of most recent maternal migration, were not found to be significantly associated with suicidal ideation among LBC.

TABLE 2 Prevalence of self-harm and suicidality indicators in LBC (n = 3344) and NLBC (n = 1663) using Chi-Square Analysis.

Variables	LBC n(%)	NLBC n(%)	χ^2	p	Total n(%)
Suicidal ideation					
Yes	240 (7.2)	92 (5.5)	4.854	0.028	332 (6.6)
No	3,104 (92.8)	1,571 (94.5)			4,675 (93.4)
Self-harm in past 6 mor	nths				
Yes	551 (16.4)	216 (13.0)	10.232	0.001	767 (15.3)
No	2,808 (83.6)	1451 (87.0)			4,259 (84.7)

TABLE 3 Comparison of negative school environment, negative psychological feeling, emotional and behavior difficulties, bothered by difficulties of LBC and NLBC.

	LBC mean (SD)	NLBC mean (SD)	t	p	Total mean (SD)
Negative school environment	8.812 (1.927)	8.638 (1.838)	3.108	< 0.001	8.754 (1.898)
2. Psychological feeling	9.427 (2.911)	8.925 (2.818)	5.795	< 0.001	9.261 (2.888)
3. Bothered by difficulty	7.914 (2.386)	7.841 (2.335)	0.882	0.189	7.891 (2.368)
4. Emotional and behavioral problems	13.089 (5.303)	12.477 (5.363)	3.846	< 0.001	12.891 (5.333)
5. Prosocial behavior	7.279 (1.945)	7.315 (2.011)	0.573	0.283	7.291 (1.966)

Discussion

Stemming from a socioecological resilience framework, our cross-sectional study examined correlates of suicidal ideation among LBC including emotional and behavioral problems, negative psychological feelings, negative school environmental in the absence of parental support, in conjunction with other unhealthy behaviors of smoking and drinking alcohol from a large representative LBC population drawn from impoverished areas of rural China. The overall prevalence of suicide ideation among left-behind was 7.2%, which was significantly different from 5.5% reported by controls. Our estimates for prevalence were markedly lower than the estimates of a recently published meta-analysis of 15 studies which reported the prevalence of suicide ideation among left-behind children as 18.7% (12). In comparing our results to Qu et al. (12), there are two possible explanations for this discrepancy. First, the majority of the studies included in their meta-analysis questions about suicidal behaviors in the last 12 months or in their lifetime, while in our study, the timeframe for self-harm and suicidal ideation was 6 months. Furthermore, some studies included provided scales for suicidality while we collected dichotomous data on self-harm and suicidal ideation.

We found 16.4% of left-behind children exhibited self-harm behaviors in the past 6 months, significantly different from the 13.0% reported by controls. Again, these estimates were substantially lower when compared to another population-based cross-sectional study of 2,898 children aimed to investigate self-harm behaviors and associated factors in LBC, and found 48%

of LBC reported self-harm behaviors (29). In our study, selfharm was the single greatest risk factor for suicidal ideation among left-behind children (OR = 2.078, 95%CI: 1.394-3.100). Adolescents are particularly vulnerable to self-harm behaviors and affective disorders perhaps due to neurodevelopment involving cortical regions of the brain (30). The motives for self-harm are vast and variable including self-punishment, intrapersonal functions, expression of distress, and punishing others (31). Self-harm behaviors can transform into suicidal behaviors when the act of self-harm no longer serves as an effective coping method (10), and repeated acts of self-harm can desensitize individuals to pain (11). One meta-analyses that aimed to disengage the association of self-injurious thoughts and behaviors with subsequent suicidal behavior in adolescence and young adulthood, found a longitudinal association existed as suicide death was 22 times more likely (95%CI: 18.40-27.58) among adolescents and young adults who described any previous self-injurious thoughts or behaviors (32).

The significant higher proportion of adolescents experienced suicidal ideation can be explained by resilience model. Individual factors including emotion and behavior problems and psychological feeling ere significantly correlated with suicidality among LBC. Our findings are consistent with previous research which found a child's strengths and difficulties can predict self-harm (33) and suicidality (34). Our study suggests the relationship between smoking, alcohol and suicidal ideation may be the manifest of negative coping in response to stressful life events when other supports from parents, peers and community were absent (35).

Zhou et al.

TABLE 4 Comparison of school environment, psychological feeling, total difficulties, prosocial behavior of LBC and NLBC by suicidality.

					LBC ($n=3$	3359)					NLBC $(n =$	1667)
	Suic ideation (SI	n mean	No suicidal ideation mean (SD)		t	p	ideatio	cidal on mean SD)	No suicidal ideation mea (SD)			p
Negative school environment	10.408 ((2.538)	8.689 (1.814)	1	0.291	< 0.001	9.913	(2.256)	8.563 (1.784)	5.63	35	<0.001
Negative psychological feeling	12.871 ((3.451)	9.161 (2.688)	1	6.274	< 0.001	12.511	1 (3.317)	8.715 (2.640)	10.7	78	< 0.001
Bothered by difficulty	9.473 (2	2.706)	7.753 (2.291)	8	3.693	< 0.001	8.944	(2.951)	7.762 (2.266)	3.30)5	< 0.001
Emotional behavioral problems	17.608 ((5.873)	12.740 (5.093)	1:	2.405	<0.001	16.703 (5.553)		12.228 (5.249)	7.87	78	< 0.001
Prosocial behavior	7.129 (1.997)	7.291 (1.940)	-	1.242	0.215	7.297	(2.068)	7.316 (2.008)	-0.0	87	0.931
		LBC $(n = 3359)$			NLBC (n = 1667)		Total chi	ildren	
	Suicide ideation mean (SD)	No suicida ideation mean (SD		p	Suicidal ideation mean (SD)	No suicidal ideation mean (SD)	t	p	Suicidal ideation mean (SD)	No suicidal ideation mean (SD)	t	p
School environment	10.41 (2.54)	8.69 (1.81)	10.291	< 0.001	9.91 (2.26)	8.56 (1.78)	5.635	< 0.001	10.27 (2.47)	8.65 (1.80)	11.760	< 0.001
Psychological feeling	12.87 (3.45)	9.16 (2.69)	16.274	< 0.001	12.51 (3.32)	8.73 (2.64)	10.778	< 0.001	12.77 (3.41)	9.01 (2.68)	19.644	< 0.001
Bothered by difficulty	9.47 (2.71)	7.75 (2.29)	8.693	< 0.001	8.94 (2.95)	7.76 (2.27)	3.305	< 0.001	9.33 (2.78)	7.76 (2.28)	9.097	< 0.001
Emotional behavioral problems	17.61 (5.87)	12.74 (5.09)	12.405	<0.001	16.70 (5.55)	12.23 (5.25)	7.878	< 0.001	17.36 (5.79)	12.57 (5.15)	14.569	<0.001
Prosocial behavior	7.13 (2.00)	7.29 (1.94)	-1.242	0.215	7.30 (2.07)	7.32 (2.01)	-0.087	0.931	7.18 (2.01)	7.30 (1.96)	-1.108	0.268

TABLE 5 Suicidal ideation stratified by demographic characteristics, smoking attempt, previous alcohol use, and self-harm in LBC and NLBC.

	I	eft-behind c	Non-left behind children				Total children					
Variables	SI (n%)	No SI n(%)	χ^2	p	SI (n%)	No SI n(%)	χ^2	p	SI (n%)	No SI n(%)	χ^2	p
Sex												
Male	100 (41.7)	1466 (47.2)	2.769	0.096	30 (32.6)	735 (46.8)	7.032	0.008	130 (39.2)	2201 (47.1)	7.822	0.005
Female	140 (58.3)	1638 (52.8)			62 (67.4)	836 (53.2)			202 (60.8)	2474 (52.9)		
Boarding status												
Yes	176 (73.3)	2189 (70.5)	0.85	0.356	60 (65.2)	981 (62.4)	0.285	0.593	236 (71.1)	3170 (67.8)	1.53	0.216
No	64 (26.7)	915 (29.5)			32 (34.8)	590 (37.6)			96 (28.9)	1505 (32.2)		
Smoking attempt												
Yes	70 (29.2)	409 (13.2)	46.413	< 0.001	30 (32.6)	187 (11.9)	32.84	< 0.001	100 (30.1)	596 (12.7)	78.163	< 0.001
Never smoked	170 (70.8)	2695 (86.8)			62 (67.4)	1384 (88.1)			232 (69.9)	4079 (87.3)		
Drinking attempt												
Yes	139 (61.9)	1131 (37.3)	52.586	< 0.001	54 (62.1)	523 (33.9)	28.533	< 0.001	192 (61.9)	1654 (36.2)	81.86	< 0.001
Never drank alcohol	85 (38.1)	1898 (62.7)			33 (37.9)	1019 (66.1)			118 (38.1)	2917 (63.8)		
Self-harm												
Yes	132 (55.0)	417 (13.4)	280.489	< 0.001	43 (46.7)	173 (11.0)	98.159	< 0.001	157 (47.3)	4085 (87.4)	384.901	< 0.001
No	108 (45.0)	2687 (86.6)			49 (53.3)	1398 (89.0)			175 (52.7)	590 (12.6)		
Outdoor activity												
Everyday	62 (25.8)	990 (31.9)	5.096	0.167	23 (25.0)	499 (31.9)	2.49	0.477	85 (25.6)	1489 (31.9)	7.309	0.063
Every week	65 (27.1)	856 (27.6)			31 (33.7)	494 (31.5)			96 (28.9)	1350 (28.9)		
Every month	14 (5.8)	146 (4.7)			7 (7.6)	82 (5.2)			21 (6.3)	228 (4.9)		
Rarely	99 (41.3)	1110 (35.8)			31 (33.7)	491 (31.4)			1731 (34.6)	1601 (34.3)		
Identity of main care	giver											
Father/Mother	4 (1.7)	43 (1.4)	3.338	0.342	82 (89.1)	1484 (94.5)	6.602	0.086	86 (25.9)	1527 (32.7)	10.591	0.014
Grandma/Grandpa	205 (85.4)	2768 (89.2)			8 (8.7)	74 (4.7)			213 (64.2)	2842 (60.8)		
Other relatives	24 (10.0)	221 (7.1)			2 (2.2)	9 (0.6)			26 (7.8)	230 (4.9)		
Non adult relatives	7 (2.9)	72 (2.3)			0 (0.0)	3 (0.2)			7 (2.1)	75 (1.6)		
Caregiver highest edu	ucation											
Never went to school	54 (23.4)	752 (24.7)	22.478	< 0.001	5 (55.6)	19 (22.9)	7.577	0.108	59 (24.6)	771 (24.6)	19.745	< 0.001
Primary school	109 (47.2)	1446 (47.5)			1 (11.1)	44 (53.0)			110 (45.8)	1490 (47.6) 686 (21.9)		
Junior high school	50 (21.6)	671 (22.0)			2 (22.2)	15 (18.1)			52 (21.7)	158 (5.0)		
Senior high school	9 (3.9)	155 (5.1)			1 (11.1)	3 (3.6)			10 (4.2)	25 (0.8)		
University	9 (3.9)	23 (0.8)			0 (0.0)	2 (2.4)			9 (3.8)			
Duration of previous	father mig	ration										
<6 months	36 (15.1)	469 (15.1)	3.439	0.329								
6 months – 1 year	134 (56.3)	1724 (55.6)										
1 year – 2 year	47 (19.7)	713 (23.0)										
>2 years	21 (8.8)	192 (6.2)										
Duration of previous	mother mi	gration										
<6 months	43 (18.0)	595 (19.2)	17.006	< 0.001								
6 months – 1 year	136 (56.9)	1835 (59.4)										
1 year – 2 year	24 (10.0)	422 (13.7)										
>2 years	36 (15.1)	239 (7.7)										

According to socioecological resilience framework, when proximal support is lacking, the distal supports such as peer and school supports may compensate the missing support when

parents were absent (19, 36), and reversely to double jeopardize adolescent's psychological development if school support is also lacking. Our study support the previous study's finding that

TABLE 6 Correlates emotional and behavioral problems, smoking attempt, previous alcohol use and school environment on suicidal ideation in LBC.

Variables		OR (95% CI)	p
Poor school environment		1.109 (1.020–1.206)	0.015
Psychological feeling		1.242 (1.162–1.328)	< 0.001
Bothered by difficulty		1.067 (0.993–1.147)	0.077
Emotional and behavioral problems		1.068 (1.031–1.108)	< 0.001
Prosocial item		1.000 (0.912–1.096)	0.997
Self-harm in past 6 months	Yes	2.078 (1.394–3.100)	< 0.001
	No	1	
Smoking	Yes	1.613 (1.053–2.473)	0.028
	$\mathrm{No^a}$	1	
Alcohol	Yes	1.311 (0.896-1.919)	0.163
	$\mathrm{No^b}$	1	
Duration of mother out to work	<6 months ^c	1	
	6 months-1yr	1.001 (0.611-1.641)	0.997
	1–2yr	0.729 (0.367-1.448)	0.367
	>2yrs	1.694 (0.897–3.200)	0.104
Education of main guardian	Never went to school ^d	1	
	Primary school	1.437 (0.917–2.250)	0.113
	Junior high school	1.400 (0.822-2.383)	0.216
	Senior high school	0.964 (0.378-2.459)	0.939
	University	3.756 (1.272–11.089)	0.017

a,b,c,d are reference groups. Nagelkerke variance explained by all independent variables are 30.2%.

poor school environment and support, particularly bullying victimization from peer, increased the likelihood of the risk outcome of suicidality in left-behind children (37). Experiences of being bullied had a significant relationship with suicide plan (38). In a study that examined the association between bullying victimization and suicidal ideation among adolescents, they found children who experienced both school bullying and cyberbullying victimization had 3.26 times higher odds (95%CI: 3.10–3.43) of experiencing suicidal ideation than controls (39). Bullying victimization is a negative life event that can be highly traumatic for individuals (40). Left-behind children who are victims of bullying had less self-compassion and hope, and greater feelings of depression, and these feelings are often associated with suicidal ideation (37), and consistent with our study finding.

Abundant evidence suggest that parental migration is a risk factor for suicidal ideation among left-behind adolescents (12, 14, 29, 41, 42). The innovation in this present study is this is the first study to implement the socioecological resilience framework to explain correlates of suicidality issues in LBC adolescent. We examined numerous factors such as individual factors (emotional and behavioral problems and psychological feeling,), negative school environment (peer support), and other negative coping behaviors of smoking and drinking alcohol. The new knowledge from the study is that coping behaviors, in particular, self-harm and smoking,

as well as negative school environment and emotional and behavioral problems have multiply jeopardize left-behind adolescent's healthy psychological development which has further led to their suicidal ideation development. These findings ultimately emphasize the need to introduce substitute coping behaviors to assist left-behind children who are more vulnerable to stress and trauma than non-left-behind children. Future research should trial initiatives such as school-based suicide prevention programs, health-awareness programs, and mindfulness training to improve resilience, overall psychological wellbeing, and reduce suicidality of left-behind children.

In addition, we recruited participants based on sample representativeness targeting rural Chinese children living in areas of low socioeconomic status. We used nationwide data from 11 provinces and 1 municipal incorporating over 5,000 students which suggests generalisability of results to left-behind children living in impoverished areas of rural China.

Several limitations of this study must be acknowledged. First, the study design implemented was cross-sectional which means causal inferences cannot be established. Our data obtained 5 years ago may also present issues for application today due to revisions and reforms to policies surrounding left-behind children; nonetheless data on the impact of these changes LBC mental health cannot yet be ascertained. The study does not clearly distinguish self-harm from suicidal ideation as the broad definition for self-harm was used rather than asking participants

specifically about non-suicidal self-injury. The potential overlap of the terms impacts on the integrity of the data, and thus results should be interpreted cautiously. While self-reported surveys are important tools to collect substantial amounts of data from many participants, the reliability of self-constructed school-based self-reported surveys may be questionable particularly due to fears for anonymity and the sensitivity of the survey asking about suicide. Many questions were retrospective in nature and recall bias could be introduced. Recruitment of participants by schools may also suggest selection bias as children who have dropped out were not included in the analysis.

Another limitation is that the study lacks generalisability to other year levels since participants were all year 1 junior high school students. Age has been reported as a predictor for adolescent suicidal ideation. One study which conducted multiple logistic regression to consider potential factors found all equations indicated risk of suicide attempts lowered as age increased (43). Finally, several key predictors such as depression, anxiety, stress, parent-child communication, for suicidal ideation were not investigated in this study. For example, one study found depression, anxiety, stress, hopelessness were the greatest risk factors of suicidal ideation in adolescents (44), while another study found healthy parent-child communication was a mediator for suicidal ideation among left-behind children (42). Future research should implement a longitudinal study design and incorporate depression and other mental health issues into the analysis to predict suicide behaviors. Stemming from a socioecological framework, further research may also explore the role of other support systems such as the government and extended family. These recommendations will help better understand the mechanism of how risk factors and protective factors influence suicide behaviors among a unique and vulnerable population of children

Conclusion

Findings in our study indicate suicidal ideation and self-harm were more prevalent among left-behind children than controls. As suggested by the socioecological resilience framework, our results support that adolescent's psychological characteristics including emotional and behavioral problems, negative psychological feeling, negative school environment, and negative coping behaviors (smoking, alcohol use, self-harm) are correlates of suicidal ideation in LBC. Self-harm was most positively associated with suicidal ideation in LBC. To prevent suicidal ideation and self-harm in left-behind children, there is urgent need for development of targeted strategies focusing on coping behaviors and emotion regulation, gatekeeper training of school teachers and peers, and psychosocial interventions for at-risk children.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of Beijing Anding Hospital affiliated with Capital Medical University under Ethical Approval Number of 2013 (06). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

Y-mZ: collected data, conducted statistical analysis, drafted the manuscript, and edited and submitted the manuscript. LM: conducted statistical analysis, drafted the manuscript, and submitted the manuscript. C-xZ: organize the program, collected data, reviewed and revised the manuscript, and approved the final manuscript as submitted. FH: collected data, reviewed and revised the manuscript, and approved the final manuscript as submitted. X-nH and X-bT: reviewed and revised the manuscript, and approved the final manuscript as submitted. Y-z: conceptualized and designed the study, collected data, and approved the final manuscript as submitted. JS: designed the study, conducted statistical analysis, critically reviewed, edited and revised the manuscript, and approved the final manuscript as submitted. All authors contributed to the article and approved the submitted version.

Funding

National "Twelfth Five-Year" Science and Technology Support Program (No: 2012BAI01B02); Research on prevention and control of major chronic non-communicable diseases in the Ministry of Science and Technology (No: 2016YFC1306100). Beijing Hospitals Authority Clinical medicine Development of special funding support, code: ZYLX202128.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Mental Health Research During the COVID-19 Pandemic: Focuses and Trends

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Background: The COVID-19 pandemic has profoundly influenced the world. In wave after wave, many countries suffered from the pandemic, which caused social instability, hindered global growth, and harmed mental health. Although research has been published on various mental health issues during the pandemic, some profound effects on mental health are difficult to observe and study thoroughly in the short term. The impact of the pandemic on mental health is still at a nascent stage of research. Based on the existing literature, we used bibliometric tools to conduct an overall analysis of mental health research during the COVID-19 pandemic.

Method: Researchers from universities, hospitals, communities, and medical institutions around the world used questionnaire surveys, telephone-based surveys, online surveys, cross-sectional surveys, systematic reviews and meta-analyses, and systematic umbrella reviews as their research methods. Papers from the three academic databases, Web of Science (WOS), ProQuest Academic Database (ProQuest), and China National Knowledge Infrastructure (CNKI), were included. Their previous research results were systematically collected, sorted, and translated and CiteSpace 5.1 and VOSviewers 1.6.13 were used to conduct a bibliometric analysis of them.

Result: Authors with papers in this field are generally from the USA, the People's Republic of China, the UK, South Korea, Singapore, and Australia. Huazhong University of Science and Technology, Hong Kong Polytechnic University, and Shanghai Jiao Tong University are the top three institutions in terms of the production of research papers on the subject. The University of Toronto, Columbia University, and the University of Melbourne played an important role in the research of mental health problems during the COVID-19 pandemic. The numbers of related research papers in the USA and China are significantly larger than those in the other countries, while co-occurrence centrality indexes in Germany, Italy, England, and Canada may be higher.

Conclusion: We found that the most mentioned keywords in the study of mental health research during the COVID-19 pandemic can be divided into three categories: keywords that represent specific groups of people, that describe influences and symptoms, and that are related to public health

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Edited by:

Liye Zou, Shenzhen University, China

Reviewed by:

Qian Yang, Zhejiang University, China M. Saqib Nawaz, Shenzhen University, China

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Specialty section:

This article was submitted to Public Mental Health, a section of the journal Frontiers in Public Health

Received: 13 March 2022 Accepted: 03 May 2022 Published: 26 July 2022

Citation:

Liang Y, Sun L and Tan X (2022) Mental Health Research During the COVID-19 Pandemic: Focuses and Trends.

Front. Public Health 10:895121. doi: 10.3389/fpubh.2022.895121 policies. The most-cited issues were about medical staff, isolation, psychological symptoms, telehealth, social media, and loneliness. Protection of the youth and health workers and telemedicine research are expected to gain importance in the future.

Keywords: COVID-19, mental health, bibliometric analysis, keyword clustering, focuses, trends

INTRODUCTION

Although the impacts of the COVID-19 pandemic will be recorded in human medical history and in socio-economic history, various psychological consequences regarding mental health among populations cannot be ignored, including stress, anxiety, depression, frustration, insomnia, and so on. Researchers from universities, hospitals, communities, and medical institutions worldwide have been focusing on mental health problems during the pandemic. They have used questionnaire surveys, telephone-based surveys, online surveys, cross-sectional surveys, systematic reviews and meta-analysis, and systematic umbrella reviews to investigate mental health problems during the pandemic. Two years after the outbreak of the COVID-19, the pandemic has gradually subsided in some countries, while others have adopted a strategy of coexisting with the virus. If more deadly mutant strains do not appear in the future, it is very likely that the pandemic will not climax again. It is pertinent to summarize and study mental health research during the pandemic, because many psychological problems have arisen as a result, and there has been significant interest in research on such issues in the previous two years.

As an effective quantitative analysis method, bibliometrics can be used not only to assess the quality and quantity of published papers, but also to explore research focuses and trends, the distribution of authors and institutions, the impact of publications, journals, and different countries regarding research contributions to the theme. Due to the rapid growth in research in this area, there are now over 1,000 academic papers, and accordingly, it would appear necessary to investigate important, valid, and meaningful information from large databases to guide scientific research. The authors used CiteSpace and VOSviewers to determine the focuses and trends in this regard.

METHODS

Data Analysis and Visualization

The authors searched the Web of Science (WOS), ProQuest Academic Database (ProQuest), and China National Knowledge Infrastructure (CNKI) to extract publications related to mental health and COVID-19. Their previous research results were systematically collected, sorted, and translated, and CiteSpace 5.1 and VOSviewers 1.6.13 were used to conduct a bibliometric analysis of them.

Data Source and Search Strategy

Our team selected 1,226 papers from 2019 to 2022 using three combinations of keywords, mental health and COVID-19, mental health and new coronavirus, and mental health and novel coronavirus, from the three academic paper databases, WOS,

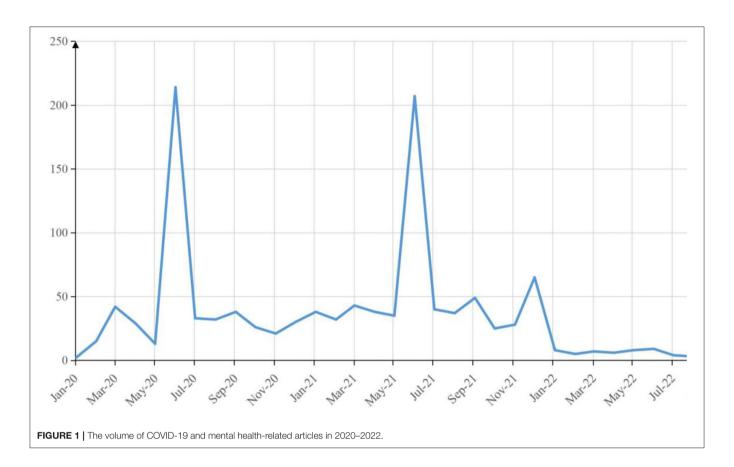
ProQuest, and CNKI. Two explanations are necessary here, the first is about the keywords and the second is about the databases. (1) The reason we used new or novel coronavirus as keywords was that the name COVID-19 has not been determined about 2 years ago. In order not to miss relevant research results, we also included these synonyms as keywords for the search. (2) Among the three databases, WOS and ProQuest, in which most of the English-language papers were published, are well-known to scholars all around the world. However, the CNKI database is not as popular as WOS or ProQuest given that most of the papers in CNKI were published in Chinese. We chose to use the CNKI data for the following three reasons: first, China was the most affected country during the COVID-19 outbreak and Chinese academic journals published significant research on mental health. Second, CNKI is the largest Chinese academic database. Third, after the outbreak, the Chinese government's virus clearance policy has been implemented and continues to date. Strict control has helped suppress the spread of the virus, but has also likely had mental health implications, given the severe reduction in social interactions. Therefore, we think that the Chinese database is appropriate and useful in this study.

About 50% of the articles were from the WOS, about 10% of the articles from ProQuest, and about 40% from CNKI. Basic information such as title, author, institution, country, abstract, keywords, methods, results, and conclusions of all articles, if not in English, are translated into English and analyzed using SiteSpaceII and VOSviewers. Since the keywords include COVID-19 and mental health, synonyms such as novel coronavirus and psychological distress spontaneously appeared while searching. Words that are closely related to the subject, such as public health, quarantine, and insomnia, were most frequently mentioned.

RESULTS

Most articles were published during the period from February 2020 to July 2022, including those pre-published online from April to July, and only one article that had been published in 2019 was included. Judging from the line chart above, since the volume of COVID-19 and mental health-related articles had already risen two times in June 2020 and June 2021 and then remained low until now, it is high time to conclude a previous study on COVID-19 and mental health, to sort out the foci of those studies, and to analyze and predict future trends (**Figure 1**).

Scholars from around the world have contributed to the study of mental health issues during the COVID-19 pandemic. The top 10 countries with the largest quantum of publications related to mental health during COVID-19 are the USA, People's Republic of China, England, Canada,



Australia, India, Italy, Japan, Iran, and Germany. Wide and active participation of several countries has laid a solid foundation for its future development. Universities, hospitals, communities, and medical institutions around the world have conducted sample surveys of patients, students, community residents, medical workers, and other sample populations of considerable sample sizes since the outbreak. Survey and research methods include questionnaire survey, telephone-based survey, online survey, cross-sectional survey, systematic review and meta-analyses, and systematic umbrella review (Table 1).

Most papers are from the USA, the People's Republic of China, England, Australia, Canada, India, Italy, Iran, Japan, and Germany. Judging from the country or region co-occurrence graph, England and Canada are in the center of this graph, with India, Poland, Denmark, Spain, South Korea, Portugal, Italy, and Canada around them. England, Australia, Canada, Japan, Brazil, India, Iran, and Germany have done significant research work in this field. In addition, the number of related research papers in the USA and China is significantly larger than that in all other countries (Figure 2).

In **Table 2**, we can see that most names of the top 20 authors are Asian names, and they are mainly from China. Six of them published more than 10 articles by the end of 2021. In the extended ranking, we find that the authors who have published a large number of papers are generally from the USA, China, the UK, South Korea, Singapore, and Australia. The authors Griffiths

TABLE 1 | Top 20 countries.

Ranking	Frequency	Country	Ranking	Frequency	Country
1	280	USA 11 27		27	Spain
2	223	China	12	26	Brazil
3	85	England	13	22	Saudi Arabia
4	69	Canada	14	19	Pakistan
5	68	Australia	15	18	Turkey
6	54	India	16	12	Bangladesh
7	50	Italy	17	11	Sweden
8	41	Japan	18	10	Singapore
9	37	Iran	18	10	Poland
10	27	Germany	20	9	Malaysia

MD, Cheung T, Xiang Y, Lin C, Wang Y, and Zhang L were very active in this field of study.

In the abovementioned graphs, we can see six groups of related authors. The VOSviewer was used to describe the partnership between them. Though six colors were used to separate these groups, there were still lines connecting the groups to represent the partnership between them. We can take Cheung T and Xiang Y as the center of the largest group. Another group with Griffiths MD and Lin C as its center was also significant (**Figures 3, 4**).

The top five institutions are Huazhong University of Science and Technology, Hong Kong Polytechnic University,

Focuses Trends Mental Health COVID-19

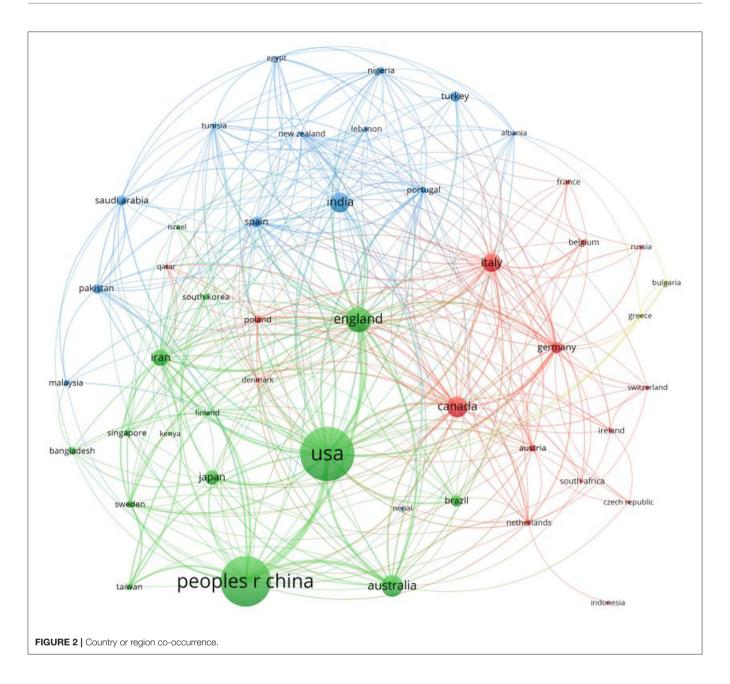
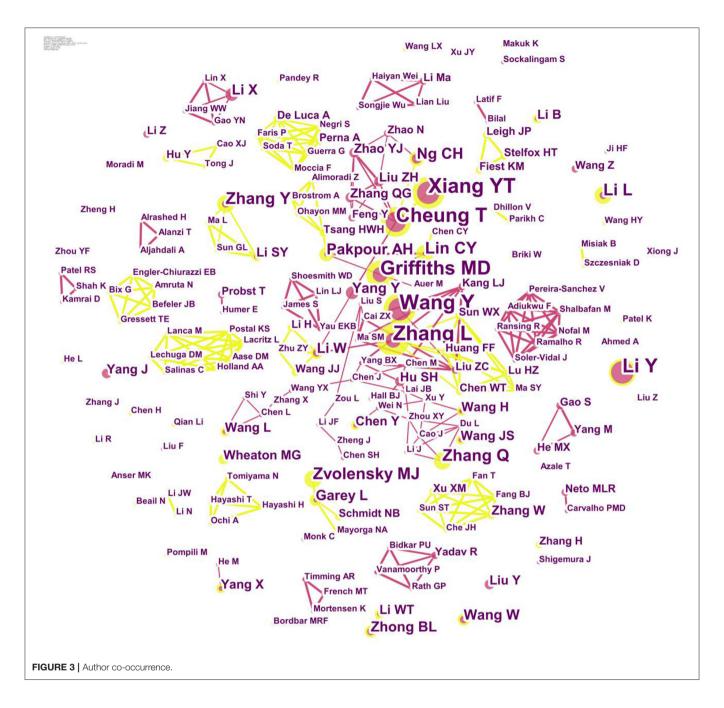


TABLE 2 | Top 20 authors.

Ranking	Frequency	Author	Ranking	Frequency	Author
1	14	Xiang YT	7	7	Zvolensky MJ
2	13	Zhang L	12	6	Ng CH
2	13	Wang Y	12	6	Pakpour AH
2	13	Cheung T	14	5	Li W
5	11	LiY	14	5	Li X
5	11	Griffiths MD	14	5	Garey L
7	7	Li L	14	5	Zhong BL
7	7	Zhang Y	14	5	Wang W
7	7	Zhang Q	14	5	Yang Y
7	7	Lin CY	20	4	Hu SH

Shanghai Jiao Tong University, Columbia University, and the University of Toronto. Meanwhile, the top five institutions in centrality are the University of Macau, the University of Melbourne, Columbia University, Wuhan University, and the University of Toronto. It is worth mentioning that Huazhong University of Science and Technology and Wuhan University are located in the city of Wuhan, one of the areas most affected by the virus through the outbreak. The society and economy of the city temporarily stagnated at the time, and its medical system was once paralyzed. Eventually, Wuhan City's medical system was fully recovered. The University of Toronto, Columbia University, and the University of Melbourne have played an important role in the research of mental

Focuses Trends Mental Health COVID-19

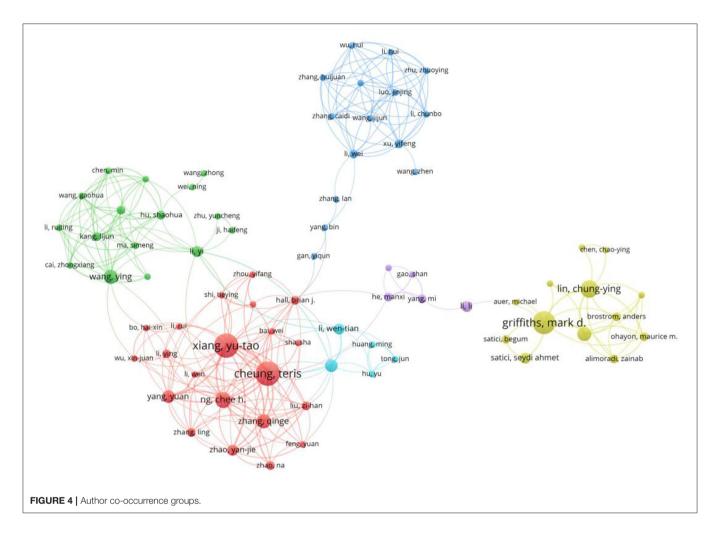


health problems during the COVID-19 pandemic (Table 3 and Figure 5).

As can be seen in **Figure 6**, Huazhong University of Science and Technology has led Chinese universities and research institutions, such as Shanghai Jiao Tong University and Peking University, in conducting research on COVID-19 and mental health. Hong Kong Polytechnic University, Fudan University, and the University of Melbourne acted as bridges, connecting famous universities and research institutions in Europe, America, and other countries in the world, such as Kings College London and Harvard Medical School, to jointly study issues in this field. In particular, they conduct joint research, directly or

indirectly, through Hong Kong Polytechnic University, which display the important communication and joint role of Hong Kong Polytechnic University.

Judging from **Table 4**, the most mentioned keywords, in addition to COVID-19 and mental health, can be roughly divided into three categories: (1) keywords representing specific groups of people, such as adolescents, young adults, doctors, nurses, medical staff, and healthcare workers; (2) keywords describing influences and symptoms, such as isolation, loneliness, anxiety, depression, stress, and insomnia; and (3) keywords related to public health policies, such as lockdown, social distancing, telehealth, telemedicine, and quarantine.



In Graph 7, we can judge that COVID-19, mental health, pandemic, and coronavirus are represented by larger red dots as their centrality indexes are naturally higher. In this bibliometric network map, other keywords emerged next to them and together formed this visualization bibliometric network. Occupational and sociodemographic characteristics are clustered together, while symptoms of mental health problems are clustered next to them. Specific groups of people and their typical symptoms and causes occupy certain areas on the map. For example, typical symptoms of university students and the possible causes of these symptoms are grouped together on the map. Similarly, quarantine policy and its influence are also classified in certain areas. In addition, research methods and solutions appeared sporadically on this map.

Table 5 shows eight groups of core keywords separated from keyword clustering I. Each of these groups contains three keywords, which proves that these keywords appear at the same time in a considerable part of the research, and are more closely related. Keyword ClusteringII cannot only present the outline of existing mental health research in academia, but also highlights the focus of research. In addition, SiteSpaceII and VOSviewers also gave us some clues about the research trends and further development.

DISCUSSION

Research Focuses

Medical Staff

The COVID-19 pandemic has exacerbated mental health problems among populations, especially medical staff, patients with COVID-19, chronic disease patients, and isolated people. Doctors, nurses, and other medical staff have significantly higher rates of insomnia than other populations (1). The researchers obtained the relevant demographic data through the WeChat questionnaire survey. Questions in the questionnaire are related to insomnia, depression, anxiety, and stress-related symptoms during the pandemic. Their research found that, since the outbreak, more than one-third of the medical staff suffered from symptoms of insomnia. Psychological intervention measures were necessary for those people (2). Research within medical institutions shows that the psychological pressure of medical staff in isolation wards was greater, but had also attracted greater attention from hospital administrators. The concern of hospital managers alleviated the pressure of medical staff to a certain extent. Further, concern for the public also reduced their psychological burden. In terms of anxiety about infection and fatigue factors, the research results showed that the psychological

Focuses Trends Mental Health COVID-19

TABLE 3 | Top 20 institutions.

Ranking	Frequency	Centrality	Institution
1	25	0.18	Huazhong University of Science and Technology
2	25	0.14	Hong Kong Polytechnic University
3	21	0.12	Shanghai Jiao Tong University
4	19	0.56	Columbia University
5	18	0.44	The University of Toronto
6	16	0.61	The University of Melbourne
7	16	0.35	Harvard Medical School
8	14	0.78	The University of Macau
9	14	0.50	Wuhan University
10	13	0.12	Kings College London
11	13	0.01	Capital Medical University
12	12	0	Nottingham Trent University
13	11	0	Peking University
14	11	0.22	New York University
15	10	0.12	Zhejiang University
16	10	0	The University of California Los Angeles
16	10	0	Sichuan University
18	9	0.21	Dalhousie University
19	9	0	Xi An Jiao Tong University
20	8	0	The University of Calgary

burden of nurses was heavier than that of doctors. Healthcare workers who lived with their own children showed more obvious fatigue and anxiety, which might be due to the fear of their children becoming infected. In terms of workload and work motivation, medical staff who have been working for more than 20 years have a heavier workload, but they can still maintain their enthusiasm to fight against the pandemic (3). Another survey showed that 73.4% of healthcare workers, mainly physicians, nurses, and auxiliary staff, reported posttraumatic stress symptoms during outbreaks, with symptoms persisting for up to 3 years in 10-40% of the cases. Depressive symptoms were reported in 27.5-50.7%, insomnia symptoms in 34-36.1%, and severe anxiety symptoms in 45% (4). A subgroup analysis revealed gender and occupational differences, with female health care practitioners and nurses exhibiting higher rates of affective symptoms compared to men and medical staff, respectively (5).

Quarantine

As a result, depressive symptoms (21%) and anxiety symptoms (19%) are higher during the COVID-19 pandemic compared to previous epidemiological data. About 16% of the subjects suffered from severe clinical insomnia during the lockdown. The pandemic and lockdown seemed to be particularly stressful for younger adults who were under 35 years old, women, people out of work, or those with low incomes (6). In the fight against the pandemic, China adopted measures to restrict population aggregation, such as the blockade of pandemic areas, individual patient isolation, and restrictions on the movement

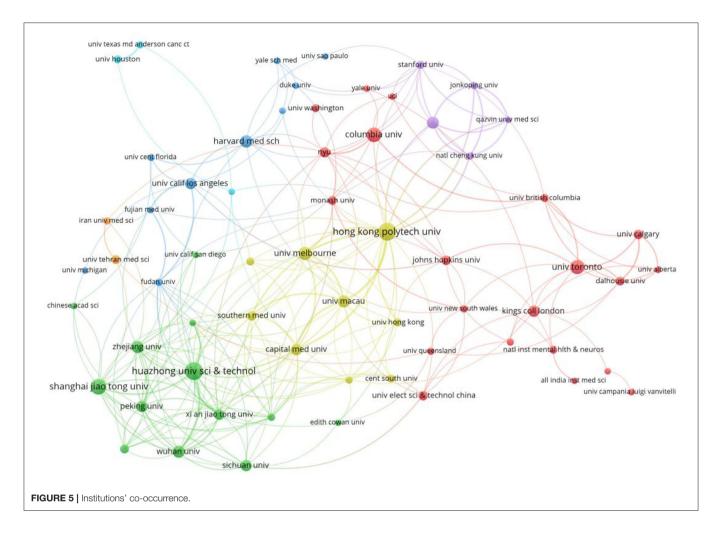
of people in non-pandemic areas. These measures effectively prevented the spread of the pandemic. At the same time, the use of health codes, grid-like community management, and the operational efficiency of infectious disease information networks have greatly improved. However, quarantine has also brought with it a number of problems, such as increasing psychological pressure on the population, affecting the daily lives of families, and hindering social and economic development (7). A large sample size study with wide coverage published in 2021 showed that young people quarantined at home in different provinces had different rates of anxiety and depression due to different severity of pandemic situations in different regions. The risk of anxiety and depression was statistically significantly higher in girls than in boys. The rate of anxiety and depression was affected by factors, such as gender, age, and area, as well as the existence of COVID-19 cases in the surrounding area (8).

Psychological Symptoms

The impact of the aforementioned isolation measures on mental health is only part of the impact of the COVID-19 on mental health. Psychological symptoms brought about by the pandemic have also been systematically sorted out by scholars. These studies show two clues. First, certain people have special psychological symptoms; second, psychological symptoms in different countries of the world are roughly the same. Several factors were associated with a higher risk of psychiatric symptoms or low psychological wellbeing, including female gender and poor self-related health (9). Relatively, severe symptoms of anxiety, depression, posttraumatic stress disorder, psychological distress, and stress were reported in the general population during the COVID-19 pandemic in China, Spain, Italy, Iran, the USA, Turkey, Nepal, and Denmark. Risk factors associated with measures of distress include female gender, younger age group, the presence of chronic or psychiatric illnesses, unemployment, student status, and frequent exposure to social media or news concerning COVID-19. The pandemic is associated with significant levels of psychological distress that, in many cases, will meet the threshold for clinical relevance. Mitigating the hazardous effects of COVID-19 on mental health is an international public health priority (1). Infectious disease pandemics often cause some people to act irrationally. The results of a survey based on psychological symptoms and irrational behaviors have drawn some conclusions. First, the vast majority of people remain in good physical and mental health, but some exhibit irrational behaviors. Second, women, elderly people, and those with confirmed cases showed more physical and mental symptoms and irrational behaviors. Finally, paradoxically, people with high education levels showed more mental symptoms, but fewer irrational behaviors (10).

Telemedicine

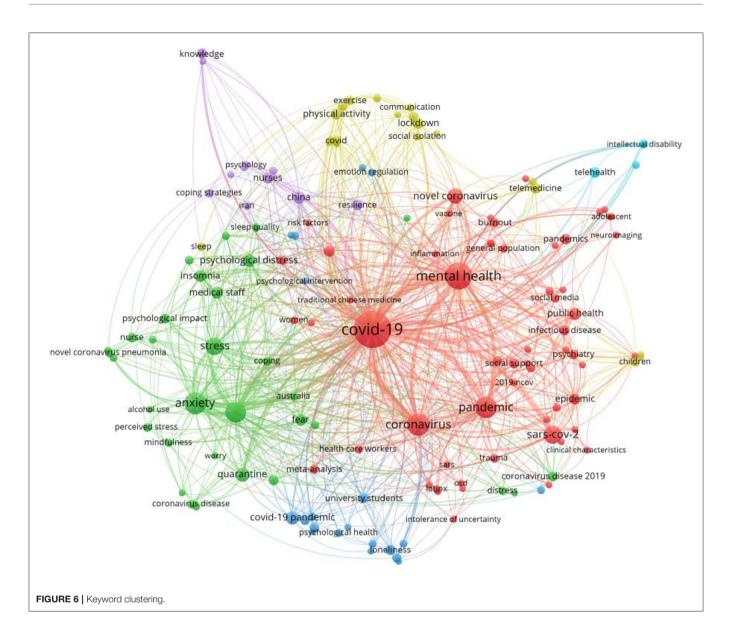
Just as the pandemic has enabled the rapid development of online education, the prospects of telemedicine are also favored by experts, observers, and investors. However, there



are two restrictive aspects, namely, telemedicine equipment and telemedicine human resources. The application of 5G communication technology, telemedicine equipment, remote monitoring equipment, remote physical sign monitoring equipment, and medical artificial intelligence triage equipment all need to be urgently developed and improved. Jiangsu, a province in China, is a model province of the national project called "Internet + Medical and Health." During the pandemic, the telemedicine by public hospitals in Jiangsu Province helped improve the efficiency of diagnosis and treatment, alleviating the pressure of offline diagnosis and treatment, and reducing the risk of cross-infection. Subsequently, medical staff were fully supportive of telemedicine. However, there was a shortage of medical staff in fever clinics, obstetrics and gynecology, pediatrics, and psychiatrists that provided telemedicine services, and they lacked corresponding incentive mechanisms (11). Effective mitigation strategies to improve mental health were developed by public health management experts. To control the rapid spread of COVID-19 and manage the crisis better, both developed and developing countries have been improving the efficiency of their health system by replacing a proportion of face-to-face clinical encounters with telemedicine solutions (12).

Social Media

There were rumors in various kinds of media during the COVID-19 pandemic. Although we can regard rumors as a disturbing error for psychological measurement, if they are not strictly controlled, their impact on people's mental health and behavior cannot be ignored. A study focusing on the spread of WeChat rumors has explored the psychological perception mechanism of audiences affected by rumor spreading in emergency situations. The study has significant results in the following terms: the form characteristics of the rumors in COVID-19, the ranking of susceptible age groups, the degree of dependence of the test subject on certain media and its psychological impact, and the follow-up behavior of the test subjects related to psychological variables (2). In 2021, another interesting study based on the data of TikTok videos released by three mainstream media in China showed that they inevitably caused some psychological trauma to the public. However, from the perspective of overall emotional orientation, short-format videos with positive reporting emotional tendencies had an advantage in attracting likes from TikTok users. Positive government responses to pandemic information were very important, and those responses could be recognized and praised by most social media users. Some of the TikTok videos, such as The Plasma of a Recovered



Patient Cured 11 Other ICU Patients, The First COVID-19 Test Kit Passed Inspection, and A Frenchman Named Fred gave up Returning to Home to Join China's Anti-COVID-19 Battle, are extremely popular among social media users. Most social media users have been providing spiritual sustenance for people in the pandemic (13). When a public health crisis occurs, social media plays an important role in increasing public vigilance, helping the public identify rumors, and boosting public morale.

University Students and Loneliness

A study that assessed the adverse impact on the mental health of university students has drawn some conclusions. First, the severity of the outbreak has an indirect effect on negative emotions by affecting sleep quality. Second, a possible mitigation strategy to improve mental health includes ensuring suitable amounts of daily physical activity and deep sleep. Third, the pandemic has reduced people's aggressiveness, probably by

making people realize the fragility and preciousness of life (14). Another research focused on social networks and mental health compared two cohorts of Swiss undergraduate students who were experiencing the crisis, and made an additional comparison with an earlier cohort who did not experience the pandemic. The researchers found that interaction and co-study networks had become sparser, and more students were studying alone. Stressors shifted from fear of missing out on social life to concern about health, family, friends, and their future (15). Young adults, women, people with lower education or lower income, the economically inactive, people living alone, and urban residents were at greater risk of being lonely during the pandemic. Being a student emerged as a higher than usual risk factor for loneliness during the lockdown (16). A study to explore the relationship between loneliness and stress among undergraduates in North America showed that the loneliness and stress among college students increased. On one hand, stress plays a key role in the

TABLE 4 | Keyword clustering I.

Count Centrality Keyword Year Cluster 0.54 Mental health 0.1 Psychological distress 0.41 Fear Lockdown 0.1 Healthcare worker Psychological impact Adolescent 0.06 Social distancing Burnout Ω Distress Stiama 0.05 Social media Trauma COVID-19 Spirituality 0.05 Nurse 0.24 Insomnia Medical staff 0.46 0.05 Resilience 0.1 Sleep Qualitative research Coping 0.1 Coping strategy 0.15 Perceived stress Prevalence Physician Telehealth 0.16 0.17 Children 0.27 Telemedicine 0.21 Mental health service Quality of life COVID College student 0.21 Coronavirus disease 0.05 COVID19 Viral infection 0.21 Novel coronavirus 0.41 Public health 0.03 Infectious disease Mentalhealth 0.12 Psychiatry 0.07 **Pandemics** 0.03Young adult Risk communication COVID-19 outbreak 0.12 Psychotherapy 0.95 Coronavirus 0.22 Physical activity Meta-analysis 0.05 University student

TABLE 4 | Continued

Count	Centrality	Keyword	Year	Cluster	
6	0.23	Exercise	2021	4	
5	0.15	Health	2021	4	
4	0	Depressive symptom	2021	4	
4	0	Attitude	2021	4	
3	0.05	Health care worker	2020	4	
537	1.08	COVID-19	2020	5	
98	0.6	Pandemic	2020	5	
19	0.15	China	2020	5	
13	0.66	Epidemic	2020	5	
11	0	Social support	2020	5	
4	0	Knowledge	2020	5	
3	0.05	Psychological stress	2020	5	
3	0	Psychological intervention	2020	5	
2	0.19	Qualitative study	2022	5	
106	0.72	Anxiety	2020	6	
95	0.66	Depression	2020	6	
57	0	SARS-CoV-2	2020	6	
54	0.61	Stress	2020	6	
10	0	Ptsd	2021	6	
6	0	Outbreak	2020	6	
4	0	Sleep quality	2020	6	
3	0.1	Isolation	2020	6	
25	0	Quarantine	2020	7	
21	0.1	COVID-19 pandemic	2020	7	
13	0.78	Loneliness	2021	7	
10	0	Wellbeing	2021	7	
7	0.78	Worry	2021	7	
2	0.2	Youth	2022	7	
2	0	Suicidal ideation	2022	7	
2	0.34	Longitudinal	2022	7	

deterioration of college students' mental health; on the other hand, reducing the loneliness of college students is expected to reduce the negative impact of stress on college students' mental health (17).

Research Trends

Due to the limited training sample of academic papers at present, it is difficult to predict the outcomes accurately. Though we cannot exactly predict the hot issues in the future, we can sort out some possible research trends in this field by analyzing existing research approaches. Psychological symptoms that affected people's mental health during the COVID-19 pandemic will be discovered further, especially those that probably continued to affect people's mental health even after the pandemic is controlled.

Studies on mild psychological symptoms, such as mild insomnia and anxiety, tend to decrease slowly, and in the case of severe problems caused by the pandemic, or severe psychological symptoms, such as clinical insomnia, depression,

(Continued)

TABLE 5 | Keyword clustering II.

Cluster ID	Size	Silhouette	Mean year	Keyword				
0	13	0.918	2020	Quarantine	COVID-19 pandemic	Psychological distress		
1	10	0.936	2020	Epidemic	Telehealth	Telemedicine		
2	10	0.925	2020	Nurse	Insomnia	Medical staff		
3	9	0.737	2020	Coronavirus	Lockdown	Physical activity		
4	9	0.863	2020	COVID-19	Mental health	Pandemic		
5	8	0.949	2020	Novel coronavirus	Public health	Mental health		
6	7	0.827	2020	Anxiety	Depression	Stress		
7	6	0.887	2021	Loneliness	Health	University student		

bipolar disorder, the corresponding in-depth research will continue. The impact of a global pandemic on the mental health of the global population must be profound and worthy of study. Due to the rapid development of COVID-19, many famous universities and research institutions have not had enough time to collect sufficient data and relevant research materials. The different effects on populations in different countries with different pandemic prevention policies are not yet fully displayed.

Regardless of how research on mental health develops, the COVID-19 pandemic has indeed brought us some new insights. As mentioned in many articles on mental health interventions for adolescents and college students, the mental health of specific populations and the development of telemedicine all deserve continued academic attention. Mental health intervention for adolescents and college students is a means to consider and prepare for the future. To ensure responsible and accountable behavior for future generations, we should all pay attention to the research and application of this method. Caring for specific groups of people, such as doctors, nurses, and other healthcare workers, and studying how to protect them in a global pandemic is a topic that global academia must study in the future, or we will lose protection the next time the virus sweeps the world. In addition, telemedicine is the trend in the future, and face-toface diagnosis and treatment will undoubtedly increase the risk of cross-infection during the pandemic. Therefore, the development of telemedicine is an important way to avoid contact between the patients. The COVID-19 pandemic has accelerated the research and development of telemedicine.

Limitations

(1) Though we have selected three databases for analysis, there are still some databases that may be related to this field that are not covered in this study. (2) Since COVID-19-related research was started just 2 years ago, the results of the bibliometric analysis may vary after adding new data. (3) The citation frequency of articles is influenced by the time of publication, thus previously published articles should be cited more frequently than new ones.

(4) Bibliometric data change over time, and different conclusions may be drawn over time. Therefore, this study should be updated in the future.

CONCLUSIONS

The most mentioned keywords, in addition to COVID-19 and mental health, can be roughly divided into three categories: keywords representing specific groups of people, keywords describing influences and symptoms, and keywords related to public health policies. The most mentioned issues were about medical staff, quarantine, psychological symptoms, telemedicine, social media, and loneliness. Mild psychological symptoms, such as insomnia, depression, and anxiety, tend to decrease slowly, while severe ones, such as severe clinical insomnia, depression, and bipolar disorder, are yet to be discovered. The importance of studies on the protection of youth medical staff and telemedicine studies will become even more significant in the future. While physical health is threatened by the pandemic, human mental health also suffers. Judging from the current situation of pandemic prevention and control, if severe prevention and control measures are taken, the impact of COVID-19 on the health of the social population is controllable; if a strategy of coexistence with the virus is adopted, as long as a new deadly mutation of COVID-19 does not emerge, the outcomes can be controllable. However, the impact of the pandemic on human mental health is not easy to predict. In addition to the abovementioned papers on mental health, the author also noted that some papers focused on neuromedicine pointed out that the virus might have some damage to the normal working mechanism of the human nervous system, but these studies are outside the scope of mental health research, at least for now. This study aims to summarize the observations, analysis, and research of scholars on mental health during the pandemic from 2020 to early 2022, with a view to provide more clues for future researchers. We hope that more researchers will build on our research to discover new research areas and new questions to help more countries, groups, and individuals affected by the COVID-19 pandemic.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

YL was responsible for the concept and design, drafting this article, and bibliometric analysis. YL, LS, and XT were responsible for the revision and data collection. All authors contributed to this article and approved the submitted version.

ACKNOWLEDGMENTS

The authors thank the study participants for their time and effort.

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SPECIALTY SECTION

This article was submitted to Public Mental Health, a section of the journal Frontiers in Psychiatry

RECEIVED 09 December 2021 ACCEPTED 11 July 2022 PUBLISHED 28 July 2022

CITATION

Zhang W, Du Y, Yang X, Wang E, Fang J, Liu Z, Wu S, Liu Q and Hu Y (2022) Comparative efficacy of face-to-face and internet-based cognitive behavior therapy for generalized anxiety disorder: A meta-analysis of randomized controlled trial.

Front. Psychiatry 13:832167.

doi: 10.3389/fpsyt.2022.832167

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Comparative efficacy of face-to-face and internet-based cognitive behavior therapy for generalized anxiety disorder: A meta-analysis of randomized controlled trial

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Objective: The study aimed to ascertain the comparative efficacy of these two forms on reducing anxiety scores of scales in patients with a generalized anxiety disorder (GAD) by examining the available evidence for face-to-face cognitive behavior therapy (CBT) and internet-based cognitive behavior therapy (ICBT). Moreover, this study attempted to determine whether ICBT can obtain similar benefits as CBT for GAD patients during coronavirus disease 2019 (COVID-19) due to the quarantine policy and the requirement of social distance.

Methods: This meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO) according to the guidelines in the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (registration number CRD42021241938). Therefore, a meta-analysis of randomized controlled trials (RCTs) examining CBT or ICBT was conducted in this study to treat GAD patients diagnosed with DMS-IV. The researchers searched PubMed, MEDLINE, Embase, PsycINFO, and the Cochrane Database of Systematic Reviews for relevant studies published from 2000 to July 5, 2022. Evidence from RCTs was synthesized by Review Manager 5.4 as mean difference (MD) for change in scores of scales through a random-effects meta-analysis.

Results: A total of 26 trials representing 1,687 participants were pooled. The results demonstrated that ICBT and CBT were very close in the effect size of treating GAD (MD = -2.35 vs. MD = -2.79). Moreover, they still exhibited a similar response (MD = -3.45 vs. MD = -2.91) after studies with active control were removed.

Conclusion: Regarding the treatment of GAD, ICBT can achieve a similar therapeutic effect as CBT and could be CBT's candidate substitute, especially in the COVID-19 pandemic era, since the internet plays a crucial role in handling social space constraints.

Systematic Review Registration: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=241938, identifier CRD42021241938.

KEYWORDS

cognitive behavior therapy, internet-based cognitive behavior therapy, generalized anxiety disorder, randomized controlled trials, meta-analysis

Introduction

Generalized anxiety disorder (GAD), as a common and disabling illness, is frequently underdiagnosed and undertreated (1). Typical symptoms include excessive anxiety and worry, which occur every day for at least 6 months and are challenging to control for sufferers (2). GAD is characterized by chronic, pervasive anxiety, and worries, accompanied by nonspecific physical symptoms. Additionally, patients with GAD usually experience psychological symptoms such as restlessness, fatigue, difficulty concentrating, irritability, muscle tension, or sleep disturbances (1).

GAD is a chronic, enduring condition. Retrospective accounts suggest that most patients with GAD experience their first episode by 31, among which a quarter experiences it by age 20, with early onset in childhood or adolescence (3). According to representative epidemiologic surveys, the estimated prevalence of GAD in the general population of the United States is 3.1% in the previous year and 5.7% over a patient's lifetime (4). GAD is twice as common in women as in men (5). Carter et al. revealed that GAD is associated with comorbid depression in 70% of cases, any anxiety disorder in over 55%, and somatoform disorders in 48% of cases (6). Consequently, patients with GAD suffer significant mental and physical pain, and are eager to find a way to get rid of these symptoms.

Cognitive behavior therapy (CBT), as a psychotherapeutic treatment, is considered the gold standard for treating GAD (7). CBT better demonstrates how the human mind functions because it is based on an experimental and scientific psychology (8). Hence, CBT for GAD involves cognitive therapy to address worry and cognitive biases and relaxation to handle tension and imaginal exposure to catastrophic images and stressful situations (9). In recent years, the effectiveness of CBT for GAD has been explored by meta-analysis, confirming that CBT is an effective treatment for GAD (10–13). It typically leads to reductions in worry. Such therapy is equal to pharmaceutical treatment and more effective 6 months after study completion (8).

Moreover, CBT may be more effective than some other psychological treatment methods in the longer term, while those

were equally effective in the short term (12). Although these results are based on a limited number of studies and should be confirmed in future research, CBT may be preferable over others as the first-line treatment of GAD. Moreover, CBT would have longer-lasting effects compared to usual care.

the continuous development of network communication, people started to find psychological treatment, removing space and time barriers. Consequently, internetbased cognitive behavior therapy (ICBT) emerged. ICBT is a psychotherapy based on CBT principles and is delivered through the Internet by an individual or program remote from the client (14). ICBT can overcome existing treatment barriers, such as a shortage of trained therapists and ethnic inequalities. The only difference is the format for the delivery of care (15). The main advantages of ICBT are that it is highly accessible, and the required therapist times can be reduced to a fraction of what is necessary for face-to-face CBT (16). ICBT is an effective treatment for GAD across adults and is delivered in routine clinical care. The existing workforce's capacity to manage those seeking help can be improved by continuing to integrate ICBT into existing services, particularly as the population ages (17). ICBT is an effective way to relieve symptoms, improve prognosis, and better GAD patients' life treatment (18-21).

Since November 2019, the outbreak of the novel coronavirus SARS-CoV-2 (coronavirus disease 2019; previously 2019-nCoV) has been spreading worldwide and influencing most people on Earth (22). Measures such as social isolation and home isolation are taken to reduce the virus's spread as much as possible, putting people into a hopeless, nervous, and isolated circumstance. Some studies (23–25) have revealed that the COVID-19 pandemic is inducing additional health problems such as stress, anxiety, depressive symptoms, insomnia, denial, anger, and fear globally, resulting in increased anxiety disorders. This is universally recognized. Therefore, ICBT could be an effective technique to alleviate people's and GAD patients' anxiety symptoms through no face-to-face interaction with each other.

To this end, it is vital to explore whether ICBT has the same effect as CBT from the perspective of evidence-based medicine. There is no related research. In this meta-analysis,

the available evidence for face-to-face CBT and web-based CBT (therapist-directed and self-help individual therapy) was examined to determine the effectiveness of both forms in treating GAD and explore whether ICBT could, to some extent, replace CBT as a safer psychotherapy option during COVID-19.

Methods

Protocol and registration

This study was registered in Prospero International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42021241938 (https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID= 241938). It followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (26).

Selection of studies

To identify eligible studies, the researchers searched MEDLINE, Embase, PsycINFO, and Cochrane Database of Systematic Reviews for relevant studies published from 2000 to July 5, 2022. The search terms were ((randomized controlled trial[Filter]) AND (((((((CBT[Title/Abstract]) OR (cognitive behavior therapy[Title/Abstract])) OR (ICBT[Title/Abstract])) (internet-based cognitive behavior therapy[Title/Abstract])) OR (applied relaxation[Title/Abstract])) OR (meta-cognitive therapy[Title/Abstract])) OR (worry exposure[Title/Abstract]) AND (randomized controlled trial[Filter])))) AND (generalized anxiety disorder[Title/Abstract]) OR (GAD[Title/Abstract]). Furthermore, other meta-analysis studies in this field were reviewed, and some original studies that we did not find before

Both authors selected the studies independently. If there is a discrepancy between the two, they will discuss whether to keep the study or not.

Studies were included in this meta-analysis if they meet the following criteria. (1) Patients were aged 18–65 and met DSM-IV diagnostic criteria for generalized anxiety disorders. (2) Patients were randomly assigned to either CBT/ICBT or control (positive or negative). Specifically, a positive placebo was defined as pills, psychological treatments, and other treatments to improve patients' symptoms; a negative placebo was defined as a waiting list and others that do not take any treatment for the patients. (3) The clinical severity of GAD was assessed through psychometrically sound measures. (4) Studies provided sufficient data of anxiety scores to calculate effect sizes. Studies were excluded if (1) not RCTs; (2) the patients presented other mental disorders; (3) the treatment was combined with other psychotherapy in the CBT/ICBT arm.

Data collection process and data items

The data was extracted in Microsoft Excel 2019 by two of the authors (Z and D) using a pre-piloted and standardized extraction tool. Details of the region, design, population, diagnosis, sample size, percentage of females, mean age, method, dose, instruments, and comparator were extracted. Moreover, we contacted the authors for additional information when missing data were encountered. Review Manager (RevMan), version 5.4, was employed to generate the risk of bias plots.

Risk of bias in individual studies

The Cochrane risk of bias tool for randomized controlled trials was adopted to assess the risk of bias within individual trials. Particularly, indicators of selection bias, performance bias, detection bias, attrition bias, and reporting bias were evaluated with the tool (27). Those assessments were completed independently by two reviewers (Z or D). Discussions were held to resolve disagreements between reviewers.

Meta-analysis

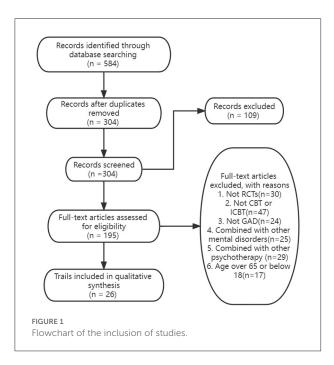
Meta-analyses were conducted on anxiety using RevMan5.4 analysis software. Besides, between-study heterogeneity was assessed using the chi-squared test and I2 statistic. According to the Cochrane guidelines, 0–39%, 40–74%, and 75–100% values were regarded as low, moderate, and high, respectively. Regardless of the heterogeneity test, a random-effects model was employed owing to the inconsistency within the patients, measurement tools, and the characteristics of included studies. Moreover, all the outcomes pooled were continuous in those studies, so as mean differences (MDs) with random-effects meta-analysis. When more than one measurement tool was used in an individual study, all the questionnaires related to generalized anxiety were pooled. The effect sizes were averaged across all outcome measures by

 $SD = \frac{\sqrt{(N_1-1)SD_1^2+(N_2-1)SD_2^2+\frac{N_1-N_2}{N_1+N_2}(M_1^2+M_2^2-2M_1M_2)}}{N_1+N_2-1}$. Preand post-treatment means and standard deviations (SDs) or the mean and SD of pre- and post-treatment change scores were utilized to calculate the effect sizes.

Results

Study selection

A total of 584 records were identified using the search strategy (Figure 1). After duplicates were removed, a total of 304 records were screened by title and abstract for potential relevance in this meta-analysis. After title and abstract screening,



109 irrelevant records were excluded, leaving 195 documents for full-text review. After a full-text review, 26 randomized controlled trials for CBT and ICBT (Table 1) satisfied the systematic review and meta-analysis.

Characteristics of studies

Details of the characteristics of included studies are listed in Table 1. All the studies included were published in English, and most of the researchers are from the Americas, Europe, and Australia. All the included studies were designed for patients with GAD diagnosed by the diagnostic and statistical manual of mental disorders fourth edition (DSM-IV). Anxiety symptoms before and after intervention were measured by some of the scales of anxiety. Specifically, most of the studies used The Penn State Worry Questionnaire (PSWQ). Other scales such as the Generalized Anxiety Disorder 7-Item (GAD-7) Scale and Statetrait anxiety inventory (STAI) were also adopted in those studies. More than 10 sessions in the intervention period were provided for 14 out of 26 trials, and at least five sessions were offered for all the studies.

Overview of results of the pairwise meta-analysis

Effect sizes and 95% CI for anxiety symptoms for different treatments are presented in Figure 2. The forest plot is from top to bottom: (1) subgroup meta-analysis of anxiety scores in

the treatment of GAD with CBT and ICBT; (2) subgroup metaanalysis of anxiety scores in the treatment of GAD with CBT and ICBT after removed trails with active comparators.

All trials reported anxiety rating scores, and it was considered the primary outcome. All the results in individual trials were combined since most of the trials pooled were used at least one measure tool. There were 18 trails in the face-to-face CBT group and eight trails in the internet-based CBT group. Figures 3, 4 illustrate a summary of the pooled meta-analysis outcomes. CBT demonstrated a greater improvement compared with ICBT (MD = -2.79, 95%CI: -6.75; 1.18 vs. MD = -2.35, 95%CI: -4.96; 0.27).

In the ICBT Group, seven trials identified the control group on a waiting list, suggesting that eventually all of these patients were treated. Nonetheless, the control group was always negative during the study period. However, part of the CBT study was an active control group; some of the control groups adopted drug therapy, and some used other forms of psychological treatment. This difference would be induced by the following factors. Patients with CBT may be either inpatients or outpatients, and few researchers utilize active controls because of the delay in patient recovery. However, patients on ICBT may be recruited from the community, and the wait-list approach is more appropriate in milder cases. Thus, the trails with active comparators were removed and analyzed again to draw a new forest graph. ICBT still exerted a similar effect compared to CBT for treating GAD (MD = -2.91, 95%CI: -5.00; -0.81 vs. MD = -3.54,95%CI: -7.05; -0.02).

Publication bias and risk of bias

The results of the publication bias assessments are depicted in Figure 3. No significant publication bias in anxiety rating scores was observed in the funnel plot. The overall quality of the 26 trials included in the meta-analysis was high, and only a handful of studies had any "high risk" domains (Figures 4, 5).

Discussions

Many factors affect the changes in patients' anxiety symptoms, and randomized controlled trials could be the most effective method to investigate the therapeutic effects of CBT and ICBT for treating GAD. Therefore, the effects of CBT and ICBT in the treatment of GAD were compared in this meta-analysis only based on randomized controlled studies to obtain more accurate and objective conclusions. In this paper, 26 randomized controlled trials were reviewed, including 18 in the CBT group and 8 in the ICBT group. The difference in the number of studies between the two groups may be induced by the following factors. First, ICBT is the type of internet-based therapy emerging in recent years, and most

Zhang et al.

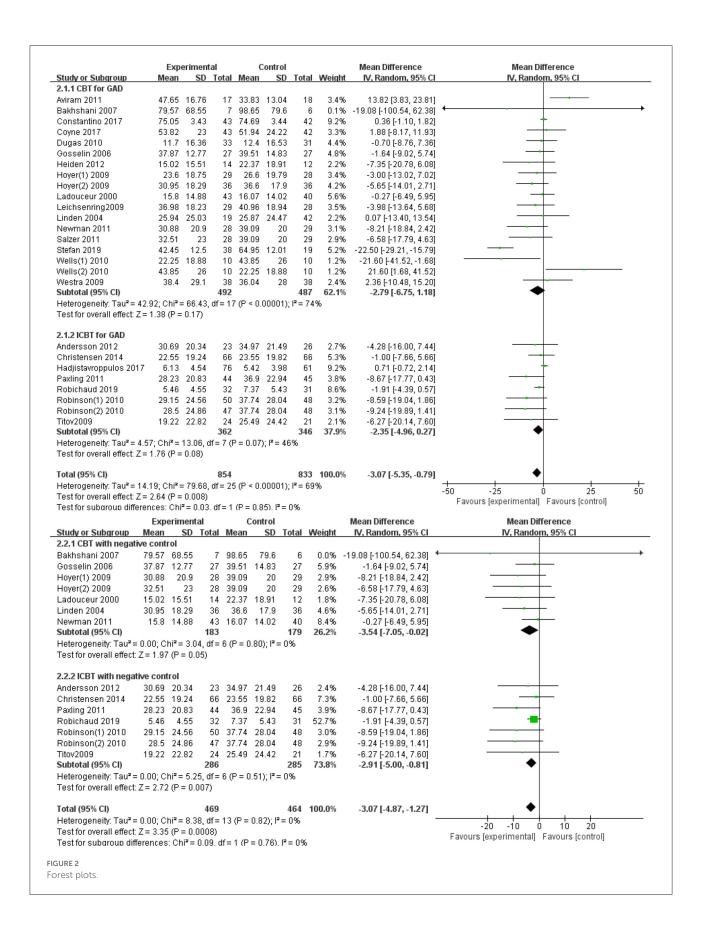
TABLE 1 Characteristics of included studies.

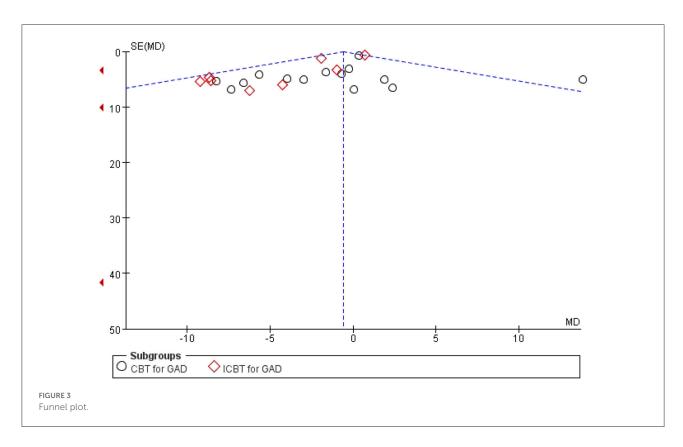
Author/Year	Region	Diagnose	Sample size (experimental/control	Female (%)	Mean age	Method	Dose	Instruments	Comparator
Dugas et al. (28)	Canada	GAD/	65 (33/32)	66%	38.5	СВТ	12 sessions,	CSRADIS	Applied relaxation
		DSM-IV					1 h		
Aviram and Westra (29)	Canada	GAD/DSM-IV	35 (17/18)	80%	40.7	CBT	6 sessions, 2 h	PSWQ	MI pre-treatment
Leichsenring et al.	Germany	GAD/	57 (29/28)	80%	42.5	CBT	30 sessions,	HARS	Short-term psychodynamic
(30)	,	DSM-IV					50 min	PSWQ	X / /
								BAI	
Linden et al. (31)	Germany	GAD/	72 (36/36)	67%	43.3	CBT	25 sessions,	HARS	Contact control
		DSM-IV					50 min	STAI-S	
Hoyer et al. (32)	Germany	GAD/	49 (18/31)	71%	45.5	Applied	15 sessions	HAMA	Waiting list
		DSM-IV				relaxation		PSWQ	
Hoyer et al. (32)	Germany	GAD/	55 (24/31)	77%	45,8	Worry	15 sessions	HAMA	Waiting list
		DSM-IV				exposure		PSWQ	
Constantino et al.	Canada	GAD/	85 (42/43)	88%	33.3	CBT	15 sessions,	PSWQ	MI
(33)		DSM-IV					50 min		CBT
Coyne et al. (34)	Canada	GAD/	85 (42/43)	88%	33.3	CBT	15 sessions,	PSWQ	MI
		DSM-IV					50 min	DASS	CBT
Gosselin et al. (35)	Canada	GAD/	61 (30/31)	59%	50.3	CBT	12 sessions,	PSWQ	Nonspecific psychological
		DSM-IV					90 min		treatment
Newman et al. (36)	United	GAD/	83 (40/43)	76%	37.2	CBT+IEP	14 sessions,	PSWQ	I/EP segment
	state	DSM-IV					50 min	CSR	
								HARS	
								STAI-S	
Wells et al. (37)	UK	GAD/	20 (10/10)	60%	49.05	Metacognitive	8-12	PSWQ	Applied relaxation
		DSM-IV				therapy	Sessions	BAI	
							50 min		
Wells et al. (37)	UK	GAD/	20 (10/10)	60%	49.05	Applied	8-12	PSWQ	Metacognitive therapy
		DSM-IV				relaxation	Sessions	BAI	
							50 min		
Heiden et al. (38)	Netherlands	GAD/	74 (54/20)	73%	35	Metacognitive	14 sessions	PSWQ	Intolerance-of-uncertainty therapy
		DSM-IV				therapy	45 min		
Bakhshani et al. (39)	Iran	GAD/	13 (7/6)	38%	26.5	CBT	8 sessions	BAI HARS	Placebo
		DSM-IV						DAS	

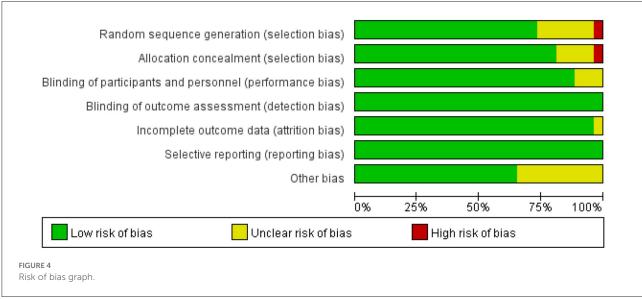
TABLE 1 Continued

Author/Year	Region	Diagnose	Sample size (experimental/control)	Female (%)	Mean age	Method	Dose	Instruments	Comparator
Salzer et al. (40) Canada	GAD/	57 (29/28)	no details	no details	CBT	mean=28.81(3.	BAI	Short-term psychodynamic	
		DSM-IV					44), 50 min	HADS	
								HARS	
								PSWQ	
								STAI-S	
Stefan et al. (41)	Romania	GAD/	71 (23/48)	85%	26.6	CT/BTP	20 sessions,	GAD-Q-IV	ACT
		DSM-IV					50 min	PSWQ	
Westra et al. (42)	United	GAD/	76 (38/38)	67%	41.9	CBT	14 sessions,	PSWQ	MI pre-treatment
	state	DSM-IV					50 min	DASS-A	
Ladouceur et al. (43)	Canada	GAD/DSM-IV	26 (12/14)	77%	39.7	CBT	16 sessions,	ADIS-IV	Waiting list
							1 h	PSWQ	
								BAI	
Titov et al. (44)	Australia	GAD/DSM-IV	45 (21/24)	no details	no details	ICBT	6 sessions	GAD-7	Waiting list
								PSWQ	
Andersson et al. (45)	Netherlands	GAD/DSM-IV	54 (27/27)	76%	42.02	ICBT	8 sessions	PSWQ	Waiting list
								GAD-Q-IV	
								STAI-state	
								STAI-trait	
								BAI	
Paxling et al. (46)	Sweden	GAD/DSM-IV	89 (44/45)	79.80%	39.3	ICBT	8 sessions	PSWQ	Waiting list
								GAD-Q-IV	
								STAI-S	
								STAI-T	
								BAI	
Hadjistavroppulos et al. (47)	Canada	GAD/DSM-IV	174 (91/83)	78.70%	38.3	ICBT	5 sessions	GAD-7	Optional weekly therapist support
Robinson et al. (48)	Australia	GAD/DSM-IV	98 (50/48)	67%	44.84	TA-ICBT	6 sessions	PSWQ	Delay treatment
								GAD-7	,
Robinson et al. (48)	Australia	GAD/DSM-IV	95 (47/48)	71.60%	45.52	CA-ICBT	6 sessions	PSWQ	Delay treatment
. ,			•					GAD-7	,
Robichaud et al. (49)	Canada	GAD/DSM-IV	63 (32/31)	87.3%	35.19	ICBT	8 sessions	GAD-7	Waiting list
Christensen et al.	Australia	GAD/DSM-IV	222 (111/111)	no details	25.85	ICBT	10 sessions	GAD-7	Placebo
(50)			, ,					PSWQ	

GAD: generalized anxiety disorder; CBT: cognitive behavior therapy; ICBT: internet-based cognitive behavior therapy; DSM: the diagnostic and statistical manual of mental disorders; CSRADIS 9- point (0 to 8): Clinician's Severity Rating of the Anxiety Disorders Interview Schedule for DSM-IV; PSWQ: Penn State Worry Questionnaire; HARS: Hamilton Anxiety Rating Scale; BAI: Beck Anxiety Inventory; DASS: Depression Anxiety Stress Scales, 21-item version; CRS Clinician's Severity Rating; GAD-Q-IV: generalized anxiety disorder questionnaire; HADS: Hospital Anxiety and Depression Scale; GAD-7: Generalized Anxiety Disorder 7-Item; MI: motivational interview; ACT: acceptance and commitment therapy; I/EP: segment interpersonal/emotional processing segment.







studies may not be conducted in hospitals. As a result, RCTs will be fewer. Second, all studies of patients with GAD were identified using the DSM-IV system, which was a step to minimize bias. Moreover, a literature search suggested that the vast majority of studies used this system. Besides, 1,687 patients were randomly assigned to the CBT, ICBT, and placebo treatment groups to treat GAD. The results revealed that

the CBT and ICBT groups were significantly better than the placebo in comparing anxiety levels before and after treatment. Compared with placebo, CBT was a treatment method with more significant benefits for anxiety-related disorders. The unique effect of CBT has gone beyond the scope of disease symptoms while presenting a bearing on the lives of patients as a positive benefit.

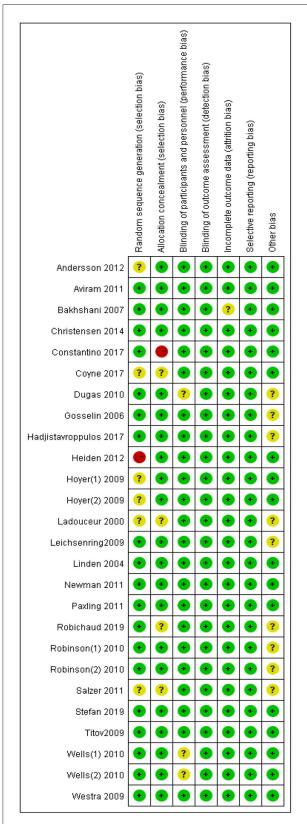


FIGURE 5
Risk of bias summary.

As unveiled by reviewing the previous studies in the field of psychiatry (51, 52), clinician-guided ICBT seems to work as effective as face-to-face CBT for some disorders. Moreover, ICBT has been discovered to be effective for somatic conditions, such as tinnitus and irritable bowel syndrome (53). A Cochrane review (54) of ICBT for anxiety disorders suggested that it is effective, with a standardized mean difference against no treatment control of 1.06, which is a large effect. Furthermore, therapist-guided ICBT may be as effective as face-to-face CBT, consistent with the conclusion of our study. Concerning GAD only, positive results of ICBT for GAD have been investigated in a few controlled studies including long-term follow-up after treatment completion. However, there are no comparative trials against face-to-face CBT and no meta-analysis related to GAD treated by ICBT compared with CBT.

Therefore, the comparative effects of CBT and ICBT for GAD were explored in this meta-analysis. Many studies have examined the effect of those two types of psychological treatments for GAD in adults. Generally, CBT and ICBT are more effective than waiting list control groups or even active control groups on worries, anxiety, and depression, regardless of whether effects were measured with which kind of instruments.

Specifically, our first goal of this meta-analysis was to determine whether ICBT can obtain similar benefits to CBT in treating GAD. The comparative effects were tested on other mental disorders, such as psychiatric and somatic disorders (55). In other words, ICBT and face-to-face treatment are similar and produce equivalent overall effects, in line with our results. Moreover, therapist-supported ICBT is more efficacious than a waiting list, attention, information, or online discussion groups only, and there may not be a significant difference in outcome between unguided CBT and therapist-supported ICBT (54). The evidence suggests that therapist-supported ICBT may not be significantly different from face-to-face CBT in reducing anxiety, similar to our conclusion. Some other studies (16, 56, 57) present the treatment format and review the evidence for mood and anxiety disorders, concluding that ICBT is becoming one of the most evidence-based forms of psychological treatment. The previous studies and our study uncover that ICBT can obtain similar benefits like CBT for treating GAD and even other mental disorders.

Nevertheless, patients treated with ICBT may have milder symptoms. Hence, the response to ICBT may be better, and patients who can complete an entire course of ICBT treatment, their desire for, and confidence in healing, were also better. This may explain why ICBT is slightly better than CBT in the overall effect.

This study aimed to reveal whether ICBT can replace CBT during the COVID-19 pandemic period for our second goal. The coronavirus disease 2019 (COVID-19) outbreak, which has caused >46 million confirmed infections and >1.2 million coronavirus-related deaths, is one of the most devastating

worldwide crises in recent years (58). Social distancing is the most visible public health response and effective mothed to the COVID-19 pandemic (59-61). Thus, a series of mandatory actions have been taken by the municipal and provincial governments supported by the central government, such as measures to restrict travel across cities, case detection and contact tracing, quarantine, guidance and information to the public, and detection kit development (62). Consequently, face-to-face psychological treatment may increase the risk of infection, and it is imperative to determine whether internet-based can replace face-to-face psychological treatment. According to the meta-analysis results, the overall effect of ICBT is better than CBT. Hence, ICBT can replace CBT during the COVID-19 pandemic and even become the primary psychological method in the future due to its characteristics such as convenience and economics.

Although ICBT has many advantages, it has some limitations. First, patients are required to have a higher level of education for self-service ICBT since the instructions are mainly provided in text form. Second, participants are generally well-educated in many studies. This would be no different from typical psychotherapeutic studies while limiting the possibility of extending the research results to conventional medical settings. Third, few studies adopt reliable attention control conditions, though direct comparison studies with face-to-face CBT exhibit small differences in results, raising questions about the specificity of the results.

Despite these limitations, research and clinical implementation studies are promising and could boost the chances of obtaining evidence-based psychotherapy. Many questions remain to be answered. Nevertheless, clinicians will increasingly combine their routine services with ICBT as a supplement or alternative for certain patients considering that information technology may be continuously developed.

This study also presents several limitations related to the included studies, such as the small number of studies using other than waiting list control groups and the lack of follow-up measurements. Besides, the measurement tools used in those trials are so different that we could not find the same one in 26 trials. As a result, those results had to be combined, and this may influence the final result.

Concurrently, the RCT studies of ICBT treatment for GAD are few and all focus on the years after 2000, while the study of CBT is more numerous, causing bias in the results. To minimize this bias, we referred to the same type of study and limited the time of publication to 2000. ICBT emerged after 2000 and was of concern to researchers, whereas CBT has been widely studied

since earlier times. Hence, studies from the same time period were compared to minimize the results bias.

Conclusion

Despite the limitations of this meta-analysis, this is the first systematic review and meta-analysis for RCTs that have compared the performance of CBT to ICBT for the treatment of GAD. The final MDs of CBT and ICBT are close, suggesting that the effect sizes of ICBT and CBT were similar in anxiety score reduction. This verified the efficacy of the internet-based CBT treatment. Nevertheless, the results demonstrated that ICBT has an equal treatment effect with CBT and can replace CBT during the COVID-19 pandemic as a safer method.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

YH reviewed the manuscript. WZ designed the research, searched the literature, extracted the data, and wrote the manuscript. YD searched the literature and extracted the data. SW and QL checked and analyzed the data. ZL reviewed and checked the language of this manuscript. XY, EW, and JF reviewed the manuscript and made changes suggestions. All authors read and approved the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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